

ADANA UNIVERSITY – INDUSTRY JOINT RESEARCH CENTER

**ALKALOIDS
&
ALKALOIDS
PLANTS**

By

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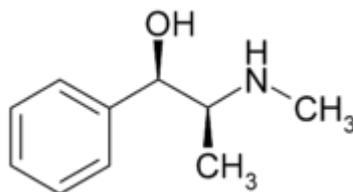
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PART – 1

ALKALOIDS



Alkaloid



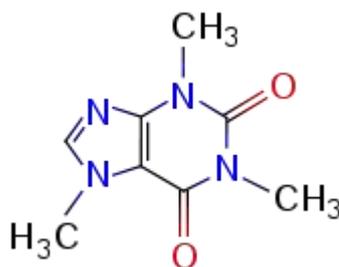
Chemical structure of ephedrine, a phenethylamine alkaloid

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1 – Introduction :

Alkaloids are naturally occurring chemical compounds containing basic nitrogen atoms . The name derives from the word alkaline and was used to describe any nitrogen - containing base. Alkaloids are produced by a large variety of organisms, including bacteria, fungi, plants, and animals and are part of the group of natural products (also called secondary metabolites) . Many alkaloids can be purified from crude extracts by acid - base extraction. Many alkaloids are toxic to other organisms. They often have pharmacological effects and are used as medications, as recreational drugs, or in entheogenic rituals. Examples are the local anesthetic and stimulant cocaine, the stimulant caffeine, nicotine, the analgesic morphine, or the antimalarial drug quinine. Some alkaloids have a bitter taste .



Caffeine

2 - Alkaloid classifications :

The classification of the alkaloids is complex and may be guided by a set of rules that take into account the structure and other chemical features of the alkaloid molecule, its biological origin, as well as the biogenetic origin where known.^{[2][3]} For example, where the biosynthesis pathway of an alkaloid is unknown, it may be grouped based on structural similarities with known compounds, including non-nitrogenous compounds, or by the organism (s) from which the alkaloid was isolated .

Pyridine group :

piperine , coniine , trigonelline , arecoline , arecaidine , guvacine, cytisine , lobeline , nicotine , anabasine , sparteine , pelletierine .

Pyrrolidine group :

hygrine , cuscohygrine , nicotine .

Tropane group :

atropine , cocaine , ecgonine , scopolamine , catuabine .

Indolizidine group :

senecionine , swainsonine .

Quinoline group :

quinine , quinidine , dihydroquinine, dihydroquinidine , strychnine , brucine , veratrine , cevadine .

Isoquinoline group :

opium alkaloids (papaverine , narcotine , narceine) , pancratistatin , sanguinarine , hydrastine , berberine , emetine , berbamine , oxyacanthine .

Phenanthrene alkaloids :

opium alkaloids (morphine , codeine , thebaine , oripavine)

Phenethylamine group :

mescaline , ephedrine , dopamine .

Indole group :

Tryptamines : serotonin , bufotenine , psilocybin

Ergolines : ergine , ergotamine , lysergic acid

Beta - carbolines : harmine , harmaline , tetra hydro harmine

Yohimbans : reserpine, yohimbine .

Vinca alkaloids : vinblastine, vincristine .

Kratom) alkaloids : mitragynine , 7- hydroxy mitragynine .

Tabernanthe iboga : ibogaine , voacangine , coronaridine .

Strychnos nux-vomica : strychnine , brucine .

Purine group :

Xanthines , caffeine , theobromine , theophylline .

Terpenoid group :

Aconitum alkaloids : aconitine .

Steroid alkaloids : (containing a steroid skeleton in a nitrogen containing structure) :

Solanum alkaloids (e.g. potato and tomato) : (solanidine , solanine , chaconine) .

Veratrum alkaloids : (veratramine , cyclo pamine , cycloposine , jervine , muldamine) :

Fire Salamander alkaloids : (samandarin) .

thers : conessine .

Quaternary ammonium compounds : muscarine , choline , neurine .

Miscellaneous : capsaicin , cynarin , phytolaccine , phytolaccotoxin .

3 - Physicochemical properties :

Low - molecular weight alkaloids without hydrogen bond donors such as hydroxy groups are often liquid at room temperature , examples are nicotine , sparteine , coniine , and phenethylamine .

The basicity of alkaloids depends on the lone pairs of electrons on their nitrogen atoms. As organic bases, alkaloids form salts with mineral acids such as hydrochloric acid and sulfuric acid and organic acids such as tartaric acid or maleic acid. These salts are usually more water-soluble than their free base form .

4 - Category : Alkaloids :

An alkaloid is a naturally occurring nitrogenous organic molecule that has a pharmacological effect on humans and other animals. The name derives from the word alkaline; originally, the term was used to describe any nitrogen - containing base (an amine in modern terms). Alkaloids are found in plants (e.g., in potatoes and tomatoes), animals (e.g., in shellfish) and fungi (e.g., in mushrooms), and can be extracted from their sources by treatment with acids (usually hydrochloric acid or sulfuric acid, though organic acids such as maleic acid and citric acid are sometimes used).

A : Acetylpsilocin . Aconitine . Ageliferin . Ajmalan . Ajmaline . Akuammine . Allopumiliotoxin . Allopumiliotoxin 267A . Anabasine . Anatoxin - a . Apomorphine . Aporphine

B : Batrachotoxin . Benzyl isoquinoline . Berberine . Brucine . Bulbocapnine

C : Calligonine . Camptothecin . Carpaine . Castanospermine . Cathinone . Chaconine . Chavicine . Chelerythrine . Cinchonidine . Cinchonine . Colchicine . Conessine . Conhydrine . Coniine . Coptisine . Coramsine . Cordycepin . Cryogenine . Cuscohygrine . Cyindrospermopsin . Cytisine .

D : Dehydro emetine . Delphinine . Demecolcine . Dihydro ergocornine . Dihydro ergocristine . Dihydro quinidine . Dihydro quinine . Docetaxel

E : Eletefine . Emetine . Epibatidine . Ergine E cont . Ergoline . Ethocybin .

G : Glaucine . Glycoalkaloid .

H : Harmine . Hasubanan . Hasubanone . Himbacine . Histrio nicotoxin . Hodgkinsine . Horsfiline . Huperzine A . Hydrastine . Hydrastinine . Hygrine .

I : Imidazole . Isovaleramide

L : Lennoxamine . Leonurine . Lobeline . Loline alkaloids .
Lupinine . Lycorine . Lysergic acid hydroxy ethylamide .

M : Methcathinone . Methoxy methyl enedioxy amphetamine .
Methoxy coronaridine . 1-Methyl - 2,3,4,9 – tetra hydro -1H – pyrido -
3,4 – b - indole . Methyl benzo dioxolyl butanamine . N –Methyl
coniine . Methyllycaconitine . Methylone .

N : Nantenine . Narcotoline . Neurine . Nicotine .
Norzoanthamine .

O : Orellanine

P : Paclitaxel . Pancratistatin . Pericine . Phenyl propanol amine .
Phenyl tropane . Physostigmine . Piperine . Prajmaline . Pseudo
aconitine . Pseudo pelletierine . Pukateine P cont . Pumiliotoxin .
Pumiliotoxin 251D . Pyrrolizidine alkaloid .

R : Rhynchophylline . Rodiasine . Ryanodine .

S : Samandaridine . Samandarin . Sanguinarine . Saxitoxin .
Scoulerine . Senecionine . Sinomenine . Solamargine . Solanine .
Solanocapsine . Solasodamine . Solasodine . Solasonine .
Solaurocidine . Solaurocine . Solenopsin . Sparteine . Spirotryprostatin.
Staurosporine . Stepholidine . Strychnine . Swainsonine .

T : Tetra hydro harman . Tetra hydro palmatine . Thebaine . Tri
gonelline . Tri methoxy amphetamine . Tropane . Tropane alkaloid .
Tropinone . Tryptoline . Tubocurarine

V : Veracevine . Veratridine . Vinblastine . Vinburnine .
Vincristine . Vindesine . Vinflunine . Vinorelbine . Voacangine .

Y : Yuremamine

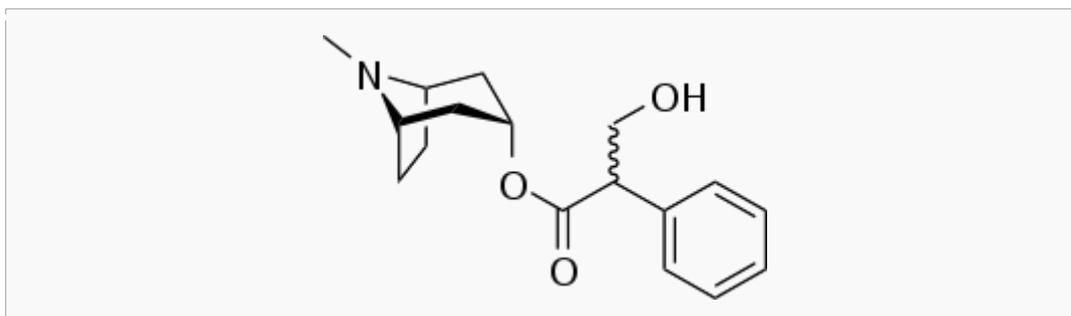
Atropine

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 - 2.5 Optical penalization
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- 3 Chemistry and pharmacology
- 4 History
- 5 Natural sources

1 – Introduction :

Atropine is a tropane alkaloid extracted from deadly nightshade (*Atropa belladonna*), jimsonweed (*Datura stramonium*), mandrake (*Mandragora officinarum*) and other plants of the family Solanaceae . It is a secondary metabolite of these plants and serves as a drug with a wide variety of effects. It is a competitive antagonist for the muscarinic acetylcholine receptor. It is classified as an anti cholinergic drug. Being potentially deadly, it derives its name from Atropos, one of the three Fates who, according to Greek mythology, chose how a person was to die. Atropine is a *core* medicine in the World Health Organization's "Essential Drugs List", which is a list of minimum medical needs for a basic health care system .



Systematic (IUPAC) name	
(8 – methyl – 8 – azabicyclo [3.2.1] oct – 3 – yl) 3 – hydroxyl – 2 – phenyl propanoate	
Formula	$C_{17}H_{23}NO_3$
Mol Mass	289
Pharmacokinetic data	
Bioavailability	25 %
Metabolism	50 % hydrolyzed to tropine and tropic acid
Half life	2 hours
Excretion	50 % excreted unchanged in urine

2 - Physiological effects and uses

Atropine increases firing of the sinoatrial node (SA) and conduction through the atrioventricular node (AV) of the heart, opposes the actions of the vagus nerve, blocks acetylcholine receptor sites, and decreases bronchial secretions.

In general, atropine lowers the parasympathetic activity of all muscles and glands regulated by the parasympathetic nervous system. This occurs because atropine is a competitive antagonist of the muscarinic acetylcholine receptors (Acetylcholine is the main neurotransmitter used by the parasympathetic nervous system). Therefore, it may cause swallowing difficulties and reduced secretions

2 -1 : Ophthalmic use

Topical atropine is used as a cyclo plegic, to temporarily paralyze the accommodation reflex, and as a mydriatic, to dilate the pupils. Atropine degrades slowly, typically wearing off in 7 to 14 days, so it

is generally used as a therapeutic mydriatic , whereas tropicamide (a shorter - acting cholinergic antagonist) or phenyl ephrine (an α -adrenergic agonist) is preferred as an aid to ophthalmic examination. Atropine induces mydriasis by blocking contraction of the circular pupillary sphincter muscle, which is normally stimulated by acetylcholine release, thereby allowing the radial pupillary dilator muscle to contract and dilate the pupil. Atropine induces cycloplegia by paralyzing the ciliary muscles, whose action inhibits accommodation to allow accurate refraction in children, helps to relieve pain associated with iridocyclitis, and treats ciliary block (malignant) glaucoma. Atropine is contraindicated in patients pre-disposed to narrow angle glaucoma . Atropine can be given to patients who have direct globe trauma .

2 – 2 : Resuscitation

Injections of atropine are used in the treatment of bradycardia (an extremely low heart rate), asystole and pulseless electrical activity (PEA) in cardiac arrest. This works because the main action of the vagus nerve of the parasympathetic system on the heart is to decrease heart rate. Atropine blocks this action and, therefore, may speed up the heart rate. The usual dosage of atropine in bradyasystolic arrest is 0.5 to 1 mg IV push every three to five minutes, up to a maximum dose of 0.04 mg/kg. For symptomatic bradycardia, the usual dosage is 0.5 to 1.0 mg IV push, may repeat every 3 to 5 minutes up to a maximum dose of 3.0 mg .

Atropine is also useful in treating second-degree heart block Mobitz Type 1 (Wenckebach block), and also third-degree heart block with a high Purkinje or AV-nodal escape rhythm. It is usually not effective in second - degree heart block Mobitz type 2, and in third-degree heart block with a low Purkinje or ventricular escape rhythm. Atropine is contraindicated in ischemia-induced conduction block, because the drug increases oxygen demand of the AV nodal tissue, thereby aggravating ischemia and the resulting heart block.

One of the main actions of the parasympathetic nervous system is to stimulate the M_2 muscarinic receptor in the heart, but atropine inhibits this action.

2 – 3 : Secretions and broncho constriction

Atropine's actions on the parasympathetic nervous system inhibits salivary, sweat, and mucus glands. This can be useful in treating hyperhidrosis, and can prevent the death rattle of dying patients. Even though atropine has not been officially indicated for either of these purposes by the FDA, it has been used by physicians for these purposes .

2 – 4 : Treatment for organophosphate poisoning

Atropine is not an actual antidote for organophosphate poisoning. However, by blocking the action of acetylcholine at muscarinic receptors, atropine also serves as a treatment for poisoning by organophosphate insecticides and nerve gases, such as Tabun (GA), Sarin (GB), Soman (GD) and VX. Troops that are likely to be attacked with chemical weapons often carry autoinjectors with atropine and obidoxime, which can be quickly injected into the thigh. Atropine is often used in conjunction with Pralidoxime chloride.

Atropine is given as a treatment for SLUDGE (Salivation, Lacrimation, Urination, Diaphoresis, Gastrointestinal motility, Emesis) symptoms caused by organophosphate poisoning .

Some of the nerve agents attack and destroy acetyl cholin esterase , so the action of acetylcholine becomes prolonged. Therefore atropine can be used to reduce the effect of acetylcholine .

2 – 5 : Optical penalization :

In refractive and accommodative amblyopia , when occlusion is not appropriate sometimes atropine is given to induce blur in the good eye

2 – 6 : Side - effects and overdose

Adverse reactions to atropine include ventricular fibrillation, supra ventricular or ventricular tachycardia, dizziness, nausea, blurred vision, loss of balance, dilated pupils, photophobia, and, possibly, notably in the elderly, extreme confusion, extreme dissociative hallucinations, and excitation. These latter effects are because atropine

is able to cross the blood - brain barrier. Because of the hallucinogenic properties, some have used the drug recreationally, though this is potentially dangerous and often unpleasant.

In overdoses, atropine is poisonous. Atropine is sometimes added to other potentially addictive drugs, particularly anti-diarrhea opioid drugs such as diphenoxylate or difenoxin, wherein the secretion-reducing effects of the atropine can also aid the anti-diarrhea effects.

Although atropine treats bradycardia (slow heart rate) in emergency settings, it can cause paradoxical heart rate slowing when given at very low doses, presumably as a result of central action in the CNS. The antidote to atropine is physostigmine or pilocarpine .

A common mnemonic used to describe the physiologic manifestations of atropine overdose is: "hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hatter".^[6] These associations reflect the specific changes of warm, dry skin from decreased sweating, blurry vision , decreased sweating / lacrimation , vasodilation, and central nervous system effects on muscarinic receptors, type 4 and 5 . This set of symptoms is known as anti cholinergic toxidrome , and may also be caused by other drugs with anti cholinergic effects, such as diphenhy dramine , phenothiazine antipsychotics and benztropine .

3 - Chemistry and pharmacology

Atropine is a racemic mixture of D - hyoscyamine and L - hyoscyamine , with most of its physiological effects due to L – hyoscyamine . Its pharmacological effects are due to binding to muscarinic acetylcholine receptors. It is an antimuscarinic agent. The most common atropine compound used in medicine is atropine sulfate ($C_{17}H_{23}NO_3$)₂ · H₂SO₄ · H₂O, the full chemical name is 1 α H , 5 α H – Tropan – 3 - α ol (\pm) – tropate (ester) , sulfate mono hydrate .

4 - History

Mandragora (mandrake) was described by Theophrastus in the fourth century B.C. for treatment of wounds, gout, and sleeplessness,

and as a love potion. By the first century A.D. Dioscorides recognized wine of mandrake as an anaesthetic for treatment of pain or sleeplessness, to be given prior to surgery or cautery . The use of Solanaceae containing tropane alkaloids for anesthesia, often in combination with opium, persisted throughout the Roman and Islamic Empires and continued in Europe until superseded by the use of ether, chloroform, and other modern anesthetics.

Atropine extracts from the Egyptian henbane were used by Cleopatra in the last century B.C. to dilate her pupils, in the hope that she would appear more alluring. In the Renaissance, women used the juice of the berries of *Atropa belladonna* to enlarge the pupils of their eyes, for cosmetic reasons; " bella donna " is Italian for "beautiful lady".^[8] This practice resumed briefly in the late nineteenth - and early twentieth - century in Paris .

The mydriatic effects of atropine were studied among others by the German chemist Friedrich Ferdinand Runge (1795–1867). In 1831, the pharmacist Mein succeeded the pure crystalline isolation of atropine. The substance was first synthesized by German chemist Richard Willstätter in 1901.

Atropinic shock therapy, also known as atropinic coma therapy, is an old and rarely - used method. It consists of induction of atropinic coma by rapid intravenous infusion of atropine. Atropinic shock treatment is considered safe with careful monitoring and preparation, but it entails prolonged coma (between four and five hours), and it has many unpleasant side-effects, such as blurred vision .

5 - Natural sources

Atropine is found in many members of the Solanaceae family. The most commonly-found sources are *Atropa belladonna*, *Datura inoxia*, *D. metel*, and *D. stramonium*. Other sources include members of the *Brugmansia* and *Hyoscyamus* genera . The *Nicotiana* genus (including the tobacco plant, *N. tabacum*) is also found in the Solanaceae family, but these plants do not contain atropine or other tropane alkaloids .

Caffeine

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1 – Introduction :

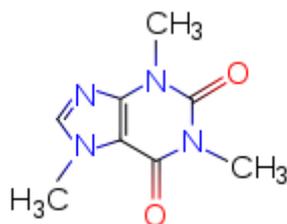
Caffeine is a bitter , white crystalline xanthine alkaloid that is a psychoactive stimulant drug . Caffeine was discovered by a German chemist , Friedrich Ferdinand Runge , in 1819 . He coined the term *kaffein* , a chemical compound in coffee , which in English became *caffeine* . Caffeine is also part of the chemical mixtures and insoluble complexes **guaranine** found in guarana , **mateine** found in mate , and **theine** found in non - herbal tea ; all of which contain additional alkaloids such as the cardiac stimulants theophylline and theobromine,

and often other chemicals such as polyphenols which can form insoluble complexes with caffeine .

Caffeine is found in varying quantities in the beans , leaves , and fruit of some plants , where it acts as a natural pesticide that paralyzes and kills certain insects feeding on the plants . It is most commonly consumed by humans in infusions extracted from the cherries of the coffee plant and the leaves of the tea bush , as well as from various foods and drinks containing products derived from the kola nut . Other sources include yerba mate , guarana berries, and the Yaupon Holly .

In humans , caffeine is a central nervous system (CNS) stimulant having the effect of temporarily warding off drowsiness and restoring alertness . Beverages containing caffeine , such as coffee , tea , soft drinks , and energy drinks enjoy great popularity . Caffeine is the world's most widely consumed psychoactive substance , but unlike many other psychoactive substances it is legal and unregulated in nearly all jurisdictions . In North America , 90 % of adults consume caffeine daily . The U.S . Food and Drug Administration lists caffeine as a " multiple purpose generally recognized as safe food substance " .

Caffeine has diuretic properties, at least when administered in sufficient doses to subjects who do not have a tolerance for it . Regular users , however , develop a strong tolerance to this effect , and studies have generally failed to support the common notion that ordinary consumption of caffeinated beverages contributes significantly to dehydration .



Other Names

1,3,7- Tri methyl xanthine ,
Tri methyl xanthine ,
Theine ,
Methyl theo bromine

Molecular Formula	$C_8 H_{10} N_4 O_2$
Molar Mass	194 g / mol
Appearance	Odorless , white needles or powder
Density	1.23 g /cm ³ , solid
Melting Point	227 – 228 °C (anhydrous) , 234 – 235 °C (monohydrate)
Boiling Point	178 °C <i>subl.</i>
Solubility in Water	2.17 g / 100 ml (25 °C) 18.0 g / 100 ml (80 °C) 67.0 g / 100 ml (100 °C)
Acidity (p <i>K</i> _a)	– 0.13 – 1.22
Dipole Moment	3.64 D (calculated)
EU classification	Harmful (Xn)
LD ₅₀	192 mg / kg (rat , oral)

2 - Occurrence :



Roasted coffee beans, a common source of caffeine

Caffeine is found in many plant species , where it acts as a natural pesticide , with high caffeine levels being reported in seedlings that are still developing foliage, but are lacking mechanical protection ; caffeine paralyzes and kills certain insects feeding upon the plant . High caffeine levels have also been found in the surrounding soil of coffee bean seedlings. It is therefore understood that caffeine has a natural function as both a natural pesticide and as an inhibitor of seed

germination of other nearby coffee seedlings thus giving it a better chance of survival .

The most commonly used sources of caffeine are coffee, tea , and to a lesser extent cacao . Less commonly used sources of caffeine include the yerba maté and guarana plants,^[15] which are sometimes used in the preparation of teas and energy drinks . Two of caffeine's alternative names, *mateine* and *guaranine* , are derived from the names of these plants . Some yerba mate enthusiasts assert that mateine is a stereoisomer of caffeine , which would make it a different substance altogether . This is not true because caffeine is an achiral molecule , and therefore has no enantiomers ; nor does it have other stereoisomers . The disparity in experience and effects between the various natural caffeine sources could be due to the fact that plant sources of caffeine also contain widely varying mixtures of other xanthine alkaloids , including the cardiac stimulants theophylline and theobromine and other substances such as polyphenols which can form insoluble complexes with caffeine .

One of the world's primary sources of caffeine is the coffee bean (which is the seed of the coffee plant) , from which coffee is brewed . Caffeine content in coffee varies widely depending on the type of coffee bean and the method of preparation used ; even beans within a given bush can show variations in concentration . In general, one serving of coffee ranges from 40 milligrams , for a single shot (30 milliliters) of *arabica* - variety espresso, to about 100 milligrams for a cup (120 milliliters) of drip coffee . Generally , dark - roast coffee has less caffeine than lighter roasts because the roasting process reduces the bean's caffeine content . *Arabica* coffee normally contains less caffeine than the *robusta* variety . Coffee also contains trace amounts of theophylline , but no theobromine .

Tea is another common source of caffeine. Although tea contains more caffeine than coffee , a typical serving contains much less , as tea is normally brewed much weaker. Besides strength of the brew , growing conditions , processing techniques and other variables also affect caffeine content . Certain types of tea may contain somewhat more caffeine than other teas . Tea contains small amounts of

theobromine and slightly higher levels of theophylline than coffee. Preparation and many other factors have a significant impact on tea, and color is a very poor indicator of caffeine content . Teas like the pale Japanese green tea gyokuro , for example , contain far more caffeine than much darker teas like lapsang souchong , which has very little .

Caffeine content of select common food and drugs :

Product	Serving size	Caffeine per serving (mg)	Caffeine per litre (mg)
Caffeine tablet (regular strength)	1 tablet	100	—
Caffeine tablet (extra strength)	1 tablet	200	—
Excedrin tablet	1 tablet	65	—
Hershey's Special Dark (45 % cacao content)	1 bar (43 g; 1.5 oz)	31	—
Hershey's Milk Chocolate (11 % cacao content)	1 bar (43 g; 1.5 oz)	10	—
Percolated coffee	207 mL (7 U.S. fl oz)	80 – 135	386 - 652
Drip coffee	207 mL (7 U.S. fl oz)	115 – 175	555–845
Coffee,decaffeinated	207 mL (7 U.S. fl oz)	5 - 15	24 - 72
Coffee , espresso	44–60 mL (2 U.S. fl oz)	100	1691- 2254
Coffee , Starbucks	(Tall 12 U.S. fl oz)	240	650 - 700
Black tea	177 mL (6 U.S. fl oz)	50	282
Green tea	177 mL (6 U.S. fl oz)	30	169
Coca - Cola Classic	355 mL (12 U.S. fl oz)	34	96

Caffeine is also a common ingredient of soft drinks such as cola , originally prepared from kola nuts. Soft drinks typically contain about 10 to 50 milligrams of caffeine per serving. By contrast , energy

drinks such as Red Bull can start at 80 milligrams of caffeine per serving . The caffeine in these drinks either originates from the ingredients used or is an additive derived from the product of decaffeination or from chemical synthesis. Guarana, a prime ingredient of energy drinks , contains large amounts of caffeine with small amounts of theobromine and theophylline in a naturally occurring slow-release excipient .

Chocolate derived from cocoa contains a small amount of caffeine. The weak stimulant effect of chocolate may be due to a combination of theobromine and theophylline as well as caffeine . A typical 28 - gram serving of a milk chocolate bar has about as much caffeine as a cup of *decaffeinated* coffee .

In recent years various manufacturers have begun putting caffeine into shower products such as shampoo and soap , claiming that caffeine can be absorbed through the skin . However, the effectiveness of such products has not been proven, and they are likely to have little stimulatory effect on the central nervous system because caffeine is not readily absorbed through the skin .

Various manufacturers market caffeine tablets , claiming that using caffeine of pharmaceutical quality improves mental alertness . These effects have been borne out by research that shows that caffeine use (whether in tablet form or not) results in decreased fatigue and increased attentiveness . These tablets are commonly used by students studying for their exams and by people who work or drive for long hours .

3 - History :

Humans have consumed caffeine since the Stone Age . Early peoples found that chewing the seeds , bark , or leaves of certain plants had the effects of easing fatigue , stimulating awareness , and elevating one's mood . Only much later was it found that the effect of caffeine was increased by steeping such plants in hot water. Many cultures have legends that attribute the discovery of such plants to people living many thousands of years ago .



A coffeehouse in Palestine , circa 1900

According to one popular Chinese legend, the Emperor of China Shennong , reputed to have reigned in about 3000 BC , accidentally discovered that when some leaves fell into boiling water , a fragrant and restorative drink resulted . Shennong is also mentioned in Lu Yu's *Cha Jing* , a famous early work on the subject of tea . The history of coffee has been recorded as far back as the ninth century . During that time, coffee beans were available only in their native habitat , Ethiopia . A popular legend traces its discovery to a goatherder named Kaldi , who apparently observed goats that became elated and sleepless at night after grazing on coffee shrubs and , upon trying the berries that the goats had been eating, experienced the same vitality. The earliest literary mention of coffee may be a reference to Bunchum in the works of the 9th century Persian physician al - Razi. In 1587 , Malaye Jaziri compiled a work tracing the history and legal controversies of coffee, entitled " Undat al safwa fi hill al - qahwa ". In this work , Jaziri recorded that one Sheikh , Jamal – al - Din al – Dhabhani , mufti of Aden , was the first to adopt the use of coffee in 1454 , and that in the 15th century the Sufis of Yemen routinely used coffee to stay awake during prayers .

Towards the close of the 16th century , the use of coffee was recorded by a European resident in Egypt , and about this time it came into general use in the Near East . The appreciation of coffee as a beverage in Europe, where it was first known as "Arabian wine," dates from the 17th century . During this time " coffee houses " were established , the first being opened in Constantinople and Venice . In

Britain , the first coffee houses were opened in London in 1652 , at St Michael's Alley , Cornhill . They soon became popular throughout Western Europe, and played a significant role in social relations in the 17th and 18th centuries .

The kola nut , like the coffee berry and tea leaf , appears to have ancient origins . It is chewed in many West African cultures, individually or in a social setting, to restore vitality and ease hunger pangs . In 1911 , kola became the focus of one of the earliest documented health scares when the US government seized 40 barrels and 20 kegs of Coca - Cola syrup in Chattanooga , Tennessee , alleging that the caffeine in its drink was " injurious to health " .^[34] On March 13 , 1911 , the government initiated *The United States v. Forty Barrels and Twenty Kegs of Coca - Cola*, hoping to force Coca - Cola to remove caffeine from its formula by making claims, such as that the excessive use of Coca - Cola at one girls' school led to " wild nocturnal freaks , violations of college rules and female proprieties, and even immoralities." Although the judge ruled in favor of Coca-Cola, two bills were introduced to the U.S. House of Representatives in 1912 to amend the Pure Food and Drug Act, adding caffeine to the list of " habit - forming " and "deleterious" substances which must be listed on a product's label .

The earliest evidence of cocoa use comes from residue found in an ancient Mayan pot dated to 600 BC. In the New World, chocolate was consumed in a bitter and spicy drink called *xocoatl*, often seasoned with vanilla, chile pepper, and achiote. Xocoatl was believed to fight fatigue , a belief that is probably attributable to the theobromine and caffeine content . Chocolate was an important luxury good throughout pre - Columbian Mesoamerica, and cocoa beans were often used as currency .

Xocoatl was introduced to Europe by the Spaniards and became a popular beverage by 1700 . They also introduced the cacao tree into the West Indies and the Philippines. It was used in alchemical processes, where it was known as Black Bean .

The leaves and stems of the Yaupon Holly (*Ilex vomitoria*) were used by Native Americans to brew a tea called Asi or the Black Drink

the use of which among Native American groups archaeologists have demonstrated to stretch back far into antiquity, possibly dating to Late Archaic times.

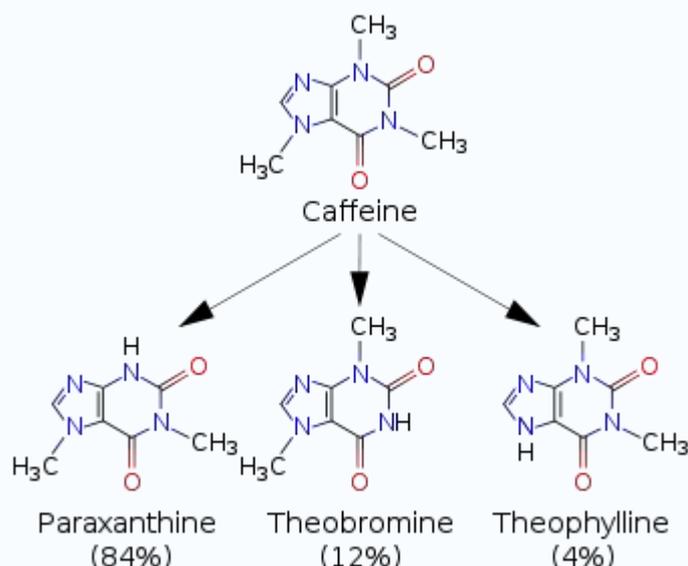
4 - Synthesis and properties :

In 1819, the German chemist Friedrich Ferdinand Runge isolated relatively pure caffeine for the first time. According to Runge , he did this at the behest of Johann Wolfgang von Goethe . In 1827 , Oudry isolated " theine " from tea, but it was later proved by Mulder and Jobat that theine was the same as caffeine . The structure of caffeine was elucidated near the end of the 19th century by Hermann Emil Fischer , who was also the first to achieve its total synthesis . This was part of the work for which Fischer was awarded the Nobel Prize in 1902 . The nitrogen atoms are all essentially planar (in sp^2 orbital hybridisation) , resulting in the caffeine molecule having aromatic character . Being readily available as a byproduct of decaffeination, caffeine is not usually synthesized . If desired, it may be synthesized from dimethylurea and malonic acid .

5 - Pharmacology :

Global consumption of caffeine has been estimated at 120,000 tonnes per year , making it the world's most popular psychoactive substance. This number equates to one serving of a caffeine beverage for every person, per day . Caffeine is a central nervous system and metabolic stimulant , and is used both recreationally and medically to reduce physical fatigue and restore mental alertness when unusual weakness or drowsiness occurs. Caffeine and other methylxanthine derivatives are also used on newborns to treat apnea and correct irregular heartbeats. Caffeine stimulates the central nervous system first at the higher levels, resulting in increased alertness and wakefulness, faster and clearer flow of thought , increased focus, and better general body coordination, and later at the spinal cord level at higher doses.^[28] Once inside the body, it has a complex chemistry, and acts through several mechanisms as described below.

5 – 1 : Metabolism and half-life



Caffeine is metabolized in the liver into three primary metabolites : paraxanthine (84 %) , theobromine (12 %) , and theophylline (4 %).

Caffeine from coffee or other beverages is absorbed by the stomach and small intestine within 45 minutes of ingestion and then distributed throughout all tissues of the body.^[41] It is eliminated by first-order kinetics.^[42] Caffeine can also be ingested rectally, evidenced by the formulation of suppositories of ergotamine tartrate and caffeine (for the relief of migraine) and chlorobutanol and caffeine (for the treatment of hyperemesis) .

The half-life of caffeine — the time required for the body to eliminate one-half of the total amount of caffeine — varies widely among individuals according to such factors as age, liver function, pregnancy, some concurrent medications, and the level of enzymes in the liver needed for caffeine metabolism. In healthy adults, caffeine's half-life is approximately 4.9 hours. In women taking oral contraceptives this is increased to 5 – 10 hours , and in pregnant women the half-life is roughly 9 – 11 hours . Caffeine can accumulate in individuals with severe liver disease , increasing its half-life up to 96 hours . In infants and young children, the half - life may be longer than in adults; half-life in a newborn baby may be as long as 30 hours. Other factors such as smoking can shorten caffeine's half - life . Fluvoxamine reduced the apparent oral clearance of caffeine by

91.3 % , and prolonged its elimination half - life by 11.4 - fold (from 4.9 hours to 56 hours) .

Caffeine is metabolized in the liver by the cytochrome P450 oxidase enzyme system (specifically , the 1A2 isozyme) into three metabolic dimethylxanthines , which each have their own effects on the body :

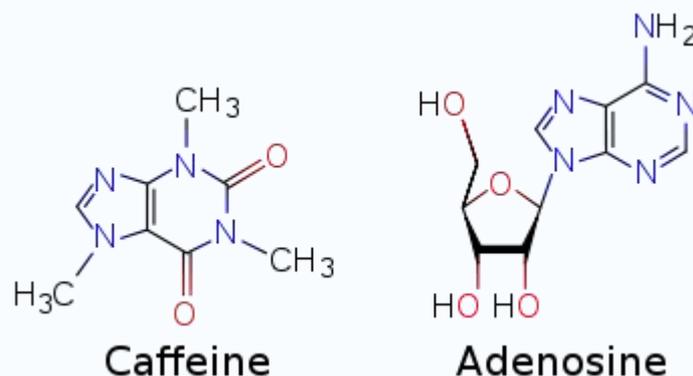
- Paraxanthine (84 %) : Has the effect of increasing lipolysis, leading to elevated glycerol and free fatty acid levels in the blood plasma.

- Theobromine (12 %) : Dilates blood vessels and increases urine volume. Theobromine is also the principal alkaloid in cocoa, and therefore chocolate.

- Theophylline (4 %) : Relaxes smooth muscles of the bronchi, and is used to treat asthma. The therapeutic dose of theophylline, however, is many times greater than the levels attained from caffeine metabolism.

Each of these metabolites is further metabolized and then excreted in the urine.

5- 2 : Mechanism of action



Caffeine's principal mode of action is as an antagonist of adenosine receptors in the brain .

Like alcohol and nicotine, caffeine readily crosses the blood–brain barrier that separates the bloodstream from the interior of the brain. Once in the brain, the principal mode of action is as an antagonist of adenosine receptors . The caffeine molecule is

structurally similar to adenosine, and binds to adenosine receptors on the surface of cells without activating them (an " antagonist " mechanism of action). Therefore, caffeine acts as a competitive inhibitor .

Adenosine is found in every part of the body, because it plays a role in the fundamental ATP - related energy metabolism, but it has special functions in the brain. There is a great deal of evidence that concentrations of brain adenosine are increased by various types of metabolic stress including anoxia and ischemia. The evidence also indicates that brain adenosine acts to protect the brain by suppressing neural activity and also by increasing blood flow through A_{2A} and A_{2B} receptors located on vascular smooth muscle . By counteracting adenosine, caffeine reduces resting cerebral blood flow between 22% and 30%.^[53] Caffeine also has a generally disinhibitory effect on neural activity. It has not been shown, however, how these effects cause increases in arousal and alertness.

Adenosine is released in the brain through a complex mechanism.^[52] There is evidence that adenosine functions as a synaptically released neurotransmitter in some cases, but stress-related adenosine increases appear to be produced mainly by extracellular metabolism of ATP. It is not likely that adenosine is the primary neurotransmitter for any group of neurons, but rather that it is released together with other transmitters by a number of neuron types. Unlike most neurotransmitters, adenosine does not seem to be packaged into vesicles that are released in a voltage - controlled manner, but the possibility of such a mechanism has not been completely ruled out.

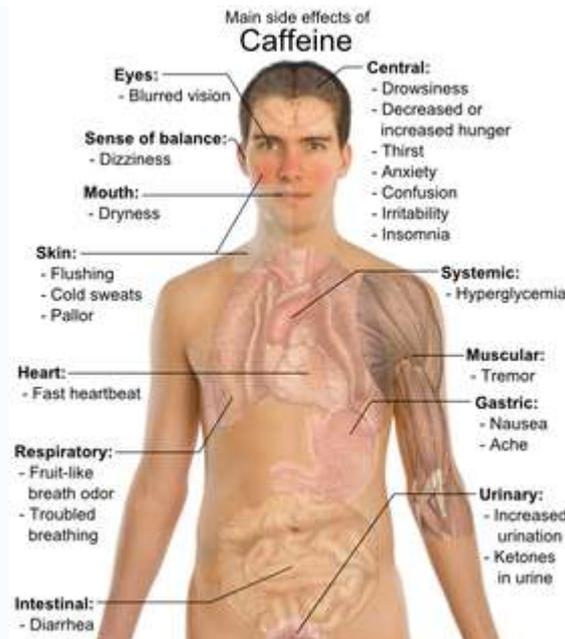
Several classes of adenosine receptors have been described, with different anatomical distributions. A₁ receptors are widely distributed, and act to inhibit calcium uptake. A_{2A} receptors are heavily concentrated in the basal ganglia, an area that plays a critical role in behavior control, but can be found in other parts of the brain as well, in lower densities. There is evidence that A_{2A} receptors interact with the dopamine system , which is involved in reward and arousal. (A_{2A} receptors can also be found on arterial walls and blood cell membranes) .

Beyond its general neuroprotective effects, there are reasons to believe that adenosine may be more specifically involved in control of the sleep-wake cycle. Robert McCarley and his colleagues have argued that accumulation of adenosine may be a primary cause of the sensation of sleepiness that follows prolonged mental activity, and that the effects may be mediated both by inhibition of wake-promoting neurons via A_1 receptors, and activation of sleep-promoting neurons via indirect effects on A_{2A} receptors.^[54] More recent studies have provided additional evidence for the importance of A_{2A} , but not A_1 , receptors. Some of the secondary effects of caffeine are probably caused by actions unrelated to adenosine. Caffeine is known to be a competitive inhibitor of the enzyme cAMP - phosphodiesterase (cAMP – PDE), which converts cyclic AMP (cAMP) in cells to its noncyclic form, thus allowing cAMP to build up in cells. Cyclic AMP participates in activation of protein kinase A (PKA) to begin the phosphorylation of specific enzymes used in glucose synthesis. By blocking its removal caffeine intensifies and prolongs the effects of epinephrine and epinephrine-like drugs such as amphetamine, methamphetamine, or methylphenidate. Increased concentrations of cAMP in parietal cells causes an increased activation of protein kinase A (PKA) which in turn increases activation of H^+ / K^+ ATPase, resulting finally in increased gastric acid secretion by the cell. Cyclic AMP also increases the activity of the funny current, which directly increases heart rate. Caffeine is also a structural analogue of strychnine and like it (though much less potent) a competitive antagonist at ionotropic glycine receptors.

Metabolites of caffeine also contribute to caffeine's effects. Paraxanthine is responsible for an increase in the lipolysis process, which releases glycerol and fatty acids into the blood to be used as a source of fuel by the muscles. Theobromine is a vasodilator that increases the amount of oxygen and nutrient flow to the brain and muscles. Theophylline acts as a smooth muscle relaxant that chiefly affects bronchioles and acts as a chronotrope and inotrope that increases heart rate and efficiency.

Caffeine has a significant effect on spiders, which is reflected in the construction of their webs.

5 – 3 : Effects when taken in moderation :



Over view of the more common side effects of caffeine, possibly appearing even at levels below overdose .

The precise amount of caffeine necessary to produce effects varies from person to person depending on body size and degree of tolerance to caffeine. It takes less than an hour for caffeine to begin affecting the body and a mild dose wears off in three to four hours.^[28] Consumption of caffeine does not eliminate the need for sleep, it only temporarily reduces the sensation of being tired throughout the day. In general, 25 to 50 milligrams of caffeine is sufficient for most people to report increased alertness and arousal as well as subjectively lower levels of fatigue.

With these effects, caffeine is an ergogenic, increasing a person's capability for mental or physical labor. A study conducted in 1979 showed a 7 % increase in distance cycled over a period of two hours in subjects who consumed caffeine compared to control subjects.^[60] Other studies attained much more dramatic results; one particular study of trained runners showed a 44 % increase in "race-pace" endurance, as well as a 51 % increase in cycling endurance, after a dosage of 9 milligrams of caffeine per kilogram of body weight.^[61] Additional studies have reported similar effects. Another study found

5.5 milligrams of caffeine per kilogram of body mass resulted in subjects cycling 29 % longer during high intensity circuits .

Caffeine citrate has proven to be of short and long term benefit in treating the breathing disorders of apnea of prematurity and bronchopulmonary dysplasia in premature infants . The only short term risk associated with caffeine citrate treatment is a temporary reduction in weight gain during the therapy , and longer term studies (18 to 21 months) have shown lasting benefits of treatment of premature infants with caffeine .

Caffeine relaxes the internal anal sphincter muscles and thus should be avoided by those with fecal incontinence .

While relatively safe for humans, caffeine is considerably more toxic to some other animals such as dogs, horses, and parrots due to a much poorer ability to metabolize this compound. Caffeine has also a pronounced effect on mollusks and various insects as well as spiders.

5 – 4 : Tolerance and with drawal :

Because caffeine is primarily an antagonist of the central nervous system's receptors for the neurotransmitter adenosine, the bodies of individuals who regularly consume caffeine adapt to the continual presence of the drug by substantially increasing the number of adenosine receptors in the central nervous system. This increase in the number of the adenosine receptors makes the body much more sensitive to adenosine, with two primary consequences . First, the stimulatory effects of caffeine are substantially reduced, a phenomenon known as a tolerance adaptation. Second, because these adaptive responses to caffeine make individuals much more sensitive to adenosine, a reduction in caffeine intake will effectively increase the normal physiological effects of adenosine, resulting in unwelcome withdrawal symptoms in tolerant users .

Other research questions the idea that up-regulation of adenosine receptors is responsible for tolerance to the locomotor stimulant effects of caffeine, noting, among other things, that this tolerance is insurmountable by higher doses of caffeine (it should be surmountable

if tolerance was due to an increase in receptors) , and that the increase in adenosine receptor number is modest and does not explain the large tolerance which develops to caffeine .

Caffeine tolerance develops very quickly, especially among heavy coffee and energy drink consumers. Complete tolerance to sleep disruption effects of caffeine develops after consuming 400 mg of caffeine 3 times a day for 7 days. Complete tolerance to subjective effects of caffeine was observed to develop after consuming 300 mg 3 times per day for 18 days, and possibly even earlier . In another experiment, complete tolerance of caffeine was observed when the subject consumed 750 – 1200 mg per day while incomplete tolerance to caffeine has been observed in those that consume more average doses of caffeine .

Because adenosine, in part, serves to regulate blood pressure by causing vasodilation, the increased effects of adenosine due to caffeine withdrawal cause the blood vessels of the head to dilate, leading to an excess of blood in the head and causing a headache and nausea. Reduced catecholamine activity may cause feelings of fatigue and drowsiness. A reduction in serotonin levels when caffeine use is stopped can cause anxiety, irritability, inability to concentrate and diminished motivation to initiate or to complete daily tasks; in extreme cases it may cause mild depression. Together, these effects have come to be known as a "crash".

Withdrawal symptoms—possibly including headache, irritability, an inability to concentrate, drowsiness, insomnia and pain in the stomach, upper body, and joints — may appear within 12 to 24 hours after discontinuation of caffeine intake, peak at roughly 48 hours, and usually last from one to five days, representing the time required for the number of adenosine receptors in the brain to revert to "normal" levels, uninfluenced by caffeine consumption. Analgesics, such as aspirin, can relieve the pain symptoms, as can a small dose of caffeine. Most effective is a combination of both an analgesic and a small amount of caffeine .

This is not the only case where caffeine increases the effectiveness of a drug. Caffeine makes pain relievers 40 % more

effective in relieving headaches and helps the body absorb headache medications more quickly, bringing faster relief . For this reason, many over - the - counter headache drugs include caffeine in their formula. It is also used with ergotamine in the treatment of migraine and cluster headaches as well as to overcome the drowsiness caused by antihistamines .

5 – 5 : Overuse

In large amounts, and especially over extended periods of time, caffeine can lead to a condition known as *caffeinism* . Caffeinism usually combines caffeine dependency with a wide range of unpleasant physical and mental conditions including nervousness, irritability, anxiety, tremulousness, muscle twitching (hyperreflexia), insomnia, headaches, respiratory alkalosis, and heart palpitations . Furthermore, because caffeine increases the production of stomach acid, high usage over time can lead to peptic ulcers, erosive esophagitis, and gastroesophageal reflux disease .

There are four caffeine - induced psychiatric disorders recognized by the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*: caffeine intoxication, caffeine-induced anxiety disorder, caffeine-induced sleep disorder, and caffeine-related disorder not otherwise specified (NOS) .

5 – 5 - 1 : Caffeine intoxication :

An acute overdose of caffeine, usually in excess of about 300 milligrams, dependent on body weight and level of caffeine tolerance, can result in a state of central nervous system over-stimulation called *caffeine intoxication* (DSM - IV 305.90) , or colloquially the "caffeine jitters". The symptoms of caffeine intoxication are not unlike overdoses of other stimulants. It may include restlessness, nervousness, excitement, insomnia, flushing of the face, increased urination, gastrointestinal disturbance, muscle twitching, a rambling flow of thought and speech, irritability, irregular or rapid heart beat, and psychomotor agitation . In cases of much larger overdoses, mania, depression, lapses in judgment, disorientation, disinhibition, delusions, hallucinations, and psychosis may occur, and

rhabdomyolysis (breakdown of skeletal muscle tissue) can be provoked .



Main symptoms of caffeine intoxication

In cases of extreme overdose, death can result. The median lethal dose (LD₅₀) given orally, is 192 milligrams per kilogram in rats . The LD₅₀ of caffeine in humans is dependent on weight and individual sensitivity and estimated to be about 150 to 200 milligrams per kilogram of body mass, roughly 80 to 100 cups of coffee for an average adult taken within a limited time frame that is dependent on half-life. Though achieving lethal dose with caffeine would be exceptionally difficult with regular coffee, there have been reported deaths from overdosing on caffeine pills, with serious symptoms of overdose requiring hospitalization occurring from as little as 2 grams of caffeine. An exception to this would be taking a drug such as fluvoxamine which blocks the liver enzyme responsible for the metabolism of caffeine, thus increasing the central effects and blood concentrations of caffeine dramatically at 5 – fold . It is not contraindicated, but highly advisable to minimize the intake of caffeinated beverages, as drinking one cup of coffee will have the same effect as drinking five under normal conditions.^{[84][85][86][87]} Death typically occurs due to ventricular fibrillation brought about by effects of caffeine on the cardiovascular system.

Treatment of severe caffeine intoxication is generally supportive, providing treatment of the immediate symptoms, but if the patient has very high serum levels of caffeine then peritoneal dialysis, hemodialysis, or hemofiltration may be required.

5 – 5 – 2 : Anxiety and sleep disorders :

Two infrequently diagnosed caffeine-induced disorders that are recognized by the American Psychological Association (APA) are *caffeine-induced sleep disorder* and *caffeine-induced anxiety disorder*, which can result from long-term excessive caffeine intake.

In the case of caffeine - induced sleep disorder , an individual regularly ingests high doses of caffeine sufficient to induce a significant disturbance in his or her sleep, sufficiently severe to warrant clinical attention .

In some individuals, the large amounts of caffeine can induce anxiety severe enough to necessitate clinical attention. This caffeine-induced anxiety disorder can take many forms, from generalized anxiety to panic attacks, obsessive-compulsive symptoms, or even phobic symptoms.^[81] Because this condition can mimic organic mental disorders, such as panic disorder, generalized anxiety disorder, bipolar disorder, or even schizophrenia, a number of medical professionals believe caffeine-intoxicated people are routinely misdiagnosed and unnecessarily medicated when the treatment for caffeine-induced psychosis would simply be to stop further caffeine intake.^[88] A study in the *British Journal of Addiction* concluded that caffeinism, although infrequently diagnosed, may afflict as many as one person in ten of the population . Co administration of theanine was shown to greatly reduce this caffeine - induced anxiety .

5 – 6 : Effects on memory and learning :

An array of studies found that caffeine could have nootropic effects, inducing certain changes in memory and learning . However , the tests performed contradict one another and the results have proven inconsistent and inconclusive .

Researchers have found that long-term consumption of low dose caffeine slowed hippocampus - dependent learning and impaired long-term memory in mice . Caffeine consumption for 4 weeks also significantly reduced hippocampal neurogenesis compared to controls during the experiment . The conclusion was that long - term consumption of caffeine could inhibit hippocampus-dependent learning and memory partially through inhibition of hippocampal neurogenesis .

In another study, caffeine was added to rat neurons *in vitro*. The dendritic spines (a part of the brain cell used in forming connections between neurons) taken from the hippocampus (a part of the brain associated with memory) grew by 33 % and new spines formed. After an hour or two, however, these cells returned to their original shape .

Another study showed that human subjects — after receiving 100 milligrams of caffeine — had increased activity in brain regions located in the frontal lobe , where a part of the working memory network is located, and the anterior cingulate cortex, a part of the brain that controls attention. The caffeinated subjects also performed better on the memory tasks .

However, a different study showed that caffeine could impair short term memory and increase the likelihood of the tip of the tongue phenomenon. The study allowed the researchers to suggest that caffeine could aid short-term memory when the information to be recalled is related to the current train of thought, but also to hypothesize that caffeine hinders short - term memory when the train of thought is unrelated.^[93] In essence, caffeine consumption increases mental performance related to focused thought while it may decrease broad - range thinking abilities .

5 – 7 : Effects on the heart :

Caffeine binds to receptors on the surface of heart muscle cells which leads to an increase in the level of cAMP inside the cells (by blocking the enzyme that degrades cAMP) , mimicking the effects of epinephrine (which binds to receptors on the cell that activate cAMP production) . cAMP acts as a " second messenger ," and activates a

large number of protein kinase A (PKA; cAMP - dependent protein kinase) . This has the overall effect of increasing the rate of glycolysis and increases the amount of ATP available for muscle contraction and relaxation. According to one study, caffeine in the form of coffee, significantly reduces the risk of heart disease in epidemiological studies. However, the protective effect was found only in participants who were not severely hypertensive (i.e. patients that are not suffering from a very high blood pressure) . Furthermore, no significant protective effect was found in participants aged less than 65 years or in cerebrovascular disease mortality for those aged equal or more than 65 years.

5 – 8 : Effects on children

It is a common myth that caffeine causes stunted growth in children.^[95] However, scientific studies have contradicted that belief . Children experience the same effects from caffeine as adults .

Energy drinks, most of which containing high amounts of caffeine, have been banned in many schools throughout the world .

5 – 9 : Caffeine intake during pregnancy :

Despite its widespread use and the conventional view that it is a safe substance, a 2008 study suggested that pregnant women who consume 200 milligrams or more of caffeine per day have about twice the miscarriage risk as women who consume none. However, another 2008 study found no correlation between miscarriage and caffeine consumption.^[97] The UK Food Standards Agency has recommended that pregnant women should limit their caffeine intake to less than 200 mg of caffeine a day – the equivalent of two cups of instant coffee or a half to two cups of fresh coffee . The FSA noted that the design of the studies made it impossible to be certain that the differences were due to caffeine per se, instead of other lifestyle differences possibly associated with high levels of caffeine consumption, but judged the advice to be prudent .

Dr De - Kun Li of Kaiser Permanente Division of Research , writing in the American Journal of Obstetrics and Gynecology,

concluded that an intake of 200 milligrams or more per day, representing two or more cups, "significantly increases the risk of miscarriage" . However, Dr. David Savitz , a professor in community and preventive medicine at New York's Mount Sinai School of Medicine and lead author of the other new study on the subject published in the January issue of Epidemiology, found no link between miscarriage and caffeine consumption .

5 – 10 : Genetics and caffeine metabolism :

A 2006 study by Dr. Ahmed El - Sohemy at the University of Toronto discovered a link between a gene affecting caffeine metabolism and the effects of coffee on health.^[101] Some people metabolize caffeine more slowly than the general population due to variations in a specific cytochrome P450 gene , and there is evidence people with this gene may be at a higher risk of myocardial infarction when consuming large amounts of coffee. For rapid metabolizers, however, coffee seemed to have a preventative effect. Slow and fast metabolizers are comparably common in the general population, and this has been blamed for the wide variation in studies of the health effects of caffeine .

5 – 11 : Intraocular Pressure and caffeine :

Recent data has suggested that caffeine consumption can raise intraocular pressure . This may be a significant consideration for those with open angle glaucoma .

6 - Decaffeination

Extraction of caffeine from coffee , to produce decaffeinated coffee and caffeine, is an important industrial process and can be performed using a number of different solvents. Benzene, chloroform, trichloroethylene and dichloromethane have all been used over the years but for reasons of safety, environmental impact, cost and flavor, they have been superseded by the following main methods :

6 – 1 : Water extraction :

Coffee beans are soaked in water. The water, which contains many other compounds in addition to caffeine and contributes to the flavor of coffee, is then passed through activated charcoal, which removes the caffeine. The water can then be put back with the beans and evaporated dry, leaving decaffeinated coffee with a good flavor.^[105] Coffee manufacturers recover the caffeine and resell it for use in soft drinks and over-the-counter caffeine tablets.

6 – 2 : Supercritical carbon dioxide extraction :

Supercritical carbon dioxide is an excellent nonpolar solvent for caffeine, and is safer than the organic solvents that are otherwise used. The extraction process is simple: CO₂ is forced through the green coffee beans at temperatures above 31.1 °C and pressures above 73 atm. Under these conditions, CO₂ is in a "supercritical" state: it has gaslike properties which allow it to penetrate deep into the beans but also liquid-like properties which dissolve 97–99% of the caffeine. The caffeine-laden CO₂ is then sprayed with high pressure water to remove the caffeine. The caffeine can then be isolated by charcoal adsorption (as above) or by distillation, recrystallization, or reverse osmosis .

6 – 3 : Extraction by organic solvents :

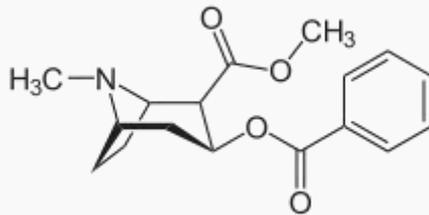
Organic solvents such as ethyl acetate present much less health and environmental hazard than previously used chlorinated and aromatic solvents. Another method is to use triglyceride oils obtained from spent coffee grounds .

Cocaine

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Systematic (IUPAC) name

methyl (1*R* , 2*R* , 3*S* , 5*S*) -3 - (benzoyloxy) – 8 – methyl – 8 – azabicyclo [3 . 2 . 1] octane – 2 - carboxylate

Formula	C₁₇ H₂₁ NO₄
Mol Mass	303 g / mol
Melt Point	195 °C (383 °F)
Solubility in Water	1800 mg / mL (20 ° C)
Bioavailability	Oral : 33 % Insufflated : 60 – 80 % Nasal Spray: 25 – 43 %
Metabolism	Hepatic CYP3A4
Half life	1 hour

1 – Introduction :

Cocaine (benzoyl methyl ecgonine) is a crystalline tropane alkaloid that is obtained from the leaves of the coca plant . The name comes from " coca " in addition to the alkaloid suffix - *ine*, forming *cocaine* . It is a stimulant of the central nervous system and an appetite suppressant. Specifically, it is a serotonin-norepinephrine - dopamine reuptake inhibitor , which mediates functionality of such as an exogenous catecholamine transporter ligand. Because of the way it affects the mesolimbic reward pathway , cocaine is addictive .

Its possession, cultivation, and distribution are illegal for non-medicinal and non - government sanctioned purposes in virtually all parts of the world. Although its free commercialization is illegal and has been severely penalized in virtually all countries, its use worldwide remains widespread in many social , cultural , and personal settings .

2 - History :

2 – 1 : Coca leaf

For over a thousand years South American indigenous peoples have chewed the coca leaf (*Erythroxylon coca*) , a plant that contains vital nutrients as well as numerous alkaloids, including cocaine. The leaf was, and is, chewed almost universally by some indigenous communities — ancient Peruvian mummies have been found with the remains of coca leaves and pottery from the time period depicts humans, cheeks bulged with the presence of something on which they are chewing . There is also evidence that these cultures used a mixture of coca leaves and saliva as an anesthetic for the performance of trepanation .

When the Spaniards conquered South America , they at first ignored aboriginal claims that the leaf gave them strength and energy, and declared the practice of chewing it the work of the Devil But after discovering that these claims were true, they legalized and taxed the leaf, taking 10 % off the value of each crop , In 1569 , Nicolás

Monardes described the practice of the natives of chewing a mixture of tobacco and coca leaves to induce " great contentment " :

[...when they wished to] make themselves drunk and [...] out of judgment [they chewed a mixture of tobacco and coca leaves which ...] make them go as they were out of their wittes [...]

In 1609, Padre Blas Valera wrote:

Coca protects the body from many ailments, and our doctors use it in powdered form to reduce the swelling of wounds, to strengthen broken bones, to expel cold from the body or prevent it from entering, and to cure rotten wounds or sores that are full of maggots. And if it does so much for outward ailments, will not its singular virtue have even greater effect in the entrails of those who eat it ?



The coca plant, *Erythroxylon coca*.

2 – 2 : Isolation :

Although the stimulant and hunger - suppressant properties of coca had been known for many centuries, the isolation of the cocaine alkaloid was not achieved until 1855. Various European scientists had attempted to isolate cocaine, but none had been successful for two reasons: the knowledge of chemistry required was insufficient at the time, and the cocaine was worsened because coca does not grow in the Eurasian region and ruined easily amidst transcontinental shipping .

The cocaine alkaloid was first isolated by the German chemist Friedrich Gaedcke in 1855. Gaedcke named the alkaloid "erythroxyline", and published a description in the journal *Archiv der Pharmazie*.

In 1856, Friedrich Wöhler asked Dr. Carl Scherzer, a scientist aboard the *Novara* (an Austrian frigate sent by Emperor Franz Joseph to circle the globe), to bring him a large amount of coca leaves from South America. In 1859 , the ship finished its travels and Wöhler received a trunk full of coca. Wöhler passed on the leaves to Albert Niemann, a Ph.D. student at the University of Göttingen in Germany, who then developed an improved purification process .

Niemann described every step he took to isolate cocaine in his dissertation titled *Über eine neue organische Base in den Cocablättern* (*On a New Organic Base in the Coca Leaves*), which was published in 1860 — it earned him his Ph.D. and is now in the British Library. He wrote of the alkaloid's "colourless transparent prisms" and said that, "Its solutions have an alkaline reaction, a bitter taste, promote the flow of saliva and leave a peculiar numbness, followed by a sense of cold when applied to the tongue." Niemann named the alkaloid " cocaine " — as with other alkaloids its name carried the "-ine" suffix (from Latin – *ina*).

The first synthesis and elucidation of the structure of the cocaine molecule was by Richard Willstätter in 1898 . The synthesis started from tropinone, a related natural product and took five steps .

2 – 3 : Medicalization :

With the discovery of this new alkaloid, Western medicine was quick to exploit the possible uses of this plant .

In 1879 , Vassili von Anrep, of the University of Würzburg, devised an experiment to demonstrate the analgesic properties of the newly-discovered alkaloid. He prepared two separate jars , one containing a cocaine-salt solution, with the other containing merely salt water. He then submerged a frog's legs into the two jars, one leg in the treatment and one in the control solution, and proceeded to

stimulate the legs in several different ways. The leg that had been immersed in the cocaine solution reacted very differently than the leg that had been immersed in salt water .

Carl Koller (a close associate of Sigmund Freud, who would write about cocaine later) experimented with cocaine for ophthalmic usage. In an infamous experiment in 1884, he experimented upon himself by applying a cocaine solution to his own eye and then pricking it with pins. His findings were presented to the Heidelberg Ophthalmological Society. Also in 1884, Jellinek demonstrated the effects of cocaine as a respiratory system anesthetic. In 1885, William Halsted demonstrated nerve-block anesthesia,^[14] and James Corning demonstrated peridural anesthesia . 1898 saw Heinrich Quincke use cocaine for spinal anaesthesia .

Today, cocaine has very limited medical use .

2 – 4 : Popularization :

In 1859, an Italian doctor, Paolo Mantegazza, returned from Peru, where he had witnessed first-hand the use of coca by the natives. He proceeded to experiment on himself and upon his return to Milan he wrote a paper in which he described the effects. In this paper he declared coca and cocaine (at the time they were assumed to be the same) as being useful medicinally, in the treatment of “a furred tongue in the morning, flatulence , [and] whitening of the teeth.”

Pope Leo XIII purportedly carried a hipflask of the coca - treated Vin Mariani with him, and awarded a Vatican gold medal to Angelo Mariani .

A chemist named Angelo Mariani who read Mantegazza’s paper became immediately intrigued with coca and its economic potential. In 1863, Mariani started marketing a wine called Vin Mariani, which had been treated with coca leaves, to become cocawine. The ethanol in wine acted as a solvent and extracted the cocaine from the coca leaves, altering the drink’s effect. It contained 6 mg cocaine per ounce of wine, but Vin Mariani which was to be exported contained 7.2 mg per ounce, to compete with the higher cocaine content of similar

drinks in the United States. A “pinch of coca leaves” was included in John Styth Pemberton's original 1886 recipe for Coca-Cola, though the company began using decocainized leaves in 1906 when the Pure Food and Drug Act was passed. The actual amount of cocaine that Coca-Cola contained during the first twenty years of its production is practically impossible to determine .

In 1879 cocaine began to be used to treat morphine addiction. Cocaine was introduced into clinical use as a local anaesthetic in Germany in 1884 , about the same time as Sigmund Freud published his work *Über Coca*, in which he wrote that cocaine causes .

exhilaration and lasting euphoria, which in no way differs from the normal euphoria of the healthy person...You perceive an increase of self-control and possess more vitality and capacity for work....In other words, you are simply normal, and it is soon hard to believe you are under the influence of any drug....Long intensive physical work is performed without any fatigue...This result is enjoyed without any of the unpleasant after-effects that follow exhilaration brought about by alcohol...Absolutely no craving for the further use of cocaine appears after the first, or even after repeated taking of the drug...

In 1885 the U.S. manufacturer Parke-Davis sold cocaine in various forms, including cigarettes, powder, and even a cocaine mixture that could be injected directly into the user's veins with the included needle. The company promised that its cocaine products would “supply the place of food, make the coward brave, the silent eloquent and ... render the sufferer insensitive to pain.”

By the late Victorian era cocaine use had appeared as a vice in literature. For example, it was injected by Arthur Conan Doyle's fictional Sherlock Holmes.

In early 20th - century Memphis , Tennessee, cocaine was sold in neighborhood drugstores on Beale Street, costing five or ten cents for a small boxful. Stevedores along the Mississippi River used the drug as a stimulant , and white employers encouraged its use by black laborers .

In 1909, Ernest Shackleton took “Forced March” brand cocaine tablets to Antarctica, as did Captain Scott a year later on his ill-fated journey to the South Pole .

2 – 5 : Prohibition :

By the turn of the twentieth century, the addictive properties of cocaine had become clear, and the problem of cocaine abuse began to capture public attention in the United States. The dangers of cocaine abuse became part of a moral panic that was tied to the dominant racial and social anxieties of the day. In 1903, the *American Journal of Pharmacy* stressed that most cocaine abusers were “bohemians, gamblers, high- and low-class prostitutes, night porters, bell boys, burglars, racketeers, pimps, and casual laborers.” In 1914, Dr. Christopher Koch of Pennsylvania’s State Pharmacy Board made the racial innuendo explicit, testifying that, “Most of the attacks upon the white women of the South are the direct result of a cocaine-crazed Negro brain.” Mass media manufactured an epidemic of cocaine use among African Americans in the Southern United States to play upon racial prejudices of the era, though there is little evidence that such an epidemic actually took place. In the same year, the Harrison Narcotics Tax Act outlawed the sale and distribution of cocaine in the United States. This law incorrectly referred to cocaine as a narcotic, and the misclassification passed into popular culture. As stated above, cocaine is a stimulant, not a narcotic. Although technically illegal for purposes of distribution and use, the distribution, sale and use of cocaine was still legal for registered companies and individuals. Because of the misclassification of cocaine as a narcotic, the debate is still open on whether the government actually enforced these laws strictly. Cocaine was not considered a controlled substance until 1970, when the United States listed it as such in the Controlled Substances Act. Until that point, the use of cocaine was open and rarely prosecuted in the US due to the moral and physical debates commonly discussed.

2 – 6 : Modern usage :

In many countries, cocaine is a popular recreational drug. In the United States, the development of " crack " cocaine introduced the substance to a generally poorer inner- city market. Use of the powder

form has stayed relatively constant, experiencing a new height of use during the late 1990s and early 2000s in the U.S., and has become much more popular in the last few years in the UK.

Cocaine use is prevalent across all socioeconomic strata, including age, demographics, economic, social, political, religious, and livelihood.

The estimated U.S. cocaine market exceeded \$ 70 billion in street value for the year 2005, exceeding revenues by corporations such as Starbucks . There is a tremendous demand for cocaine in the U.S. market, particularly among those who are making incomes affording luxury spending, such as single adults and professionals with discretionary income. Cocaine's status as a club drug shows its immense popularity among the " party crowd ".

In 1995 the World Health Organization (WHO) and the United Nations Interregional Crime and Justice Research Institute (UNICRI) announced in a press release the publication of the results of the largest global study on cocaine use ever undertaken. However, a decision in the World Health Assembly banned the publication of the study. In the sixth meeting of the B committee the US representative threatened that "If WHO activities relating to drugs failed to reinforce proven drug control approaches, funds for the relevant programs should be curtailed". This led to the decision to discontinue publication. A part of the study has been recuperated . Available are profiles of cocaine use in 20 countries .

A problem with illegal cocaine use, especially in the higher volumes used to combat fatigue (rather than increase euphoria) by long-term users, is the risk of ill effects or damage caused by the compounds used in adulteration. Cutting or "stamping on" the drug is commonplace, using compounds which simulate ingestion effects, such as Novocain (procaine) producing temporary anaesthesia as many users believe a strong numbing effect is the result of strong and/or pure cocaine, ephedrine or similar stimulants that are to produce an increased heart rate. The normal adulterants for profit are inactive sugars, usually mannitol, creatine or glucose, so introducing active adulterants gives the illusion of purity and to 'stretch' or make it

so a dealer can sell more product than without the adulterants . The adulterant of sugars therefore allows the dealer to sell the product for a higher price because of the illusion of purity and allows to sell more of the product at that higher price, enabling dealers to make a lot of revenue with little cost of the adulterants. Cocaine trading carries large penalties in most jurisdictions, so user deception about purity and consequent high profits for dealers are the norm .

3 - Biosynthesis

The first synthesis and elucidation of the **cocaine** molecule was by Richard Willstätter in 1898.^[21] Willstätter's synthesis derived cocaine from tropinone. Since then, Robert Robinson and Edward Leete have made significant contributions to the mechanism of the synthesis .

2 – 1 : Biosynthesis of *N* – methyl - pyrrolinium cation :

3

The biosynthesis begins with L-Glutamine, which is derived to L-ornithine in plants. The major contribution of L-ornithine and L-arginine as a precursor to the tropane ring was confirmed by Edward Leete.^[22] Ornithine then undergoes a Pyridoxal phosphate-dependent decarboxylation to form putrescine. In animals, however, the urea cycle derives putrescine from ornithine. L - ornithine is converted to L-arginine,^[23] which is then decarboxylated via PLP to form agmatine. Hydrolysis of the imine derives *N* - carbamoylputrescine followed with hydrolysis of the urea to form putrescine. The separate pathways of converting ornithine to putrescine in plants and animals have converged. A SAM - dependent *N*-methylation of putrescine gives the *N*-methylputrescine product, which then undergoes oxidative deamination by the action of diamine oxidase to yield the aminoaldehyde. Schiff base formation confirms the biosynthesis of the *N* – methyl - Δ^1 - pyrrolinium cation .

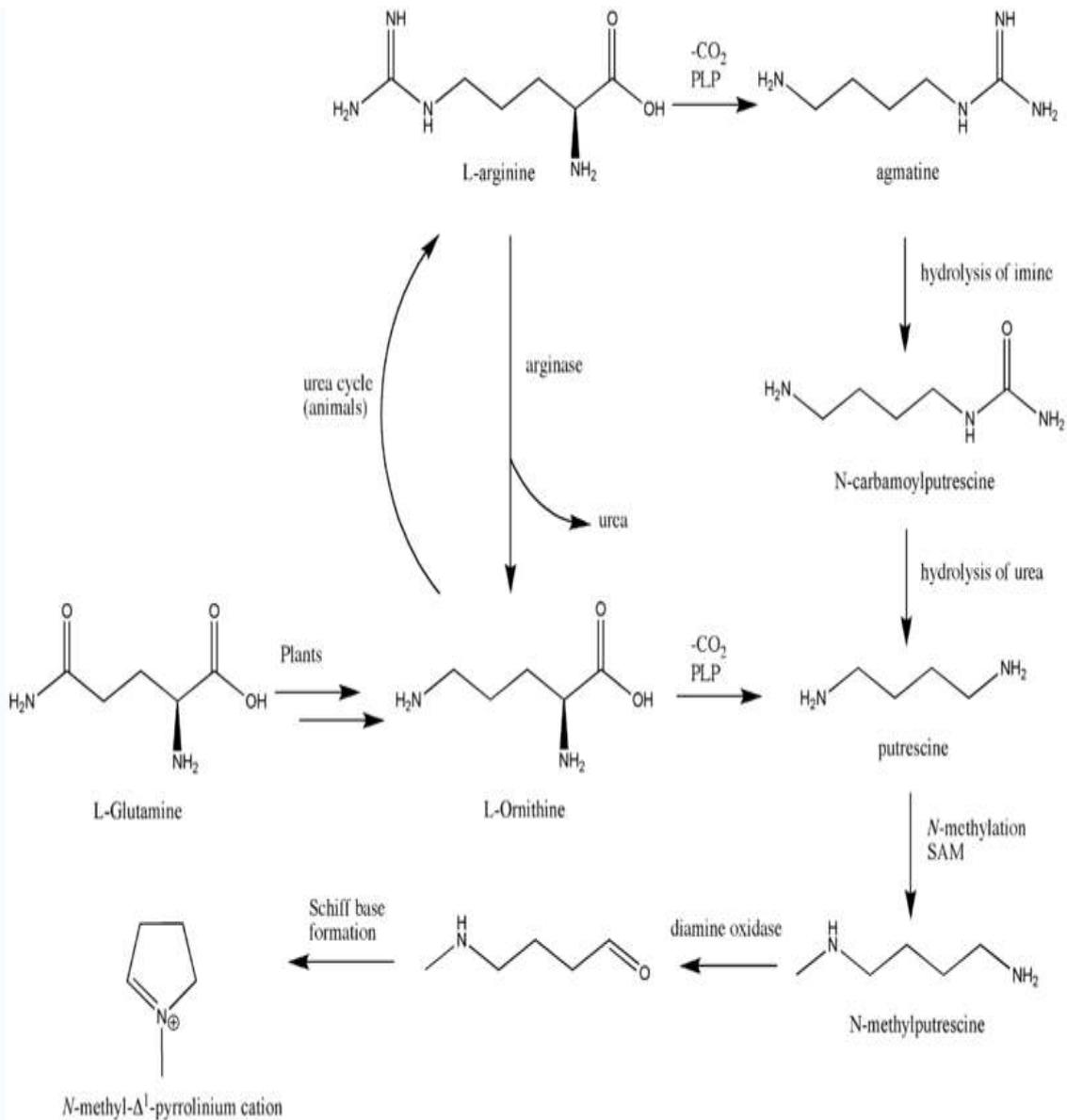
3 – 2 : Biosynthesis of cocaine :

The additional carbon atoms required for the synthesis of cocaine are derived from acetyl – CoA , by addition of two acetyl - CoA units

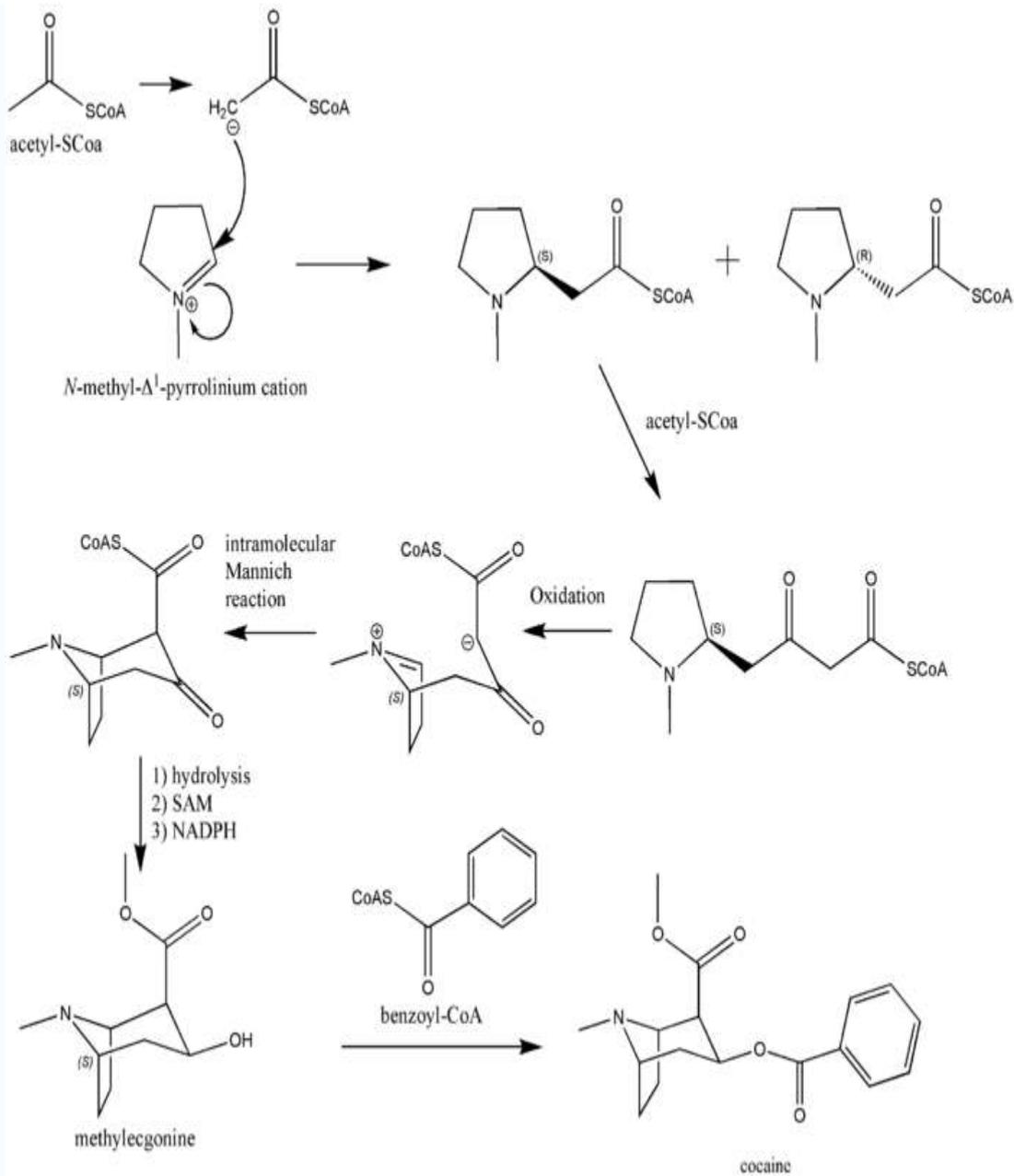
to the *N*-methyl- Δ^1 -pyrrolinium cation. The first addition is a Mannich-like reaction with the enolate anion from acetyl-CoA acting as a nucleophile towards the pyrrolinium cation. The second addition occurs through a Claisen condensation. This produces a racemic mixture of the 2-substituted pyrrolidine, with the retention of the thioester from the Claisen condensation. In formation of tropinone from racemic ethyl [2,3-¹³C₂]4-(*N*-methyl-2-pyrrolidinyl)-3-oxobutanoate there is no preference for either stereoisomer. In the biosynthesis of cocaine, however, only the (*S*)-enantiomer can cyclize to form the tropane ring system of cocaine. The stereoselectivity of this reaction was further investigated through study of prochiral methylene hydrogen discrimination^[26]. This is due to the extra chiral center at C-2. This process occurs through an oxidation, which regenerates the pyrrolinium cation and formation of an enolate anion, and an intramolecular Mannich reaction. The tropane ring system undergoes hydrolysis, SAM-dependent methylation, and reduction via NADPH for the formation of methylecgonine. The benzoyl moiety required for the formation of the cocaine diester is synthesized from phenylalanine via cinnamic acid. Benzoyl-CoA then combines the two units to form cocaine.

3 – 3 : Robert Robinson's acetonedicarboxylate :

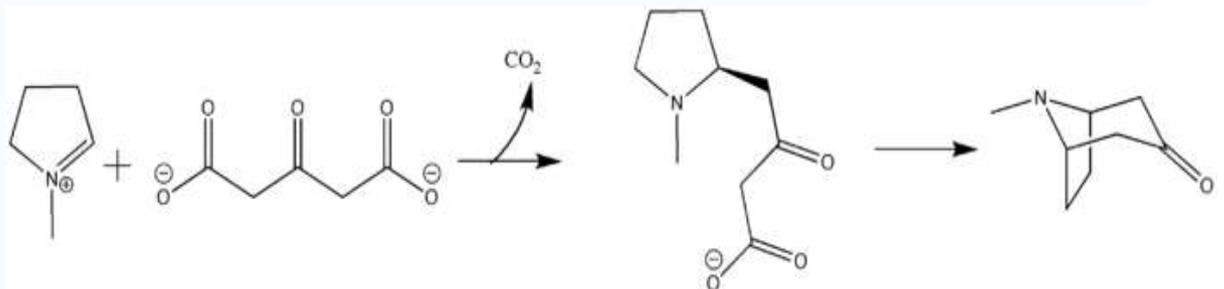
The biosynthesis of the tropane alkaloid, however, is still uncertain. Hemscheidt proposes that Robinson's acetonedicarboxylate emerges as a potential intermediate for this reaction^[29]. Condensation of *N*-methylpyrrolinium and acetonedicarboxylate would generate the oxobutyrate. Decarboxylation leads to tropane alkaloid formation.



Biosynthesis of N – methyl - pyrrolium cation



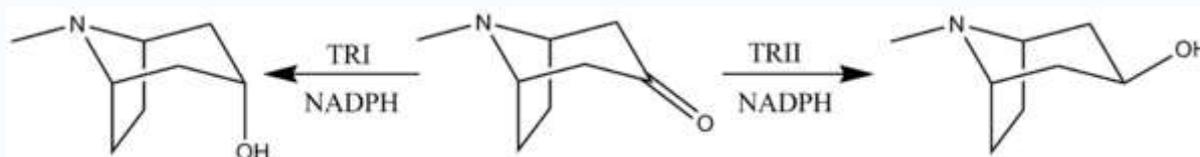
Biosynthesis of cocaine



Robinson biosynthesis of tropine

3 – 4 : Reduction of tropinone

The reduction of tropinone is mediated by NADPH-dependent reductase enzymes, which have been characterized in multiple plant species . These plant species all contain two types of the reductase enzymes, tropinone reductase I and tropinone reductase II. TRI produces tropine and TRII produces pseudotropine. Due to differing kinetic and pH/activity characteristics of the enzymes and by the 25 - fold higher activity of TRI over TRII , the majority of the tropinone reduction is from TRI to form tropine .



Reduction of tropinone

4 – Pharmacology :

4 – 1 : Appearance :

Cocaine in its purest form is a white, pearly product . Cocaine appearing in powder form is a salt, typically cocaine hydro chloride (CAS 53 - 21 - 4) . Street market cocaine is frequently adulterated or “cut” with various powdery fillers to increase its weight; the substances most commonly used in this process are baking soda; sugars, such as lactose, dextrose, inositol, and mannitol; and local anesthetics, such as lidocaine or benzocaine, which mimic or add to cocaine's numbing effect on mucous membranes. Cocaine may also be "cut" with other stimulants such as methamphetamine . Adulterated cocaine is often a white, off - white or pinkish powder .

The color of “ crack ” cocaine depends upon several factors including the origin of the cocaine used, the method of preparation – with ammonia or baking soda – and the presence of impurities, but will generally range from white to a yellowish cream to a light brown. Its texture will also depend on the adulterants, origin and processing of the powdered cocaine, and the method of converting the base. It ranges from a crumbly texture, sometimes extremely oily, to a hard, almost crystalline nature .

4 – 2 : Forms of cocaine :

4 – 2 – 1 : Salts :

Cocaine, like many alkaloids can form many different salts, such as hydrochloride (HCl) and sulfate (- SO₄) . Different salts have different solvency in solvents. Its hydrochloride , like many alkaloid hydrochloride is polar and is soluble in water .

4 – 2 – 2 : Basic

As the name implies, “ free base ” is the base form of cocaine, as opposed to the salt form. It is practically insoluble in water whereas hydrochloride salt is water soluble.

Smoking freebase cocaine has the additional effect of releasing methylecgonidine into the user's system due to the pyrolysis of the substance (a side effect which insufflating or injecting powder cocaine does not create) . Some research suggests that smoking freebase cocaine can be even more cardiotoxic than other routes of administration because of methylecgonidine's effects on lung tissue and liver tissue .

Pure cocaine is prepared by neutralizing its compounding salt with an alkaline solution which will precipitate to non - polar basic cocaine. It is further refined through aqueous-solvent Liquid - liquid extraction .

4 – 2 – 3 : Crack cocaine :

Crack is a lower purity form of free-base cocaine and contains sodium bicarbonate as impurity. Freebase and crack are often administered by smoking . The origin of the name is from the crackling sound (hence the onomatopoeic “ crack ”) produced when cocaine containing impurities are heated .



A woman smoking crack cocaine .

4 – 2 – 4 : Coca leaf infusions :

Coca herbal infusion (also referred to as Coca tea) is used in coca-leaf producing countries much as any herbal medicinal infusion would elsewhere in the world. The free and legal commercialization of dried coca leaves under the form of filtration bags to be used as "coca tea" has been actively promoted by the governments of Peru and Bolivia for many years as a drink having medicinal powers. Visitors to the city of Cuzco in Peru, and La Paz in Bolivia are greeted with the offering of coca leaf infusions (prepared in tea pots with whole coca leaves) purportedly to help the newly - arrived traveler overcome the malaise of high altitude sickness. The effects of drinking coca tea are a mild stimulation and mood lift. It does not produce any significant numbing of the mouth nor does it give a rush like snorting cocaine. In order to prevent the demonization of this product, its promoters publicize the unproven concept that much of the effect of the ingestion of coca leaf infusion would come from the secondary alkaloids, as being not only quantitatively different from pure cocaine but also qualitatively different.

It has been promoted as an adjuvant for the treatment of cocaine dependence. In one controversial study, coca leaf infusion was used - in addition to counseling- to treat 23 addicted coca-paste smokers in Lima, Peru. Relapses fell from an average of four times per month before treatment with coca tea to one during the treatment. The duration of abstinence increased from an average of 32 days prior to

treatment to 217 days during treatment. These results suggest that the administration of coca leaf infusion plus counseling would be an effective method for preventing relapse during treatment for cocaine addiction.^[38] Importantly, these results also suggest strongly that the primary pharmacologically active metabolite in coca leaf infusions is actually cocaine and not the secondary alkaloids .

The cocaine metabolite benzoylecgonine can be detected in the urine of people a few hours after drinking one cup of coca leaf infusion .

4 – 3 : Routes of administration :

4 – 3 – 1 : Oral :

A spoon containing baking soda, cocaine, and a small amount of water. Used in a " poor - man's " crack - cocaine production

Many users rub the powder along the gum line, or onto a cigarette filter which is then smoked, which numbs the gums and teeth - hence the colloquial names of " numbies " , " gummers " or "cocoa puffs " for this type of administration. This is mostly done with the small amounts of cocaine remaining on a surface after insufflation. Another oral method is to wrap up some cocaine in rolling paper and swallow it. This is sometimes called a " snow bomb " .

4 – 3 – 1 – 1 : Coca leaf :

Coca leaves are typically mixed with an alkaline substance (such as lime) and chewed into a wad that is retained in the mouth between gum and cheek (much in the same as chewing tobacco is chewed) and sucked of its juices. The juices are absorbed slowly by the mucous membrane of the inner cheek and by the gastrointestinal tract when swallowed. Alternatively, coca leaves can be infused in liquid and consumed like tea. Ingesting coca leaves generally is an inefficient means of administering cocaine. Advocates of the consumption of the coca leaf state that coca leaf consumption should not be criminalized as it is not actual cocaine, and consequently it is not properly the illicit drug. Because cocaine is hydrolyzed and rendered inactive in the

acidic stomach, it is not readily absorbed when ingested alone. Only when mixed with a highly alkaline substance (such as lime) can it be absorbed into the bloodstream through the stomach. The efficiency of absorption of orally administered cocaine is limited by two additional factors. First, the drug is partly catabolized by the liver. Second, capillaries in the mouth and esophagus constrict after contact with the drug, reducing the surface area over which the drug can be absorbed. Nevertheless, cocaine metabolites can be detected in the urine of subjects that have sipped even one cup of coca leaf infusion. Therefore, this is an actual additional form of administration of cocaine, albeit an inefficient one .

Orally administered cocaine takes approximately 30 minutes to enter the bloodstream. Typically, only a third of an oral dose is absorbed, although absorption has been shown to reach 60% in controlled settings. Given the slow rate of absorption, maximum physiological and psychotropic effects are attained approximately 60 minutes after cocaine is administered by ingestion. While the onset of these effects is slow, the effects are sustained for approximately 60 minutes after their peak is attained.

Contrary to popular belief, both ingestion and insufflation result in approximately the same proportion of the drug being absorbed: 30 to 60 %. Compared to ingestion, the faster absorption of insufflated cocaine results in quicker attainment of maximum drug effects. Snorting cocaine produces maximum physiological effects within 40 minutes and maximum psychotropic effects within 20 minutes, however, a more realistic activation period is closer to 5 to 10 minutes, which is similar to ingestion of cocaine. Physiological and psychotropic effects from nasally insufflated cocaine are sustained for approximately 40 – 60 minutes after the peak effects are attained .

Mate de coca or coca-leaf infusion is also a traditional method of consumption and is often recommended in coca producing countries, like Peru and Bolivia, to ameliorate some symptoms of altitude sickness. This method of consumption has been practiced for many centuries by the native tribes of South America. One specific purpose

of ancient coca leaf consumption was to increase energy and reduce fatigue in messengers who made multi-day quests to other settlements.

In 1986 an article in the *Journal of the American Medical Association* revealed that U.S. health food stores were selling dried coca leaves to be prepared as an infusion as “ Health Inca Tea ” . While the packaging claimed it had been “ decocainized ”, no such process had actually taken place. The article stated that drinking two cups of the tea per day gave a mild stimulation, increased heart rate, and mood elevation, and the tea was essentially harmless. Despite this, the DEA seized several shipments in Hawaii , Chicago , Illinois , Georgia, and several locations on the East Coast of the United States , and the product was removed from the shelves .

4 – 3 – 2 : Insufflation :

Insufflation (known colloquially as " snorting ", " sniffing ", or " blowing ") is the most common method of ingestion of recreational powdered cocaine in the Western world. The drug coats and is absorbed through the mucous membranes lining the sinuses. When insufflating cocaine, absorption through the nasal membranes is approximately 30 – 60 % , with higher doses leading to increased absorption efficiency. Any material not directly absorbed through the mucous membranes is collected in mucus and swallowed (this " drip " is considered pleasant by some and unpleasant by others) . In a study of cocaine users, the average time taken to reach peak subjective effects was 14.6 minutes. Any damage to the inside of the nose is because cocaine highly constricts blood vessels – and therefore blood and oxygen/nutrient flow – to that area .

Prior to insufflation, cocaine powder must be divided into very fine particles. Cocaine of high purity breaks into fine dust very easily, except when it is moist (not well stored) and forms " chunks " , which reduces the efficiency of nasal absorption .

Rolled up banknotes, hollowed-out pens, cut straws, pointed ends of keys, specialized spoons, long fingernails, and (clean) tampon applicators are often used to insufflate cocaine. Such devices are often called "tooters" by users. The cocaine typically is poured onto a flat,

hard surface (such as a mirror , CD case or book) and divided into "bumps" , " lines " or "rails", and then insufflated . As tolerance builds rapidly in the short- term (hours) , many lines are often snorted to produce greater effects .

A study by Bonkovsky and Mehta reported that, just like shared needles, the sharing of straws used to " snort " cocaine can spread blood diseases such as Hepatitis C .

In the United States, as far back as 1992 many of the people sentenced by federal authorities for charges related to powder cocaine were Hispanic; more Hispanics than non - Hispanic White and non-Hispanic Black people received sentences for crimes related to powder cocaine .

4 – 3 – 3 : Injection :

Drug injection provides the highest blood levels of drug in the shortest amount of time. Subjective effects not commonly shared with other methods of administration include a ringing in the ears moments after injection (usually when in excess of 120 milligrams) lasting 2 to 5 minutes including tinnitus & audio distortion. This is colloquially referred to as a "bell ringer" . In a study of cocaine users, the average time taken to reach peak subjective effects was 3.1 minutes. The euphoria passes quickly. Aside from the toxic effects of cocaine, there is also danger of circulatory emboli from the insoluble substances that may be used to cut the drug. As with all injected illicit substances, there is a risk of the user contracting blood-borne infections if sterile injecting equipment is not available or used.

An injected mixture of cocaine and heroin, known as “speedball” is a particularly popular and dangerous combination, as the converse effects of the drugs actually complement each other, but may also mask the symptoms of an overdose. It has been responsible for numerous deaths, including celebrities such as John Belushi, Chris Farley , Mitch Hedberg , River Phoenix and Layne Staley .

Experimentally, cocaine injections can be delivered to animals such as fruit flies to study the mechanisms of cocaine addiction .

4 – 3 – 4 : Inhalation :

Inhalation or smoking is one of the several means cocaine is administered. Cocaine is smoked by inhaling the vapor by sublimating solid cocaine by heating . In a 2000 Brookhaven National Laboratory medical department study , based on self reports of 32 abusers who participated in the study," peak high " was found at mean of 1.4 min + / - 0.5 minutes .

Smoking freebase or crack cocaine is most often accomplished using a pipe made from a small glass tube, often taken from "Love roses," small glass tubes with a paper rose that are promoted as romantic gifts . These are sometimes called "stems", "horns", "blasters" and "straight shooters". A small piece of clean heavy copper or occasionally stainless steel scouring pad – often called a "brillo" (actual Brillo pads contain soap, and are not used), or "chore", named for *Chore Boy* brand copper scouring pads, – serves as a reduction base and flow modulator in which the "rock" can be melted and boiled to vapor. Crack smokers also sometimes smoke through a soda can with small holes in the bottom.

Crack is smoked by placing it at the end of the pipe; a flame held close to it produces vapor, which is then inhaled by the smoker. The effects, felt almost immediately after smoking, are very intense and do not last long – usually five to fifteen minutes.

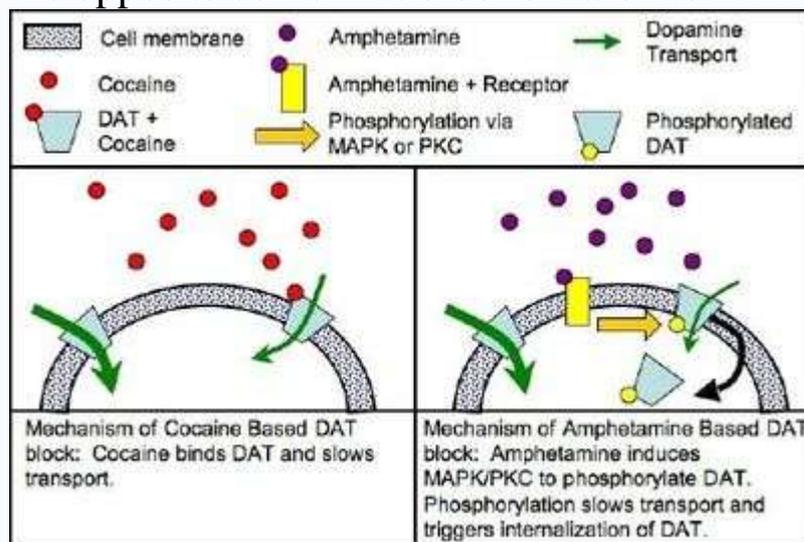
When smoked, cocaine is sometimes combined with other drugs, such as cannabis, often rolled into a joint or blunt. Powdered cocaine is also sometimes smoked, though heat destroys much of the chemical; smokers often sprinkle it on marijuana.

The language referring to paraphernalia and practices of smoking cocaine vary, as do the packaging methods in the street level sale.

4 – 4 : Physical mechanisms :

Cocaine binds directly to the DAT1 transporter, inhibiting reuptake with more efficacy than amphetamines which phosphorylate it causing internalization; instead primarily releasing DAT (which cocaine does not do) and only inhibiting its reuptake as a secondary,

and much more minor, mode of action than cocaine and in another manner: from the opposite conformation/orientation to DAT.



The pharmacodynamics of cocaine involve the complex relationships of neurotransmitters (inhibiting monoamine uptake in rats with ratios of about : serotonin : dopamine = 2 : 3 , serotonin : norepinephrine = 2 : 5) The most extensively studied effect of cocaine on the central nervous system is the blockade of the dopamine transporter protein. Dopamine transmitter released during neural signaling is normally recycled via the transporter; i.e., the transporter binds the transmitter and pumps it out of the synaptic cleft back into the presynaptic neuron, where it is taken up into storage vesicles. Cocaine binds tightly at the dopamine transporter forming a complex that blocks the transporter's function. The dopamine transporter can no longer perform its reuptake function, and thus dopamine accumulates in the synaptic cleft. This results in an enhanced and prolonged postsynaptic effect of dopaminergic signaling at dopamine receptors on the receiving neuron. Prolonged exposure to cocaine, as occurs with habitual use, leads to homeostatic dysregulation of normal (i.e. without cocaine) dopaminergic signaling via down - regulation of dopamine receptors and enhanced signal transduction. The decreased dopaminergic signaling after chronic cocaine use may contribute to depressive mood disorders and sensitize this important brain reward circuit to the reinforcing effects of cocaine (e.g. enhanced dopaminergic signalling only when cocaine is self – administered) . This sensitization contributes to the intractable nature of addiction and relapse .

Dopamine - rich brain regions such as the ventral tegmental area, nucleus accumbens, and prefrontal cortex are frequent targets of cocaine addiction research. Of particular interest is the pathway consisting of dopaminergic neurons originating in the ventral tegmental area that terminate in the nucleus accumbens. This projection may function as a "reward center", in that it seems to show activation in response to drugs of abuse like cocaine in addition to natural rewards like food or sex . While the precise role of dopamine in the subjective experience of reward is highly controversial among neuroscientists, the release of dopamine in the nucleus accumbens is widely considered to be at least partially responsible for cocaine's rewarding effects. This hypothesis is largely based on laboratory data involving rats that are trained to self - administer cocaine. If dopamine antagonists are infused directly into the nucleus accumbens, well-trained rats self - administering cocaine will undergo extinction (i.e. initially increase responding only to stop completely) thereby indicating that cocaine is no longer reinforcing (i.e. rewarding) the drug - seeking behavior .

Cocaine's effects on serotonin (5 – hydroxytryptamine , 5 – HT) show across multiple serotonin receptors, and is shown to inhibit the re-uptake of 5 - HT3 specifically as an important contributor to the effects of cocaine. The overabundance of 5 - HT3 receptors in cocaine conditioned rats display this trait, however the exact effect of 5 - HT3 in this process is unclear . The 5 - HT2 receptor (particularly the subtypes 5 - HT2AR , 5 - HT2BR and 5 - HT2CR) show influence in the evocation of hyperactivity displayed in cocaine use .

In addition to the mechanism shown on the above chart, cocaine has been demonstrated to bind as to directly stabilize the DAT transporter on the open outward-facing conformation whereas other stimulants (namely phenethyl amines) stabilize the closed conformation . Further, cocaine binds in such a way as to inhibit a hydrogen bond innate to DAT that otherwise still forms when amphetamine and similar molecules are bound. Cocaine's binding properties are such that it attaches so this hydrogen bond will not form and is blocked from formation due to the tightly locked orientation of the cocaine molecule. Research studies have suggested that the

affinity for the transporter is not what is involved in habituation of the substance so much as the conformation and binding properties to where & how on the transporter the molecule binds.^[54]

Sigma receptors are effected by cocaine , as cocaine functions as a sigma ligand agonist . Further specific receptors it has been demonstrated to function on are NMDA and the D1 dopamine receptor .

Cocaine also blocks sodium channels, thereby interfering with the propagation of action potentials; thus, like lignocaine and novocaine, it acts as a local anesthetic. Cocaine also causes vasoconstriction, thus reducing bleeding during minor surgical procedures. The locomotor enhancing properties of cocaine may be attributable to its enhancement of dopaminergic transmission from the substantia nigra. Recent research points to an important role of circadian mechanisms and clock genes in behavioral actions of cocaine .

Because nicotine increases the levels of dopamine in the brain, many cocaine users find that consumption of tobacco products during cocaine use enhances the euphoria. This, however, may have undesirable consequences, such as uncontrollable chain smoking during cocaine use (even users who do not normally smoke cigarettes have been known to chain smoke when using cocaine) , in addition to the detrimental health effects and the additional strain on the cardiovascular system caused by tobacco .

In addition to irritability , mood disturbances , restlessness, paranoia , and auditory hallucinations, cocaine use can cause several dangerous physical conditions. It can lead to disturbances in heart rhythm and heart attacks, as well as chest pains or even respiratory failure. In addition, strokes, seizures and headaches are common in heavy users.

Cocaine can often cause reduced food intake, many chronic users lose their appetite and can experience severe malnutrition and significant weight loss. Cocaine effects, further, are shown to be potentiated for the user when used in conjunction with new surroundings and stimuli, and otherwise novel environs .

4 – 5 : Metabolism and excretion :

Cocaine is extensively metabolized, primarily in the liver, with only about 1 % excreted unchanged in the urine. The metabolism is dominated by hydrolytic ester cleavage, so the eliminated metabolites consist mostly of benzoylecgonine (BE), the major metabolite, and other significant metabolites in lesser amounts such as ecgonine methyl ester (EME) and ecgonine. Further minor metabolites of cocaine include norcocaine, p – hydroxy cocaine , m – hydroxy cocaine , p – hydroxy benzoyl ecgonine (pOHBE) , and m - hydroxy benzoyl ecgonine . These do not include metabolites created beyond the standard metabolism of the drug in the human body, like for example by the process of pyrolysis such as is the case with methyl ecgonidine .

Depending on liver and kidney function, cocaine metabolites are detectable in urine. Benzoylecgonine can be detected in urine within four hours after cocaine intake and remains detectable in concentrations greater than 150 ng / ml typically for up to eight days after cocaine is used. Detection of accumulation of cocaine metabolites in hair is possible in regular users until the sections of hair grown during use are cut or fall out.

If consumed with alcohol, cocaine combines with alcohol in the liver to form cocaethylene. Studies have suggested cocaethylene is both more euphorogenic, and has a higher cardiovascular toxicity than cocaine by itself.

4 – 6 : Effects and health issues :

Health problems resulting from cocaine use can lead to severe mental, physical and social problems .

4 – 6 – 1 : Acute :

Cocaine is a potent central nervous system stimulant. Its effects can last from 20 minutes to several hours, depending upon the dosage of cocaine taken, purity, and method of administration .

The initial signs of stimulation are hyperactivity, restlessness, increased blood pressure, increased heart rate and euphoria. The euphoria is sometimes followed by feelings of discomfort and depression and a craving to experience the drug again. Sexual interest and pleasure can be amplified. Side effects can include twitching, paranoia, and impotence, which usually increases with frequent usage.

With excessive or prolonged use, the drug can cause itching, tachycardia, hallucinations, and paranoid delusions. Overdoses cause tachyarrhythmias and a marked elevation of blood pressure. These can be life-threatening, especially if the user has existing cardiac problems. The LD₅₀ of cocaine when administered intraperitoneally to mice is 95.1 mg/kg . Toxicity results in seizures , followed by respiratory and circulatory depression of medullar origin. This may lead to death from respiratory failure, stroke, cerebral hemorrhage, or heart - failure. Cocaine is also highly pyrogenic, because the stimulation and increased muscular activity cause greater heat production. Heat loss is inhibited by the intense vasoconstriction . Cocaine - induced hyperthermia may cause muscle cell destruction and myoglobinuria resulting in renal failure. Emergency treatment often consists of administering a benzodiazepine sedation agent, such as diazepam (Valium) to decrease the elevated heart rate and blood pressure. Physical cooling (ice, cold blankets, etc...) and paracetamol (acetaminophen) may be used to treat hyperthermia, while specific treatments are then developed for any further complications.^[67] There is no officially approved specific antidote for cocaine overdose, and although some drugs such as dexmedetomidine and rimcazole have been found to be useful for treating cocaine overdose in animal studies, no formal human trials have been carried out .

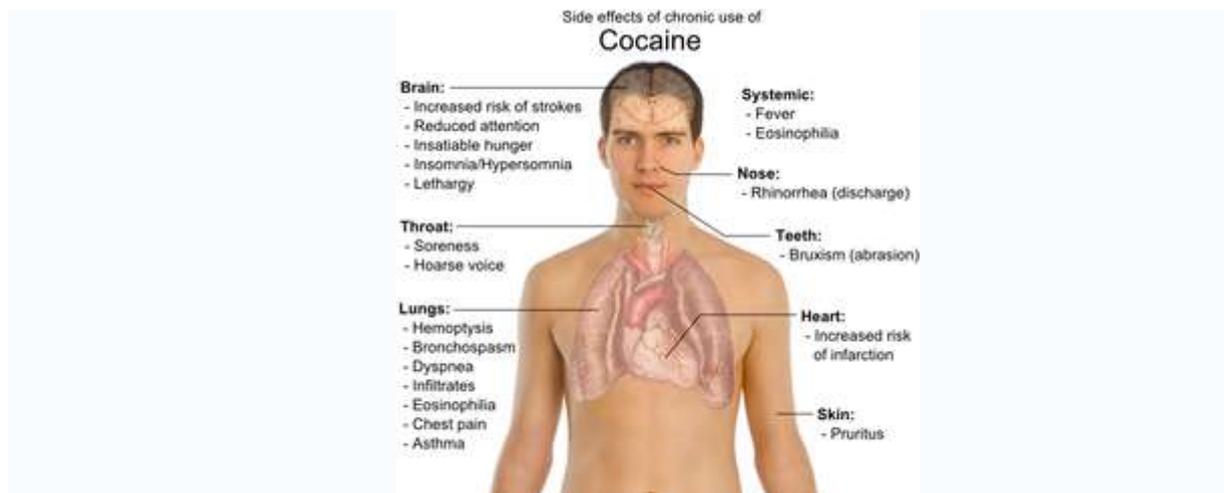
In cases where a patient is unable or unwilling to seek medical attention, cocaine overdoses resulting in mild - moderate tachycardia (i.e.: a resting pulse greater than 120 bpm) , may be initially treated with 20 mg of orally administered diazepam or equivalent benzodiazepine (eg: 2 mg lorazepam) . Acetaminophen and physical cooling may likewise be used to reduce mild hyperthermia (< 39 C) . However, a history of high blood pressure or cardiac problems puts the patient at high risk of cardiac arrest or stroke , and requires

immediate medical treatment. Similarly, if benzodiazepine sedation fails to reduce heart rate or body temperatures fails to lower, professional intervention is necessary .

Cocaine's primary acute effect on brain chemistry is to raise the amount of dopamine and serotonin in the nucleus accumbens (the pleasure center in the brain) ; this effect ceases, due to metabolism of cocaine to inactive compounds and particularly due to the depletion of the transmitter resources (tachyphylaxis). This can be experienced acutely as feelings of depression, as a "crash" after the initial high. Further mechanisms occur in chronic cocaine use. The "crash" is accompanied with muscle spasms throughout the body, also known as the "jitters", muscle weakness, headaches, dizziness, and suicidal thoughts. Not all users will experience these, but most tend to experience some or all of these symptoms .

Studies have shown that cocaine usage during pregnancy triggers premature labor^[71] and may lead to abruptio placentae.^[72]

5 – 6 – 2 : Chronic :



Main effects of chronic cocaine use.

Chronic cocaine intake causes brain cells to adapt functionally to strong imbalances of transmitter levels in order to compensate extremes. Thus, receptors disappear from the cell surface or reappear on it, resulting more or less in an "off" or "working mode" respectively, or they change their susceptibility for binding partners

(ligands) – mechanisms called down-/upregulation. However, studies suggest cocaine abusers do not show normal age - related loss of striatal DAT sites, suggesting cocaine has neuroprotective properties for dopamine neurons . The experience of insatiable hunger, aches, insomnia/oversleeping, lethargy, and persistent runny nose are often described as very unpleasant. Depression with suicidal ideation may develop in very heavy users. Finally, a loss of vesicular monoamine transporters, neurofilament proteins, and other morphological changes appear to indicate a long term damage of dopamine neurons. All these effects contribute a rise in tolerance thus requiring a larger dosage to achieve the same effect .

The lack of normal amounts of serotonin and dopamine in the brain is the cause of the dysphoria and depression felt after the initial high. Physical withdrawal is not dangerous, and is in fact restorative. The diagnostic criteria for cocaine withdrawal are characterized by a dysphoric mood , fatigue , unpleasant dreams, insomnia or hypersomnia , erectile dysfunction , increased appetite , psychomotor retardation or agitation, and anxiety .

Physical side effects from chronic smoking of cocaine include hemoptysis, bronchospasm, pruritus, fever, diffuse alveolar infiltrates without effusions, pulmonary and systemic eosinophilia, chest pain, lung trauma, sore throat, asthma, hoarse voice , dyspnea (shortness of breath) , and an aching, flu - like syndrome. A common but untrue belief is that the smoking of cocaine chemically breaks down tooth enamel and causes tooth decay . However, cocaine does often cause involuntary tooth grinding, known as bruxism, which can deteriorate

tooth enamel and lead to gingivitis . Chronic intranasal usage can degrade the cartilage separating the nostrils (the septum nasi), leading eventually to its complete disappearance. Due to the absorption of the cocaine from cocaine hydrochloride, the remaining hydrochloride forms a dilute hydrochloric acid .

Cocaine may also greatly increase this risk of developing rare autoimmune or connective tissue diseases such as lupus , Goodpasture's disease , vasculitis , glomerulonephritis , Stevens-

Johnson syndrome and other diseases . It can also cause a wide array of kidney diseases and renal failure .

Cocaine abuse doubles both the risks of hemorrhagic and ischemic strokes^[82], as well as increases the risk of other infarctions, such as myocardial infarction .

4 – 6 - 3 : Addiction :

Cocaine dependence (or **addiction**) is physical and psychological dependency on the regular use of cocaine. It can result in physiological damage , lethargy , psychosis , depression , or a potentially fatal overdose .

4 – 7 : Cocaine as a local anesthetic

Cocaine was historically useful as a topical anesthetic in eye and nasal surgery, although it is now predominantly used for nasal and lacrimal duct surgery. The major disadvantages of this use are cocaine's intense vasoconstrictor activity and potential for cardiovascular toxicity. Cocaine has since been largely replaced in Western medicine by synthetic local anaesthetics such as benzocaine, proparacaine, lignocaine/xylocaine/lidocaine, and tetracaine though it remains available for use if specified. If vasoconstriction is desired for a procedure (as it reduces bleeding), the anesthetic is combined with a vasoconstrictor such as phenylephrine or epinephrine. In Australia it is currently prescribed for use as a local anesthetic for conditions such as mouth and lung ulcers. Some ENT specialists occasionally use cocaine within the practice when performing procedures such as nasal cauterization. In this scenario dissolved cocaine is soaked into a ball of cotton wool, which is placed in the nostril for the 10 –15 minutes immediately prior to the procedure, thus performing the dual role of both numbing the area to be cauterized and also vasoconstriction. Even when used this way, some of the used cocaine may be absorbed through oral or nasal mucosa and give systemic effects.

In 2005, researchers from Kyoto University Hospital proposed the use of cocaine in conjunction with phenylephrine administered in the form of an eye drop as a diagnostic test for Parkinson's disease .

5 – Etymology:

The word "cocaine" was made from "coca" + the suffix "-ine"; from its use as a local anaesthetic a suffix "-caine" was extracted and used to form names of synthetic local anaesthetics .

6 - Current prohibition:

The production, distribution and sale of cocaine products is restricted (and illegal in most contexts) in most countries as regulated by the Single Convention on Narcotic Drugs, and the United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. In the United States the manufacture, importation, possession, and distribution of cocaine is additionally regulated by the 1970 Controlled Substances Act .

Some countries, such as Peru and Bolivia permit the cultivation of coca leaf for traditional consumption by the local indigenous population, but nevertheless prohibit the production, sale and consumption of cocaine .

Some parts of Europe and Australia allow processed cocaine for medicinal uses only .

6 – 1 : Interdiction :

In 2004 , according to the United Nations, 589 metric tons of cocaine were seized globally by law enforcement authorities. Colombia seized 188 tons , the United States 166 tons , Europe 79 tons, Peru 14 tons, Bolivia 9 tons, and the rest of the world 133 tons .

7 - Illicit trade ;

Because of the extensive processing it undergoes during preparation, cocaine is generally treated as a 'hard drug', with severe penalties for possession and trafficking. Demand remains high, and consequently black market cocaine is quite expensive. Unprocessed cocaine, such as coca leaves, are occasionally purchased and sold, but this is exceedingly rare as it is much easier

and more profitable to conceal and smuggle it in powdered form. The scale of the market is immense : 770 tonnes times \$100 per gram retail = up to \$ 77 billion .



Bricks of cocaine, a form in which it is commonly transported.

7 – 1 : Production :

Colombia is the world's leading producer of cocaine.^[86] Due to Colombia's 1994 legalization of small amounts of cocaine for personal use, while sale of cocaine was still prohibited, the result was the spread of local coca crops, partly justified by the local demand.

Three-quarters of the world's annual yield of cocaine has been produced in Colombia, both from cocaine base imported from Peru (primarily the Huallaga Valley) and Bolivia, and from locally grown coca. There was a 28 % increase from the amount of potentially harvestable coca plants which were grown in Colombia in 1998 . This, combined with crop reductions in Bolivia and Peru, made Colombia the nation with the largest area of coca under cultivation after the mid-1990s. Coca grown for traditional purposes by indigenous communities, a use which is still present and is permitted by Colombian laws, only makes up a small fragment of total coca production, most of which is used for the illegal drug trade.

Attempts to eradicate coca fields through the use of defoliants have devastated part of the farming economy in some coca growing regions of Colombia , and strains appear to have been developed that

are more resistant or immune to their use. Whether these strains are natural mutations or the product of human tampering is unclear. These strains have also shown to be more potent than those previously grown, increasing profits for the drug cartels responsible for the exporting of cocaine. Although production fell temporarily, coca crops rebounded as numerous smaller fields in Colombia, rather than the larger plantations.

The cultivation of coca has become an attractive, and in some cases even necessary, economic decision on the part of many growers due to the combination of several factors, including the persistence of worldwide demand, the lack of other employment alternatives, the lower profitability of alternative crops in official crop substitution programs, the eradication - related damages to non-drug farms, and the spread of new strains of the coca plant.

Estimated Andean region coca cultivation and potential pure cocaine production , 2000 – 2004 .					
	2000	2001	2002	2003	2004
Net cultivation (km ²)	1875	2218	2007.5	1663	1662
Potential pure cocaine production (tonnes)	770	925	830	680	645

7 - 2 : Synthesis :

Synthetic cocaine would be highly desirable to the illegal drug industry, as it would eliminate the high visibility and low reliability of offshore sources and international smuggling, replacing them with clandestine domestic laboratories, as are common for illicit methamphetamine. However, natural cocaine remains the lowest cost and highest quality supply of cocaine.

Actual full synthesis of cocaine is rarely done. Formation of inactive enantiomers (cocaine has 4 chiral centres - 1R,2R,3S,5S - hence a total potential of 16 possible enantiomers and diastereoisomers) plus synthetic by - products limits the yield and purity .

7 – 3 : Trafficking and distribution :

Organized criminal gangs operating on a large scale dominate the cocaine trade. Most cocaine is grown and processed in South America, particularly in Colombia, Bolivia, Peru, and smuggled into the United States and Europe, the United States being the world's largest consumer of Cocaine, where it is sold at huge markups; usually in the US at \$ 50 – \$ 75 for 1 gram (or a " fitty rock "), and \$ 125 – 200 for 3.5 grams (1/8 th of an ounce , or an " eight ball ") .

Cocaine shipments from South America transported through Mexico or Central America are generally moved over land or by air to staging sites in northern Mexico. The cocaine is then broken down into smaller loads for smuggling across the U.S.– Mexico border . The primary cocaine importation points in the United States are in Arizona, southern California, southern Florida, and Texas. Typically, land vehicles are driven across the U.S.- Mexico border. Sixty five percent of cocaine enters the United States through Mexico, and the vast majority of the rest enters through Florida .

Another route of cocaine traffic goes through Chile, this route is primarily used for cocaine produced in Bolivia since the nearest seaports lie in northern Chile. The arid Bolivia-Chile border is easily crossed by 4 x 4 vehicles that then heads to the seaports of Iquique and Antofagasta. While the price of cocaine is higher in Chile than in Peru and Bolivia the final destination is usually Europe , specially Spain where drug dealing networks exist among South American immigrants.

Cocaine is also carried in small , concealed, kilogram quantities across the border by couriers known as “ mules ” (or “mulas”) , who cross a border either legally, e.g. through a port or airport, or illegally elsewhere. The drugs may be strapped to the waist or legs or hidden in bags, or hidden in the body. If the mule gets through without being caught, the gangs will reap most of the profits. If he or she is caught however, gangs will sever all links and the mule will usually stand trial for trafficking alone .

Cocaine traffickers from Colombia, and recently Mexico, have also established a labyrinth of smuggling routes throughout the Caribbean, the Bahama Island chain, and South Florida. They often hire traffickers from Mexico or the Dominican Republic to transport the drug. The traffickers use a variety of smuggling techniques to transfer their drug to U.S. markets. These include airdrops of 500–700 kg in the Bahama Islands or off the coast of Puerto Rico, mid-ocean boat - to - boat transfers of 500 – 2,000 kg , and the commercial shipment of tonnes of cocaine through the port of Miami.

Bulk cargo ships are also used to smuggle cocaine to staging sites in the western Caribbean–Gulf of Mexico area. These vessels are typically 150 – 250 - foot (50 – 80 m) coastal freighters that carry an average cocaine load of approximately 2.5 tonnes. Commercial fishing vessels are also used for smuggling operations. In areas with a high volume of recreational traffic , smugglers use the same types of vessels, such as go - fast boats , as those used by the local populations.

Sophisticated drug subs are the latest tool drug runners are using to bring cocaine north from Colombia, it was reported on March 20, 2008. Although the vessels were once viewed as a quirky sideshow in the drug war, they are becoming faster, more seaworthy, and capable of carrying bigger loads of drugs than earlier models, according to those charged with catching them .

7 – 4 : Sales to consumers :

Cocaine is readily available in all major countries' metropolitan areas. According to the *Summer 1998 Pulse Check*, published by the U.S. Office of National Drug Control Policy, cocaine use had stabilized across the country, with a few increases reported in San Diego, Bridgeport, Miami, and Boston. In the West, cocaine usage was lower, which was thought to be due to a switch to methamphetamine among some users; methamphetamine is cheaper and provides a longer - lasting high. Numbers of cocaine users are still very large, with a concentration among urban youth.

In addition to the amounts previously mentioned, cocaine can be sold in " bill sizes" : for example, \$ 10 might purchase a "dime bag," a

very small amount (0.1 – 0.15 g) of cocaine . Twenty dollars might purchase . 15 – .3 g. However, in lower Texas , it's sold cheaper due to it being easier to receive: a dime for \$ 10 is .4 g , a 20 is . 8 - 1.0 gram and a 8 - ball (3.5g) is sold for \$ 60 to \$80 dollars , depending on the quality and dealer. These amounts and prices are very popular among young people because they are inexpensive and easily concealed on one's body. Quality and price can vary dramatically depending on supply and demand, and on geographic region.^[91]

However, UK prices are astronomical compared to those in the USA, with £ 40 (typically \$ 80) getting 1 gram of cocaine (compared to \$ 20 – \$ 40 in the USA) .

The European Monitoring Centre for Drugs and Drug Addiction reports that the typical retail price of cocaine varied between 50€ and 75€ per gram in most European countries , although Cyprus , Romania , Sweden and Turkey reported much higher values .



Bags of cocaine, adulterated with fruit flavoring.

7 – 5 : Consumption :

World annual cocaine consumption currently stands at around 600 metric tons, with the United States consuming around 300 metric tons, 50% of the total, Europe about 150 metric tons, 25 % of the total, and the rest of the world the remaining 150 metric tons or 25% .

8 - Cocaine adulterants :

Cocaine is " cut " with many substances such as :

Anesthetics :

- Lidocaine
- Benzocaine
- Procaine

Other stimulants :

- Caffeine
- Ephedrine
- Methamphetamine

Inert powder :

- Baking soda
- Inositol

9 – Usage :

According to a 2007 United Nations report , Spain is the country with the highest rate of cocaine usage (3.0 % of adults in the previous year) . Other countries where the usage rate meets or exceeds 1.5 % are the United States (2.8 %) , England and Wales (2.4 %) , Canada (2.3 %) , Italy (2.1 %) , Bolivia (1.9 %) , Chile (1.8 %) , and Scotland (1.5 %) .

9 – 1 : In the United States

9 – 1 – 1 : General usage :

Cocaine is the second most popular illegal recreational drug in the U.S. (behind marijuana) and the U.S. is the world's largest consumer of cocaine . Cocaine is commonly used in middle to upper class communities. It is also popular amongst college students, to aid in studying and as a party drug. Its users span over different ages, races, and professions. In the 1970s and 80's , the drug became particularly popular in the disco culture as cocaine usage was very common and popular in many discos such as Studio 54 .

The National Household Survey on Drug Abuse (NHSDA) reported in 1999 that cocaine was used by 3.7 million Americans, or 1.7 % of the household population age 12 and older . Estimates of the

current number of those who use cocaine regularly (at least once per month) vary , but 1.5 million is a widely accepted figure within the research community.

Although cocaine use had not significantly changed over the six years prior to 1999, the number of first-time users went up from 574,000 in 1991, to 934,000 in 1998 – an increase of 63 %. While these numbers indicated that cocaine is still widely present in the United States, cocaine use was significantly less prevalent than it was during the early 1980s .

9 – 1 – 2 : Usage among youth :

The 1999 Monitoring the Future (MTF) survey found the proportion of American students reporting use of powdered cocaine rose during the 1990s. In 1991, 2.3 % of eighth - graders stated that they had used cocaine in their lifetime. This figure rose to 4.7% in 1999. For the older grades, increases began in 1992 and continued through the beginning of 1999. Between those years, lifetime use of cocaine went from 3.3 % to 7.7 % for tenth-graders and from 6.1% to 9.8% for high school seniors. Lifetime use of crack cocaine, according to MTF, also increased among eighth - , tenth - , and twelfth - graders, from an average of 2 % in 1991 to 3.9 % in 1999.

Perceived risk and disapproval of cocaine and crack use both decreased during the 1990s at all three grade levels . The 1999 NHSDA found the highest rate of monthly cocaine use was for those aged 18 – 25 at 1.7 %, an increase from 1.2 % in 1997 . Rates declined between 1996 and 1998 for ages 26 – 34, while rates slightly increased for the 12–17 and 35 + age groups. Studies also show people are experimenting with cocaine at younger ages. NHSDA found a steady decline in the mean age of first use from 23.6 years in 1992 to 20.6 years in 1998 .

9 – 2 : In Europe :

9m- 2 – 1 : General usage :

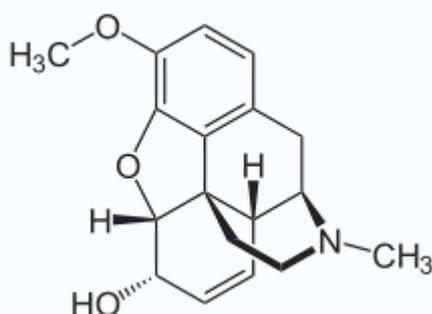
Cocaine is the second most popular illegal recreational drug in Europe (behind marijuana). Since the mid - 1990s , overall cocaine usage in Europe has been on the rise, but usage rates and attitudes tend to vary between countries. Countries with the highest usage rates are: The United Kingdom , Spain , Italy , and Ireland .

Approximately 12 million Europeans (3.6 %) have used cocaine at least once, 4 million (1.2 %) in the last year, and 2 million in the last month (0.5 %) .

9 – 2 – 2 : Usage among young adults :

About 3.5 million or 87.5 % of those who have used the drug in the last year are young adults (15 –34 years old). Usage is particularly prevalent among this demographic : 4 % to 7 % of males have used cocaine in the last year in Spain, Denmark, Ireland, Italy, and the United Kingdom . The ratio of male to female users is approximately 3.8 : 1 , but this statistic varies from 1 : 1 to 13 : 1 depending on country .

Codeine



Contents :

- 1 Introduction
- 2 History
- 3 Pharmacology
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- 6 Narcotic Content Numbers (US & Canada)
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- 8 Relation to other opiates
- 9 Adverse effects
 - 9.1 Withdrawal effects
- 10 Recreational use
- 11 Controlled substance

1 – Introduction :

Codeine (INN) or **methyl morphine** is an opiate used for its analgesic , anti tussive , and anti diarrheal properties .

Systematic (IUPAC) name	
(5 α , 6 α) – 7 , 8 – didehydro – 4 , 5 – epoxy - 3 – methoxy – 17 – methyl morphinan – 6 - ol	
Formula	C ₁₈ H ₂₁ N O ₃
Mol. mass	299 g / mol
Pharmacokinetic data	

Bioavailability	~ 90 % Oral
Metabolism	Hepatic , via CYP2D6 (Cytochrome P450 2D6)
Half life	2.5 – 3 hours
Routes	Oral , intra – rectally , SC , IM

2 - History

Codeine is an alkaloid found in opium and other poppy saps like *Papaver bracteatum*, the Iranian poppy, in concentrations ranging from 0.3 to 3.0 percent. While codeine can be extracted from opium, most codeine is synthesized from morphine through the process of O - methylation. It was first isolated in 1832 in France by Jean - Pierre Robiquet.

The effects of the Nixon War On Drugs by 1972 or so had caused across-the - board shortages of illicit and licit opiates because of a scarcity of natural opium, poppy straw and other sources of opium alkaloids, and the geopolitical situation was getting less helpful for the United States. After a large percentage of the opium and morphine in the US National Stockpile of Strategic & Critical Materials had to be tapped in order to ease severe shortages of medicinal opiates — the codeine - based anti tussives in particular — in late 1973 , researchers were tasked with and quickly succeeded in finding a way to synthesize codeine and its derivatives and precursors from scratch from petroleum or coal tar using a process developed at the United States' National Institutes of Health.

Numerous codeine salts have been prepared since the drug was discovered. The most commonly used are the hydrochloride (freebase conversion ratio 0.805), phosphate (0.736), sulphate (0.859) and citrate (0.842). Others include a salicylate NSAID, codeine salicylate (0.686), and at least four codeine - based barbiturates , the cyclo hexenyl ethyl barbiturate (0.559) , cyclo pentenyl allyl barbiturate (0.561), diallyl barbiturate (0.561), and diethyl barbiturate (0.619).

3 - Pharmacology

Codeine is considered a prodrug, since it is metabolised *in vivo* to the primary active compounds morphine and codeine-6-glucuronide (C6G). Roughly 5 - 10 % of codeine will be converted to morphine, with the remainder either free, conjugated to form codeine-6-glucuronide (~ 70 %), or converted to norcodeine (~10%) and hydro morphine (~1 %). It is less potent than morphine and has a correspondingly lower dependence-liability than morphine. Like all opioids, continued use of codeine induces physical dependence and can be psychologically addictive. However, the withdrawal symptoms are relatively mild and as a consequence codeine is considerably less addictive than the other opiates.

A dose of approximately 200 mg (oral) of codeine must be administered to give analgesia approximately equivalent to 30 mg (oral) of morphine (Rossi, 2004). However, codeine is generally not used in single doses of greater than 60 mg (and no more than 240 mg in 24 hours). When analgesia beyond this is required, stronger opioids such as hydrocodone or oxycodone are favored.

Codeine is metabolized to C6G by uridine diphosphate glucuronosyl transferase (UGT) 2B7 and since only about 5 % of codeine is metabolized by cytochrome P450 CYP2D6, the current evidence is that C6G is the primary active compound. Claims about the supposed "ceiling effect" of codeine doses seemed to rest on the assumption that high doses of codeine saturated CYP2D6 which prevented further conversion of codeine to morphine, which is simply incorrect. There is also no evidence that CYP2D6 inhibition is useful in treating codeine dependence, though the metabolism of codeine to morphine (and hence further metabolism to glucuronide morphine conjugates) does have an effect on the abuse potential of codeine.

4 – Pharmacokinetics

The conversion of codeine to morphine occurs in the liver and is catalysed by the cytochrome P450 enzyme CYP2D6. CYP3A4 produces norcodeine and UGT2B7 conjugates codeine, norcodeine and morphine to the corresponding 3- and 6- glucuronides.

Approximately 6 – 10 % of the Caucasian population, 2 % of Asians, and 1 % of Arabs are " poor meta bolizers " ; they have little CYP2D6 and codeine is less effective for analgesia in these patients (Rossi , 2004) , although it is speculated that codeine - 6 - glucuronide is responsible for a large percentage of the analgesia of codeine and thus these patients should experience some analgesia . Many of the adverse effects will still be experienced in poor meta bolizers . Conversely , 0.5 – 2 % of the population are " extensive meta bolizers " ; multiple copies of the gene for 2D6 produce high levels of CYP2D6 and will metabolize drugs through that pathway more quickly than others.

Some medications are CYP2D6 inhibitors and reduce or even completely block the conversion of codeine to morphine. The most well - known of these are two of the selective serotonin reuptake inhibitors, paroxetine (Paxil) and fluoxetine (Prozac) as well as the anti histamine diphenhydramine and the antidepressant , bupropion (Wellbutrin, also known as Zyban). Other drugs, such as rifampicin and dexamethasone , induce CYP450 isozymes and thus increase the conversion rate.

While a CYP2D6 extensive meta boliser (EM) needs higher doses of drugs metabolized by CYP2D6 to maintain sufficient plasma levels for therapeutic effect and a poor meta boliser (PM) may suffer from drug toxicity due to slow drug clearance and excessive plasma concentration, prodrugs like codeine have the opposite effect. Thus an EM may have adverse effects from a rapid buildup of codeine metabolites while a PM may get little or no pain relief . The active metabolites of codeine , notably morphine, exert their effects by binding to and activating the μ - opioid receptor.

5 - Indications

Approved indications for codeine include :

- Cough , though its efficacy in low dose over the counter formulations has been disputed .
- Diarrhea
- Mild to severe pain
- Irritable bowel syndrome

Codeine is marketed as both a single - ingredient drug and in combination preparations with the analgesic acetaminophen (paracetamol), as co - codamol , paracod , panadeine , or the Tylenol With Codeine series (e.g. Tylenol 3 and 4 tablets and elixir) ; with the analgesic acetylsalicylic acid (aspirin), as co-codaprin; or with the NSAID (non-steroidal anti- inflammatory drug) ibuprofen, as Nurofen Plus. These combinations provide greater pain relief than either agent alone (drug synergy). Codeine is also commonly marketed in products containing codeine with other pain killers or muscle relaxers such as Fioricet with Codeine, Soma Compound / Codeine, as well as codeine mixed with phenacetin (Emprazol With Codeine No. 1, 2, 3, and 4) , naproxen , indomethacin , diclofenac and others as well as more complex mixtures including such mixtures as aspirin + paracetamol + codeine ± caffeine ± antihistamines and other agents such as mentioned above .

Codeine - only products can be obtained with a prescription as a time release tablet (e.g. Codeine Contin 100 mg and Perduretas 50 mg) . Codeine is also marketed in cough syrups with zero to a half - dozen other active ingredients, and a linctus (e.g. Paveral®) for all of the uses for which codeine is indicated.

Injectable codeine is available for subcutaneous or intramuscular injection; intravenous injection can cause a serious reaction which can progress to anaphylaxis. Codeine suppositories are also marketed in some countries.

6 - Narcotic Content Numbers (US & Canada) :

The narcotic content number in the US names of codeine tablets and combination products like Tylenol With Codeine No. 3, Emprin With Codeine No. 4, and pure codeine tablets are as follows: No. 1 - 7½ or 8 mg (1/8 grain), No. 2 - 15 or 16 mg (1/4 grain), No. 3 - 30 or 32 mg (1/2 grain), No. 4 - 60 or 64 mg (1 grain). The Canadian 222 series is identical to the above list 222=1/8 grain, 292=1/4 grain, 293=1/2 grain, and 294=1 grain of codeine. This system, which is also used at present in the trade names of some dihydro codeine and ethyl morphine products both in and outside of North America, was inaugurated with the Pure Food and Drug Act of 1906 and related

legislation and refined since. Equivalent scales for labeling stronger opioids such as diacetylmorphine (heroin), morphine, opium salts mixtures, and others were in common use in the past, and on occasion one can find past references to brand names for hydro codone (invented 1920, introduced in US 1943), hydro morphone (invented 1926), oxy codone (invented 1916), paregoric and similar drugs containing narcotic content numbers

Contrary to the advertising matter of some pharmacies, 60 mg is No. 4, not No. 6, and tablets with 45 mg of codeine are not No. 4 and would in all likelihood be classified as No. 3½ under that system. Whether the scale goes to No. 5 and higher is moot at this point as in the United States and Canada single-dose-unit concentrations of more than 64 mg are not manufactured. The Controlled Substances Act of 1970 does place dosage unit strengths of 90 mg of codeine and higher in Schedule II, even if mixed with another active ingredient, and oral tablets, hypodermic tablets, liquid forms, and capsules of less common doses such as 5, 10, 12, 20, 25, 40, 45, 50, 75, 80, 90, 96, 100, 105, 120 and 128 mg and others and in some cases the equivalent dihydro codeine, dionine, benzyl morphine, and opium dosages were available in North America (and in most cases still are in other countries, the 45 mg para cetamol/codeine and 50 and 100 mg single-ingredient codeine tablets)

7 - Availability :

Codeine phosphate and sulfate are marketed in the United States and Canada. Codeine hydrochloride is more commonly marketed in continental Europe and other regions, and codeine hydroiodide and codeine citrate round out the top five most-used codeine salts worldwide. Codeine is usually present in raw opium as free alkaloid in addition to codeine meconate, codeine pectinate, and possibly other naturally-occurring codeine salts. Codeine bitartrate , tartrate , nitrate , picrate , acetate , hydro bromide and others are occasionally encountered on the pharmaceutical market and in research.

In certain jurisdictions , codeine is available over - the - counter in combination with guaifenesin or promethazine to be sold at the pharmacist's discretion, though many pharmacists decline to do so

8 - Relation to other opiates :

Codeine is the starting material and prototype of a large class of mainly mild to moderately strong opioids such as hydrocodone, dihydrocodeine and its derivatives such as nicocodeine. Other series of codeine derivatives include isocodeine and its derivatives, which were developed in Germany starting around 1920. As an analgesic, codeine compares moderately to other opiates. Related to codeine in other ways are Codeine - N - Oxide (Geno codeine), related to the nitrogen morphine derivatives as is codeine methobromide, and heterocodeine which is a drug six times stronger than morphine and 72 times stronger than codeine due to a small re-arrangement of the molecule, viz. moving the methyl group from the 3 to the 6 position on the morphine carbon skeleton. Drugs bearing resemblance to codeine in effects due to close structural relationship are variations on the methyl groups at the 3 position including ethyl morphine a.k.a. codethyline (Dionine) and benzyl morphine (Peronine). While having no narcotic effects of its own, the important opioid precursor thebaine differs from codeine only slightly in structure. Pseudo codeine and some other similar alkaloids not currently used in medicine are found in trace amounts in opium as well.

9 - Adverse effects :

Common effects other than analgesia associated with the use of codeine include euphoria, itching, nausea, vomiting, drowsiness, dry mouth, miosis, orthostatic hypotension, urinary retention, depression and constipation.^[11] Another side effect commonly noticed is the lack of sexual drive and increased complications in erectile dysfunction. Some people may also have an allergic reaction to codeine, such as the swelling of skin and rashes.

Tolerance to many of the effects of codeine develops with prolonged use, including therapeutic effects. The rate at which this occurs develops at different rates for different effects, with tolerance to the constipation-inducing effects developing particularly slowly for instance.

A potentially serious adverse drug reaction, as with other opioids, is respiratory depression. This depression is dose - related and is the mechanism for the potentially fatal consequences of overdose. As codeine is metabolized to morphine, morphine can be passed through breast milk in potentially lethal amounts, fatally depressing the respiration of a breastfed baby .

9 – 1 : With drawal effects :

As with other opiate - based pain killers, chronic use of codeine can cause physical dependence. When physical dependence has developed, withdrawal symptoms may occur if a person suddenly stops the medication. Withdrawal symptoms include: drug craving, runny nose, yawning, sweating, insomnia, weakness, stomach cramps, nausea, vomiting, diarrhea, muscle spasms, chills, irritability and pain. To minimize withdrawal symptoms, long-term users should gradually reduce their codeine medication under the supervision of a healthcare professional . A support group called CodeineFree exists to help people who have found themselves dependent on codeine.

10 - Recreational use :

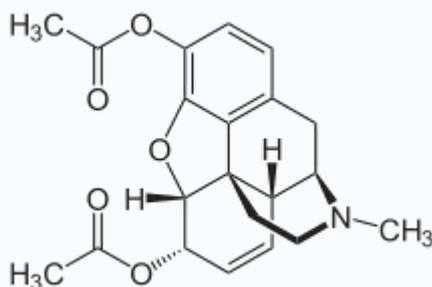
Codeine can be used as a recreational drug. However, it has much less abuse potential than some other opiates or opioids, such as oxy codone and hydro codone .

In some countries, cough syrups and tablets containing codeine are available without prescription ; some potential recreational users are reported to buy codeine from multiple pharmacies so as not to arouse suspicion . A heroin addict may use codeine to ward off the effects of a withdrawal .

Codeine is also available in conjunction with the anti-nausea medication promethazine in the form of a syrup. Brand named as Phenergan with Codeine or generically as promethazine with codeine this medication is quickly becoming one of the most highly abused codeine preparations .

Codeine is also demethylated by reaction with pyridine to illicitly synthesize morphine. Pyridine is toxic and possibly carcinogenic, so morphine illicitly produced in this manner (and potentially contaminated with pyridine) may be particularly harmful. Codeine can also be turned into α - chlorodide which is used in the clandestine synthesis of desomorphine (Permonid) . Codeine can also be turned directly into stronger derivatives of the dihydro codeine and hydrocodone families and a few others with various chemicals and equipment .

Heroin



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1 – Introduction :

Heroin, or **diacetylmorphine** (INN) , also known as **diamorphine** (BAN) , is a semi - synthetic opioid drug synthesized from morphine, a derivative of the opium poppy. It is the 3,6-diacetyl ester of morphine (*di* (two)-*acetyl-morphine*). The white crystalline form is commonly the hydrochloride salt **diacetylmorphine hydrochloride**, however heroin freebase is typically a white powder .

As with other opioids, heroin is used as both a pain-killer and a recreational drug and has an extremely high potential for abuse. Frequent and regular administration is associated with tolerance, moderate physical dependence, and severe psychological dependence which develops into addiction.

Internationally, heroin is controlled under Schedules I and IV of the Single Convention on Narcotic Drugs. It is illegal to manufacture, possess, or sell diacetylmorphine without a licence in Belgium, Denmark, Germany, Iran, India, the Netherlands, the United States, Australia, Canada, Ireland, Pakistan, the United Kingdom and Swaziland.

Under the name diamorphine, it is a legally prescribed controlled drug in the United Kingdom. It is available for prescription to long-term addicts in the Netherlands, the United Kingdom, Switzerland, Germany and Denmark.

Systematic (IUPAC) name	
(5 α ,6 α)-7,8-didehydro- 4,5-epoxy- 17-methylmorphinan-3,6-diol diacetate	
Formula	C₂₁ H₂₃ N O₅
Mol. mass	369 g / mol
Synonyms	Di amorphine , Diacetyl morphine , Aceto morphine , (Dual) Acetylated morphine , Morphine di acetate
Pharmacokinetic data	
Bioavailability	< 35 % (oral) , 44 – 61 % (inhaled)
Protein binding	0 % (morphine metabolite 35 %)
Metabolism	hepatic
Half life	3 – 5 min (IV, inhaled)

Excretion	90 % renal as glucuronides , rest biliary
Routes	Inhalation , Trans mucosal , Intra enous , Oral , Intra nasal , Rectal , Intramuscular

2 – Etymology :

Bayer named its new over the counter drug "Heroin" in 1898.^[5] Because Bayer is a German company, the name was most likely derived from the common German word "*heroisch*" (heroic), related to the Greek ἥρως, "*hero*." The name originated from to its perceived effects on a user.^[5] It was also developed as a morphine substitute that did not have its addictive side - effects . Contrary to Bayer's advertising as a non - addictive morphine substitute, its new drug, Heroin would cause an addiction worse than any drug ever previously known.

3 – History :

The opium poppy was cultivated in lower Mesopotamia as long ago as 3400 BC . The chemical analysis of opium in the 19th century revealed that most of its activity could be ascribed to two alkaloids, codeine and morphine.

Diacetylmorphine was first synthesized in 1874 by C. R. Alder Wright, an English chemist working at St. Mary's Hospital Medical School in London. He had been experimenting with combining morphine with various acids. He boiled anhydrous morphine alkaloid with acetic anhydride for several hours and produced a more potent, acetylated form of morphine, now called *diacetylmorphine*. The compound was sent to F. M. Pierce of Owens College in Manchester for analysis. Owens told Wright :

Doses ... were subcutaneously injected into young dogs and rabbits ... with the following general results ... great prostration, fear, and sleepiness speedily following the administration, the eyes being sensitive, and pupils constrict, considerable salivation being produced in dogs, and slight tendency to vomiting in some

cases, but no actual emesis. Respiration was at first quickened, but subsequently reduced, and the heart's action was diminished, and rendered irregular. Marked want of coordinating power over the muscular movements, and loss of power in the pelvis and hind limbs, together with a diminution of temperature in the rectum of about 4°.^[8]

Wright's invention did not lead to any further developments, and diacetylmorphine only became popular after it was independently re-synthesized 23 years later by another chemist, Felix Hoffmann. Hoffmann, working at the Aktiengesellschaft Farbenfabriken (today the Bayer pharmaceutical company) in Elberfeld, Germany, was instructed by his supervisor Heinrich Dreser to acetylate morphine with the objective of producing codeine, a constituent of the opium poppy, pharmacologically similar to morphine but less potent and less addictive. Instead the experiment produced an acetylated form of morphine one and a half to two times more potent than morphine itself.

From 1898 through to 1910 diacetylmorphine was marketed under the name heroin as a non - addictive morphine substitute and cough suppressant. Bayer marketed heroin as a cure for morphine addiction before it was discovered that it rapidly metabolizes into morphine. As such, heroin is essentially a quicker acting form of morphine. The company was embarrassed by the new finding, which became a historic blunder for Bayer .

In the U.S.A. the Harrison Narcotics Tax Act was passed in 1914 to control the sale and distribution of " heroin " and other opioids, which allowed the drug to be prescribed and sold for medical purposes. In 1924 the United States Congress banned its sale, importation or manufacture. It is now a Schedule I substance, which makes it illegal for non - medical use in signatory nations of the Single Convention on Narcotic Drugs treaty, including the United States.

Later, as with Aspirin, Bayer lost some of its trademark rights to "heroin" under the 1919 Treaty of Versailles following the German defeat in World War I .

4 – Pharmacology :

When taken orally, diacetylmorphine undergoes extensive first-pass metabolism via deacetylation, making it a prodrug for the systemic delivery of morphine . When the drug is injected, however, it avoids this first - pass effect, very rapidly crossing the blood-brain barrier due to the presence of the acetyl groups, which render it much more lipid-soluble than morphine itself . Once in the brain, it then is deacetylated into 6-monoacetylmorphine (6 – MAM) and morphine which bind to μ -opioid receptors, resulting in the drug's euphoric, analgesic (pain relief) , and anxiolytic (anti - anxiety) effects ; diacetylmorphine itself exhibits relatively low affinity for the μ receptor.^[13] Unlike hydromorphone and oxycodone, however, administered intravenously, diacetylmorphine creates a larger histamine release, similar to morphine, resulting in the feeling of a greater subjective "body high" to some, but also instances of pruritus (itching) when they first start using .

Both morphine and 6 - MAM are μ - opioid agonists which bind to receptors present throughout the brain, spinal cord and gut of all mammals. The μ - opioid receptor also binds endogenous opioid peptides such as β - endorphin, Leu - enkephalin, and Met-enkephalin. Repeated use of diacetylmorphine results in a number of physiological changes, including decreases in the number of μ - opioid receptors . These physiological alterations lead to tolerance and dependence, so that cessation of diacetylmorphine use results in a set of extremely uncomfortable symptoms including pain, anxiety, muscle spasms, and insomnia called the opioid withdrawal syndrome. Depending on usage it has an onset 4 to 24 hours after the last dose of diacetylmorphine. Morphine also binds to δ - and κ - opioid receptors .There is also evidence that 6-MAM binds to a subtype of μ - opioid receptors which are also activated by the morphine metabolite morphine – 6 β - glucuronide but not morphine itself. The contribution of these receptors to the overall pharmacology of heroin remains unknown .

A subclass of morphine derivatives, namely the 3,6 esters of morphine, with similar effects and uses includes the clinically-used strong analgesics nicomorphine (Vilan), and dipropanoylmorphine; there is also the latter's dihydromorphine analogue, diacetyl dihydro morphine (Paralaudin) .

5 - Usage and effects :

5 – 1 : Medical use :

Under the name diamorphine, heroin is prescribed as a strong analgesic in the United Kingdom, where it is given via subcutaneous, intramuscular, intrathecal or intravenous route. Its use includes treatment for acute pain, such as in severe physical trauma, myocardial infarction, post - surgical pain, and chronic pain, including end - stage cancer and other terminal illnesses. In other countries it is more common to use morphine or other strong opioids in these situations.

In 2005, there was a shortage of diamorphine in the UK, due to a problem at the main UK manufacturers . Due to this, many hospitals changed to using morphine instead of diamorphine. Although there is no longer a problem with its manufacture, many hospitals have continued to use morphine .

Diamorphine continues to be widely used in palliative care in the United Kingdom, where it is commonly given by the subcutaneous route, often via a syringe driver, if patients could not easily swallow oral morphine solution. The advantage of diamorphine over morphine is that diamorphine is more soluble and smaller volumes of diamorphine are needed for the same analgesic effect. Both of these factors are advantageous if giving high doses of opioids via the subcutaneous route, which is often necessary in palliative care.

The medical use of diamorphine (in common with other strong opioids such as morphine, fentanyl and oxycodone) is controlled in the United Kingdom by the Misuse of Drugs Act 1971. In the UK, it is a class A controlled drug. Registers of its use are required to be kept in hospitals .

Heroin is also used as a maintenance drug in the treatment of heroin addicts. Though this is somewhat controversial among proponents of a zero tolerance drug policy it has proven superior to methadone in improving the social and health situation of addicts.^[17] See the section Heroin prescription for addicts. Heroin has been proven to act as a fever reducer .

5 – 2 : Recreational use :



Recreational heroin user under the influence.

Diacetylmorphine is used as a recreational drug for the profound relaxation and intense euphoria it produces, although the latter effect diminishes with increased tolerance. Its popularity with recreational drug users, compared to morphine, reportedly stems from its perceived different effects . In particular, users report an intense "rush" that occurs while the diacetylmorphine is being metabolized into 6-monoacetylmorphine (6-MAM) and morphine in the brain. Any intravenous opioid will induce rapid, profound effects, but diacetylmorphine produces more euphoria than other opioids upon injection. One possible explanation is the presence of 6-monoacetylmorphine, a metabolite unique to diacetylmorphine. While other opioids of abuse, such as codeine, produce only morphine, heroin also leaves 6-MAM, also a psycho-active metabolite. However, this perception is not supported by the results of clinical studies comparing the physiological and subjective effects of injected diacetylmorphine and morphine in individuals formerly addicted to opioids; these subjects showed no preference for one drug over the other. Equipotent, injected doses had comparable action courses, with

no difference in subjects' self - rated feelings of euphoria, ambition, nervousness, relaxation, drowsiness, or sleepiness . Short - term addiction studies by the same researchers demonstrated that tolerance developed at a similar rate to both diacetylmorphine and morphine. When compared to the opioids hydromorphone, fentanyl, oxycodone, and pethidine/meperidine, former addicts showed a strong preference for diacetylmorphine and morphine, suggesting that diacetylmorphine and morphine are particularly susceptible to abuse and addiction. Morphine and diacetylmorphine were also much more likely to produce euphoria and other positive subjective effects when compared to these other opioids .

One of the most common methods of illicit heroin use is via intravenous injection (colloquially termed " shooting up ") . Heroin base (commonly found in the UK and Europe), when prepared for injection will only dissolve in water when mixed with an acid (most commonly citric acid powder or lemon juice) and heated. Heroin in the US is most commonly its hydrochloride salt, requiring just water to dissolve. Users tend to initially inject in the easily accessible veins in the arm, but as these veins collapse over time through damage caused by the acid, the user will often resort to injecting in other veins.

Recreational users may also administer the drug through means of snorting, or smoking by inhaling its vapors when heated; either with tobacco in a rolled cigarette or by heating the drug on aluminium foil from underneath . When heated the heroin powder changes to a thick liquid, similar in consistency to molten wax, and it will run across the foil giving off smoke which the user inhales through a tube, usually made from foil also so that any heroin that collects on the inside of the tube can be smoked afterward. The user follows the "blob" of heroin with the intention of inhaling, through the tube, as much of the smoke as possible - i.e. " chasing the dragon " .

The onset of diacetylmorphine's effects depends upon the route of administration . Orally , since diacetylmorphine is completely metabolized in vivo to morphine before crossing the blood-brain barrier the effects are the same as with oral morphine . Snorting

results in an onset within 3 to 5 minutes; smoking results in an almost immediate effect that builds in intensity; intravenous injection induces a rush and euphoria usually taking effect within 30 seconds; intramuscular and subcutaneous injection take effect within 3 to 5 minutes .

The diacetyl morphine dose used for recreational purposes depends strongly on the frequency of use. A first - time user typically ingests between 5 and 20 mg of diacetylmorphine, but an individual who is heavily dependent on the drug may require several hundred mg per day . Large doses of heroin can cause fatal respiratory depression, and the drug has been used for suicide or as a murder weapon .

5 – 3 : Effects :

Central nervous system :

- Drowsiness
- Disorientation
- Delirium

Neurological :

- Analgesia
- Tolerance
- Addiction (Physical Dependence)

Psychological :

- Addiction (Psychological Dependence)
- Anxiolysis
- Confusion
- Euphoria
- Somnolence

Cardiovascular & Respiratory :

- Bradycardia
- Hypotension
- Hypoventilation

- Shallow breathing
- Respiratory depression

Gastrointestinal :

- Nausea
- Vomiting (protracted)
- Constipation
- Dyspepsia

Musculoskeletal :

- Analgesia
- Ataxia
- Muscle spasticity

Skin :

- Itching
- Flushing/Rash

Miscellaneous :

- Dry mouth (Xerostomia)
- Miosis, or pupil constriction (" pinpoint pupils ")
- Urinary retention

Recreational uses :

- Euphoria
- Relaxation

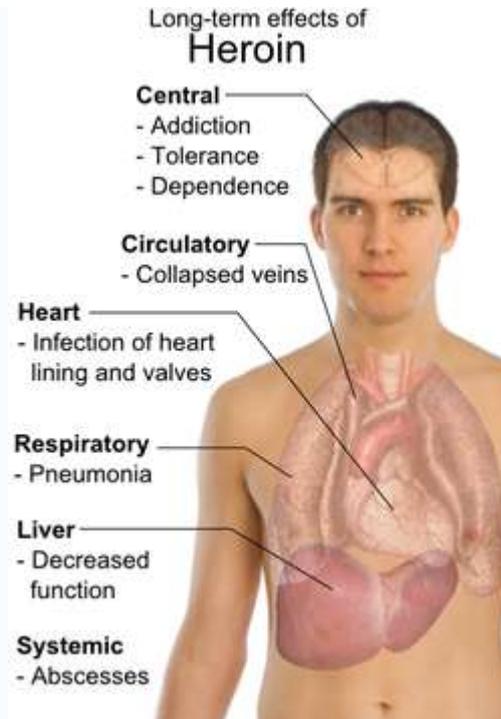
Medicinal uses :

- Powerful analgesic
- Cough suppressant
- Anti - diarrheal

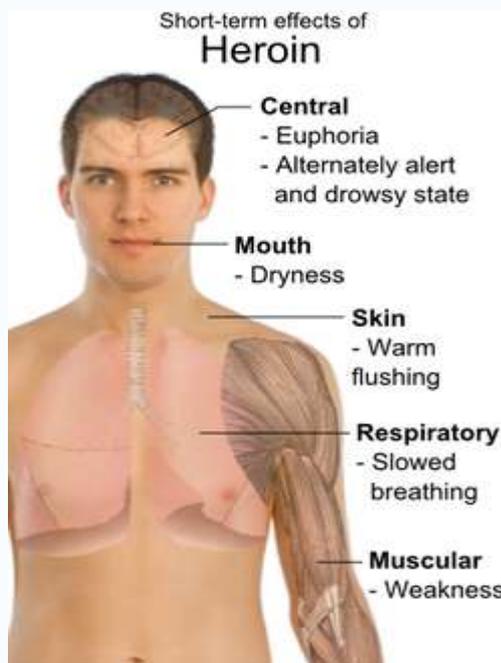
Contraindications :

- Alcohol

- Barbiturates and Benzodiazepines
- Stimulants
- Other opioids (depends heavily on tolerance)



Main long - term effects of usage



Main short-term effects of heroin usage

6 – Regulation :

In the Netherlands, diamorphine (heroin) is a List I drug of the Opium Law. It is available for prescription under tight regulation to long-term heroin addicts for whom methadone maintenance treatment has failed. Heroin is exclusively available for prescription to long-term heroin addicts, and cannot be used to treat severe pain or other illnesses.

In the United States, heroin is a schedule I drug according to the Controlled Substances Act of 1970, making it illegal to possess without a DEA license. Possession of more than 100 grams of heroin or a mixture containing heroin is punishable with a minimum mandatory sentence of 5 years of imprisonment in a federal prison.

In Canada , heroin is a controlled substance under Schedule I of the Controlled Drugs and Substances Act (CDSA). Any person who seeks or obtains heroin without disclosing authorization 30 days prior to obtaining another prescription from a practitioner is guilty of an indictable offense and subject to imprisonment for a term not exceeding seven years. Possession of heroin for the purpose of trafficking is guilty of an indictable offense and subject to imprisonment for life.

In Hong Kong, heroin is regulated under Schedule 1 of Hong Kong's Chapter 134 *Dangerous Drugs Ordinance*. It is available by prescription. Anyone who supplies heroin without a valid prescription can be fined \$10,000 (HKD). The penalty for trafficking or manufacturing heroin is a \$5,000,000 (HKD) fine and life imprisonment. Possession of heroin without a license from the Department of Health is illegal with a \$1,000,000 (HKD) fine and/or 7 years of jail time.

In the United Kingdom, heroin is available by prescription, though it is a restricted Class A drug. According to the 50th edition of the British National Formulary (BNF), diamorphine hydrochloride may be used in the treatment of acute pain, myocardial infarction, acute pulmonary oedema, and chronic pain. The treatment of chronic non-malignant pain must be supervised by a specialist. The BNF notes

that all opioid analgesics cause dependence and tolerance but that this is "no deterrent in the control of pain in terminal illness". When used in the palliative care of cancer patients, heroin is often injected using a syringe driver.

7 – Price :

The European Monitoring Centre for Drugs and Drug Addiction reports that the retail price of brown heroin varies from €14.5 per gram in Turkey to €110 per gram in Sweden, with most European countries reporting typical prices of €35-40 per gram. The price of white heroin is reported only by a few European countries and ranged between €27 and €110 per gram

8 - Production and trafficking : The Golden Triangle

8 – 1 : Manufacturing :

Heroin, also known as diacetyl morphine is produced from acetylation of morphine derived from natural opium sources. Numerous mechanical and chemical means are used to purify the final product. The final product have different appearance depending on purity and have different names .

8 – 2 : History of heroin traffic :

The origins of the present international illegal heroin trade can be traced back to laws passed in many countries in the early 1900s that closely regulated the production and sale of opium and its derivatives including heroin. At first, heroin flowed from countries where it was still legal into countries where it was no longer legal. By the mid-1920s, heroin production had been made illegal in many parts of the world. An illegal trade developed at that time between heroin labs in China (mostly in Shanghai and Tianjin) and other nations. The weakness of government in China and conditions of civil war enabled heroin production to take root there. Chinese triad gangs eventually came to play a major role in the heroin trade. The French Connection route started in the 1930s.

Heroin trafficking was virtually eliminated in the U.S. during World War II due to temporary trade disruptions caused by the war. Japan's war with China had cut the normal distribution routes for heroin and the war had generally disrupted the movement of opium.

After World War II, the Mafia took advantage of the weakness of the postwar Italian government and set up heroin labs in Sicily. The Mafia took advantage of Sicily's location along the historic route opium took westward into Europe and the United States.^[27]

Large scale international heroin production effectively ended in China with the victory of the communists in the civil war in the late 1940s . The elimination of Chinese production happened at the same time that Sicily's role in the trade developed.

Although it remained legal in some countries until after World War II, health risks, addiction, and widespread recreational use led most western countries to declare heroin a controlled substance by the latter half of the 20th century.

In late 1960s and early 70s, the CIA supported anti-Communist Chinese Nationalists settled near Sino-Burmese border and Hmong tribesmen in Laos. This helped the development of the Golden Triangle opium production region, which supplied about one-third of heroin consumed in US after 1973 American withdrawal from Vietnam. As of 1999, Myanmar (formerly Burma), the heartland of the Golden Triangle remained the second largest producer of heroin, after Afghanistan .

Soviet-Afghan war led to increased production in the Pakistani-Afghani border regions, as U.S.- backed mujaheddin militants raised money for arms from selling opium, contributing heavily to the modern Golden Crescent creation. By 1980, 60 % of heroin sold in the U.S. originated in Afghanistan . It increased international production of heroin at lower prices in the 1980s. The trade shifted away from Sicily in the late 1970s as various criminal organizations violently fought with each other over the trade. The fighting also led to a stepped up government law enforcement presence in Sicily.

8 – 3 : Trafficking :

Traffic is heavy worldwide, with the biggest producer being Afghanistan . According to U.N. sponsored survey , as of 2004, Afghanistan accounted for production of 87 percent of the world's heroin .

The cultivation of opium in Afghanistan reached its peak in 1999, when 225,000 acres — 350 square miles — of poppies were sown. The following year the Taliban banned poppy cultivation, a move which cut production by 94 percent. By 2001 only 30 square miles of land were in use for growing opium poppies. A year later, after American and British troops had removed the Taliban and installed the interim government, the land under cultivation leapt back to 285 square miles, with Afghanistan supplanting Burma to become the world's largest opium producer once more.^[32] Opium production in that country has increased rapidly since, reaching an all-time high in 2006. War once again appeared as a facilitator of the trade .

At present, opium poppies are mostly grown in Afghanistan, and in Southeast Asia, especially in the region known as the Golden Triangle straddling Myanmar, Thailand, Vietnam, Laos and Yunnan province in the People's Republic of China. There is also cultivation of opium poppies in the Sinaloa region of Mexico and in Colombia. The majority of the heroin consumed in the United States comes from Mexico and Colombia. Up until 2004, Pakistan was considered one of the biggest opium-growing countries.

Conviction for trafficking in heroin carries the death penalty in most South-east Asian, some East Asian and Middle Eastern countries (see Use of death penalty worldwide for details), among which Malaysia, Singapore and Thailand are the most strict. The penalty applies even to citizens of countries where the penalty is not in place, sometimes causing controversy when foreign visitors are arrested for trafficking, for example the arrest of nine Australians in Bali, the death sentence given to Nola Blake in Thailand in 1987, or the hanging of an Australian citizen Van Tuong Nguyen in Singapore ,

9 - Risks of use :

- For intravenous users of heroin (and any other substance), the use of non-sterile needles and syringes and other related equipment leads to several serious risks:
 - the risk of contracting blood-borne pathogens such as HIV and hepatitis
 - the risk of contracting bacterial or fungal endocarditis and possibly venous sclerosis
 - abscesses
- Poisoning from contaminants added to "cut" or dilute heroin
- Chronic constipation
- Addiction and increasing tolerance
- Physical dependence can result from prolonged use of all opioids, resulting in withdrawal symptoms on cessation of use
- Decreased kidney function (although it is not currently known if this is due to adulterants or infectious diseases)

Many countries and local governments have begun funding programs that supply sterile needles to people who inject illegal drugs in an attempt to reduce these contingent risks and especially the contraction and spread of blood-borne diseases. The Drug Policy Alliance reports that up to 75 % of new AIDS cases among women and children are directly or indirectly a consequence of drug use by injection. The United States federal government does not operate needle exchanges, although some state and local governments do support needle exchange programs.

Anthropologists Philippe Bourgois and Jeff Schonberg, who did a decade of field work among homeless heroin and crack addicts in San Francisco, reported that the African-American addicts they observed was more inclined to "direct deposit" heroin into a vein, rather than "skin-popping" their injections. (Skin - popping was a far more widespread practice among the white addicts: "By the midpoint of our fieldwork, most of the whites had given up searching for operable veins and skin - popped. They sank their needles perfunctorily, often through their clothing, into their fatty tissue ") . Bourgois and Schonberg describes how the cultural difference between the African-

Americans and the whites leads to this contrasting behavior, and also points out that the two different ways to inject heroin comes with different health risks. Skin-popping more often results in abscesses, and direct injection more often leads to fatal overdose and also to hepatitis C and HIV infection .

A heroin overdose is usually treated with an opioid antagonist, such as naloxone (Narcan) , or naltrexone, which has high affinity for opioid receptors but does not activate them. This reverses the effects of heroin and other opioid agonists and causes an immediate return of consciousness but may precipitate withdrawal symptoms. The half-life of naloxone is much shorter than that of most opioid agonists, so that antagonist typically has to be administered multiple times until the opioid has been metabolized by the body .

Depending on drug interactions and numerous other factors, death from overdose can take anywhere from several minutes to several hours due to anoxia because the breathing reflex is suppressed by μ -opioids. An overdose is immediately reversible with an opioid antagonist injection. Heroin overdoses can occur due to an unexpected increase in the dose or purity or due to diminished opioid tolerance. However, many fatalities reported as overdoses are probably caused by interactions with other depressant drugs like alcohol or benzodiazepines . It should also be noted that since heroin can cause nausea and vomiting, a significant number of deaths attributed to heroin overdose are caused by aspiration of vomit by an unconscious victim. Some sources give a figure of between 75 and 375 mg for a 75 kg being fatal for 50 % of opiate naive people . Street heroin is of widely varying and unpredictable purity. This means that the user may prepare what they consider to be a moderate dose while actually taking far more than intended. Also, tolerance typically decreases after a period of abstinence. If this occurs and the user takes a dose comparable to their previous use, the user may experience drug effects that are much greater than expected, potentially resulting in a dangerous overdose.

It has been speculated that an unknown portion of heroin related deaths are the result of an overdose or allergic reaction to quinine, which may sometimes be used as a cutting agent .

A final factor contributing to overdoses is place conditioning. Heroin use is a highly ritualized behavior. While the mechanism has yet to be clearly elucidated, longtime heroin users display increased tolerance to the drug in locations where they have repeatedly administered heroin. When the user injects in a different location, this environment-conditioned tolerance does not occur, resulting in a greater drug effect. The user's typical dose of the drug, in the face of decreased tolerance, becomes far too high and can be toxic, leading to overdose .

A small percentage of heroin smokers and occasionally IV users may develop symptoms of toxic leukoencephalopathy. The cause has yet to be identified, but one speculation is that the disorder is caused by an uncommon adulterant that is only active when heated.^{[40][41][42]} Symptoms include slurred speech and difficulty walking.

Cocaine sometimes proves to be fatal when used in combination with heroin. Though " speedballs " (when injected) or " moon rocks " (when smoked) are a popular mix of the two drugs among users, combinations of stimulants and depressants can have unpredictable and sometimes fatal results. In the United States in early 2006, a rash of deaths was attributed to either a combination of fentanyl and heroin, or pure fentanyl masquerading as heroin particularly in the Detroit Metro Area; one news report refers to the combination as ' laced heroin ' , though this is likely a generic rather than a specific term .

10 - Harm reduction :

Proponents of the harm reduction philosophy seek to minimize the harms that arise from the recreational use of heroin. Safer means of taking the drug, such as smoking or nasal, oral and rectal insertion, are encouraged, due to injection having higher risks of overdose, infections and blood-borne viruses. Where the strength of the drug is unknown, users are encouraged to try a small amount first to gauge

the strength, to minimize the risks of overdose. For the same reason, poly drug use (the use of two or more drugs at the same time) is discouraged. Users are also encouraged to not use heroin on their own, as others can assist in the event of an overdose. Heroin users who choose to inject should always use new needles , syringes , spoons / ster - cups and filters every time they inject and not share these with other users. Governments that support a harm reduction approach often run Needle & Syringe exchange programs, which supply new needles and syringes on a confidential basis, as well as education on proper filtering prior to injection, safer injection techniques, safe disposal of used injecting gear and other equipment used when preparing heroin for injection may also be supplied including citric acid sachets/vitamin C sachets, steri-cups, filters, alcohol pre-injection swabs, sterile water ampules and tourniquets (to stop use of shoe laces or belts) .

11 – Heroin With drawal :

The withdrawal syndrome from heroin may begin within 6 to 24 hours of discontinuation of the drug; however, this time frame can fluctuate with the degree of tolerance as well as the amount of the last consumed dose. Symptoms may include: sweating, malaise, anxiety, depression, priapism, extra sensitivity of the genitals in females, general feeling of heaviness, cramp-like pains in the limbs, excessive yawning or sneezing, tears, rhinorrhea, sleep difficulties (insomnia), cold sweats, chills, severe muscle and bone aches; nausea and vomiting, diarrhea, cramps, and fever .

12 - Heroin prescription for addicts :

The UK Department of Health's Rolleston Committee report in 1926 established the British approach to heroin prescription to users, which was maintained for the next forty years: dealers were prosecuted, but doctors could prescribe heroin to users when withdrawing from it would cause harm or severe distress to the patient. This "policing and prescribing" policy effectively controlled the perceived heroin problem in the UK until 1959 when the number of heroin addicts doubled every sixteenth month during a period of ten years, 1959–1968 . The failure changed the attitudes; in 1964 only

specialized clinics and selected approved doctors were allowed to prescribe heroin to users. The law was made more restrictive in 1968. Beginning in the 1970s , the emphasis shifted to abstinence and the use of methadone, until now only a small number of users in the UK are prescribed heroin .

In 1994 Switzerland began a trial heroin maintenance program for users that had failed multiple withdrawal programs. The aim of this program is to maintain the health of the user in order to avoid medical problems stemming from the use of illicit street heroin. Reducing drug-related crime and preventing overdoses were two other goals. The first trial in 1994 involved 340 users, although enrollment was later expanded to 1000 based on the apparent success of the program. Participants are allowed to inject heroin in specially designed pharmacies for 15 Swiss Francs per dose . A national referendum in November 2008 showed 68 % of voters supported the plan , introducing heroin prescription into federal law. The trials before were based on time - limited executive ordinances.

The success of the Swiss trials led German, Dutch,^[49] and Canadian cities to try out their own heroin prescription programs . Some Australian cities (such as Sydney) have instituted legal heroin supervised injecting centers , in line with other wider harm minimization programs .

Starting in January 2009 Denmark is also going to prescribe heroin to a few addicts that have tried methadone and subutex without success.^[52] In July 2009, the German Bundestag passed a law allowing heroin prescription as a standard treatment for addicts; while heroin prescription was started in 2002, it was only authorized as a large-scale trial .

□

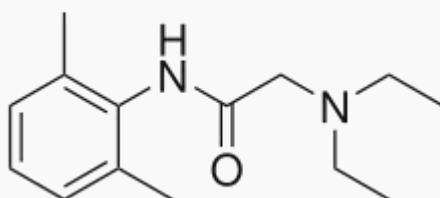
Lidocaine

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1 – Introduction :

Lidocaine (INN) or **lignocaine** (former BAN) is a common local anesthetic and antiarrhythmic drug . Lidocaine is used topically to relieve itching, burning and pain from skin inflammations, injected as a dental anesthetic, and in minor surgery .



Systematic (IUPAC) name

2- (diethyl amino) -N- (2,6 - dimethyl phenyl) acetamide

Formula **C₁₄H₂₂N₂O**

Mol. mass 234 g / mol

Synonyms N - (2 , 6 - dimethyl phenyl) - N², N² - diethyl
glycin amide

Melt Point 68 °C (154 °F)

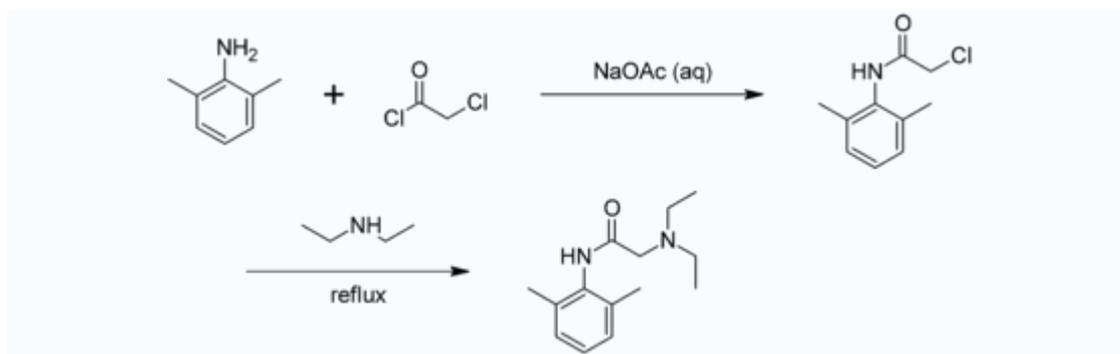
Pharmacokinetic data	
Bioavailability	35 % (oral) 3 % (topical)
Metabolism	Hepatic , 90 % CYP1A2 - mediated
Half life	1.5 – 2 hours
Excretion	renal

2 - History :

Lidocaine , the first amino amide - type local anesthetic , was first synthesized under the name xylocaine by Swedish chemist Nils Löfgren in 1943 . His colleague Bengt Lundqvist made the first injection anesthesia experiments on himself .

3 - Preparation :

Lidocaine may be prepared in two steps by the reaction of 2 , 6 - xylidine with chloro acetyl chloride , followed by the reaction with diethyl amine :



4 - Pharma cokinetics :

Lidocaine is approximately 90 % metabolized (de – ethylated) in the liver by CYP1A2 (and to a minor extent CYP3A4) to the pharmacologically - active metabolites mono ethyl glycine xylidide and glycine xylidide .

The elimination half-life of lidocaine is approximately 1.5 – 2 hours in most patients . This may be prolonged in patients with

hepatic impairment (average 343 minutes) or congestive heart failure (average 136 minutes) .

5 – Pharmacodynamics :

5 – 1 : Anesthesia :

Lidocaine alters signal conduction in neurons by blocking the fast voltage gated sodium (Na^+) channels in the neuronal cell membrane, which are responsible for signal propagation^[4]. With sufficient blockade, the membrane of the postsynaptic neuron will not depolarize and so fail to transmit an action potential, leading to its anaesthetic effects. Careful titration allows for a high degree of selectivity in the blockage of sensory neurons , whereas higher concentrations will also affect other modalities of neuron signaling .

6 - Clinical use :

6 – 1 : Indications

Topical lidocaine has been shown to relieve postherpetic neuralgia in some patients, though there is not enough study evidence to recommend it as a first - line treatment . It also has uses as a temporary fix for tinnitus. Although not completely curing the illness, it has been shown to reduce the effects by around two thirds .

The efficacy profile of lidocaine as a local anesthetic is characterized by a rapid onset of action and intermediate duration of efficacy. There fore , lidocaine is suitable for infiltration , block and surface anesthesia. Longer-acting substances such as bupivacaine are sometimes given preference for spinal and peridural anesthetics; lidocaine, on the other hand, has the advantage of a rapid onset of action. Adrenaline supplements delay the resorption; the duration of efficacy can thus almost be doubled. For surface anesthesia several formulations are available that can be used e.g. for endoscopies , before intubations etc.

Lidocaine is also the most important class 1B antiarrhythmic drug: it is used intravenously for the treatment of ventricular arrhythmias (for acute myocardial infarction, digitalis poisoning,

cardioversion or cardiac catheterization) . However, a routine prophylactic administration is no longer recommended for acute cardiac infarction; the overall benefit of this measure is not convincing. Lidocaine has also been efficient in refractory cases of status epilepticus .

6 – 2 : Contraindications

Contraindications for the use of lidocaine include :

- Heart block, second or third degree (without pacemaker)
- Severe sinoatrial block (without pacemaker)
- Serious adverse drug reaction to lidocaine or amide local anaesthetics
- Concurrent treatment with quinidine, flecainide , disopyramide, procainamide (Class I antiarrhythmic agents)
- Prior use of Amiodarone hydrochloride
- Hypotension not due to Arrhythmia
- Bradycardia
- Accelerated idioventricular rhythm
- Pacemaker

6 – 3 : Adverse drug reactions

Adverse drug reactions (ADRs) are rare when lidocaine is used as a local anesthetic and is administered correctly. Most ADRs associated with lidocaine for anesthesia relate to administration technique (resulting in systemic exposure) or pharmacological effects of anesthesia, but allergic reactions only rarely occur .

Systemic exposure to excessive quantities of lidocaine mainly result in central nervous system (CNS) and cardiovascular effects – CNS effects usually occur at lower blood plasma concentrations and additional cardiovascular effects present at higher concentrations, though cardiovascular collapse may also occur with low concentrations . CNS effects may include CNS excitation (nervousness , tingling around the mouth (also known as circumoral paraesthesia) , tinnitus , tremor , dizziness , blurred vision , seizures) followed by depression, and with increasingly heavier exposure:

drowsiness, loss of consciousness, respiratory depression and apnoea). Cardiovascular effects include hypotension, bradycardia, arrhythmias, and/or cardiac arrest – some of which may be due to hypoxemia secondary to respiratory depression .

ADRs associated with the use of intravenous lidocaine are similar to toxic effects from systemic exposure above. These are dose-related and more frequent at high infusion rates (≥ 3 mg / minute) . Common ADRs include : headache , dizziness , drowsiness , confusion , visual disturbances, tinnitus, tremor, and/or paraesthesia. Infrequent ADRs associated with the use of lidocaine include: hypotension, bradycardia, arrhythmias, cardiac arrest, muscle twitching, seizures, coma, and/or respiratory depression .

On September 25 , 2009 , a Florida woman was hospitalized because of lidocaine complications during a minimally invasive liposuction procedure at a day spa . The spa was not a licensed clinic or healthcare facility. After having a seizure , the woman was rushed from the spa to the hospital where she was declared brain dead .

6 – 4 : Insensitivity to lidocaine

Relative insensitivity to lidocaine runs in families . In hypokalemic sensory overstimulation , relative insensitivity to lidocaine has been described in people who also have attention deficit hyperactivity disorder . In dental anesthesia, a relative insensitivity to lidocaine can occur for anatomical reasons due to unexpected positions of nerves. Some people with Ehlers-Danlos syndrome are insensitive to lidocaine .

6 – 5 : Dosage forms

Lidocaine , usually in the form of **lidocaine hydrochloride** , is available in various forms including :

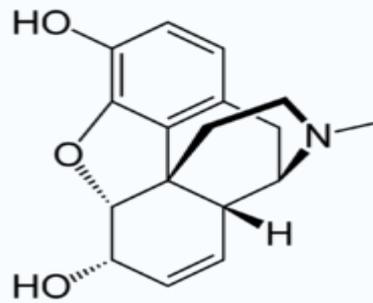
- Injected local anesthetic (some times combined with epinephrine to reduce bleeding)
- Dermal patch (some times combined with prilocaine)

- Intravenous injection (some times combined with epinephrine to reduce bleeding)
- Intravenous infusion
- Nasal instillation / spray (combined with phenyl ephrine)
- Oral gel (often referred to as " viscous lidocaine " or abbreviated " lidocaine visc " or " lidocaine HCl visc " in pharmacology ; used as teething gel)
- Oral liquid
- Topical gel (as with Aloe Vera gels that include Lidocaine)
- Topical liquid
- Topical patch (Lidocaine 5 % patch is marketed as " Lidoderm " in the US (since 1999) and " Versatis " in the UK (since 2007 by Grünenthal))
- Topical aerosol Spray

7 - Additive in cocaine :

Lidocaine is often added to cocaine as a diluent . Cocaine numbs the gums when applied, and since lidocaine causes stronger numbness users get the impression of high-quality cocaine when in actuality, the user is receiving a diluted product .

Morphine



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1 – Introduction :

Morphine (INN) (pronounced /'mɔːfɪːn/) (**MS Contin, MSIR, Avinza, Kadian, Oramorph, Roxanol**) is a highly potent opiate analgesic psychoactive drug, is the principal active ingredient in *Papaver somniferum* (opium poppy, or simply opium), is considered to be the prototypical opioid. Like other opioids, e.g. oxycodone (OxyContin, Percocet, Percodan), hydromorphone (Dilaudid, Palladone) , and diacetylmorphine (Heroin), morphine acts directly on the central nervous system (CNS) to relieve pain. Morphine has a high potential for addiction; tolerance and both physical and psychological dependence develop rapidly.

Systematic (IUPAC) name	
(5 α , 6 α) – 7 , 8 – didehydro - 4 , 5 - epoxy -17- methyl morphinan – 3 , 6 - diol	
Chemical data	
Formula	C ₁₇ H ₁₉ N O ₃
Mol . mass	285
Pharmacokinetic data	
Bioavailability	~ 25 % (oral) ; 100 % (IV) ;
Protein binding	30 – 40 %
Metabolism	Hepatic 90 %
Half life	2 – 3 h
Excretion	Renal 90 % , biliary 10%

Indications :

- Pain relief or analgesia
- Cough suppressance
- Anti diarrheal effects

Recreational uses :

- Anti depressant effects
- Anxiolysis
- Drowsiness or somnolence (nodding)
- Euphoria
- Relaxation
- Sedation
- Stress relief

Contraindications :

- ☆ Dissociatives like ketamine (K) , phencyclidine (PCP) , dextro methorphan (DXM) , and nitrous oxide (N₂O)
- ☆ Sympatholytics like alpha blockers and beta blockers
- ☆ Tranquilizers like alcohol (ethanol), gamma-Hydroxy butyrate , barbiturates , benzo diazepines , and non benzo diazepines
- ☆ Other opiates and opioids (narcotics or analgesics)
- ☆ Miscellaneous depressants , anesthetics , hypnotics , and sedatives

Side effects :

Cardiovascular :

- Bradycardia or decreased heart rate
- Cardiac arrest, cessation of heartbeat, or heart failure
- Hypotension or decreased blood pressure
- Palpitation or abnormal heart beat
- Faintness or syncope
- Flushing of the face
- Orthostatic hypotension or very low blood pressure

Ear, nose , throa t, and skin :

- Flushing
- Pruritus or itching
- Xerostomia or dry mouth

Eye:

- Intermittent blurring
- Pupil constriction or miosis
- Visual distortions

Gastrointestinal:

- Constipation
- Nausea and vomiting or emesis

Hepatological:

- Hepatotoxicity or liver damage (due to acetaminophen or paracetamol (APAP; Tylenol) in many morphine preparations)
- Liver failure (again, due to acetaminophen)
- Renal failure or kidney failure

Musculoskeletal:

- Fasciculation or muscle twitch

Neurological:

- Analgesia

Psychological:

- Antidepressant effects
- Anxiolysis
- Confusion
- Drowsiness or somnolence (nodding)
- Dysphoria
- Euphoria
- Relaxation
- Sedation
- Stress relief

Respiratory:

- Bradypnea or slow breathing

- Dyspnea or shortness of breath
- Hypoventilation , respiratory depression , or shallow breathing
- Respiratory acidosis or an abnormal decrease in the pH of the blood
- Respiratory arrest or cessation of breathing

Miscellaneous / Severe :

- Miscarriage or spontaneous abortion
- Coma or unconsciousness
- Death or termination of life

2 - Trade Names :

Morphine is marketed under many different brand names in various parts of the world .

3 – History :

A poppyseed - based elixir similar to morphine was used by alchemists of Byzantine times, but when the Ottoman Turks conquered Byzantium, it was lost. Around 1522, Paracelsus, who fancied himself as a travelling doctor, recovered the formula for this elixir. He named it, *laudanum* from the Latin word *laudare* meaning "to praise," presumably on account of its pleasant side effects. This elixir was used by Paracelsus as a potent painkiller, and he did not sell it to the public often. Later, between the 18th and 19th century, laudanum became a medical standard and every doctor carried it in his medical bag.

Morphine was discovered as the first active alkaloid extracted from the opium poppy plant in 1804 in Paderborn, Germany,^{[3][4]} The drug was first marketed to the general public by Sertürner and Company in 1817 as an analgesic, and also as a treatment for opium and alcohol addiction. Later it was found that morphine was more addictive than either alcohol or opium, and its extensive use during the American Civil War allegedly resulted in over 400,000 sufferers from the "soldier's disease" of morphine addiction . This idea has been a

subject of controversy, as there have been suggestions that such a disease was in fact a hoax .

Diacetylmorphine (better known as heroin) was synthesized from morphine in 1874 and brought to market by Bayer in 1898. Heroin is approximately 1.5–2 times more potent than morphine on a milligram-for-milligram basis. Using a variety of subjective and objective measures, one study estimated the relative potency of heroin to morphine administered intravenously to post - addicts to be 1.80 – 2.66 mg of morphine sulfate to 1 mg of diamorphine hydro chloride (heroin) .

Morphine became a controlled substance in the U.S. under the Harrison Narcotics Tax Act of 1914, and possession without a prescription in the U.S. is a criminal offense. Morphine was the most commonly abused narcotic analgesic in the world up until heroin was synthesized and came into use. Until the synthesis of dihydromorphine (c.a. 1900), the dihydromorphinone class of opioids (1920s), and oxycodone (1916) and similar drugs, there generally were no other drugs in the same efficacy range as opium, morphine and heroin, with synthetics still several years away (pethidine was invented in Germany in 1937) and opioid agonists amongst the semi-synthetics were analogues and derivatives of codeine such as dihydro codeine (Paracodin) , ethyl morphine (Dionine) , and benzyl morphine (Peronine) . Even today, morphine is the most sought after prescription narcotic by heroin addicts when heroin is scarce, all other things being equal; local conditions and user preference may cause hydromorphone, oxymorphone, high - dose oxycodone, or methadone as well as dextromoramide in specific instances such as 1970s Australia, to top that particular list. The stop-gap drugs used by the largest absolute number of heroin addicts is probably codeine, with significant use also of dihydro codeine , poppy straw derivatives like poppy pod and poppy seed tea , propoxyphene , and tramadol .

The structural formula of morphine was determined by 1925. At least three methods of total synthesis of morphine from starting materials such as coal tar and petroleum distillates have been patented, the first of which was announced in 1952, by Dr. Marshall D. Gates,

Jr at the University of Rochester . Still, the vast majority of morphine is derived from the opium poppy by either the traditional method of gathering latex from the scored unripe pods of the poppy, or processes using poppy straw, the dried pods and stems of the plant, the most widespread of which was invented in Hungary in 1925 and announced in 1930 by chemist János Kábay.

In 2003 there was discovery of endogenous morphine occurring naturally in the human body. Thirty years of speculation were made on this subject because there was a receptor that apparently only reacted to morphine, the mu₃ opiate receptor in human tissue.^[12] Human cells that form in reaction to cancerous neuroblastoma cells have been found to contain trace amounts of endogenous morphine .

4 - Indications :

Morphine can be used as an analgesic in hospital settings to relieve :

- pain in myocardial infarction
- pain in sickle cell crisis
- pain associated with surgical conditions, pre- and postoperatively
- pain associated with trauma
- severe chronic pain, eg.,
 - cancer
 - pain from kidney stones (renal colic, ureterolithiasis)
 - severe back pain

Morphine can also be used :

- as an adjunct to general anesthesia
- in epidural anesthesia or intrathecal analgesia
- for palliative care (i.e., to alleviate pain without curing the underlying reason for it, usually because the latter is found impossible)
- as an antitussive for severe cough

- in nebulized form, for treatment of dyspnea, although the evidence for efficacy is slim . Evidence is better for other routes .
- as an antidiarrheal in chronic conditions (e.g., for diarrhea associated with AIDS , although loperamide (a non - absorbed opioid acting only on the gut is the most commonly used opioid for diarrhea) .

5 - Side effects :

5 – 1 : Constipation :

Like loperamide and other opioids, morphine acts on the myenteric plexus in the intestinal tract, reducing gut motility, causing constipation. The gastrointestinal effects of morphine are mediated primarily by μ - opioid receptors in the bowel. By inhibiting gastric emptying and reducing propulsive peristalsis of the intestine, morphine decreases the rate of intestinal transit. Reduction in gut secretion and increases in intestinal fluid absorption also contribute to the constipating effect . Opioids also may act on the gut indirectly through tonic gut spasms after inhibition of nitric oxide generation.^[16] This effect was shown in animals when a nitric oxide precursor, L-Arginine, reversed morphine - induced changes in gut motility .

5 – 2 : Addiction :

In controlled studies comparing the physiological and subjective effects of injected heroin and morphine in individuals formerly addicted to opiates, subjects showed no preference for one drug over the other. Equipotent, injected doses had comparable action courses, with no difference in subjects' self-rated feelings of euphoria, ambition, nervousness, relaxation, drowsiness, or sleepiness.^[10] Short-term addiction studies by the same researchers demonstrated that tolerance developed at a similar rate to both heroin and morphine. When compared to the opioids hydromorphone, fentanyl, oxycodone, and pethidine/meperidine, former addicts showed a strong preference for heroin and morphine, suggesting that heroin and morphine are particularly susceptible to abuse and addiction. Morphine and heroin

were also much more likely to produce euphoria and other positive subjective effects when compared to these other opioids.^[10]

Other studies such as the Rat Park experiments suggest that morphine is less physically addictive than others suggest, and most studies on morphine addiction merely show that "severely distressed animals, like severely distressed people, will relieve their distress pharmacologically if they can ". In these studies rats with a morphine "addiction" overcome their addiction themselves when placed in decent living environments with enough space, good food, companionship, areas for exercise, areas for privacy . More recent research has shown that an enriched environment may decrease morphine addiction in mice .

Morphine is a potentially highly addictive substance, as it can cause psychological dependence and physical dependence as well as tolerance, with an addiction potential identical to that of heroin. When used illicitly, a very serious narcotic habit can develop in a matter of weeks whereas iatrogenic morphine addiction rates have, according to a number of studies, remained nearly constant at one case in 150 to 200 for at least two centuries . In the presence of pain and the other disorders for which morphine is indicated for use, a combination of psychological and physiological factors tend to prevent true addiction from developing, although physical dependence and tolerance will develop with protracted opioid therapy, and these two factors do *not* add up to addiction without psychological dependence which manifests primarily as a morbid seek orientation for the drug .

5 – 3 : Tolerance :

Tolerance to the analgesic effects of morphine is fairly rapid. There are several hypotheses about how tolerance develops, including opioid receptor phosphorylation (which would change the receptor conformation) , functional decoupling of receptors from G - proteins (leading to receptor desensitization) , mu - opioid receptor internalization and/or receptor down - regulation (reducing the number of available receptors for morphine to act on) , and upregulation of the cAMP pathway (a counterregulatory mechanism to opioid effects) , CCK might mediate some counter-regulatory

pathways responsible of opioid tolerance. CCK - antagonist drugs , specifically proglumide , have been shown to slow down the development of tolerance to morphine .

5 – 4 : With drawal :

The withdrawal symptoms associated with morphine addiction are usually experienced shortly before the time of the next scheduled dose, sometimes within as early as a few hours (usually between 6 – 12 hours) after the last administration. Early symptoms include watery eyes, insomnia, diarrhea, runny nose, yawning, dysphoria, and sweating and in some cases a strong drug craving. Severe headache, restlessness, irritability, loss of appetite, body aches, severe abdominal pain, nausea and vomiting, tremors, and even stronger and more intense drug craving appear as the syndrome progresses. Severe depression and vomiting are very common. During the acute withdrawal period systolic and diastolic blood pressure increase, usually beyond pre-morphine levels, and heart rate increases , which could potentially cause a heart attack, blood clot, or stroke.

Chills or cold flashes with goose bumps ("cold turkey") alternating with flushing (hot flashes), kicking movements of the legs ("kicking the habit") and excessive sweating are also characteristic symptoms . Severe pains in the bones and muscles of the back and extremities occur, as do muscle spasms. At any point during this process, a suitable narcotic can be administered that will dramatically reverse the withdrawal symptoms. Major withdrawal symptoms peak between 48 and 96 hours after the last dose and subside after about 8 to 12 days. Sudden withdrawal by heavily dependent users who are in poor health is very rarely fatal. Morphine withdrawal is considered less dangerous than alcohol , barbiturate , or benzo diazepam with drawal .

The psychological dependence associated with morphine addiction is complex and protracted. Long after the physical need for morphine has passed, the addict will usually continue to think and talk about the use of morphine (or other drugs) and feel strange or overwhelmed coping with daily activities without being under the influence of morphine . Psychological with drawal from morphine is a

very long and painful process . Addicts often suffer severe depression, anxiety, insomnia, mood swings, amnesia (forgetfulness) , low self – esteem , confusion , paranoia , and other psychological disorders . The psychological dependence on morphine can, and usually does, last a lifetime . There is a high probability that relapse will occur after morphine withdrawal when neither the physical environment nor the behavioral motivators that contributed to the abuse have been altered. Testimony to morphine's addictive and reinforcing nature is its relapse rate. Abusers of morphine (and heroin) , have one of the highest relapse rates among all drug users.

5 – 4 – 1 : Hepatitis C :

Researchers at the University of Pennsylvania have demonstrated that morphine withdrawal complicates hepatitis C by suppressing IFN-alpha-mediated immunity and enhancing virus replication. Hepatitis C virus (HCV) is common among intravenous drug users. This high association has piqued interest in determining the effects of drug abuse, specifically morphine and heroin, on progression of the disease. The discovery of such an association would impact treatment of both HCV infection and drug abuse .

6 - Contraindications :

The following conditions are relative contraindications for morphine :

- acute respiratory depression
- renal failure (due to accumulation of the metabolites morphine – 3 - glucuronide and morphine – 6 - glucuronide
- chemical toxicity (potentially lethal in low tolerance subjects)
- raised intracranial pressure, including head injury (risk of worsening respiratory depression)
- Biliary colic .

Although it has previously been thought that morphine was contraindicated in acute pancreatitis , a review of the literature shows no evidence for this .

7 - Pharmacology :

Endogenous opioids include endorphins, enkephalins, dynorphins, and even **morphine** itself. Morphine appears to mimic endorphins. Endogenous endorphins are responsible for analgesia (reducing pain), causing sleepiness, and feelings of pleasure. They can be released in response to pain, strenuous exercise, orgasm, or excitement.

Morphine is the prototype narcotic drug and is the standard against which all other opioids are tested. It interacts predominantly with the μ - opioid receptor. These μ -binding sites are discretely distributed in the human brain, with high densities in the posterior amygdala, hypothalamus, thalamus, nucleus caudatus, putamen, and certain cortical areas. They are also found on the terminal axons of primary afferents within laminae I and II (substantia gelatinosa) of the spinal cord and in the spinal nucleus of the trigeminal nerve .

Morphine is a phenanthrene opioid receptor agonist – its main effect is binding to and activating the μ - opioid receptors in the central nervous system. In clinical settings, morphine exerts its principal pharmacological effect on the central nervous system and gastrointestinal tract. Its primary actions of therapeutic value are analgesia and sedation. Activation of the μ -opioid receptors is associated with analgesia, sedation, euphoria, physical dependence, and respiratory depression. Morphine is a rapid - acting narcotic, and it is known to bind very strongly to the μ - opioid receptors, and for this reason, it often has a higher incidence of euphoria/dysphoria, respiratory depression, sedation, pruritus, tolerance, and physical and psychological dependence when compared to other opioids at equianalgesic doses. Morphine is also a κ - opioid and δ - opioid receptor agonist , κ - opioid's action is associated with spinal analgesia, miosis (pinpoint pupils) and psychotomimetic effects . δ - opioid is thought to play a role in analgesia . Although morphine does not bind to the σ -opioid receptor, it has been shown that sigma agonists, such as (+) pentazocine, antagonize morphine analgesia, and sigma antagonists enhance morphine analgesia , suggesting some interaction between morphine and the σ - opioid receptor .

The effects of morphine can be countered with opioid antagonists such as naloxone and naltrexone; the development of tolerance to morphine may be inhibited by NMDA antagonists such as ketamine or dextromethorphan . The rotation of morphine with chemically dissimilar opioids in the long-term treatment of pain will slow down the growth of tolerance in the longer run, particularly agents known to have significantly incomplete cross - tolerance with morphine such as levorphanol, ketobemidone, piritramide, and methadone and its derivatives; all of these drugs also have NMDA antagonist properties. It is believed that the strong opioid with the most incomplete cross-tolerance with morphine is either methadone or dextro moramide .

7 – 1 : Gene expression :

Studies have shown that morphine can alter the expression of a number of genes. A single injection of morphine has been shown to alter the expression of two major groups of genes, for proteins involved in mitochondrial respiration and for cytoskeleton-related proteins .

7 - 2 : Effects on the immune system :

Morphine has long been known to act on receptors expressed on cells of the central nervous system resulting in pain relief and analgesia. In the 1970s and '80s, evidence suggesting that opiate drug addicts show increased risk of infection (such as increased pneumonia, tuberculosis, and HIV) led scientists to believe that morphine may also affect the immune system. This possibility increased interest in the effect of chronic morphine use on the immune system.

The first step of determining that morphine may affect the immune system was to establish that the opiate receptors known to be expressed on cells of the central nervous system are also expressed on cells of the immune system. One study successfully showed that dendritic cells, part of the innate immune system, display opiate receptors. Dendritic cells are responsible for producing cytokines, which are the tools for communication in the immune system. This same study showed that dendritic cells chronically treated with morphine during their differentiation produce more interleukin-12 (IL-

12) , a cytokine responsible for promoting the proliferation, growth, and differentiation of T-cells (another cell of the adaptive immune system) and less interleukin-10 (IL-10), a cytokine responsible for promoting a B - cell immune response (B cells produce antibodies to fight off infection) .

This regulation of cytokines appear to occur via the p38 MAPKs (mitogen activated protein kinase) dependent pathway. Usually, the p38 within the dendritic cell expresses TLR 4 (toll-like receptor 4), which is activated through the ligand LPS (lipopolysaccharide). This causes the p38 MAPK to be phosphorylated. This phosphorylation activates the p38 MAPK to begin producing IL-10 and IL-12. When the dendritic cell is chronically exposed to morphine during their differentiation process then treated with LPS, the production of cytokines is different. Once treated with morphine, the p38 MAPK does not produce IL-10, instead favoring production of IL-12. The exact mechanism through which the production of one cytokine is increased in favor over another is not known. Most likely, the morphine causes increased phosphorylation of the p38 MAPK. Transcriptional level interactions between IL-10 and IL-12 may further increase the production of IL-12 once IL-10 is not being produced. Future research may target the exact mechanism that increases the production of IL-12 in morphine treated dendritic cells. This increased production of IL-12 causes increased T-cell immune response. This response is due to the ability of IL-12 to cause T helper cells to differentiate into the Th1 cell, causing a T cell immune response .

Further studies on the effects of morphine on the immune system have shown that morphine influences the production of neutrophils and other cytokines. Since cytokines are produced as part of the immediate immunological response (inflammation), it has been suggested that they may also influence pain. In this way, cytokines may be a logical target for analgesic development. Recently, one study has used an animal model (hind - paw incision) to observe the effects of morphine administration on the acute immunological response. Following hind-paw incision, pain thresholds and cytokine production were measured. Normally, cytokine production in and around the

wounded area increases in order to fight infection and control healing (and, possibly, to control pain), but pre-incisional morphine administration (0.1-10.0 mg/kg) reduced the number of cytokines found around the wound in a dose-dependent manner. The authors suggest that morphine administration in the acute post - injury period may reduce resistance to infection and may impair the healing of the wound .

8 - Pharmacokinetics :

8 – 1 : Absorption and metabolism :

Morphine can be taken orally , rectally , subcutaneously , intravenously, intrathecally or epidurally. On the streets, it is becoming more common to inhale (“chasing the dragon”), but for medicinal purposes, intravenous (IV) injection is the most common method of administration. Morphine is subject to extensive first-pass metabolism (a large proportion is broken down in the liver), so if taken orally, only 40-50% of the dose reaches the central nervous system. Resultant plasma levels after subcutaneous (SC), intramuscular (IM), and IV injection are all comparable. After IM or SC injections, morphine plasma levels peak in approximately 20 minutes, and after oral administration levels peak in approximately 30 minutes.^[36] Morphine is metabolised primarily in the liver and approximately 87 % of a dose of morphine is excreted in the urine within 72 hours of administration. Morphine is primarily metabolized into morphine-3-glucuronide (M3G) and morphine - 6 - glucuronide (M6G) via glucuronidation by phase II metabolism enzyme UDP-glucuronosyl transferase - 2B7 (UGT2B7). About 60 % of morphine is converted to M3G, and 6–10% is converted to M6G.^[38] The cytochrome P450 (CYP) family of enzymes involved in phase I metabolism plays a lesser role.^[citation needed] Not only does the metabolism occur in the liver but it may also take place in the brain and the kidneys. M3G does not undergo opioid receptor binding and has no analgesic effect. M6G binds to mu-receptors and is a more potent analgesic than morphine.^[38] Morphine may also be metabolized into small amounts of normorphine, codeine, and hydromorphone. Metabolism rate is determined by gender, age, diet, genetic makeup, disease state (if any) and use of other

medications. The elimination half - life of morphine is approximately 120 minutes, though there may be slight differences between men and women. Morphine can be stored in fat, and thus can be detectable even after death. Morphine is able to cross the blood - brain barrier but because of poor lipid solubility, protein binding, rapid conjugation with glucuronic acid and ionization, it does not cross easily. Diamorphine, which is derived from morphine, crosses the blood-brain barrier more easily, making it more potent .

9 - Effects on human performance :

Most reviews conclude that opioids produce minimal impairment of human performance on tests of sensory, motor, or attentional abilities. However, recent studies have been able to show some impairments caused by morphine, which is not surprising given that morphine is a central nervous system depressant. Morphine has resulted in impaired functioning on critical flicker frequency (a measure of overall CNS arousal) and impaired performance on the Maddox Wing test (a measure of deviation of the visual axes of the eyes). Few studies have investigated the effects of morphine on motor abilities; a high dose of morphine can impair finger tapping and the ability to maintain a low constant level of isometric force (ie. fine motor control is impaired) , though no studies have shown a correlation between morphine and gross motor abilities .

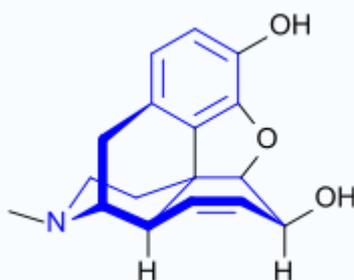
In terms of cognitive abilities, one study has shown that morphine may have a negative impact on anterograde and retrograde memory^[41], but these effects are minimal and are transient. Overall, it seems that acute doses of opioids in non - tolerant subjects produce minor effects in some sensory and motor abilities, and perhaps also in attention and cognition. It is likely that the effects of morphine will be more pronounced in opioid-naive subjects than chronic opioid users.

In chronic opioid users, such as those on Chronic Opioid Analgesic Therapy (COAT) for managing severe, chronic pain, behavioural testing has shown normal functioning on perception, cognition, coordination and behaviour in most cases. One recent study^[42] analysed COAT patients in order to determine whether they were able to safely operate a motor vehicle. The findings from this

study suggest that stable opioid use does not significantly impair abilities inherent in driving (this includes physical, cognitive and perceptual skills). COAT patients showed rapid completion of tasks which require speed of responding for successful performance (eg. Rey Complex Figure Test) but made more errors than controls. COAT patients showed no deficits in visual-spatial perception and organization (as shown in the WAIS-R Block Design Test) but did show impaired immediate and short-term visual memory (as shown on the Rey Complex Figure Test – Recall). These patients showed no impairments in higher order cognitive abilities (ie. Planning). COAT patients appeared to have difficulty following instructions and showed a propensity towards impulsive behaviour, yet this did not reach statistical significance. Importantly, this study reveals that COAT patients have no domain - specific deficits, which supports the notion that chronic opioid use has minor effects on psychomotor, cognitive, or neuropsychological functioning.

It is difficult to study the performance effects of morphine without considering why a person is taking morphine. Opioid-naive subjects are volunteers in a pain-free state. However, most chronic-users of morphine use it to manage pain. Pain is a stressor and so it can confound performance results, especially on tests that require a large degree of concentration. Pain is also variable, and will vary over time and from person to person. It is unclear to what extent the stress of pain may cause impairments, and it is also unclear whether morphine is potentiating or attenuating these impairments.

10 – Chemistry :



Morphine is a benzyl iso quinoline alkaloid with two additional ring closures .

Most of the licit morphine produced is used to make codeine by methylation . It is also a precursor for many drugs including heroin (di acetyl morphine) , hydro morphone , and oxy morphone . Replacement of the N- methyl group of morphine with an N-phenylethyl group results in a product that is 18 times more powerful than morphine in its opiate agonist potency. Combining this modification with the replacement of the 6 - hydroxyl with a 6 - methylene produces a compound some 1,443 times more potent than morphine, stronger than the Bentley compounds such as etorphine.

The structure - activity relationship of morphine has been extensively studied. The structural formula of morphine was determined in 1925 and confirmed in 1952 when two methods of total synthesis were also published. As a result of the extensive study and use of this molecule, more than 200 morphine derivatives (also counting codeine and related drugs) have been developed since the last quarter of the 19th Century. These drugs range from 25 per cent the strength of codeine or a little over 2 per cent of the strength of morphine, to several hundred times the strength of morphine to several powerful opioid antagonists including naloxone (Narcan), naltrexone (Trexan), and nalorphine (Nalline) for human use and also the amongst strongest antagonists known, such as diprenorphine (M5050), the reversing agent in the Immobilon large animal tranquilliser dart kit; the tranquilliser is another ultra-potent morphine derivative/structural analogue, viz., etorphine (M99). Morphine-derived agonist-antagonist drugs have also been developed. Elements of the morphine structure have been used to create completely synthetic drugs such as the morphinan family (levorphanol, dextromethorphan and others) and other groups which have many members with morphine - like qualities. The modification of morphine and the aforementioned synthetics has also given rise to non-narcotic drugs with other uses such as emetics, stimulants, anti tussives, anti cholinergics , muscle relaxants , local anaesthetics , general anaesthetics , and others .

Most semi - synthetic opioids, both of the morphine and codeine subgroups, are created by modifying one or more of the following :

- Halogenating or making other modifications at positions 1 and/or 2 on the morphine carbon skeleton.

- The methyl group which makes morphine into codeine can be removed or added back, or replaced with another functional group like ethyl and others to make codeine analogues of morphine-derived drugs and vice versa. Codeine analogues of morphine-based drugs often serve as prodrugs of the stronger drug, as in codeine & morphine, hydro codone & hydro morphine, oxy codone & oxy morphine, nico codeine & nico morphine, dihydro codeine and dihydro morphine, &c. &c.

- Saturating, opening, or other changes to the bond between positions 7 and 8, as well as adding, removing, or modifying functional groups to these positions; saturating, reducing, eliminating, or otherwise modifying the 7-8 bond and attaching a functional group at 14 yields hydromorphanol; the oxidation of the hydroxyl group to a carbonyl and changing the 7-8 bond to single from double changes codeine into oxycodone.

- Attachment, removal or modification of functional groups to positions 3 and / or 6 (dihydro codeine and related, hydro codone, nico morphine) ; in the case of moving the methyl functional group from position 3 to 6, codeine becomes hetero codeine which is 72 times stronger, and therefore six times stronger than morphine.

- Attachment of functional groups or other modification at position 14 (oxy morphine, oxy codone, naloxone)

- Modifications at positions 2, 4, 5 or 17, usually along with other changes to the molecule elsewhere on the morphine skeleton. Often this is done with drugs produced by catalytic reduction, hydrogenation, oxidation, or the like, producing strong derivatives of morphine and codeine.

Both morphine and its hydrated form, $C_{17}H_{19}NO_3 \cdot H_2O$, are sparingly soluble in water. In five liters of water, only one gram of the hydrate will dissolve. For this reason, pharmaceutical companies produce sulfate and hydrochloride salts of the drug, both of which are over 300 times more water-soluble than their parent molecule. Whereas the pH of a saturated morphine hydrate solution is 8.5, the

salts are acidic. Since they derive from a strong acid but weak base, they are both at about pH = 5; as a consequence, the morphine salts are mixed with small amounts of NaOH to make them suitable for injection .

A number of salts of morphine are used, with the most common in current clinical use being the hydrochloride, sulphate, tartrate, acetate, citrate; less commonly methobromide, hydrobromide, hydroiodide, lactate, chloride, and bitartrate and the others listed below. Morphine meconate is a major form of the alkaloid in the poppy, as is morphine pectinate, nitrate and some others. Like codeine, dihydrocodeine and other, especially older, opiates, morphine has been used as the salicylate salt by some suppliers and can be easily compounded, imparting the therapeutic advantage of both the opioid and the NSAID ; multiple barbiturate salts of morphine were also used in the past, as was/is morphine valerate, the salt of the acid being the active principle of valerian. Calcium morphenate is the intermediate in various latex and poppy - straw methods of morphine production. Morphine ascorbate and other salts such as the tannate, citrate, and acetate, phosphate, valerate and others may be present in poppy tea depending on the method of preparation. Morphine valerate produced industrially was one ingredient of a medication available for both oral and parenteral administration popular many years ago in Europe and elsewhere called Trivalin (not to be confused with the current, unrelated herbal preparation of the same name) which also included the valerates of caffeine and cocaine, with a version containing codeine valerate as a fourth ingredient being distributed under the name Tetravalin.

Closely related to morphine are the opioids morphine - N - oxide (geno morphine) which is a pharmaceutical which is no longer in common use ; and pseudomorphine, an alkaloid which exists in opium form as degradation products of morphine .

10 - 1 : Production :

A Hungarian chemist, János Kabay , found and internationally patented a method to extract morphine from " poppy straw " : dried poppy pods and stem, and other parts of the dry plant , except for

seeds and root. In natural form, in poppy plant, the alkaloids are bound to meconic acid. The method is to extract from the crushed plant with diluted sulfuric acid, which is a stronger acid than meconic acid, but not so strong to react with alkaloid molecules. The extraction is performed in many steps (one amount of crushed plant is at least six to ten times extracted, so practically every alkaloid goes into the solution). From the solution obtained at the last extraction step, the alkaloids are precipitated by either ammonium hydroxide or sodium carbonate. The last step is purifying and separating morphine from other opium alkaloids. Opium poppy contains at least 40 different alkaloids, but most of them are of very low concentration. Morphine is the principal alkaloid in raw opium and constitutes ~ 8 - 19 % of opium by dry weight (depending on growing conditions) . In the 1950s and 1960s, Hungary supplied nearly 60 % of Europe's total medication-purpose morphine production. To this day , poppy farming is legal in Hungary, but poppy farms are limited by law to 2 acres (8 , 100 m²) . It is also legal to sell dried poppy in flower shops for use in floral arrangements .

It was announced in 1973 that a team at the National Institutes of Health in the United States had developed a method for total synthesis of morphine, codeine, and thebaine using coal tar as a starting material. A shortage in codeine-hydrocodone class cough suppressants (all of which can be made from morphine in one or more steps, as well as from codeine or thebaine) was the initial reason for the research .

Most morphine produced for pharmaceutical use around the world is actually converted into codeine as the concentration of the latter in both raw opium and poppy straw is much lower than that of morphine; in most countries the usage of codeine (both as end - product and precursor) is at least an order of magnitude greater than that of morphine on a weight basis and codeine is by far the most commonly-used opioid in the world. Whilst strains of poppies have been engineered to produce much higher yields of the other useful opioid pharmaceutical precursors thebaine and oripavine, no known strain of *P. somniferum* will produce more codeine than morphine under most or all possible conditions .

11 - Illicit use :

The euphoria, comprehensive alleviation of distress and therefore all aspects of suffering, promotion of sociability and empathy, "body high", and anxiolysis provided by narcotic drugs including the opioids can cause the use of high doses in the absence of pain for a protracted period, which can impart a morbid craving for the drug in the user. Being the prototype of the entire opioid class of drugs means that morphine has properties that may lend it to misuse. Morphine addiction is the model upon which the current perception of addiction is based.

Animal and human studies and clinical experience back up the contention that morphine is one of the most euphoric of drugs, and via all but the IV route heroin and morphine cannot be distinguished according to studies. Chemical changes to the morphine molecule yield other powerful euphorigenics such as dihydromorphine, hydromorphone (Dilaudid, Hydral) and oxymorphone (Numorphan , Opana) as well as the latter three's methylated equivalents dihydrocodeine, hydrocodone and oxycodone respectively; in addition to heroin , there are dipropan oyl morphine , diacetyl dihydro morphine and other members of the 3 , 6 morphine diester category like nicomorphine and other similar semi-synthetic opiates like deso morphine, hydro morphinol &c . used clinically in many countries of the world but in many cases also produced illicitly in rare instances.

Misuse of morphine generally entails taking more than prescribed or outside of medical supervision, injecting oral formulations, mixing it with unapproved potentiators such as alcohol, cocaine, and the like, and/or defeating the extended-release mechanism by chewing the tablets or turning into a powder for snorting or preparing injectables. The latter method can be every bit as time-consuming and involved as traditional methods of smoking opium . This and the fact that the liver destroys a large percentage of the drug on the first pass impacts the demand side of the equation for clandestine re-sellers, as many customers are not needle users and may have been disappointed with ingesting the drug orally. As morphine is generally as hard or harder to divert than oxy codone in a lot of cases, morphine in any form is

uncommon on the street, although ampoules and phials of morphine injection, pure pharmaceutical morphine powder, and soluble multi-purpose tablets are very popular where available.

Morphine is also available in a paste which is used in the production of heroin which can be smoked by itself or turned to a soluble salt and injected; the same goes for the penultimate products of the Kompot (Polish Heroin) and black tar processes. Poppy straw as well as opium can yield morphine of purity levels ranging from poppy tea to near-pharmaceutical grade morphine by itself or with all of the more than 50 other alkaloids. It also is the active narcotic ingredient in opium and all of its forms, derivatives, and analogues as well as forming from breakdown of heroin and otherwise being present in many batches of illicit heroin as the result of incomplete acetylation .

11 – 1 : Precursor to other opioids, in a pharmaceutical manufacturing setting :

Morphine is a precursor in the manufacture in a large number of opioids such as dihydromorphine, hydromorphone, nicomorphine, and heroin as well as codeine, which itself has a large family of semi-synthetic derivatives. Morphine is commonly treated with acetic anhydride and ignited to yield heroin.^[44] The pharmacology of heroin and morphine is identical except the two acetyl groups increase the lipid solubility of the heroin molecule, causing it to cross the blood-brain barrier and enter the brain more rapidly. Once in the brain, these acetyl groups are removed to yield morphine, which causes the subjective effects of heroin. Thus, heroin may be thought of as a more rapidly acting form of morphine .

11 - 2 : Precursor to other opioids, in an underground and illicit setting :

Illicit morphine is rarely produced from codeine found in over the counter cough and pain medicines. This demethylation reaction is often performed using pyridine and hydrochloric acid .

Another source of illicit morphine comes from the extraction of morphine from extended release morphine products, such as MS-Contin. Morphine can be extracted from these products with simple extraction techniques to yield a morphine solution that can be injected. Alternatively, the tablets can be crushed and snorted, injected or swallowed, although this provides much less euphoria although retaining some of the extended-release effect and the extended-release property is why MS - Contin is used in some countries alongside methadone, dihydro codeine, buprenorphine, dihydro etorphine, piritramide, levo - alpha - acetyl methadol (LAAM) and special 24 - hour formulations of hydro morphone for maintenance and detoxification of those physically dependent on opioids.

Another means of using or misusing morphine is to use chemical reactions to turn it into heroin or another stronger opioid. Morphine can, using a technique reported in New Zealand (where the initial precursor is codeine) and elsewhere known as home-bake, be turned into what is usually a mixture of morphine, heroin, 3 - mono acetyl morphine, 6 - mono acetyl morphine, and codeine derivatives like acetyl codeine if the process is using morphine made from demethylating codeine by mixing acetic anhydride or acetyl chloride with the morphine and cooking it in an oven between 80 and 85°C for several hours.

Since heroin is one of a series of 3,6 diesters of morphine, it is possible to convert morphine to nicomorphine (Vilan) using nicotinic anhydride, dipropanoyl morphine with propionic anhydride, dibutanoyl morphine and disalicyloyl morphine with the respective acid anhydrides. Glacial Acetic acid can be used to obtain a mixture high in 6 - monoacetylmorphine, nicotinic acid (Vitamin B3) in some form would be precursor to 6 - nicotinylmorphine, salicylic acid may yield the salicyoyl analogue of 6 - MAM, and so on.

Homebake or other clandestinely - produced heroin produced from extended - release morphine tablets may be known as Blue Heroin because of the blue colour of some of these tablets, even though the coloured coating of the tablet is usually removed before processing, many strengths of the tablets are not blue, bluish or a

related colour like purple, and the final product tends not to be blue. A writer of a 2006 description of producing heroin from 100 mg as well as some 30 and 15 mg MS - Contin type tablets coined the term Blue Heroin to distinguish his, her or their product from New Zealand - style homebake as the process was shorter and began with uncoated tablets which in the case of the 100 mg tablet was at or above 35 per cent morphine sulphate by weight, resulting in a final liquid injectable which was brown-purple and quite potent . The drugs present in the final product are limited to heroin, 6 – mono acetyl morphine , 3 – monoacetyl morphine, and morphine , with the 6 - MAM being just as or more sought than the heroin for reasons elucidated in the Wikipedia heroin article .

The clandestine conversion of morphine to ketones of the hydromorphone class or other derivatives like dihydro morphine (Paramorfan) , desomorphine (Permonid) , metopon &c. and codeine to hydrocodone (Dicodid) , dihydro codeine (Paracodin) &c . is more involved, time consuming, requires lab equipment of various types , and usually requires expensive catalysts and large amounts of morphine at the outset and is less common but still has been discovered by authorities in various ways during the last 20 years or so. Dihydro morphine can be acetylated into another 3 , 6 morphine diester , namely diacetyl dihydro morphine (Paralaudin) , and hydrocodone into thebacon .

12 - Legal classification :

- In the United Kingdom, morphine is listed as a Class A drug under the Misuse of Drugs Act 1971 and a Schedule 2 Controlled Drug under The Misuse of Drugs Regulations 2001.
- In the United States, morphine is classified as a Schedule II drug under the Controlled Substances Act.
- In Canada, morphine is classified as a Schedule I drug under the Controlled Drugs and Substances Act.
- In Australia, morphine is classified as a Schedule 8 drug under the variously titled State and Territory Poisons Acts.
- In the Netherlands, morphine is classified as a List 1 drug under the Opium Law.

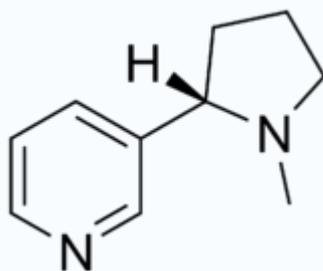
- In Japan, morphine is classified as a narcotic under the Narcotics and Psychotropics Control Act.
- Internationally, morphine is a Schedule I drug under the Single Convention on Narcotic Drugs .

13 - Access to morphine in poor countries :

Although morphine is cheap, people in poorer countries often do not have access to it. According to a 2005 estimate by the International Narcotics Control Board , six countries (Australia , Britain , Canada , France , Germany , and the United States) consume 79 percent of the world's morphine . The less affluent countries , accounting for 80 percent of the world's population, consumed only about 6 percent of the global morphine supply . Some countries import virtually no morphine, and in others the drug is rarely available even for relieving severe pain while dying .

Experts in pain management attribute the under-distribution of morphine to an unwarranted fear of the drug's potential for addiction and abuse. While morphine is clearly addictive, Western doctors believe it is worthwhile to use the drug and then wean the patient off when the treatment is over .

Nicotine



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1 – Introduction :

Nicotine is an alkaloid found in the nightshade family of plants (*Solanaceae*) which constitutes approximately 0.6 – 3.0 % of dry weight of tobacco , with biosynthesis taking place in the roots, and accumulating in the leaves. It functions as an antiherbivore chemical with particular specificity to insects; therefore nicotine was widely used as an insecticide in the past , and currently nicotine analogs such as imidacloprid continue to be widely used.

In low concentrations (an average cigarette yields about 1 mg of absorbed nicotine), the substance acts as a stimulant in mammals and is the main factor responsible for the dependence-forming properties of tobacco smoking. According to the American Heart Association, the "nicotine addiction has historically been one of the hardest addictions to break". The pharmacological and behavioral characteristics that determine tobacco addiction are similar to those that determine addiction to drugs such as heroin and cocaine.^[5] Nicotine content in cigarettes has actually slowly increased over the years, and one study found that there was an average increase of 1.6% per year between the years of 1998 and 2005. This was found for all major market categories of cigarettes .

Systematic (IUPAC) name	
3 - [(2S) -1- methyl pyrrolidin – 2 - yl]pyridine	
Formula	C₁₀ H₁₄ N₂
Mol. mass	162 g / mol
SMILES	eMolecules & Pub Chem
Density	1.01 g / cm ³
Melt. Point	-79 °C (-110 °F)
Boiling Point	247 °C (477 °F)
Pharmacokinetic data	
Bioavailability	20 to 45 % (oral)
Half life	2 hours

2 - History and name :

Nicotine is named after the tobacco plant *Nicotiana tabacum*, which in turn is named after Jean Nicot de Villemain, French ambassador in Portugal, who sent tobacco and seeds from Brazil to Paris in 1560 and promoted their medicinal use. Nicotine was first isolated from the tobacco plant in 1828 by German chemists Posselt & Reimann, who considered it a poison . Its chemical empirical formula was described by Melsens in 1843 , its structure was discovered by

Garry Pinner in 1893 , and it was first synthesized by A . Pictet and Crepieux in 1904 .

3 – Chemistry :

Nicotine is a hygroscopic, oily liquid that is miscible with water in its base form. As a nitrogenous base, nicotine forms salts with acids that are usually solid and water soluble. Nicotine easily penetrates the skin. As shown by the physical data, free base nicotine will burn at a temperature below its boiling point, and its vapors will combust at 308 K (35 °C ; 95 °F) in air despite a low vapor pressure. Because of this, most of the nicotine is burned when a cigarette is smoked; however, enough is inhaled to provide the desired effects. The amount of nicotine inhaled with tobacco smoke is a fraction of the amount contained in the tobacco leaves.

4 - Optical activity :

Nicotine is optically active, having two enantiomeric forms . The naturally - occurring form of nicotine is levo rotatory , with $[\alpha]_D = -166.4^\circ$. The dextro rotatory form , (+) – nicotine , has only one - half the physiological activity of (–) - nicotine. It is therefore weaker in the sense that a higher dose is required to attain the same effects.^[10] The salts of (+) - nicotine are usually dextro rotatory .

5 - Pharmacology :

5 – 1 : Pharma cokinetics :

As nicotine enters the body , it is distributed quickly through the bloodstream and can cross the blood - brain barrier . On average it takes about seven seconds for the substance to reach the brain when inhaled . The half life of nicotine in the body is around two hours .

The amount of nicotine absorbed by the body from smoking depends on many factors, including the type of tobacco, whether the smoke is inhaled, and whether a filter is used. For chewing tobacco, dipping tobacco, snus and snuff, which are held in the mouth between the lip and gum, or taken in the nose, the amount released into the body tends to be much greater than smoked tobacco. Nicotine is

metabolized in the liver by cytochrome P450 enzymes (mostly CYP2A6, and also by CYP2B6) . A major metabolite is cotinine .

Other primary metabolites include nicotine N'- oxide , nornicotine , nicotine isomethonium ion , 2 – hydroxy nicotine and nicotine glucuronide .

Gluconuration and oxidative metabolism of nicotine to cotinine are both inhibited by menthol , an additive to mentholated cigarettes, thus increasing the half-life of nicotine *in vivo* .

5 – 2 : Pharma codynamics :

Nicotine acts on the nicotinic acetylcholine receptors , specifically the ganglion type nicotinic receptor and one CNS nicotinic receptor . The former is present in the adrenal medulla and elsewhere , while the latter is present in the central nervous system (CNS) . In small concentrations, nicotine increases the activity of these receptors . Nicotine also has effects on a variety of other neurotransmitters through less direct mechanisms .

5 – 2 – 1 : In CNS :

By binding to nicotinic acetylcholine receptors, nicotine increases the levels of several neurotransmitters - acting as a sort of "volume control". It is thought that increased levels of dopamine in the reward circuits of the brain are responsible for the euphoria and relaxation and eventual addiction caused by nicotine consumption. A single amino-acid difference between brain and muscle acetylcholine receptors explains why nicotine activates the CNS but does not activate skeletal muscles and cause instant death. Nicotine addiction is therefore a biological oddity .

Tobacco smoke contains the monoamine oxidase inhibitors harman, norharman , anabasine, anatabine, and nornicotine . These compounds significantly decrease MAO activity in smokers . MAO enzymes break down mono aminergic neuro transmitters such as dopamine, norepinephrine , and serotonin .

Chronic nicotine exposure via tobacco smoking up - regulates alpha 4 beta 2 * n AChR in cerebellum and brainstem regions but not habenulopeduncular structures. Alpha 4 beta 2 and alpha 6 beta 2 receptors , present in the ventral tegmental area , play a crucial role in mediating the reinforcement effects of nicotine .

5 -2 -2 : In PNS :

Nicotine also activates the sympathetic nervous system,^[21] acting via splanchnic nerves to the adrenal medulla, stimulates the release of epinephrine. Acetylcholine released by preganglionic sympathetic fibers of these nerves acts on nicotinic acetylcholine receptors, causing the release of epinephrine (and norepinephrine) into the blood stream. Nicotine also has an affinity for melanin - containing tissues due to its precursor function in melanin synthesis or its irreversible binding of melanin and nicotine. This has been suggested to underlie the increased nicotine dependence and lower smoking cessation rates in darker pigmented individuals .

5 -2 -3 : In adrenal medulla :

By binding to ganglion type nicotinic receptors in the adrenal medulla nicotine increases flow of adrenaline (epinephrine) , a stimulating hormone . By binding to the receptors, it causes cell depolarization and an influx of calcium through voltage-gated calcium channels . Calcium triggers the exocytosis of chromaffin granules and thus the release of epinephrine (and norepinephrine) into the blood stream . The release of epinephrine (adrenaline) causes an increase in heart rate , blood pressure and respiration , as well as higher blood glucose levels .

Cotinine is a byproduct of the metabolism of nicotine which remains in the blood for up to 48 hours. It can therefore be used as an indicator of a person's exposure to nicotine .

6 - Psychoactive effects

Nicotine's mood - altering effects are different by report: in particular it is both a stimulant and a relaxant . First causing a release

of glucose from the liver and epinephrine (adrenaline) from the adrenal medulla, it causes stimulation. Users report feelings of relaxation, sharpness, calmness, and alertness . By reducing the appetite and raising the metabolism, some smokers may lose weight as a consequence .

When a cigarette is smoked , nicotine - rich blood passes from the lungs to the brain within seven seconds and immediately stimulates the release of many chemical messengers including acetylcholine, norepinephrine , epinephrine, vasopressin , arginine , dopamine , autocrine agents , and beta - endorphin . This release of neurotransmitters and hormones is responsible for most of nicotine's effects. Nicotine appears to enhance concentration and memory due to the increase of acetyl choline . It also appears to enhance alertness due to the increases of acetyl choline and norepinephrine. Arousal is increased by the increase of norepinephrine . Pain is reduced by the increases of acetyl choline and beta - endorphin . Anxiety is reduced by the increase of beta - endorphin. Nicotine also extends the duration of positive effects of dopamine and increases sensitivity in brain reward systems . Most cigarettes (in the smoke inhaled) contain 0.1 to 2.8 milligrams of nicotine .

Research suggests that, when smokers wish to achieve a stimulating effect, they take short quick puffs, which produce a low level of blood nicotine . This stimulates nerve transmission. When they wish to relax, they take deep puffs , which produce a high level of blood nicotine, which depresses the passage of nerve impulses, producing a mild sedative effect. At low doses, nicotine potently enhances the actions of norepinephrine and dopamine in the brain, causing a drug effect typical of those of psychostimulants. At higher doses, nicotine enhances the effect of serotonin and opiate activity, producing a calming , pain - killing effect. Nicotine is unique in comparison to most drugs, as its profile changes from stimulant to sedative / pain killer in increasing dosages and use .

Technically, nicotine is not significantly addictive, as nicotine administered alone does not produce significant reinforcing properties. However , only after coadministration with an MAOI , such as those

found in tobacco , nicotine produces significant behavioral sensitization , a measure of addiction potential . This is similar in effect to amphetamine .



A 21 mg patch applied to the left arm

Nicotine gum , usually in 2 - mg or 4 - mg doses , and nicotine patches are available, as well as smokeless tobacco which do not have all the other ingredients in smoked tobacco .

7 - Dependence and withdrawal :

Modern research shows that nicotine acts on the brain to produce a number of effects. Specifically, its addictive nature has been found to show that nicotine activates reward pathways — the circuitry within the brain that regulates feelings of pleasure and euphoria .

Dopamine is one of the key neurotransmitters actively involved in the brain. Research shows that by increasing the levels of dopamine within the reward circuits in the brain, nicotine acts as a chemical with intense addictive qualities. In many studies it has been shown to be more addictive than cocaine and heroin, though chronic treatment has an opposite effect on reward thresholds . Like other physically addictive drugs, nicotine causes down-regulation of the production of dopamine and other stimulatory neurotransmitters as the brain attempts to compensate for artificial stimulation. In addition, the sensitivity of nicotinic acetylcholine receptors decreases. To compensate for this compensatory mechanism, the brain in turn upregulates the number of receptors, convoluting its regulatory effects with compensatory mechanisms meant to counteract other compensatory mechanisms. The net effect is an increase in reward pathway sensitivity, opposite of other drugs of abuse such as cocaine and heroin, which reduce reward pathway sensitivity . This neuronal

brain alteration persists for months after administration ceases. Due to an increase in reward pathway sensitivity, nicotine withdrawal is relatively mild compared to alcohol or heroin withdrawal . Nicotine also has the potential to cause dependence in many animals other than humans. Mice have been administered nicotine and exhibit withdrawal reactions when its administration is stopped .

A study found that nicotine exposure in adolescent mice retards the growth of the dopamine system, thus increasing the risk of substance abuse during adolescence .

8 - Toxicology :

The LD₅₀ of nicotine is 50 mg / kg for rats and 3 mg / kg for mice. 40 – 60 mg (0.5 - 1.0 mg / kg) can be a lethal dosage for adult humans . Nicotine therefore has a high toxicity in comparison to many other alkaloids such as cocaine, which has an LD₅₀ of 95.1 mg/kg when administered to mice. It is impossible however to overdose on nicotine through smoking alone (though a person can overdose on nicotine through a combination of nicotine patches , nicotine gum, and/or tobacco smoking at the same time) . Spilling an extremely high concentration of nicotine onto the skin can result in intoxication or even death since nicotine readily passes into the bloodstream from dermal contact .

The carcinogenic properties of nicotine in standalone form, separate from tobacco smoke, have not been evaluated by the IARC, and it has not been assigned to an official carcinogen group. The currently available literature indicates that nicotine, on its own, does not promote the development of cancer in healthy tissue and has no mutagenic properties. However, nicotine and the increased cholinergic activity it causes have been shown to impede apoptosis, which is one of the methods by which the body destroys unwanted cells (programmed cell death). Since apoptosis helps to remove mutated or damaged cells that may eventually become cancerous, the inhibitory actions of nicotine may create a more favourable environment for cancer to develop, though this also remains to be proven .

The teratogenic properties of nicotine have not yet been adequately researched, and while the likelihood of birth defects caused by nicotine is believed to be very small or nonexistent, nicotine replacement product manufacturers recommend consultation with a physician before using a nicotine patch or nicotine gum while pregnant or nursing .

Women who use nicotine gum and patches during the early stages of pregnancy face an increased risk of having babies with birth defects, says a study that looked at about 77,000 pregnant women in Denmark. The study found that women who use nicotine-replacement therapy in the first 12 weeks of pregnancy have a 60 percent greater risk of having babies with birth defects, compared to women who are non-smokers, the Daily Mail reported . The findings were published in the journal Obstetrics and Gynaecology .

9 - Nicotine and oxidative stress :

Nicotine is detoxified by the cytochrome p 450 in the liver.

10 - Link to circulatory disease :

Nicotine has very powerful effects on arteries throughout the body. Nicotine is a stimulant, it raises blood pressure, and is a vasoconstrictor, making it harder for the heart to pump through the constricted arteries. It causes the body to release its stores of fat and cholesterol into the blood .

Nicotine has been speculated to increase the risk of blood clots by increasing plasminogen activator inhibitor – 1 , though this has not been proven. Plasma fibrinogen levels are elevated in smokers and are further elevated during acute COPD exacerbation. Also , Factor XIII , which stabilizes fibrin clots, is increased in smokers. But neither of the two previous effects have been shown yet to be caused by nicotine. If blood clots in an artery, blood flow is reduced or halted, and tissue loses its source of oxygen and nutrients and dies in minutes .

11 - Therapeutic uses :

The primary therapeutic use of nicotine is in treating nicotine dependence in order to eliminate smoking with its risks to health. Controlled levels of nicotine are given to patients through gums, dermal patches , lozenges , electronic / substitute cigarettes or nasal sprays in an effort to wean them off their dependence .

However, in a few situations, smoking has been observed to apparently be of therapeutic value to patients. These are often referred to as " Smoker's Paradoxes ". Although in most cases the actual mechanism is understood only poorly or not at all, it is generally believed that the principal beneficial action is due to the nicotine administered, and that administration of nicotine without smoking may be as beneficial as smoking, without the higher risk to health due to tar and other ingredients found in tobacco.

For instance, recent studies suggest that smokers require less frequent repeated revascularization after percutaneous coronary intervention (PCI) . Risk of ulcerative colitis has been frequently shown to be reduced by smokers on a dose - dependent basis; the effect is eliminated if the individual stops smoking . Smoking also appears to interfere with development of Kaposi's sarcoma , breast cancer among women carrying the very high risk BRCA gene , preeclampsia , and atopic disorders such as allergic asthma .

A plausible mechanism of action in these cases may be nicotine acting as an anti - inflammatory agent, and interfering with the inflammation-related disease process , as nicotine has vasoconstrictive effects .

With regard to neurological diseases, evidence suggests that the risk of developing Parkinson's disease or Alzheimer's disease might be 50 % lower in smokers, compared to non – smokers . Tobacco smoke has been shown to contain compounds capable of inhibiting MAO. Monoamine oxidase is responsible for the degradation of dopamine in the human brain. When dopamine is broken down by MAO-B, neurotoxic by - products are formed, possibly contributing to Parkinson's and Alzheimers disease . Many such papers regarding

Alzheimer's disease and Parkinson's Disease have been published . More recent studies find that there's no beneficial link between smoking and Alzheimer's, and in some cases suggest that it actually results in an earlier onset of the disease .

Recent studies have indicated that nicotine can be used to help adults suffering from Autosomal dominant nocturnal frontal lobe epilepsy. The same areas that cause seizures in that form of epilepsy are also responsible for processing nicotine in the brain .

It has been noted that the majority of people diagnosed with schizophrenia smoke tobacco. Estimates for the number of schizophrenics that smoke range from 75 % to 90 %. It was recently argued that the increased level of smoking in schizophrenia may be due to a desire to self-medicate with nicotine . More recent research has found that mildly-dependent users got some benefit from nicotine, but not those who were highly - dependent . All of these studies are based only on observation, and no interventional (randomized) studies have been done. Research on nicotine as administered through a patch or gum is ongoing .

Nicotine improves ADHD symptoms and appears to have effects in the brain that are similar to those of stimulants. Although such findings should certainly not encourage anyone to smoke , some studies are focusing on benefits of nicotine therapy in adults with ADHD .

12 - Research as a potential basis for an antipsychotic agent :

However, when the metabolites of nicotine were isolated and their effect on first the animal brain and then the human brain in people with schizophrenia were studied, it was shown that the effects helped with cognitive and negative symptoms of schizophrenia. Therefore, the nicotinic agents, as antipsychotics which do not contain nicotine but act on the same receptors in the brain are showing promise as adjunct antipsychotics in early stages of FDA studies on schizophrenia. The prepulse inhibition (PPI) is a phenomenon in which a weak prepulse attenuates the response to a subsequent startling stimulus. Therefore, PPI is believed to have face, construct,

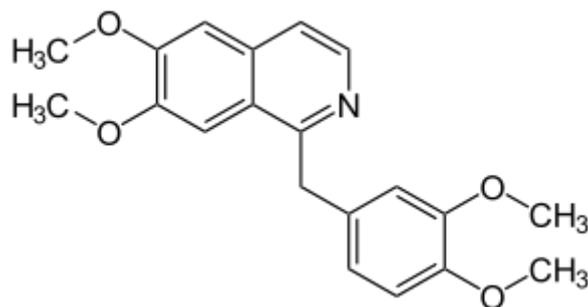
and predictive validity for the PPI disruption in schizophrenia, and it is widely used as a model to study the neurobiology of this disorder and for screening antipsychotics . Additionally, studies have shown that there are genes predisposing people with schizophrenia to nicotine use .

Therefore with these factors taken together the heavy usage of cigarettes and other nicotine related products among people with schizophrenia may be explained and novel antipsychotic agents developed that have these effects in a manner that is not harmful and controlled and is a promising arena of research for schizophrenia.

Nicotine and its metabolites are being researched for the treatment of a number of disorders, including ADHD, Schizophrenia and Parkinson's Disease .

The therapeutic use of nicotine as a means of appetite-control and to promote weight loss is anecdotally supported by many ex-smokers who claim to put on weight after quitting. Studies of nicotine in mice suggest it may play a role in weight - loss that is independent of appetite and studies involving the elderly suggest that nicotine affects not only weight loss , but also prevents some weight gain .

Papaverine



Contents :

- 1 Introduction
- 2 Uses
- 3 Mechanism
- 4 Side effects
- 5 Formulations and trade names

1 – Introduction :

Papaverine (pronounced / pə'pævəri:n/) is an opium alkaloid used primarily in the treatment of visceral spasm, vasospasm (especially those involving the heart and the brain) , and occasionally in the treatment of erectile dysfunction.^[3] While it is found in the opium poppy, papaverine differs in both structure and pharmacological action from the analgesic (morphine – related) opium alkaloids (opiates). In 1979 , a Food and Drug Administration Advisory Committee evaluated studies on papaverine and concluded that there was a lack of objective data to support the therapeutic use of papaverine for these conditions. Papaverine remains available despite the committee's recommendation that it be withdrawn from the market

Systematic (IUPAC) name	
1- (3,4 – dimethoxy benzyl) - 6 ,7- dimethoxy iso quinoline	
Formula	C ₂₀ H ₂₁ NO ₄
Mol mass	339 g / mol

Pharmacokinetic data	
Bioavailability	80 %
Protein binding	~ 90 %
Metabolism	Hepatic
Half life	1.5 – 2 hours

2 - Uses :

Papaverine is approved to treat spasms of the gastrointestinal tract, bile ducts and ureter and for use as a cerebral and coronary vasodilator in subarachnoid hemorrhage (combined with balloon angioplasty) and coronary artery bypass surgery . Papaverine may also be used as a smooth muscle relaxant in microsurgery where it is applied directly to blood vessels .

It is also commonly used in cryopreservation of blood vessels along with the other glycosaminoglycans and protein suspensions . Functions as a vasodilator during cryopreservation when used in conjunction with verapamil , phentolamine , nifedipine , tolazoline or nitroprusside .

Papaverine is also being investigated as a topical growth factor in tissue expansion with some success .

Papaverine is also present in combinations of opium alkaloid salts such as Omnopon, Pantopon , Papaveretum , and others along with morphine , codeine, and in some cases noscapine and others in a percentage similar to that in opium or modified for a given application

3 - Mechanism :

The in vivo mechanism of action is not entirely clear, but an inhibition of the enzyme phosphodiesterase causing elevation of cyclic AMP levels is significant . It may also alter mitochondrial respiration .

Papaverine has also been demonstrated to be a selective phosphodiesterase inhibitor for the PDE_{10A} subtype found mainly in the striatum of the brain. When administered chronically to mice it

produced motor and cognitive deficits and increased anxiety, but conversely may produce an antipsychotic effect .

4 - Side effects :

Frequent side effects of papaverine treatment include polymorphic ventricular tachycardia, constipation, interference with sulpho bromo phthalein retention test (used to determine hepatic function) , increased tran saminase levels , increased alkaline phosphatase levels , somnolence , and vertigo .

Rare side effects include flushing of the face , hyperhidrosis (excessive sweating) , cutaneous eruption, arterial hypotension , tachycardia , loss of appetite, jaundice, eosinophilia, thrombopenia, mixed hepatitis, headache , allergic reaction, chronic active hepatitis , and paradoxical aggravation of cerebral vasospasm .

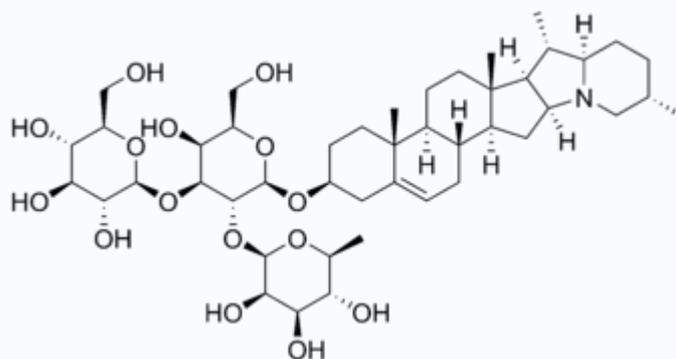
5 - Formulations and trade names :

Papaverine is available as a conjugate of hydrochloride, codecarboxylate, adenylate, and teprosylate . It was also once available as a salt of hydro bromide , camsylate , cromesilate , nicotinate, and phenyl glycolate. The hydrochloride salt is available for intra muscular , intra venous , rectal and oral administration . The teprosylate is available in intravenous, intramuscular, and orally administered formulations . The codecarboxylate is available in oral form, only , as is the adenylate .

The code carboxylate is sold under the name Albatran , the adenylate as Dicertan , and the hydro chloride salt is sold under variously name as :

Artegodan , Cardioverina , Dispamil , Opdensit , Panergon, Paverina Houde , Pavacap , Pavadyl , Papaverin – Hamelin , Paveron , Spasmo - Nit , Cardiospan , Papaversan , Cepaverin , Cerespan , Drapavel , Forpaven , Papalease , Pavatest , Paverolan , Therapav , Vasospan, Cerebid , Delapav , Dilaves , Durapav , Dynovas , Optenyl, Pameion , Papacon , Pavabid , Pavacen , Pavakey , Pavased , Pavnell , Alapav , Myobid , Vasal , Pamelon , Pavadel , Pavagen , Ro – Papav .

Solanine



Contents

- 1 Introduction
- 2 Solanine poisoning
 - 2.1 Symptoms
 - 2.2 Mechanism of Action
 - 2.3 Correlation with birth defects
- 3 Solanine in potatoes
- 4 Solanine in green tomatoes
- 5 Other uses of solanine

Solanine is a glyco alkaloid poison found in species of the nightshade family (solanaceae) , such as potatoes. It can occur naturally in any part of the plant, including the leaves, fruit, and tubers. It is very toxic even in small quantities. Solanine has both fungicidal and pesticidal properties, and it is one of the plant's natural defenses. Solanine was first isolated in 1820 by Desfosses from the berries of the European Black Night shade , *Solanum nigrum*, after which it was named .

Molecular formula	$C_{45} H_{73} NO_{15}$
Molar mass	868
Appearance	crystalline solid
Melting point	271 - 273 °C

2 - Solanine poisoning :

2 – 1 : Symptoms :

Solanine poisoning is primarily displayed by gastro intestinal and neurological disorders . Symptoms include nausea , diarrhea , vomiting , stomach cramps , burning of the throat , heart arrhythmia , headache and dizziness . Hallucinations, loss of sensation, paralysis, fever, jaundice, dilated pupils and hypothermia have been reported in more severe cases .

In large quantities , solanine poisoning can cause death. One study suggests that doses of 2 to 5 mg per kilogram of body weight can cause toxic symptoms , and doses of 3 to 6 mg per kilogram of body weight can be fatal.

Symptoms usually occur 8 to 12 hours after ingestion, but may occur as rapidly as 30 minutes after eating high-solanine foods.

The lowest dose to cause symptoms of nausea is about 25 mg solanine for adults , a life-threatening dose for a regular-weight adult ranges about 400 mg Solanine .

2 – 2 : Mechanism of Action :

One study suggests that the toxic mechanism of solanine is caused by the chemical's interaction with mitochondrial membranes . Experiments show that solanine exposure opens the potassium channels of mitochondria, increasing their membrane potential. This in turn leads to Ca^{2+} being transported down its concentration gradient into the mitochondria, and it is this increased concentration of Ca^{2+} in the cell that triggers cell damage and apoptosis .

2 – 3 : Correlation with birth defects :

Some studies show a correlation between the consumption of potatoes suffering from late - blight (which increases solanine and other glycol alkaloid levels) and the incidence of congenital spina bifida in humans. However, other studies have shown no correlation between potato consumption and the incidence of birth defects .

3 - Solanine in potatoes

Solanine occurs naturally in many species of the genus *Solanum*, including potatoes (*Solanum tuberosum*), tomatoes (*Solanum lycopersicum*), eggplant (*Solanum melongena*), and bitter-sweet nightshade (*Solanum dulcamara*).

Potatoes naturally produce solanine and chaconine , a related glycol alkaloid, as a defense mechanism against insects, disease, and predators. Potato leaves, stems and shoots are naturally high in glycol alkaloids .

When potato tubers are exposed to light, they turn green and increase glycol alkaloid production. This is a natural defense to help prevent the uncovered tuber from being eaten. The green colour is from chlorophyll, and is itself harmless. However, it is an indication that increased level of solanine and chaconine may be present .

Some diseases, such as potato blight, can dramatically increase the levels of glycol alkaloids present in potatoes. Mechanically damaged potatoes also produce increased levels of glycoalkaloids. This is believed to be a natural reaction of the plant in response to disease and damage .

Commercial varieties of potatoes are screened for solanine levels and most have a solanine content of less than 0.2 mg/g. However, potatoes that have been exposed to light and started to green can show concentrations of 1 mg / g or more. In these situations a single unpeeled potato can result in a dangerous dose .

In potato tubers 30 – 80 % of the solanine develops in and close to the skin .

Showing green under the skin strongly suggests solanine build - up in potatoes although each process can occur without the other. A bitter taste in a potato is another, potentially more reliable indicator of toxicity. Because of the bitter taste and appearance of such potatoes, solanine poisoning is rare outside conditions of food shortage. The symptoms are mainly vomiting and diarrhea, and the condition may be

misdiagnosed as gastroenteritis. Most potato poisoning victims recover fully, although fatalities are known especially when victims are undernourished or do not receive suitable treatment.^[4] Fatalities are also known from solanine poisoning from other plants in the nightshade family, such as the berries of *Solanum dulcamara* (woody nightshade) .

The National Institute of Health's information on solanine says to never eat potatoes that are green below the skin .

Deep - frying potatoes at 170° C (306°F) is known to effectively lower glycol alkaloid levels (because they move into the frying fat) , whereas microwaving is only somewhat effective, freeze drying or dehydration has little effect and boiling has no effect .

4 - Solanine in green tomatoes :

While ripe (red or yellow) tomatoes do not contain significant amounts of solanine, the amount of solanine in unripe (green) tomatoes is quite high. A dose of 25 mg is about the dose where symptoms of nausea start to show , Depending on the variety of tomatoes the amount of 25 mg solanine may be reached with less than 80 g of raw green tomatoes, and the potentially life - threatening dose for adults of 400 mg may be reached between 1.25 kg to 4.5 kg of raw green tomatoes , As with potatoes, deep - frying them does reduce the solanine level significantly (up to 50 %) while solanine dissolves into the frying fat. Therefore only small portions of no more than 80 g of raw green tomatoes or 150 g of deep - fried green tomatoes should be consumed per day by adults .

5 - Other uses of solanine :

Solanine has fungicidal and pesticidal properties , and solanine hydrochloride (a salt of solanine) has been used as a commercial pesticide, but never on a large scale .

Solanine has sedative and anticonvulsant properties, and has been used as a treatment for asthma, as well as for cough and cold medicines . However, its effectiveness for either use is questionable .

PART – 2

**ALKALOIDS
PLANTS**



Atropa Belladonna



Deadly Night Shade

Contents :

- 1 Introduction
- 2 Description
- 3 Naming and taxonomy
- 4 Toxicity
- 5 Uses
 - 5.1 Cosmetics
 - 5.2 Medicine
 - 5.3 Traditional and alternative medicine
 - 5.4 Recreational drug
 - 5.5 Poison
- 6 Folklore

1 – Introduction :

Atropa belladonna , commonly known as **belladonna** or **deadly night shade** , is a perennial herbaceous plant in the family Solanaceae native to Europe , North Africa, and Western Asia . The foliage and berries are extremely toxic, containing tropane alkaloids . These toxins include scopolamine and hyoscyamine which cause a bizarre delirium and hallucinations . The drug atropine is derived from the plant. When atropine, pralidoxime (2 – PAM) , and diazepam are combined , they can be injected and used to combat poisoning by organophosphates or acetyl cholinesterase inhibitors (nerve agents) .

It has a long history of use as a medicine, cosmetic , and poison. Before the Middle Ages , it was used as an anesthetic for surgery , and it was used as a poison by early men , ancient Romans, including the wives of two Emperors , and by Macbeth of Scotland before he became a Scottish King .

The genus name " atropa " comes from Atropos , one of the three Fates in Greek mythology , and the name " atropa belladonna " is derived from an admonition in Italian and Greek meaning " do not betray a beautiful lady " .

Kingdom : Plantae
unranked : Angiosperms
unranked : Eudicots
Unranked : Asterids
Order : Solanales
Family : Solanaceae
Genus : *Atropa*
Species : *A . belladonna*

2 - Description:



Atropa belladonna

Atropa belladonna is a branching herbaceous perennial , often growing as a sub shrub , from a fleshy rootstock . Plants grow to 1.5 meters (4.9 ft) tall with 18 centimeters (7.1 in) long ovate leaves. The bell - shaped flowers are dull purple with green tinges and faintly scented . The fruits are berries , which are green ripening to a shiny black , and approximately 1 centimeter (0.39 in) in diameter . The

berries are sweet and are consumed by animals that disperse the seeds in their droppings, even though the seeds contain toxic alkaloids . There is a pale yellow flowering form called *Atropa belladonna* var . *lutea* with pale yellow fruit .

Atropa belladonna is rarely used in gardens, but when grown it is usually for its large upright habit and showy berries . It is naturalized in parts of North America, where it is often found in shady , moist locations with limestone-rich soils. It is considered a weed species in parts of the world , where it colonizes areas with disturbed soils . Germination of the small seeds is often difficult , due to hard seed coats that cause seed dormancy . Germination takes several weeks under alternating temperature conditions but can be sped up with the use of gibberellic acid . The seedlings need sterile soil to prevent damping off and resent root disturbance during transplanting .

3 - Naming and taxonomy :

The first botanical description was by Linnaeus in *Species Plantarum* in 1753 . It is in the nightshade family (*Solanaceae*) , which it shares with potatoes , tomatoes , eggplants , jimsonweed , tobacco, wolfberry , and chili peppers . The common names for this species include belladonna , deadly nightshade , divale , dwale , banewort , devil's cherries, naughty man's cherries, black cherry, devil's herb , great morel , and dwayberry .

The name *Atropa* is thought to be derived from that of the Greek goddess Atropos , one of the three Greek fates or destinies who would determine the course of a man's life by the weaving of threads that symbolized their birth , the events in their life and finally their death; with Atropos cutting these threads to mark the latter . The name " belladonna " comes from the Italian language , meaning " beautiful lady " ; originating either from its usage as cosmetic for the face , or , more probably , from its usage to increase the pupil size in ladies .

4 - Toxicity :

Belladonna is one of the most toxic plants found in the Western hemisphere . All parts of the plant contain tropane alkaloids . The berries pose the greatest danger to children because they look attractive and have a some what sweet taste . The consumption of two to five berries by children and ten to twenty berries by adults can be lethal . The root of the plant is generally the most toxic part, though this can vary from one specimen to another. Ingestion of a single leaf of the plant can be fatal to an adult .



Flowers of *belladonna*

The active agents in Belladonna , atropine , hyoscine (scopolamine) , and hyoscyamine , have anticholinergic properties . The symptoms of belladonna poisoning include dilated pupils , sensitivity to light, blurred vision , tachycardia, loss of balance , staggering , headache , rash , flushing , dry mouth and throat, slurred speech , urinary retention, , constipation, confusion, hallucinations, delirium, and convulsions . The plant's deadly symptoms are caused by atropine's disruption of the parasympathetic nervous system's ability to regulate non - volitional /subconscious activities such as sweating , breathing, and heart rate. The antidote for belladonna poisoning is physostigmine or pilocarpine , the same as for atropine .

Atropa belladonna is also toxic to many domestic animals , causing narcosis and paralysis . However, cattle and rabbits seem to eat the plant without suffering harmful effects . Its anti cholinergic properties will cause in humans the disruption of cognitive capacities like memory and learning .

5 - Uses :

5 – 1 : Cosmetics

The common name *belladonna* originates from its historic use by women - *Bella Donna* is Italian for *beautiful lady* . Drops prepared from the belladonna plant were used to dilate women's pupils , an effect considered attractive . Today it is known that the atropine in belladonna acts as an antimuscarinic , blocking receptors in the muscles of the eye that constrict pupil size . Belladonna is currently rarely used cosmetically, as it carries the adverse effects of causing minor visual distortions, inability to focus on near objects, and increased heart rate . Prolonged usage was reputed to cause blindness .

5 – 2 : Medicine

There is currently insufficient scientific evidence to recommend the use of *A. belladonna* in its natural form for any condition,^[14] although some of its components, in particular *l*-atropine which was purified from belladonna in the 1830s , have accepted medical uses . Don natal is a prescription pharmaceutical , approved in the United States by the FDA , that combines natural belladonna alkaloids in a specific, fixed ratio with pheno barbital to provide peripheral anti cholinergic / anti spasmodic action and mild sedation . According to its labeling , it is possibly effective for use as adjunctive therapy in the treatment of irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis .

5 – 3 : Traditional and alternative medicine :



Berries of *belladonna*

A. belladonna has been used in traditional treatments for centuries for an assortment of conditions including headache , menstrual symptoms , peptic ulcer disease, histaminic reaction , inflammation , and motion sickness , with at least one 19th century eclectic medicine journal explaining how to prepare a Belladonna tincture for direct administration to patients .

Homeopathic remedies prepared from the belladonna plant have been sold as treatments for various conditions, although there is no scientific evidence to support the efficacy of this use . Clinically and in research trials, the most common preparation is diluted to the 30 C level in homeopathic notation. This level of dilution contains no molecules of the original plant , although preparations with much lesser dilutions (which may contain trace amounts of the plant) are occasionally sold.

5 – 4 : Recreational drug

Atropa belladonna , along with related plants such as jimson weed (*Datura stramonium*) , has occasionally been used as a recreational drug because of the vivid hallucinations and delirium that it produces . These hallucinations are most commonly described as very unpleasant, however, and recreational use is considered extremely dangerous because of the high risk of unintentional fatal overdose . In addition, the central nervous system effects of atropine include memory disruption, which may lead to severe confusion .

5 – 5 : Poison :

It was used by early men in poisonous arrows .

In Ancient Rome , it was used as a poison by Agrippina the Younger , wife of Emperor Claudius , and Livia, who is rumored to have used it to kill her husband Emperor Augustus . Macbeth of Scotland , when he was still one of the lieutenants of King Duncan I of Scotland, used it during a truce to poison the troops of the invading Harold Hare foot , King of England, to the point that the English troops were unable to stand their ground and had to retreat to their ships .

6 - Folklore :



Leaves of *belladonna*

In the past, it was believed that witches used a mixture of belladonna , opium poppy , and other plants , typically poisonous (such as monkshood and poison hemlock) in flying ointment they applied to help them fly to gatherings with other witches . Carlo Ginzburg and others have argued that flying ointments were preparations meant to encourage hallucinatory dreaming ; a possible explanation for the inclusion of belladonna and opium poppy in flying ointments concerns the known antagonism between tropane alkaloids of belladonna (specifically scopolamine) and opiate alkaloids in the opium poppy , *Papaver somniferum* (specifically morphine) , which produces a dream - like waking state . This antagonism was known in folk medicine , discussed in eclectic (botanical) medicine formularies and posited as the explanation of how flying ointments might have actually worked in contemporary writing on witchcraft . The antagonism between opiates and tropanes is the original basis of the Twilight Sleep that was provided to Queen Victoria to deaden pain as well as consciousness during childbirth , and which was later modified so that isolated alkaloids were used instead of plant materials . The belladonna herb was also notable for its unpredictable effects from toxicity .

Cannabis



Common hemp

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- 2 Etymology
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 - 6.4 Religious use
- 7 Aspects of Cannabis production and use

1 – Introduction :

Cannabis (*Cán-na-bis*) is a genus of flowering plants that includes three putative species, *Cannabis sativa* L.,^[1] *Cannabis indica* Lam.,^[1] and *Cannabis ruderalis* Janisch. These three taxa are indigenous to Central Asia, and South Asia. *Cannabis* has long been used for fibre (hemp), for medicinal purposes, and as a recreational drug. Industrial hemp products are made from *Cannabis* plants selected to produce an abundance of fiber and minimal levels of THC (Δ^9 - tetra hydro cannabinol), a psychoactive molecule that produces the "high" associated with marijuana. The psychoactive product consists of dried flowers and leaves of plants selected to produce high levels of THC. Various extracts including hashish and hash oil are also produced from the plant .

Scientific classification

Kingdom : Plantae

Division : Magnoliophyta

Class : Magnoliopsida

Order : Rosales

Family : Cannabaceae

Genus : *Cannabis* L .

2 - Etymology :

The word **cannabis** is from Greek κάnnαβις (*kánnabis*) (see Latin *cannabis*) , which was originally Scythian or Thracian. It is related to the Persian *kanab*, the English *canvas* and possibly even to the English *hemp* (Old English *hænep*) . In Hebrew, the word is קַנְבִּיץ [qan:a'bo:s]. Old Akkadian *qunnabtu* , Neo - Assyrian and Neo - Babylonian *qunnabu* were used to refer to the plant meaning "a way to produce smoke " .

3 – Description :

Cannabis is an annual, dioecious, flowering herb. The leaves are palmately compound or digitate, with serrate leaflets. The first pair of

leaves usually have a single leaflet, the number gradually increasing up to a maximum of about thirteen leaflets per leaf (usually seven or nine), depending on variety and growing conditions. At the top of a flowering plant, this number again diminishes to a single leaflet per leaf. The lower leaf pairs usually occur in an opposite leaf arrangement and the upper leaf pairs in an alternate arrangement on the main stem of a mature plant.

Cannabis normally has imperfect flowers, with staminate "male" and pistillate "female" flowers occurring on separate plants . It is not unusual, however, for individual plants to bear both male and female flowers . Although monoecious plants are often referred to as "hermaphrodites," true hermaphrodites (which are less common) bear staminate and pistillate structures on individual flowers, whereas monoecious plants bear male and female flowers at different locations on the same plant. Male flowers are normally borne on loose panicles, and female flowers are borne on racemes .

All known strains of *Cannabis* are wind - pollinated and produce "seeds" that are technically called achenes . Most strains of *Cannabis* are short day plants , with the possible exception of *C. sativa* subsp. *sativa* var. *spontanea* (= *C. ruderalis*) , which is commonly described as "auto - flowering" and may be day - neutral.

Cannabis, like many organisms, is diploid, having a chromosome complement of $2n = 20$, although polyploid individuals have been artificially produced . The plant is believed to have originated in the mountainous regions northwest of the Himalayas. It is also known as hemp, although this term is often used to refer only to varieties of *Cannabis* cultivated for non - drug use. *Cannabis* plants produce a group of chemicals called cannabinoids, which produce mental and physical effects when consumed . Cannabinoids, terpenoids, and other compounds are secreted by glandular trichomes that occur most abundantly on the floral calyxes and bracts of female plants . As a drug it usually comes in the form of dried flower buds (marijuana), resin (hashish), or various extracts collectively known as hashish oil . In the early 20th century, it became illegal in most of the world to cultivate or possess *Cannabis* for drug purposes .

4 – Taxonomy :



Leaf of a *Cannabis* plant.

The genus *Cannabis* was formerly placed in the Nettle (Urticaceae) or Mulberry (Moraceae) family, but is now considered along with hops (*Humulus* sp.) to belong to the Hemp family (Cannabaceae) . Recent phylogenetic studies based on cpDNA restriction site analysis and gene sequencing strongly suggest that the Cannabaceae arose from within the Celtidaceae clade, and that the two families should be merged to form a single monophyletic group .

Various types of *Cannabis* have been described, and classified as species , subspecies , or varieties :

plants cultivated for fiber and seed production , described as low – intoxicant , non – drug , or fiber types

- Plants cultivated for drug production, described as high-intoxicant or drug types
- Rscaped or wild forms of either of the above types.

Cannabis plants produce a unique family of terpeno-phenolic compounds called cannabinoids, which produce the "high" one experiences from smoking marijuana. The two cannabinoids usually produced in greatest abundance are cannabidiol (CBD) and / or Δ^9 – tetra hydro cannabinol (THC), but only THC is psychoactive. Since the early 1970s, *Cannabis* plants have been categorized by their chemical phenotype or "chemotype," based on the overall amount of THC produced, and on the ratio of THC to CBD . Although overall cannabinoid production is influenced by environmental factors, the THC / CBD ratio is genetically determined and remains fixed

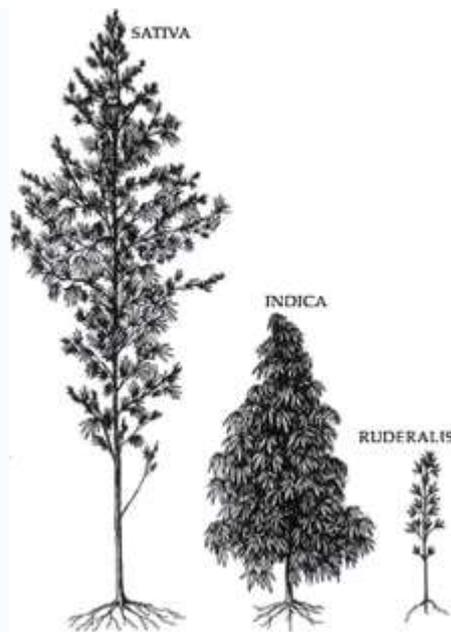
throughout the life of a plant. Non - drug plants produce relatively low levels of THC and high levels of CBD, while drug plants produce high levels of THC and low levels of CBD. When plants of these two chemotypes cross-pollinate, the plants in the first filial (F_1) generation have an intermediate chemotype and produce similar amounts of CBD and THC. Female plants of this chemotype may produce enough THC to be utilized for drug production .

Whether the drug and non – drug , cultivated and wild types of *Cannabis* constitute a single, highly variable species, or the genus is polytypic with more than one species , has been a subject of debate for well over two centuries. This is a contentious issue because there is no universally accepted definition of a species . One widely applied criterion for species recognition is that species are "groups of actually or potentially interbreeding natural populations which are reproductively isolated from other such groups " . Populations that are physiologically capable of interbreeding, but morphologically or genetically divergent and isolated by geography or ecology, are sometimes considered to be separate species . Physiological barriers to reproduction are not known to occur within *Cannabis*, and plants from widely divergent sources are interfertile . However, physical barriers to gene exchange (such as the Himalayan mountain range) might have enabled *Cannabis* gene pools to diverge before the onset of human intervention, resulting in speciation . It remains controversial whether sufficient morphological and genetic divergence occurs within the genus as a result of geographical or ecological isolation to justify recognition of more than one species .

4 – 1 : Early classifications :

The *Cannabis* genus was first classified using the "modern" system of taxonomic nomenclature by Carolus Linnaeus in 1753, who devised the system still in use for the naming of species . He considered the genus to be monotypic, having just a single species that he named *Cannabis sativa* L. (L. stands for Linnaeus, and indicates the authority who first named the species). Linnaeus was familiar with European hemp, which was widely cultivated at the time. In 1785, noted evolutionary biologist Jean - Baptiste de Lamarck published a

description of a second species of *Cannabis*, which he named *Cannabis indica* Lam . Lamarck based his description of the newly named species on plant specimens collected in India. He described *C. indica* as having poorer fiber quality than *C. sativa*, but greater utility as an inebriant. Additional *Cannabis* species were proposed in the 19th century, including strains from China and Vietnam (Indo – China) assigned the names *Cannabis chinensis* Delile, and *Cannabis gigantea* Delile ex Vilmorin . However, many taxonomists found these putative species difficult to distinguish. In the early 20th century, the single-species concept was still widely accepted, except in the Soviet Union where *Cannabis* continued to be the subject of active taxonomic study. The name *Cannabis indica* was listed in various Pharmacopoeias, and was widely used to designate *Cannabis* suitable for the manufacture of medicinal preparations .



Relative size of varieties of *Cannabis*

4 – 2 : 20 th Century :

In 1924, Russian botanist D.E. Janichevsky concluded that ruderal *Cannabis* in central Russia is either a variety of *C. sativa* or a separate species, and proposed *C. sativa* L. var. *ruderalis* Janisch. and *Cannabis ruderalis* Janisch. as alternative names . In 1929, renowned

plant explorer Nikolai Vavilov assigned wild or feral populations of *Cannabis* in Afghanistan to *C. indica* Lam. var. *kafiristanica* Vav., and ruderal populations in Europe to *C. sativa* L. var. *spontanea* Vav.^{[23][32]} In 1940, Russian botanists Serebriakova and Sizov proposed a complex classification in which they also recognized *C. sativa* and *C. indica* as separate species. Within *C. sativa* they recognized two subspecies: *C. sativa* L. subsp. *cultata* Serebr. (consisting of cultivated plants), and *C. sativa* L. subsp. *spontanea* (Vav.) Serebr. (consisting of wild or feral plants). Serebriakova and Sizov split the two *C. sativa* subspecies into 13 varieties, including four distinct groups within subspecies *cultata*. However, they did not divide *C. indica* into subspecies or varieties.^{[20][34]} This excessive splitting of *C. sativa* proved too unwieldy, and never gained many adherents.

In the 1970s, the taxonomic classification of *Cannabis* took on added significance in North America. Laws prohibiting *Cannabis* in the United States and Canada specifically named products of *C. sativa* as prohibited materials. Enterprising attorneys for the defense in a few drug busts argued that the seized *Cannabis* material may not have been *C. sativa*, and was therefore not prohibited by law. Attorneys on both sides recruited botanists to provide expert testimony. Among those testifying for the prosecution was Dr. Ernest Small, while Dr. Richard E. Schultes and others testified for the defense. The botanists engaged in heated debate (outside of court), and both camps impugned the other's integrity . The defense attorneys were not often successful in winning their case, because the intent of the law was clear .

In 1976 , Canadian botanist Ernest Small^[36] and American taxonomist Arthur Cronquist published a taxonomic revision that recognizes a single species of *Cannabis* with two subspecies : *C. sativa* L. subsp. *sativa*, and *C. sativa* L. subsp. *indica* (Lam.) Small & Cronq . The authors hypothesized that the two subspecies diverged primarily as a result of human selection; *C. sativa* subsp. *sativa* was presumably selected for traits that enhance fiber or seed production, whereas *C. sativa* subsp. *indica* was primarily selected for drug production. Within these two subspecies, Small and Cronquist described *C. sativa* L. subsp. *sativa* var. *spontanea* Vav. as a wild or

escaped variety of low - intoxicant *Cannabis*, and *C. sativa* subsp. *indica* var. *kafiristanica* (Vav.) Small & Cronq. as a wild or escaped variety of the high - intoxicant type. This classification was based on several factors including interfertility, chromosome uniformity, chemotype, and numerical analysis of phenotypic characters .

Professors William Emboden, Loran Anderson, and Harvard botanist Richard E. Schultes and coworkers also conducted taxonomic studies of *Cannabis* in the 1970s, and concluded that stable morphological differences exist that support recognition of at least three species, *C. sativa*, *C. indica*, and *C. ruderalis*.^{[38][39][40][41]} For Schultes, this was a reversal of his previous interpretation that *Cannabis* is monotypic, with only a single species.^[42] According to Schultes' and Anderson's descriptions, *C. sativa* is tall and laxly branched with relatively narrow leaflets, *C. indica* is shorter, conical in shape, and has relatively wide leaflets, and *C. ruderalis* is short, branchless, and grows wild in central Asia. This taxonomic interpretation was embraced by *Cannabis* aficionados who commonly distinguish narrow-leafed "sativa" drug strains from wide-leafed "indica" drug strains.^[43]

4 – 3 : Ongoing research :

Molecular analytical techniques developed in the late twentieth century are being applied to questions of taxonomic classification. This has resulted in many reclassifications based on evolutionary systematics. Several studies of Random Amplified Polymorphic DNA (RAPD) and other types of genetic markers have been conducted on drug and fiber strains of *Cannabis*, primarily for plant breeding and forensic purposes . Dutch *Cannabis* researcher E.P.M. de Meijer and coworkers described some of their RAPD studies as showing an "extremely high" degree of genetic polymorphism between and within populations, suggesting a high degree of potential variation for selection, even in heavily selected hemp cultivars . They also commented that these analyses confirm the continuity of the *Cannabis* gene pool throughout the studied accessions, and provide further confirmation that the genus comprises a single species, although theirs was not a systematic study *per se*.

Karl W. Hillig, a graduate student in the laboratory of long-time *Cannabis* researcher Paul G. Mahlberg at Indiana University, conducted a systematic investigation of genetic, morphological, and chemotaxonomic variation among 157 *Cannabis* accessions of known geographic origin, including fiber, drug, and feral populations. In 2004, Hillig and Mahlberg published a chemotaxonomic analysis of cannabinoid variation in their *Cannabis* germplasm collection. They used gas chromatography to determine cannabinoid content and to infer allele frequencies of the gene that controls CBD and THC production within the studied populations, and concluded that the patterns of cannabinoid variation support recognition of *C. sativa* and *C. indica* as separate species, but not *C. Ruderalis*. The authors assigned fiber/seed landraces and feral populations from Europe, central Asia, and Asia Minor to *C. sativa*. Narrow-leaflet and wide-leaflet drug accessions, southern and eastern Asian hemp accessions, and feral Himalayan populations were assigned to *C. indica*. In 2005, Hillig published a genetic analysis of the same set of accessions (this paper was the first in the series, but was delayed in publication), and proposed a three-species classification, recognizing *C. sativa*, *C. indica*, and (tentatively) *C. Ruderalis*. In his doctoral dissertation published the same year, Hillig stated that principal components analysis of phenotypic (morphological) traits failed to differentiate the putative species, but that canonical variates analysis resulted in a high degree of discrimination of the putative species and infraspecific taxa.^[50] Another paper in the series on chemotaxonomic variation in the terpenoid content of the essential oil of *Cannabis* revealed that several wide-leaflet drug strains in the collection had relatively high levels of certain sesquiterpene alcohols, including guaiol and isomers of eudesmol, that set them apart from the other putative taxa. Hillig concluded that the patterns of genetic, morphological, and chemotaxonomic variation support recognition of *C. sativa* and *C. indica* as separate species. He also concluded there is little support to treat *C. ruderalis* as a separate species from *C. sativa* at this time, but more research on wild and weedy populations is needed because they were underrepresented in their collection.

In September 2005, New Scientist reported that researchers at the Canberra Institute of Technology had identified a new type of

Cannabis based on analysis of mitochondrial and chloroplast DNA.^[52] The New Scientist story, which was picked up by many news agencies and web sites, indicated that the research was to be published in the journal *Forensic Science International*. When the article was finally published, there was no mention of "Rasta".

As of 2007, most taxonomy web sites continue to list *Cannabis* as a single species .

4 – 4 : Popular usage :

The scientific debate regarding taxonomy has had little effect on the terminology in widespread use among cultivators and users of drug-type *Cannabis*. *Cannabis* aficionados recognize three distinct types based on such factors as morphology, native range, aroma, and subjective psychoactive characteristics. "Sativa" is the term used to describe the most widespread variety, which is usually tall, laxly branched, and found in warm lowland regions. "Indica" is used to designate shorter, bushier plants adapted to cooler climates and highland environments. "Ruderalis" is the term used to describe the short plants that grow wild in Europe and central Asia.

Breeders, seed companies, and cultivators of drug type *Cannabis* often describe the ancestry or gross phenotypic characteristics of cultivars by categorizing them as "pure indica," "mostly indica," "indica/sativa," "mostly sativa", or "pure sativa."

5 – Reproduction :

5 – 1 : Breeding systems :



Cannabis sativa seeds



Male *Cannabis* pollen sacs

Cannabis is predominantly dioecious , although many mono - ecious varieties have been described . Subdioecy (the occurrence of monoecious individuals and dioecious individuals within the same population) is widespread . Many populations have been described as sexually labile .

As a result of intensive selection in cultivation, *Cannabis* exhibits many sexual phenotypes that can be described in terms of the ratio of female to male flowers occurring in the individual, or typical in the cultivar . Dioecious varieties are preferred for drug production, where typically the female flowers are used. Dioecious varieties are also preferred for textile fiber production, whereas monoecious varieties are preferred for pulp and paper production. It has been suggested that the presence of monoecy can be used to differentiate licit crops of monoecious hemp from illicit drug crops . However, the so - called "sativa" drug strains often produce monoecious individuals, probably as a result of inbreeding .

5 -2 : Mechanisms of sex determination :

Cannabis has been described as having one of the most complicated mechanisms of sex determination among the dioecious plants . Many models have been proposed to explain sex determination in *Cannabis* .

Based on studies of sex reversal in hemp , it was first reported by K. Hirata in 1924 that an XY sex - determination system is present .

At the time, the XY system was the only known system of sex determination. The X:A system was first described in *Drosophila* spp in 1925. Soon thereafter, Schaffner disputed Hirata's interpretation, and published results from his own studies of sex reversal in hemp, concluding that an X:A system was in use and that furthermore sex was strongly influenced by environmental conditions.

Since then, many different types of sex determination systems have been discovered, particularly in plants. Dioecy is relatively uncommon in the plant kingdom, and a very low percentage of dioecious plant species have been determined to use the XY system. In most cases where the XY system is found it is believed to have evolved recently and independently.

Since the 1920s, a number of sex determination models have been proposed for *Cannabis*. Ainsworth describes sex determination in the genus as using "an X / auto some dosage type".

	
<p>A male hemp plant</p>	<p>Dense raceme of carpellate flowers typical of drug - type varieties of <i>Cannabis</i></p>

The question of whether heteromorphic sex chromosomes are indeed present is most conveniently answered if such chromosomes were clearly visible in a karyotype. *Cannabis* was one of the first plant species to be karyotyped; however, this was in a period when

karyotype preparation was primitive by modern standards (see History of Cytogenetics). Heteromorphic sex chromosomes were reported to occur in staminate individuals of dioecious "Kentucky" hemp, but were not found in pistillate individuals of the same variety. Dioecious "Kentucky" hemp was assumed to use an XY mechanism. Heterosomes were not observed in analyzed individuals of monoecious "Kentucky" hemp, nor in an unidentified German cultivar. These varieties were assumed to have sex chromosome composition X X . According to other researchers, no modern karyotype of *Cannabis* had been published as of 1996 . Proponents of the X Y system state that Y chromosome is slightly larger than the X , but difficult to differentiate cytologically .

More recently, Sakamoto and various co-authors^{[72][73]} have used RAPD to isolate several genetic marker sequences that they name Male-Associated DNA in *Cannabis* (MADC), and which they interpret as indirect evidence of a male chromosome. Several other research groups have reported identification of male-associated markers using RAPD and AFLP . Ainsworth commented on these findings, stating .

" It is not surprising that male - associated markers are relatively abundant. In dioecious plants where sex chromosomes have not been identified, markers for maleness indicate either the presence of sex chromosomes which have not been distinguished by cytological methods or that the marker is tightly linked to a gene involved in sex determination " .

Environmental sex determination is known to occur in a variety of species . Many researchers have suggested that sex in *Cannabis* is determined or strongly influenced by environmental factors . Ainsworth reviews that treatment with auxin and ethylene have feminizing effects, and that treatment with cytokinins and gibberellins have masculinizing effects . It has been reported that sex can be reversed in *Cannabis* using chemical treatment . A PCR - based method for the detection of female-associated DNA polymorphisms by genotyping has been developed .

6 - Industrial and Personal Uses :

Cannabis is used for a wide variety of purposes .

6 – 1 : Hemp :

Hemp is the natural, durable soft fiber from the stalk of *Cannabis sativa* plants that grow upwards of 20 feet tall . *Cannabis* plants used for hemp production are not valued for recreational uses as the plants that are cultivated for hemp produce minimal levels of THC, analogous to attempting to get drunk from low-alcohol beer. *Cannabis* plants intended for any drug cultivation cannot be hidden in a hemp field either, as the size and height of each are significantly different .

Hemp producers sell hemp seeds as a health food, as they are rich in heart - healthy, essential fatty acids, amino acids (both essential and non essential) , vitamins and minerals. Hemp "milk" is a milk substitute also made from hemp seeds that is both dairy and gluten - free .

Hemp is fairly easy to grow and matures very fast compared to many crops, most notably trees used for paper. Compared to cotton for clothing, hemp cloth is known to be of superior strength and last longer. The fibers may also be used to form cordage for industrial-strength ropes. Hemp plants also require little pesticides and herbicides due to its height, density and foliage. This also makes the hemp plant very environmentally - friendly.

Hemp can be utilized for 25,000 very durable textile products,^[78] ranging from paper and clothing to biofuels (from the oils found in the seeds) , medicines and construction material. Hemp has been used by many civilizations, from China to Europe (and later North America) for the last 12,000 years of history .

6 – 2 : Recreational use :

Cannabis is an immensely popular recreational drug around the world, only behind alcohol, caffeine (as a stimulant) and tobacco. In the United States alone, it is believed that over 100 million Americans

have tried Cannabis, with 25 million Americans using it within the past year .

The psychoactive effects of Cannabis are known to have a biphasic nature. The main psychoactive compound found in cannabis is tetrahydrocannabinol, or THC. The first psychoactive effects include a state of relaxation, and to a lesser degree, euphoria. The latter effects include an increase in heart rate and hunger, believed to be caused by 11 - Hydroxy - THC, a psychoactive metabolite of THC produced in the liver. In addition to euphoria, other psychoactive effects such as introspection, metacognition, anxiety or paranoia and a facility for philosophical thinking are also commonly reported.^[83] Cannabidiol (CBD) , which has no psychotropic effects by itself,^[84] has been shown to attenuate the higher anxiety levels caused by THC alone.^[85] Some studies show that cannabidiol actually has a small stimulant effect similar to caffeine . The *Cannabis sativa* plant is known to cause more of a " high " by stimulating hunger, and producing comedic and energetic effects. Conversely, the *Cannabis indica* plant is known to cause more of the " stoned " effect, possibly due to a higher CBD to THC ratio .

Normal cognition is restored in approximately three hours for larger doses via a smoking pipe, bong or vaporizer . However, if a large amount is taken orally the effects may last much longer. Minuscule psychoactive effects may be felt up to 24 hours to a few days, depending on dosage, frequency and tolerance .

According to the UK medical journal *The Lancet*, Cannabis has a lower rate of dependence compared to both nicotine and alcohol.^[87] However, everyday use of Cannabis is correlated with some withdrawal symptoms such as irritability, anxiety, and insomnia . There is also evidence to suggest that if a user experiences stress, the likeliness of getting a panic attack increases due to an increase in THC metabolites . However, any Cannabis withdrawal symptoms are typically mild to moderate and are never life - threatening alone . Various extracts including hashish and hash oil are also produced from the plant .

6- 3 : Medical use :

A synthetic form of the main psychoactive cannabinoid in *Cannabis*, Δ^9 – tetra hydro cannabinol (THC), is used as a treatment for a wide range of medical conditions.

In the United States, although the Food and Drug Administration (FDA) does acknowledge that " there has been considerable interest in its use for the treatment of a number of conditions, including glaucoma, AIDS wasting, neuropathic pain, treatment of spasticity associated with multiple sclerosis, and chemotherapy-induced nausea," the agency has not approved "medical marijuana". There are currently 2 oral forms of cannabis (cannabinoids) available by prescription in the United States for nausea and vomiting associated with cancer chemotherapy: dronabinol (Marinol) and nabilone (Cesamet) . Dronabinol is also approved for the treatment of anorexia associated with AIDS . The FDA does facilitate scientific investigations into the medical uses of cannabinoids .

In a collection of writings on medical marijuana by 45 researchers, a literature review on the medicinal uses of *Cannabis* and cannabinoids concluded that established uses include easing of nausea and vomiting, anorexia, and weight loss ; " well - confirmed effect " was found in the treatment of spasticity, painful conditions (i.e. neurogenic pain), movement disorders, asthma, and glaucoma. Reported but "less-confirmed" effects included treatment of allergies, inflammation, infection , epilepsy , depression , bipolar disorders , anxiety disorder , dependency and withdrawal . Basic level research was being carried out at the time on autoimmune disease, cancer, neuroprotection, fever, disorders of blood pressure .

Clinical trials conducted by the American Marijuana Policy Project, have shown the efficacy of cannabis as a treatment for cancer and AIDS patients, who often suffer from clinical depression, and from nausea and resulting weight loss due to chemotherapy and other aggressive treatments . A synthetic version of the cannabinoid THC named dronabinol has been shown to relieve symptoms of anorexia and reduce agitation in elderly Alzheimer's patients . Dronabinol has been approved for use with anorexia in patients with HIV / AIDS and

chemotherapy - related nausea. This drug, while demonstrating the effectiveness of *Cannabis* at combating several disorders , is more expensive and less available than " pot " and has not been shown to be effective or safe .

Glaucoma, a condition of increased pressure within the eyeball causing gradual loss of sight, can be treated with medical marijuana to decrease this intraocular pressure. There has been debate for 25 years on the subject. Some data exist, showing a reduction of IOP in glaucoma patients who smoke cannabis , but the effects are short - lived, and the frequency of doses needed to sustain a decreased IOP can cause systemic toxicity. There is also some concern over its use since it can also decrease blood flow to the optic nerve. Marijuana lowers IOP by acting on a cannabinoid receptor on the ciliary body called the CB receptor . Although *Cannabis* is not a good therapeutic choice for glaucoma patients, it may lead researchers to more effective, safer treatments. A promising study shows that agents targeted to ocular CB receptors can reduce IOP in glaucoma patients who have failed other therapies .

Medical cannabis is also used for analgesia, or pain relief. It is also reported to be beneficial for treating certain neurological illnesses such as epilepsy, and bipolar disorder . Case reports have found that *Cannabis* can relieve tics in people with obsessive compulsive disorder and Tourette syndrome . Patients treated with tetra hydro cannabinol , the main psychoactive chemical found in *Cannabis*, reported a significant decrease in both motor and vocal tics, some of 50% or more . Some decrease in obsessive-compulsive behavior was also found . A recent study has also concluded that cannabinoids found in *Cannabis* might have the ability to prevent Alzheimer's disease.^[103] THC has been shown to reduce arterial blockages .

Another potential use for medical cannabis is movement disorders *Cannabis* is frequently reported to reduce the muscle spasms associated with multiple sclerosis; this has been acknowledged by the Institute of Medicine, but it noted that these abundant anecdotal reports are not well-supported by clinical data. Evidence from animal studies suggests that there is a possible role for cannabinoids in the

treatment of certain types of epileptic seizures . A synthetic version of the major active compound in *Cannabis*, THC, is available in capsule form as the prescription drug dronabinol (Marinol) in many countries. The prescription drug Sativex, an extract of cannabis administered as a sublingual spray, has been approved in Canada for the treatment of multiple sclerosis .

6 – 4 : Religious use :

Cannabis is first referred to in Hindu Vedas between 2000 and 1400 BCE, in the *Atharvaveda*. By the tenth century CE, it was being referred to in India as "food of the gods" . Cannabis use eventually became a ritual part of the Hindu festival of Holi. In Buddhism, cannabis has been used in meditation and regarded as a holy plant since 500 BCE . Shamanic use of *Cannabis* in China has been dated to at least 1000 BCE . In ancient Germanic culture , *Cannabis* was associated with the Norse love goddess, Freya . An anointing oil mentioned in Exodus is, by some translators, said to contain *Cannabis* . Sufis have used *Cannabis* in a spiritual context since the thirteenth century CE .

In modern times the Rastafari movement has embraced *Cannabis* as a sacrament . Elders of the modern religious movement known as the Ethiopian Zion Coptic Church consider *Cannabis* to be the Eucharist, claiming it as an oral tradition from Ethiopia dating back to the time of Christ, even though the movement was founded in the United States in 1975 and has no ties to either Ethiopia or the Coptic Church.^[115] Like the Rastafari, some modern Gnostic Christian sects have asserted that *Cannabis* is the Tree of Life . Other organized religions founded in the 20th century that treat *Cannabis* as a sacrament are the THC Ministry , the Way of Infinite Harmony, Cantheism , the Cannabis Assembly and the Church of Cognizance .

7 - Aspects of Cannabis production and use :

- Medical Cannabis discusses its use as a medication.
- Cannabis (drug) discusses its use as a recreational drug.
- Spiritual use of cannabis discusses sacramental and religious use.

- Hemp discusses its uses as a source of housing, oil, food, fibers, and industrial materials. See *The Hemp Chronicles* for uses of hemp.
- Cannabis cultivation discusses aspects of cultivation for medicinal and recreational drug purposes
- Legality of cannabis focuses on the law and enforcement aspects of growing , transporting , selling and using *Cannabis* as a drug .

Cannabis (drug)

Contents :

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1- Introduction :

Cannabis – also known as marijuana or marihuana , and ganja (from Sanskrit : गांजा *gañjā*, meaning *hemp*) , among many other names^{a[>]} – refers to any number of preparations of the *Cannabis* plant intended for use as a psychoactive drug. The most common form of cannabis used as a drug is the dried herbal form.

The typical herbal form of cannabis consists of the flowers and subtending leaves and stalks of mature pistillate or female plants. The resinous form of the drug is known as hashish (or merely as ' hash') .

The major psychoactive chemical compound in cannabis is Δ^9 -tetra hydro cannabinol (commonly abbreviated as THC) . At least 66 other cannabinoids are also present in cannabis , including cannabidiol (CBD) , cannabinol (CBN) and tetra hydro cannabivarin (THCV) among many others , which are believed to influence the effects of THC alone .

Cannabis use has been found to have occurred as long ago as the third millennium B.C . In modern times, the drug has been used for recreational, religious or spiritual, and medicinal purposes. The United Nations (UN) estimated that in 2004 about 4 % of the world's adult population (162 million people) use cannabis annually, and about 0.6 % (22.5 million) use it on a daily basis . The possession, use, or sale of cannabis preparations containing psychoactive cannabinoids became illegal in most parts of the world in the early twentieth century. Since then, some countries have intensified the enforcement of cannabis prohibition, while others have reduced it.

2 – History :

The use of cannabis, at least as fiber, has been shown to go back at least 10,000 years in Taiwan . Má (Pinyin pronunciation), the Chinese expression for hemp, is a pictograph of two plants under a shelter .

Cannabis is indigenous to Central and South Asia.^[9] Evidence of the inhalation of cannabis smoke can be found as far back as the 3rd millennium B.C., as indicated by charred cannabis seeds found in a ritual brazier at an ancient burial site in present day Romania.^[5] Cannabis is also known to have been used by the ancient Hindus of India and Nepal thousands of years ago. The herb was called *ganjika* in Sanskrit (गांजा/गाँजा *ganja* in modern Indic languages) . The ancient drug soma , mentioned in the Vedas as a sacred intoxicating hallucinogen, was sometimes associated with cannabis .

Cannabis was also known to the ancient Assyrians, who discovered its psychoactive properties through the Aryans . Using it in some religious ceremonies, they called it *qunubu* (meaning "way to produce smoke") , a probable origin of the modern word "cannabis" .

Cannabis was also introduced by the Aryans to the Scythians and Thracians/Dacians, whose shamans (the *kapnobatai*—“those who walk on smoke/clouds”) burned cannabis flowers to induce a state of trance . Members of the cult of Dionysus, believed to have originated in Thrace (Bulgaria , Greece and Turkey) , are also thought to have inhaled cannabis smoke. In 2003, a leather basket filled with cannabis leaf fragments and seeds was found next to a 2,500 - to 2,800 – year - old mummified shaman in the northwestern Xinjiang Uygur Autonomous Region of China .



Cannabis sativa from Vienna Dioscurides, 512 A.D.

Cannabis has an ancient history of ritual use and is found in pharmacological cults around the world. Hemp seeds discovered by archaeologists at Pazyryk suggest early ceremonial practices like eating by the Scythians occurred during the 5th to 2nd century B.C., confirming previous historical reports by Herodotus . One writer has claimed that cannabis was used as a religious sacrament by ancient Jews and early Christians due to the similarity between the Hebrew word "*qannabbos*" ("*cannabis*") and the Hebrew phrase "*qené bósem*" ("aromatic cane"). It was used by Muslims in various Sufi orders as early as the Mamluk period, for example by the Qalandars .

A study published in the South African Journal of Science showed that "pipes dug up from the garden of Shakespeare's home in Stratford

upon Avon contain traces of cannabis " . The chemical analysis was carried out after researchers hypothesized that the "noted weed" mentioned in Sonnet 76 and the "journey in my head" from Sonnet 27 could be references to cannabis and the use thereof.^[22]

Cannabis was criminalized in the United States in 1937 due to Marihuana Tax Act of 1937. Several theories try to explain why it is illegal in most Western societies. Jack Herer, a cannabis legalization activist and writer, argues that the economic interests of the paper and chemical industry were a driving force to make it illegal.^{[23][24][25]} Another explanation is that beneficial effects of hemp would lower the profit of pharmaceutical companies which therefore have a vital interest to keep cannabis illegal . Those economic theories were criticized for not taking social aspect into account. The illegalization was rather a result of racism directed to associate American immigrants of Mexican and African descent with cannabis abuse .

3 – Form ;

3 – 1 : Cannabis (Herbal Form) :



*Dried Cannabis flowers in its herbal form
commonly known as marijuana.*

The terms *cannabis* or *marijuana* generally refer to the dried flowers and subtending leaves and stems of the female *Cannabis* plants . This is the most widely consumed form, containing 3 % to 22 % THC . In contrast, cannabis strains used to produce industrial hemp contain less than 1 % THC and are thus not valued for recreational use .

3 - 2 : Hashish :



Hashish

Hashish (also spelled hasheesh) or hash is a concentrated resin produced from the flowers of the female cannabis plant . Hash is more potent than marijuana and can be smoked or chewed . It varies in color from black to golden brown depending upon purity.

3 – 3 : Hash oil :

Hash oil , or honey oil , is an essential oil extracted from the cannabis plant through the use of various solvents . It has a high proportion of cannabinoids (ranging from 40 – 90 %) , This oil is also used in the process of making a variety of cannabis foods .

3 - 4 : Kief :

Kief is a powder made from trichomes removed from the leaves and flowers of cannabis plants. Kief can also be compressed to produce one form of hashish, or consumed in powder form.^[33]

3 – 5 : Cannabis (hashish) rosin :



Resin collected from a pipe.

Because of THC's adhesive properties, resin builds up inside the paraphernalia when cannabis is smoked. It has tar - like properties but still contains THC as well as other cannabinoids. This resin still has all

the psychoactive properties of cannabis but is more difficult to smoke due to the discomfort caused to the throat and lungs. Cannabis users typically only smoke resin when cannabis is unavailable. Glass may be water-steamed at a low temperature prior to scraping in order to make the resin easier to remove .

4 – Potency ;

According to the United Nations Office on Drugs and Crime (UNODC) , "the amount of THC present in a cannabis sample is generally used as a measure of cannabis potency " . The three main forms of cannabis products are the herb (marijuana) , resin (hashish), and oil (hash oil). The UNODC states that marijuana often contains 5 % THC content, resin "can contain up to 20 % THC content", and that " Cannabis oil may contain more than 60 % THC content " .

A scientific study published in 2000 in the Journal of Forensic Sciences (JFS) found that the potency of confiscated cannabis in the United States (US) rose from approximately 3.3 % in 1983 and 1984 to 4.47 % in 1997 . It also concluded that " other major cannabinoids (i.e. , CBD , CBN , and CBC) showed no significant change in their concentration over the years" . More recent research undertaken at the University of Mississippi's Potency Monitoring Project^[37] has found that average THC levels in cannabis samples between 1975 and 2007 have increased from 4 % in 1983 to 9.6 % in 2007.

Australia's National Cannabis Prevention and Information Centre (NCPIC) states that the buds (flowers) of the female cannabis plant contain the highest concentration of THC , followed by the leaves. The stalks and seeds have " much lower THC levels " , The UN states that the leaves can contain ten times less THC than the buds, and the stalks one hundred times less THC .

5 - Routes of administration :

The most commonly used include screened bowls , bongos , one - hitters , chillums , paper - wrapped joints and tobacco – leaf - wrapped blunts. Local methods differ by the preparation of the cannabis plant before use, the parts of the cannabis plant which are used, and the treatment of the smoke before inhalation .

A vaporizer heats herbal cannabis to 185 – 210 °C) , which causes the active ingredients to evaporate into a gas without burning the plant material (the boiling point of THC is 392°F (200 °C) at 0.02 mmHg pressure, and somewhat higher at standard atmospheric pressure) , A lower proportion of toxic chemicals are released than by smoking, although this may vary depending on the design of the vaporizer and the temperature at which it is set. This method of consuming cannabis produces markedly different effects than smoking due to the flash points of different cannabinoids; for example, CBN has a flash point of 212.7°C and would normally be present in smoke but might not be present in vapor .

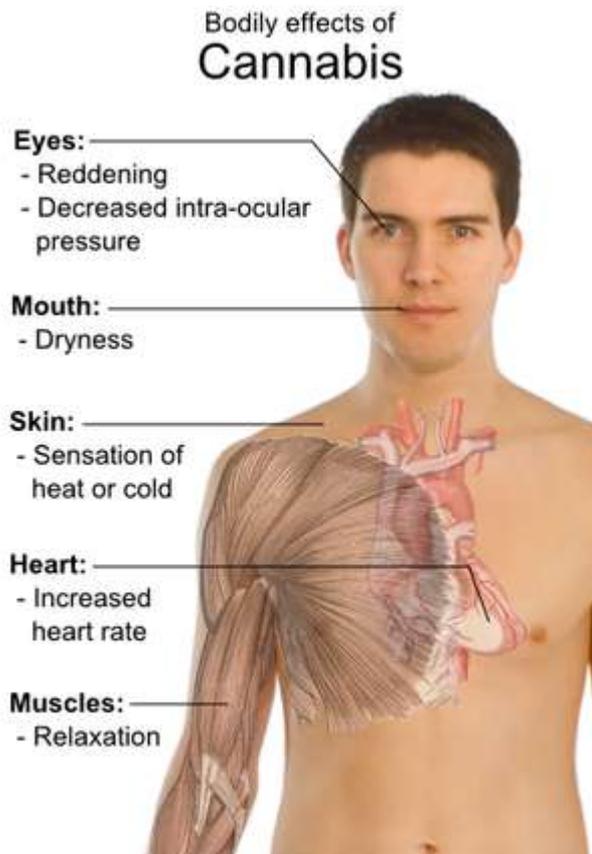
As an alternative to smoking, cannabis may be consumed orally. However, the cannabis or its extract must be sufficiently heated or dehydrated to cause decarboxylation of its most abundant cannabinoid, tetra hydro cannabinolic acid (THCA) , into psychoactive THC .

Cannabinoids can be leached from cannabis plant matter using high-proof spirits (often grain alcohol) to create a tincture, often referred to as Green Dragon .

Cannabis can also be consumed as a tea . THC is lipophilic and only slightly water soluble (with a solubility of 2.8 mg per liter) , so tea is made by first adding a saturated fat to hot water (i.e. cream or any milk except skim) with a small amount of cannabis, green or black tea leaves and honey or sugar, steeped for approximately 5 minutes.

6 - Effects of cannabis :

Cannabis has psychoactive and physiological effects when consumed. The minimum amount of THC required to have a perceptible psychoactive effect is about 10 micrograms per kilogram of body weight . Aside from a subjective change in perception, the most common short-term physical and neurological effects include increased heart rate, lowered blood pressure, impairment of psychomotor coordination, concentration, and short-term episodic and working memory . Long - term effects are less clear .



Main short - term physical effects of cannabis

6 – 1 : Classification :

Or : Effects of cannabis # Psychoactive effects

While many drugs clearly fall into the category of either stimulant, depressant, or hallucinogen, cannabis exhibits a mix of all properties, perhaps leaning the most towards hallucinogen or psychedelic properties, though with other effects quite pronounced as well. Though THC is typically considered the primary active component of the cannabis plant, various scientific studies have suggested that certain other cannabinoids like CBD may also play a significant role in its psychoactive effects .

6 – 2 : Health issues :

6 – 2 – 1 : Medical use :

Although the extent of the medicinal value of cannabis has been debated, it does have several well - documented beneficial effects .

Cannabis is indicated for treating and preventing nausea and vomiting, stimulating hunger in chemotherapy and AIDS patients and for the treatment of glaucoma due to its lowering of intraocular pressure, as well as a non-addictive general analgesic or painkiller. Other studies have show that CBD or cannabidiol a cannabinoid can lower the affects or stop schizophrenia. Individual studies also have been conducted indicating cannabis to be beneficial to a gamut of conditions running from multiple sclerosis to depression. Synthesized cannabinoids are also sold as prescription drugs, including Marinol (dronabinol in the United States and Germany) and Cesamet (nabilone in Canada, Mexico , The United States and The United Kingdom) .

Currently , the FDA has not approved smoked marijuana for any condition or disease in the United States. Regardless, thirteen states have legalized cannabis for medical use . Canada, Spain, The Netherlands and Austria have also legalized cannabis for medicinal use .

6 – 2 – 2 : Long - term effects :

The smoking of cannabis is the most harmful method of consumption, as the inhalation of smoke from organic materials can cause various health problems .

By comparison, studies on the vaporization of cannabis found that subjects were " only 40 % as likely to report respiratory symptoms as users who do not vaporize, even when age , sex , cigarette use , and amount of cannabis consumed are controlled " . Another study found vaporizers to be " a safe and effective cannabinoid delivery system " .

Cannabis is ranked one of the least harmful drugs by the UK medical journal, The Lancet .

While a study in New Zealand of 79 lung-cancer patients suggested daily cannabis smokers have a 5.7 times higher risk of lung cancer than non-users,^[59] another study of 2252 people in Los Angeles failed to find a correlation between the smoking of cannabis and lung, head or neck cancers . These effects have been attributed to the well documented anti - tumoral properties of cannabinoids, specifically tetrahydrocannabinol (THC) and cannabidiol. Some studies have also

found that moderate cannabis use may protect against head and neck cancers , as well as lung cancer.^[62] Some studies have shown that cannabidiol may also be useful in treating breast cancer .

Cannabis use has been assessed by several studies to be correlated with the development of anxiety, psychosis, and depression,^{[64][65]} however, no causal mechanism has been proven, and the meaning of the correlation and its direction is a subject of debate that has not been resolved in the scientific community. Some studies assess that the causality is more likely to involve a path from cannabis use to psychotic symptoms rather than a path from psychotic symptoms to cannabis use , while others assess the opposite direction of the causality , or hold cannabis to only form parts of a "causal constellation", while not inflicting mental health problems that would not have occurred in the absence of the cannabis use .

Though cannabis use has at times been associated with stroke, there is no firmly established link, and potential mechanisms are unknown . Similarly, there is no established relationship between cannabis use and heart disease, including exacerbation of cases of existing heart disease . Though some fMRI studies have shown changes in neurological function in long term heavy cannabis users, no long term behavioral effects after abstinence have been linked to these changes .

6 – 3 : Adulterants :

Adulterants in cannabis are less common than in other drugs of abuse. Chalk (in the Netherlands) and glass particles (in the UK) have been used at times to make cannabis appear to be higher quality . Increasing the weight of hashish products in Germany with lead caused lead intoxication in at least 29 users . In the Netherlands two chemical analogs of Sildenafil (Viagra) were found in adulterated marijuana .

7 - Gateway drug theory :

Some claim that trying cannabis increases the probability that users will eventually use " harder " drugs. This hypothesis has been one of the central pillars of anti - cannabis drug policy in the United

States , though the validity and implications of these hypotheses are highly debated . Studies have shown that tobacco smoking is a better predictor of concurrent illicit hard drug use than smoking cannabis .

No widely accepted study has ever demonstrated a cause-and-effect relationship between the use of cannabis and the later use of harder drugs like heroin and cocaine. However, the prevalence of tobacco cigarette advertising and the practice of mixing tobacco and cannabis together in a single large joint, common in Europe, are believed to be a factor in promoting nicotine dependency among young persons investigating cannabis .

A 2005 comprehensive review of the literature on the cannabis gateway hypothesis found that pre - existing traits may predispose users to addiction in general, the availability of multiple drugs in a given setting confounds predictive patterns in their usage, and drug sub-cultures are more influential than cannabis itself. The study called for further research on " social context , individual characteristics, and drug effects" to discover the actual relationships between cannabis and the use of other drugs .

The main variant of the gateway hypothesis is that people, upon trying cannabis for the first time and not finding it dangerous, are then tempted to try other, harder drugs . In such a scenario, a new user of cannabis who feels there is a difference between anti-drug information and their own experiences will apply this distrust to public information about other, more powerful drugs. Some studies state that while there is no proof for this gateway hypothesis, young cannabis users should still be considered as a risk group for intervention programs . Other findings indicate that hard drug users are likely to be " poly - drug " users, and that interventions must address the use of multiple drugs instead of a single hard drug .

Another gateway hypothesis is that while cannabis is not as harmful or addictive as other drugs, a gateway effect may be detected as a result of the " common factors " involved with using any illegal drug. Because of its illegal status, cannabis users are more likely to be in situations which allow them to become acquainted with people who use and sell other illegal drugs . By this argument, some studies have

shown that alcohol and tobacco may be regarded as gateway drugs.^[79] However, a more parsimonious explanation could be that cannabis is simply more readily available (and at an earlier age) than illegal hard drugs, and alcohol / tobacco are in turn easier to obtain earlier than cannabis (though the reverse may be true in some areas) , thus leading to the " gateway sequence " in those people who are most likely to experiment with any drug offered .

8 - Legal status :

Since the beginning of the 20th century, most countries have enacted laws against the cultivation, possession, or transfer of cannabis for recreational use. These laws have impacted adversely on the cannabis plant's cultivation for non - recreational purposes, but there are many regions where, under certain circumstances, handling of cannabis is legal or licensed. Many jurisdictions have lessened the penalties for possession of small quantities of cannabis, so that it is punished by confiscation or a fine, rather than imprisonment, focusing more on those who traffic the drug on the black market.

In some areas where cannabis use has been historically tolerated, some new restrictions have been put in place, such as the closing of cannabis coffee shops near the borders of the Netherlands,^[86] closing of coffee shops near secondary schools in the Netherlands and crackdowns on " Pusher Street " in Christiania, Copenhagen in 2004 .

Some jurisdictions use free voluntary treatment programs and/or mandatory treatment programs for frequent known users. Simple possession can carry long prison terms in some countries, particularly in East Asia, where the sale of cannabis may lead to a sentence of life in prison or even execution.

9 – Price :

The price or street value of Cannabis varies strongly by region and area. Alternatively, some dealers may also sell potent buds at a higher price .

In the United States however, Cannabis is overall the # 4 crop with it being the # 1 or # 2 crop in many states, including California ,

New York and Florida , averaging \$ 3,000 / lb . It is believed to generate an estimated \$ 36 billion market . Most of the money is spent not on growing and producing but on smuggling the supply to buyers. The United Nations Office on Drugs and Crime claims in its 2008 World Drug Report that typical U.S. retail prices are 10-15 dollars per gram (approximately \$ 290 to \$ 430 per ounce. Street prices in North America are known to range at about \$ 150 to \$ 250 per ounce .

The European Monitoring Centre for Drugs and Drug Addiction reports that typical retail prices in Europe for cannabis varies from 2 € to 14 € per gram , with a majority of European countries reporting prices in the range 4 – 10 € . In the United Kingdom, a Cannabis plant has an approximate street value of £ 300 .

10 - Truth serum :

Cannabis was used as a truth serum by the Office of Strategic Services (OSS) , a US government intelligence agency formed during World War II. In the early 1940s , it was the most effective truth drug developed at the OSS labs at St. Elizabeths Hospital ; it caused a subject " to be loquacious and free in his impartation of information " .

In May 1943, Major George Hunter White, head of OSS counter-intelligence operations in the US, arranged a meeting with Augusto Del Gracio, an enforcer for gangster Lucky Luciano. Del Gracio was given cigarettes spiked with THC concentrate from cannabis, and subsequently talked openly about Luciano's heroin operation. On a second occasion the dosage was increased such that Del Gracio passed out for two hours .

11 - Breeding and cultivation :

It is often claimed by growers and breeders of herbal cannabis that advances in breeding and cultivation techniques have increased the potency of cannabis since the late 1960s and early '70s , when THC was first discovered and understood. However, potent seedless marijuana such as " Thai sticks " were already available at that time. Sinsemilla (Spanish for " without seed ") is the dried, seedless inflorescences of female cannabis plants. Because THC production

drops off once pollination occurs, the male plants (which produce little THC themselves) are eliminated before they shed pollen to prevent pollination. Advanced cultivation techniques such as hydroponics, cloning, high - intensity artificial lighting , and the sea of green method are frequently employed as a response (in part) to prohibition enforcement efforts that make outdoor cultivation more risky. These intensive horticultural techniques have made it possible to grow strains with fewer seeds and higher potency. It is often cited that the average levels of THC in cannabis sold in United States rose dramatically between the 1970s and 2000, but such statements are likely skewed because of undue weight given to much more expensive and potent, but less prevalent samples .



Maturing female Cannabis plant

" Skunk " cannabis is a potent strain of cannabis, grown through selective breeding and usually hydroponics, which is a cross - breed of

Cannabis sativa and *C. indica*. Skunk cannabis potency ranges usually from 6% to 15% and rarely as high as 20 %. The average THC level in coffee shops in the Netherlands is about 18 – 19 % .

In revisions to cannabis rescheduling in the UK, the government has rescheduled cannabis back from C to B. One of the purported reasons is the high-potency cannabis .

A Dutch double - blind, randomized, placebo-controlled, cross-over study examining male volunteers aged 18 – 45 years with a self-reported history of regular cannabis use concluded that smoking of cannabis with high THC levels (marijuana with 9 – 23 % THC) , as currently sold in coffee shops in the Netherlands, may lead to higher THC blood - serum concentrations. This is reflected by an increase of the occurrence of impaired psychomotor skills, particularly among younger or inexperienced cannabis smokers, who do not adapt their smoking - style to the higher THC content . High THC concentrations in cannabis was associated with a dose-related increase of physical effects (such as increase of heart rate, and decrease of blood pressure) and psychomotor effects (such as reacting more slowly, being less concentrated, making more mistakes during performance testing, having less motor control , and experiencing drowsiness) . It was also observed during the study that the effects from a single joint at times lasted for more than eight hours. Reaction times remained impaired five hours after smoking, when the THC serum concentrations were significantly reduced, but still present. The researchers suggested that THC may accumulate in blood-serum when cannabis is smoked several times per day .

Another study showed that consumption of 15 mg of Δ^9 - THC resulted in no impairment to learning whatsoever occurring over a three - trial selective reminding task after two hours. In several tasks, Δ^9 - THC increased both speed and error rates, reflecting “riskier” speed–accuracy trade - offs .

12 - Cannabis strains :

There are hundreds of named strains of cannabis, but their origins (particularly the drug varieties) are often shrouded in mystery. The

names of many legendary strains , such as Panama Red and Purple Haze, are ubiquitous in the pop - culture, but the origins of some of these infamous strains, such as G - 13 , are acknowledged to be urban legends, and some people even doubt their existence .

13 - Strains of cannabis include :

Acapulco Gold , AK – 47 , Big Bud , Blueberry Bud , British Columbia Bud (B.C. Bud) , Chocolate Thai , Durban Poison , Holland's Hope , G -13 (Gaby) , Jack Herer , Juicy Fruit , Kush , Mauwie Wauwie , Netherlands Weed (Nederwiet) , Northern Lights , NYC Diesel , Panama Red , PG - 13 (Purple Gaby) , Purple Haze , Quebec Gold , Silver Haze , Skunk , Sour Diesel , Swiss Miss , White Widow

The names of some strains have become embedded in the mass culture . For example , *Chocolate Thai* , which was popular in the early 1990s due to its supposed high potency , was adopted as the stage name of a jazz performer whose album *The Real McCoy* was released in 2006 , Because there is no state control over the production or sale of cannabis, many so - called " strains " may in fact be just marketing brands adopted by drug dealers to increase sales .

Cannabis Cultivation

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1- Introduction :

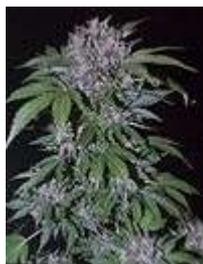
This article deals with the cultivation of the flowering plant cannabis primarily for the production and consumption of marijuana buds, which contain the main psychoactive ingredient tetra hydro cannabinol or THC. Cultivation techniques for other purposes such as the production of hemp vary dramatically. A basic description of hemp cultivation can be seen in the US propaganda film *Hemp for Victory*, shot during WWII. While it is possible to grow cannabis simply for the purpose of a houseplant or as a hobby, the practice is quite challenging due to the need to keep the annual plant in a near perpetual vegetative state, which requires root pruning and artificial lighting for the winter months .

2 - General aspects :

2 - 1 : Brief History ;

Evidence found in ancient burial sites indicates that humans have been experimenting with cannabis recreationally, spiritually and medicinally since the 3rd millenium BC . Herodotus, an important Greek historian of the 5th century BC , described how the Scythians of the Middle East used cannabis in steam baths . The status of cannabis has changed in recent years. In 1937 the USA outlawed cannabis for reasons possibly related to racism and / or industrial economic interests . In the 2000s, the vast majority of states has outlawed the cultivation, consumption and trade of cannabis with penalties ranging from a small fine to jail time .

2 – 2 : Botany :



Autoflowering hybrid auto AK47 during flowering stage

Cannabis belongs to the genus *Cannabis* in the family Cannabaceae , along with hops. It comprises four species : *C. sativa*, *C. Indica* , *C. Ruderalis* ," C . Afgannica " .

(APG II system) and is usually a dioecious (has separate pistillate (female) and staminate (male) plants) annual plant (life period : April – September) .

Generally only non - drug cultivars of *C. ruderalis* are grown for industrial/agricultural purposes whereas for consumption high-cannabinoid cultivars of both *C. indica* and *C. sativa* can be used. *C. sativa* generally grows tall (some varieties can reach 3 meters) and is possible to grow in a very close matrix. The resultant plants (often referred to as hemp) will have very fine yet strong fibers which can be used among many others for the creation of durable fine cloth resembling silk . *C. ruderalis* bears great differences relative to *C. sativa* and *C. indica*. It's very short, produces only traces of THC and flowers independently of the photoperiod and according to age. The other two species flower as they sense light hours diminishing due to forthcoming winter . However, commercial cross-bred hybrids containing both ruderalis, indica and/or sativa genes exist (usually called autoflowering). Such strains are advantageous for some growers due to their small size and early harvests. The *lowrider* can be harvested within 60 days from germination .

Cannabis needs five things to prosper :

- A grow medium (like soil) ,
- light (natural or artificial) ,
- warmth ,
- water ,
- nutrients (food) .

2 – 2 – 1 : Air Temperature :

Cannabis is a summer plant . The optimal day temperature range for cannabis is believed to be 24 to 30 °C . At night temperature may fall as low as 15.5 °C . Temperatures above 31 °C and below 15.5 °C seem to decrease THC potency and slow growth. At 13 °C a plant will

undergo a mild shock, though sometimes cannabis has been observed to withstand (only temporarily) freezing temperatures .

2 – 2 – 2 : Soil :

Soil is the natural growing medium of cannabis and very popular among growers . Certain characteristics are recommended . Good drainage to facilitate nutrient absorption and prevent root drowning .

Ideal pH between 6.5 and 7.0. To increase pH one can add agricultural lime during watering . For decrease ground coffee or lemon peels may be used. Commercial fertilizers (even organic) almost always make the soil more acidic (decrease its pH) .

Ideal temperature range: 18 - 24 C .

Fertilization : NPK stands for the percentage of Nitrogen, Phosphorus and Potassium respectively, the most essential elements a plant needs to thrive. NPK shows the degree of fertilization in commercial soils. For example if a bag of soil reads " N – P – K : 12 - 12 – 12 " this means 12 % N , 12 % P , 12 % K . Proper soil for cannabis must contain all three in both stages of growth, with more N required for the vegetative stage and more P for the flowering stage. A vegetative fertilizer may say 3 – 1 - 1 or 30 – 10 – 10 . A flowering fertilizer may say 1 – 3 - 1 or 10 – 30 – 10 . There are wide choices of chemical fertilizer NPK ratios available commercially . Loam soil and compost are considered most effective and cheap choices.

2 – 2 – 3 : Water :

Watering frequency indoors is determined by many factors, including the age of the plant, the stage of growth, the medium used, the medium's makeup, the grow room's temperature, the light used and container volume. It is not possible to recommend a specific interval good for all plants in all stages of growth. A very common way to determine when to water is to keep an empty planter filled with dry soil next to your plants. Compare the weights daily and do not let your plants get as light as your dry example . A conspicuous sign of water problems is the downward wilting of leaves .

2 – 2 – 4 : Nutrients :



Fertilizer burn on a leaf

Nutrients are the food of plants and come in the form of fertilizers which can be chemical or organic, liquid or powder and may contain several elements . Commercial fertilizers must indicate the levels of NPK (mentioned above) . During vegetative stage cannabis needs more amounts of N than of P , K while during flowering P is more essential than N , K . The presence of secondary nutrients (Calcium , Magnesium , Sulphur) is recommended . Also there are seven micronutrients (Iron , Boron , Chlorine , Manganese , Copper , Zinc , Molybdenum) that are not extremely important and rarely manifest as deficiencies .

Fertilizers although vital for good cannabis growth, must be used frugally otherwise they could burn the plant. As a general rule, half the amount suggested in a bottle may be given each time .

As a plant acclimatized to virtually every growing region on Earth, its nutrient needs vary widely with its genetics and can truly only be determined with experience. Chemical plant foods vary greatly maker to maker, and some can be used at full strength, or the strength listed for plants with large fruits like the tomato .

2 – 2 – 5 : Organic cannabis :

Organic cultivation of marijuana is similar to the organic food movement in recent times. It is superficially similar to the hydroponic methods, with the exception of tending towards soil and nutrients which are derived from organic sources. In general, these sources are items like guano. The use of soil (generally in buckets or ally printed on the container. For this reason, the supposed organic cultivation of

cannabis, especially indoors, resembles other controlled cultivation methods where the intake of the plants is closely monitored.

2 – 3 : Stages Of Development :

2 – 3 - 1 : Germination :



C. sativa seeds

Duration: 12 hours to 8 days. Warmth, darkness and moisture initiate metabolic processes such as the activation of hormones which in turn trigger the expansion of the embryo within the seed. Then the coating cracks open and produces a small embryonic root that begins growing downwards due to gravitropism, if placed in a proper growing medium. Soon (after 2 – 4 days) the root is anchored and two circular embryonic leaves (cotyledons) emerge in search of light, as the remains of the seed shell are pushed away. This marks the beginning of the seedling stage .

Seeds may be germinated by soaking them between wet paper towels, in a cup of water at room temperature for 24 hours, or in wet peat pellets. Regardless of the method used however, distilled water is often employed since it has the proper pH. In most cases tap water is sufficient. Peat pellets are often used as a germinating medium as they make it unnecessary to transplant the fragile seedlings; the saturated pellets with their seedlings can be planted directly into the intended growing medium with a minimum of trouble and effort, or shock to the plant.

A technique that achieves high germination rates is the following: First the seeds are inserted into a cup of water. All will initially flow over the surface so forcing them to immerse completely is recommended. Then the cup is left in a warm dark place for no more than 24 hours (otherwise seeds might drown) . Shortly most will go down the bottom, an indicator that water has penetrated the shell. Finally, the seeds are placed carefully in a constantly damp, warm and

dark environment such as wet cotton or towel. Dirty hands (even traces of nicotine on them) can damage the seeds. As soon as the root can be distinctly seen, the seeds are ready to be placed in a growing medium.

2 – 3 – 2 : Seedling phase :

Duration: 1– 4 weeks. The seedling stage begins when the seed breaks and exposes its round “seed leaves” or cotyledons. This is the most fragile time during the entire life cycle of the cannabis plant. It is important to keep a constant atmosphere with a high humidity level and medium to high light intensity. Most indoor growers use compact fluorescents or T5 fluorescents during this stage as they give off little heat. HPS and MH lights give off large amounts of radiant heat and increase the rate of transpiration in the plant. Seedlings have small root systems and can dry out very quickly, thus keeping the medium moist is important at this stage. During the seedling stage fertilizers are not necessary and should not be given to the plant. As plant needs vary strain to strain, watch for discolored lower leaves, as this may be a sign the plant is ready for food. By the end of the seedling stage the plant can have 4 - 8 new leaves.

The plant can begin to sex itself in this stage but if time is an issue one can induce sexing by switching to a 12 / 12 hour period. Once sex is determined you can remove the males and switch the cycle back to vegetation stage by inducing an 18 / 6 hour period.

2 – 3 – 3 : Vegetative phase :

Duration: 1–2 months indoors. In this stage the plant needs all the light (at least 18 hours) and nutrients (food) it can get. It will continue to grow upwards and produce new leaves. The sex is starting to reveal which is a sign that the next stage begins. Concurrently the root system expands downwards in search of more water and food. Some newly developed strains (autoflowering hybrids) omit the vegetative stage and pass directly from seedling to pre - flowering .



A young male cannabis plant during early flowering stage

When the plant possesses 4 sets of true leaves and the 5th is barely visible in the center of the growth tip, or shoot apical meristem (SAM), the plant has entered the vegetative phase of growth. During the vegetative phase of growth, the plant directs its energy resources primarily to the growth of leaves, stems, and roots. A strong root system is imperative, as it is required for strong floral development. A plant needs 1 or 2 months to mature before blooming. The plant is ready when it has revealed its sex. The males are then culled when they are identified, because they don't produce buds or flowers. If males are allowed to pollinate the females their potency will be greatly reduced, as energy that would have been used to make large, potent buds instead goes to making seeds .

During the vegetative phase of growth, cultivators generally employ an 18 to 24 hour photoperiod, as the plants grow more quickly if they receive more light, although a warmer and cooler period are required for optimal health. While no dark period is required, there is debate among cultivators as to whether a dark period is beneficial, and many continue to employ a dark period.

The amount of time to grow a cannabis plant indoors in the vegetative stage depends on the size of the flower light you use, the size of the space you're flowering in and how many plants you wish to flower at once and how big your strain gets in 'the stretch' - the first two weeks of flowering .

Marijuana cultivators employ fertilizers high in nitrogen and potassium during this stage, as well as a complete micronutrient fertilizer. The strength of the fertilizer is gradually increased as the plants grow and become more hardy.

The modification of a plant's growth habit is called training. Indoor cultivators employ many training techniques in order to encourage shorter plants and denser canopy growth. For example, unless the crop is too large to be extensively pruned, cultivators will remove adventitious growth shoots, often called suckers, that are near the bottom of the plant and/or receive little light and will produce poor quality buds .

Many cultivators also employ other techniques :

Topping :

Is done by removing the top of the apical meristem (dominant central stem) , called the apex or terminal bud, in order to transfer apical dominance (the tendency for the apex to grow more rapidly than the rest of the plant) to the shoots emanating from the two nodes immediately beneath the pruning cut. This process can be repeated on one or both of the two new meristems, when they become apically dominant, with the same results. This process can actually be repeated almost infinitely, but over - diffusion of apical dominance will produce smaller, lower quality buds, so it is usually done no more than a few times. Topping also causes more rapid growth of all of the branches below the cut while the plant heals.

Pinching :

Pinching (also called super cropping) is similar to topping in that it causes the lower branches to grow more rapidly, but the apical meristem will maintain apical dominance, which is especially useful if the plant has already been topped. Pinching is performed by firmly pinching the apical meristem(s) so as to substantially damage vascular and structural cells but without totally breaking the stem. This will cause the lower limbs to grow more rapidly while the pinched tissue heals, after which time the stem will resume apical dominance .

2 – 3 – 4 : Pre - flowering phase :

Duration: 1 day to 2 weeks. Also called 'the stretch' . In most plants will last for 10 – 14 days after switching the light cycle to 12/12. The plant development increases dramatically, with the plant doubling in size or more (see reproductive development below) . The production of more branches and nodes occurs in this stage as the structure for flowering is built. The plant will start to show a calyx which appears where the branches meet the stem (nodes) . Pre-flowering indicates that the plant is ready to flower .

2 – 3 – 5 : Reproductive/Flowering phase :



The flowers of a male cannabis plant

Duration : 4 – 16 weeks . The sex is clearly revealed. Males produce little balls clustered together like grapes. Most plants (except autoflowering strains which flower independently of photoperiod) will flower under diminished light. In nature, cannabis plants sense the forthcoming winter as the earth turns and daylight reduces in duration. If females are not pollinated (fertilized by male pollen) they will start to produce buds containing sticky white resin glands or trichomes in a final attempt to attract male pollen (THC is very sticky and thus the plant produces more when it is not fertilized) . The trichomes contain the largest amounts of THC and CBD, the two main psychoactive substances. Indoors, flowering is induced by keeping the plant in complete dark for 12 hours every day, until it is ready to be harvested. If manipulated, a female can either generate a seedless bud, a bud with a few seeds, or a bud that is almost totally seeds. The first case is achieved by removing all the male plants before any of their flowers open, the second occurs when one or more male flowers have barely

burst open and then removed and the third case occurs if the males are let to fully pollinate the females.

Buds of the first case are called *sinsemilla* (it is really two words: " sin semilla " , which translates to " without seeds " in Spanish, but is often misspelled as one word). The resultant cannabis contains the most Cannabinoids possible . The amount of Cannabinoids in *sinsemilla* is considerably more in comparison to cannabis that has been grown in a pollinated environment, because the production of seeds requires an immense amount of energy, and if left unpollinated a female plant will divert all her energy to calyx production in an effort to seize pollen . This is especially desirable, as the calyx is where the highest concentration of trichomes exists, and the more densely packed a plant is with calyces, the greater psychoactive effect that plant will likely have. Potent sinsemilla is especially important to medical users, to minimize the amount of cannabis they must consume in order to be afforded relief . Cannabis with seeds is generally considered to be of inferior quality and/or grown with inferior technique. Common terms for seeded , or otherwise low – quality , cannabis are " mids " , *schwag* , " regs " , " booty " , " greta" or *mersh*.

Indoors , plants like cannabis are induced into flowering by decreasing its photoperiod to at least 10 hours of darkness per day. Traditionally most growers change their plants lighting cycle to 12 hours on and 12 hours off. This change in photoperiod mimics the plant's natural outdoor cycle; with up to 18 hours of light per day in the summer and down to less than 12 hours of light come fall and winter .

While the flowering hormone in most plants (including cannabis) is present during all phases of growth, it is inhibited by exposure to light. To induce flowering, the plant must be subject to at least 8 hours of darkness per day ; this number is very strain-specific and most growers flower with 12 hours of darkness to be safe. The flowering hormone is very quickly inhibited, taking less than two minutes of exposure.

Flowering usually lasts from 45 to 90 days indoors. If growing outdoors it may take somewhat longer, depending on the natural onset

of the colder seasons. The flowering length is mainly genetically determined with plants (as pure cannabis "indica" strains) flowering in as low as 45 days, while plants (as cannabis "sativa") can take up to 4 months to finish and the harvest yields significantly less. This is also the main reason why certain plants (as cannabis indica) are almost always grown indoors (unlike cannabis sativa, which is also grown outdoors) .

Some plants, specifically members of the subspecies Ruderalis, will begin the flowering cycle without a significant reduction in their photoperiod .

Flowers from certain plants (eg cannabis) are called Calyx, and are (with cannabis) the most prized part of the plant. In late flowering the calyx are easily visible to the naked eye. Calyx development begins approximately 1–2 weeks after the photoperiod is reduced. In the first weeks of flowering a plant usually doubles in size and can triple. Calyx development ends around 5 weeks into flowering and is preceded by a period of Calyx “swelling”. During this time the buds greatly increase in weight and size.

3 : Outdoor Cannabis Cultivation :



Guerrilla cannabis plot in a forest clearing

A chart demonstrating the reflective qualities of cannabis in comparison with other common plants, which may be used for cover.

Cannabis can be planted outdoors under the sun, either on natural soil or in pots of pre-made or commercial soil. In most places of the subtropics cannabis is germinated from late spring to early summer and harvested from late summer to early autumn.

Outdoor cultivation is common in both rural and urban areas, with outdoor cultivators tending to grow indica-based strains due to their heavy yields, quick maturing time, and shortness. Some growers prefer sativa because of its clear-headed (cerebral) high, better response to sunlight, and lower odor emissions.

One can cultivate on his own property or practice guerrilla farming i.e. plant cannabis in remote areas such as forest clearings or mountain cliffs and visit rarely. However such a method is prone to ripoffs - so much so that some ingenious growers even attach pots on trees to decrease this possibility.

When cultivated outdoors, the chosen areas are those which receive twelve hours or more of sunlight in a given day. In the Northern Hemisphere cannabis seeds are typically planted in late May or early June, so the plants can have a full four months of growth. Typically, the plants are harvested anywhere from mid September to early October. In North America, northern locations are preferred (Humboldt County, California and British Columbia being particularly notable), but southern locations (such as Maui, Hawaii) are also known to be good producers.

In instances where the local laws do not permit growing cannabis, cultivators may choose to grow in forests or rugged and rural areas where the local population are not likely to find the crop. Another technique is to grow cannabis in a crop that is larger and obscures the plants, such as maize. This is reported by the United States government to be common in the midwestern states. Bamboo and elderberry are also used as camouflage companion plants.¹

Some government organizations have claimed that in state and national parks, people have been injured by "rebel farmers" protecting their crops, including a well documented developing problem with Mexican cartels growing cannabis in US national parks and forests.

3 – 1 : Detection :

Often simple camouflage techniques can avert detection, such as mixing cannabis plants with other bushy, leafy species. Plants started

outdoors late in the season do not grow as tall, attracting less attention when placed next to plants of similar or taller stature.

A common technique used by many outdoor growers is to dig a hole and put a potted plant in it. This can reduce a plant's height by at least a foot, reducing visibility to neighbours, visitors and guests. Also, some growers top the plant when it is only 12 inches (30 cm) high, and grow the 2 tops horizontally along a trellis. When using this technique, it is unlikely the plant will grow to be over 3 feet (1 m) tall.

Law enforcement agencies often monitor certain wider areas, particularly areas of countryside with a significant history of outdoor cannabis cultivation. In helicopters, they use infrared cameras and other equipment that can detect cannabis by measuring the heat and reflective signature of the vegetation below. Cannabis has higher reflectivity at certain wavelengths than other rural crops, such as corn. Law enforcement agencies have found that the use of this technology has become necessary in their detection efforts because many growers hide cannabis among other plants, making detection with the naked eye difficult even from the air. These techniques are effective and difficult to defeat because a plant's reflective signature is difficult to change or mask. It has been said that if the cannabis plant is planted by a pine or cedar tree the heat from the tree will overlap the cannabis plant heat making it harder to detect from helicopters .

4 - Indoor Cannabis Cultivation :



Indoor Cannabis cultivation.

Cultivating Cannabis indoors traditionally has to do with growing the plants in a soil - like medium and adding fertilizer when the plants are given water. Cultivating marijuana indoors is more complicated and expensive than growing outdoors, but it allows the cultivator

complete control over the growing environment. Cannabis grown outdoors can be just as potent as its indoor counterpart if tended to properly.

Cultivating plants indoors can also be done through the use of hydroponics; however, this method is somewhat less common .

In order to grow plants indoors, a growing medium (eg soil or growing substrate) , water, nutrients, light and air need to be supplied to the plant .

4 – 1 : Supply of light :

To determine the appropriate lighting (and the best lamp to use), the specific needs of the plant must be considered, as well as the room size and ventilation. To arrange optimal lighting, the lighting present in the plant's natural environment needs to be imitated.^[20] For example vegetables grow best in full sunlight, which means in practice that as much light as possible must be supplied to grow cannabis indoors (high intensity discharge (HID) lights such as high pressure sodium (HPS) and metal halide (MH) are preferred. fluorescent lamps can also be used). Incandescents and mercury vapor lighting are not used in cannabis cultivation.

In addition, plants also require both dark and light ("photo"-) periods. As such, lights need to be timed to switch them on and off at set intervals. The optimum photo/dark-periods is specific depending on each plant (some prefer long days and short nights an others preferring the opposite, or something in between)

Most plants will grow under most light spectra, yet always prefer a full spectrum light. A test done by Ed Rosenthal found that when a room was set up using both high pressure sodium (HPS) and metal halide (MH) lamps the plants in between the two lights did better than those under MH alone but not as well as those under HPS. However, certain plants (as cannabis) can be grown successfully under both types of light. MH is used for vegetative phase of growth, as it encourages short internodes (distance between sets of leaves) , and inhibits cell elongation, creating a shorter, stockier plant. Metal halide lamps produce more ultraviolet radiation than high pressure sodium

lamps, which may play a role in increasing the flowering (and for certain plants as cannabis the amount of working substances as THC) produced by the plant. High pressure sodium lamps trigger a greater flowering response in the plant and are thus used for the second (or reproductive) phase of the growth, or they are used by those people who only wish to purchase 1 single lamp.^[21] If high pressure sodium lamps are used for the vegetative phase, plants will usually grow slightly more quickly, but will also have longer internodes, and may be taller .

Recent advancements in LEDs have allowed for the production of relatively cheap, bright and long lasting grow lights that emit only the colors of light required for plant growth. These lights are attractive to indoor-growers since they do not consume as much power, do not require ballasts, and produce a fraction of the heat of HID lamps. The lamps consist of arrays of many wide - spectrum red and a few narrow-spectrum blue LEDs of specific wavelengths. Although LED grow lights have shown promise through plant research by NASA and many universities, it is unknown whether the results are applicable to Cannabis cultivation, as their luminous efficiency is much lower. However, luminous efficiency is not applicable to plant growth since it is based on what wavelengths humans see best. A plant is, for example very sensitive to far - red, while humans can barely see that wavelength. Therefore , LED's can be more efficient for plant growth, while their lumniuous efficiency is lower compared to other solutions.

According to the inverse square law, the intensity of light radiating from a point source (in this case a bulb) is inversely proportional to the square of the distance from the source. So if an object is twice as far away, it receives only 1 / 4 the light. This is a serious hurdle for indoor marijuana growers, and many techniques are employed to use light as efficiently as possible.

Reflectors are often used in the lamps to maximize light efficiency. Plants or lights are moved as close together as possible so that they receive equal lighting and that all light coming from the lamps wind up on the plants (rather than partly besides it). Often, the distance between lamp and plant is in the range of 0.6 m (2 ft) with incandescent lamps, to 10 cm (4 in) with other lamps, such as

compact, large and high - output fluorescent lamps. Some marijuana cultivators cover the walls of their grow - room with some type of reflective material, or alternatively, white paint to maximise efficiency.

One commonly used covering is 6 millimeter (150 μm) PVC plastic sheeting that is white on one side and black on the other. The plastic is installed with the white side facing in to the room to reflect light, and the black facing the wall, to reduce fungus and mold growth. Another common covering is flat white paint, with a high titanium dioxide content to maximize reflectivity. Mylar sheeting from a grow store is very effective when it lines grow room walls, along with Astrofoil (which also reflects heat) , and Foylon (a foil – laminated , reinforced fabric) .

4 – 2 : Control of the atmosphere :

When growing indoors, the cultivator should maintain as close to an ideal atmosphere inside the grow-room as possible. The air temperature should be maintained within a specific range, typically with deviations no larger than 10 °C. with a cooler night and warmer day. Adequate levels of CO₂ must be maintained in order for the plants to grow most efficiently. It is also important to promote vigorous air circulation within the grow room, which is usually accomplished by mounting an extraction fan and one or more oscillating fans.

Assuming adequate light and nutrients are available to plants, the limiting factor in plant growth is the level of carbon dioxide (CO₂) . Plants grown with supplemental carbon dioxide will grow more quickly, have larger stomata, and can utilize more light. Ways of increasing carbon dioxide levels in the grow-room include: bottled carbon dioxide, carbon dioxide generators, a milk jug and yeast solution (in which yeast grows in a container hereby emitting CO₂) , a baking soda and vinegar mixture in a container, or dry ice .

Certain plants (eg most strains of cannabis) emit a distinctive odor during their reproductive phase. This presents difficulties to those who are cultivating in places where it is illegal. The most common way of eliminating odor is by pulling odorous air through a

carbon filter. Many cultivators simply attach a large carbon filter to their air extraction system, thereby filtering any smell before the air is expelled from the grow-room. Another way of eliminating odor is by installing an ozone generator in the extraction ducting. The air is forced past the ozone generator by the extraction fan, and the odorous air is neutralized as it mixes with the ozone; however the cultivator must ensure that the air is thoroughly mixed before it is expelled outside, lest some odor escape. Care must be taken to prevent excessive ozone concentrations in the garden itself, or where it might be inhaled by the grower or his/her family. Ozone itself has a distinctive smell and is harmful to living things, although the molecule breaks down quickly (20 minutes to an hour) in atmospheric conditions.

4 – 3 : Popularity :

Indoor growing has become increasingly common over the past decade, in part due to increased availability of equipment, seeds and instructions on how to cultivate. So - called grow- ops (growing operations, often located in grow houses) are seen by many marijuana enthusiasts as a much cheaper way in which to gain a steady, higher-quality supply of cannabis. On a larger scale they have proven a viable commercial venture, with some law enforcement agencies finding grow-ops large enough to yield several kilograms of marijuana. More expansive grow - ops, however , are generally more susceptible to detection than smaller operations .

Since individual grow light power generally ranges from 250 watts to in excess of 1000 watts and remains lit for a long time each day, differences in utility bill costs are a significant security issue. It is not uncommon for power companies to work with law enforcement if they witness significant increases in power usage relative to a household's previous electricity costs. Employing energy saving methods is a common way to alleviate this, for instance; switching off light bulbs when leaving rooms, purchasing energy efficient appliances, using TVs or computers less, buying lower power light bulbs and so forth.

Some plants (eg cultivars of *Cannabis sativa* subsp. *Índica*) , can give off strong odors as they grow, resulting in detection of illegal growing operations. Growers frequently use carbon scrubbers in conjunction with ventilation in order to control odors. This typically involves forcing air from the grow room through a device containing activated carbon, before being vented outdoors. Others use an ozone generator. Ozone reacts with odor molecules in the air, permanently eliminating them. However, ozone can build up to levels that may be hazardous both for the grower and the plant. As a last resort, strong air fresheners are used to control smells as well as keeping windows firmly shut. This is a risky method, as the smell of air fresheners may often arouse suspicion by police officers. Checking outside to see if any smells are emanating from indoors is often a necessary precaution, as many growers become acclimated to the smell, and fail to realize just how pervasive the odor may be. Many store plants in more isolated areas such as a basement or attic to prevent smell detection. Another less common solution is to simply grow a strain which possesses a weaker odor.

Storing plants and lights away from windows and areas which may be seen by visitors is also a common practice, as is keeping the entire grow op in an attic or basement. Some growers, finding this impractical, may cover their windows with light - resistant materials. This can solve the problem of escaping bright light but may arouse suspicion amongst neighbours and local residents.

Many cultivators face detection by fire. Fires normally originate from faulty electrical equipment or wiring. Shoddy fixtures and sockets, improperly grounded equipment, and faulty circuit breakers are some of the most prevalent causes. Due to the large amount of electricity needed for large-scale cultivation, old or damaged wiring is prone to melt and short. Some commercial growers resort to power theft in order to hide electricity usage and many do not take precautions to ensure that their connections are safe. Many growers adapt light cycles so that the lights are on when they are home and off when they are away.

Another fire hazard is plants making contact with hot HID bulbs. Growers using fluorescent bulbs with reasonable air circulation do not have this problem.

Word of mouth can of course be as much a threat to growers as any of the above issues. Often, a few sentences of conversation overheard can result in a tip - off and thus speedy detection. It is for this reason that many growers are reticent to talk about their cultivation.

5 - Harvesting, drying and curing ;

A typical indicator that a plant is ready to be harvested is when 2/3 of the pistils have turned from white to reddish brown or other color. In general, harvesting consists of drying and curing . Curing is essential for the even distribution of moisture in the buds . A popular alternate method is the following:

Dry : Buds left in well ventilated dark place for 24 hours

Cure : Buds stored in sealed bag and left in dark place for 8 hours

Dry : Buds left in well ventilated dark place for 16 hours

Cure : Buds stored in sealed bag and left in dark place for 6 hours

Dry : Buds left in well ventilated dark place for 12 hours

Steps continued likewise as necessary

In 3 – 4 days buds are ready for consumption .

Cannabis buds are typically harvested when fully ripe. Generally, ripeness is defined as when the white pistils start to turn dark yellow, orange, light to mid red, etc. and the trichomes, "crystals", barely begin to turn milky from clear. These trichomes can range from completely clear (generally deemed underdeveloped), to amberish-red. Ideally, professionals will use a decent power magnifying glass, a brix meter (to measure "sugar" content), and a microscope. The potential seed pods swell with resins usually reserved for seed production, thus improving the quality of the buds (called *colitas*, Spanish for "little tails"), which will swell to form full "colas" (Spanish for "tails") . If

harvested early on with only a few of the pistils turned color, the buds will have a more pure THC content and less of the cannabinoids CBD and CBN. The latter cannabinoids are non-psychoactive; they contribute to the bouquet of the marijuana and modulate the overall nature of the high anywhere from purely psychedelic to purely sedative.

Contrary to sinsemilla (bud production focused cultivation), seeds are harvested when fully developed and often after the accompanying buds have begun to deteriorate. In contrast, hemp grown for fiber is harvested before flowering, and cannabis grown for cloning is not flowered at all.

5 – 1 : Drying :

The plants are dried at room temperature in a dark space. This process can take from a few days to two weeks, depending on the size and density of the buds and the relative humidity of the air. A stable temperature preserves cannabinoids well. Some believe flowers are hung by their stalks, allowing the internal fluids of the plant to remain in the flowers. Others believe the cut stem is simply a handy non-sticky place from which to hang the plant. Roots are removed. When the stems in the middle of the largest buds can be snapped easily, the plant is dry enough to be cured. Drying is done in a dark place, as THC resins will deteriorate if exposed to light and the degradation product CBN will be formed, thus significantly altering the cannabinoid profile of the dried flowers.

5 – 2 : Curing :

The curing process continues breaking down sugars and helps develop taste and smoothness of smoke. Usually, the dried product is packed (not compressed) into glass canning jars which are airtight. Initially the product is checked periodically (every few hours) to make sure it was properly dried and has not remoistened itself. After several days, when the product is dried to satisfaction, the jars are sealed off and opened just once a week. Curing is highly varied — the minimum is usually two weeks. Some growers even cure as long as six months, while others do not cure at all. As with tobacco, curing

can make the cannabis more pleasant to smoke. For the same reasons as when drying , curing jars are stored in a cool , dark , place .

A recent method of curing is called water curing. This method is quicker and can improve a lower quality product. The freshly cut buds are submersed in water for a period of 7 straight days, changing the water daily. The buds are then dried and are ready to use. Nutrients can be added to the plants up until they are harvested. When water curing, the water will flush out harmful chemicals (such as the ones used to feed the plants) as well as proteins, sugars, pigments, chlorophyll and some resins. This will also increase the THC to weight ratio.^[25] Many believe the finished product is not as attractive as using a standard dry and cure >

Tincture . Ethanol is used to extract cannabinoids from the marijuana plant (THC is soluble in alcohol) . The extraction process takes longer, but results in an edible product . Marijuana stems, leaves and buds can all be used. The resulting mixture can be eaten straight, mixed with food or even smoked. Many smokers prefer to dip cigarettes in the mixture, which allows them to smoke in public without detection. Contact with direct flame causes this liquid to lose its THC content (THC vaporizes at 180 °C) . Smokers usually heat the liquid and inhale the vapors through a straw .

5 – 3 : Hash or Hashish :

Hashish can be expensive but like everything else in cannabis cultivation, it can be an investment that pays for itself. After a harvest, there are typically many green leaves - particularly large shade leaves- which themselves cannot be smoked, but have collected over time many fallen trichomes. Rather than letting them go to waste, these are soaked in a bucket of cold water. The liquid is then passed through a succession of bags with decreasing screen sizes which capture the trichomes, which are then pressed into shape and let dry. The result is called *bubble hash*, due to the bubbling which occurs when it is heated for smoking. This bubbling is due to its purity, as adulterants tend to cause hash not to bubble .

Hash Oil . Allowing the ethanol in a tincture to evaporate makes hash oil . **Ethanol should never be evaporated with direct heat , or near an open flame!** The resultant hash oil is often very strong in terms of THC content (depending on parent material) , and can be then smoked. Delta 9 THC is most strongly soluble in petroleum ether and less so in ethanol. Adding petroleum ether to tincture will extract D9 THC, and leave water soluble chemicals in the ethanol (certain cannabinoids, proteins, chlorophyll, etc). Hash oil purified this way can exceed 90 % D9 THC.

6 - Pests And Insects :

Outdoor growers are more likely to have problems caused by pests. If these need to be treated with chemicals only pesticides and insecticides which are safe to use on food crops should be used. Popular and safe pesticides include :

Pyrethrins : Organic and very effective , although sometimes hard to find and expensive due to high production cost.

Azadirachtin : Meeting most criteria to be classified as a natural insecticide. Biodegradable, non-toxic to mammals. Cheap and easier to find.

Indoor growers also have problems with pests, usually caused by the grower or a pet bringing them in from the outdoors. If caught too late, eradication of many destructive insect species indoors may be impossible until all infected plants are removed from the space and sterilization methods employed.

7 - Advanced Cultivation Methods :

The legal status of cannabis has led growers to implement novel cultivation methods for indoor growing which involves the use of lamps, in order to avoid aerial surveillance of outdoor plots.^[27] These methods include :

using a water or air - based growth medium (known as hydroponics and aeroponics respectively) .

the use of homemade , organic composted fertilizers .

training and trellising techniques such as *Screen of Green* (also known as *SCROG*) , *Sea of Green* (also known as *SOG*) "Supercropping" and LST supercropping; and entire systems and methods such as the *NIMBY no-dump* method, *Hempy Bucket*, and the *Krusty Freedom Bucket* methods. Research into the production of cannabis for the drug Marinol and other more profitable and marketable forms of cannabis based medicines has further pushed the envelope of cannabis cultivation in all forms of laboratory, both public and private.

The emphasis on advanced cultivation techniques, as well as the availability of hybrid strains (with names like *Northern Lights*, *Master Kush*, *NYC Diesel*), is believed to be a factor in the increase in the overall quality and variety of commercially-available cannabis over the past few decades. The internet in particular has brought together widely diverse genetics from around the world through trading and purchasing . However , well - grown heirloom strains (e.g. island sweet skunk , fruity Thai etc). are used to produce 1gram per watt harvest.

7 – 1 : SOG :

In contrast to the "Screen of Green" method, *Sea of Green* (or *SOG*) growing depends on the high density of plants (as high as 60 per square meter) to create uniformity in the crop. In this technique, which is often grown in hydroponic media, only the colas of the plants are harvested. Containers are used to enforce the geometric distribution of flowers and plant material, as well as their exposure to lighting and atmosphere. Sea of green is popular with commercial cultivators, as it minimizes the amount of time a plant spends in vegetative stage, and allows very efficient light distribution, keeping the plants much closer to the lights than when grown to full size. However, the individual plants grown with this method typically give smaller yields than those grown with other methods .

7 – 2 : SCROG :

SCROG, short for SCReen Of Green, is an advanced training technique for Cultivating Cannabis , mainly indoors . Closely

resembles SOG (or Sea Of Green) with the difference being that SCROG uses extensive training to produce the same field of bud effect with only one plant. Medical growers may find this a helpful technique to maximize harvest if they are only allowed a certain number of plants. A screen such as chicken wire is hung over plants so that the tips of branches are kept at the same level. This allows even light distribution to all of the nodes/bud sites. Once the flowering stage is initiated, the flower tips will reach through the wire and all be at relatively equal distances from the light source.

Light Depreciation: The Inverse Square Law ^[28] states, as the distance from the light source is doubled, the light intensity is quartered. Cannabis growers realize this and want to get the maximum use for their lights. With an untrained plant the lower branches of their plants don't produce as well as the upper branches, being too far from the light. The SCROG method reduces this problem by putting basically the whole plant on one vertical plane, allowing all bud sites to receive nearly maximum light. This is beneficial because it produces more by getting light where the plant needs it. Vegetative State: The plant should remain in the vegetative state until 70 to 80 percent of the net is full As a branch reaches three to four inches above the wire it is pulled back under the wire and so trained to grow vertically until flowering. Due to the amount of plant required to fill the net, the vegetative period may require longer than normal to be ready for flowering.

Timing: Timing is vital to the success of a SCROG grow. If the net is not full at harvest, valuable space has been wasted. If the net is too full then the buds will be too crowded to develop properly. Knowing how a plant grows can help to visualize when to flower for maximum effect .

7 – 3 ; Hydroponics :

Hydroponic cultivation generally occurs indoors, although there is no practical obstacle to growing outdoors . In general, it consists of a non-soil medium which is exposed to a nutrient and water flow .

There are many types of hydroponic systems. If the nutrient solution floods the loose growing medium and recedes for aeration, this is an *ebb and flow* or *flood and drain* system. Systems that gradually drip solution onto the medium are *drip systems*. Systems that intermittently spray roots floating in air are called *aeroponic systems*. If aerated water runs down a channel lined with a film of rooting medium, this is a *nutrient film technique* system. A series of tubes intermittently running high flow nutrient solution into the tops of growing containers use a *top feed system*.

Hydroponic systems greatly increase aeration of plant roots, and increase control of nutrient uptake. Hydroponic systems are decidedly more difficult to operate for the amateur or hobby grower, as over-fertilization is common, because there is no soil to act as a nutrient buffer. For this reason, many growers now use coconut fibre as a soilless medium due to its high drainage and buffering capabilities, making it almost impossible to over - fertilize. Additionally, if a hydroponic system fails, the crop has a high probability of dying as the roots rapidly dry out (this is especially true of aeroponic systems)

There is now a new breed of hydroponic configurations such as the Omega Garden and the Ecosystem that use circular designs to maximize efficiency. This consists of plants being placed or in the case of the Omega Garden revolving around a central light which maximizes the lumen output of the lights used.

8 - Genetics and breeding :

8 – 1 : Selection of mother plants :

An important factor in cannabis cultivation is selecting the best genetics for one's crop. This is frequently done by selecting one or more known strains, or strains with preferred genetics (in the case of marijuana, one might use seeds from a batch that was particularly enjoyed) , and then growing a number of the seeds to find out which exhibit the characteristics most desirable to the cultivator. These genetics should typically yield at least 1 gram per watt.

Plant characteristics which are generally selected for include :

Overall yield , Time to fruition , Resistance to pests , Geometric traits (uniformity , compactness , flower density , etc) , Color , Flavor and / or aroma , Appeal to end buyer (known as "bag appeal") , Psychoactive qualities , Trichome density and type (stalked or sessile).

When a cultivator has decided which plant or plants exhibit the most desirable traits, a cutting is taken and grown to maturity but never allowed to flower. This plant is referred to as a *mother*, and can be kept for years, producing thousands of clones genetically identical to the mother .

8 – 2 ; Feminized seeds :

It is possible to use a combination of cloning and "shocking" plants to get them to produce feminized seeds.^[31] A clone will retain the same sex throughout its life, so if a female plant is cloned, its clones will also be female, precluding reproduction.

Some claim (particularly vendors of feminized seeds produced with certain methods) that while environmental stresses have been used to create pollen bearing male flowers on female plants- known as 'hermaphroditing' or 'hermying', this method is not preferred when creating feminized seeds; due to those plants most likely to revert to seed making being the ones which hermie soonest; hence passing on the genetic trait of instability of gender - desirable in the wild but not in cultivation .

Spraying selected leaves, branches and in cases where large amount of seed desired whole plants with colloidal silver solution has become a preferred method since the colloidal silver suppresses ethylene production in bud sites, stimulating male characteristics. Gibberellic acid has been used frequently; but is harder to find than colloidal silver, which involves nothing more than a small wall d.c. power supply and two pieces of solid silver jeweler's wire, or 99.99 % silver coin. A method used by organic growers and promulgated by the famous Cannabis breeder Soma, is called 'Rodelization', or letting unpollinated female plants live several weeks longer than the normal harvest time. In such plants a hermaphroditic trait will self express in effort to continue the genetic line; the fact this method utilizes auto

hermaphroditic traits which could contribute to instability in a plant's genetics is offset by grower observations that the tendency to auto-switch sex is not great in plants grown from seeds made this way, and the fact that it occurs naturally without effort on the part of the cultivator.

However, other cultivators claim that the genes responsible for hermaphroditism are present and may be activated under stress from any of the above methods and that once activated can be passed to seeds regardless of how it was activated. Previous theories would not have allowed for the passing of genetic alterations an adult has acquired after birth but there is evidence that when a gene is activated in a mother after her birth that expression can be passed to offspring .

8 – 3 : Hybrid vigor :

When crossing two strains of cannabis (or two of any plant), the resultant hybrid may possess what is called *hybrid vigor*. In general, this produces a plant which is healthier, stronger, or quicker growing than its predecessors. Sometimes, in the case of a plant which has been brought back from fruiting (fruition, as mentioned above), it may be beneficial to cross it back with another (close) relative, in the hopes that it will become invigorated .

Caution should be exercised, as one does not always attain a beneficial cross with hybridizing.

8 – 4 : Cloning from cuttings :

Like many plants, cloning of cannabis is possible through a relatively simple process. The process itself is quite similar to the cloning of most other plants and involves rooting branch cuttings from donor (" mother ") plants .

There are many methods of cloning available, from store bought purpose built cloning machines to inserting a cutting in a cup of water and waiting for roots to grow. Most methods will take anywhere from 5 – 21 days . Certain strains of cannabis have proven harder to clone than others.

Rooting hormone gel or powder mixes are then applied to the cut to promote root growth and inhibit fungal infection. The cutting is then placed in a rooting medium which may be a soil mix or a soil-less medium. Typical soil - less media are Perlite, vermiculite, peat moss, sand, rock wool or Oasis foam. A good medium is one that drains well, holds moisture and air well also. Oxygen is important for healthy root growth .

The cuttings in their new medium should be kept at a constant temperature (around 78 F) and with high humidity. Elevated humidity levels can be achieved by use of a humidifier or a humidity dome. Elevated humidity levels slow the transpiration rate which is important because without a root system the water uptake is very slow; If the transpiration rate exceeds the uptake rate the cutting is losing water and will wilt and die .

Many growers use a humidity dome as they are very inexpensive, around \$ 7 , and are easy to use. Many others improvise domes with simple plastic baggies secured with rubber bands (even less expensive and equally easy to use). When using a humidity dome, the dome should be removed at least twice a day and the rooting clones should be fanned to prevent mold and to give them some air circulation. Alternatively, you can cut off the bottom of a clear 3-liter bottle and temporarily put it over a single plant. The cap can easily be removed a couple times a day to easily refreshen air .

During other stages of growth one is advised to allow the soil to dry out to allow the roots to get oxygen and to prevent root rot. Since cuttings do not have roots this is not of concern. What is of concern is that a cutting will dry out and die, which occurs very rapidly.

Light intensity should be very low during the rooting process. High light intensities will force the plant to focus on photosynthesis at the expense of rooting. Light intensity should be increased during the last week up to normal illumination levels.

Cuttings usually take 7 – 14 days to develop root systems. Drooping is common within the first week. Cuttings that have not regained rigidity after 7 days are weak and are culled by most

growers. To speed the rooting process keep the cuttings at constant temperature. Allowing the parent plant to become mildly nitrogen deficient before the cutting is taken will also speed rooting.

If performed correctly, the cuttings should stay green during their rooting time, and condensation should appear on the plastic coverings for the cuttings, which indicates proper humidity. After 7 days, healthy cuttings will appear strong with leaves reaching upward. Yellowing leaf tips are a common indicator of successful rooting. Browning likely indicates too much sunlight, too little humidity, cutting rotting in sitting water, or unsanitary cloning conditions.

In recent years, stores selling hydroponic grow equipment began offering automated machines (i.e.: *EZCloner*, etc.) in which trimmed cuttings are placed and left alone for approximately two weeks. Anecdotal accounts from established growers indicate these automated machines have near 100% success rates. Unfortunately, the cost (more than \$ 300 USD) is prohibitive for most people that grow at home for personal use .

Coca



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- 2 Species and classification
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- 6 Traditional uses
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10.1 Photographs

10.2 Videos

1 - Introduction :

Coca is a plant in the family Erythroxylaceae, native to north-western South America. The plant plays a significant role in

traditional Andean culture. Coca leaves contain many alkaloids including cocaine, which is a powerful stimulant.

The plant resembles a blackthorn bush, and grows to a height of 2–3 m (7–10 ft). The branches are straight, and the leaves, which have a green tint, are thin, opaque, oval, and taper at the extremities. A marked characteristic of the leaf is an areolated portion bounded by two longitudinal curved lines, one line on each side of the midrib, and more conspicuous on the under face of the leaf.

The flowers are small, and disposed in little clusters on short stalks; the corolla is composed of five yellowish-white petals, the anthers are heart-shaped, and the pistil consists of three carpels united to form a three-chambered ovary. The flowers mature into red berries.

The leaves are sometimes eaten by the larvae of the moth *Eloria noyesi*.

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Malpighiales
Family : Erythroxylaceae
Genus : *Erythroxylum*
Species : *E. coca*

2 - Species and classification :

There are twelve main species and varieties. Two subspecies, *Erythroxylum coca* var. *coca* and *Erythroxylum coca* var. *ipadu*, are almost indistinguishable phenotypically ; a related high cocaine-bearing species has two subspecies, *Erythroxylum novogranatense* var. *novogranatense* and *Erythroxylum novogranatense* var. *truxillense* that are phenotypically similar, but morphologically distinguishable. Under the older Cronquist system of classifying flowering plants, this was placed in an order Linales; more modern systems place it in the order Malpighiales.

3 - Cultivation



Leaves and berries

Coca is traditionally cultivated in the lower altitudes of the eastern slopes of the Andes (the Yungas) , or the highlands depending on the species grown. Since ancient times, its leaves have been an important trade commodity between the lowlands where it is grown and the higher altitudes where it is widely consumed by the Andean peoples of Peru, Colombia, Ecuador, Venezuela, and Bolivia.

Fresh samples of the dried leaves are uncurled, are of a deep green on the upper, and a grey - green on the lower surface, and have a strong tea-like odor. When chewed, they produce a pleasurable numbness in the mouth, and have a pleasant, pungent taste. They are traditionally chewed with lime to increase the release of the active ingredients from the leaf. Older species have a camphoraceous smell and a brownish color, and lack the pungent taste .

The seeds are sown from December to January in small plots (*almacigas*) sheltered from the sun, and the young plants when at 40 – 60 cm in height are placed in final planting holes (*aspi*), or if the ground is level, in furrows (*uachos*) in carefully weeded soil. The plants thrive best in hot, damp and humid locations, such as the clearings of forests; but the leaves most preferred are obtained in drier areas, on the hillsides. The leaves are gathered from plants varying in age from one and a half to upwards of forty years, but only the new fresh growth is harvested. They are considered ready for plucking when they break on being bent. The first and most abundant harvest is

in March after the rainy season, the second is at the end of June, and the third in October or November. The green leaves (*matu*) are spread in thin layers on coarse woollen cloths and dried in the sun; they are then packed in sacks, which must be kept dry in order to preserve the quality of the leaves.

4 - Pharmacological aspects :

The pharmacologically active ingredient of coca is the alkaloid cocaine, which is found in the amount of about 0.3 to 1.5%, averaging 0.8%^[1], in fresh leaves. Besides cocaine, the coca leaf contains a number of other alkaloids, including methyl ecgonine cinnamate , benzoyl ecgonine , truxilline, hydroxy tropacocaine , tropacocaine , ecgonine , cuscohygrine , dihydro cuscohygrine , nicotine and hygrine . When chewed , coca acts as a mild stimulant and suppresses hunger , thirst, pain , and fatigue .

Absorption of cocaine from the leaf is much less rapid and efficient than from the purified forms of cocaine, and it does not cause the euphoric and psychoactive effects associated with use of the drug. Some proponents have claimed that cocaine itself is not an active ingredient when unprocessed coca leaf is chewed or brewed as an infusion. However, studies have shown that small but measurable amounts of cocaine are present in the bloodstream after consumption of coca tea . Addiction or other deleterious effects from the consumption of the leaf in its natural form have not been documented.

5 - History :

Traces of coca have been found in mummies dating 3000 years back . Extensive archeological evidence for the chewing of coca leaves dates back at least to the sixth century A.D. Moche period, and the subsequent Inca period, based on mummies found with a supply of coca leaves, pottery depicting the characteristic cheek bulge of a coca chewer, spatulas for extracting alkali and figured bags for coca leaves and lime made from precious metals, and gold representations of coca in special gardens of the Inca in Cuzco Coca chewing may originally have been limited to the eastern Andes before its introduction to the Incas. As the plant was viewed as having a divine origin, its

cultivation became subject to a state monopoly and its use restricted to nobles and a few favored classes (court orators, couriers, favored public workers, and the army) by the rule of the Topa Inca (1471-1493) . As the Incan empire declined, the leaf became more widely available. After some deliberation, Philip II of Spain issued a decree recognizing the drug as essential to the well - being of the Andean Indians but urging missionaries to end its religious use. The Spanish are believed to have effectively encouraged use of coca by an increasing majority of the population to increase their labor output and tolerance for starvation, but it is not clear that this was planned deliberately .

Coca was first introduced to Europe in the 16th century, but did not become popular until the mid -19th century, with the publication of an influential paper by Dr. Paolo Mantegazza praising its stimulating effects on cognition. This led to invention of cocawine and the first production of pure cocaine. Cocawine (of which Vin Mariani was the best-known brand) and other coca - containing preparations were widely sold as patent medicines and tonics, with claims of a wide variety of health benefits. The original version of Coca-cola was among these. These products became illegal in most countries outside of South America in the early 20th century, after the addictive nature of cocaine was widely recognized. In 1859, Albert Niemann of the University of Gottingen became the first person to isolate the chief alkaloid of coca, which he named " cocaine " .

In recent times (2007), the governments of several South American countries , such as Peru , Bolivia and Venezuela , have defended and championed the traditional use of coca , as well as the modern uses of the leaf and its extracts in household products such as teas and toothpaste .

6 - Traditional uses :

Traditional medical uses of coca are foremost as a stimulant to overcome fatigue, hunger, and thirst. It is considered particularly effective against altitude sickness. It also is used as an anesthetic to alleviate the pain of headache, rheumatism, wounds and sores, etc. Before stronger anaesthetics were available, it also was used for

broken bones , childbirth , and during trephining operations on the skull. Because cocaine constricts blood vessels, the action of coca also serves to oppose bleeding , and coca seeds were used for nosebleeds. Indigenous use of coca has also been reported as a treatment for malaria, ulcers, asthma, to improve digestion, to guard against bowel laxity, as an aphrodisiac, and credited with improving longevity. Modern studies have supported a number of these medical applications .

Coca has also been a vital part of the religious cosmology of the Andean peoples of Peru, Bolivia, Ecuador, Colombia and northern Argentina and Chile from the pre-Inca period through the present. Coca leaves play a crucial part in offerings to the apus (mountains), Inti (the sun) , or Pachamama (the earth) . Coca leaves are also often read in a form of divination analogous to reading tea leaves in other cultures. As one example of the many traditional beliefs about coca, it is believed by the miners of Cerro de Pasco to soften the veins of ore, if masticated (chewed) and thrown upon them (see also Cocomama) .



Coca leaves

The activity of chewing coca is called *mambear*, *chacchar* or *acullicar*, borrowed from Quechua, or in Bolivia, *picchar*, derived from the Aymara language. The Spanish *masticar* is also frequently used, along with the slang term "bolear," derived from the word "bola" or ball of coca pouched in the cheek while chewing. Typical coca consumption is about two ounces per day, and contemporary methods are believed to be unchanged from ancient times. Coca is kept in a

woven pouch (*chuspa* or *huallqui*). A few leaves are chosen to form a quid (*acullico*) held between the mouth and gums. Doing so usually causes users to feel a tingling and numbing sensation in their mouths. (The common dental anaesthetic Novocaine has a similar effect.) Chewing coca leaves is most common in indigenous communities across the central Andean region, particularly in places like the highlands of Colombia, Ecuador, Bolivia and Peru, where the cultivation and consumption of coca is as much a part of the national culture similar to chicha, like wine is to France or beer is to Germany. It also serves as a powerful symbol of indigenous cultural and religious identity, amongst a diversity of indigenous nations throughout South America. Bags of coca leaves are sold in local markets and by street vendors. Commercially manufactured coca teas, granola bars, cookies, hard candies, etc. are also available in most stores and supermarkets, including upscale suburban supermarkets .

Coca is still chewed in the traditional way, with a tiny quantity of *ilucta* (a preparation of the ashes of the quinoa plant) added to the coca leaves; it softens their astringent flavor and activates the alkaloids. Other names for this basifying substance are *llipta* in Peru and the Spanish word *lejía*, *lye* in English. The consumer carefully uses a wooden stick (formerly often a spatula of precious metal) to transfer an alkaline component into the quid without touching his flesh with the corrosive substance. The alkali component, usually kept in a gourd (*ishcupuro* or *poporo*), can be made by burning limestone to form unslaked quicklime, burning quinoa stalks, or the bark from certain trees, and may be called *ilipta*, *tocra* or *mambe* depending on its composition.^{[6][7]} Many of these materials are salty in flavor, but there are variations. The most common base in the La Paz area of Bolivia is a product known as *lejía dulce* (*sweet lye*), which is made from quinoa ashes mixed with anise and cane sugar, forming a soft black putty with a sweet and pleasing licorice flavor. In some places, baking soda is used under the name *bico*.

In the Sierra Nevada de Santa Marta, on the Caribbean Coast of Colombia, coca is consumed by the Kogi, Arhuaco and Wiwa by using a special device called *poporo*. The *poporo* is the mark of manhood. It represents the womb and the stick is a phallic symbol.

The movements of the stick in the poporo symbolize the sexual act. For a man the poporo is a good companion that means "food", "woman", "memory" and "meditation". Women are prohibited from using coca. It is important to stress that poporo is the symbol of manhood. But it is the woman who gives men their manhood. When the boy is ready to be married, his mother will initiate him in the use of the coca. This act of initiation is carefully supervised by the mama, a traditional priest-teacher-leader .

Although coca leaf chewing is common only among the indigenous populations, the consumption of coca tea (*Mate de coca*) is common among all sectors of society in the Andean countries, and is widely held to be beneficial to health, particularly in the high altitudes. Coca leaf is sold packaged into teabags in most grocery stores in the region, and establishments that cater to tourists generally feature coca tea .

In the city of Salta, in northern Argentina, one can buy a cup of Coca tea for 4 pesos at the cafe inside the Museo De Arqueologia De Alta Montana (MAAM) in the city center. This is one of the biggest museums in Northern Argentina with a focus on Inca culture in the Andes.

6 - 1 : Industrial use :

Coca is used industrially in the cosmetics and food industries. A de-cocainized extract of coca leaf is reportedly one of the flavoring ingredients in Coca - Cola . Coca tea is produced industrially from coca leaves in South America by a number of companies, including Enaco S.A. (National Company of the Coca) a government enterprise in Peru . Coca leaves are also found in a brand of herbal liqueur called "Agwa de Bolivia" (grown in Bolivia and de-cocainized in Amsterdam) , and a natural flavouring ingredient in Red Bull Cola, that was launched in March 2008 .

Beginning in the early 21st century, there has been a movement in Bolivia, Peru, and Venezuela to promote and expand legal markets for the crop. The presidents of these three countries have personally identified with this movement. In particular, Evo Morales of Bolivia

(elected in December 2005) was a coca growers union leader. Morales asserts that " *la coca no es cocaína* " — the coca leaf is not cocaine. During his speech to the General Assembly of the United Nations on September 19, 2006, he held a coca leaf in his hand to demonstrate its innocuity .

Alan García, president of Peru, has recommended its use in salads and other edible preparations . A Peruvian-based company has announced plans to market a modern version of Vin Mariani, which will be available in both natural and de - cocainized varieties.

In Venezuela, president Hugo Chávez said in a speech on January 2008 that he chews coca every day, and that his "hook up" is Bolivian president Evo Morales. Chávez reportedly said "I chew coca every day in the morning... and look how I am" before showing his biceps to his audience, the Venezuelan National Assembly.

On the other hand, the Colombian government has recently moved in the opposite direction. For years, Bogotá has allowed indigenous coca farmers to sell coca products, promoting the enterprise as one of the few successful commercial opportunities available to recognized tribes like the Nasa, who have grown it for years and regard it as sacred . In December 2005, the Paeces, a Tierradentro (Cauca) indigenous community, started in December to produce a carbonated soft drink called " Coca Sek " . The production method belongs to the resguardos of Calderas (Inzá) and takes about 150 kg of coca per 3,000 produced bottles. The drink was never sold widely in Colombia, the efforts to do so ended in May 2007 when it was abruptly banned by the Colombian government .

7 - Literary references :

Probably the earliest reference to coca in English literature is Abraham Cowley's poem " The Legend of Coca " in his 1662 collection of poems " Six Books of Plants ".

One of the best known examples of coca's reference in fiction is Patrick O ' Brian's character, Stephen Maturin. In many of the more than twenty book series, a.k.a. Aubrey - Maturin series , Maturin

expounds the benefits of coca. However, the reader is made aware of the truly addictive effects of the drug when rats, who have found the coca (*Erythroxylum coca*), become seriously addicted and scour the ship looking for it .

8 - Legal status :

Coca leaf is the raw material for the manufacture of the drug cocaine, a powerful stimulant and anaesthetic extracted chemically from large quantities of coca leaves. Today, since it has mostly been replaced as a medical anaesthetic by synthetic analogues such as procaine, cocaine is best known as an illegal recreational drug. The cultivation, sale, and possession of unprocessed coca leaf (but not of any processed form of cocaine) is generally legal in the countries – such as Bolivia, Peru, Chile and Argentina – where traditional use is established, although cultivation is often restricted in an attempt to prevent the production of cocaine.

The prohibition of the use of the coca leaf except for medical or scientific purposes was established by the United Nations in the 1961 Single Convention on Narcotic Drugs. The coca leaf is listed on Schedule I of the 1961 Single Convention together with cocaine and heroin. The Convention determined that “The Parties shall so far as possible enforce the uprooting of all coca bushes which grow wild. They shall destroy the coca bushes if illegally cultivated” (Article 26), and that, “Coca leaf chewing must be abolished within twenty- five years from the coming into force of this Convention ” .

The rationale for including the coca leaf in the 1961 Single Convention is mainly rooted in a report requested of the United Nations by the permanent representative of Peru that was prepared by a commission that visited Bolivia and Peru briefly in 1949 to “investigate the effects of chewing the coca leaf and the possibilities of limiting its production and controlling its distribution.” The Commission of Enquiry on the Coca Leaf study, published in 1950, concluded that the effects of chewing coca leaves were negative, even though chewing coca was defined as a habit, not an addiction.^{[21][22]}

The report was sharply criticised for its arbitrariness, lack of precision and racist connotations. The team members' professional qualifications and parallel interests were also criticised, as were the methodology used and the incomplete selection and use of existing scientific literature on the coca leaf. Nowadays, a similar study would never pass the scrutiny and critical review to which scientific studies are routinely subjected .

Despite the legal restriction, coca chewing and drinking of coca tea is carried out daily by millions of people in the Andes as well as considered sacred within indigenous cultures. They claim that most of the information provided about the traditional use of the coca leaf and its modern adaptations are erroneous. This has made it impossible to shed light on the plant's positive aspects and its potential benefits for the physical, mental and social health of the people who consume and cultivate it .

In an attempt to obtain legal recognition for the traditional use of coca, Peru and Bolivia negotiated paragraph 2 of Article 14 into the 1988 United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances, stipulating that measures to eradicate illicit cultivation and to eliminate illicit demand “should take due account of traditional licit use, where there is historic evidence of such use ” . Bolivia also made a formal reservation to the 1988 Convention, which required countries to adopt measures to establish the use, consumption, possession, purchase or cultivation of the coca leaf for personal consumption as a criminal offence. Bolivia stated that “the coca leaf is not, in and of itself, a narcotic drug or psychotropic substance” and stressed that its “legal system recognizes the ancestral nature of the licit use of the coca leaf, which, for much of Bolivia's population, dates back over centuries ” .

However, the International Narcotics Control Board (INCB) – the independent and quasi-judicial control organ for the implementation of the United Nations drug conventions – denied the validity of article 14 in the 1988 Convention over the requirements of the 1961 Convention, or any reservation made by parties, since it does not

" absolve a party of its rights and obligations under the other international drug control treaties " .

In recent years the current legal status of the coca leaf is more and more questioned. Even the INCB stated in its 1994 Annual Report that "mate de coca, which is considered harmless and legal in several countries in South America, is an illegal activity under the provisions of both the 1961 Convention and the 1988 Convention, though that was not the intention of the plenipotentiary conferences that adopted those conventions " . It implicitly also dismissed the original report of the Commission of Enquiry on the Coca Leaf by recognizing that "there is a need to undertake a scientific review to assess the coca-chewing habit and the drinking of coca tea " .

Nevertheless , the INCB on other occasions did not show signs of an increased sensitivity towards the Bolivian claim on the rights of their indigenous population, and the general public, to consume the coca leaf in a traditional manner by chewing the leaf, and even goes as far as to consider drinking coca tea, as "not in line with the provisions of the 1961 Convention " . The Board considered Bolivia, Peru and a few other countries that allow such practises to be in breach with their treaty obligations, and insisted that "each party to the Convention should establish as a criminal offence, when committed intentionally, the possession and purchase of coca leaf for personal consumption " .

8 – 1 : Legal status by country :

Outside of South America, most countries' laws make no distinction between the coca leaf and any other substance containing cocaine , so the possession of coca leaf (except for de - cocainized leaf) is prohibited.

In the Netherlands, coca leaf is legally in the same category as cocaine, both are List I drugs of the Opium Law. The Opium Law specifically mentions the leafs of the plants of the species *Erythroxylon*. However, the possession of living plants of the species *Erythroxylon* are not actively prosecuted, even though they are legally forbidden.

In the United States, the Stepan Company of Maywood, New Jersey has the only license to legally import coca leaf. The company manufactures pure cocaine for medical use and also produces a cocaine-free extract of the coca leaf, which is used as a flavoring ingredient in Coca - Cola . According to the Bolivian press, Coca - Cola legally imported 204 tons of coca leaf in 1996 .

Since the 1980s, the countries in which coca is grown have come under political and economic pressure from the United States to restrict the cultivation of the crop, in order to reduce the supply of cocaine on the international market .

Article 26 of the Single Convention on Narcotic Drugs requires nations that allow the cultivation of coca to designate an agency to regulate said cultivation and take physical possession of the crops as soon as possible after harvest, and to destroy all coca which grows wild or is illegally cultivated. The effort to enforce these provisions, referred to as coca eradication, has involved many strategies, ranging from aerial spraying of herbicides on coca crops to assistance and incentives to encourage farmers to grow alternate crops .

This effort has been politically controversial, with proponents claiming that the production of cocaine is several times the amount needed to satisfy legal demand, and inferring that the vast majority of the coca crop is destined for the illegal market, which not only contributes to the major social problem of drug abuse, but also financially supports insurgent groups that collaborate with drug traffickers in some cocaine - producing territories. Critics of the effort claim that it creates hardship primarily for the coca growers, many of whom are poor and have no viable alternative way to make a living, causes environmental problems, that it is not effective in reducing the supply of cocaine, in part because cultivation can move to other areas, and that any social harm created by drug abuse is only made worse by the war on drugs .

mm

Coffee



A cup of coffee

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1 – Introduction :

Coffee is a brewed beverage prepared from roasted seeds, commonly called coffee beans, of the coffee plant. They are seeds of

"coffee cherries" that grow on trees in over 70 countries. It has been said that green coffee is the second most traded commodity in the world behind crude oil . Due to its caffeine content, coffee can have a stimulating effect in humans. Today, coffee is one of the most popular beverages worldwide .

It is thought that the energizing effect of the coffee bean plant was first recognized in the south west of Ethiopia, and the cultivation of coffee expanded in the Arab world . The earliest credible evidence of coffee drinking appears in the middle of the fifteenth century, in the Sufi monasteries of the Yemen in southern Arabia.^[3] From the Muslim world, coffee spread to Italy, then to the rest of Europe, to Indonesia, and to the Americas .

Coffee berries, which contain the coffee bean, are produced by several species of small evergreen bush of the genus *Coffea*. The two most commonly grown species are *Coffea canephora* (also known as *Coffea robusta*) and *Coffea arabica*; less popular species are *liberica*, *excelsa*, *stenophylla*, *mauritiana*, *racemosa*. These are cultivated primarily in Latin America, Southeast Asia, and Africa. Once ripe, coffee berries are picked, processed, and dried. The seeds are then roasted, undergoing several physical and chemical changes. They are roasted to varying degrees, depending on the desired flavour. They are then ground and brewed to create coffee. Coffee can be prepared and presented in a variety of ways.

Coffee has played an important role in many societies throughout history. In Africa and Yemen, it was used in religious ceremonies. As a result, the Ethiopian Church banned its secular consumption until the reign of Emperor Menelik II of Ethiopia . It was banned in Ottoman Turkey in the 17th century for political reasons . and was associated with rebellious political activities in Europe.

Coffee is an important export commodity. In 2004 , coffee was the top agricultural export for 12 countries , and in 2005, it was the world's seventh - largest legal agricultural export by value .

Some controversy is associated with coffee cultivation and its impact on the environment. Many studies have examined the

relationship between coffee consumption and certain medical conditions; whether the overall effects of coffee are positive or negative is still disputed .

Type	Hot or cold beverage
Country of origin	Ethiopia
Introduced	Approx . 15th century AD (beverage)
Color	Brown

2 - Etymology :

The term coffee was introduced to Europe by the Ottoman Turkish *kahve*, which is, in turn, derived from the Arabic: قهوة , *qahweh*.^{[10][11]} The origin of the Arabic term is derived either from the name of the Kaffa region in western Ethiopia, where coffee was cultivated, or by a truncation of *qahwat al - būnn*, meaning "wine of the bean " in Arabic . The English word *coffee* first came to be used in the early to mid-1600s, but early forms of the word date to the last decade of the 1500s . In Ethiopia's neighbor Eritrea, "būnn" (also meaning " wine of the bean " in Tigrinya) is used . The Amharic and Afan Oromo name for coffee is *bunna*.

3 – History :

It is supposed that the Ethiopians, the ancestors of today's Oromo people, were the first to have discovered and recognized the energizing effect of the coffee bean plant . However, no direct evidence has ever been found revealing exactly where in Africa coffee grew or who among the natives might have used it as a stimulant or even known about it there earlier than the seventeenth century . The story of Kaldi, the 9th - century Ethiopian goatherd who discovered coffee, did not appear in writing until 1671 and is probably apocryphal.^[3] The earliest credible evidence of either coffee drinking or knowledge of the coffee tree appears in the middle of the fifteenth century, in the Sufi monasteries of the Yemen in southern Arabia.^[3] From Ethiopia, coffee spread to Egypt and Yemen . It was in Arabia that coffee beans were first roasted and brewed, similar to how it is

done today. By the 15th century, it had reached the rest of the Middle East, Persia, Turkey, and northern Africa. From the Muslim world, coffee spread to Italy, then to the rest of Europe, to Indonesia, and to the Americas .

In 1583, Leonhard Rauwolf, a German physician, gave this description of coffee after returning from a ten - year trip to the Near East :

A beverage as black as ink, useful against numerous illnesses, particularly those of the stomach. Its consumers take it in the morning, quite frankly, in a porcelain cup that is passed around and from which each one drinks a cupful. It is composed of water and the fruit from a bush called bunnu.

From the Muslim world , coffee spread to Italy . The thriving trade between Venice and North Africa, Egypt, and the Middle East brought many goods, including coffee, to the Venetian port. From Venice, it was introduced to the rest of Europe. Coffee became more widely accepted after it was deemed a Christian beverage by Pope Clement VIII in 1600, despite appeals to ban the "Muslim drink." The first European coffee house opened in Italy in 1645 . The Dutch were the first to import coffee on a large scale, and they were among the first to defy the Arab prohibition on the exportation of plants or unroasted seeds when Pieter van den Broeck smuggled seedlings from Aden into Europe in 1616 . The Dutch later grew the crop in Java and Ceylon . The first exports of Indonesian coffee from Java to the Netherlands occurred in 1711 . Through the efforts of the British East India Company, coffee became popular in England as well. It was introduced in France in 1657, and in Austria and Poland after the 1683 Battle of Vienna, when coffee was captured from supplies of the defeated Turks .

When coffee reached North America during the Colonial period, it was initially not as successful as it had been in Europe. During the Revolutionary War, however, the demand for coffee increased so much that dealers had to hoard their scarce supplies and raise prices dramatically; this was also due to the reduced availability of tea from

British merchants . After the War of 1812, during which Britain temporarily cut off access to tea imports, the Americans' taste for coffee grew, and high demand during the American Civil War together with advances in brewing technology secured the position of coffee as an everyday commodity in the United States .

Coffee has become a vital cash crop for many Third World countries . Over one hundred million people in developing countries have become dependent on coffee as their primary source of income (Ponte 1). Coffee has become the primary export and backbone for African countries like Uganda, Burundi, Rwanda, and Ethiopia as well as many Central American countries .

4 - Biology of Coffea :



Illustration of Coffea arabica plant and seeds

The *Coffea* plant is native to subtropical Africa and southern Asia.^[23] It belongs to a genus of ten species of flowering plants of the family *Rubiaceae*. It is an evergreen shrub or small tree that may grow 5 meters tall when unpruned. The leaves are dark green and glossy, usually 100–150 millimeters long and 60 millimeters wide. It produces clusters of fragrant white flowers that bloom simultaneously. The fruit berry is oval, about 15 millimeters long , and green when immature, but ripens to yellow, then crimson, becoming black on drying. Each berry usually contains two seeds, but 5 – 10 % of the berries have only one; these are called peaberries . Berries ripen in seven to nine months .

5 - Cultivation :

Coffee is usually propagated by seeds. The traditional method of planting coffee is to put 20 seeds in each hole at the beginning of the rainy season; half are eliminated naturally. Coffee is often intercropped with food crops, such as corn, beans, or rice, during the first few years of cultivation .



Map showing areas of coffee cultivation:

The two main cultivated species of the coffee plant are *Coffea canephora* and *Coffea arabica*. Arabica coffee (from *C. arabica*) is considered more suitable for drinking than robusta coffee (from *C. canephora*); robusta tends to be bitter and have less flavor but better body than arabica. For these reasons, about three-quarters of coffee cultivated worldwide is *C. Arabica* . However, *C. canephora* is less susceptible to disease than *C. arabica* and can be cultivated in environments where *C. arabica* will not thrive. Robusta coffee also contains about 40 –50 % more caffeine than arabica.^[27] For this reason, it is used as an inexpensive substitute for arabica in many commercial coffee blends. Good quality robustas are used in some espresso blends to provide a better foam head, a full-bodied result, and to lower the ingredient cost . Other cultivated species include *Coffea liberica* and *Coffea esliaca*, believed to be indigenous to Liberia and southern Sudan, respectively .

Most arabica coffee beans originate from either Latin America , eastern Africa, Arabia, or Asia. Robusta coffee beans are grown in western and central Africa, throughout southeast Asia, and to some extent in Brazil . Beans from different countries or regions usually have distinctive characteristics such as flavor, aroma, body, and

acidity . These taste characteristics are dependent not only on the coffee's growing region, but also on genetic subspecies (varietals) and processing . Varietals are generally known by the region in which they are grown, such as Colombian, Java or Kona.

5 – 1 : Production :

Brazil is the world leader in production of green coffee , followed by Vietnam and Colombia the last of which produces a much softer coffee .

Top twenty green coffee producers — Tonnes (2007) and Bags thousands (2007)		
Country	Tonnes	Bags thousands
 Brazil	2,249,010	36,070
 Vietnam	961,200	16,467
 Colombia	697,377	12,515
 Indonesia	676,475	7,751
 Ethiopia	325,800	4,906
 India	288,000	4,148
 Mexico	268,565	4,150
 Guatemala	252,000	4,100
 Peru	225,992	2,953
 Honduras	217,951	3,842
 Côte d'Ivoire	170,849	2,150
 Uganda	168,000	3,250
 Costa Rica	124,055	1,791
 Philippines	97,877	431
 El Salvador	95,456	1,626
 Nicaragua	90,909	1,700
 Papua New Guinea	75,400	968
 Venezuela	70,311	897
 Madagascar	62,000	604

 Thailand	55,660	653
 World	7,742,675	117,319

5 – 2 : Ecological effects :



A flowering Coffea arabica tree in a Brazilian plantation

Originally, coffee farming was done in the shade of trees, which provided a habitat for many animals and insects . This method is commonly referred to as the traditional shaded method or " shade – grown " . Many farmers have decided to switch their production method to sun cultivation, a method in which coffee is grown in rows under full sun with little or no forest canopy. This causes berries to ripen more rapidly and bushes to produce higher yields, but requires the clearing of trees and increased use of fertilizer and pesticides.^[32] When compared to the sun cultivation method, traditional coffee production causes berries to ripen more slowly and produce lower yields, but the quality of the coffee is allegedly superior . In addition, the traditional shaded method is environmentally friendly and provides living space for many wildlife species. Opponents of sun cultivation say environmental problems such as deforestation, pesticide pollution, habitat destruction, and soil and water degradation are the side effects of these practices . The American Birding Association, Smithsonian Migratory Bird Center, Rainforest Alliance, and the Arbor Day Foundation have led a campaign for " shade - grown" and organic coffees, which it says are sustainably harvested . However, while certain types of shaded coffee cultivation systems show greater biodiversity than full-sun systems, they still compare poorly to native forest in terms of habitat value .

Another issue concerning coffee is its use of water. According to New Scientist, it takes about 140 litres of water to grow the coffee beans needed to produce one cup of coffee , and the coffee is often grown in countries where there is a water shortage , such as Ethiopia .

5 - 3 : Economics :

Coffee ingestion on average is about a third of that of tap water in North America and Europe . Worldwide, 6.7 million metric tons of coffee were produced annually in 1998 – 2000, and the forecast is a rise to 7 million metric tons annually by 2010 .

Brazil remains the largest coffee exporting nation, but in recent years, Vietnam has become a major producer of robusta beans.^[37] Indonesia is the third-largest exporter and the largest producer of washed arabica coffee. Robusta coffees, traded in London at much lower prices than New York's arabica, are preferred by large industrial clients, such as multinational roasters and instant coffee producers because of the lower cost.

The concept of fair trade labeling, which guarantees coffee growers a negotiated preharvest price, began with the Max Havelaar Foundation's labeling program in the Netherlands. In 2004 , 24,222 metric tons (of 7,050,000 produced worldwide) were fair trade ; in 2005, 33,991 metric tons out of 6,685,000 were fair trade , an increase from 0.34 % to 0.51 % . A number of studies have shown that fair trade coffee has a positive impact on the communities that grow it. A study in 2002 found that fair trade strengthened producer organizations, improved returns to small producers, and positively affected their quality of life . A 2003 study concluded that fair trade has "greatly improved the well - being of small-scale coffee farmers and their families" by providing access to credit and external development funding and greater access to training, giving them the ability to improve the quality of their coffee . The families of fair trade producers were also more stable than those who were not involved in fair trade , and their children had better access to education . A 2005 study of Bolivian coffee producers concluded that fair trade certification has had a positive impact on local coffee prices, economically benefiting all coffee producers, fair trade-certified or not

The production and consumption of fair trade coffee has grown in recent years as some local and national coffee chains have started to offer fair trade alternatives .

5 - 4 : Coffee as a commodity :

While coffee is not technically a commodity (it is fresh produce; its value is directly affected by the length of time it is held), coffee is bought and sold by roasters, investors and price speculators as a tradable commodity. Coffee futures contracts for Grade 3 washed arabicas are traded on the New York Mercantile Exchange (NYMEX) under ticker symbol **KT**, with contract deliveries occurring every year in March, May, July, September, and December.^[47] Higher and lower grade arabica coffees are sold through other channels. Futures contracts for robusta coffee are traded on the London Liffe exchange and, since 2007, on the New York ICE exchange. As of 2006 green coffee is the second most traded commodity in the world.

6 - Processing :

6 -1 : Roasting :



Roasted coffee beans

Coffee berries and their seeds undergo several processes before they become the familiar roasted coffee. First, coffee berries are picked, generally by hand. Then they are sorted by ripeness and color and the flesh of the berry is removed, usually by machine, and the seeds—usually called beans — are fermented to remove the slimy layer of mucilage still present on the bean. When the fermentation is finished, the beans are washed with large quantities of fresh water to remove the fermentation residue, which generates massive amounts of

highly polluted coffee wastewater. Finally, the seeds are dried. The best (but least utilized) method of drying coffee is using drying tables. In this method the pulped and fermented coffee is spread thinly on raised beds, which allows the air to pass on all sides of the coffee; then the coffee is mixed by hand. In this method the drying that takes place is more uniform, and fermentation is less likely. Most African Coffee is dried in this manner and certain coffee farms around the world are starting to use this traditional method. Next, the coffee is sorted, and labeled as green coffee. Another way to let the coffee beans dry is to let them sit on a cement patio and rake over them in the sunlight. Some companies use cylinders to pump in heated air to dry the coffee beans, though this is generally in places where the humidity is very high .

The next step in the process is the roasting of the green coffee. Coffee is usually sold in a roasted state, and all coffee is roasted before it is consumed. It can be sold roasted by the supplier, or it can be home roasted . The roasting process influences the taste of the beverage by changing the coffee bean both physically and chemically. The bean decreases in weight as moisture is lost and increases in volume, causing it to become less dense. The density of the bean also influences the strength of the coffee and requirements for packaging. The actual roasting begins when the temperature inside the bean reaches 200°C , though different varieties of beans differ in moisture and density and therefore roast at different rates.^[50] During roasting, caramelization occurs as intense heat breaks down starches in the bean, changing them to simple sugars that begin to brown, changing the color of the bean . Sucrose is rapidly lost during the roasting process and may disappear entirely in darker roasts. During roasting, aromatic oils, acids, and caffeine weaken, changing the flavor; at 205°C, other oils start to develop . One of these oils is *caffeol*, created at about 200°C, which is largely responsible for coffee's aroma and flavor .

Depending on the color of the roasted beans as perceived by the human eye, they will be labeled as light, medium light, medium, medium dark, dark, or very dark. A more accurate method of discerning the degree of roast involves measuring the reflected light

from roasted beans illuminated with a light source in the near infrared spectrum. This elaborate light meter uses a process known as spectroscopy to return a number that consistently indicates the roasted coffee's relative degree of roast or flavor development. Such devices are routinely used for quality assurance by coffee-roasting businesses.

Darker roasts are generally smoother, because they have less fiber content and a more sugary flavor. Lighter roasts have more caffeine, resulting in a slight bitterness, and a stronger flavor from aromatic oils and acids otherwise destroyed by longer roasting times.^[52] A small amount of chaff is produced during roasting from the skin left on the bean after processing . Chaff is usually removed from the beans by air movement, though a small amount is added to dark roast coffees to soak up oils on the beans . Decaffeination may also be part of the processing that coffee seeds undergo. Seeds are decaffeinated when they are still green. Many methods can remove caffeine from coffee, but all involve either soaking beans in hot water or steaming them, then using a solvent to dissolve caffeine-containing oils.^[17] Decaffeination is often done by processing companies, and the extracted caffeine is usually sold to the pharmaceutical industry .

6 – 2 : Storage :

Once roasted, coffee beans must be stored properly to preserve the fresh taste of the bean. Ideally, the container must be airtight and kept cool. In order of importance, air, moisture, heat, and light are the environmental factors responsible for deteriorating flavor in coffee beans .

Folded - over bags, a common way consumers often purchase coffee, are generally not ideal for long - term storage because they allow air to enter. A better package contains a one - way valve, which prevents air from entering .

6 – 3 : Coffee Preparation :

Coffee beans must be ground and brewed in order to create a beverage. All methods of preparing coffee require the beans to be ground and mixed with hot water for long enough to extract the flavor,

but without boiling for more than an instant; boiling develops an unpleasant "cooked" flavor. Finally the spent grounds are removed from the liquid, and the liquid is drunk. There are many variations in the fineness of grind, the ways in which the water extracts the flavor, additional flavorings (sugar , milk , spices) , and the removal of the spent grounds .



Espresso brewing, with dark reddish - brown crema

The criteria for choosing a method include flavor and economy. Extracting as much as possible from the beans (for economy) tends to impair flavor .

The roasted coffee beans may be ground at a roastery, in a grocery store, or in the home. Most coffee is roasted and ground at a roastery and sold in packaged form, though roasted coffee beans can be ground at home, and it is possible, though complex, to roast raw beans .

Coffee beans may be ground in several ways. A burr mill uses revolving elements to shear the bean; an electric grinder smashes the beans with blunt blades moving at high speed; and a mortar and pestle crushes the beans .

The type of grind is often named after the brewing method for which it is generally used. Turkish grind is the finest grind, while coffee percolator or French press are the coarsest grinds. The most common grinds are between the extremes; a medium grind is used in most common home coffee - brewing machines . Coffee may be brewed by several methods : boiled , steeped , or pressured .

Brewing coffee by boiling was the earliest method, and Turkish coffee is an example of this method . It is prepared by grinding or pounding the beans to a fine powder, then adding it to water and bringing it to the boil for no more than an instant in a pot called a *cezve* or, in Greek, a *briki*. This produces a strong coffee with a layer of foam on the surface and sediment (which is not meant for drinking) settling on the bottom of the cup .

Coffee percolators and automatic coffeemakers brew coffee by gravity. In an automatic coffeemaker hot water drips onto coffee grounds held in a coffee filter made of paper, plastic, or perforated metal, allowing the water to seep through the ground coffee while extracting its oils and essences. The liquid drips through the coffee and the filter into a carafe or pot, and the spent grounds are retained in the filter . (The Chemex coffeemaker operates under a similar principle but uses only an hourglass shaped flask.) In a percolator, boiling water is forced into a chamber above a filter by steam pressure created by boiling. The water then seeps through the grounds, and the process is repeated until terminated by removing from the heat, by an internal timer^[57], or by a thermostat that turns off the heater when the entire pot reaches a certain temperature. This thermostat also serves to keep the coffee warm (it turns on when the pot cools), but requires the removal of the basket holding the grounds after the initial brewing to avoid additional brewing as the pot reheats. Repeated boiling spoils the flavor of coffee .

Coffee may be brewed by steeping in a device such as a French press (also known as a *cafetière* or coffee press). Ground coffee and hot water are combined in a cylindrical vessel and left to brew for a few minutes. A circular filter which fits tightly in the cylinder fixed to a plunger is then pushed down from the top to force the grounds to the bottom. Because the coffee grounds are in direct contact with the water, all the coffee oils remain in the beverage, making it stronger and leaving more sediment than in coffee made by an automatic coffee machine . The coffee is poured from the container ; the filter retains the grounds at the bottom .

The espresso method forces hot (but not boiling) pressurized water through ground coffee. As a result of brewing under high pressure (ideally between 9 – 10 atm) , the espresso beverage is more concentrated (as much as 10 to 15 times the amount of coffee to water as gravity-brewing methods can produce) and has a more complex physical and chemical constitution. A well-prepared espresso has a reddish-brown foam called *crema* that floats on the surface.^[55] The drink "Americano" is popularly thought to have been named after American soldiers in WW II who found the European way of drinking espresso too strong; baristas would cut the espresso with hot water for them.

Coffee may also be brewed in cold water by steeping coarsely-ground beans in cold water for several hours, then filtering^[citation needed].

6 – 4 : Presentation :



French petit noir

Once brewed, coffee may be presented in a variety of ways. Drip-brewed, percolated, or French – pressed / cafetière coffee may be served with no additives or sugar (colloquially known as *black*) or with milk, cream, or both. When served cold, it is called *iced coffee* .

Espresso-based coffee has a wide variety of possible presentations. In its most basic form, it is served alone as a *shot* or in the more watered-down style café americano — a shot or two of espresso with hot water added (reversing the process by adding espresso to hot water preserves the crema, and is known as a long black) . Milk can be added in various forms to espresso: steamed milk makes a caffè latte , equal parts steamed milk and milk froth make a cappuccino , and a dollop of hot foamed milk on top creates a caffè

macchiato . The use of steamed milk to form patterns such as hearts or maple leaves is referred to as latte art .

A number of products are sold for the convenience of consumers who do not want to prepare their own coffee. Instant coffee is dried into soluble powder or freeze - dried into granules that can be quickly dissolved in hot water . Canned coffee has been popular in Asian countries for many years, particularly in China, Japan, and South Korea. Vending machines typically sell varieties of flavored canned coffee, much like brewed or percolated coffee, available both hot and cold. Japanese convenience stores and groceries also have a wide availability of bottled coffee drinks, which are typically lightly sweetened and preblended with milk. Bottled coffee drinks are also consumed in the United States.^[63] Liquid coffee concentrates are sometimes used in large institutional situations where coffee needs to be produced for thousands of people at the same time. It is described as having a flavor about as good as low - grade robusta coffee, and costs about 10¢ a cup to produce. The machines used can process up to 500 cups an hour, or 1,000 if the water is preheated .

7 - Social aspects :



A coffeehouse in Palestine (1900)

Coffee was initially used for spiritual reasons. At least 1,000 years ago, traders brought coffee across the Red Sea into Arabia (modern - day Yemen) , where Muslim monks began cultivating the shrub in their gardens. At first, the Arabians made wine from the pulp of the fermented coffee berries. This beverage was known as *qishr* (*kisher* in modern usage) and was used during religious ceremonies .

Coffee became the substitute beverage in spiritual practices where wine was forbidden . Coffee drinking was briefly prohibited by Muslims as *haraam* in the early years of the 16th century, but this was quickly overturned. Use in religious rites among the Sufi branch of Islam led to coffee's being put on trial in Mecca: it was accused of being a heretical substance, and its production and consumption were briefly repressed. It was later prohibited in Ottoman Turkey under an edict by the Sultan Murad IV . Coffee, regarded as a Muslim drink, was prohibited by Ethiopian Orthodox Christians until as late as 1889; it is now considered a national drink of Ethiopia for people of all faiths. Its early association in Europe with rebellious political activities led to its banning in England , among other places .

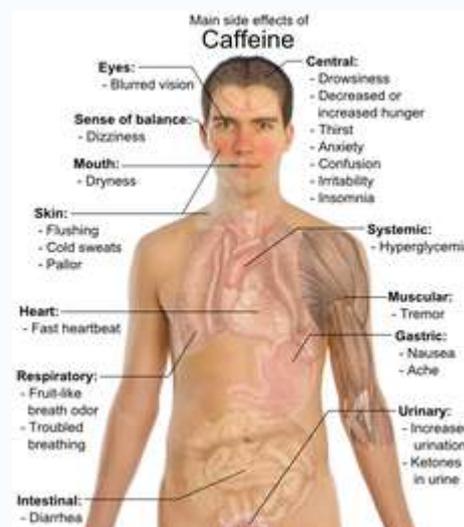
A contemporary example of coffee prohibition can be found in The Church of Jesus Christ of Latter-day Saints.^[68] The organization claims that it is both physically and spiritually unhealthy to consume coffee.^[69] This comes from the Mormon doctrine of health, given in 1833 by Mormon founder Joseph Smith in a revelation called the Word of Wisdom. It does not identify coffee by name, but includes the statement that "hot drinks are not for the belly," which has been interpreted to forbid both coffee and tea .

Quite a number of members of the Seventh-day Adventist Church also avoid caffeinated drinks. In its teachings, the Church requires members to avoid tea and coffee and other stimulants. Studies conducted on Adventists have shown a small but statistically significant association between coffee consumption and mortality from ischemic heart disease, other cardiovascular disease, all cardiovascular diseases combined, and all causes of death .

8 - Health and pharmacology :

Scientific studies have examined the relationship between coffee consumption and an array of medical conditions. Findings are contradictory as to whether coffee has any specific health benefits, and results are similarly conflicting regarding the negative effects of coffee consumption .

Coffee consumption has been shown to have minimal or no impact, positive or negative, on cancer development ; however, researchers involved in an ongoing 22 - year study by the Harvard School of Public Health state that "the overall balance of risks and benefits [of coffee consumption] are on the side of benefits."^[72] Various other studies have shown apparent reductions in the risks of Alzheimer's disease, Parkinson's disease, heart disease, diabetes mellitus type 2 , cirrhosis of the liver , and gout. A longitudinal study in 2009 showed that moderate drinkers of coffee (3-5 cups per day) had lower chances of developing dementia, in addition to Alzheimer's disease . It increases the risk of acid reflux and associated diseases . Some health effects of coffee are due to its caffeine content, as the benefits are only observed in those who drink caffeinated coffee while others appear to be due to other components . For example, the antioxidants in coffee prevent free radicals from causing cell damage .



Overview of the more common effects of caffeine,^[71] a main active component of coffee

Caffeine is the major coffee constituent affecting individual's tolerance or intolerance. In a healthy liver, the majority of caffeine is degraded by the hepatic microsomal enzymatic system. Caffeine is mostly degraded to paraxanthine substances, partially to theobromine and theophylline, and a small amount of unchanged caffeine is excreted by urine. Therefore, the metabolism of caffeine depends on the state of this enzymatic system of the liver. Elderly individuals with a depleted enzymatic system do not tolerate coffee with caffeine. They

are recommended to take decaffeinated coffee, and this only if their stomach is healthy, because both decaffeinated coffee and coffee with caffeine cause heartburn. Moderate amounts of coffee (50 - 100 mg of caffeine or 5 - 10 g of coffee powder a day) are well tolerated by a majority of elderly people. Excessive amounts of coffee, however, can in many individuals cause very unpleasant, exceptionally even life-threatening side effects .

Coffee consumption can lead to iron deficiency anemia in mothers and infants . Coffee also interferes with the absorption of supplemental iron .

American scientist Yaser Dorri has suggested that the smell of coffee can restore appetite and refresh olfactory receptors. He suggests that people can regain their appetite after cooking by smelling coffee beans, and that this method can also be used for research animals.^[81] Many high end perfume shops now offer coffee beans to refresh the receptors between perfume tests .

Over 1,000 chemicals have been reported in roasted coffee; more than half of those tested (19 / 28) are rodent carcinogens . Coffee's negative health effects are often blamed on its caffeine content. Research suggests that drinking caffeinated coffee can cause a temporary increase in the stiffening of arterial walls . Coffee is no longer thought to be a risk factor for coronary heart disease . Some studies suggest that it may have a mixed effect on short - term memory , by improving it when the information to be recalled is related to the current train of thought but making it more difficult to recall unrelated information . About 10 % of people with a moderate daily intake (235 mg per day) reported increased depression and anxiety when caffeine was withdrawn . About 15 % of the general population report having stopped drinking coffee altogether, citing concern about health and unpleasant side effects of caffeine .

8 - 1 : Caffeine content :



Caffeine molecule

Depending on the type of coffee and method of preparation, the caffeine content of a single serving can vary greatly. On average, a single cup of coffee (about 200 milliliters) or a single shot of espresso (about 30 mL) can be expected to contain the following amounts of caffeine :

- Drip coffee : 115 – 175 mg (560 – 850 mg / L)
- Espresso : 185 mg (2000 mg / L)
- Brewed / Pressed : 80 – 135 mg (390 – 650 mg / L)
- Instant : 65 – 100 mg (310 – 480 mg / L)
- Decaf , brewed : 3 – 4 mg
- Decaf , instant : 2 – 3 mg

Datura stramonium



Thorn apple / Jimson weed

Contents

- 1 Introduction
- 2 Growth
- 3 Distribution
- 4 Nomenclature
- 5 Toxicity
 - 5.1 Effects
- 6 History
- 7 Mistaken identity
- 8 Gallery

1 – Introduction :

Datura stramonium, known by the common names **jimson weed**, **angel's trumpet**, **devil's weed**, **thorn apple**, **tolguacha**, **Jamestown weed**, **stinkweed**, **datura**, **moonflower** , and, in South Africa, **malpitte** and **mad seeds** is, along with *Datura metel* (zombie cucumber), a common weed in the *Solanaceae* (the nightshade family). It contains tropane alkaloids that are sometimes used as a hallucinogen. The active ingredients are atropine, hyoscyamine and scopolamine which are classified as deliriant, or anticholinergics. Due to the elevated risk of overdose in uninformed users, many hospitalizations, and some deaths, are reported from recreational use .

Scientific classification

Kingdom : Plantae
(unranked): Angiosperms
(unranked): Eudicots
(unranked): Asterids
Order: Solanales
Family: Solanaceae
Genus: *Datura*
Species: *D. stramonium*

2 - Growth :

Datura stramonium is an erect annual herb forming a bush up to 3 – 5 ft (1 – 1.5 m) tall . The foliage and stems have a pungent smell that becomes stronger if any part of it is crushed or even touched . The leaves are soft, irregularly undulate, and toothed. The fragrant flowers are trumpet - shaped, white to creamy or violet, and 2.5 to 3.5 in. long. They rarely open completely. The egg - shaped seed capsule is walnut-sized and either covered with spines or bald. At maturity it splits into four chambers, each with dozens of small black seeds.

3 - Distribution :

The native range of *Datura stramonium* is unclear. It was scientifically described and named by Swedish botanist Carl Linnaeus in 1753, although it was earlier described by many herbalists such as Nicholas Culpeper . It was mentioned earlier by the Arab physician Avicenna in 11th century Persia . Today, it grows wild in all the world's warm and moderate regions, where it is found along roadsides and in dung heaps . In Europe, it is found as a weed on wastelands and in garbage dumps .

The seed is thought to be carried by birds and spread in their droppings. It can lie dormant underground for years and germinate when the soil is disturbed. People surprised to discover it growing in their gardens have contacted organisations such as the Royal

Horticultural Society to identify it. If worried about its toxicity they are advised to dig it up or have it otherwise removed .

4 - Nomenclature :

The genus name was derived from "dhatura", a Hindu name itself derived from *D'hustúra* (an ancient Sanskrit word for *Datura fastuosa*, a related plant) , *Stramonium* is originally from Greek , *strychnos* (night shade) and *manikos* (mad) .

5 – Toxicity :

All parts of *Datura* plants contain dangerous levels of poison and may be fatal if ingested by humans or animals, including livestock and pets. Some municipalities prohibit the purchase, sale, or cultivation of *Datura* plants .

5 – 1 : Effects :



Blooming Datura

There is a mnemonic device for the physiological effects of datura/atropine intoxication: "blind as a bat, mad as a hatter, red as a beet, hot as hell, dry as a bone, the bowel and bladder lose their tone, and the heart runs alone." Another rhyme describing its effects is, "Can't see, can't spit, can't pee, can't shit." Regarding *Datura*, among the Navajo is the folk admonition, "Eat a little, and go to sleep. Eat some more, and have a dream. Eat some more, and don't wake up." The physiological effects are reported to be cycloplegia and mydriasis (extreme dilation of the pupil), flushed, warm and dry skin, dry mouth, urinary retention and ileus (slowing or stopping of intestinal movement), tachycardia, hypertension or hypotension, and choreoathetosis/jerky movements. In case of overdose the effects are

hyperthermia, coma, respiratory arrest and seizures. The vast majority of atropine - poisoning cases are accompanied by delirium with visual and auditory hallucinations .

The effects of *Datura* have been described as a living dream: consciousness falls in and out, people who don't exist or are miles away are conversed with, etc. The effects can last for days. Tropane alkaloids are some of the few substances which cause true hallucinations which cannot be distinguished from reality. It may be described as a "real" trance when a user under the effect can be awake but completely disconnected from his or her immediate environment. In this case, the user would ignore most stimuli and respond to unreal ones. This is unlike psilocybin or LSD, which only cause sensory distortions .

If taken recreationally and the user does not notice any conscious effects, many people redose thinking it's not working, which is why overdoses are common. The user doesn't realize that he or she was hallucinating. Some users have reported seeing an array of people from their lives. A few anecdotal reports also mention the user's perception of "phantom cigarettes"; the person believes that he or she is smoking a cigarette only to find that it has disappeared later, thus realizing that it never existed. This hallucination is reported among both smokers and non - smokers . There have been reports of the user interacting with other unreal objects also, such as looking down and seeing a cigarette lighter in one's hand and then dropping it, and after a minute or two of searching, the user often realizes that this lighter or any other unreal object never existed. Returning to "reality" from datura-induced hallucinations is often coupled with momentary disorientation. At the peak of such experiences users often enter a true psychotomimetic state, in which they "lose touch with reality" altogether; at this point, many find it difficult or impossible to communicate with others .

The majority of users who have written reports on experiences with datura have described those experiences as quite unpleasant and often terrifying. This is possibly due to their having taken excessive

doses. The powerful effects of *Datura* continue until the body metabolizes the tropane alkaloids .

Scopolamine is the primary hallucinogen in *Datura wrightii* from California and other *Datura* species. Scopolamine can be slowly and erratically absorbed into the brain. In most people, scopolamine reaches the brain within an hour or so after ingestion and causes visual and auditory hallucinations. In about 25 % of people, scopolamine is very slowly absorbed into the brain, taking up to 13 hours to enter the brain. These are the people who are at the highest risk of overdosing. They become impatient waiting for the recreational high and take more of the plant extract .

6 – History :

Datura stramonium is native to either India or Central America . It was used as a mystical sacrament in both possible places of origin. Aboriginal Americans in the United States have used this plant in sacred ceremonies. In some tribes datura was involved in the ceremonies of manhood. The sadhus of Hinduism also used datura as a spiritual tool, smoking it with cannabis in their traditional chillums. It was also widely used by the Magyar (Hungarian) spiritual leaders (the Táltos) since ancient times. There is a Hungarian phrase "Nem veszem be ezt a maszlagot" (I will not eat *Datura stramonium*), meaning " you cannot fool me " .

In the United States it is called jimson weed, or more rarely Jamestown weed; it got this name from the town of Jamestown, Virginia, where British soldiers were drugged with it while attempting to suppress Bacon's Rebellion. They spent eleven days generally appearing to have gone insane :

The James - Town Weed (which resembles the Thorny Apple of Peru, and I take to be the plant so call'd) is supposed to be one of the greatest coolers in the world. This being an early plant, was gather'd very young for a boil'd salad, by some of the soldiers sent thither to quell the rebellion of Bacon (1676) ; and some of them ate plentifully of it, the effect of which was a very pleasant comedy, for they turned natural fools upon it for several days: one would blow up a feather in

the air; another would dart straws at it with much fury; and another, stark naked, was sitting up in a corner like a monkey, grinning and making mows [grimaces] at them; a fourth would fondly kiss and paw his companions, and sneer in their faces with a countenance more antic than any in a Dutch droll .

In this frantic condition they were confined, lest they should, in their folly, destroy themselves — though it was observed that all their actions were full of innocence and good nature. Indeed, they were not very cleanly; for they would have wallowed in their own excrements, if they had not been prevented. A thousand such simple tricks they played, and after eleven days returned themselves again, not remembering anything that had passed. — The History and Present State of Virginia , 1705 .

There was a time when stramonium, a drug obtained from the leaves and seeds of *Datura stramonium*, was used medicinally (Herbalgram). The alkaloid was known as daturine. From the seeds was made extractum stramonii. The tinctura stramonii was made from the leaves. Stramonium was used to relax the smooth muscle of the bronchial tubes, and thus it was used to treat an asthmatic's bronchial spasm. Cigarettes were made of stramonium leaves which could be smoked; or the tincture was taken internally. Frequently the leaves were powdered together with equal quantities of the leaves of cannabis and lobelia mixed with potassium nitrate, and were burned in an open dish. The preparation was reported to give off dense fumes which afforded great relief to the asthmatic paroxysm. Around the turn of the century numerous patent "cures" for asthma contained these ingredients in varying proportions. Daturine was also used to treat acute mania as hyoscyamine was said to produce sleep. Because of the dangers of tropane poisoning, datura is not used medicinally today, and the Food and Drug Administration (FDA) has claimed it to be unfit for human consumption. However, atropine, scopolamine and hyoscyamine are FDA approved drugs that are used every day for a variety of conditions.

The antidote of choice for overdose or poisoning is physostigmine.

7 - Mistaken identity :

The plant achieved some notoriety in the press^{[7][12][13]} and other media^{[14][15][16]} during the silly season of 2009 when several stories mistakenly identified it with Devil's Snare, an imaginary plant mentioned in the first of UK author J.K. Rowling's *Harry Potter* books, *Harry Potter and the Philosopher's Stone* .

8 - Gallery :

	
<i>D.stramonium</i> var. <i>tatula</i>	<i>D.stramonium</i> var. <i>Tatula</i> , flower (front)
	
<i>D.stramonium</i> var. <i>Tatula</i> , flower (side)	<i>D.stramonium</i> var. <i>tatula</i> , fruit

Datura



Contents

- 1 Introduction
- 2 Description
- 3 Species and cultivars
- 4 Cultivation
- 5 Toxicity
 - 5 .1 Effects of ingestion
 - 5 .2 Treatment

1 - Introduction :

Datura is a genus of nine species of vespertine flowering plants belonging to the family Solanaceae. Its precise and natural distribution is uncertain, owing to its extensive cultivation and naturalization throughout the temperate and tropical regions of the globe. Its distribution within the Americas, however, is most likely restricted to the United States and Mexico, where the highest species diversity occurs.

Some South American plants formerly thought of as *Daturas* are now treated as belonging to the distinct genus *Brugmansia* { this genus differs in being woody, making shrubs or small trees, and in having pendulous flowers }. Other related genera include *Hyoscyamus* and *Atropa*.

Scientific classification

Kingdom : Plantae
(unranked) : Angiosperms
(unranked) : Eudicots
(unranked) : Asterids
Order : Solanales
Family : Solanaceae
Genus : *Datura* L .

2 - Description :

Datura are woody-stalked, leafy annuals and short-lived perennials which can reach up to 2 meters in height. The leaves are alternate, 10–20 cm long and 5–18 cm broad, with a lobed or toothed margin. The flowers are erect or spreading (not pendulous like those of the closely allied *Brugmansia*), trumpet-shaped , 5 – 20 cm long and 4 – 12 cm broad at the mouth; colors vary from white to yellow, pink, and pale purple. The fruit is a spiny capsule 4 – 10 cm long and 2 – 6 cm broad, splitting open when ripe to release the numerous seeds . The seeds disperse freely over pastures , fields and even wasteland locations .

Datura belongs to the classic "witches' weeds," along with deadly nightshade, henbane, and mandrake. Most parts of the plants contain toxic hallucinogens, and *Datura* has a long history of use for causing delirious states and death. It was well known as an essential ingredient of love potions and witches' brews .

Common names include Thorn Apple (from the spiny fruit), Pricklyburr (similarly) , Jimson Weed, Moonflower, Hell's Bells, Devil's Weed, Devil's Cucumber, and Devil's Trumpet, (from their large trumpet-shaped flowers). Nathaniel Hawthorne refers to one type in *The Scarlet Letter* as Apple - Peru. The word *datura* comes from the Hindi *Dhatūrā* (thorn apple) ; record of this name dates back to 1662 (OED). In Tamil it is called " oomathai " (ஊமத்தை) .

Datura species are food plants for the larvae of some Lepidoptera (butterfly and moth) species including *Hypercompe indecisa*.

3 - Species and cultivars :

It is difficult to classify a *datura* as to its species, and it often happens that descriptions of new species are accepted prematurely. Later it is found that these "new species" are simply varieties that have evolved due to conditions at a specific location. They usually disappear in a few years. Contributing to the confusion are the facts that various species such as *D. wrightii* and *D. inoxia* are very similar in appearance, and that the variation within a species can be extreme. For example, *Datura* have the interesting property of being able to change size of plant, size of leaf, and size of flowers, all depending on location. The same species, when growing in a half-shady damp location can develop into a magnificent flowering bush half as tall as a person, but when growing in a very dry location will only grow into a thin little plant just higher than his ankles, with tiny flowers and a few miniature leaves .

Today , experts classify only nine species of *Datura*:^[2]

- *Datura ceratocaula*
- *Datura discolor* - Desert Thorn - apple
- *Datura ferox* - Long Spined Thorn-apple
- *Datura inoxia* or *Datura innoxia* – Thorn – apple , downy thorn - apple, Indian-apple, moonflower, sacred datura, toloatzin, or toloache
 - *Datura leichhardtii* (syn. *D. Pruinosa*) - Leichhardt's *Datura*
 - *Datura metel*
 - *Datura quercifolia* - Oak-leaf Thorn-apple
 - *Datura stramonium* (syn. *D. inermis*) - Jimsonweed, Thorn - apple
 - *Datura wrightii* - Sacred datura , Sacred Thorn - apple

American Brugmansia & Datura Society, Inc. (ABADS), is designated in the 2004 edition of the International Code of Nomenclature for Cultivated Plants as the official International

Cultivar Registration Authority for *Datura*. This role was delegated to ABADS by the International Society for Horticultural Science in 2002 .

4 - Cultivation:



Fruit



D. inoxia with ripe, split-open fruit

Datura are usually planted annually from the seed produced in the spiny pods, but with care, plants can be overwintered. Most species are suited to being planted outside or in containers. As a rule, they need warm, sunny places and soil that will keep their roots dry. When grown outdoors in good locations, the plants tend to reseed themselves and may become invasive. In containers, they should have porous, aerated potting soil with adequate drainage. The plants are susceptible to fungi in the root area, so organic enrichers such as compost and manure should be avoided

4 - Toxicity :

All *Datura* plants contain tropane alkaloids such as scopolamine, hyoscyamine, and atropine, primarily in their seeds and flowers. Because of the presence of these substances, *Datura* has been used for centuries in some cultures as a poison and hallucinogen.^{[2][3]} There can be a 5:1 toxin variation across plants, and a given plant's toxicity depends on its age, where it is growing, and the local weather conditions. This variation makes *Datura* exceptionally hazardous, as a drug. In traditional cultures, a great deal of experience with, and detailed knowledge of, "Datura" was critical in order to minimize harm.^[2] Many tragic incidents result from modern recreational users ingesting *Datura*. For example, in the 1990s and 2000s, the United States media contained stories of adolescents and young adults dying or becoming seriously ill from intentionally ingesting *Datura*.^{[4][5]} There are also several reports in the medical literature of deaths from *Datura stramonium* and *Datura ferox* intoxication . Children are especially vulnerable to atropine poisoning, and their prognosis is likely to be fatal.^{[9][10]} In some parts of Europe and India, *Datura* has been a popular poison for suicide and murder. From 1950 – 1965 , the State Chemical Laboratories in Agra , India investigated 2,778 deaths that were caused by ingesting *Datura* .

5 – 1 : Effects of ingestion :

Due to the potent combination of anticholinergic substances it contains, *Datura* intoxication typically produces effects similar to that of an anticholinergic delirium: a complete inability to differentiate reality from fantasy (delirium , as contrasted to hallucination) ; hyperthermia ; tachycardia ; bizarre , and possibly violent behavior ; and severe mydriasis with resultant painful photophobia that can last several days . Pronounced amnesia is another commonly reported effect .

According to the drug information site Erowid, no other substance has received as many " Train Wreck " (i.e., severely negative experience) reports as has *Datura* , noting that " the overwhelming majority of those who describe to us their use of *Datura* (and to a lesser extent , Belladonna , Brugmansia and Brunfelsia) find their

experiences extremely mentally and physically unpleasant and not infrequently physically dangerous."

The full listing of reports can be found at www.erowid.org. Numerous stories of *Datura* - related deaths and critical illnesses can also be found at the Lycaeum Datura Index [here](#).

5 – 2 : Treatment :

Due to their agitated behavior and confused mental state, victims of *Datura* poisoning are typically hospitalized . Gastric lavage (stomach pumping) and the administration of activated charcoal can be used to reduce the stomach's absorption of the ingested material. The drug physostigmine is used to reverse the effect of the poisons. Benzodiazepines can be given to curb the patient's agitation, and supportive care with oxygen, hydration, and symptomatic treatment is often provided. Observation of the patient is indicated until the symptoms resolve, usually from 24 – 36 hours after ingestion of the *Datura* .

Hashish



" Blonde " hashish

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1 – Introduction :

Hashish (pronounced /hæ'ʃi:ʃ/ or /'hæʃi:ʃ/) (from Arabic: حشيش *ḥashīsh*, lit . " grass " , from *hashsha* " to become dry " ; also **hash**) is a preparation of cannabis composed of the compressed stalked resin glands called trichomes, collected from the cannabis plant. It contains the same active ingredients but in higher concentrations than other parts of the plant such as the buds or the leaves. Psychoactive effects are the same as those of other cannabis preparations such as marijuana. It is sometimes believed that the

effects are different, but those differences usually stem from variations between regionally different Cannabis specimens that are typically processed into hashish.

Hashish is often a solid or paste - like substance of varying hardness and pliability, and will soften under heat. Its color can vary from green, yellow, black, reddish brown, or most commonly light to dark brown.

It is consumed in much the same way as cannabis buds, used by itself in a screened miniature smoking pipe, hookah, bong or bubbler, vaporized, hot knifed, or smoked in joints mixed with tobacco, cannabis buds, or other herbs.

It can also be eaten alone as well as used as an ingredient in food.

2 - History :

It is believed that hash first originated from Middle East, as this region was among the first to be populated by the cannabis plant, although the plant itself is thought to have originated in the Hindu Kush . More reliably, it may have originated in Northern India which also has a very long social tradition in the production of Hashish which is locally known as Charas. *Cannabis sativa subsp. indica* grows wild almost everywhere in the Indian sub-continent and special strains have been particularly cultivated for production of 'ganja' and 'hashish' particularly in Kerala, Rajasthan and the Himalayas . The earliest hashish was created without the use of sieves. The ancients would gently rub their palms and fingers on cannabis buds for hours while resin accumulated on their hands and then scrape that resin off. This sort of primitive harvesting is undertaken even today in the Cannabis growing farms of Manali, Naggar and Upper Himachal Pradesh.

Consumption of hashish saw an increase in the 20th century, in Europe and America, associated with the hippie scene which promoted pacifism and introspection. Hashish use declined significantly in the United States starting in the 1980s for several reasons, including U.S. political pressures against Afghanistan and the

ensuing Soviet invasion, the Reagan - escalated War on Drugs, a huge jump in price, and the success of marijuana cultivators in North America with new growing methods for increasing THC production, such as growing marijuana indoors.

No reports of a statistical linkage between hashish and violent crime have been published in known scientific literature, instead it has been found to generally inhibit aggressive impulses .

3 - Manufacturing processes :

Hashish is made from cannabinoid - rich glandular hairs known as trichomes, as well as varying amounts of cannabis flower and leaf fragments. The flowers of a mature female plant contain the most trichomes, though trichomes are found on other parts of the plant. Certain strains of cannabis are cultivated specifically for their ability to produce large amounts of trichomes. The resin reservoirs of the trichomes, sometimes erroneously called pollen, are separated from the plant through various methods. The resulting powder is compressed into blocks of hashish aided by heat, which can be easily stored and transported. Alternatively, the powder consisting of uncompressed, dry trichomes is often referred to as 'kief' instead of 'hashish'.

Mechanical separation methods use physical action to remove the trichomes from the plant. Sieving through a fine screen is a vital part of most methods. The plants may be sifted by hand or in motorized tumblers. Hash made in this way is sometimes called 'dry sift'. 'Finger hash' is produced by rolling the ripe trichome - covered flowers of the plant between the fingers, rupturing the trichomes, and collecting the freed resin that sticks to the fingers.

Ice water separation is a more modern mechanical separation method which submerges the plant's leaves in ice and water and agitates the mixture, sometimes in a Washing machine. The low temperature solidifies the resinous trichomes. They become brittle, and the mechanical agitation breaks them off the leaves. The waste plant matter, detached trichomes, and water are separated by filtering through a series of increasingly fine screens or bags (with pore sizes

ranging from 220 to 25 microns) . The trichomes of various sizes are then dried and pressed into solid blocks of hash. Kits are commercially available which provide a series of filter bags meant to fit inside standard bucket sizes. Hash made in this way is sometimes called 'ice hash', or 'bubble hash'. This method produces valuable product from leaf matter that would otherwise be discarded (after the plant's "buds" are trimmed for sale). The advent of this process has made hashish much more readily available in North America.

Chemical separation methods generally use a solvent such as ethanol or hexane to dissolve the lipophilic desirable resin. The remaining plant material is then filtered out of the solution and sent to the compost.^[3] The solvent is then evaporated, leaving behind the desirable resins, called honey oil, 'hash oil', or just 'oil'. Honey oil still contains waxes and essential oils and can be further purified by vacuum distillation to yield 'red oil'. The product of chemical separations is more commonly referred to as 'honey oil'.

4 - Quality :

The main factors affecting quality are potency and purity. Different cannabis plants will produce resins with unique chemical profiles that vary in potency. Some forms of hashish are described as producing a "body stone" while others are more of a "head high". This is usually due to whether it was extracted from a sativa or indica plant.

Tiny pieces of leaf matter or even purposefully added adulterants introduced when the hash is being produced will reduce the purity of the material. The tetrahydrocannabinol (THC) content of hashish usually ranges from 15 – 20 % , and that of hash oil from 30 – 40 % .

Fresh hashish of good quality is soft and pliable and becomes progressively harder and less potent as its THC content oxidizes to cannabinol and as essential oils evaporate.

Hash is generally said to be black, brown or blond. There is also hashish of greenish or reddish hue. A green tinge may indicate that the hashish contains a large amount of leaf material. Hashish color usually reflects the methods of harvesting, manufacturing, and storage.

5 - Hashish by region :

5 – 1 : Production :



Cannabis crop in Afghanistan

Hashish is traditionally produced in warm conditions. It is traditionally found in a belt extending from North Africa, Egypt to North India and into Central Asia . The primary hash-producing countries are Iran, India , Afghanistan , Pakistan, Nepal , Morocco , Lebanon and Egypt .

Charas is the name of hashish that has been hand-rubbed directly from the cannabis plant. It is primarily produced in Afghanistan and Pakistan and to a smaller extent the rest of the subcontinent. Today, the word charas is common word for hash in a majority of the subcontinent, despite the fact that different methods may be used other than the hand-rubbed method.

The most popular and sought after form of charas is produced in the tribal areas of Pakistan bordering Afghanistan. Popular destinations include the tribal areas themselves as well as adjacent Pakistani states such as Peshawar.

A visitor to the Rif Mountains and the town of Ketama in Morocco in December 1976 described the production of hashish. In unheated huts, each worker placed his hands and arms inside a fertilizer sack. The depths of the bag was filled with leaves of the cannabis plant. In the mouth of the bag was a plastic washing-up bowl, over which was stretched a sheet of "zero - zero" grade muslin. The worker rubbed the leaves of the cannabis plant against the muslin, resulting in a fine powder falling into the bowl. 100 grams of the powder would be wrapped in more of the same fine muslin, put onto a

heated metal plate, and rolled down with a bottle. This process produces a slightly sticky solid brown mass in the form of a rectangular slab, quite a bit smaller than a paperback book and 5 mm thick. The block was then wrapped in cellophane. Sellers of this Moroccan hashish pointed to the imprint of the muslin on the surface of the block, and declared it proof that the product was " zero – zero " , top quality.

In Afghanistan there is a method of making hash that resembles charas. First, cannabis resin is placed on a heated mortar about the size of a box, then the resin is threshed with a heavy object. The result is a very gooey, sticky black hash. This method is mostly used in villages around the Hindu Kush mountain region .

Hashish is also produced in the deserts of northern Mexico, and throughout the western United States and Canada.

6 - Preparation and methods of use :

Like ordinary cannabis preparations, hashish is usually smoked, though it can also be eaten (more commonly than cannabis plant) or vaporised.

Hash is sometimes prepared for smoking by heating it with a flame for a couple of seconds, sometimes producing some bubbling or sizzling as moisture and essential oils evaporate. It then softens and can be sliced with a sharp knife, crumbled into tiny pieces obtain maximum surface area when burning. The resulting lower burning temperature permits more THC to be released in its active form .

6 – 1 : Vaporization :

Used with hashish as with any cannabis, tobacco or other herb material, a vaporizer can volatilize cannabinoids at temperatures as low as 140 °C, protecting against loss of this ingredient which occurs in burning, and eliminating carbon monoxide and other toxic combustion gases. Since hashish is solid, its surface area may be enlarged by cutting slices or breaking into small crumbs to achieve maximum cannabinoid vaporization.

6 – 2 : Pipe :

A narrow screened single - toke midwakh (made in the U.A.E.), shown here, or kiseru achieves lowest burning temperature, reducing waste of THC. Such a utensil may be connected to a long draw-tube, such as those used on hookahs, to cool the smoke before it reaches the user's trachea.

Hashish may be smoked through a pipe , either alone or mixed with loose herb to aid igniting, with a screen to prevent small parts of burning hashish rushing into the user's throat(colloquially 'shooters'). A hookah pipe or a bong provides water filtration, cooling the smoke for a smoother inhalation.

6 - 2 - 1 : Semi - vaporizer technique :

When using a screened long-stemmed glass or metal utensil, vaporization is achieved by holding a moderate (2 - cm) lighter flame for several seconds near enough below the crater opening to heat the contents inside but delaying as long as possible their catching on fire, all the while continually sucking slowly through the drawtube. After a serving is completed, breathing numerous times in and out of a one-liter paper or plastic sack protects against health issues arising from overheating or drying the respiratory tract.

6 - 2 -2 : Auxiliary herbs :

Of herbs that may be burned to vaporize from hashish, hops (*Humulus lupulus*) flowers, previously ground to a fine particle size in a mesh-16 screen strainer, are the most delicate and interfere least with perceiving the taste of the hashish. Eucalyptus leaf also has a low combustion point but adds a strong flavor, as does oregano. Mild species include various flowers, basil, catnip (*Nepeta cataria*), damiana, dandelion, ginseng (leaf), lemon balm (melissa) , marjoram, parsley, savory, tarragon, thyme, uva ursi (kinnickinnick) .

6 -3 : Dabous :

A piece of hash may be ignited by cigarette coals or other means and placed inside a container, such as a plastic bottle. The smoke that collects inside can then be inhaled. 'Dabous' or 'Khabour', but most commonly "shisha" (glass in Arabic) is a North African technique. This technique is commonly referred to as "Bots" or "BTs" ("Bottle-Tokes") or simply "Ts/Tees" in Canada. "Hash under Glass" is for smoking with minimal equipment. A small ball of hash can be stuck onto a Safety pin opened and inserted through paper. The ball is ignited and then covered by a Drinking glass. Smoke collects in the glass and can then be inhaled by tipping the glass slightly .

7 - *Cooking* :

As cannabinoids are fat-soluble, they dissolve in oils and fats, including butter. Finely crumbled or dissolved hashish can be used for cooking . .

Khat



Catha edulis

Contents

- 1 Introduction
- 2 Description
- 3 History
- 4 Cultivation and uses
- 5 Chemistry and pharmacology
- 6 Growing
- 7 Effects
- 8 Demographics

1 – Introduction :

Khat (*Catha edulis* , family Celastraceae ; pronounced / 'kɑ:t / ; Arabic : قات ; Ge'ez ሻሻ ṣāt ; Somali : qaat) , also known as **qat** , **qaat** , **quat** , **gat** , **jaad** , **chat** , **chad** , **chaad** and **miraa** , is a flowering plant native to tropical East Africa and the Arabian Peninsula .

Khat contains the alkaloid called cathinone , an amphetamine - like stimulant which is said to cause excitement, loss of appetite and euphoria. In 1980 the World Health Organization classified khat as a drug of abuse that can produce mild to moderate psychological dependence. The plant has been targeted by anti-drug organizations like the DEA . It is a controlled/illegal substance in many countries, but is legal for sale and production in many others .

Scientific classification

Kingdom :	Plantae
Division :	Magnoliophyta
Class :	Magnoliopsida
Order :	Celastrales
Family :	Celastraceae
Genus :	Catha
Species:	C. edulis

2 - Description

Khat is a slow - growing shrub or tree that grows to between 1.5 meters and 20 meters tall , depending on region and rainfall, with evergreen leaves 5 – 10 cm long and 1 – 4 cm broad . The flowers are produced on short axillary cymes 4 –8 cm long , each flower small, with five white petals . The fruit is an oblong three - valved capsule containing 1 – 3 seeds .

3 - History



Man consuming khat in Sana'a, Yemen

It's believed that it is Ethiopian in origin, from where it spread to the hillsides of East Africa and Yemen . Others believe that khat originated in Yemen before spreading to Ethiopia and nearby countries. Sir Richard Burton explains that khat was introduced to the Yemen from Ethiopia in the 15th century . There is also evidence to suggest this may have occurred as early as the 13th century. Through botanical analysis, Revri (1983) supports Yemen origins of the plant . From Ethiopia and Yemen the trees spread to Arabia , Kenya , Uganda , Tanzania , the Congo , Malawi , Zimbabwe , Zambia , and South

Africa . The earliest recorded use of khat medically is believed to be within the New Testament , The ancient Egyptians considered the khat plant a " divine food " which was capable of releasing humanity's divinity. The Egyptians used the plant for more than its stimulating effects; they used it as a metamorphic process and transcended into "apotheosis", intending to make the user god - like .

The earliest documented description of khat dates back to the Kitab al - Saidana fi al - Tibb, an 11th century work on pharmacy and materia medica written by Abū Rayhān al-Bīrūnī, a Persian scientist and biologist. Unaware of its origins , al -Bīrūnī wrote that khat is : " a commodity from Turkestan . It is sour to taste and slenderly made in the manner of batan – alu . But qat is reddish with a slight blackish tinge . It is believed that batan - alu is red, coolant , relieves biliousness, and is a refrigerant for the stomach and the liver . "

In 1854, the Malay writer Abdullah bin Abdul Kadir noted that the custom of chewing Khat was prevalent in Al Hudaydah in Yemen : " I observed a new peculiarity in this city — everyone chewed leaves as goats chew the cud . There is a type of leaf, rather wide and about two fingers in length, which is widely sold, as people would consume these leaves just as they are; unlike betel leaves, which need certain condiments to go with them, these leaves were just stuffed fully into the mouth and munched. Thus when people gathered around, the remnants from these leaves would pile up in front of them. When they spat, their saliva was green. I then queried them on this matter: ‘What benefits are there to be gained from eating these leaves?’ To which they replied , ‘ None whatsoever , it’s just another expense for us as we’ve grown accustomed to it’. Those who consume these leaves have to eat lots of ghee and honey, for they would fall ill otherwise. The leaves are known as Kad " .

4 - Cultivation and uses :

The khat plant is known by a variety of names, such as qat and ghat in Yemen , qaat and jaad in Somalia , and chat in Ethiopia. It is also known as Jimma in the Oromo language. Khat has been grown for use as a stimulant for centuries in the Horn of Africa and the Arabian Peninsula. There, chewing khat predates the use of coffee and

is used in a similar social context. Its fresh leaves and tops are chewed or, less frequently, dried and consumed as tea, in order to achieve a state of euphoria and stimulation; it also has anorectic side - effects. Its use is generally not limited by religion, though the Ethiopian Orthodox Tewahedo Church (along with its Eritrean counterpart) has forbidden Christians from using it due to its stimulating effects . Due to the availability of rapid, inexpensive air transportation , the plant has been reported in England , Wales , Rome , Amsterdam , Canada , Australia , New Zealand and the United States . The international community has become more aware of this plant through media reports pertaining to the United Nations mission in Somalia, where khat use is widespread , and its role in the Arabian Gulf.



Bundles of khat

Khat use has traditionally been confined to the regions where khat is grown, because only the fresh leaves have the desired stimulating effects. In recent years improved roads, off-road motor vehicles and air transport have increased the global distribution of this perishable commodity. Traditionally, khat has been used as a socializing drug, and this is still very much the case in Yemen where khat - chewing is predominantly, although not exclusively, a male habit.^[11] In other countries, khat is consumed largely by single individuals and at parties. It is mainly a recreational drug in the countries which grow khat, though it may also be used by farmers and laborers for reducing physical fatigue or hunger and by drivers and students for improving attention. Within the counter-culture segments of the Kenyan elite population, Khat (referred to as veve or mirra) is used to counter the

effects of a hangover or binge drinking, similar to the use of the coca leaf in South America. In Yemen, some women have their own saloons for the occasion, and participate in chewing Khat with their husbands on weekends. In many places where it is grown, khat has become mainstream enough for many children to start chewing the plant before puberty..

Khat is so popular in Yemen that its cultivation consumes much of the country's agricultural resources. It is estimated that 40 % of the country's water supply goes towards irrigating it, with production increasing by about 10 % to 15 % every year. Water consumption is so high that groundwater levels in the Sanaa basin are diminishing; because of this, government officials have proposed relocating large portions of the population of Sanaa to the coast of the Red Sea . One reason for cultivating khat in Yemen so widely is the high income it provides for farmers. Some studies done in 2001 estimated that the income from cultivating khat was about 2.5 million Yemeni rials per hectare, while it was only 0.57 million rials per hectare if fruits were cultivated. This is a strong reason farmers prefer to cultivate khat over coffee and fruits. It is estimated that between 1970 and 2000, the area on which khat was cultivated grew from 8,000 hectares to 103,000 hectares .

In Somalia, the Supreme Islamic Courts Council, which took control of much of the country in 2006, banned khat during Ramadan, sparking street protests in Kismayo . In November 2006, Kenya banned all flights to Somalia , citing security concerns, prompting protests by Kenyan khat growers. The Kenyan Member of Parliament from Ntonyiri, Meru North District stated that local land had been specialized in khat cultivation, that 20 tons worth \$800,000 were shipped to Somalia daily and that a flight ban could devastate the local economy.^[13] With the victory of the Provisional Government backed by Ethiopian forces in the end of December 2006, khat has returned to the streets of Mogadishu, though Kenyan traders have noted demand has not yet returned to pre - ban levels .

5 - Chemistry and pharmacology :

The stimulant effect of the plant was originally attributed to "katin", cathine, a phenethyl amine - type substance isolated from the plant. However, the attribution was disputed by reports showing the plant extracts from fresh leaves contained another substance more behaviorally active than cathine. In 1975, the related alkaloid cathinone was isolated, and its absolute configuration was established in 1978. Cathinone is not very stable and breaks down to produce cathine and norephedrine. These chemicals belong to the PPA (phenyl propanol amine) family, a subset of the phenethylamines related to amphetamines and the catechol amines epinephrine and norepinephrine.

Both of khat's major active ingredients — cathine and cathinone — are phenyl alkyl amines, meaning they are in the same class of chemicals as amphetamines. In fact, cathinone and cathine have a very similar molecular structure to amphetamine.

When khat leaves dry, the more potent chemical, cathinone, decomposes within 48 hours leaving behind the milder chemical, cathine. Thus, harvesters transport khat by packaging the leaves and stems in plastic bags or wrapping them in banana leaves to preserve their moisture and keep the cathinone potent. It is also common for them to sprinkle the plant with water frequently or use refrigeration during transportation.

When the khat leaves are chewed, cathine and cathinone are released and absorbed through the mucous membranes of the mouth and the lining of the stomach. The action of cathine and cathinone on the reuptake of epinephrine and norepinephrine has been demonstrated in lab animals, showing that one or both of these chemicals cause the body to recycle these neurotransmitters more slowly, resulting in the wakefulness and insomnia associated with khat use.

Receptors for serotonin show a high affinity for cathinone suggesting that this chemical is responsible for feelings of euphoria associated with chewing khat. In mice, cathinone produces the same types of nervous pacing or repetitive scratching behaviors associated with amphetamines. The effects of cathinone peak after 15 to 30

minutes with nearly 98 % of the substance metabolized into norephedrine by the liver .

Cathine is somewhat less understood, being believed to act upon the adrenergic receptors causing the release of epinephrine and norepinephrine . It has a half - life of about 3 hours in humans . Because the receptor effect are similar to those of cocaine medication, treatment of the occasional addiction is similar to that of cocaine. The medication bromo criptine can reduce cravings and withdrawal symptoms within 24 hours .

6 - Growing :

It takes nearly seven to eight years for the Khat plant to reach its full height. Other than access to sun and water, Khat requires little maintenance. Ground water is often pumped from deep wells by diesel engines to irrigate the crops, or brought in by water trucks. The plants are watered heavily starting around a month before it is harvested to make the leaves and stems soft and moist. A good Khat plant can be harvested four times a year, providing a year long source of income for the farmer.

7 – Effects :

Khat consumption induces mild euphoria and excitement. A meta-analysis in *The Lancet* has stated that khat creates a pleasuring effect to the same degree as ecstasy. Individuals become very talkative under the influence of the drug and may appear to be unrealistic and emotionally unstable. Khat can induce manic behaviors and hyperactivity. Khat is an effective anorectic and its use also results in constipation . Dilated pupils (mydriasis) , which are prominent during khat consumption, reflect the sympathomimetic effects of the drug, which are also reflected in increased heart rate and blood pressure. A state of drowsy hallucinations (hypnagogic hallucinations) may result coming down from khat use as well. Withdrawal symptoms that may follow occasional use include mild depression and irritability. Withdrawal symptoms that may follow prolonged khat use include lethargy, mild depression, nightmares, and slight tremor. Long-term use can precipitate the following effects: negative impact

on liver function, permanent tooth darkening (of a greenish tinge) , susceptibility to ulcers, and diminished sex drive. Those who abuse the drug generally cannot stay without it for more than 4 – 5 days, feeling tired and having difficulty concentrating . Occasionally a psychosis can result, resembling a hypo manic state in presentation .

8 – Demographics :

It is estimated that several million people are frequent users of khat. Many of the users originate from countries between Sudan and Madagascar and in the southwestern part of the Arabian Peninsula, especially Yemen. In Yemen , 80 % of the males and 45 % of the females were found to be khat users who had chewed daily for long periods of their life. The traditional form of khat chewing in Yemen involves only male users; khat chewing by females is less formal and less frequent. In Saudi Arabia, the cultivation and consumption of khat are forbidden, and the ban is strictly enforced. The ban on khat is further supported by the clergy on the grounds that the Qur'an forbids anything that is harmful to the body. In Somalia, 61 % of the population reported that they do use khat, 18 % report habitual use, and 21 % are occasional users .

Researchers estimate that about 70 – 80 % of Yemenis between 16 and 50 years old chew khat , at least on occasion, and it has been estimated that Yemenis spend about 14.6 million person-hours per day chewing khat. The local researcher Ali Al-Zubaidi has estimated that the amount of money spent on khat has increased from 14.6 billion rials in 1990 to 41.2 billion rials in 1995 . Researchers have also estimated that families spend about 17 % of their income on khat (the real number may be less) .

Opium



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1 – Introduction :

Opium is a narcotic formed from the latex released by lacerating (or "scoring") the immature seed pods of opium poppies (*Papaver somniferum*). It contains up to 12 % morphine, an opiate alkaloid, which is most frequently processed chemically to produce heroin for the illegal drug trade. The resin also includes codeine and non-narcotic alkaloids, such as papaverine, thebaine and noscapine. **Meconium** historically referred to related, weaker preparations made from other parts of the poppy or different species of poppies. Modern opium production is the culmination of millennia of production, in which the source poppy, methods of extraction and processing, and methods of consumption have become increasingly potent.

Cultivation of opium poppies for food, anesthesia, and ritual purposes dates back to at least the Neolithic Age. The Sumerian, Assyrian, Egyptian, Minoan, Greek, Roman, Persian and Arab Empires each made widespread use of opium, which was the most potent form of pain relief then available, allowing ancient surgeons to perform prolonged surgical procedures. Opium is mentioned in the most important medical texts of the ancient world, including the Ebers Papyrus and the writings of Dioscorides , Galen, and Avicenna. Widespread medical use of unprocessed opium continued through the American Civil War before giving way to morphine and its successors, which could be injected at a precisely controlled dosage. American morphine is still produced primarily from poppies grown and processed in India in the traditional manner and remains the standard of pain relief for casualties of war .

In China recreational use of the drug began in the fifteenth century but was limited by its rarity and expense. Opium trade became more regular by the seventeenth century, when it was mixed with tobacco for smoking, and addiction was first recognized . Opium prohibition in China began in 1729 yet was followed by nearly two centuries of increasing opium use .

China had a positive balance sheet in trading with the British, which led to a decrease of the British silver stocks. Therefore, the British tried to encourage Chinese opium use to enhance their balance, and they delivered it from Indian provinces under British control. A massive confiscation of opium by the Chinese emperor, who tried to stop the opium deliveries, led to two Opium Wars in 1839 and 1858, in which Britain suppressed China and traded opium all over the country. After 1860, opium use continued to increase with widespread domestic production in China, until more than a quarter of the male population was addicted by 1905. Recreational or addictive opium use in other nations remained rare into the late nineteenth century, recorded by an ambivalent literature that sometimes praised the drug.

Global regulation of opium began with the stigmatization of Chinese immigrants and opium dens in San Francisco, leading rapidly from town ordinances in the 1870s to the formation of the International Opium Commission in 1909. During this period, the portrayal of opium in literature became squalid and violent, British opium trade was largely supplanted by domestic Chinese production, purified morphine and heroin became widely available for injection, and patent medicines containing opiates reached a peak of popularity. Opium was prohibited in many countries during the early twentieth century, leading to the modern pattern of opium production as a precursor for illegal recreational drugs or tightly regulated legal prescription drugs. Illicit opium production, now dominated by Afghanistan, was decimated in 2000 when production was banned by the Taliban, but has increased steadily since the fall of the Taliban in 2001 and over the course of the War in Afghanistan , Worldwide production in 2006 was 6610 metric tones - nearly one - fifth the level of production in 1906. Opium for illegal use is often converted into heroin, which multiplies its potency to approximately twice that of morphine, can be taken by intravenous injection, and is easier to smuggle .

Botanical	Opium
Source plant (s)	Papaver somniferum
Part (s) of plant	sap
Geographic origin	Indochina Region u.s.a (?)
Active ingredients	Morphine, Codeine
Main producers	Afghanistan (primary) , Northern India , Thailand , Laos , Myanmar , Mexico , Colombia , Hungary ,
Whole sale price	\$ 3,000 per kilogram
Retail price	\$ 16,000 per kilogram

2 – History :

2 - 1 : Ancient use (4200 BC - 800 AD)

At least seventeen finds of *Papaver somniferum* from Neolithic settlements have been reported throughout Switzerland, Germany, and Spain, including the placement of large numbers of poppy seed capsules at a burial site (the *Cueva de los Murciélagos* , or " Bat cave ," in Spain) , which have been carbon - 14 dated to 4200 B.C. Numerous finds of *Papaver somniferum* or *Papaver setigerum* from Bronze Age and Iron Age settlements have also been reported.^[5] The first known cultivation of opium poppies was in Mesopotamia, approximately 3400 B.C., by Sumerians who called the plant *Hul Gil*, the " joy plant " . Tablets found at Nippur, a Sumerian spiritual center south of Baghdad , described the collection of poppy juice in the morning and its use in production of opium.^[4] Cultivation continued in the Middle East by the Assyrians, who also collected poppy juice in the morning after scoring the pods with an iron scoop; they called the juice *aratpa - pal*, possibly the root of *Papaver* . Opium production continued under the Babylonians and Egyptians .

Opium was used with poison hemlock to put people quickly and painlessly to death, but it was also used in medicine. The Ebers Papyrus, ca. 1500 B.C., describes a way to "stop a crying child" using grains of the poppy-plant strained to a pulp. *Spongia somnifera*, sponges soaked in opium, were used during surgery.^[6] The Egyptians cultivated *opium thebaicum* in famous poppy fields around 1300 B.C. Opium was traded from Egypt by the Phoenicians and Minoans to destinations around the Mediterranean Sea, including Greece, Carthage, and Europe. By 1100 B.C., opium was cultivated on the Mediterranean island of Cyprus, where surgical - quality knives were used to score the poppy pods, and opium was cultivated, traded, and smoked.^[8] Opium was also mentioned after the Persian conquest of Assyria and Babylonia in the sixth century B.C .

From the earliest finds, opium has appeared to have ritual significance, and anthropologists have speculated that ancient priests may have used the drug as a proof of healing power.^[6] In Egypt, the use of opium was generally restricted to priests, magicians, and warriors, its invention credited to Thoth, and it was said to have been given by Isis to Ra as treatment for a headache.^[4] A figure of the Minoan "goddess of the narcotics," wearing a crown of three opium poppies, ca. 1300 B.C., was recovered from the Sanctuary of Gazi, Crete, together with a simple smoking apparatus . The Greek gods Hypnos (Sleep) , Nyx (Night) , and Thanatos (Death) were depicted wreathed in poppies or holding poppies. Poppies also frequently adorned statues of Apollo, Asklepios , Pluto, Demeter, Aphrodite, Kybele and Isis, symbolizing nocturnal oblivion .

2 - 2 : Islamic Societies (600 - 1500 A . D) :

As the power of the Roman Empire declined, the lands to the south, and east of the Mediterranean sea became incorporated into the Islamic Empire, which assembled the finest libraries and the most skilled physicians of the era. Many Muslims believe that the hadith of al - Bukhari prohibits every intoxicating substance as haraam , but the use of intoxicants in medicine has been widely permitted by Scholars,

even though it is prohibited under Islamic Law . Dioscorides ' five - volume *De Materia Medica*, the precursor of pharmacopoeias, remained in use (with some improvements in Arabic versions) from the 1st to 16th centuries and described opium , meconium and the wide range of uses prevalent in the ancient world.^[12] Somewhere between 400 and 1200 AD , Arab traders introduced opium to China . The Persian physician Abu Bakr Muhammad ibn Zakariya al - Razi Rhazes (845 - 930 A.D) maintained a laboratory and school in Baghdad , and was a student and critic of Galen, made use of opium in anesthesia and recommended its use for the treatment of melancholy in *Fi ma-yahdara al-tabib* (In the Absence of a Physician) , a home medical manual directed toward ordinary citizens for self-treatment if a doctor was not available.^{[14][15]} The renowned ophthalmologic surgeon Abu al - Qasim Ammar (936 - 1013 AD) relied on opium and mandrake as surgical anaesthetics and wrote a treatise, *al-Tasrif*, that influenced medical thought well into the sixteenth century.^{[16][17]} The Persian physician Abū 'Alī al - Husayn ibn Sina (Avicenna) described opium as the most powerful of the stupeficients, by comparison with mandrake and other highly effective herbs, in *The Canon of Medicine*. This classic text was translated into Latin in 1175 and later into many other languages and remained authoritative into the seventeenth century . Şerafeddin Sabuncuoğlu used opium in the fourteenth century Ottoman Empire to treat migraine headaches, sciatica, and other painful ailments .

2 – 3 : Reintroduction to Western medicine :

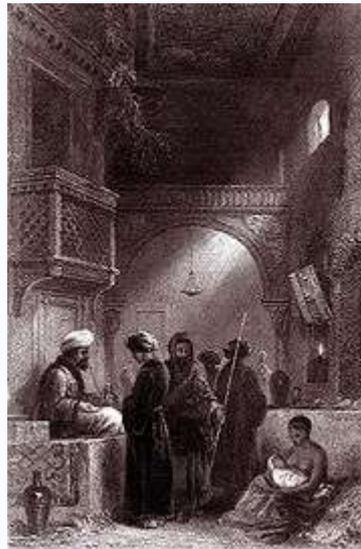
Opium became stigmatized in Europe during the Inquisition as a Middle Eastern influence and became a taboo subject in Europe from approximately 1300 to 1500 A.D . Manuscripts of Pseudo - Apuleius's fifth - century work from the tenth and eleventh centuries refer to the use of wild poppy *Papaver agreste* or *Papaver rhoeas* (identified as *Papaver silvaticum*) instead of *Papaver somniferum* for inducing sleep and relieving pain .

The use of Paracelsus' laudanum was introduced to Western medicine in 1527, when Philip Aureolus Theophrastus Bombast von Hohenheim, better known by the name Paracelsus, returned from his wanderings in Arabia with a famous sword, within the pommel of which he kept "Stones of Immortality" compounded from opium thebaicum, citrus juice, and "quintessence of gold". The name "Paracelsus" was a pseudonym signifying him the equal or better of Aulus Cornelius Celsus, whose text, which described the use of opium or a similar preparation, had recently been translated and reintroduced to medieval Europe.^[23] *The Canon of Medicine*, the standard medical textbook that Paracelsus burned in a public bonfire three weeks after being appointed professor at the University of Basel, also described the use of opium, though many Latin translations were of poor quality.^[21] *Laudanum* was originally the sixteenth-century term for a medicine associated with a particular physician that was widely well-regarded, but became standardized as "tincture of opium," a solution of opium in ethyl alcohol, which Paracelsus has been credited with developing. During his lifetime, Paracelsus was viewed as an adventurer who challenged the theories and mercenary motives of contemporary medicine with dangerous chemical therapies, but his therapies marked a turning point in Western medicine. In the seventeenth century laudanum was recommended for pain, sleeplessness, and diarrhea by Thomas Sydenham, the renowned "father of English medicine" or "English Hippocrates," to whom is attributed the quote, "Among the remedies which it has pleased Almighty God to give to man to relieve his sufferings, none is so universal and so efficacious as opium". Use of opium as a cure-all was reflected in the formulation of mithridatium described in the 1728 *Chambers Cyclopaedia*, which included true opium in the mixture. Subsequently, laudanum became the basis of many popular patent medicines of the nineteenth century.

The standard medical use of opium persisted well into the nineteenth century. U.S. president William Henry Harrison was treated with opium in 1841, and in the American Civil War, the Union Army used 2.8 million ounces of opium tincture and powder and about 500,000 opium pills.^[4] During this time of popularity, users called opium "God's Own Medicine".

The most important reason for the increase in opiate consumption in the United States during the 19th century was the prescribing and dispensing of legal opiates by physicians and pharmacist to women with "female problems" (mostly to relieve painful menstruation. Between 150,000 and 200,000 opiate addicts lived in the United States in the late 19th century and between two-thirds and three - quarters of these addicts were women .

2 – 4 : Recreational use in Islamic Societies :



An imaginary view of an Ottoman opium seller

In Islamic societies, opium is said to have been used for recreational purposes from the 14th century onwards. Testimonies of historians, diplomats, religious scholars, intellectuals and travelers , Ottoman and European, confirm that, from the 16th to the 19th century, Anatolian opium was eaten in Constantinople as much as it was exported to Europe. From eating it, dervishes drew ecstasy, soldiers courage, dignitaries and people bliss and voluptuousness. It is not only to the pleasures of coffee and tulips that the Ottomans initiated Europe. It was also Turkey which, long before China, supplied the West with opium . According to Fynes Moryson, who travelled in Turkey in 1595 – 7 , “ The Turkish Souldiers being to fight , if they can find no wine , drinke the juyce of blacke poppy, called Opium, to raise their spirits to a kind of fury, thinking themselves made more valiant thereby; For howsoever we thinke this

hearbe, especially taken largely, to be dangerous for the health, yet there is not a Turke from the highest to the lowest, who doth not as it were daily use it, nothing being more frequently sowed, nothing more plentifully growing, especially in Natolia, nothing more easily finding a buyer; yea, if their Cammels and Dromidaries faile by the way, or upon necessity must goe further than they use to journey, as sometimes it fals out in Armies and other Journeys, then they give them this hearbe, by which they report their spirits so to be stirred up, as they will goe till they fall downe dead ” . In his “Confessions of an English Opium - eater ” (1821, p. 188) , it is still about Ottoman, not Chinese, addicts that Thomas de Quincey writes : “ I question whether any Turk, of all that ever entered the paradise of opium-eaters, can have had half the pleasure I had ” .

Extensive textual and pictural sources also show that poppy cultivation and opium consumption were widespread in Safavid Iran and Moghol India .

2 – 5 : Recreational use in China :

The earliest clear description of the use of opium as a recreational drug in China came from Xu Boling, who wrote in 1483 that opium was "mainly used to aid masculinity, strengthen sperm and regain vigor," and that it "enhances the art of alchemists, sex and court ladies." He described an expedition sent by the Chenghua Emperor in 1483 to procure opium for a price "equal to that of gold" in Hainan, Fujian, Zhejiang, Sichuan and Shaanxi where it is close to Xiyu. A century later, Li Shizhen listed standard medical uses of opium in his renowned *Compendium of Materia Medica* (1578) , but also wrote that "lay people use it for the art of sex," in particular the ability to " arrest seminal emission " . This association of opium with sex continued in China until the twentieth century. Opium smoking began as a privilege of the elite and remained a great luxury into the early nineteenth century, but by 1861, Wang Tao wrote that opium was used even by rich peasants, and even a small village without a rice store would have a shop where opium was sold .

Smoking of opium came on the heels of tobacco smoking and may have been encouraged by a brief ban on the smoking of tobacco

by the Ming emperor, ending in 1644 with the Qing dynasty, which had encouraged smokers to mix in increasing amounts of opium . In 1705, Wang Shizhen wrote that "nowadays, from nobility and gentlemen down to slaves and women, all are addicted to tobacco." Tobacco in that time was frequently mixed with other herbs (this continues with clove cigarettes to the modern day) , and opium was one component in the mixture. Tobacco mixed with opium was called madak (or madat) and became popular throughout China and its seafaring trade partners (such as Taiwan, Java and the Philippines) in the seventeenth century . In 1712 , Engelbert Kaempfer described addiction to madak: "No commodity throughout the Indies is retailed with greater profit by the Batavians than opium, which [its] users cannot do without, nor can they come by it except it be brought by the ships of the Batavians from Bengal and Coromandel " .

Fueled in part by the 1729 ban on madak , which at first effectively exempted pure opium as a potentially medicinal product, the smoking of pure opium became more popular in the eighteenth century. In 1736 , the smoking of pure opium was described by Huang Shujing, involving a pipe made from bamboo rimmed with silver, stuffed with palm slices and hair, fed by a clay bowl in which a globule of molten opium was held over the flame of an oil lamp. This elaborate procedure, requiring the maintenance of pots of opium at just the right temperature for a globule to be scooped up with a needle-like skewer for smoking, formed the basis of a craft of "paste-scooping" by which servant girls could become prostitutes as the opportunity arose .

Beginning in 19th-century China, famine and political upheaval, as well as rumors of wealth to be had in nearby Southeast Asia, led to the Chinese Diaspora. Chinese emigrants to cities such as San Francisco, London, and New York brought with them the Chinese manner of opium smoking and the social traditions of the opium den . The Indian Diaspora distributed opium-eaters in the same way, and both social groups survived as " lascars " (seamen) and "coolies" (manual laborers) . French sailors provided another major group of opium smokers, having contracted the habit in French Indochina, where the drug was promoted by the colonial government as a

monopoly and source of revenue . Among white Europeans, opium was more frequently consumed as laudanum or in patent medicines. Britain's All - India Opium Act of 1878 formalized social distinctions, limiting recreational opium sales to registered Indian opium - eaters and Chinese opium - smokers and prohibiting its sale to workers from Burma . Likewise, American law sought to contain addiction to immigrants by prohibiting Chinese from smoking opium in the presence of a white man.^[33]

Because of the low social status of immigrant workers, contemporary writers and media had little trouble portraying opium dens as seats of vice, white slavery, gambling, knife and revolver fights, a source for drugs causing deadly overdoses, with the potential to addict and corrupt the white population. By 1919, anti - Chinese riots attacked Limehouse, the Chinatown of London. Chinese men were deported for playing pock-apu, a popular gambling game, and sentenced to hard labor for opium possession. Both the immigrant population and the social use of opium fell into decline . Yet despite lurid literary accounts to the contrary, nineteenth - century London was not a hotbed of opium smoking. The total lack of photographic evidence of opium smoking in Britain, as opposed to the relative abundance of historical photos depicting opium smoking in North America and France, indicates that the infamous Lime house opium smoking scene was little more than fantasy on the part of British writers of the day who were intent on scandalizing their readers while drumming up the threat of the " yellow peril " .

5 – 6 : Prohibition and conflict in China :

Opium prohibition began in 1729 , when Emperor Yongzheng of the Qing Dynasty, disturbed by madak smoking at court and carrying out the government's role of upholding Confucian virtue, officially prohibited the sale of opium, except for a small amount for medicinal purposes. The ban punished sellers and opium den keepers, but not users of the drug.^[13] Opium was banned completely in 1799 and this prohibition continued until 1860 .

Under the Qing Dynasty, China opened itself to foreign trade under the Canton System through the port of Guangzhou (*Canton*),

and traders from the British East India Company began visiting the port by the 1690s. Due to the growing British demand for Indian tea and the Chinese lack of interest in British commodities other than silver, the British became interested in opium as a high-value commodity for which China was not self-sufficient. The British traders had been purchasing small amounts of opium from India for trade since Ralph Fitch first visited in the mid-sixteenth century.^[13] Trade in opium was standardized, with production of balls of raw opium, 1.1 to 1.6 kilograms, 30 % water content, wrapped in poppy leaves and petals, and shipped in chests of 60 - 65 kilograms (one picul) . Chests of opium were sold in auctions in Calcutta with the understanding that the independent purchasers would then smuggle it into China .

After the 1757 Battle of Plassey and 1764 Battle of Buxar, the British East India Company gained the power to act as diwan of Bengal, Bihar, and Orissa . This allowed the company to pursue a monopoly on opium production and export in India, to encourage ryots to cultivate the cash crops of indigo and opium with cash advances, and to prohibit the "hoarding" of rice. This strategy led to the increase of the land tax to 50 % of the value of crops, the starvation of ten million people in the Bengal famine of 1770, and the doubling of East India Company profits by 1777. Beginning in 1773, the British government began enacting oversight of the company's operations, culminating in the establishment of British India in response to the Indian Rebellion of 1857. Bengal opium was highly prized, commanding twice the price of the domestic Chinese product, which was regarded as inferior in quality . The Sassoon family was heavily involved in the opium trade in both China and India

India is also an opium producing nation. In India , Nimach , Mandsour (Madhya Pradesh) , and Chittorgarh (Rajasthan) are major centers for opium production because these areas are suitable for the opium crop i.e. climate, soil. It is the major crop of this region. Nimach has a opium & alkaloid factory which is the organisation of Govt. of India producing alkaloids from opium for pharmaceutical medicine .

Some competition came from the newly independent United States, which began to compete in Guangzhou (*Canton*) selling Turkish opium in the 1820s. Portuguese traders also brought opium from the independent Malwa states of western India, although by 1820, the British were able to restrict this trade by charging "pass duty" on the opium when it was forced to pass through Bombay to reach an entrepot . Despite drastic penalties and continued prohibition of opium until 1860, opium importation rose steadily from 200 chests per year under Yongzheng to 1,000 under Qianlong , 4,000 under Jiaqing, and 30,000 under Daoguang . The illegal sale of opium became one of the world's most valuable single commodity trades and has been called " the most long continued and systematic international crime of modern times "

In response to the ever - growing number of Chinese people becoming addicted to opium, Daoguang of the Qing Dynasty took strong action to halt the import of opium, including the seizure of cargo. In 1838, the Chinese Commissioner Lin Zexu destroyed 20,000 chests of opium in Guangzhou (*Canton*) , Given that a chest of opium was worth nearly \$ 1,000 in 1800 , this was a substantial economic loss. The British, not willing to replace the cheap opium with costly silver, began the First Opium War in 1840, winning Hong Kong and trade concessions in the first of a series of Unequal Treaties .

Following China's defeat in the Second Opium War in 1858, China was forced to legalize opium and began massive domestic production. Importation of opium peaked in 1879 at 6,700 tons, and by 1906, China was producing 85 % of the world's opium, some 35,000 tons, and 27 % of its adult male population was addicted — 13.5 million addicts consuming 39,000 tons of opium yearly . From 1880 to the beginning of the Communist era, the British attempted to discourage the use of opium in China, but this effectively promoted the use of morphine, heroin, and cocaine, further exacerbating the problem of addiction .

Scientific evidence of the pernicious nature of opium use was largely undocumented in the 1890s when Protestant missionaries in China decided to strengthen their opposition to the trade by compiling

data which would demonstrate the harm the drug did. Faced with the problem that many Chinese associated Christianity with opium, partly due to the arrival of early Protestant missionaries on opium clippers, at the 1890 Shanghai Missionary Conference, they agreed to establish the Permanent Committee for the Promotion of Anti - Opium Societies in an attempt to overcome this problem and to arouse public opinion against the opium trade. The members of the committee were John Glasgow Kerr , MD , American Presbyterian Mission in Canton ; B.C. Atterbury , MD , American Presbyterian Mission in Peking; Archdeacon Arthur E. Moule, Church Missionary Society in Shanghai; Henry Whitney, MD, American Board of Commissioners for foreign Missions in Foochow; the Rev. Samuel Clarke, China Inland Mission in Kweiyang; the Rev. Arthur Gostick Shorrocks, English Baptist Mission in Taiyuan; and the Rev. Griffith John, London Mission Society in Hankow . These missionaries were generally outraged over the British government's Royal Commission on Opium visiting India but not China. Accordingly, the missionaries first organized the Anti - Opium League in China among their colleagues in every mission station in China. American missionary Hampden Coit DuBose acted as first president. This organization, which had elected national officers and held an annual national meeting, was instrumental in gathering data from every Western-trained medical doctor in China, which was then published as William Hector Park compiled *Opinions of Over 100 Physicians on the Use of Opium in China* (Shanghai: American Presbyterian Mission Press , 1899) . The vast majority of these medical doctors were missionaries ; the survey also included doctors who were in private practices, particularly in Shanghai and Hong Kong, as well as Chinese who had been trained in medical schools in Western countries. In England, the home director of the China Inland Mission, Benjamin Broomhall, was an active opponent of the Opium trade, writing two books to promote the banning of opium smoking : *The Truth about Opium Smoking* and *The Chinese Opium Smoker*. In 1888, Broomhall formed and became secretary of the Christian Union for the Severance of the British Empire with the Opium Traffic and editor of its periodical, *National Righteousness*. He lobbied the British Parliament to stop the opium trade. He and James Laidlaw Maxwell appealed to the London Missionary Conference of 1888 and the Edinburgh Missionary

Conference of 1910 to condemn the continuation of the trade. When Broomhall was dying, his son Marshall read to him from *The Times* the welcome news that an agreement had been signed ensuring the end of the opium trade within two years .

Official Chinese resistance to opium was renewed on September 20, 1906, with an anti - opium initiative intended to eliminate the drug problem within ten years. The program relied on the turning of public sentiment against opium, with mass meetings at which opium paraphernalia was publicly burned, as well as coercive legal action and the granting of police powers to organizations such as the Fujian Anti - Opium Society. Smokers were required to register for licenses for gradually reducing rations of the drug. Addicts sometimes turned to missionaries for treatment for their addiction, though many associated these foreigners with the drug trade. The program was counted as a substantial success, with a cessation of direct British opium exports to China (but not Hong Kong) and most provinces declared free of opium production. Nonetheless, the success of the program was only temporary , with opium use rapidly increasing during the disorder following the death of Yuan Shikai in 1916 .

Beginning in 1915 , Chinese nationalist groups came to describe the period of military losses and Unequal Treaties as the " Century of National Humiliation ," later defined to end with the conclusion of the Chinese Civil War in 1949 . The Mao Zedong government is generally credited with eradicating both consumption and production of opium during the 1950s using unrestrained repression and social reform. Ten million addicts were forced into compulsory treatment, dealers were executed, and opium-producing regions were planted with new crops. Remaining opium production shifted south of the Chinese border into the Golden Triangle region, at times with the involvement of Western intelligence agencies.^[43] The remnant opium trade primarily served Southeast Asia, but spread to American soldiers during the Vietnam War, with 20% of soldiers regarding themselves as addicted during the peak of the epidemic in 1971. In 2003 , China was estimated to have four million regular drug users and one million registered drug addicts .

2 -7 : Prohibition outside China :

There were no legal restrictions on the importation or use of opium in the United States until the San Francisco, California, Opium Den Ordinance, which banned dens for public smoking of opium in 1875, a measure fueled by anti - Chinese sentiment and the perception that whites were starting to frequent the dens. This was followed by an 1891 California law requiring that narcotics carry warning labels and that their sales be recorded in a registry, amendments to the California Pharmacy and Poison Act in 1907 making it a crime to sell opiates without a prescription, and bans on possession of opium or opium pipes in 1909 .

At the US federal level, the legal actions taken reflected constitutional restrictions under the Enumerated powers doctrine prior to reinterpretation of the Commerce clause, which did not allow the federal government to enact arbitrary prohibitions but did permit arbitrary taxation . Beginning in 1883, opium importation was taxed at \$ 6 to \$ 300 per pound, until the Opium Exclusion Act of 1909 prohibited the importation of opium altogether. In a similar manner the Harrison Narcotics Tax Act of 1914, passed in fulfillment of the International Opium Convention of 1912, nominally placed a tax on the distribution of opiates, but served as a *de facto* prohibition of the drugs. Today, opium is regulated by the Drug Enforcement Administration under the Controlled Substances Act.

Following passage of a regional law in 1895, Australia's Aboriginal Protection and restriction of the sale of opium act 1897 addressed opium addiction among Aborigines, though it soon became a general vehicle for depriving them of basic rights by administrative regulation. Opium sale was prohibited to the general population in 1905, and smoking and possession was prohibited in 1908 .

Hardening of Canadian attitudes toward Chinese opium users and fear of a spread of the drug into the white population led to the effective criminalization of opium for non-medical use in Canada between 1908 and the mid – 1920 s .

In 1909, the International Opium Commission was founded, and by 1914, thirty-four nations had agreed that the production and importation of opium should be diminished. In 1924, sixty-two nations participated in a meeting of the Commission. Subsequently, this role passed to the League of Nations, and all signatory nations agreed to prohibit the import, sale, distribution, export, and use of all narcotic drugs, except for medical and scientific purposes. This role was later taken up by the International Narcotics Control Board of the United Nations under Article 23 of the Single Convention on Narcotic Drugs, and subsequently under the Convention on Psychotropic Substances. Opium-producing nations are required to designate a government agency to take physical possession of licit opium crops as soon as possible after harvest and conduct all wholesaling and exporting through that agency.

2 - 8 : Obsolescence :

Opium has gradually been superseded by a variety of purified, semi-synthetic, and synthetic opioids with progressively stronger effect, and by other general anesthetics. This process began in 1804, when Friedrich Wilhelm Adam Sertürner first isolated morphine from the opium poppy. The process continued until 1817, when Sertürner published the isolation of pure morphine from opium after at least thirteen years of research and a nearly disastrous trial on himself and three boys. The great advantage of purified morphine was that a patient could be treated with a known dose—whereas with raw plant material, as Gabriel Fallopius once lamented, "if soporifics are weak they do not help; if they are strong they are exceedingly dangerous." Morphine was the first pharmaceutical isolated from a natural product, and this success encouraged the isolation of other alkaloids: by 1820, isolations of narcotine, strychnine, veratrine, colchicine, caffeine, and quinine were reported. Morphine sales began in 1827, by Heinrich Emanuel Merck of Darmstadt, and helped him expand his family pharmacy into the massive Merck KGaA pharmaceutical company.

Codeine was isolated in 1832 by Robiquet.

The use of diethyl ether and chloroform for general anesthesia began in 1846 – 1847 , and rapidly displaced the use of opiates and tropane alkaloids from Solanaceae due to their relative safety .

Heroin, the first semi - synthetic opiate, was first synthesized in 1874, but was not pursued until its rediscovery in 1897 by Felix Hoffmann at the Bayer pharmaceutical company in Elberfeld, Germany. From 1898 to 1910 heroin was marketed as a non-addictive morphine substitute and cough medicine for children. By 1902, sales made up 5% of the company's profits, and " heroinism " had attracted media attention . Oxycodone, a thebaine derivative similar to codeine, was introduced by Bayer in 1916 and promoted as a less-addictive analgesic. Preparations of the drug such as Percocet and Oxy Contin remain popular to this day.

A range of synthetic opioids such as methadone (1937), pethidine (1939), fentanyl (late 1950s) , and derivatives thereof have been introduced, and each is preferred for certain specialized applications. Nonetheless, morphine remains the drug of choice for American combat medics, who carry packs of syrettes containing 16 milligrams each for use on severely wounded soldiers . No drug has yet been found that can match the painkilling effect of opioids without also duplicating much of its addictive potential .

3 - Modern production and usage :

3 – 1 : *Papaver somniferum* :

In South American countries, opium poppies (*Papaver somniferum*) are technically illegal, but nonetheless appear in some nurseries as ornamentals. They are popular and attractive garden plants, whose flowers vary greatly in color, size and form. A modest amount of domestic cultivation in private gardens is not usually subject to legal controls. In part, this tolerance reflects variation in addictive potency: a cultivar for opium production, *Papaver somniferum L. elite*, contains 92 % morphine, codeine, and thebaine in its latex alkaloids, whereas the condiment cultivar "Marianne" has only one-fifth this total, with the remaining alkaloids made up mostly of narcotoline and noscapine .



Scored poppy pod showing latex exudates



Raw opium

Seed capsules can be dried and used for decorations, but they also contain morphine, codeine, and other alkaloids. These pods can be boiled in water to produce a bitter tea that induces a long-lasting intoxication (*See Poppy tea*). If allowed to mature, poppy pods can be crushed into "poppy straw" and used to produce lower quantities of morphinans. In poppies subjected to mutagenesis and selection on a mass scale, researchers have been able to use poppy straw to obtain large quantities of oripavine, a precursor to opioids and antagonists such as naltrexone .

Poppy seeds are a common and flavorsome topping for breads and cakes. One gram of poppy seeds contains up to 33 micrograms of morphine and 14 micrograms of codeine, and the Substance Abuse and Mental Health Services Administration formerly mandated that all drug screening laboratories use a standard cutoff of 300 nanograms per milliliter in urine samples. A single poppy seed roll (0.76 grams

of seeds) usually did not produce a positive drug test, but a positive result was observed from eating two rolls. A slice of poppy seed cake containing nearly five grams of seeds per slice produced positive results for 24 hours. Such results are viewed as false positive indications of drug abuse and were the basis of a legal defense . On November 30, 1998, the standard cutoff was increased to 2000 nanograms (two micrograms) per milliliter . During the Communist era in Eastern Europe, poppy stalks sold in bundles by farmers were processed by users with household chemicals to make *kompot* (" Polish heroin ") , and poppy seeds were used to produce *koknar*, an opiate .

3 – 2 : Harvesting and processing :

When grown for opium production, the skin of the ripening pods of these poppies is scored by a sharp blade at a time carefully chosen so that neither rain, wind, nor dew can spoil the exudation of white, milky latex, usually in the afternoon. Incisions are made while the pods are still raw, with no more than a slight yellow tint, and must be shallow to avoid penetrating hollow inner chambers or *loculi* while cutting into the lactiferous vessels. In Indian Subcontinent, Afghanistan, Central Asia and Iran, the special tool used to make the incisions is called a *nushtar* or " nishtar " (from Persian, meaning a lancet) and carries three or four blades three millimeters apart, which are scored upward along the pod. Incisions are made three or four times at intervals of two to three days, and each time the "poppy tears," which dry to a sticky brown resin, are collected the following morning. One acre harvested in this way can produce three to five kilograms of raw opium.^[69] In the Soviet Union, pods were typically scored horizontally, and opium was collected three times, or else one or two collections were followed by isolation of opiates from the ripe capsules. Oil poppies, an alternative strain of *P. somniferum*, were also used for production of opiates from their capsules and stems .

Raw opium may be sold to a merchant or broker on the black market, but it usually does not travel far from the field before it is refined into **morphine base**, because pungent, jelly - like raw opium is bulkier and harder to smuggle . Crude laboratories in the field are

capable of refining opium into morphine base by a simple acid - base extraction. A sticky, brown paste, morphine base is pressed into bricks and sun-dried, and can either be smoked, prepared into other forms or processed into heroin .

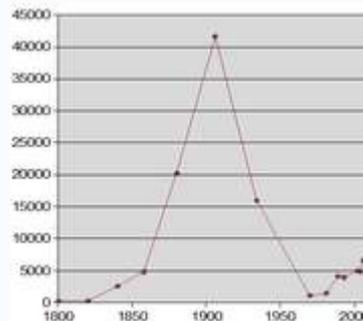
Other methods of preparation (besides smoking) , include processing into regular opium tincture (*tinctura opii*), laudanum, paregoric (*tinctura opii camphorata*), herbal wine (eg *vinum opii*), opium powder (*pulvis opii*), opium sirup (*sirupus opii*) and opium extract (*extractum opii*)^[71]. *Vinum opii* is made by combining sugar, white wine, cinnamon, and cloves. Opium syrup is made by combining 997.5 part sugar syrup with 2.5 parts opium extract. Opium extract (*extractum opii*) finally can be made by macerating raw opium with water. To make opium extract, 20 parts water are combined with 1 part raw opium which has been boiled for 5 minutes (the latter to ease mixing) .

Heroin is widely preferred because of increased potency. One study in postaddicts found heroin to be approximately 2.2 times more potent than morphine by weight with a similar duration; at these relative quantities, they could distinguish the drugs subjectively but had no preference . Heroin was also found to be twice as potent as morphine in surgical anesthesia . Morphine is converted into heroin by a simple chemical reaction with acetic anhydride, followed by a varying degree of purification . Especially in Mexican production, opium may be converted directly to "black tar heroin" in a simplified procedure. This form predominates in the U.S. west of the Mississippi. Relative to other preparations of heroin, it has been associated with a dramatically decreased rate of HIV transmission among intravenous drug users (4 % in Los Angeles vs. 40 % in New York) due to technical requirements of injection, although it is also associated with greater risk of venous sclerosis and necrotizing fasciitis .

3 – 3 : Illegal production :

Opium production has fallen greatly since 1906 , when 41,000 tons were produced, but because 39,000 tons of that year's opium were consumed in China, overall usage in the rest of the world was much lower. In 1980, 2,000 tons of opium supplied all legal and illegal uses

. Recently, opium production has increased considerably, surpassing 5,000 tons in 2002. In 2002, the price for one kilogram of opium was \$ 300 for the farmer, \$ 800 for purchasers in Afghanistan, and \$ 16,000 on the streets of Europe before conversion into heroin .



Approximate global opium production for recreational purposes

Following documented trends of increasing availability mirroring increased American military and geo - political regional involvement, Afghanistan is currently the primary producer of the drug. After regularly producing 70 % of the world's opium, Afghanistan decreased production to 74 tons per year under a ban by the Taliban in 2000, a move which cut production by 94 per cent. A year later, after American and British troops invaded Afghanistan, removed the Taliban and installed the interim government, the land under cultivation leapt back to 285 square miles, with Afghanistan supplanting Burma to become the world's largest opium producer once more. Opium production in that country has increased rapidly since, reaching an all - time high in 2006. According to DEA statistics, Afghanistan's production of oven-dried opium increased to 1,278 tons in 2002, more than doubled by 2003, and nearly doubled again during 2004. In late 2004, the U.S. government estimated that 206,000 hectares were under poppy cultivation, 4.5% of the country's total cropland, and produced 4,200 metric tons of opium, 76 % of the world's supply, yielding 60 % of Afghanistan's gross domestic product . In 2006, the UN Office on Drugs and Crime estimated production to have risen 59 % to 407,000 acres (1,650 km²) in cultivation , yielding 6,100 tons of opium, 82 % of the world's supply . The value of the resulting heroin was estimated at \$3.5 billion, of which Afghan farmers were estimated to have received \$ 700 million in revenue (of which the Taliban have been estimated to have collected any where

from tens of millions to \$ 140 million in taxes) . For farmers, the crop can be up to ten times more profitable than wheat. The price of opium is around \$ 138 per kilo (INR 7,000 per kg) .

An increasingly large fraction of opium is processed into morphine base and heroin in drug labs in Afghanistan. Despite an international set of chemical controls designed to restrict availability of acetic anhydride, it enters the country, perhaps through its Central Asian neighbors which do not participate. A counternarcotics law passed in December 2005 requires Afghanistan to develop registries or regulations for tracking, storing, and owning acetic anhydride .

Besides Afghanistan, smaller quantities of opium are produced in Pakistan, the Golden Triangle region of Southeast Asia (particularly Myanmar) , Colombia and Mexico.

3 - 4 : Legal production :

Legal opium production is allowed under the United Nations Single Convention on Narcotic Drugs and other international drug treaties, subject to strict supervision by the law enforcement agencies of individual countries. The leading legal production method is the Gregory process, whereby the entire poppy, excluding roots and leaves, is mashed and stewed in dilute acid solutions. The alkaloids are then recovered via acid-base extraction and purified. This process was developed in the UK during World War II, when wartime shortages of many essential drugs encouraged innovation in pharmaceutical processing .

Legal opium production in India is much more traditional. As of 2008, opium was collected by farmers who were licensed to grow 0.1 hectare of opium poppies (0.24 acre) , who to maintain their licenses needed to sell 56 kilograms of unadulterated raw opium paste. The price of opium paste is fixed by the government according to the quality and quantity tendered. The average is around 1500 rupees (\$ 29 US) per kilogram . Some additional money is made by drying the poppy heads and collecting poppy seeds, and a small fraction of opium beyond the quota may be consumed locally or diverted to the black market. The opium paste is dried and processed in two

government opium and alkaloid factories before it is packed into cases of 60 kilograms for export. Purification of chemical constituents is done in India for domestic production, but typically done abroad by foreign importers .

Legal opium importation from India and Turkey is conducted by Mallinckrodt, Noramco, Abbott Laboratories, and Purdue Pharma in the United States, and legal opium production is conducted by GlaxoSmithKline, Johnson and Johnson, Johnson Matthey, and Mayne in Tasmania, Australia; Sanofi Aventis in France; Shionogi Pharmaceutical in Japan; and MacFarlan Smith in the United Kingdom . The United Nations UN treaty requires that every country submit annual reports to the International Narcotics Control Board, stating that year's actual consumption of many classes of controlled drugs as well as opioids and projecting required quantities for the next year. This is to allow trends in consumption to be monitored and production quotas allotted.

A recent proposal from the European Senlis Council hopes to solve the problems caused by the massive quantity of opium produced illegally in Afghanistan, most of which is converted to heroin and smuggled for sale in Europe and the USA. This proposal is to license Afghan farmers to produce opium for the world pharmaceutical market, and thereby solve another problem, that of chronic underuse of potent analgesics where required within developing nations. Part of the proposal is to overcome the " 80 - 20 rule " that requires the U.S. to purchase 80% of its legal opium from India and Turkey to include Afghanistan, by establishing a second - tier system of supply control that complements the current INCB regulated supply and demand system by providing poppy - based medicines to countries who cannot meet their demand under the current regulations. Senlis arranged a conference in Kabul that brought drug policy experts from around the world to meet with Afghan government officials to discuss internal security, corruption issues, and legal issues within Afghanistan.^[86] In June 2007, the Council launched a "Poppy for Medicines" project that provides a technical blueprint for the implementation of an integrated control system within Afghan village-based poppy for medicine projects: the idea promotes the economic diversification by redirecting

proceeds from the legal cultivation of poppy and production of poppy-based medicines . However, there has been criticism of the Senlis report findings by Macfarlan Smith, who argue that though they produce morphine in Europe, they were never asked to contribute to the report .

3 - 5 : Cultivation in the UK :

In late 2006 , the British government permitted the pharmaceutical company Macfarlan Smith (a Johnson Matthey company) to cultivate opium poppies in England for medicinal reasons, after Macfarlan Smith's primary source, India, decided to increase the price of export opium latex. This move is well received by British farmers, with a major opium poppy field based in Didcot, England. The British government has contradicted the Home Office's suggestion that opium cultivation can be legalized in Afghanistan for exports to the United Kingdom, helping lower poverty and internal fighting whilst helping NHS to meet the high demand for morphine and heroin. Opium poppy cultivation in the United Kingdom does not need a licence; however, a licence is required for those wishing to extract opium for medicinal products .

3 – 6 : Consumption :



An Akha man smokes a pipe containing opium mixed with tobacco.

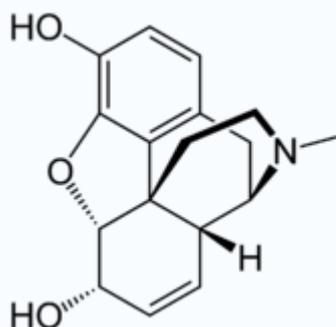
In the industrialized world, the USA is the world's biggest consumer of prescription opioids, with Italy one of the lowest.^[90] Most opium imported into the United States is broken down into its alkaloid constituents, and whether legal or illegal, most current drug use occurs with processed derivatives such as heroin rather than with pure and untouched opium.

Intravenous injection of opiates is most used: by comparison with injection, "dragon chasing" (heating of heroin with barbitol on a piece of foil) , and madak and " ack ack " (smoking of cigarettes containing tobacco mixed with heroin powder) are only 40 % and 20 % efficient, respectively . One study of British heroin addicts found a 12-fold excess mortality ratio (1.8 % of the group dying per year).^[92] Most heroin deaths result not from overdose *per se* , but combination with other depressant drugs such as alcohol or benzodiazepines .

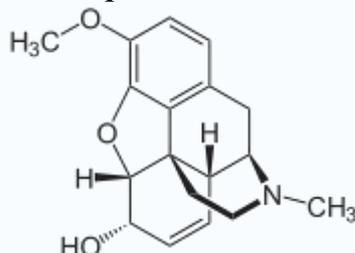
The smoking of opium does not involve the pyrolysis of the material as might be imagined. Rather, the prepared opium is indirectly heated to temperatures at which the active alkaloids, chiefly morphine, are vaporized. In the past, smokers would utilize a specially designed opium pipe which had a removable knob-like pipe - bowl of fired earthenware attached by a metal fitting to a long, cylindrical stem . A small "pill" of opium about the size of a pea would be placed on the pipe - bowl, which was then heated by holding it over an opium lamp, a special oil lamp with a distinct funnel - like chimney to channel heat into a small area. The smoker would lie on his or her side in order to guide the pipe-bowl and the tiny pill of opium over the stream of heat rising from the chimney of the oil lamp and inhale the vaporized opium fumes as needed. Several pills of opium were smoked at a single session depending on the smoker's tolerance to the drug. The effects could last up to twelve hours. Opium in its rawest form contains half the potency of synthetically compared drugs; such as Oxy Contin, morphine patches or trentanol .

In Eastern culture, opium is more commonly used in the form of paregoric to treat diarrhea. This is a weaker solution than laudanum, an alcoholic tincture which was prevalently used as a pain medication and sleeping aid. Tincture of opium has been prescribed for, among other things, severe diarrhea . Taken thirty minutes prior to meals, it significantly slows intestinal motility, giving the intestines greater time to absorb fluid in the stool .

4 - Chemical and physiological properties :



Morphine is the primary biologically active chemical constituent of opium.



Codeine is another biologically active chemical constituent of opium.

Opium contains two main groups of alkaloids . Phenanthrenes include morphine , codeine , and thebaine are the main narcotic constituents. Iso quinolines such as papaverine have no significant central nervous system effects and are not regulated under the Controlled Substances Act. Morphine is by far the most prevalent and important alkaloid in opium, consisting of 10 % - 16 % of the total, and is responsible for most of its harmful effects such as lung edema, respiratory difficulties, coma, or cardiac or respiratory collapse, with a normal lethal dose of 120 to 250 milligrams^[96]—the amount found in approximately two grams of opium.^[69] Morphine binds to and activates μ -opioid receptors in the brain, spinal cord, stomach and intestine. Regular use leads to physical tolerance and dependence. Chronic opium addicts in 1906 China or modern - day Iran consume an average of eight grams daily .

Both analgesia and drug addiction are functions of the mu opioid receptor, the class of opioid receptor first identified as responsive to

morphine. Tolerance is associated with the superactivation of the receptor, which may be affected by the degree of endocytosis caused by the opioid administered, and leads to a superactivation of cyclic AMP signaling . Long-term use of morphine in palliative care and management of chronic pain cannot be managed without the development of drug tolerance or physical dependence. However, it is important to note that " physical dependence " is the expected clinical outcome of using opioids in pain management; it should not be confused with addiction or other forms of " dependence " that are associated with the disease of addiction. Just as a diabetic is physically dependent on insulin to treat the disease of diabetes, so a chronic pain patient will become physically dependent on opioids such as morphine to treat the disease of chronic pain or to palliate end - of - life pain. With respect to drug tolerance, the distinction between chronic pain patients and drug abusers is that the former will ultimately find that at an appropriate dose of medication, tolerance develops to the euphoric and other side-effects of opioid use while pain is successfully controlled for years at the same dose. A drug abuser or addict posing as a pain patient will quickly develop tolerance to the euphoric side-effects of the opioids he is prescribed for pain. As a result, such patients will demand an increase in their dose at every opportunity (because as explained previously, tolerance to euphoria develops much more quickly than tolerance to analgesia) .

Many techniques of drug treatment exist, including pharmacologically based treatments with naltrexone, methadone, or ibogaine . However, it should be emphasized that these treatments are for those suffering from true opioid addiction, and not from physical dependence resulting from the appropriate use of opioids for chronic pain. In the event that a patient with chronic pain no longer suffers from the same degree of pain, it is not difficult for the patient and treating physician to gradually taper down the prescribed opioids until the patient has entirely discontinued opioids use. Of course this is only possible if the patient's underlying pain has been mitigated, successfully treated, or otherwise been resolved.

5 - Slang terms (drug - related) :

There are a number of slang terms used for opium as a drug, often by peddlers and users in doing business . Several are especially prevalent:

- Dope
- Big O
- Tar

6 - Cultural references :

There is a longstanding literary history by and about opium users. Thomas de Quincey's 1822 *Confessions of an English Opium-Eater* is one of the first and most famous literary accounts of opium addiction written from the point of view of an addict and details both the pleasures and the dangers of the drug. De Quincey writes about the great English Romantic poet Samuel Taylor Coleridge (1772 - 1834) , whose poem "Kubla Khan" is also widely considered to be a poem of the opium experience. Coleridge began using opium in 1791 after developing jaundice and rheumatic fever and became a full addict after a severe attack of the disease in 1801, requiring 80-100 drops of laudanum daily.^[100] George Crabbe is another early writer who wrote about opium. " The Lotos - Eaters ", an 1832 poem by Alfred Lord Tennyson, reflects the generally favorable British attitude toward the drug. In *The Count of Monte Cristo* (1844) by Alexandre Dumas, père, the Count is assuaged by an edible form of opium, and his experience with it is depicted vividly.

Edgar Allan Poe presents opium in a more disturbing context in his 1838 short story " Ligeia " , in which the narrator, deeply distraught for the loss of his beloved, takes solace in opium until he "had become a bounden slave in the trammels of opium," unable to distinguish fantasy from reality after taking immoderate doses of opium. In music, Hector Berlioz' 1830 *Symphony Fantastique* tells the tale of an artist who has poisoned himself with opium while in the depths of despair for a hopeless love. Each of the symphony's five movements takes place at a different setting and with increasingly audible effects from the drug. For example, in the fourth movement,

"Marche au Supplice," the artist dreams that he is walking to his own execution . In the fifth movement , " Songe d'une Nuit du Sabbat " . he dreams that he is at a witch's orgy , where he witnesses his beloved dancing wildly along to the demented Dies Irae.

Towards the end of the nineteenth century, references to opium and opium addiction in the context of crime and the foreign underclass abound within English literature, such as in Wilkie Collins' *The Moonstone* (1868), where it is used to attempt to uncover the jewel thief. Opium features in the opening paragraphs of Charles Dickens's 1870 serial *The Mystery of Edwin Drood* and in Arthur Conan Doyle's 1891 Sherlock Holmes short story "The Man with the Twisted Lip." In Oscar Wilde's 1890 *The Picture of Dorian Gray*, the protagonist visits an opium den "for forgetfulness," unable to bear the guilt and shame of committing murder. Opium likewise underwent a transformation in Chinese literature, becoming associated with indolence and vice by the early twentieth century . Perhaps the best-known literary reference to opium is Karl Marx's metaphor in his "Contribution to the Critique of Hegel's 'Philosophy of Right'," where he refers to religion as "the opium of the people." (This phrase is more commonly quoted as "the opiate of the masses ") .

In the twentieth century, as the use of opium was eclipsed by morphine and heroin, its role in literature became more limited, and often focused on issues related to its prohibition. In *The Good Earth* by Pearl S. Buck, Wang Lung, the protagonist, gets his troublesome uncle and aunt addicted to opium in order to keep them out of his hair. William S. Burroughs autobiographically describes the use of opium beside that of its derivatives. His associate Jack Black's memoir *You Can't Win* chronicles one man's experience both as an onlooker in the opium dens of San Francisco, and later as a "hop fiend" himself. The book and subsequent movie *The Wonderful Wizard of Oz* may allude to opium at one point in the story, when Dorothy and her friends are drawn into a field of poppies, in which they fall asleep .

1 - Whole Opium Preparations	
	Compote / Kompot / Polish Heroin • Diascordium • B & O Suppettes • Dover's powder • Laudanum • Mithridate • Opium • Paregoric • Concentrate of Poppy Straw (CPS) • Poppy tea • Smoking Opium • Theriac
2 - Natural Opiates	
Opium Alkaloids	Codeine • Morphine • Oripavine • Pseudo morphine • Thebaine
Alkaloid Salts Mixtures	Pantopon • Papaveretum (Omnopon) • Tetrapon
3 - Semi Synthetics	
Morphine Family	14 - Hydroxy morphine • 14 β - Hydroxy morphine • 14 β - Hydroxy morphone • 2,4 - Dinitro phenyl morphine • 6 - Methyl dihydro morphine • 6 - ethylene dihydro desoxy morphine • 6 - Acetyl dihydro morphine / 6 - Mono acetyl dihydro morphine • Acetyl dihydro morphine • Azido morphine • Chlornaltrexamine • Chloro morphide • Dihydro desoxy morphine (Desomorphine) • Dihydro morphine •

	<ul style="list-style-type: none"> Ethyl dihydro morphine • Hydro morphinol • Methyl desorphine • N - Phenethylnormorphine • Pseudomorphine
3 , 6 Diesters of Morphine	<ul style="list-style-type: none"> Diacetyl dihydro morphine (Dihydroheroin) • Dibenzoyl morphine • Dibutanoyl morphine • Dipropanoyl morphine • Disalicyl oylmorphine • Heroin (Diacetyl morphine) • Heroin - 7 , 8 - Oxide • Nico morphine
Codeine - Dionine Family	<ul style="list-style-type: none"> 14 - Hydroxy dihydro codeine • Acetyl codeine • Benzyl morphine • Codeine methyl bromide • Deso codeine • Methyl dihydro morphine (Dihydro hetero codeine) • Ethyl morphine (Dionine) • Hetero codeine • Iso codeine • Morpholinyl ethyl morphine (Pholcodine) • Myrophine • Nalodeine • Transiso codeine
Morphinones	<ul style="list-style-type: none"> 14 - Ethoxy metopon • 14 - Methoxy metopon • 14 β - Hydroxy morphone • 14 - O - Methyloxy morphone • 14 - phenyl propoxy-5-methyl-hydro morphone • 14 - Phenyl propoxy metopon • 7 - Spiroindanyloxy morphone • 8 ,14 - Dihydroxy dihydro morphinone • Acetyl morphone • Ethyl dihydro morphinone •

	<ul style="list-style-type: none"> Hydro morphinone • Hydro morphone • Hydroxy codeine • Methyl dihydro morphinone • Metopon • Morphinol • Morphinone • N - Phenethyl - 14 - ethoxy metopon • Oxy morphol • Oxy morphone • Penta morphone • Semorphone
Codeinones	<ul style="list-style-type: none"> 1- carboxy-14 - hydroxydihydro codeinone • 1- carbethoxy-14-hdroxy dihydro codeinone • Thebacon (Acetyl dihydro codeinone / Dihydro codeinone enol acetate) • Codeinone • Codorphone • Codoxime • Hydro codone • Mono dihydro codeineone • Oxy codone
Dihydrocodeine Series	<ul style="list-style-type: none"> 14 - hydroxydihydro codeine • Acetyldihydrocodeine • Dihydro codeine • Dihydro desoxy codeine / Deso codeine • Dihydro iso codeine • Nico codeine • Nico dicodeine
Nitrogen Morphine Derivatives	<ul style="list-style-type: none"> Codeine - N - Oxide • Heroin - N - Oxide • Hydro morphone – N - Oxide • Morphine – N - Oxide
Hydrazones	<ul style="list-style-type: none"> Hydro morphazone • Morphazone • Oxy morphazone
Others	<ul style="list-style-type: none"> α – chloro codide • Pholcodine

Active Opiate Metabolites
Codeine - N - Oxide (Geno codeine) • Hydro morphone – N - Oxide • Heroin - 7 , 8 - Oxide • Morphine - 3 - glucuronide • Morphine - 6 - glucuronide • Mono acetyl morphine • Morphine - N - Oxide (Genomorphine) • Naltrexol • Nor codeine • Nor morphine
Morphinan Series
4 – chloro phenyl pyrido morphinan • Cyclorphan • Dextro - 3 – hydroxy - N – allyl morphinan • Dimemorfan • Levargorphan • Levallorphan • Levo rphanol • Levo rphan • Levo phenacyl morphan • Levo methorphan • Norlevo rphanol • N – Methyl morphinan • Oxilo rphan • Pheno morphan • Metho rphan / Race methorphan • Morphanol / Racemorphanol • Stephodeline • Xorphanol
Others
1 - Nitro aknadinine • 14 - episinomenine • 5 , 6 - Dihydro norsalutaridine • 6 - Ketonalbuphine • Aknadinine • Buto rphanol • Cephakicine •

<ul style="list-style-type: none"> Cephasamine • Cyprodime • Drotebanol • Fenfangjine G • Nalbuphine • Sinococuline • Sinomenine (Cocculine) • Tannagine
Pethidines (Meperidines)
<ul style="list-style-type: none"> Allylnorp ethidine • Anileridine • Benz ethidine • Carperidine • Difenoxin • Diphenoxylate • Etox eridine (Carbetidine) • Fur ethidine • Hydroxy pethidine (Bemidone) • Hydroxy methoxy pethidine • Morpheridine • Oxpheneridine (Carbam ethidine) • Meperidine - N - Oxide • Pethidine (Meperidine) • Pethidine Intermediate A • Pethidine Intermediate B (Norp ethidine) • Pethidine Intermediate C (Pethidinic Acid) • Pheneridine • Pheno peridine • Piminodine • Properidine (Ipro pethidine) • Sameridine
Prodines
<ul style="list-style-type: none"> Allyl prodine • Iso promedol • Me prodine (α - meprodine / β - meprodine) • MPPP (Desmethyl prodine) • Prodine (α - prodine / β – prodine) • Prosidol •

Tri meperidine (Promedol)
Ketobemidones
Acetoxy keto bemidone • Droxy propine • Keto bemidone • Methyl keto bemidone • Propyl keto bemidone
Others
Alvimopan • Loperamide • Picenadol
Amidones
Dextro iso methadone • Dipipanone • Hexalgon (Nor pipanone) • Iso methadone • Levo iso methadone • Levo methadone • Methadone • Methadone intermediate • Nor methadone • Nor pipanone • Phenadoxone (Heptazone) • Pipidone
Methadols
Dimepheptanol (Racemethadol) • Lev acetyl methadol • Levo methadyl acetate (Acetyl methadol) • Nor acetyl methadol
Moramides
Dextro moramide • Levo moramide • Moramide intermediate • Racemoramide
Thiambutenes
Diethyl thiambutene • Dimethyl thiambutene •

Ethyl methyl thiambutene • Piperidyl thiambutene • Pyrrolidinyl thiambutene • Thiambutene • Tipepidine
Phenalkoxams
Dextro propoxy phene (Propoxyphene) • Dimenoxadol • Dioxaphetyl Butyrate • Levo propoxy phene • Nor propoxy phene
Ampromides
Diampromide • Phenampromide • Propiram
Others
Iso aminile • Lefetamine

Opium poppy



Opium Poppy

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1 - Introduction :

The **Opium Poppy**, *Papaver somniferum*, is the type of poppy from which opium and many refined opiates, including morphine, thebaine, codeine, papaverine, and noscapine, are extracted. The binomial name means, loosely, the "sleep - bringing poppy", referring to its narcotic properties. The seeds are important food items,

and contain healthy oils used worldwide in the culinary arts . The plant itself is valuable for ornamental purposes, and has been known as the "common garden poppy". It is widely grown in ornamental gardens throughout Europe, North America, South America, and Asia.

Scientific classification

Kingdom : Plantae
Division : Magnoliophyta
Class : Magnoliopsida
Order : Ranunculales
Family : Papaveraceae
Genus : *Papaver*
Species : *P. somniferum*

2 - Varieties :

Papaver somniferum is a species of plant with many sub-groups or varieties. Colors of the flower vary widely, as do other physical characteristics such as number and shape of petals, number of pods, production of morphine, etc.

Papaver somniferum Paeoniflorum Group (sometimes called *Papaver paeoniflorum*) is a sub-type of opium poppy whose flowers are highly double, and are grown in many colors. *Papaver somniferum* Laciniatum Group (sometimes called *Papaver laciniatum*) is a sub-type of opium poppy whose flowers are highly double and deeply lobed, to the point of looking like a ruffly pompon .

A few of the varieties, notably the Norman and Przemko varieties, have low morphine content (less than one percent), but have much higher concentrations of other alkaloids. Most varieties, however, including those most popular for ornamental use or seed production, have a higher morphine content, with the average content being 10 % .

3 – Legality :

Opium poppy cultivation in the United Kingdom does not need a license, however, a license is required for those wishing to extract opium for medicinal products .

In the United States, opium is listed as a Schedule II controlled substance by the Drug Enforcement Administration . In addition, "Opium poppy and poppy straw" are also prohibited . However, this is not typically enforced for poppies grown or sold for ornamental or food purposes.^[1] There is a common misconception that there is a clear distinction between poppies useful for opium extraction and ornamental or food poppies. It is not difficult to manufacture opium tea with a high morphine content from poppies readily available at flower shops .

The seeds themselves contain very low levels of opiates.^[1] However, the television show *MythBusters* demonstrated that one could test positive for narcotics after consuming four poppy seed bagels. The show *Brainiac: Science Abuse* had subjects who tested positive with only two poppy seed bagels. As a result, the U.S. standard for urinalysis raised the threshold for a positive result by a considerable amount . However, many labs have not implemented the increased detection threshold and many believe that the new threshold is still too low. In the UAE , where the drug law is especially stern , at least one man was reported to have been imprisoned for possessing poppy seeds obtained from a bread roll .

4 - Poppies as medicine :



Commercial poppy cultivation in France



Capsule of *Papaver somniferum* showing latex (opium)

Tasmania , Turkey and India are the major producers of poppy for medicinal purposes and poppy - based drugs , such as morphine or codeine . The USA has a policy of sourcing 80 % of its narcotic raw materials from the traditional producers, India and Turkey .

A recent initiative to extend opium production for medicinal purposes called Poppy for Medicine was launched by The Senlis Council which proposes that Afghanistan could produce medicinal opium under a scheme similar to that operating in Turkey and India.^[10] The Council proposes licensing poppy production in Afghanistan, within an integrated control system supported by the Afghan government and its international allies, to promote economic growth in the country, create vital drugs and combat poverty and the diversion of illegal opium to drug traffickers and terrorist elements. Interestingly, Senlis is on record advocating reintroduction of poppy into areas of Afghanistan, specifically Kunduz, which has been poppy free for some time.

The Senlis proposal is based in part on the assertion that there is an acute global shortage of opium poppy - based medicines some of which (morphine) are on the World Health Organisation's list of essential drugs as they are the most effective way of relieving severe pain. This assertion is contradicted by the International Narcotics Control Board (INCB) the "independent and quasi-judicial control organ monitoring the implementation of the United Nations drug

control conventions". INCB reports that the supply of opiates is greatly in excess of demand .

The British government has given the go-ahead to the pharmaceutical company Macfarlan Smith (a Johnson Matthey company) to cultivate opium poppies in England for medicinal reasons. This move is well - received by British farmers, with a major opium poppy field based in Didcot, England .

5 - Use as food :



Polish makowiec cake . The dark filling is made mainly from poppy seeds.

The seeds of the poppy are widely used in and on many food items such as bagels , bialys , muffins and cakes . The seeds can be pressed to form poppy seed oil , which can be used in cooking , or as a carrier for oil - based paints . The primary flavor compound is : 2 - pentyl furan .

The seeds themselves contain very low levels of opiates .

Poppy seed production in tones (2007)		
Source: FAO STAT		
Country	Tones	%
Czech Republic	33,101	54.32
Turkey	8,981	14.74
France	5,000	8.2
Hungary	3,300	5.42
Germany	2,800	4.59

Israel	2,200	3.61
Austria	1,964	3.22
Romania	1,600	2.63
Serbia	700	1.15
Netherlands	500	0.82
Slovakia	482	0.79
Republic of Macedonia	161	0.26
Spain	100	0.16
Croatia	50	0.08
World total	60,939	100
The sum does not equal 100 % due to rounding		

6 - Ornamental cultivation :



A red opium poppy flower used for ornamental purposes

Many seed companies and nurseries grow and sell live plants and seeds in many highly beautiful variations. They are also sold dried for dried flower arrangements. This is technically illegal in the United States, but this is not generally enforced unless the plants are being sold for drug production .

Many countries grow the plants; some of which rely heavily on the commercial production of the drug as a major source of income. As an additional source of profit, the same seeds are sold in the culinary trade shortly thereafter, making cultivation of the plant a significant source of income . This international trade in seeds of *Papaver somniferum* was addressed by a UN resolution " to fight the international trade in illicit opium poppy seeds " on July 28 , 1998.

7 - History :

Use of the opium poppy predates written history. Images of opium poppies have been found in ancient Sumerian artifacts (*ca.* 4000 BC). The opium poppy was also known to the ancient Greeks, from whom it gained its modern name of *opium*. Remains have been discovered at sites such as Kalapodi and Kastanas .

Opium was used for treating asthma, stomach illnesses, and bad eye sight. The Opium Wars between China and the British Empire took place in the late 1830s when the Chinese attempted to stop the sale of opium by Britain , in China .

Many modern writers, particularly in the nineteenth century, have written on the opium poppy and its effects, notably L. Frank Baum in *The Wonderful Wizard of Oz* and Thomas de Quincey in *Confessions of an English Opium Eater*

The French Romantic composer Hector Berlioz used an opium hallucination for the program of his *Symphonie Fantastique*. In this work, a young artist overdoses on opium and experiences a series of visions of his unrequited love .

Tea



Green Tea leaves in a Chinese gaiwan



A tea bush



Plantation workers picking tea in Tanzania.

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Tea plant (*Camellia sinensis*) from *Köhler's Medicinal Plants*.



Loose dried tea leaves

1- Introduction :

Tea refers to the agricultural products of the leaves, leaf buds, and internodes of the *Camellia sinensis* plant, prepared and cured by various methods. "Tea" also refers to the aromatic beverage prepared from the cured leaves by combination with hot or boiling water,^[1] and is the common name for the *Camellia sinensis* plant itself.

After water, tea is the most widely - consumed beverage in the world.^[2] It has a cooling, slightly bitter, astringent flavour which many enjoy .

The four types of tea most commonly found on the market are black tea, oolong tea, green tea and white tea,^[4] all of which can be made from the same bushes, processed differently, and in the case of fine white tea grown differently. Pu - erh tea , a double - fermented black tea, is also often classified as amongst the most popular types of tea .

The term "herbal tea" usually refers to an infusion or tisane of leaves, flowers, fruit, herbs or other plant material that contains no *Camellia sinensis*.^[6] The term "red tea" either refers to an infusion made from the South African rooibos plant, also containing no *Camellia sinensis*, or, in Chinese, Korean, Japanese and other East Asian languages, refers to black tea.

2 - Traditional Chinese Tea Cultivation and Technologies :

Camellia sinensis is an evergreen plant that grows mainly in tropical and sub-tropical climates. Nevertheless, some varieties can also tolerate marine climates and are cultivated as far north as Cornwall on the UK mainland and Seattle in the United States.

In addition to a zone 8 climate or warmer, tea plants require at least 50 inches of rainfall a year and prefer acidic soils . Traditional Chinese Tea Cultivation and Studies believes that high-quality tea plants are cultivated at elevations of up to 1500 meters (5,000 ft) : at these heights , the plants grow more slowly and acquire a better flavour .

Only the top 1 - 2 inches of the mature plant are picked. These buds and leaves are called *flushes* . A plant will grow a new flush every seven to ten days during the growing season.

A tea plant will grow into a tree if left undisturbed, but cultivated plants are pruned to waist height for ease of plucking .

Two principal varieties are used: the small - leaved China plant (*C. sinensis sinensis*) , used for most Chinese, Formosan and Japanese teas (but not Pu - erh) ; and the large-leaved Assam plant (*C. sinensis assamica*) , used in most Indian and other teas (but not Darjeeling). Within these botanical varieties, there are many strains and modern Indian clonal varieties. Leaf size is the chief criterion for the classification of tea plants : tea is classified into (1) Assam type, characterized by the largest leaves ; (2) China type, characterized by the smallest leaves ; and (3) Cambod, characterized by leaves of intermediate size .

3 - Processing and classification :

A tea's type is determined by the processing which it undergoes. Leaves of *Camellia sinensis* soon begin to wilt and oxidize if not dried quickly after picking. The leaves turn progressively darker as their chlorophyll breaks down and tannins are released. This process, *enzymatic oxidation*, is called *fermentation* in the tea industry, although it is not a true fermentation: it is not caused by microorganisms, and is not an anaerobic process. The next step in processing is to stop the oxidation process at a predetermined stage by heating, which deactivates the enzymes responsible. With black tea this is done simultaneously with drying .

Without careful moisture and temperature control during manufacture and packaging, the tea will grow fungi. The fungus causes real fermentation that will contaminate the tea with toxic and sometimes carcinogenic substances, as well as off-flavors, rendering the tea unfit for consumption .

Tea is traditionally classified based on the techniques with which it is produced and processed :

- White tea : Unwilted and unoxidized
- Yellow tea : Unwilted and unoxidized but allowed to yellow
- Green tea : Wilted and unoxidized
- Oolong : Wilted , bruised , and partially oxidized
- Black tea : Wilted , sometimes crushed , and fully oxidized
- Post - fermented tea : Green Tea that has been allowed to ferment / compost

4 - Blending and additives :

Almost all teas in bags and most other teas sold in the West are blends. Blending may occur in the tea-planting area (as in the case of Assam), or teas from many areas may be blended. The aim is to obtain better taste, higher price, or both, as a more expensive, better-tasting tea may cover the inferior taste of cheaper varieties.

Some teas are not pure varieties, but have been enhanced through additives or special processing. Tea is highly receptive to inclusion of various aromas; this may cause problems in processing, transportation and storage, but also allows for the design of an almost endless range of scented and flavored variants, such as vanilla, caramel, and many others.

5 – Content :

Tea contains catechins, a type of antioxidant. In a freshly-picked tea leaf, catechins can compose up to 30 % of the dry weight. Catechins are highest in concentration in white and green teas, while black tea has substantially fewer due to its oxidative preparation.^{[14][15]} Research by the U.S. Department of Agriculture has suggested that levels of antioxidants in green and black tea do not differ greatly, with green tea having an Oxygen Radical Absorbance Capacity (ORAC) of 1253 and black tea an ORAC of 1128 (measured in $\mu\text{mol TE} / 100\text{g}$) . Tea also contains theanine and the stimulant caffeine at about 3 % of its dry weight, translating to between 30 mg and 90 mg per 8 oz (250 ml) cup depending on type , brand and brewing method , Tea also contains small amounts of theobromine and theophylline , as

well as fluoride ' with certain types of brick tea made from old leaves and stems having the highest levels .

Dry tea has more caffeine by weight than coffee; nevertheless, more dried coffee is used than dry tea in preparing the beverage,^[21] which mean that a cup of brewed tea contains significantly less caffeine than a cup of coffee of the same size.

Tea has no carbohydrates , fat , or protein .

6 - Origin and history :

According to Mondal (2007 , p . 519) : " *Camellia sinensis* originated in southeast Asia , specifically around the intersection of latitude 29 °N and longitude 98°E , the point of confluence of the lands of northeast India, north Burma, southwest China and Tibet. The plant was introduced to more than 52 countries , from this 'centre of origin' " .

Based on morphological differences between the Assamese and Chinese varieties, botanists have long asserted a dual botanical origin for tea ; however, statistical cluster analysis, the same chromosome number ($2n = 30$) , easy hybridization, and various types of intermediate hybrids and spontaneous polyploids all appear to demonstrate a single place of origin for *Camellia sinensis* — the area including the northern part of Burma, and Yunnan and Sichuan provinces of China . According to this theory, tea plants in southeast Asia may have been the products of the 19th Century and 20th Century hybridizing experiments .

Yunnan Province has also been identified as "the birthplace of tea...the first area where humans figured out that eating tea leaves or brewing a cup could be pleasant" , Fengqing County in the Lincang City Prefecture of Yunnan Province is said to be home to the world's oldest cultivated tea tree, some 3,200 years old .

6 -1 : Origin myths :

In one popular Chinese legend, Shennong , the legendary Emperor of China and inventor of agriculture and Chinese medicine was drinking a bowl of boiling water some time around 2737 BC when a few leaves were blown from a nearby tree into his water, changing the color. The emperor took a sip of the brew and was pleasantly surprised by its flavor and restorative properties. A variant of the legend tells that the emperor tested the medical properties of various herbs on himself, some of them poisonous, and found tea to work as an antidote . Shennong is also mentioned in Lu Yu's famous early work on the subject , *Cha Jing* . A similar Chinese legend goes that the god of agriculture would chew the leaves, stems, and roots of various plants to discover medicinal herbs. If he consumed a poisonous plant , he would chew tea leaves to counteract the poison .

A rather gruesome legend dates back to the Tang Dynasty. In the legend, Bodhidharma, the founder of Chan Buddhism, accidentally fell asleep after meditating in front of a wall for nine years. He woke up in such disgust at his weakness that he cut off his own eyelids. They fell to the ground and took root, growing into tea bushes.^[28] Sometimes, another version of the story is told with Gautama Buddha in place of *Bodhidharma* .

Whether or not these legends have any basis in fact, tea has played a significant role in Asian culture for centuries as a staple beverage, a curative, and a status symbol. It is not surprising, therefore, that theories of its origin are often religious or royal in nature.

6 – 2 : History of tea in China

The Chinese have consumed tea for thousands of years. People of the Han Dynasty used tea as medicine (though the first use of tea as a stimulant is unknown) . China is considered to have the earliest records of tea consumption , with records dating back to the 10th century BC .

Laozi (ca. 600 - 517 BC) , the classical Chinese philosopher, described tea as "the froth of the liquid jade" and named it an indispensable ingredient to the elixir of life. Legend has it that master Lao was saddened by society's moral decay and, sensing that the end of the dynasty was near, he journeyed westward to the unsettled territories, never to be seen again. While passing along the nation's border, he encountered and was offered tea by a customs inspector named Yin Hsi. Yin Hsi encouraged him to compile his teachings into a single book so that future generations might benefit from his wisdom. This then became known as the *Dao De Jing*, a collection of Laozi's sayings.

In 59 BC, Wang Bao wrote the first known book with instructions on buying and preparing tea .

In 220 , famed physician and surgeon Hua Tuo wrote *Shin Lun*, in which he describes tea's ability to improve mental functions.

During the Sui Dynasty (589 - 618 AD) tea was introduced to Japan by Buddhist monks .

According to *Cha Jing* tea drinking was widespread . The book describes how tea plants were grown, the leaves processed, and tea prepared as a beverage. It also describes how tea was evaluated. The book also discusses where the best tea leaves were produced. Teas produced in this period were mainly tea bricks which were often used as currency, especially further from the center of the empire where coins lost their value.

During the Song Dynasty (960 – 1279) , production and preparation of all tea changed. The tea of Song included many loose-leaf styles (to preserve the delicate character favored by court society), but a new powdered form of tea emerged. Steaming tea leaves was the primary process used for centuries in the preparation of tea. After the transition from compressed tea to the powdered form, the production of tea for trade and distribution changed once again. The Chinese learned to process tea in a different way in the mid-13th century. Tea leaves were roasted and then crumbled rather than steamed. This is the origin of today's loose teas and the practice of brewed tea .

Tea production in China, historically, was a laborious process, conducted in distant and often poorly accessible regions. This led to the rise of many apocryphal stories and legends surrounding the harvesting process. For example, one story that has been told for many years is that of a village where monkeys pick tea. According to this legend, the villagers stand below the monkeys and taunt them. The monkeys, in turn, become angry, and grab handfuls of tea leaves and throw them at the villagers . There are products sold today that claim to be harvested in this manner, but no reliable commentators have observed this firsthand, and most doubt that it happened at all.^[33] For many hundreds of years the commercially - used tea tree has been, in shape, more of a bush than a tree . "Monkey picked tea" is more likely a name of certain varieties than a description of how it was obtained .

In 1391, the Ming court issued a decree that only loose tea would be accepted as a "tribute." As a result, loose tea production increased and processing techniques advanced. Soon, most tea was distributed in full-leaf, loose form and steeped in earthenware vessels.

6 – 3 : History of tea in Japan :



Ancient Tea Urns used by merchants to store tea



Japanese tea ceremony

Tea use spread to Japan about the sixth century , Tea became a drink of the religious classes in Japan when Japanese priests and envoys, sent to China to learn about its culture, brought tea to Japan. Ancient recordings indicate the first batch of tea seeds were brought by a priest named Saichō in 805 and then by another named Kūkai in 806 . It became a drink of the royal classes when Emperor Saga , the Japanese emperor, encouraged the growth of tea plants. Seeds were imported from China, and cultivation in Japan began .

In 1191, the famous Zen priest Eisai (1141-1215) brought back tea seeds to Kyoto. Some of the tea seeds were given to the priest Myoe Shonin, and became the basis for Uji tea. The oldest tea specialty book in Japan, *Kissa Yōjōki* (*How to Stay Healthy by Drinking Tea*) , was written by Eisai. The two - volume book was written in 1211 after his second and last visit to China. The first sentence states, “Tea is the ultimate mental and medical remedy and has the ability to make one’s life more full and complete.” Eisai was also instrumental in introducing tea consumption to the warrior class, which rose to political prominence after the Heian Period.

Green tea became a staple among cultured people in Japan—a brew for the gentry and the Buddhist priesthood alike. Production grew and tea became increasingly accessible, though still a privilege enjoyed mostly by the upper classes. The tea ceremony of Japan was introduced from China in the 15th century by Buddhists as a semi-religious social custom. The modern tea ceremony developed over several centuries by Zen Buddhist monks under the original guidance of the monk Sen no Rikyū (1522-1591) . In fact, both the beverage and the ceremony surrounding it played a prominent role in feudal diplomacy .

In 1738, Soen Nagatani developed Japanese *sencha* (煎茶?), literally *roasted tea*, which is an unfermented form of green tea. It is the most popular form of tea in Japan today. In 1835, Kahei Yamamoto developed *gyokuro* , literally *jewel dew* , by shading tea trees during the weeks leading up to harvesting. At the end of the Meiji period (1868 – 1912) , machine manufacturing of green tea was introduced and began replacing handmade tea .

6 - 4 : Korea :



Korean tea ceremony

The first historical record documenting the offering of tea to an ancestral god describes a rite in the year 661 in which a tea offering was made to the spirit of King Suro, the founder of the Geumgwan Gaya Kingdom (42 – 562) . Records from the Goryeo Dynasty (918-1392) show that tea offerings were made in Buddhist temples to the spirits of revered monks .

During the Joseon Dynasty (1392 – 1910), the royal Yi family and the aristocracy used tea for simple rites. The "Day Tea Rite" was a common daytime ceremony, whereas the "Special Tea Rite" was reserved for specific occasions. Toward the end of the Joseon Dynasty, commoners joined the trend and used tea for ancestral rites, following the Chinese example based on Zhu Xi's text formalities of Family.

Stoneware was common, ceramic more frequent, mostly made in provincial kilns, with porcelain rare, imperial porcelain with dragons the rarest. The earliest kinds of tea used in tea ceremonies were heavily pressed cakes of black tea, the equivalent of aged pu-erh tea still popular in China. However, importation of tea plants by Buddhist monks brought a more delicate series of teas into Korea, and the tea ceremony. Green tea, "chaksol" or "chugno," is most often served. However other teas such as "Byeoksoryung" Chunhachoon, Woojeon, Jakseol, Jookro, Okcheon, as well as native chrysanthemum tea, persimmon leaf tea, or mugwort tea may be served at different times of the year.

6 – 5 : Taiwan :

Taiwan is famous for the making of Oolong tea and green tea, as well as many western - styled teas. Bubble Tea or "Zhen Zhu Nai Cha" is black tea mixed with sweetened condensed milk and tapioca. Since the island was known to Westerners for many centuries as *Formosa* - short for the Portuguese *Ilha Formosa*, or "beautiful island" - tea grown in Taiwan is often identified by that name.

6 – 6 : Thailand :

Thai tea or " cha – yen " in Thailand, is a drink made from strongly - brewed black tea ("red tea" in East Asia) . Other ingredients may include added orange blossom water, star anise, crushed tamarind seed or red and yellow food coloring, and sometimes other spices as well. This tea is sweetened with sugar and condensed milk.

Usually, Thai people drink Thai hot tea in the morning, frequently with Yau ja gwai or *Pa - tong - ko* as it is called by most Thais.

- * *Thai hot tea* (cha - ron) Thai tea served hot.

- * *Dark Thai hot tea* (cha - dam - ron) Thai tea served hot with no milk content, sweetened with sugar only.

6 – 7 : Vietnam :



Vietnamese green teas have been largely unknown outside of mainland Asia until the present day. Recent free - enterprise initiatives are introducing these green teas to outside countries through new export activities.

Types :

- Lotus tea is a specialty product of the Vietnamese tea industry. Generally, high - quality green tea leaves are placed within lotus flowers for a day to acquire the scent, then are removed and packaged. A higher grade of lotus tea is made with lotus petals mixed in with high quality green tea leaves. Green tea style of Vietnam is to roll the leaves gently into crescents, and minimal handling. Vietnamese green teas are typically very potent. They are best brewed for most tastes for under 2 minutes using water temperature of 160°F. Beyond this time the tea will acquire a bitter taste that is nevertheless fancied by many tea lovers, as it reflects the potency of the tea leaves. Some fanciers will brew 3 - 4 times from one set of leaves, preferring the narrower flavor range of the later brewings .

- Jasmine tea is produced in two grades similar to lotus tea. Lotus tea is considered a specialty and is reserved for events or special meals. Jasmine tea is popular as a "chaser" for Vietnamese iced coffee, and is poured into the glass after the coffee is consumed, allowed to chill, and then enjoyed as a follow-up to the iced coffee in coffee shop cafes, particularly in the night life of major cities, where coffee shops are a popular social rendezvous on hot evenings .

- Artichoke Tea

Vietnamese teas are produced in many areas that have been known for tea - house " retreats " . For example some are, located amidst immense tea forests of the Lamdong highlands , where there is a community of ancient Ruong houses built at the end of the 18th century .



Middle Eastern tea

6 – 8 : Tea spreads to the world :



A conical urn - shaped silver-plated samovar used for boiling water for tea in Russia and some Middle eastern countries

The earliest record of tea in a more occidental writing is said to be found in the statement of an Arabian traveler, that after the year 879 the main sources of revenue in Canton were the duties on salt and tea. Marco Polo records the deposition of a Chinese minister of finance in 1285 for his arbitrary augmentation of the tea taxes. The travelers Giovanni Batista Ramusio (1559), L. Almeida (1576), Maffei (1588), and Teixeira (1610) also mentioned tea. In 1557, Portugal established a trading port in Macau and word of the Chinese drink "chá" spread quickly, but there is no mention of them bringing any samples home.

In the early 17th century, a ship of the Dutch East India Company brought the first green tea leaves to Amsterdam from China. Tea was known in France by 1636. It enjoyed a brief period of popularity in Paris around 1648. The history of tea in Russia can also be traced back to the seventeenth century. Tea was first offered by China as a gift to Czar Michael I in 1618. The Russian ambassador tried the drink; he did not care for it and rejected the offer, delaying tea's Russian introduction by fifty years. In 1689, tea was regularly imported from China to Russia via a caravan of hundreds of camels traveling the year-long journey, making it a precious commodity at the time. Tea was appearing in German apothecaries by 1657 but never gained much esteem except in coastal areas such as Ostfriesland.^[37] Tea first appeared publicly in England during the 1650s, where it was introduced through coffee houses. From there it was introduced to British colonies in America and elsewhere.

6 – 9 : United Kingdom :



Tea plantation in the Cameron Highlands , Malaysia .

The importing of tea into Britain began in the 1660s with the marriage of King Charles II to the Portuguese princess Catherine of Braganza, who brought to the court the habit of drinking tea . On 25 September of the same year Samuel Pepys recorded in his diary: "I did send for a cup of tee (a China drink) of which I never had drank before". It is probable that early imports came via Amsterdam or through sailors on eastern boats . Regular trade began in Guangzhou (Canton) . Trade was controlled by two monopolies: the Chinese *Hongs* (trading companies) and the British East India Company . The Hongs acquired tea from ' the tea men ' who had an elaborate supply chain into the mountains and provinces where the tea was grown .

The East India Company brought back many products, of which tea was just one, but it was to prove one of the most successful.^[38] It was initially promoted as a medicinal beverage or tonic . By the end of the seventeenth century tea was taken as a drink, albeit mainly by the aristocracy . In 1690 nobody would have predicted that by 1750 tea would be the national drink . The origin of large trade in tea was the need for a return cargo from the East Indies. Merchantmen ships delivered fabrics manufactured in Britain to India and China but would return empty or partially full. To solve this problem the East India Company began a vigorous public relations campaign to popularise tea among the common people in Britain and develop it as a viable return cargo.

The escalation of tea importation and sales over the period 1690 to 1750 is mirrored closely by the increase in importation and sales of cane sugar: the British were not drinking just tea but *sweet* tea . Thus, two of Britain's trading triangles were to meet within the cup: the sugar sourced from Britain's trading triangle encompassing Britain, Africa and the West Indies and the tea from the triangle encompassing Britain, India and China .

Britain had to pay China for its tea, but China had little need of British goods, so much of it was paid for with silver bullion. Although the Chinese did not need the silver, China's government eventually accepted the silver as the payments for the first few good Chinese tea shipments . A few years on, India used its opium to influence the then East India Company, Britain to pay all of their gold and silver for their addiction of Indian opium, and forced the Chinese Tea Growers to accept the illegal Indian opium for the exchange of shipments of the good Chinese tea . Critics of the tea trade at this time would point to the damage caused to Britain's wealth by this loss of bullion.^[38] As an alternative, Britain began producing opium in India and forced China to trade tea for opium as part of several treaties after the Opium wars. And to circumvent its dependence on Chinese tea, the East India Company sent Scottish botanist Robert Fortune to China to steal and smuggle out of China tea plants, which were then taken to India, where by the end of the 19th century they matured and produced Indian tea .

Tea became a very important item in Britain's global trade, contributing to Britain's global dominance by the end of the eighteenth century. To this day tea is seen worldwide as a symbol of 'Britishness', but also, to some, as a symbol of old British Colonialism .

The London 2012 section of the paralympic handover in Beijing included tea as part of the routine . Tea in Britain is taken differently to in China and other Eastern countries, with over 90 % of tea consumed being black tea, often with milk, and with teabags now being a far more popular way to make a cup of tea than in Oriental countries .

6 – 10 : United States of America :

While coffee is by far more popular, hot brewed black tea is enjoyed both with meals and as a refreshment by much of the population. Similarly, iced tea is consumed throughout. In the Southern states sweet tea, sweetened with large amounts of sugar or an artificial sweetener and chilled, is the fashion. Outside the South, sweet tea is sometimes found, but primarily because of cultural migration and commercialization .

The American specialty tea market has quadrupled in the years from 1993-2008, now being worth \$6.8 billion a year.^[40] Similar to the trend of better coffee and better wines, this tremendous increase was partly due to consumers who choose to trade up. Specialty tea houses and retailers also started to pop up during this period .

The Boston Tea Party was an act of protest by the American colonists against the British Government in which they destroyed many crates of tea belonging to the British East India Company on ships in Boston Harbor. The incident, which took place on Thursday, December 16, 1773, has been seen as helping to spark the American Revolution .

6 – 11 : India

Tea had been known for millennia in India as a medicinal plant, but was not drunk for pleasure until the British began to establish

plantations in the 19th century. The Chinese variety is used for Darjeeling tea, and the Assamese variety, native to the Indian state of Assam, everywhere else. The British started commercial tea plantations in India and in Ceylon: "In 1824 tea plants were discovered in the hills along the frontier between Burma and the Indian state of Assam. The British introduced *tea culture* into India in 1836 and into Ceylon (Sri Lanka) in 1867. At first they used seeds from China, but later seeds from the Assam plant were used " · Only black tea was produced until recent decades.



Tea Garden in Assam, India

India was the top producer of tea for nearly a century, but was displaced by China as the top tea producer in the 21st century.^[43] Indian tea companies have acquired a number of iconic foreign tea enterprises including British brands Tetley and Typhoo.^[43] While India is the largest consumer of tea worldwide, the per-capita consumption of tea in India remains a modest 750 grams per person every year.^[43] A lot of huge companies have emerged including 'Golden Tips Tea Co', and many other major brands that specialise and emphasize on Darjeeling tea and tourism in Darjeeling, one of the prime beautiful locations famous for tea .

6 – 12 : Sri Lanka / Ceylon :



Tea Garden in Sri Lanka

Sri Lanka is renowned for its high quality tea and as the fourth biggest tea producing country globally , after China , India and Kenya and has a production share of 9 % in the international sphere . The total extent of land under tea cultivation has been assessed at approximately 187,309 hectares .

The plantations started by the British were initially taken over by the government in the 1960s, but have been privatized and are now run by 'plantation companies' which own a few 'estates' or tea plantations each.

Ceylon tea is divided into 3 groups as Upcountry, Mid country and Low country tea based on the geography of the land on which it is grown .

6 – 13 : Africa and South America :

Africa and South America have seen greatly increased tea production in recent decades, the great majority for export to Europe and North America respectively, produced on large estates, often owned by tea companies from the export markets. Almost all production is of basic mass-market teas, processed by the Crush, Tear, Curl method. Kenya is now the third largest global producer (figures below), after China and India, and is now the largest exporter of tea to the United Kingdom. There is also a great consumption of tea in Chile. In South Africa , the non - *Camellia sinensis* beverage rooibos is popular. In South America, yerba mate, a tisane, is popular.

7 - Health effects :

The health benefits of tea is a controversial topic with many proponents and detractors. An article from the Nutrition (1999 , pp. 946 – 949) journal as related on PubMed states :

The possible beneficial effects of tea consumption in the prevention of cancer and cardiovascular diseases have been demonstrated in animal models and suggested by studies in vitro. Similar beneficial effects, however, have not been convincingly demonstrated in humans: beneficial effects have been demonstrated in some studies but not in others. If such beneficial effects do exist in humans, they are likely to be mild, depending on many other lifestyle-related factors, and could be masked by confounding factors in certain populations. Another concern is that the amounts of tea consumed by humans are lower than the doses required for demonstrating the disease-prevention effects in animal models. Caution should be applied, however, in the use of high concentrations of tea for disease prevention. Ingestion of large amounts of tea may cause nutritional and other problems because of the caffeine content and the strong binding activities of tea polyphenols, although there are no solid data on the harmful effects of tea consumption. More research is needed to elucidate the biologic activities of green and black tea and to determine the optimal amount of tea consumption for possible health-beneficial effects.

In summary, the health benefits of tea have been shown in animal studies, but at doses much higher than regularly consumed by humans, at which dosage levels may prove to be harmful to health.

Several of the potential health benefits proposed for tea are outlined in this excerpt from Mondal (2007, pp.519–520) as following:

Tea leaves contain more than 700 chemicals, among which the compounds closely related to human health are flavanoides, amino acids, vitamins (C, E and K), caffeine and polysaccharides. Moreover, tea drinking has recently proven to be associated with cell - mediated immune function of the human body. Tea plays an important role in

improving beneficial intestinal microflora, as well as providing immunity against intestinal disorders and in protecting cell membranes from oxidative damage. Tea also prevents dental caries due to the presence of fluorine. The role of tea is well established in normalizing blood pressure, lipid depressing activity, prevention of coronary heart diseases and diabetes by reducing the blood-glucose activity. Tea also possesses germicidal and germistatic activities against various gram - positive and gram negative human pathogenic bacteria. Both green and black tea infusions contain a number of antioxidants, mainly catechins that have anti - carcinogenic , anti - mutagenic and anti - tumoric properties .

In a large study of over 11,000 Scottish men and women completed in 1993 and published in the 1999 Journal of Epidemiology and Community Health (1999 , pp. 481 – 487) , there was an increase in the risk of coronary disease with the regular consumption of tea, although it disappeared after adjustment for confounding factors (age and occupational status).

8 - Etymology and cognates in other languages :

The Chinese character for tea is 茶 , but it is pronounced differently in the various Chinese dialects. Two pronunciations have made their way into other languages around the world.^[45] One is *tê*, which comes from the Amoy Min Nan dialect, spoken around the port of Xiamen (Amoy) . This pronunciation is believed to come from the old words for tea 荼 (tú) or 荼 (tú) . The other is *chá*, used by the Cantonese dialect spoken around the ports of Guangzhou (Canton), Hong Kong, Macau, and in overseas Chinese communities, as well as in the Mandarin dialect of northern China. This term was used in ancient times to describe the first flush harvest of tea. Yet another different pronunciation is *zu*, used in the Wu dialect spoken around Shanghai. The words for tea in Korea and Japan are 茶 and 茶 (ちゃ), respectively. Both are transliterated as *cha*. (In Japanese , it is sometimes 御茶 (おちゃ) or *ocha*, which is more polite) .

8 – 1 : The derivatives from *tê* :

Language	Name	Language	Name	Language	Name	Language	Name	Language	Name
Afrikaans	<i>tee</i>	Armenian, Catalan	<i>te</i>	Czech	<i>té</i> or <i>thé</i>	Danish	<i>te</i>	Dutch	<i>thee</i>
English	<i>tea</i>	Esperanto	<i>teo</i>	Estonian	<i>tee</i>	Faroese	<i>te</i>	Finnish	<i>tee</i>
French	<i>thé</i>	West Frisian	<i>tee</i>	Galician	<i>té</i>	German	<i>Tee</i>	Hebrew	תה, <i>te</i>
Hungarian	<i>tea</i>	Icelandic	<i>te</i>	Indonesian	<i>teh</i>	Irish	<i>tae</i>	Italian	<i>tè</i> or <i>thè</i>
Javanese	<i>tèh</i>	Korean	茶, 다 <i>da</i> [ta] ⁽²⁾	scientific Latin	<i>thea</i>	Latvian	<i>tēja</i>	Leonese	<i>té</i>
Limburgish	<i>tiè</i>	Low Saxon	<i>Tee</i> [tʰɛː] or <i>Tei</i> [tʰaː]	Malay	<i>teh</i>	Filipino	<i>tsaa</i>	Norwegian	<i>te</i>
Occitan	<i>tè</i>	Sesotho	<i>tea, chá</i>	Scots Gaelic	<i>tì, teatha</i>	Sinhalese	<i>thé</i>	Spanish	<i>té</i>
Scots	<i>tea</i> [ti:] ~ [te:]	Sundanese	<i>entèh</i>	Swedish	<i>te</i>	Tamil	தேநீர் <i>thenir</i> (nīr = water) "theyilai" means "tea leaf" (ilai=leaf)	Telugu	తేనీళ్లు <i>tēnīru</i>
Welsh	<i>te</i>								

8 - 2 : Derivatives from *cha* or *chai* :

The Polish word for a tea - kettle is *czajnik* , which could be derived directly from *cha* or from the cognate Russian word. However, tea in Polish is *herbata*, which, as well as Lithuanian *arbata*, was derived from the Latin *herba thea*, meaning " tea herb " .

It is tempting to correlate these names with the route that was used to deliver tea to these cultures, although the relation is far from simple at times. As an example, the first tea to reach Britain was traded by the Dutch from Fujian, which uses *te*, and although later most British trade went through Canton, which uses *cha*, the Fujianese pronunciation continued to be the more popular .

In Ireland, or at least in Dublin, the term *cha* is sometimes used for " tea " , as is pre-vowel-shift pronunciation " tay " (from which the Irish Gaelic word " tae " is derived) . *Char* was a common slang

term for tea throughout British Empire and Commonwealth military forces in the 19th and 20th centuries, crossing over into civilian usage.

The British English slang word "char" for "tea" arose from its Mandarin Chinese pronunciation " *cha* " with its spelling affected by the fact that *ar* is a more common way of representing the phoneme /ɑ:/ in British English .

In North America, the word *chai* is used to refer almost exclusively to the Indian *masala chai* (spiced tea) beverage.

The original pronunciation "cha" in the Cantonese and Mandarin languages has no [j] ending. The forms with this ending in many Eurasian languages come from the Chinese compound word denoting "tea leaves" (Mandarin 茶叶 chá yè) . The different articulations of the word for tea into the two main groups: " teh – derived " (Min Chinese dialects) and " cha – derived " (Mandarin , Cantonese and other non-Min Chinese dialects) is an interesting one, as it reveals the particular Chinese local cultures where non-Chinese nations acquired their tea and "tea cultures". Not surprisingly, India and the Arab world most likely got their tea cultures from the Cantonese or the Southwestern Mandarin speakers, whereas the Russians got theirs from the northern Mandarin speakers. The Portuguese, the first Europeans to import the herb in large amounts, took the Cantonese form "chá", as used in their trading posts in the south of China, especially Macau. Conversely, other Western Europeans who copied the Min articulation "teh" probably traded with the Hokkienese while in Southeast Asia.

Quite recently, no earlier than 1980, "chai" entered North American English with a particular meaning: Indian masala black tea. Of course this is not the case in other languages, where "chai" usually just means black tea (as people traditionally drink more black tea than green outside of East Asia) . English is thus one of the few languages that allow for the dual articulations of "tea" into a "teh-derived" word and a " cha - derived " one, such as Moroccan colloquial Arabic (Darija): in the case of Moroccan Arabic , " ash – shay " means "generic, or black Middle Eastern tea" whereas "atay" means a

specialty tea: Zhejiang or Fujian green tea with fresh mint leaves. The Moroccans are said to have acquired a unique penchant in the Arab world for East Chinese green tea after the ruler Mulay Hassan exchanged some European hostages captured by the Barbary Pirates for a whole ship of Chinese tea. They have thus acquired a word for this special tea different from the generic "ash – shay" .

Perhaps the only place in which a word unrelated to tea is used to describe the beverage is South America (particularly Andean countries), because a similar stimulant beverage, *yerba mate*, was consumed there long before tea arrived.

9 - Tea culture :

In many cultures, tea is often had at high class social events, such as afternoon tea and the tea party. It may be consumed early in the day to heighten alertness; it contains theophylline and bound caffeine^[3] (sometimes called "theine"), although there are also decaffeinated teas. In many cultures such as Arab culture tea is a focal point for social gatherings. Moreover, the history of tea in Iran - in the Persian culture- is another to explore. One source cites: "the first thing you will be offered when a guest at an Iranian household is tea".^[46]

There are tea ceremonies which have arisen in different cultures, Japan's complex, formal and serene one being one of the most well known. Other examples are the Chinese tea ceremony which uses some traditional ways of brewing tea. One form of Chinese tea ceremony is the *Gongfu tea ceremony*, which typically uses small Yixing clay teapots and oolong tea.

The American poet Wallace Stevens, a tea-fancier, is credited by Eleanor Cook with a "delicately implicit trope of drinking tea as a metaphor for reading (ingesting a drink from leaves)."^[47] See for instance his "Tea".

10 - Preparation:



Korean tea kettle over hot coal

The traditional method of making a cup of tea is to place loose tea leaves, either directly, or in a tea infuser, into a tea pot or teacup and pour hot water over the leaves. After a couple of minutes the leaves are usually removed again, either by removing the infuser, or by straining the tea while serving.

Most green teas should be allowed to steep for about three minutes, although some types of tea require as much as ten. The strength of the tea should be varied by changing the amount of tea leaves used, not by changing the steeping time. The amount of tea to be used per amount of water differs from tea to tea but one basic recipe may be one slightly heaped teaspoon of tea (about 5 ml) for each teacup of water (200 ml) (8 oz) prepared as above. Stronger teas, such as Assam, to be drunk with milk are often prepared with more leaves, and more delicate high grown teas such as a Darjeeling are prepared with a little less (as the stronger mid-flavors can overwhelm the champagne notes).

The best temperature for brewing tea depends on its type. Teas that have little or no oxidation period, such as a green or white tea, are best brewed at lower temperatures between 60 °C and 85 °C (140-185 °F), while teas with longer oxidation periods should be brewed at higher temperatures around 100 °C (212 °F) . The higher temperatures are required to extract the large, complex, flavorful phenolic molecules found in fermented tea, although boiling the water reduces the amount of dissolved oxygen in the water.

Type	Water Temp	Steep Time	Infusions
White Tea	150 °F (66 °C) – 160 °F (71 °C)	1–2 minutes	3
Yellow Tea	160 °F (71 °C) – 170 °F (77 °C)	1–2 minutes	3
Green Tea	170 °F (77 °C) – 180 °F (82 °C)	1–2 minutes	4 - 6
Oolong Tea	180 °F (82 °C) – 190 °F (88 °C)	2–3 minutes	4 - 6
Black Tea	210 °F (99 °C)	2–3 minutes	2 - 3
Pu-erh Tea	200 °F (93 °C) – 210 °F (99 °C)	Limitless	Several
Herbal Tea	210 °F (99 °C)	3–6 minutes	Varied

Some tea sorts are often brewed several times using the same tea leaves. Historically, in China, tea is divided into a number of infusions. The first infusion is immediately poured out to wash the tea, and then the second and further infusions are drunk. The third through fifth are nearly always considered the best infusions of tea, although different teas open up differently and may require more infusions of hot water to bring them to life .

One way to taste a tea, throughout its entire process, is to add hot water to a cup containing the leaves and after about 30 seconds to taste the tea. As the tea leaves unfold (known as "The Agony of the Leaves") they give up various parts of themselves to the water and thus the taste evolves. Continuing this from the very first flavours to the time beyond which the tea is quite stewed will allow an appreciation of the tea throughout its entire length .



Black tea infusion.

10 -1 : Black tea :

The water for black teas should be added near boiling point 210 °F (99 °C). Many of the active substances in black tea do not develop at temperatures lower than 90 °C. For some more delicate teas lower temperatures are recommended. The temperature will have as large an effect on the final flavor as the type of tea used. The most common fault when making black tea is to use water at too low a temperature. Since boiling point drops with increasing altitude, this makes it difficult to brew black tea properly in mountainous areas. It is also recommended that the teapot be warmed before preparing tea, easily done by adding a small amount of boiling water to the pot, swirling briefly, before discarding. Black teas are usually brewed for about 4 minutes and should not be allowed to steep for less than 30 seconds or more than about five minutes (a process known as *brewing* or *mashing* in Britain). It is commonly said that a steeping time above five minutes make the tea bitter (at this point it is referred to as being *stewed* in Britain), but in reality the precise time depends on a number factors, such as the type of tea and the water quality, and bitterness can occur as early as three minutes, or not at all even after prolonged steeping. When the tea has brewed long enough to suit the tastes of the drinker, it should be strained while serving. The popular varieties of black tea include the Assam tea, the Darjeeling tea and the black Ceylon tea.

10 – 2 : Green tea :

Water for green tea, according to most accounts, should be around 80 °C to 85 °C (176 °F to 185 °F) ; the higher the quality of the leaves, the lower the temperature. Hotter water will burn green - tea leaves, producing a bitter taste. Preferably, the container in which the tea is steeped, the mug, or teapot should also be warmed beforehand so that the tea does not immediately cool down. High-quality green and white teas can have new water added as many as five or more times, depending on variety, at increasingly high temperatures.

10 – 3 : Oolong tea (or *Wulong*) :

Oolong teas should be brewed around 90 °C to 100 °C (194 °F to 212 °F), and again the brewing vessel should be warmed before pouring in the water. Yixing purple clay teapots are the traditional brewing vessel for oolong tea. For best results use spring water, as the minerals in spring water tend to bring out more flavor in the tea. High quality oolong can be brewed multiple times from the same leaves, and unlike green tea it improves with reuse. It is common to brew the same leaves three to five times, the third steeping usually being the best.

10 – 4 : Premium or delicate tea :

Some teas, especially green teas and delicate Oolong teas, are steeped for shorter periods, sometimes less than 30 seconds. Using a tea strainer separates the leaves from the water at the end of the brewing time if a tea bag is not being used. However black Darjeeling tea, the premium Indian tea, needs a longer than average steeping time. Elevation and time of harvest offer varying taste profiles, proper storage and water quality also have a large impact on taste.

10 – 5 : Pu - erh tea (or *Pu'er*) :

Pu-erh teas require boiling water for infusion. Some prefer to quickly rinse pu-erh for several seconds with boiling water to remove tea dust which accumulates from the aging process. Infuse pu-erh at the boiling point (100 °C or 212 °F), and allow to steep for 30 seconds or up to five minutes.

10 – 6 : Serving :

In order to preserve the pre - tannin tea without requiring it all to be poured into cups, a second teapot may be used. The steeping pot is best unglazed earthenware; Yixing pots are the best known of these, famed for the high quality clay from which they are made. The serving pot is generally porcelain, which retains the heat better. Larger teapots are a post-19th century invention, as tea before this time was very rare and very expensive. Experienced tea-drinkers often insist

that the tea should not be stirred around while it is steeping (sometimes called *winding* in the UK). This, they say, will do little to strengthen the tea, but is likely to bring the tannins out in the same way that brewing too long will do. For the same reason one should not squeeze the last drops out of a teabag; if stronger tea is desired, more tea leaves should be used.

10 – 7 : Adding milk to tea



Tea is some times taken with milk

The addition of milk to tea was first mentioned in 1680 by the epistolist Madame de Sévigné . Many teas are traditionally drunk with milk. These include Indian masala chai, and British tea blends. These teas tend to be very hearty varieties which can be tasted through the milk, such as Assams, or the East Friesian blend. Milk is thought to neutralize remaining tannins and reduce acidity . The Chinese do not usually drink milk with tea (or indeed use milk at all) but the Manchurians do, and the elite of the Manchu Dynasty continued to do so. Hong Kong - style milk tea is based on British colonial habits .

The order of steps in preparing a cup of tea is a much-debated topic. Some say that it is preferable to add the milk before the tea, as the high temperature of freshly brewed tea can denature the proteins found in fresh milk, similar to the change in taste of UHT milk, resulting in an inferior tasting beverage . Others insist that it is better to add the milk after brewing the tea, as most teas need to be brewed as close to boiling as possible. The addition of milk chills the beverage during the crucial brewing phase, meaning that the delicate flavor of a good tea cannot be fully appreciated. By adding the milk afterwards, it is easier to dissolve sugar in the tea and also to ensure

that the desired amount of milk is added, as the color of the tea can be observed .



Moroccan tea being served. It is poured from a distance to produce a foam on the tea

A 2007 study published in the *European Heart Journal* found that certain beneficial effects of tea may be lost through the addition of milk .

10 - 8 : Other additives :

Many flavourings are added to varieties of tea during processing. Among the best known are Chinese Jasmine tea, with jasmine oil or flowers, the spices in Indian Masala chai and Earl Grey tea, which contains oil of bergamot. A great range of modern flavours have been added to these traditional ones .

Other popular additives to tea by the tea - brewer or drinker include sugar, liquid honey or a solid Honey Drop, lemon (traditional in Russia and Italy) , fruit jams, and mint. In China sweetening tea was traditionally regarded as a feminine practice. In colder regions such as Mongolia , Tibet and Nepal, butter is added to provide necessary calories . Tibetan butter tea contains rock salt and dre (yak) butter, which is then churned vigorously in a cylindrical vessel closely resembling a butter churn . The same may be said for salt tea, which is consumed in some cultures in the Hindu Kush region of northern

Pakistan . Alcohol may also be added to tea, such as whisky or brandy.

The flavor of the tea can also be altered by pouring it from different heights, resulting in varying degrees of oxidization. The art of high-altitude pouring is used principally by people in Northern Africa (e.g. Morocco), but also in West Africa (e.g. Guinea , Mali , Senegal) and can positively alter the flavor of the tea, but it is more likely a technique to cool the beverage destined to be consumed immediately. In certain cultures the tea is given different names depending on the height it is poured from. In Mali, gunpowder tea is served in series of three, starting with the highest oxidization or strongest, unsweetened tea (cooked from fresh leaves) , locally referred to as " bitter as death " . Follows a second serving, where the same tea leaves are boiled again with some sugar added (" pleasant as life ") , and a third one, where the same tea leaves are boiled for the third time with yet more sugar added (" sweet as love ") . Green tea is the central ingredient of a distinctly Malian custom, the "Grin", informal social gathering that cuts across social and economic lines, starting in front of family compound gates in the afternoons, extending late in the night, and widely popular in Bamako and other large urban areas.

In Southeast Asia, particularly in Malaysia, the practice of pouring tea from a height has been refined further using black tea to which condensed milk is added, poured from a height from one cup to another several times in alternating fashion and in quick succession, to create a tea with entrapped air bubbles creating a frothy "head" in the cup. This beverage, teh tarik, literally, "pulled tea", has a creamier taste than flat milk tea and is extremely popular in the region. Tea pouring in Malaysia has been further developed into an art form in which a dance is done by people pouring tea from one container to another, which in any case takes skill and precision. The participants, each holding two containers, one full of tea, pour it from one to another. They stand in lines and squares and pour the tea into each others' pots. The dance must be choreographed to allow anyone who has both pots full to empty them and refill whoever has no tea at any one point .

11 - Economics of tea :

Tea is the most popular drink in the world in terms of consumption. Its consumption equals all other manufactured drinks in the world — including coffee, chocolate, soft drinks, and alcohol — put together . Most tea consumed outside East Asia is produced on large plantations in India or Sri Lanka, and is destined to be sold to large businesses. Opposite this large - scale industrial production there are many small " gardens ", sometimes minuscule plantations, that produce highly sought-after teas prized by gourmets. These teas are both rare and expensive, and can be compared to some of the most expensive wines in this respect .

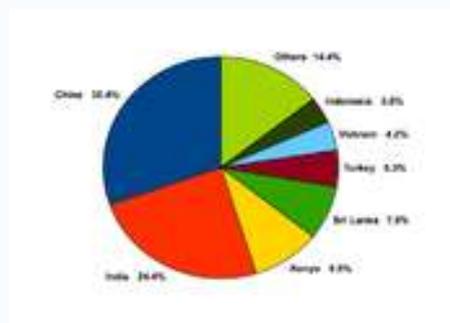
India is the world's largest tea - drinking nation although the per capita consumption of tea remains a modest 750 grams per person every year. The United Kingdom, with 2.3 kg of tea consumed per person per year, is the world's greatest per capita consumer .

12 - Statistics :

12 – 1 : Production :

In 2003, world tea production was 3.15 million tonnes annually. The largest producer was India, followed by China (the order has since reversed) , followed by Kenya and Sri Lanka. China is the only country today to produce in industrial quantities all different kinds of tea (white tea , yellow tea , green tea , blue - green tea , red tea and black tea) . Percentage of total tea production in 2003

■ Tea not grown in significant quantities
■ Less than 5%. ■ From 5 to 10%.
■ More than 10%



Percentage of total global tea production by country in 2007

Production in tones . Figures for 2006 - 2007 from FAO data base		
Country	2006	2007
 China	1,047,345	1,183,502
 India	928,000	949,220
 Kenya	310,580	369,600
 Sri Lanka	310,800	305,220
 Turkey	201,866	206,160
 Vietnam	151,000	164,000
 Indonesia	146,858	150,224
 Japan	91,800	94,100
 Argentina	72,129	72,000
 Iran	59,180	60,000
 Bangladesh	58,000	58,500
 Malawi	45,009	46,000
 Uganda	34,334	35,000
Other countries	189,551	193,782
Total	3,646,452	3,887,308

12 – 1 – 1 : Tea production certification :

There are a number of bodies that independently certify the production of tea. Tea from certified estates can be sold with a certification label on pack. The most important certification schemes are Rainforest Alliance, Fairtrade, UTZ Certified, and Organic. All these schemes certify other crops (like coffee , cocoa and fruit) as well. Rainforest Alliance certified tea is sold by Unilever brands Lipton and PG Tips in Western Europe, Australia and the US. Fairtrade certified tea is sold by a large number of suppliers around the world. UTZ Certified announce a partnership in 2008 with Sara Lee brand Pickwick tea .

Production of organic tea is rising; 3,500 tonnes of organic tea were grown in 2003. The majority of this tea (about 75 %) is sold in France, Germany, Japan, the United Kingdom and the United States.

12 – 2 : Trade :



Evolution of the average price of tea since 1989

12 - 2 - 1 : Export :

The largest exporter of tea is Kenya .

12 – 2 – 2 : Import :

The principal importers are the CIS , the EU , Pakistan , the United States , Egypt , and Japan . In 2003, 1.39 million tons were imported – an increase of 1 % over 2002 .

12 – 2 – 3 : Prices :

The large quantities produced in 2003 did not greatly affect the prices, which were relatively stable in that year. In August 2009, Dubai warned of a tea price hike .

13 : Packaging :

13 – 1 : Tea bags :



Tea Bags

In 1907, American tea merchant Thomas Sullivan began distributing samples of his tea in small bags of Chinese silk with a drawstring. Consumers noticed that they could simply leave the tea in the bag and re-use it with fresh tea. However, the potential of this distribution/packaging method would not be fully realized until later on. During World War II, tea was rationed. In 1953 (after rationing in the UK ended), Tetley launched the *tea bag* to the UK and it was an immediate success.

Tea leaves are packed into a small envelope (usually composed of paper) known as a tea bag. The use of tea bags is easy and convenient, making tea bags popular for many people today. However, the tea used in tea bags has an industry name - it is called fannings or "dust" and is the waste product produced from the sorting of higher quality loose leaf tea.^[citation needed] It is commonly held among tea aficionados that this method provides an inferior taste and experience. The paper used for the bag can also be tasted by many, which can detract from the tea's flavor. Because fannings and dust are a lower quality of the tea to begin with, the tea found in tea bags is less finicky when it comes to brewing time and temperature. Additional reasons why bag tea is considered less well - flavored include :

- Dried tea loses its flavor quickly on exposure to air. Most bag teas (although not all) contain leaves broken into small pieces; the great surface area to volume ratio of the leaves in tea bags exposes them to more air, and therefore causes them to go stale faster. Loose tea leaves are likely to be in larger pieces, or to be entirely intact.
- Breaking up the leaves for bags extracts flavored oils.
- The small size of the bag does not allow leaves to diffuse and steep properly.
- Some tea bags are made using a wet paper strength-reinforcing coating using epichlorohydrin, a known carcinogen .

13 - 2 : Pyramid tea bags :



Pyramid tea bag

The " pyramid tea bag " , introduced by Lipton and PG Tips in 1996 , has a unique design that addresses one of connoisseurs' arguments against paper tea bags, because its three - dimensional tetrahedron shape allows more room for tea leaves to expand while steeping. However, some types of pyramid tea bags have been criticized as being environmentally unfriendly , since their synthetic material does not break down in landfills as loose tea leaves and paper tea bags do .

13 – 3 : Loose tea :



Loose-leaf tea

The tea leaves are packaged loosely in a canister or other container. Rolled gunpowder tea leaves, which resist crumbling, are commonly vacuum packed for freshness in aluminized packaging for storage and retail. The portions must be individually measured by the consumer for use in a cup, mug, or teapot. This allows greater flexibility, letting the consumer brew weaker or stronger tea as desired, but convenience is sacrificed. Strainers, "tea presses", filtered teapots, and infusion bags are available commercially to avoid having to drink the floating loose leaves and to prevent over - brewing. A more traditional, yet perhaps more effective way around this problem

is to use a three - piece lidded teacup, called a gaiwan. The lid of the gaiwan can be tilted to decant the leaves while pouring the tea into a different cup for consumption.

13 – 4 : Compressed tea :

Some teas (particularly Pu - erh tea) are still compressed for transport, storage, and aging convenience. The tea brick remains in use in the Himalayan countries. The tea is prepared and steeped by first loosening leaves off the compressed cake using a small knife. Compressed teas can usually be stored for longer periods of time without spoilage when compared with loose leaf tea .

13 – 5 : Instant tea :

In recent times , " instant teas " are becoming popular, similar to freeze dried instant coffee. Instant tea was developed in the 1930s, but not commercialized until the late 1950s, and is only more recently becoming popular. These products often come with added flavors, such as vanilla, honey or fruit, and may also contain powdered milk. Similar products also exist for instant iced tea, due to the convenience of not requiring boiling water. Tea connoisseurs tend to criticize these products for sacrificing the delicacies of tea flavor in exchange for convenience .

13 – 6 : Canned tea :

Canned tea was first launched in 1981 in Japan. As such, it is a fairly recent innovation, and it has mostly benefits in marketing .

14 : Storage :

Tea has a shelf life that varies with storage conditions and type of tea. Black tea has a longer shelf life than green tea. Some teas such as flower teas may go bad in a month or so. An exception, Pu-erh tea improves with age. Tea stays freshest when stored in a dry, cool, dark place in an air-tight container . Black tea stored in a bag inside a sealed opaque canister may keep for two years. Green tea loses its freshness more quickly, usually in less than a year. Gunpowder tea, its leaves being tightly rolled, keeps longer than the more open-leafed

Chun Mee tea. Storage life for all teas can be extended by using desiccant packets or oxygen absorbing packets, and by vacuum sealing.

When storing green tea, discreet use of refrigeration or freezing is recommended. In particular, drinkers need to take precautions against temperature variation .

Improperly stored tea may lose flavor, acquire disagreeable flavors or odors from other foods, or become moldy .



Da Hong Pao
tea an Oolong
tea



Fuding Bai Hao
Yinzen tea, a
white tea



Green Pu - erh tuo
cha, a type of
compressed raw
pu- erh



Huoshan
Huangya tea, a
Yellow tea

Tobacco



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1 – Introduction :

Tobacco is an agricultural product processed from the leaves of plants in the genus *Nicotiana*. It can be consumed, used as an organic pesticide, and in the form of nicotine tartrate it is used in some medicines . In consumption it most commonly appears in the forms of smoking, chewing, snuffing, or dipping tobacco, or snus. Tobacco has long been in use as an entheogen in the Americas. However, upon the arrival of Europeans in North America, it quickly became popularized

as a trade item and as a recreational drug. This popularization led to the development of the southern economy of the United States until it gave way to cotton. Following the American Civil War, a change in demand and a change in labor force allowed for the development of the cigarette. This new product quickly led to the growth of tobacco companies until the scientific controversy of the mid - 1900s.

There are many species of tobacco, which are all encompassed by the plant genus *Nicotiana*. The word *nicotiana* (as well as *nicotine*) was named in honor of Jean Nicot, French ambassador to Portugal, who in 1559 sent it as a medicine to the court of Catherine de Medici .

Because of the addictive properties of nicotine, tolerance and dependence develop. Absorption quantity, frequency, and speed of tobacco consumption are believed to be directly related to biological strength of nicotine dependence, addiction, and tolerance.^{[3][4]} The usage of tobacco is an activity that is practiced by some 1.1 billion people, and up to 1 / 3 of the adult population.^[5] The World Health Organization reports it to be the leading preventable cause of death worldwide and estimates that it currently causes 5.4 million deaths per year.^[6] Rates of smoking have leveled off or declined in developed countries, however they continue to rise in developing countries.

Tobacco is cultivated similarly to other agricultural products. Seeds are sown in cold frames or hotbeds to prevent attacks from insects, and then transplanted into the fields. Tobacco is an annual crop, which is usually harvested in a large single-piece farm equipment. After harvest, tobacco is stored to allow for curing, which allow for the slow oxidation and degradation of carotenoids. This allows for the agricultural product to take on properties that are usually attributed to the " smoothness " of the smoke. Following this, tobacco is packed into its various forms of consumption which include smoking, chewing, sniffing, and so on.

2 - Etymology :

The Spanish word " *tabaco* " is thought to have its origin in Arawakan language, particularly, in the Taino language of the Caribbean. In Taino, it was said to refer either to a roll of tobacco

leaves (according to Bartolome de Las Casas, 1552) , or to the *tabago*, a kind of Y- shaped pipe for sniffing tobacco smoke (according to Oviedo ; with the leaves themselves being referred to as *Cohiba*) .

However, similar words in Spanish and Italian were commonly used from 1410 to define medicinal herbs , originating from the Arabic *tabbaq*, a word reportedly dating to the 9th century, as the name of various herbs .

3 – History :

3 – 1 : Early developments :

Tobacco had already long been used in the Americas when European settlers arrived and introduced the practice to Europe, where it became popular. At high doses, tobacco can become hallucinogenic ; accordingly , Native Americans never used the drug recreationally. Instead, it was often consumed as an entheogen; among some tribes, this was done only by experienced shamans or medicine men Eastern North American tribes would carry large amounts of tobacco in pouches as a readily accepted trade item and would often smoke it in pipes, either in defined ceremonies that were considered sacred, or to seal a bargain,^[9] and they would smoke it at such occasions in all stages of life, even in childhood . It was believed that tobacco was a gift from the Creator and that the exhaled tobacco smoke was capable of carrying one's thoughts and prayers to heaven .

3 – 2 : Popularization :

Following the arrival of the Europeans, tobacco became increasingly popular as a trade item. It fostered the economy for the southern United States until it was replaced by cotton. Following the American civil war, a change in demand and a change in labor force allowed inventor James Bonsack to create a machine which automated cigarette production.

This increase in production allowed tremendous growth in the tobacco industry until the scientific revelations of the mid-1900s.

3 – 3 : Contemporary :

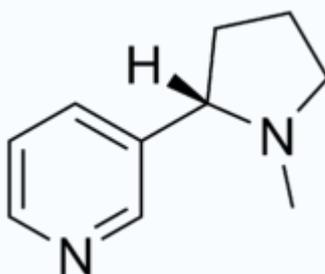
Following the scientific revelations of the mid-1900s, tobacco became condemned as a health hazard, and eventually became encompassed as a cause for cancer, as well as other respiratory and circulatory diseases. This led to the Tobacco Master Settlement Agreement (MSA) which settled the lawsuit in exchange for a combination of yearly payments to the states and voluntary restrictions on advertising and marketing of tobacco products.

In the 1970s Brown & Williamsons cross - bred a strain of tobacco to produce Y1. This strain of tobacco contained an unusually high amount of nicotine, nearly doubling its content from 3.2 - 3.5 % to 6.5 %. In the 1990s, this prompted Food and Drug Administration (FDA) to use this strain as evidence that tobacco companies were intentionally manipulating the nicotine content of cigarettes .

In 2003, in response to tobaccos growth in developing countries, the World Health Organization (WHO) successfully rallied 168 countries to sign the Framework Convention on Tobacco Control. The Convention is designed to push for effective legislation and its enforcement in all countries to reduce the harmful effects of tobacco. This led to the development of tobacco cessation products .

4 – Biology :

4 – 1 : Nicotiana :



Nicotine , a carcinogen , is the compound responsible for the addictive nature of Tobacco use .



Tobacco flower, leaves, and buds

There are many species of tobacco, which are encompassed by the genus of herbs *Nicotiana*. It is part of the nightshade family (Solanaceae) indigenous to North and South America , Australia , south west Africa and the South Pacific.

Many plants contain nicotine, a powerful neurotoxin that is particularly harmful to insects. However, tobaccos contain a higher concentration of nicotine than most other plants. Unlike many other Solanaceae they do not contain tropane alkaloids, which are often poisonous to humans and other animals.

Despite containing enough nicotine and other compounds such as germacrene and anabasine and other piperidine alkaloids (varying between species) to deter most herbivores,^[13] a number of such animals have evolved the ability to feed on *Nicotiana* species without being harmed. Nonetheless, tobacco is unpalatable to many species and therefore some tobacco plants (chiefly Tree Tobacco , *N. glauca*) have become established as invasive weeds in some places .

4 – 2 : Types of tobacco :

There are a number of types of tobacco include but are not limited to :

- **Aromatic Fire - cured** , it is cured by smoke from open fires. In the United States, it is grown in northern middle Tennessee, central Kentucky and in Virginia. Fire-cured tobacco

grown in Kentucky and Tennessee are used in some chewing tobaccos, moist snuff, some cigarettes, and as a condiment in pipe tobacco blends. Another fire - cured tobacco is Latakia and is produced from oriental varieties of *N. tabacum*. The leaves are cured and smoked over smoldering fires of local hardwoods and aromatic shrubs in Cyprus and Syria .

- **Brightleaf tobacco** , Brightleaf is commonly known as " Virginia tobacco " , often regardless of which state they are planted. Prior to the American Civil War, most tobacco grown in the US was fire - cured dark - leaf. This type of tobacco was planted in fertile lowlands, used a robust variety of leaf, and was either fire cured or air cured. Most Canadian cigarettes are made from 100 % pure Virginia tobacco .

- **Burley tobacco** , is an air - cured tobacco used primarily for cigarette production. In the U.S., burley tobacco plants are started from palletized seeds placed in polystyrene trays floated on a bed of fertilized water in March or April.

- **Cavendish** is more a process of curing and a method of cutting tobacco than a type of it. The processing and the cut are used to bring out the natural sweet taste in the tobacco. Cavendish can be produced out of any tobacco type but is usually one of , or a blend of Kentucky, Virginia, and Burley and is most commonly used for pipe tobacco and cigars .

- **Criollo tobacco** is a type of tobacco, primarily used in the making of cigars. It was, by most accounts, one of the original Cuban tobaccos that emerged around the time of Columbus.

- **Dokham**, is a tobacco originally grown in Iran, mixed with leaves, bark, and herbs for smoking in a midwakh.

- **Turkish tobacco** , is a sun - cured, highly aromatic, small-leafed variety (*Nicotiana tabacum*) that is grown in Turkey, Greece, Bulgaria, and Macedonia. Originally grown in regions historically part of the Ottoman Empire, it is also known as "Oriental". Many of the early brands of cigarettes were made mostly or entirely of Turkish tobacco; today, its main use is in blends of pipe and especially cigarette tobacco (a typical American cigarette is a blend of bright Virginia, burley and Turkish) .

- **Perique** , A farmer called Pierre Chenet is credited with first turning this local tobacco into the Perique in 1824 through the technique of pressure-fermentation. Considered the truffle of pipe tobaccos, it is used as a component in many blended pipe tobaccos, but is too strong to be smoked pure. At one time, the freshly moist Perique was also chewed, but none is now sold for this purpose. It is typically blended with pure Virginia to lend spice, strength, and coolness to the blend.

- **Shade tobacco** , is cultivated in Connecticut and Massachusetts. Early Connecticut colonists acquired from the Native Americans the habit of smoking tobacco in pipes and began cultivating the plant commercially, even though the Puritans referred to it as the "evil weed". The industry has weathered some major catastrophes, including a devastating hailstorm in 1929, and an epidemic of brown spot fungus in 2000, but is now in danger of disappearing altogether, given the value of the land to real estate speculators.

- **White Burley** , In 1865 , George Webb of Brown County, Ohio planted Red Burley seeds he had purchased, and found that a few of the seedlings had a whitish, sickly look. The air - cured leaf was found to be more mild than other types of tobacco.

- **Wild Tobacco**, is native to the southwestern United States, Mexico, and parts of South America. Its botanical name is *Nicotiana rustica*.

- **Y1** is a strain of tobacco cross-bred by Brown & Williamson in the 1970s in order to obtain an unusually high nicotine content. In the 1990s the United States Food and Drug Administration (FDA) used it as evidence that tobacco companies were intentionally manipulating the nicotine content of cigarettes .

5 – Impact :

5 – 1 : Social :

Smoking in public was for a long time something reserved for men and when done by women was sometimes associated with promiscuity . In Japan during the Edo period, prostitutes and their

clients would often approach one another under the guise of offering a smoke and the same was true for 19th century Europe .

Following the American Civil War the usage of tobacco, primarily in cigarettes, became associated with masculinity and power and is an iconic image associated with the stereotypical capitalist. Today tobacco is often rejected. This has spawned quitting associations and anti-smoking campaigns. Bhutan is the only country in the world where tobacco sales are illegal .

5 – 2 : Demographic :

Research is limited mainly to tobacco smoking, which has been studied the more extensively than any other form of consumption. As of 2000, smoking is practiced by some 1.22 billion people, of which men are more likely to smoke than women (however the gender gap declines with age) , poor more likely than rich, and people in developing countries or transitional economies are more likely than people in developed countries.^[21] As of 2004, the World Health Organization (WHO) reports that of the 58.8 million deaths to occur globally , 5.4 million are tobacco – attributed .

5 – 3 : Health effects of tobacco :

Tobacco use leads most commonly to diseases affecting the heart and lungs, with smoking being a major risk factor for heart attacks, strokes, chronic obstructive pulmonary disease (COPD) , emphysema , and cancer (particularly lung cancer , cancers of the larynx and mouth , and pancreatic cancer) .

The World Health Organization estimate that tobacco caused 5.4 million deaths in 2004 and 100 million deaths over the course of the 20th century. Similarly, the United States Centers for Disease Control and Prevention describes tobacco use as " the single most important preventable risk to human health in developed countries and an important cause of premature death worldwide " .

Rates of smoking have leveled off or declined in the developed world. Smoking rates in the United States have dropped by half from

1965 to 2006 falling from 42 % to 20.8 % in adults . In the developing world, tobacco consumption is rising by 3.4 % per year .

5 - 4 : Economic :

" Much of the disease burden and premature mortality attributable to tobacco use disproportionately affect the poor " , and of the 1.22 billion smokers , 1 billion of them live in developing or transitional economies .

In Indonesia, the lowest income group spends 15% of its total expenditures on tobacco. In Egypt, more than 10% of households expenditure in low-income homes is on tobacco. The poorest 20% of households in Mexico spend 11 % of their income on tobacco .^[29]

5 – 5 : Tobacco Political

The tobacco lobby gives money to politicians to vote in favor of deregulating tobacco. It is estimated that the United States tobacco lobby spends an average of \$ 106,415 each day legislature meets; however the industry lost its support when the U.S. National Association of Attorneys General (NAAG) filed charges against the Tobacco Institute, a tobacco industry advocacy group.^[30] This resulted in the Master Settlement Agreement, which forced the organization to disband and place all records on a website .

6 – Production :

6 – 1 : Cultivation :



Tobacco plants growing in a field in Intercourse, Pennsylvania

Tobacco is cultivated similar to other agricultural products. Seeds were at first quickly scattered onto the soil. However, young plants came under increasing attack from flea beetles (*Epitrix cucumeris* or *Epitrix pubescens*), which caused destruction of half the tobacco crops in United States in 1876. By 1890 successful experiments were conducted that placed the plant in a frame covered by thin fabric. Today, tobacco is sown in cold frames or hotbeds, as their germination is activated by light .

In the United States, tobacco is often fertilized with the mineral apatite, which partially starves the plant of nitrogen to produce a more desired flavor. Apatite, however, contains radium, lead 210, and polonium 210 — which are known radioactive carcinogens.

After the plants have reached relative maturity, they are transplanted into the fields, in which a relatively large hole is created in the tilled earth with a tobacco peg. Various mechanical tobacco planters were invented in the nineteenth and twentieth to automate the process : making the hole, fertilizing it, guiding the plant in — all in one motion .

Tobacco is cultivated annually, and can be harvested in several ways. In the oldest method, the entire plant is harvested at once by cutting off the stalk at the ground with a sickle. In the nineteenth century, bright tobacco began to be harvested by pulling individual leaves off the stalk as they ripened. The leaves ripen from the ground upwards, so a field of tobacco may go through several so-called "pullings," more commonly known as topping (topping always refers to the removal of the tobacco flower before the leaves are systematically removed and, eventually, entirely harvested. As the industrial revolution took hold, harvesting wagons used to transport leaves were equipped with man-powered stringers, an apparatus which used twine to attach leaves to a pole. In modern times large fields are harvested by a single piece of farm equipment, although topping the flower and in some cases the plucking of immature leaves is still done by hand.

6 – 2 : Curing of tobacco :



Sun - cured tobacco, Bastam, Iran.

Curing and subsequent aging allows for the slow oxidation and degradation of carotenoids in tobacco leaf. This produces certain compounds in the tobacco leaves very similar and give a sweet hay, tea, rose oil, or fruity aromatic flavor that contribute to the "smoothness" of the smoke. Starch is converted to sugar which glycosylates protein and is oxidized into advanced glycation endproducts (AGEs), a caramelization process that also adds flavor. Inhalation of these AGEs in tobacco smoke contributes to atherosclerosis and cancer . Levels of AGE's is dependent on the curing method used.

Tobacco can be cured through several methods which include but are not limited to :

- **Air cured** tobacco is hung in well - ventilated barns and allowed to dry over a period of four to eight weeks. Air-cured tobacco is low in sugar, which gives the tobacco smoke a light, sweet flavor, and high in nicotine. Cigar and burley tobaccos are air cured.

- **Fire cured** tobacco is hung in large barns where fires of hardwoods are kept on continuous or intermittent low smoulder and takes between three days and ten weeks, depending on the process and the tobacco. . Fire curing produces a tobacco low in sugar and high in nicotine. Pipe tobacco, chewing tobacco, and snuff are fire cured.

- **Flue cured** tobacco was originally strung onto tobacco sticks, which were hung from tier - poles in curing barns (Aus : kilns, also traditionally called Oasts) . These barns have flues which run from externally fed fire boxes, heat-curing the tobacco without exposing it to smoke, slowly raising the temperature over the course of the curing. The process will generally take about a week. This method produces cigarette tobacco that is high in sugar and has medium to high levels of nicotine.

- **Sun - cured** tobacco dries uncovered in the sun. This method is used in Turkey , Greece and other Mediterranean countries to produce oriental tobacco . Sun - cured tobacco is low in sugar and nicotine and is used in cigarettes .

6 – 3 : Consumption :

Tobacco is consumed in many forms and through a number of different methods. Below are examples including, but not limited to , such forms and usage :

- **Beedi** are thin , often flavored, south Asian cigarettes made of tobacco wrapped in a tendu leaf, and secured with colored thread at one end .

- **Chewing tobacco** is one of the oldest ways of consuming tobacco leaves. It is consumed orally , in two forms: through sweetened strands , or in a shredded form. When consuming the long sweetened strands the tobacco is lightly chewed and

compacted into a ball. When consuming the shredded tobacco, small amounts are placed at the bottom lip, between the gum and the teeth, where it is gently compacted, thus it can oftentimes be called *dipping tobacco*. Both methods stimulate the saliva glands, which led to the development of the spittoon.

- **Cigars** are tightly rolled bundle of dried and fermented tobacco which is ignited so that its smoke may be drawn into the smoker's mouth.

- **Cigarettes** are a product consumed through the inhalation of smoke and manufactured out of cured and finely cut tobacco leaves and reconstituted tobacco, often combined with other additives, then rolled or stuffed into a paper-wrapped cylinder.

- **Creamy snuff** are tobacco paste, consisting of tobacco, clove oil, glycerin, spearmint, menthol, and camphor, and sold in a toothpaste tube. It is marketed mainly to women in India, and is known by the brand names Ipco (made by Asha Industries), Denobac, Tona, Ganesh. It is locally known as "mishri" in some parts of Maharashtra.

- **Dipping tobacco** are a form of smokeless tobacco. Dip is occasionally referred to as "chew", and because of this, it is commonly confused with chewing tobacco, which encompasses a wider range of products. A small clump of dip is 'pinched' out of the tin and placed between the lower or upper lip and gums.

- **Electronic cigarette** is an alternative to tobacco smoking, although no tobacco is consumed. It is a battery-powered device that provides inhaled doses of nicotine by delivering a vaporized propylene glycol/nicotine solution.

- **Gutka** are a preparation of crushed betel nut, tobacco, and sweet or savory flavorings. It is manufactured in India and exported to a few other countries. A mild stimulant, it is sold across India in small, individual-size packets.

- **Hookah** are a single or multi-stemmed (often glass-based) water pipe for smoking. Originally from India, the hookah has gained immense popularity, especially in the middle east. A hookah operates by water filtration and indirect heat. It can be used for smoking herbal fruits, tobacco, or cannabis.

- **Kreteks** are cigarettes made with a complex blend of tobacco, cloves and a flavoring "sauce". It was first introduced

in the 1880s in Kudus , Java , to deliver the medicinal eugenol of cloves to the lungs.

- **Roll – Your - Own** , often called rollies or roll ups, are very popular particularly in European countries. These are prepared from loose tobacco, cigarette papers and filters all bought separately. They are usually much cheaper to make.

- **Pipe smoking** typically consists of a small chamber (the bowl) for the combustion of the tobacco to be smoked and a thin stem (shank) that ends in a mouthpiece (the bit) . Shredded pieces of tobacco are placed into the chamber and ignited.

- **Snuff** are a generic term for fine-ground smokeless tobacco products. Originally the term referred only to dry snuff, a fine tan dust popular mainly in the eighteenth century. Snuff powder originated in the UK town of Great Harwood and was famously ground in the town's monument prior to local distribution and transport further up north to Scotland. There are two major varieties which include European (dry) and American (moist) ; although American snuff is often referred to as dipping tobacco .

- **Snus** is steam - cured moist powder tobacco product that is not fermented and does not induce salivation. It is consumed by placing it in the mouth against the gums for an extended period of time. It is a form of snuff that is used in a manner similar to American dipping tobacco, but does not require regular spitting.

- **Topical tobacco paste** are sometimes recommended as a treatment for wasp, hornet, fire ant, scorpion, and bee stings.^[33] An amount equivalent to the contents of a cigarette is mashed in a cup with about a 0.5 to 1 teaspoon of water to make a paste that is then applied to the affected area.

- **Tobacco water** are traditional organic insecticide used in domestic gardening. Tobacco dust can be used similarly. It is produced by boiling strong tobacco in water, or by steeping the tobacco in water for a longer period. When cooled the mixture can be applied as a spray, or 'painted' on to the leaves of garden plants, where it will prove deadly to insects .

7 – Gallery :



Tobacco can also be pressed into plugs and sliced into flakes.



Broadleaf tobacco inspected in Chatham , Virginia , United States .

Yerba mate



Ilex Para guaricensis

Contents :

- 1 Introduction
- 2 Infusion
- 3 Nomenclature
- 4 Cultivation
- 5 Chemical composition and properties
 - 5.1 Caffeine
 - 5.1.1 Stereoisomer claims
 - 5.1.2 Comparison of effects with coffee
 - 5.2 Mineral content
 - 5.3 Phenolic content and anti - carcinogenic potential
 - 5.4 Anti obesity properties
 - 5.5 Cholesterol lowering properties
 - 5.6 Carcinogenic potential
 - 5.7 Possible MAO activity
 - 5.8 E - NTPD ase activity
- 6 Antioxidant potential
- 7 The Culture of Yerba Mate

1 - Introduction :

Yerba mate (Spanish : *yerba mate* , Portuguese: *erva – mate*) , *Ilex Para guariensis*, is a species of holly (family Aquifoliaceae) native to subtropical South America in northeastern Argentina, eastern Paraguay and southern Brazil . It was first scientifically classified by Swiss botanist Moses Bertoni , who settled in Paraguay in 1895 .

The yerba mate plant is a shrub or small tree growing up to 15 meters tall. The leaves are evergreen , 7 – 11 cm long and 3 – 5.5 cm wide, with a serrated margin. The flowers are small, greenish-white, with four petals. The fruit is a red drupe 4 – 6 mm diameter .

Scientific Classification

Kingdom :	Plantae
Unranked :	Angiosperms
Unranked :	Eudicots
Unranked :	Asterids
Order :	Aquifoliales
Family :	Aquifoliaceae
Genus :	<i>Ilex</i>
Species :	<i>I. Para guariensis</i>

2 – Infusion :

The infusion called mate is prepared by steeping dry leaves (and twigs) of yerba mate in hot water, rather than in boiling water like black tea. Drinking mate with friends from a shared hollow gourd (also called a *mate* in Spanish , or *cabaça* or *cuia* in Portuguese) with a metal straw (a *bombilla* in Spanish, *bomba* in Portuguese) is a common social practice in Argentina , Uruguay, Paraguay, southern Chile, eastern Bolivia and southern and western Brazil and has been cultivated in Syria , Lebanon and Jordan .



Steaming yerba mate infusion in its customary gourd .

The flavor of brewed yerba mate is strongly vegetal, herbal, and grassy, reminiscent of some varieties of green tea. Many consider the flavor to be very agreeable, but it is generally bitter if steeped in boiling water. Unlike most teas, it does not become bitter and astringent when steeped for extended periods, and the leaves may be infused several times. Additionally, one can purchase flavored mate in many varieties.

In Brazil, a toasted version of mate, known as *chá mate* or "mate tea", is sold in teabag and loose form, and served, sweetened, in specialized shops, either hot or iced with fruit juice or milk. An iced, sweetened version of toasted mate is sold as an un carbonated soft drink , with or without fruit flavoring. The toasted variety of mate has less of a bitter flavor and more of a spicy fragrance. When shaken it becomes creamy (since the formed foam gets well mixed and lasts for some time), known as *mate batido*. It is more popular in the coastal cities of Brazil, as opposed to the far southern states where it is consumed in the traditional way (green , drunk with a silver straw from a shared gourd) , and called " chimarrão " .



Yerba mate

Similarly, a form of mate is sold in Uruguay, Argentina and Paraguay in tea bags to be drunk in a similar way to tea. This is known in Spanish as *mate cocido* or *cocido*. In Argentina this is commonly drunk with breakfast or as part of *merienda* (roughly, afternoon tea) , often with a selection of *facturas* (sweet pastries) . It is also made by heating yerba in water and straining it as it cools .

In Paraguay, western Brazil (Mato Grosso and west of São Paulo) and the Litoral Argentino, yerba mate infusion is also drunk as a cold or iced beverage and called *tereré* or *tererê* (in spanish and portuguese, respectively). Usually sucked out of a horn cup called *guampa* with a *bombilla*. Medicinal herbs, known as "yuyos", are mixed in a mortar and pestle and added to the water for taste or medicinal reasons. *Tereré* consumed in Paraguay may also be made as an infusion of yerba mate with grapefruit or lemon juice.

3 - Nomenclature :



Yerba mate growing in the wild.

The pronunciation of *yerba mate* in Spanish is ['jerβa 'mate] . The word *hierba* is Spanish for grass or herb; *yerba* is a variant spelling of it which is quite common in Argentina. *Mate* is from the Quechua *mati*, meaning "cup". "Yerba mate" is therefore literally the "cup herb".

The (Brazilian) Portuguese name is *erva - mate* ['ɛrva 'mati] (also pronounced ['ɛrva 'mate] in some regions) and is also used to prepare the drinks *chimarrão* (hot) or *tereré* (cold). While the tea is

made with the toasted leaves, these drinks are made with green ones, and are very popular in the south of the country. The name given to the plant in Guaraní (Guarani , in Portuguese), language of the indigenous people who first cultivated and enjoyed yerba mate, is *ka'a*, which has the same meaning as *yerba*. "Congonha", in Portuguese, is derived from the Tupi expression for "erva mate", meaning something like "what keeps us alive".

Both the spellings "mate" and "maté" are used in English . The acute accent on the final letter indicates that the word and its pronunciation are distinct from the common English word "mate" /'meɪt/, meaning a partner (US) or friend (UK, Aus, NZ). However, the Yerba Mate Association of the Americas states that it is always improper to accent the second syllable, since doing so confuses the word with an unrelated Spanish word for killing^[11] ("Maté" literally means " (I) killed " in Spanish) .

4 - Cultivation



Plantation in Misiones , Argentina

The plant is grown and processed mainly in South America, more specifically in Northern Argentina (Corrientes, Misiones), Paraguay, Uruguay and southern Brazil (Rio Grande do Sul, Santa Catarina Paraná and Mato Grosso do Sul). The Guaraní are reputed to be the first people who cultivated the plant; the first Europeans to do this were Jesuit missionaries, who spread the drinking habit as far as Ecuador and Southern Chile .

When the yerba is harvested, the branches are dried sometimes with a wood fire, imparting a smoky flavor. Then the leaves and sometimes the twigs are broken up.

There are many brands and types of yerba, with and without twigs (*con palo* or *sin palo*), some with low powder content. Some types are less strong in flavor (*suave*, "mild") and there are blends flavored with mint, orange and grapefruit skin, etc.

The plant *Ilex paraguariensis* can vary in strength of the flavor, caffeine levels and other nutrients depending on whether it is a male or female plant. Female plants tend to be milder in flavor, and lower in caffeine. They are also relatively scarce in the areas where yerba mate is planted and cultivated, not wild – harvested, compared to the male plants.

5 - Chemical composition and properties :



Yerba mate with stems

5 – 1 : Caffeine

Mate contains xanthines, which are alkaloids such as caffeine, theophylline, and theobromine, well-known stimulants also found in coffee and chocolate. Caffeine content varies between 0.2% and 2% of dry weight (compared with 0.3 – 9% for tea leaves, 2.5 - 7.5% in guarana, and up to 3.2% for ground coffee).

5 – 1 – 1 : Stereo isomer claims :

However, caffeine is not chiral, and thus cannot have a stereoisomer, and "mateine" is an official synonym of caffeine in the chemical databases.

Studies of mate, though very limited, have shown preliminary evidence that the mate xanthine cocktail is different from other plants containing caffeine most significantly in its effects on muscle tissue , as opposed to those on the central nervous system, which are similar to those of other natural stimulants . The three xanthenes present in mate have been shown to have a relaxing effect on smooth muscle tissue , and a stimulating effect on myocardial (heart) tissue .

5 -1 – 2 : Comparison of effects with coffee :

Mate's negative effects are anecdotally claimed to be of a lesser degree than those of coffee, though no explanation for this is offered or even credibly postulated, except for its potential as a placebo effect.^[16] Some users report that drinking yerba mate does not prevent them from being able to fall asleep, as is often the case with some more common stimulating beverages, while still enhancing their energy and ability to remain awake at will .

However, the net amount of caffeine in one preparation of yerba mate is typically quite high, in large part because the repeated filling of the mate with hot water is able to extract the xanthenes very effectively . It is for this reason that one mate may be shared among several people and yet produce the desired stimulating effect in all of them .



Yerba mate soda

From reports of personal experience with mate , its physiological effects are similar to (yet distinct from) more widespread caffeinated beverages like coffee , tea , or guarana drinks . Some users report a mental state of wakefulness, focus and alertness reminiscent of most

stimulants, but often remark on mate's unique lack of the negative effects typically created by other such compounds, such as anxiety , " jitteriness " , and heart palpitations.

5 – 2 : Mineral content :

Mate also contains elements such as potassium , magnesium and manganese .

5 – 3 : Phenolic content and anti - carcinogenic potential :

In vivo and *in vitro* studies are showing yerba mate to exhibit significant cancer - fighting activity . Researchers at the University of Illinois (2005) found yerba mate to be " rich in phenolic constituents " and to " inhibit oral cancer cell proliferation " while it promoted proliferation of oral cancer cell lines at certain concentrations . This activity was due in part to inhibition of topoisomerase II activity in yeast .

In contrast , researchers in Mississippi found that both cold and hot water extractions of yerba mate contained high levels (8.03 to 53.3 ng / g dry leaves) of carcinogenic polycyclic aromatic hydrocarbons (PAHs) (i.e. [[Benzo [a] pyrene]]) .

5 – 4 : Anti obesity properties :

In mouse studies , *ilex paraguensis* tea has been shown to mitigate the tendency towards obesity induced by a high - fat diet .

5 – 5 : Cholesterol lowering properties :

Consumption of yerba mate (*Ilex para guariensis*) improves serum lipid parameters in healthy dyslipidemic subjects and provides an additional LDL - cholesterol reduction in individuals on statin therapy .

5 – 6 : Carcinogenic potential :

Conversely, a study by the International Agency for Research on Cancer showed a limited correlation between oral cancer and the

drinking of hot maté and on large quantities of mate . Smaller quantities (less than 1 liter daily) and warm rather than hot mate consumption were found to increase risk only slightly ; alcohol and tobacco consumption had a synergistic effect on increasing oral, throat, and esophageal cancer . Given the influence of the temperature of water, as well as the lack of complete adjustment for age, alcohol consumption and smoking, the study concludes that maté is "not classifiable as to its carcinogenicity to humans " .

Yerba maté consumption has been associated with increased incidence of bladder, esophageal, oral, squamous cell of the head and neck, and lung cancer . However, a case - control study showed no increased incidence of bladder cancer in mate drinkers.

The pyrrolizidine alkaloids contained in maté tea are known to produce a rare condition of the liver , veno - occlusive disease , which produces liver failure due to progressive occlusion of the small venous channels in the liver . One fatal case has been reported in a young British woman who consumed large quantities of maté tea from Paraguay for years .

5 – 7 : Possible MAO activity :

In August 11 , 2005 , United States patent application (documents # 20050176777 , # 20030185908 , and # 20020054926) cites yerba maté extract as a mono amine oxidase inhibitor ; the maximal inhibition observed *in vitro* was 40 – 50 % . MAOIs being anti depressants , there is speculation that this may contribute to the calming effect of yerba mate .

In addition, it has been noted by the U.S. Army Center for Health Promotion and Preventive Medicine that yerba maté can cause high blood pressure when used in conjunction with other MAO inhibitors (such as Nardil and Parnate) .

5 – 8 : E - NTPDase activity :

Research also shows that yerba maté preparations can alter the concentration of members of the ecto - nucleoside tri phosphate

diphospho hydrolase (E – NTPDase) family , resulting in an elevated level of extracellular ATP, ADP, and AMP . This was found with chronic ingestion (15 days) of an aqueous yerba mate extract, and may { OR } lead to a novel mechanism for manipulation of vascular regenerative factors, i.e., treating heart disease .

6 - Antioxidant potential :

In an investigation of yerba mate antioxidant activity, there was a correlation found between content of caffeoyl - derivatives and antioxidant capacity (AOC) .

Amongst a group of Ilex species , *Ilex para guariensis* antioxidant activity was the highest .

7 - The Culture of Yerba Mate :

The Argentina experience is not complete without daily servings of yerba mate. It is common for friends to convene to " matear " several times a week. In cold weather the beverage is served hot and in warm weather the hot water is often substituted for lemonade. Children often take yerba mate with lemonade as well .

As Americans often meet at a coffee shop, drinking mate is the impetus for gathering with friends in Argentina. Sharing mate is ritualistic and has its own set of rules. Usually one person, the host or whoever brought the mate, prepares the drink and refills the gourd with water.

The gourd is passed around, often in a circle, and each person finishes the gourd before giving it back to the brewer. The gourd (also called "mate") is passed in a clockwise order. Since mate can be re-brewed many times, the gourd is passed until the water runs out. When a person no longer wants to take mate, they say "gracias" to the brewer when returning the gourd to signify they don't want any more.

In Argentina (specifically east and south regions) , " yerba " is pronounced " sherba " (the accent in most parts of Argentina changes the " ll " and " y " sounds to a " sh " sound) .

PART – 3

TIME LINE

OF SOME

ALKALOIDS

Cannabis Time line

6000 BCE	Cannabis seeds used for food in China.
4000 BCE	Textiles made of hemp are used in China. Remains have been found of hemp fibers from this period and from Turkestan a century later .
2727 BCE	First recorded use of cannabis as medicine in Chinese pharmacopoeia. In every part of the world humankind has used cannabis for a wide variety of health problems .
1500 BCE	Cannabis cultivated in China for food and fiber
1500 BCE	Scythians cultivate cannabis and use it to weave fine hemp cloth. (Sumach 1975)
1200 - 800 BCE	Bhang (dried cannabis leaves, seeds and stems) is mentioned in the Hindu sacred text Atharva veda (Science of Charms) as "Sacred Grass", one of the five sacred plants of India. It is used by medicinally and ritually as an offering to Shiva .
700 - 600 BCE	The Zoroastrian Zend-Avesta, an ancient Persian religious text of several hundred volumes, and said to have been written by Zarathustra (Zoroaster), refers to bhang as Zoroaster's "good narcotic" (Vendidad or The Law Against Demons)
700 - 300 BCE	Scythian tribes leave Cannabis seeds as offerings in royal tombs.
700 BCE	A grave dating from circa 700 BCE in Yanghai Tombs near Turpan, China contains psychoactive cannabis (not fiber-source hemp) .
500 BCE	Scythian couple die and are buried with two small tents covering censors. Attached to one tent stick was a decorated leather pouch containing wild Cannabis seeds. This closely matches the stories told by Herodotus. The gravesite, discovered in the late 1940s, was in Pazryk, northwest of the Tien Shan Mountains in modern-day Khazakistan.
500 BCE	Hemp is introduced into Northern Europe by the Scythians. An urn containing leaves and seeds of the Cannabis plant, unearthed near Berlin, is dated to about this time.
500 - 100 BCE	Hemp spreads throughout northern Europe.
430 BCE	Herodotus reports on ritual , cleansing, and recreational use of Cannabis by the Scythians .
100 - 0 BCE	The psychotropic properties of Cannabis are mentioned in the newly compiled herbal <i>Pen Ts'ao Ching</i> which is attributed to an emperor c. 2700 B.C.
0 - 100 CE	Construction of Samartian gold and glass paste stash box for storing hashish, coriander, or salt, buried in Siberian tomb.
70	Dioscorides mentions the use of Cannabis as a Roman medicament.
170	Galen (Roman) alludes to the psychoactivity of Cannabis seed confections.
500 - 600	The Jewish Talmud mentions the euphoriant properties of Cannabis. (Abel 1980)
900 - 1000	Scholars debate the pros and cons of eating hashish. Use spreads throughout Arabia.
1090 - 1256	In Khorasan, Persia, Hasan ibn al-Sabbah, the Old Man of the Mountain, recruits followers to commit assassinations...legends develop around their supposed use of hashish. These legends are some of the earliest written tales of the discovery of the inebriating powers of Cannabis and the supposed use of Hashish. 1256 Alamut falls
Early 12th Century	Hashish smoking very popular throughout the Middle East.
12th Century	Cannabis is introduced in Egypt during the reign of the Ayyubid dynasty on the occasion of the flooding of Egypt by mystic devotees coming from Syria. (M.K. Hussein 1957 - Soueif 1972)
1155 - 1221	Persian legend of the Sufi master Sheik Haidar's of Khorasan's personal discovery of Cannabis and it's subsequent spread to Iraq, Bahrain, Egypt and Syria. Another of the ealiest written narratives of the use of Cannabis as an inebriant.
13th Century	The oldest monograph on hashish, Zahr al-'arish fi tahrim al-hashish, was written. It has since been lost.
13th Century	Ibn al-Baytar of Spain provides a description of psychoactive Cannabis.
13th Century	Arab traders bring Cannabis to the Mozambique coast of Africa.

1231	Hashish introduced to Iraq in the reign of Caliph Mustansir (Rosenthal 1971)
1271 - 1295	Journeys of Marco Polo in which he gives second-hand reports of the story of Hasan ibn al-Sabbah and his "assassins" using hashish. First time reports of Cannabis have been brought to the attention of Europe.
1378	Ottoman Emir Soudoun Scheikhouni issues one of the first edicts against the eating of hashish.
1526	Babur Nama, first emperor and founder of Mughal Empire learned of hashish in Afghanistan.
1549	Angolan slaves brought cannabis with them to the sugar plantations of northeastern Brazil. They were permitted to plant their cannabis between rows of cane, and to smoke it between harvests .
mid 16th Century	The epic poem, Benk u Bode, by the poet Mohammed Ebn Soleiman Foruli of Baghdad, deals allegorically with a dialectical battle between wine and hashish.
Apr 10, 1563	"Conversations on the simples, drugs and materia medica of India" is published by Portuguese physician Garcia de Orta. It discusses Cannabis, Opium, and Nutmeg, among more than 50 medicinal plants and substances .
17th Century	Use of hashish, alcohol, and opium spreads among the population of occupied Constantinople
1606 -1632	French and British cultivate Cannabis for hemp at their colonies in Port Royal (1606), Virginia (1611), and Plymouth (1632). ³
Late 17th Century	Hashish becomes a major trade item between Central Asia and South Asia.
1798	Napoleon discovers that much of the Egyptian lower class habitually uses hashish (Kimmens 1977). He declares a total prohibition. Soldiers returning to France bring the tradition with them.
19th Century	Hashish production expands from Russian Turkestan into Yarkand in Chinese Turkestan.
1809	Antoine Sylvestre de Sacy, a leading Arabist, reveals the etymology of the words "assassin" and "hashishin"
1840	In America, medicinal preparations with a Cannabis base are available. Hashish available in Persian pharmacies.
1843	Le Club des Hachichins, or Hashish Eater's Club, is established in Paris. ³
after 1850	Hashish appears in Greece.
1856	British tax ganja and charas trade in India
1870 - 1880	First reports of hashish smoking on Greek mainland
c. 1875	Cultivation for hashish introduced to Greece
1877	Kerr reports on Indian ganja and charas trade.
1890	Greek Department of Interior prohibits importation, cultivation and use of hashish.
1890	Hashish made illegal in Turkey
1893 - 1894	The India Hemp Drugs Commission Report is issued.
1893 - 1894	70,000 to 80,000 kg of hashish legally imported into India from Central Asia each year.
1906	Pure Food and Drug Act is passed, regulating the labelling of products containing Alcohol, Opiates, Cocaine, and Cannabis, among others. The law went into effect Jan 1, 1907 .
Early 20th Century	Hashish smoking very popular throughout the Middle East.
1915 - 1927	Cannabis begins to be prohibited for nonmedical use in the U.S., especially in SW states...California (1915), Texas (1919), Louisiana (1924), and New York (1927).
1920	Metaxus dictators in Greece crack down on hashish smoking.
1920s	Hashish smuggled into Egypt from Greece, Syria, Lebanon, Turkey, and Central Asia
1926	Lebanese hashish production peaks after World War I until prohibited in 1926.
1928	Recreational use of Cannabis is banned in Britain.
1920s - 1930s	High - quality hashish produced in Turkey near Greek border.
1930	Yarkand region of Chinese Turkestan exports 91,471 kg of hashish legally into the

	Northwest Frontier and Punjab regions of India
1930s	Legal taxed imports of hashish continue into India from Central Asia.
1934 - 1935	Chinese government moves to end all Cannabis cultivation in Yarkand and charas traffic from Yarkand. Both licit and illicit hashish production become illegal in Chinese Turkestan.
1936	Propaganda film "Reefer Madness" made to scare American youth away from using Cannabis.
1937	U.S.: The Marihuana Tax Act is passed, making it illegal to buy, sell, barter, or give away cannabis without paying a transfer tax. This is the first federal law in the U.S. regulating the possession and sale of cannabis. Declared unconstitutional in 1969 in U.S. vs Timothy Leary.
1938	Supply of hashish from Chinese Turkestan nearly ceases.
1940s	Greek hashish smoking tradition fades.
1941	Indian government considers cultivation in Kashmir to fill void of hashish from Chinese Turkestan.
1941 - 1942	Hand-rubbed charas from Nepal is choicest hashish in India during World War II.
1945	Legal hashish consumption continues in India
1945 - 1955	Hashish use in Greece flourishes again
1950s	Hashish still smuggled into India from Chinese Central Asia
1950s	Moroccan government tacitly allows kif cultivation in Rif Mountains.
1962	First hashish made in Morocco.
1963	Turkish police seize 2.5 tons of hashish
1965	First reports of C. afghanica use for hashish production in northern Afghanistan
1965	Mustafa comes to Ketama in Morocco to make hashish from local kif.
Dec 22, 1965	Timothy Leary and 18-year-old daughter Susan searched and arrested by U.S. Customs in Laredo, Texas, after being turned back at the boarder while heading ⁷ into Mexico. Susan was carrying three ounces of cannabis; Tim said it was his.
1966	The Moroccan government attempts to purge kif growers from Rif Mountains.
Mar 11, 1966	Timothy Leary convicted on marijuana charges, fined \$30,000, and sentence to a maximum of 30 years in Federal prison; his 18-year-old daughter Susan who had also been arrested was ordered sent to a Federal reformatory. ⁸ [Details]
1967	"Smash", the first hashish oil appears. Red Lebanese reaches California.
Late 1960s - Early 1970s	The Brotherhood popularizes Afghani hashish.
Aug 21, 1968	Synthetic THC's were placed under control of the DCA in the U.S .
1970 - 1973	Huge fields of Cannabis cultivated for hashish production in Afghanistan. Last years that truly great afghani hashish is available
1972	The Nixon - appointed Shafer Commission urged use of cannabis be re-legalized, but their recommendation was ignored. Medical research continues .
Early 1970s	Lebanese red and blonde hashish of very high-quality exported. The highest quality Turkish hashish from Gaziantep near Syria appears in western Europe.
Early 1970s	Afghani hashish varieties introduced to North America for sinsemilla production. Westerners bring metal sieve cloths to Afghanistan. Law enforcement efforts against hashish begin in Afghanistan
1973	Nepal bans the Cannabis shops and charas (hand-rolled hash) export.
1973	Afghan government makes hashish production and sales illegal. Afghani harvest is pitifully small.
1975	FDA establishes Compassionate Use program for medical marijuana.
1976 - 1977	Quality of Lebanese hashish reaches zenith.
1978	Westerners make sieved hashish in Nepal from wild Cannabis.
Late 1970s	Increasing manufacture of "modern" Afghani hashish. Cannabis varieties from Afghanistan imported into Kashmir for sieved hashish production.
1980s	Morocco becomes one of, if not the largest, hashish producing and exporting nations.
1980s	"Border" hashish produced in northwestern Pakistan along the Afghan border to avoid Soviet-Afghan war.

Early 1980s	Quality of Lebanese hashish declines.
1983 - 1984	Small amounts of the last high - quality Turkish hashish appear.
1985	Hashish still produced by Muslims of Kashgar and Yarkland (NW China) .
1986	Most private stashes of pre-war Afghani hashish in Amsterdam, Goa, and America are nearly finished.
May 13, 1986	Dronabinol is placed into Schedule II by the DEA.
1987	Moroccan government cracks down upon Cannabis cultivation in lower elevations of Rif Mountains.
1988	DEA administrative law Judge Francis Young finds after thorough hearings that marijuana has clearly established medical use and should be reclassified as a prescriptive drug. His recommendation is ignored.
1993	Cannabis eradication efforts resume in Morocco.
1994	Heavy fighting between rival Muslim clans continues to upset hashish trade in Afghanistan
1994	Border hashish still produced in Pakistan.
1995	Introduction of hashish - making equipment and appearance of locally produced hashish in Amsterdam coffee shops.
Oct 23, 2001	Britain's Home Secretary, David Blunkett, proposes relaxing the classification of cannabis from a class B to class C. As of June 10, 2002, this has not taken effect .

Cannabis Time line

A historical timeline of Cannabis through the ages :

6000 B.C.

Cannabis seeds used for food in China

4000 B.C.

Textiles made of hemp are used in China. Remains have been found of hemp fibers from this period and from Turkestan a century later.

2727 B.C.

First recorded use of cannabis as medicine in Chinese pharmacopoeia. In every part of the world humankind has used cannabis for a wide variety of health problems.

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Scythians cultivate cannabis and use it to weave fine hemp cloth.

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700 - 300 B.C.

Scythian tribes leave Cannabis seeds as offerings in royal tombs.

500 B.C.

Scythian couple die and are buried with two small tents covering censers. Attached to one tent stick was a decorated leather pouch containing wild Cannabis seeds. This closely matches the stories told by Herodotus. The gravesite, discovered in the late 1940s, was in Pazryk, northwest of the Tien Shan Mountains in modern-day Khazakstan.

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Hemp is introduced into Northern Europe by the Scythians. An urn containing leaves and seeds of the Cannabis plant, unearthed near Berlin, is dated to about this time.

500 - 100 BC

Hemp spreads throughout northern Europe.

430 B.C.

Herodotus reports on both ritual and recreation use of Cannabis by the Scythians (Herodotus *The Histories* trans. G. Rawlinson).

100 - 0 B.C.

The psychotropic properties of Cannabis are mentioned in the newly compiled herbal *Pen Ts'ao Ching* which is attributed to an emperor c. 2700 B.C.

0 - 100 A.D.

Construction of Samartian gold and glass paste stash box for storing hashish, coriander, or salt, buried in Siberian tomb.

70

Dioscorides mentions the use of Cannabis as a Roman medicament.

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Galen (Roman) alludes to the psychoactivity of Cannabis seed confections.

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Scholars debate the pros and cons of eating hashish. Use spreads throughout Arabia.

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In Khorasan, Persia, Hasan ibn al-Sabbah, the Old Man of the Mountain, recruits followers to commit assassinations...legends develop around their supposed use of hashish. These legends are some of the earliest written tales of the discovery of the inebriating powers of Cannabis and the supposed use of Hashish.

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Arab traders bring Cannabis to the Mozambique coast of Africa.

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Hashish introduced to Iraq in the reign of Caliph Mustansir (Rosenthal 1971)

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1378

Ottoman Emir Soudoun Scheikhouni issues one of the first edicts against the eating of hashish.

1526

Babur Nama, first emperor and founder of Mughal Empire learned of hashish in Afghanistan.

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Angolan slaves brought cannabis with them to the sugar plantations of northeastern Brazil. They were permitted to plant their cannabis between rows of cane, and to smoke it between harvests.

mid 16th Century

The epic poem, Benk u Bode, by the poet Mohammed Ebn Soleiman Foruli of Baghdad, deals allegorically with a dialectical battle between wine and hashish.

17th Century

Use of hashish, alcohol, and opium spreads among the population of occupied Constantinople.

1606-1632

French and British cultivate Cannabis for hemp at their colonies in Port Royal (1606), Virginia (1611), and Plymouth (1632).

Late 17th Century

Hashish becomes a major trade item between Central Asia and South Asia.

1798

Napoleon discovers that much of the Egyptian lower class habitually uses hashish (Kimmens 1977). He declares a total prohibition. Soldiers returning to France bring the tradition with them.

19th Century

Hashish production expands from Russian Turkestan into Yarkand in Chinese Turkestan.

1809

Antoine Sylvestre de Sacy, a leading Arabist, reveals the etymology of the words "assassin" and "hashishin".

1840

In America, medicinal preparations with a Cannabis base are available. Hashish available in Persian pharmacies.

1843

Le Club des Hachichins, or Hashish Eater's Club, established in Paris.

c.1850

Hashish appears in Greece.

1856

British tax ganja and charas trade in India.

1870 - 1880

First reports of hashish smoking on Greek mainland.

c. 1875

Cultivation for hashish introduced to Greece.

1877

Kerr reports on Indian ganja and charas trade.

1890

Greek Department of Interior prohibits importation, cultivation and use of hashish.

1890

Hashish made illegal in Turkey.

1893 - 1894

The India Hemp Drugs Commission Report is issued.

1893 - 1894

70,000 to 80,000 kg of hashish legally imported into India from Central Asia each year.

1906

Pure Food and Drug Act is passed, regulating the labelling of products containing Alcohol, Opiates, Cocaine, and Cannabis, among others. The law went into effect Jan 1, 1907.

Early 20th Century

Hashish smoking very popular throughout the Middle East.

1915 - 1927

Cannabis begins to be prohibited for nonmedical use in the U.S., especially in SW states.

1920

Metaxas dictators in Greece crack down on hashish smoking.

1920s

Hashish smuggled into Egypt from Greece, Syria, Lebanon, Turkey, and Central Asia.

1926

Lebanese hashish production peaks after World War I until prohibited in 1926.

1928

Recreational use of Cannabis is banned in Britain.

1920s - 1930s

High-quality hashish produced in Turkey near Greek border.

1930

Yarkand region of Chinese Turkestan exports 91,471 kg of hashish legally into the Northwest Frontier and Punjab regions of India.

1930s

Legal taxed imports of hashish continue into India from Central Asia.

1934 - 1935

Chinese government moves to end all Cannabis cultivation in Yarkand and charas traffic from Yarkand. Both licit and illicit hashish production become illegal in Chinese Turkestan.

1936

Propaganda film "Reefer Madness" made to scare American youth away from using Cannabis.

1937

Cannabis made federally illegal in the U.S. with the passage of the Marihuana Tax Act.

1938

Supply of hashish from Chinese Turkestan nearly ceases.

1940s

Greek hashish smoking tradition fades.

1941

Indian government considers cultivation in Kashmir to fill void of hashish from Chinese Turkestan.

1941 - 1942

Hand-rubbed charas from Nepal is choicest hashish in India during World War II.

1945

Legal hashish consumption continues in India.

1945 - 1955

Hashish use in Greece flourishes again.

1950s

Hashish still smuggled into India from Chinese Central Asia.

1950s

Moroccan government tacitly allows kif cultivation in Rif Mountains.

1962

First hashish made in Morocco.

1963

Turkish police seize 2.5 tons of hashish.

1965

First reports of *C. afghanica* use for hashish production in northern Afghanistan.

1965

Mustafa comes to Ketama in Morocco to make hashish from local kif.

1966

The Moroccan government attempts to purge kif growers from Rif Mountains.

1966

England win the World Cup.

1967

"Smash", the first hashish oil appears. Red Lebanese reaches California.

Late 1960s - Early 1970s

The Brotherhood popularizes Afghani hashish.

1970 - 1973

Huge fields of Cannabis cultivated for hashish production in Afghanistan. Last years that truly great afghani hashish is available.

1972

The Nixon-appointed Shafer Commission urged use of cannabis be re-legalized, but their recommendation was ignored. Medical research continues.

Early 1970s

Lebanese red and blonde hashish of very high-quality exported. The highest quality Turkish hashish from Gaziantep near Syria appears in western Europe.

Early 1970s

Afghani hashish varieties introduced to North America for sinsemilla production. Westerners bring metal sieve cloths to Afghanistan. Law enforcement efforts against hashish begin in Afghanistan.

1973

Nepal bans the Cannabis shops and charas (hand-rolled hash) export.

1973

Afghan government makes hashish production and sales illegal. Afghani harvest is pitifully small.

1975

FDA establishes Compassionate Use program for medical marijuana.

1976 - 1977

Quality of Lebanese hashish reaches peak.

1978

Westerners make sieved hashish in Nepal from wild Cannabis.

Late 1970s

Increasing manufacture of "modern" Afghani hashish. Cannabis varieties from Afghanistan imported into Kashmir for sieved hashish production.

1980s

Morocco becomes one of, if not the largest, hashish producing and exporting nations.

1980s

"Border" hashish produced in northwestern Pakistan along the Afghan border to avoid Soviet-Afghan war.

Early 1980s

Quality of Lebanese hashish declines.

1983 - 1984

Small amounts of the last high-quality Turkish hashish appear.

1985

Hashish still produced by Muslims of Kashgar and Yarkland (NW China).

1986

Most private stashes of pre-war Afghani hashish in Amsterdam, Goa, and America are nearly finished.

1987

Moroccan government cracks down upon Cannabis cultivation in lower elevations of Rif Mountains.

1988

DEA administrative law Judge Francis Young finds after thorough hearings that marijuana has clearly established medical use and should be reclassified as a prescriptive drug. His recommendation is ignored.

1993

Cannabis eradication efforts resume in Morocco.

1994

Heavy fighting between rival Muslim clans continues to upset hashish trade in Afghanistan.

1994

Border hashish still produced in Pakistan.

1995

Introduction of hashish-making equipment and appearance of locally produced hashish in Amsterdam coffee shops.

Oct 23, 2001

Britain's Home Secretary, David Blunkett, proposes relaxing the classification of cannabis from a class B to class C. As of June 10, 2002, this has not taken effect.

COCA TIME LINE

- c. 3000 BCE Coca chewing is practiced throughout South America. Coca is believed to be a gift from God.
- 15th Century Coca plantations are operated by Incas in Peru.
- 1505 First hand accounts of coca use made their way back to Europe. Amerigo Vespucci (1505), G Frenandez de Oviedo (1535), and Nicholas Monardes (1565).
- Early 1500s Incan Coca plantations are taken over by holders of Spanish land grants. Spanish tax laws are revised to allow land owners to make their tax payments in coca leaves.
- 1539 The Bishop of Cuzco tithes coca, taking 1/10 of the value of each crop in taxes.
- Mid 1500s Inca Empire. Pizarro invades and destroys the Inca Empire (1553); Coca production in Peru expands quickly causing a glut of leaf on the market which in turn precipitated a drop in the price of coca. Nicolas Monardes reports an increase in coca chewing particularly among lower classes of Andean Indians, as traditional controls disappear (1569).
- 1574 Monardes' text on Coca is first translated into other European languages from Spanish; Latin (1574), Italian (1576), English (1577).
- c. 1575 Forced laborors working in the Spanish silver mines were kept well supplied with Coca leaves. Roughly 8% of the Europeans living in Peru were involved in the Coca trade.
- 1580 Europe. Monardes brings coca leaves to Europe; unlike tobacco, it fails to generate interest or use, probably because most coca leaves lost their

potency during the long voyage.

- 1662 Abraham Cowley writes a poem titled "A Legend of Coca". This is the first independent mention of coca in English literature.
- 1708 Coca is first mentioned in a materia medica, *Institutiones Medicae*, written by German physician and botanist Herman Boerhaave.
- 1835 First accurate drawing of Coca appears in popular English press. The illustration by Sir William Hooker, director of the Kew gardens, was published in *Companion to the Botanical Magazine*.
- c. 1850 Coca tinctures used in throat surgery.
- c. 1855 Cocaine first extracted from Coca leaves.
- 1862 Merck produces 1/4 pound of cocaine.
- 1863 Angelo Mariani patents a preparation of coca extract and Bordeaux wine called Vin Mariani.
- 1869 Seeds from the commercial variety of Coca arrived at Kew Gardens.
- 1870 Vin Mariani (Coca wine) is for sale throughout France, containing 6 mg cocaine per ounce of wine. Exported Vin Mariani contained 7.2 mg per ounce to compete with the higher cocaine content of American competitors.
- 1870s Parke, Davis manufactures a fluid extract of coca.
- 1876 - 1885 Race walkers in England chew Coca leaves to improve their performance.
- 1883 Merck produces 3/4 pound of Cocaine.
- 1883 German physician Theodor Aschenbrandt administered cocaine to members of the Bavarian army to enhanced their endurance on

- manoeuvres. Aschenbrandt's study published in a German medical journal would be read by young Viennese neurologist, Sigmund Freud.
- 1884 Cocaine's use as a local anesthetic in eye surgery is popularized.
- 1884 Freud publishes *On Coca* in which he recommends the use of cocaine to treat a variety of conditions including morphine addiction.
- 1884 Merck produces 3,179 pounds of Cocaine.
- 1886 Merck produces 158,352 pounds of Cocaine.
- 1886 Coca - Cola is first introduced by John Pemberton, containing cocaine laced syrup and caffeine.
- Late 1880s Parke,Davis starts to manufacture refined cocaine.
- c. 1901 Coca - Cola removed Coca from their formula.
- 1903 The expiration of a patent on the cocaine extraction process increases demand for coca.
- c. 1905 Snorting cocaine becomes popular.
- 1906 Pure Food and Drug Act is passed, regulating the labelling of products containing Alcohol, Opiates, Cocaine, and Cannabis, among others. The law went into effect Jan 1, 1907
- 1910 First cases of nasal damage from Cocaine snorting are written of in medical literature.
- 1910 First cases of nasal damage from Cocaine snorting are seen in hospitals.
- 1912 U.S. government reports 5,000 Cocaine related fatalities in one year.
- Dec 17, 1914 The Harrison Narcotics Tax Act is passed, regulating and imposing a tax upon the sale of

	Opium, Heroin and Cocaine for the first time. The Act took effect Mar 1, 1915.
Early 1930s	Japan is the world's leading cocaine producer (23.3%) followed by the United States (21.3%), Germany (15%), U.K. (9.9%), France (8.3%).
1920-1970	Cocaine use subsides in the U.S. One Bureau of Narcotics supervisor in New York City reported in 1940 that they "rarely hear of cocaine being used".
Oct 27, 1970	The Comprehensive Drug Abuse Prevention and Control Act is passed. Part II of this is the Controlled Substance Act (CSA) which defines a scheduling system for drugs. It places most of the known hallucinogens (LSD, psilocybin, psilocin, mescaline, peyote, cannabis, & MDA) in Schedule I. It places coca, cocaine and injectable methamphetamine in Schedule II. Other amphetamines and stimulants, including non-injectable methamphetamine are placed in Schedule III.
c. 1976	Freebase cocaine first developed (probably in California). It would soon be popularized by dealers and glamorized by Hollywood media.
1981	Wholesale cost of 1 kg of cocaine is \$55,000.
1984	Wholesale cost of 1 kg cocaine is \$25,000.
Mid 1980's	Freebase cocaine becomes popular.

Coffee Time line

In the Beginning :

In the Coffee timeline, myth has it that roughly around the ninth century an Abyssinian goat herder named Kaldi discovered some of coffees stimulant properties.

Coffee timeline Pre - 1400's

Before 1000 A.D.: When the people of the Galla tribe in Ethiopia, mixed a particular berry ground up with animal fat they noticed a rise in their energy.

1000 A.D.: When Arab traders first brought the coffee bean back to their homeland to farm the bean for the first time. Also made a drink out of the coffee bean that they called "qahwa".

Coffee timeline 1400's

1453: Ottoman Turks pioneered coffee for the first time. A little unknown possible fact is that if a Turkish man doesn't give his wife a daily portion of coffee she can divorce him.

1475: Legend has it that the first known coffee diner opened in Kiva Han making this one more to add to the history of coffees legend.

Coffee timeline 1500's

1511: The foul Governor Khair Beg of the land of Mecca attempted a ban on coffee for fear of a riot against him. For this act the King of Mecca made coffee sacred and had Khair Beg put to death.

Coffee timeline 1600's

1607: It is believed that North America was introduced to coffee by Capt. John Smith at the Jamestown colony in Virginia.

1615: Pope Clement the VIII heard of an Italian merchant selling coffee and was informed by his priests that coffee was the tool of the devil. Clement, not to be foolish, requested a sample of the coffee and

in doing so fell in love with it, so he baptized it and made it a "truly Christian Beverage."

1645: It's believed that the first coffee diner opened in Italy.

1652: The first coffee house opens in England. By popular demand more coffee diners open for the rich and commoners. Due to quality discussions the coffee shops were labeled "Penny Universities" because of the price of coffee.

1668: Beer: New York's City's favorite breakfast drink was replaced by coffee.

1668: Lloyd's of London, the most purchased insurance provider in London became famous from when it first opened as a coffee diner. Travel merchants and insurance salesman frequented this diner.

1672: The first Paris coffee diner opens.

1675: Franz Georg Kolschitzky escaped the Rebel Turkish Soldier's in Vienna to lead military aid back to the city. The skedaddling Turkish rebels left behind a bag of coffee grounds. Snatching the grounds as his reward, Franz used the grounds to open Europe's first coffee diner and in doing so refined the method of filtering the grounds and adding sugar for sweetener.

1690: The Dutch smuggled a coffee plant out of the Arab port "Mocha" for transplantation and cultivation. This is where the name "Java" comes from which is one of the cities that opened a plantation.

Coffee timeline 1700's

1713: Gabriel Mathieu do Clieu in 1723 steals a seedling from France. Within 50 years an estimated 19 million coffee plants, 90 percent of the world's coffee spreads from this plant.

1721: Berlins' first coffee diner opens.

1727: Lieutenant colonel Francisco de Melo Palheta woos France's Governor of Guiana's wife into stealing and smuggling germinated coffee seedlings in a flowers basket for him. He returns to Brazil from which he was dispatched to settle a feud between the French and

Dutch about country border lines, only to have successfully stolen coffee while settling the dispute.

1732: Johann Sebastian Bach's famous one-act operetta, the "Coffee Cantata," was a not so liked operatic criticism of the extraordinary lengths the royal and upperclass took to keep commoners from drinking coffee.

1773: In America the Boston Tea Party allowed the experimentation with and also a popular form of protest when drinking coffee.

1775: "Prussia's" Frederick the Great's wealth is diminished trying to stop imports of coffee and the public scorn of his foolishness leads to a change of heart.

Coffee timeline 1800's

1886: Wholesale grocer Joel Cheek names a coffee blend "Maxwell House," after the hotel in Nashville, TN where it was served.

Coffee timeline 1900's

Early 1900's: In Germany, "Kaffee klatsch" is coined to describe woman's gossip. These afternoon coffee gatherings become a standard occasion.

1900: When the Hills Brothers start packaging coffee in metal tins, they half heartedly kill the coffee shop diners and mills.

1901: Satori Kato Japanese-American chemist of Chicago invents instant coffee.

1903: Sanka is introduced to the United States in 1923. Ludwig Roselius admits a batch of destroyed coffee beans over to chemist's, who remove caffeine from the coffee beans without losing the flavor. Then sells it as the brand name "Sanka."

1906: George Constant Washington, an English chemist living in Guatemala, notices a powdery condensation forming on the spout of his silver coffee holder. After experimentation, he creates the first mass-produced instant coffee (his brand is called Red E Coffee).

1920: United States institute prohibition, and coffee sales explode.

1938: Having been asked by Brazil to help find a solution to their coffee surpluses, Nestle company invents freeze-dried coffee. Nestle develops Nescafe and introduces it in Switzerland.

1940: The US imports 70 percent of the worlds coffee.

1942: During W.W.II, American soldiers are issued instant Maxwell House coffee in their ration kits. Back home, widespread hoarding leads to coffee rationing.

1946: Achilles Gaggia finishes his espresso machine In Italy. Cappuccino is named for the resemblance of its color to the robes of the monks of the Capuchin monastery.

1969: One week before Woodstock premiers the Manson Family murders coffee mogul Abigail Folger as she visits film maker Roman Polanski with Sharon Tate.

1971: The first Starbucks opens in Seattle's Pike Place public market.

This concludes the Coffee timeline for now.

Datura Time line

c. 5th Century BCE
Legend has it that when the Buddha preaches, dew or raindrops fall from the heaven onto Datura plants .
c. 301 BCE
Theophrastus, a student of Aristotle, writes about the hallucinogenic effects of Datura stramonium. The text contains one of the earliest references to the concept of tolerance to a drug .
c. 4th - 6th Century CE
The <i>Kamasutra</i> of Vātsyāyana includes at least two references to datura. One reference instructs a man to annoint his penis with honey infused with datura before sexual intercourse, to make his partner "subject to his will " .
c. 8th Century
The Buddhist scripture <i>Guhyasamāja Tantra</i> instructs in the ritual use of datura .
c. 10th Century
The Buddhist scripture <i>Vajramahabhairava Tantra</i> refers to Datura metel several times .
11th - 12th century
Datura is associated with the worship of Shiva, the Indian god associated with the creative and destructive aspects of the universe .
11th Century
Arabian doctor Avicenna reported on Datura metel under then name 'Jouzmatal ('metel nut'). This report was later repeated in Dioscorides's writings .
1543
Leonard Fuchs includes a drawing of Datura stramonium in his herbal .
1578
Datura is used as an aphrodisiac in the East Indies .
1676
A group of soldiers in Jamestown, Virginia ingest boiled datura and become delirious for days .
1968

Datura over – the - counter remedies for asthma are banned after people begin using them recreationally

1968

Carlos Castaneda gives a fictionalized account of the use of datura in his best - selling book The Teachings of Don Juan .

Oct 24, 1968

In response to reports of the recreational use of medications containing Datura stramonium, the FDA adopted a policy that preparations of D. stramonium that are labelled with directions for use in self - medication will be considered " misbranded " , a federal crime.

HASHISH TIME LINE

6000 B.C

Cannabis seeds used for food in China

2000 B.C. - 1400 B.C

Cannabis mentioned in the *Atharvaveda* (Science of Charms) as "sacred grass". Referred to as bhang or bhanga. The legend of Shiva, Lord of Bhang .

1500 B.C.

Cannabis cultivated in China for food and fiber , but not hashish

1500 B.C

Scythians cultivate *Cannabis* and weave fine hemp cloth from it .
(Sumach 1975)

700 B.C. - 600 B.C.

The Zoroastrian *Zend - Avesta*, an ancient Persian religious text of several hundred volumes, and said to have been written by Zarathustra (Zoroaster) , refers to bhang as Zoroaster's " good narcotic " (*Vendidad* or *The Law Against Demons*) .

700 B.C. - 300 B.C.

Scythian tribes leave *Cannabis* seeds as offerings in royal tombs

500 B.C.

Scythian couple die and are buried (at grave site in Pazryk , north west of the Tien Shan Mountains in modern - day Khazakstan) with two small tents covering censors. Attached to one tent stick was a decorated leather pouch containing wild *Cannabis* seeds. Unknown whether this was for purely ritual or also intoxicating use of *Cannabis*.

430 B.C.

Herodotus reports on both ritual and recreation use of *Cannabis* by the Scythians (Herodotus *The Histories* 430 B.C. trans. G. Rawlinson) .

100 B.C. - 0 A.D.

The *Pen Ts'ao* mentions Cannabis for medical use

0 A.D. - 100 A.D.

Construction of Samartian gold and glass paste stash box for storing hashish, coriander , or salt , buried in Siberian tomb .

70 A.D.

Dioscorides mentions the use of Cannabis as a medicament (Roman)

170 A.D.

Galen alludes to the psychoactiity of *Cannabis* seed confections (Roman) .

500 A.D. - 600 A.D.

The Jewish Talmud mentions the euphoriant properties of *Cannabis* (Abel 1980)

900 A.D. - 1000 A.D.

Scholars debate the pros and cons of eating hashish. Use spreads throughout Arabia

1090 A.D. - 1256 A.D.

In Khorasan , Persia , Hasan ibn al – Sabbah , the Old Man of the Mountain , recruits followers to commit assassinations...legends develop around their supposed use of hashish . These legends are some of the earliest written tales of the discovery of the inebriating powers of *Cannabis* and the supposed use of Hashish. 1256 Alamut falls .

1155 A.D. - 1221 A.D.

Persian legend of the Sufi master Sheik Haidar's of Khorasan's

personal discovery of *Cannabis* and its subsequent spread to Iraq, Bahrain, Egypt and Syria. Another of the earliest written narratives of the use of *Cannabis* as an inebriant .

Early 12th Century

Hashish smoking very popular throughout the Middle East.

12th Century A.D.

Cannabis introduced in Egypt during the reign of the Ayyubid dynasty on the occasion of the flooding of Egypt by mystic devotees coming from Syria (M.K. Hussein 1957 - Soueif 1972)

1231 A.D.

Hashish introduced to Iraq in the reign of Caliph Mustansir (Rosenthal 1971)

1271 A.D. -1295 A.D.

Journeys of Marco Polo in which he gives second-hand reports of the story of Hasan ibn al - Sabbah and his "assassins" using hashish. (link)

13th Century A.D.

The oldest monograph on hashish, *Zahr al-'arish fi tahrir al-hashish*, was written. It has since been lost.

13th Century A.D .

Ibn al-Baytar of Spain provides a description of psychoactive *Cannabis* .

1378 A.D.

Ottoman Emir Soudoun Scheikhouni issues one of the first edicts against the eating of hashish .

1526 A.D.

Babur Nama, first emperor and founder of Mughal Empire learned of hashish in Afghanistan.

mid 16 th Century A.D.

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1994 : Border hashish still produced in Pakistan

1995 : Introduction of hashish - making equipment and appearance of locally produced hashish in Amsterdam coffee shops.

Khat Time line

6th Century
One scholarly theory describes that khat use began in Yemen before the 6th Century at which time it was brought to Ethiopia. Another theory is that khat use began in Ethiopia itself before this time .
1065
The earliest printed reference to khat is found in the Kitab al-Saidana fi al-Tibb, a work on pharmacy and materia medica written by Abu al - Biruni .
1222
Khat is first identified as a plant useful for its healing properties in an Arabic book of medicinal remedies by Nagib ad - Din as - Samarkandi of Turkestan .
c. 1400
Al - Maqrizi (1364 – 1442) describes khat use in a history of the Ethiopian wars of the period .
14th or 15th Century
The popular use of khat in Yemen begins in the southern part of the western highlands .
17th Century
A poetic play written by Yemeni Jew Sholem bin Joseph al - Shibezi presents a dialog between coffee and khat, evidence that khat was in use by Yemeni Jews at this time .
1775
Swedish botanist Pehr Forsskal provides the first concise description of khat in European literature after visiting Yemen in 1763 .
Late 19 Century
European scientists investigate the chemistry and pharmacology of khat .
1920s and 1930s
Khat - based pharmaceuticals and " agents of pleasure " are sold in London , including catha-cocoa milk ,

1930
Cathine is first isolated from <i>Catha edulis</i> .
1970s
Cathinone is first isolated from <i>Catha edulis</i> .
1980
WHO classifies khat as a drug of abuse.
Mar 26, 1982
The U.S. FDA issues the first of several Import Alerts about <i>Catha edulis</i> declaring it an unapproved drug and stating that it should be seized at the border.
May 17, 1988
The DEA places cathine, one of the psychoactive alkaloids in khat, in Schedule IV on a temporary basis in order to comply with international treaties. Though formal scheduling was required within a "reasonable" period of time, no formal scheduling procedures have been undertaken and the temporary scheduling is still in effect.
Feb 9, 1993
The FDA issues an additional Import Alert stating <i>Catha edulis</i> "will be subject to the same controls as cathine" and should be seized at the U.S. border.
1993
Cathinone is placed in Schedule I under the Controlled Substances Act in the United States.

Poppy & Opium Time line

3400 BCE
Opium poppy cultivated in lower Mesopotamia...called <i>Hul Gil</i> , or " joy plant " by the Sumerians
1300 BCE
Egyptians cultivate opium poppies during the reign of Thutmose IV, Akhenaton and King Tutankhamen. They reportedly trade the item across the Mediterranean into Greece and Europe .
1100 BCE
On the island of Cyprus, the " Peoples of the Sea " craft surgical - quality culling knives to harvest opium, which they would cultivate, trade and smoke before the fall of Troy .
330 BCE
Alexander the Great introduces opium to the people of Persia and India.
300 BCE
Opium used by Arabs, Greeks, and Romans as a sedative and soporific .
160 - 180
Marcus Aurelius, emperor of Rome, habitually took opium to sleep and to cope with the difficulty of military campaigns .
400
Opium thebaicum, from the Egyptian fields at Thebes, is first introduced to China by Arab traders .
c. 1000
India . Opium is cultivated, eaten, and drunk by all classes as a household remedy; it is used by rulers as an indulgence , and given to soldiers to increase their courage
c. 1000
China. The medicinal use of opium poppy seeds is widespread . By 1100, the more potent capsule is in use, but pure opium is not extracted from the capsule

1300s
Opium disappears from European historical record due to the Holy Inquisition. " In the eyes of the Inquisition, anything from the East was linked to the Devil " .
c. 1500
China. The medicinal use of pure opium is fully established ; native opium is manufactured , but recreational use is still limited .
c. 1500
India. Earliest western records of opium as a product of India and its widespread use occur .
1526
India. The first Moghul dynasty is founded - poppy cultivation and opium sales become a state monopoly .
1527
Opium is reintroduced into European medical literature by Paracelsus as " laudanum ". These black pills or " Stones of Immortality " were made of opium thebaicum , citrus juice and quintessence of gold and prescribed as painkillers .
15th - 16th Century
" Syrup of poppy " and other poppy preparations are commonly prepared and used medicinally by monastic communities that devoted major efforts to the production and improvement of herbal medicines .
Apr 10, 1563
" Conversations on the simples, drugs and materia medica of India " is published by Portuguese physician Garcia de Orta. It discusses Cannabis, Opium, and Nutmeg, among more than 50 medicinal plants and substances .
17th Century
Use of hashish, alcohol, and opium spreads among the population of occupied Constantinople
c. 1700
Use of tobacco-opium mixtures (madak) begins in the East Indies (probably Java) spreads to Formosa , Fukien and the South China coast (refs). In 1689, Engelberg

Kaempfer inspects primitive dens where the mixture is dispensed .
1729
Reports reach Peking of the evils of opium smoking (shrivelling up the features ; early deaths) in Formosa and Fukien ; Emperor Yung Chen prohibits the sale of opium and the operation of smoking houses .
c. 1750
The British East India Company assumes control of Bengal and Bihar, the opium growing districts of eastern India; British shipping dominates the Bengal opium trade out of Calcutta .
1757
Britain annexes Bengal ; the Chinese confine foreign trade to Canton where it can be restricted and controlled in the interests of revenue for the Chinese . Hong Kong merchants serve as intermediaries between the foreigners and the Chinese authorities .
1767
Opium from Bengal continues to enter China despite the edict of 1729 prohibiting smoking. It increases in frequency from 200 chests annually in 1729 to 1000 annually by 1767 . However, much is for medicinal use. Tariffs are collected on the opium .
1772
The East India company establishes a limited monopoly over Bengal opium .
1773 - 1786
Warren Hastings, the first governor general of India, recognizes that opium is harmful and at first opposes increasing production; later he encourages the control of opium by the company hoping that by monopolizing and limiting the supply he will discourage its consumption. This limited monopoly lasts throughout his administration and beyond, but when the Chinese market is discovered, the monopoly shifts from controlling to expanding cultivation .

1779
First mention of actual trading in opium at Canton .
1780
British traders establish an opium depot at Macao . Another imperial edict prohibits consumption of opium and reiterates prohibition of its sale .
1787
Trade in opium is still less important than trade in commodities ; directors of the East India Company , recognizing China's objections to the importation of opium, make offers to prohibit the export of Indian opium to China . However, company representatives in Canton declare that the Chinese are never sincere in their declared intentions of suppressing illicit traffic , as long as the officials issue prohibitory edicts with one hand and extend the other to receive bribes from the illegal trade .
1796
Alarmed by increasing use, the emperor of China issues an edict forbidding importation of opium , as well as export of Chinese silver that is being used as a medium of exchange. Now even legitimate trade is limited to barter . Nonetheless , illegal purchase of opium with silver continues .
1797
The East India Company assumes full control of Bengal opium .
1799
The 1799 edict increases traffic through Macao and other areas beyond government control enabling UNPRECEDENTED GROWTH . The British declare only their legitimate cargo, leave opium on board to be picked up by Chinese mercahnts who smuggle it ashore in small, fast boats .
1799
A strong edict by authorities at Canton, supporting the emperor's decree of 1796 , forbids opium trade at that port. A concurrent drive against native poppy growing is

initiated. Opium becomes an illicit commodity .
1800 - 1820
Domestic opium cultivation is encouraged by increased opium use , along with rising prices and problems with adulteration . It declines after the 1820s , but there does not appear to have been any call for controls .
1800s
Patent medicines and opium preparations such as _ Dover's Powder were readily available without restrictions . Indeed, Laudanum (opium mixed with alcohol) was cheaper than beer or wine and readily within the means of the lowest-paid worker . As a result, throughout the first half of the 19th century, the incidence of opium dependence appears to have increased steadily in England , Europe and the United States. Working-class medicinal use of opium-bearing _ nostrums _ as sedatives for children was especially prominent in England. However, despite some well known cases among 19th century English literary and creative personalities -- Thomas de Quincey , Byron , Shelley , Coleridge , and Dickens -- recreational use was limited, and there is no evidence that use was so excessive as to be a medical or social concern .
1800
Opium becomes identified with official corruption, criminals and antigovernment secret societies. An imperial edict prohibits domestic cultivation and repeats the prohibition against importing opium. China develops an anti-opium policy, at least on paper. Edicts continue to be issued reiterating prohibitions against importation, sale, and consumption of opium .
1803
Morphine isolated from poppies by 20 – year - old German pharmacist Friedrich Wilhelm Adam Serturmer . This may have been the first plant alkaloid ever isolated and set off a firestorm of research into plant alkaloids. Within half a century, dozens of alkaloids, such as atropine, caffeine,

cocaine, and quinine, had been isolated from other plants and were being used in precisely measured doseages for the first time .
1804
Opium trading resumes at the port of Canton. Though the 1799 edict is still in force, it has little effect and no immediate practical change in policy ensues .
1834 - 1850
An awareness grows of endemic opium use among Fenish peoples, who both tolerate and successfully control their use by informal social mechanisms. Use is particularly widespread among poorer classes, agricultural populations, the inhabitants of small hamlets and isolated farms, and women and babies. Contemporary observers attribute initiation of use for the rheumatic pains which plague almost everyone in this low-lying marshy area .
1839
Opium and its preparations are responsible for more premature deaths than any other chemical agent. Opiates account for 186 of 543 poisonings, including no fewer than 72 among children .
1850 - 1865
U.S.: Tens of thousands of chinese laborers immigrate to the U.S . in a period of labor shortage, bringing the habit of opium smoking with them .
1878
U.S. : San Francsico passes an ordinance making it a misdemeanor to " keep , or maintain , or visit , or in any way contribut to the support of any place, house, or room, where opium is smoked " . Importation , sales and possession of opium remain legal .
1887
U.S.: The importation of opium by Chinese (but not by Americans) is forbidden .
1900-1906
China : 27 % of the adult male population of China is addicted to opium. This is about 3.5 % of the total

population of the country .
1906
More than 50,000 opium containing medicines have been patented .
1906
Pure Food and Drug Act is passed , regulating the labelling of products containing Alcohol , Opiates , Cocaine , and Cannabis, among others. The law went into effect Jan 1 , 1907 .
1912
U.S. government publication reports 5,000 fatal poisonings in one year, mostly related to opium and cocaine .
Dec 17, 1914
The Harrison Narcotics Tax Act is passed, regulating and imposing a tax upon the sale of Opium, Heroin and Cocaine for the first time. The Act took effect Mar 1, 1915
1942
The Opium Poppy Control Act prohibits the possession or growing of the opium poppy without a license .

Tea Time line

2,737 BCE
Chinese tradition places the discovery of tea by the Emperor Shen Nung. At this time the only tea produced is " green " tea.
3rd Century BCE
first drying processes developed. Before this time fresh leaves are brewed. Now leaves are dried and powdered.
1027 BCE
King Wen, founder of the Zhou Dynasty, receives tea as tribute from leaders in the Szechwan district.
551 - 479 BCE
Confucius documented as a tea drinker.
221 - 206 BCE
Liu Kun, a military leader in the Qin Dynasty writes to his nephew requesting "real tea" to lift his spirits.
74 - 49 BCE
Slave contract indicating duties including the buying and making of tea.
59 BCE
Wang Boa gives instructions in his book on how to buy tea and brew it .
206 BCE – CE 220
(Han Dynasty) Emperor specifies proper pronunciation of the word tea - Cha, distinguishing it from other plants that are described by the same character.
350
First entry of the word " tea " (cha) in the revised Erya Encyclopedia (600 year old reference work).
420 – 588
Wong Mong a government officer during Southern and Northern Dynasty is described as a man unable to live without tea. His tendency to inundate his guests with tea was referred to as " flooding " .
542 – 476
Tea bartered with the Turkic peoples.
542

The Myth of Ta Mo or Bodhidharma. Buddhist master from India who brought Buddhism to China and founded the Zen School, Said to discover the virtues of tea (cha) after cutting off his eyelids to stay awake during meditation .
618 – 907
Tang Dynasty. By this time tea is a universal drink. Brick tea is made by steaming the fresh leaves, which are then powdered, and formed into cakes. Cakes can be stored for long periods of time and pieces are broken off and boiled when needed. Early forms of the Tea ceremony develop. Tibet and India trading for tea.
Eight Century
A unique character for the word Cha is developed.
729
Japanese Emperor Shomu serves tea to 100 monks in the palace.
780
Lu Yu (the father of tea) publishes the Cha Ching (or Tea Classic) , summing up everything that is known about tea at that point. Tea drinking is developed into an art with prescribed rituals. China is the largest empire on the earth, trading tea with most of its neighbors. Kukai, patriarch of the Shingon sect of Buddhism, brought tea in the brick form from China to the Japanese court in the early ninth century.
805
Buddhist priest Saicho, spends 3 years visiting Chinese Buddhist temples on orders from the Japanese emperor, and he returns to Japan with tea seeds .
960 – 1280
Sung (Song) Dynasty. Cultivation techniques are improved and tea becomes affordable even to the poorest households. In the early part of the Dynasty brick tea is still powdered and whipped with a bamboo whisk. During this period tea is flavored with onions, pickle juice, ginger and orange peels. Some brick teas, especially those sent for imperial tribute, are perfumed with essences of camphor, musk, or other spices, although the people in the tea - producing regions usually drank un-perfumed tea. Tea related ceramics achieve legendary beauty. The first tearooms are built .
1101-1126
emperor Hui - tsung who spent time and resources searching for new

types of tea generally preferred un-perfumed "white tea" a form of green tea made with leaves that have white hairs and produce an almost clear tea. Because of his influence, perfumed teas are eventually abandoned. Meanwhile, the appreciation of leaf tea spreads among the literati. Leaves are ground to a powder and whisked in bowls in the same way that brick teas are .
1012
Cai Xiang is born. Becomes Fijian Province's tea commissioner and widely accepted as the most discerning tea palette of his day . " Tea tastings " at this time are popular entertainment among the government officials .
1191
Zen Buddhism is re - introduced to Japan by the priest Aesai, after returning from a visit to China. Aesai plants tea seeds, and in 1214 makes several medicinal claims for tea .
1200 – 1253
Dogen, disciple of Aesai (Eisais) is recognized as the founder of the Soto sect of Zen Buddhism. Dogen is an enthusiastic tea drinker.
1227
Dogen returns from China with a wide assortment of tea utensils. In his instructions on daily life at the Eiheiiji temple, he gives instructions for tea ceremonies .
1280 – 1368
Mongol conquest of China (1279) - Yuan Dynasty. Tea drinking discouraged .
1368 – 1644
Ming Dynasty - Chinese cultural revival.
1391
Chu Yuan-chang decrees that brick tea should no longer be produced, and that all tribute tea should be leaf tea . (The production of brick tea for the imperial court had been a highly complex and very expensive process, an extravagant source of corruption and waste) . Once cake tea was no longer available, the ritual of preparing whisked tea from powdered tea is abandoned. Brewed tea becomes the most popular way to prepare tea. Early forms of teapots are used .
1394 – 1481
Ikkyu, a prince who became a priest, was successful in guiding the

nobles away from their corruption of the tea ceremony.
1500
Teapots in China take on the familiar shape used today. In the fifteenth and sixteenth centuries a newly prosperous and influential merchant class develops in Japan and tea becomes available to a wider circle of people .
1422 – 1502
Murata Shuko a tea master in Japan, pupil of Ikkyu, saw that tea could be more than an opportunity for a party, could be more than a light medicine, and could have meaning outside of the temple ceremony. He realized that the preparation and drinking of tea could be an expression of the Zen belief that every act of daily life is a potential act that can lead to enlightenment. Shuko breaks all convention to perform the tea ritual for an aristocratic audience in a humble four – and – a – half - mat room .
1448
Japan's Shogun Yoshimasa encourages painting, drama and tea.
1522 – 1591
Sen no Rikyu (Rikkyu) the son of a rich merchant in Sakai, near Osaka, grows up in the most prosperous trading port in Japan in the sixteenth century. His background brings him into contact with the tea ceremonies of the rich, but he becomes more interested in the way priests approached the tea ritual as an embodiment of Zen principles for appreciating the sacred in the everyday. Taking a cue from Suko's example, Rikyu strips everything non-essential from the tearoom and the style of preparation, and developed a tea ritual in which there is no wasted movement and no object that is superfluous.
1559
A Venetian diplomat and traveler Giambattista Ramusio writes a book called the Voyages and Travels in which he describes " Chai Catai " (Tea of China) .
1606 or 1610
Dutch East India Company imports the first shipments of Chinese tea.
1618
first tea served to the Czar of Russia by Chinese embassy.
1644
Manchus invade China and take power as the Quing dynasty. Tea

makers discover the secrets of controlled " fermentation " or oxidation of the leaves before and during the drying process. Oolong and Black (red) teas are developed. As a result the coloration of tea cups changes to lighter hues .
1657
East India Company advertises tea's health benefits and begins sales in London. Tea is recommended as a treatment for apoplexy, catarrh, colic , consumption , drowsiness , epilepsy , gallstones , lethargy, migraine, paralysis, and vertigo .
1658
Thomas Garway advertises tea in his coffeehouse in London.
1675
tea becomes available in Holland in regular food stores.
1717
Thomas Twining opens first " tea - only " house and invites women to enjoy the previously " men – only " drink .
1773
United States Boston colonists, protesting the taxation of tea by Great Britain, board a ship from the Dutch East India Company and dump its cargo of tea into the bay.
1824
John Cadbury, a young English Quaker fresh from his apprenticeship at teahouses in Leeds, opens a grocery store at 93 Bull Street in Birmingham. Tea and coffee are his main commodities along with a newly imported product, cocoa. In 1831 he shifts the focus of his business to drinking chocolate and in 1849 manufactures his first chocolate bars.
1839
1839Black Assam tea arrives in London from India in large quantities. From this point on Black tea sales increase and Green tea sales decrease.
1850
The first U.S. clipper ship to visit London arrives after a 97-day voyage from Hong Kong. Named the " Oriental " she carries 1,600 - tons of tea and her \$48,000 cargo fee nearly covers the cost of her construction .
1876

Glasgow grocer Thomas Lipton opens his first shop at the age of 26. His success is due in large part to the marketing techniques he learned from his time spent working in New York department stores . 1908 Thomas Sullivan sends samples of tea to customers in silk bags. Infusions are made with the tea still in the bags and soon Sullivan is selling out of " bagged tea " .

TOBACCO TIME LINE

Oct 12, 1492

Christopher Columbus lands on the beaches of San Salvador in the West Indies and is offered fruit, wooden spears, and dried tobacco leaves by the natives .

Nov 1492

Two of Columbus's crew (Rodrigo de Jerez and Luis de Torres) become the first Europeans to witness the custom of tobacco smoking. de Jerez becomes a confirmed tobacco smoker, probably the first European to do so .

16th Century

Xochipilli statue carved. Aztec statue depicts the Prince of Flowers decorated with 6 psychoactive plants: mushrooms, tobacco, morning glory, sinicuichi, cacahuaxochitl, and one unidentified.

1518

Juan de Grijalva lands in Yucatan, observes cigarette smoking by natives .

1530

Bernardino de Sahagun, a missionary in Mexico, distinguishes between sweet commercial tobacco (*N. tabacum*) and coarse tobacco (*N. rustica*) .

1535

First printed source to contain a reference to tobacco smoking is published in Gonzalo Fernandez de Oviedo y Valdes's *Historia general y natural de las Indias, islas y tierra-firme del mar oceano* .

1556

Andre Thevet brought the first tobacco (*N. tabacum*) to France from Brazil .

1559

Tobacco is dubbed " Nicotina" in honor of Jean Nicot, the French ambassador to Portugal, who sent it from Portugal to the French court as a medicine, beginning its spread in upper - class circles .

1560

Indians along the Rio Guaviare in Colombia take Yopo along with tobacco .

1561

Tobacco first introduced in Italy by Cardinal Prospero di Santa Croce .

1565

Tobacco seeds are introduced into England, but smoking does not spread until Sir Walter Raleigh makes it fashionable in the court in the mid – 1570 s .

1570

First known picture of a tobacco plant printed in Europe. Accompanied by a diagram of a smoking tube made of plant materials used by Indians and sailors .

1571

Although smoking for pleasure is still controversial , tobacco as a medicine is almost universally approved. Nicolas Monardes devotes the second part of his book on New World plants to a lengthy section on tobacco , recommending it as an infallible cure for 36 different ailments. Summing up current beliefs regarding this much - praised herba panacea, or holy herb, Monardes' work (1571 , 1574) becomes the fundamental source for all subsequent pro-tobacco literature.

1575 – 1600

China/Japan. Limited smoking is apparent in S . China, probably introduced by Portuguese sailors and merchants .

1575 – 1600

England. Smoking becomes the " duty " of every man of fashion; tobacco is worth its weight in silver. Numerous

publications praise its medicinal virtues , starting with John Frampton's translation of Monardes, titled *Joyful Newes Oute of the Newe Founde Worlde* (1577) .

1575 – 1600

Italy. Tobacco is cultivated as a medicinal herb in Tuscany and Rome, but there is no evidence that it is widely smoked.

1575 – 1600

Turkey. Sultan Murad II cultivates tobacco as a novelty and a medicine after smoking is introduced by the English .

1585

Tobacco was being cultivated by European settlers in North Carolina .

1603

Japan. Cultivation of Tobacco begins and smoking spreads among all classes, prompting several severe imperial prohibitions (1603 +) . Prohibitions are governed by fears over outbreaks of fires, foreign influences, and interference in the cultivation of more valuable food crops such as rice. Despite increasing penalties, including property confiscations , death threats , fines and imprisonment , all bans fail . The prohibitions gradually fall into disuse from lack of enforcement .

1628

Virginia was given a monopoly on tobacco exports to England. 500,000 pounds of tobacco were shipped .

1638

1,400,000 pounds of tobacco shipped from America to Britain .

1638

China. The Ming emperor decrees any person trafficking in tobacco will be decapitated (1638), the decree proves ineffectual as smoking spreads within the court. A second prohibition is issued in 1641 .

1639

Governor Kieft bans smoking in New Amsterdam (New York). The populace ignores his decree .

1642

Papacy. Two papal bulls ban tobacco use by the clergy under penalty of excommunication (1642,1650) .

1644

China. The Manchu, having conquered China, revoke all existing smoking bans. China becomes the great smoking nation of Asia. Snuff is introduced by the Jesuits .

1650 – 1675

Japan. All Tobacco prohibitions are repealed .

1655

Papacy. Pope Alexander VII farms out spirits and tobacco monopolies (1655 , 1660) .

1659

Italy. Venice establishes the first tobacco appalto or state monopoly, selling the exclusive right to import, manufacture, or trade in tobacco to a private party .

1674

France. Louis XIV establishes a tobacco monopoly in imitation of the Italians .

1674

Russia. A Tobacco smoking ban is established, with a death penalty (1674) . Use continues to increase and restraints are lifted two years later (c. 1676). Smoking spreads from the court and foreign circles to the general population .

1730

The first American tobacco factories began in Virginia, in the form of small snuff mills .

1780

"Tobacco War" waged by Lord Cornwallis in Virginia to

destroy America's credit abroad .

1809

Nicotine is first observed as an active product in tobacco juice by French scientist Vauguelin.

1832

First documented use of tobacco rolled in paper, by Egyptian canoneer at siege of the Turkish city of Acre .

1843

First French commercial production of rolled cigarettes .

Mid 1800s

Xochipilli statue discovered by Europeans in central Mexico.

1856

First British cigarette factory opens .

1856

Health issues related to smoking tobacco cigarettes are discussed in *The Lancet* .

1880

The four leading cigarette companies did 80 % of US business in cigarettes and sold 532,718 cigarettes in 1880 along with 2.4 billion cigars .

1880 – 1881

Cigarette rolling machine invented by 18-yr-old James Bonsack. Prior to this, all cigarettes were hand-rolled .

1883 – 1884

James B. Duke of Durham, North Carolina, bought the rights to the first cigarette-making machine, which had previously been discarded as mechanically flawed. After improving the technology he adopted the machine in his factory, dropping the cost of production, leading to an increase in cigarette smoking .

1889

Annual cigarette production in US is 2 , 413 ,349 , 000 (2.4 billion) .

late 1890' s

Cigarette sales slump in US as tax was raised from \$.50 to \$ 1.50 per thousand to help pay for Spanish - American War .

Aprox 1885 – 1910

Most cigarette packages came with trading cards, a practice which later switched to bubble gum in the 20 h Century .

circa 1900

Sales dropped from 600 million to 40 million cigarettes in 2 years .

1900

Japan bans the use of cigarettes by anyone under the age of 20 .

1902

US tax lowered to \$.54 per thousand , sales increase .

1904

3 billion cigarettes sold in US .

1907

American Tobacco Company is split by US Government in anti-trust (monopoly) law suit. It had been formed in 1889 after James B. Duke merged five separate companies .

1907 – 1950

The health implications of smoking are debated. Cigarettes are still marketed as "healthy" while the medical community gathers more evidence of health problems associated in particular with heavy smoking .

1912

13 billion cigarettes sold .

1918

Camel cigarette company controls 40 % of US cigarette market .

1939

German scientists propose a link between smoke inhalation and lung cancer .

1965

New "Federal Cigarette Labeling and Advertising Act" requires all cigarette packages in the United States to carry a warning stating " Caution - cigarette smoking may be hazardous to your health " .

1967

U.S. Federal Trade Commission releases first tar and nicotine report .

1972

Australia requires packs of cigarettes to display a health warning .

1996

President Clinton announces a comprehensive anti-smoking program in the U.S. which includes granting the FDA jurisdiction to regulate cigarettes as nicotine delivery devices

1998

California becomes the first U.S. state to ban tobacco smoking in nearly all bars .

2000

Canada begins requiring cigarette label warnings that include color pictures.

2000

U.S. Supreme Court finds that the FDA does not have the authority to regulate tobacco, invalidating Clinton's 1996 regulations .

Yerba Mate Time line

Pre – Colombian
Though no archeological evidence has been found to date the beginning of Mate use in South America, it was used in Paraguay before the Spanish arrived in the early 1500s.
early 16th century
Spanish explorer Juan de Sols reported that the Guarani Indians of Paraguay made a tea from leaves that " produced exhilaration and relief from fatigue " . Yerba mate became known as Paraguay tea .
1670
Demand for yerba maté grew throughout the South American colonies , and by 1670 , Jesuit missionaries had set up maté plantations in Paraguay, leading to the common name " Jesuit tea ". Jesuit missions were encouraged to set up agricultural plantations on mission grounds using indigenous labor, in order to make the missions self sustaining . They are believed to be the first to have cultivated maté (Ilex paraguariensis) . At this point, the product was distributed almost exclusively within the Spanish colonies, rather than exported back to Europe .
1673
A letter written by the Jesuit priest Nicolaus del Techo described the character of maté. "Too many virtues are attributed to the herb," he complained. "It acts as a soporific at the same time as it stimulates; calms the appetite at the same time it aids digestion. It restores strength, brings happiness, and cures many diseases. All I see is that those who develop the habit can't seem to get along without it " .
1767
Maté cultivation is significantly curtailed when the Jesuits are expelled from Spanish territories. Harvesting continued, but using forest harvesting methods rather than cultivation methods .
1770s
Yerba mate had become a popular social drink throughout the Andes, served at all hours of the day. ³
1820s
Brazil began commercial harvesting of forest maté. Its product was considered inferior to that of Paraguay.
1800s
Maté harvesting, trade, and consumption continues in South America, but on a small scale. The introduction of Oriental tea (Camellia sinensis) in the early 1800 s provided significant competition to the maté market .
1897
Exploitation of forest maté resources leads to the renewal of some maté plantations in Nueva Germania, Paraguay and in Santa Ana, Argentina .



PART – 4

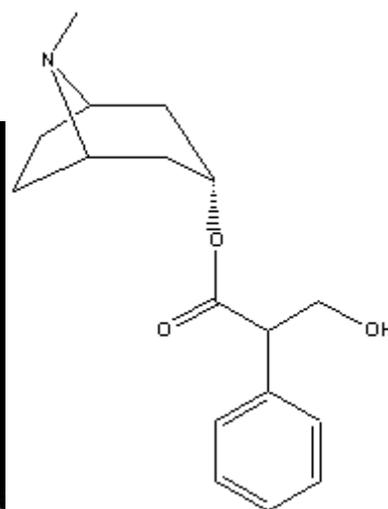
Extension and supplements

Night Shade Alkaloid Toxins Atropine , Scopolamine and Solanine



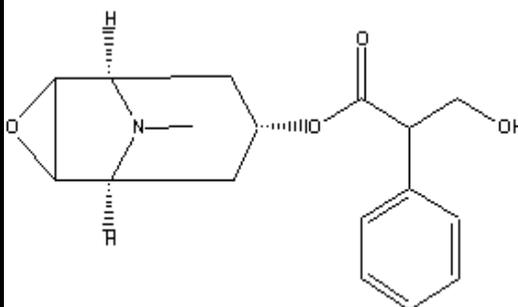
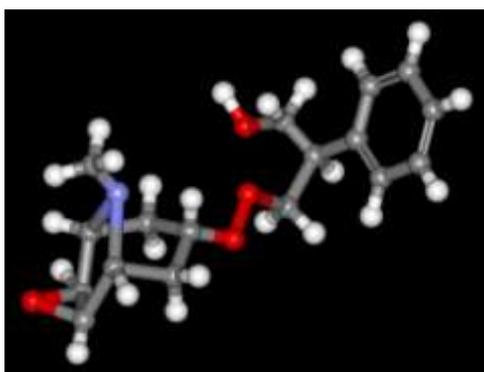
Black Nightshade

Nightshade is just not one plant , but the term represents a family of toxic plants , Solanaceae . The plants are present throughout the world , with different species prevalent in different areas. These plants produce several toxins , such as atropine , scopolamine , and solanine . These toxins are most concentrated in the berries , even though all of the parts of the plant are considered toxic . These alkaloid toxins affect the neurotransmitter acetyl choline . Atropine and scopolamine are cholinergic antagonists, while solanine is a cholinesterase inhibitor . The antagonists cause excessive sympathetic stimulation , while cholinesterase inhibitors will cause parasympathetic effects . Since they are so toxic , thank goodness , the nightshade plants are bitter tasting .



Atropine

Soluble in alcohol , benzene , glycerol , and dilute acids
 LD₅₀ in rats : 750 mg / kg orally



Scopolamine

Soluble in water , alcohol . insoluble in ether
 LD₅₀: 3800 mg / kg subcutaneous



Scopolamine and Atropine

Scopolamine and Atropine are found naturally in the plants of the Solanaceae family . Jimson weed (*Datura stramonium*) , belladonna (*Atropa Belladonna*) , and henbane (*Hyocyamus Niger*) are found in all corners of the United States and throughout the world . Animal poisoning with these plants is rare , since the alkaloids present in the plant make it bitter tasting and most animal savoid them .

Poisoning with any of these plants can be deadly, even with small doses . Atropine and Scopolamine are cholinergic antagonists , which means they inter act with acetyl choline binding sites of neurons . Acetyl choline is the neuro trans mitter found at the terminals of all preganglionic neurons and at the ending of all postganglionic fibers of the parasympathetic nervous system and mediates the impulses for skeletal muscle control . The autonomic nervous system is the " fight or flight " response , consisting of para sympathetic and sympathetic branches . The para sympathetic branch commands the day today actions of the body , while the sympathetic branch is involved in the immediate survival response . The sympathetic system will increase heart rate , respiration ate , dilate the pupils, decrease digestion, decrease salivation, increase body temperature , shunt blood to the limbs , and increase alertness The para sympathetic system has just the opposite effect ; it calms the body back into a state of normal rhythms and digestion . These two systems work against each other and are both active at all times . The effects of one are seen when that system is stimulated or the other systemic inhibited .

Since atropine and scopolamine bind to the receptors for acetyl choline , there is a lack of para sympathetic stimulation. Symptoms would be like that of excessive sympathetic stimulation . Mydriasis , or dilation of the pupils , impaired vision , muscle spasms , flushed skin , increased body temperature with a lack of sweating and increased heart rate and respiration are seen in patients poisoned by atropine . Different animals have different tolerance levels for possible digestion of these plants . Horses have a very high death rate after consumption of Jimson weed . In one equine study , eleven out of 15 horses showing symptoms died . Pigs can tolerate 2.2 mg of Jimson weed seeds , but at 2.7 mg , pigs begin to show signs of poisoning . Poultry on the other hand, can eat up to 15 g of seed a day and have no ill effects .



Jimson Weed Plants and seeds

Once poisoned with atropine or scopolamine , seek emergency medical attention ! Treatment at the emergency room will include stomach lavage and/or irrigation of the colon to remove the plant material and toxin as quickly as possible . These poisons have a short half life and are quickly bio trans formed and excreted from the body . Morphine can be titrated intravenously to counteract or amyl nitrate can be inhaled . Physostigmine , a cholinesterase inhibitor , can be cautiously used if the situation is dire . If no medical facilities are available , vinegar can be given to the victim orally. Vinegar is acidic and since these molecules can be protonated , rendering them lipophobic and unable to be absorbed by the body and thus quickly excreted in the urine .

These poisons also have therapeutic uses. Atropine is used as a " antidote " for organo phosphate poisoning , Organo phosphates are choline esterase inhibitors , preventing the break down of acetyl choline and causing prolonged stimulation . Atropine is used to block the sites for acetyl choline and reduce the stimulation . This buys time to treat the organophosphate poisoning effectively . Atropine can also be used to dilate the eyes for wide angle glaucoma . Atropine can also be used for treating tremor disorders , since it effects the acetyl choline at the neuromuscular junctions also . Scopolamine is widely used as an anti nausea drug and as a precursor to general anesthesia .

Interesting Facts about Atropine and Scopolamine :

In William Shakespeare 's Hamlet , Hamlet's father , the king of Denmark was poisoned with " henbone " dripped into his ear while he slept . Shakespeare 's henbone was quite possibly the plant today known as henbane . The membranes of the ear would have been permeable to scopolamine (toxic principle of henbane) and the quick absorption into the blood stream would resulted in a fast onset of symptoms and death. Such a quick death resulted, that the King of Denmark was unable to confess his sins and was condemned to wander through purgatory forever .



Henbane

Henbane was widely used as a way of making beer more potent. In one of stories of ancient Egypt , Hath or was created by her father Re as the Sekmet , or the destroyer of men , who were disobedient to him. Later Re changed his mind, but even he could not stop her from killing men. He then disguised beer as blood, laced the beer with henbane and when Sekemt became drunk , she could no longer kill and was known thereafter as Hath or , a goddess of love . The

Egyptians must have believed that not only was beer fun , but that it saved the world and could change a killer into a lover .

Atropine was used in witches ointment , which was thought to allow the witch to have sex with the devil . The ointment was applied all over the body and in orifices (vaginally , anally) . This created feelings of flying , dancing , love , and hallucinations . Ointment users couldn't discern reality from the drug - induced state. It was even thought that the plant from which the ointment was made were only found under the gallows where a evil person was hanged . Their urine or semen were the seed for these plants .

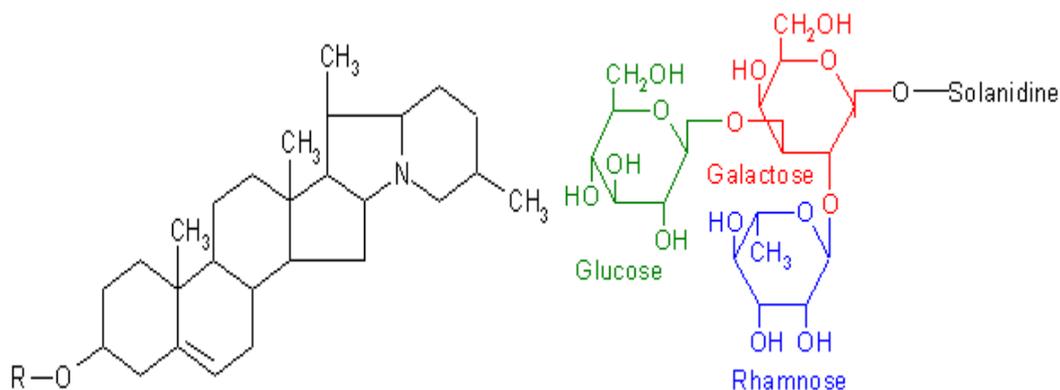


Blue Nightshade

Solanine :

Solanine is found in blue nightshade (*Solanum dulcamara*) , black nightshade (*Solanum nigrum*) , potatoes (*Solanum tuberosum*) , tomatoes (*Lycopersicon esculentum*) ,green peppers , and ornamental Jerusalem cherries (*Solanum pseudo capsicum*) .The most poisonous component is the unripe berries , but all of parts of the plant contain solanine . The alkaloids are very bitter tasting and are found in disturbed soil , such as in gardens , fence posts , and along high ways . Poisoning is very rare , since most animals have no interest in this plant . Only curious young animals or bored confined animals , will sample the plant . Animals will also eat this plant if no other nutrition is available . Human poisoning is usually accidental . The huckleberry looks very similar to black night shade ; it is even thought to be a domesticated form of the deadly night shade plant .

Children who eat huckleberries may mistake the purple –black berries of the black night shade for the delicious huckleberry and become poisoned . Unripe potatoes and tomatoes peelings also have high levels of the toxin and poison in shave been reported .



Solanidine

Solanine

This glycol alkaloid is has a sugar component attached to a steroid – like part , solanidine . Solandine alone is much less toxic . The sugar is necessary for the extreme toxicity . Solanineis very poisonous even in very small quantities . The LD50 in mice is 42 mg / kg when injected peritoneally . A fatal human dose can be as little as 420mg.It is much more toxic when injected since solanine is poorly absorbed through the gut wall . If not absorbed, the body will begin biotransformation and cleave the glycol alkaloid into the sugar and solanidine . These are excreted from the body via the feces.

Solanine acts to cause destruction in two different ways. It is a gastrointestinal irritant. It directly irritates the mucous membranes of the gastrointestinal tract and if absorbed into the bloodstream, will cause the hemolysis of erythrocytes . In addition to directly causing cellular damage, it causes neurologic effects . Unlike atropine and scopolamine, solanine affects the enzyme that breaks down acetylcholine. Likethe organo phosphates , it inhibits the breakdown of the para sympathetic neurotransmitter , acetyl choline . Solanine neural effects are characterized by excessive stimulation of the para sympathetic nervous system . Signs of solanine poisoning are apathy ,

excessive salivation , diarrhea , and a decrease in heart rate and respiration which can lead to cardiac arrest .

Treatment for solanine poisoning is mostly supportive. In animals, fluid levels must be monitored and maintained . Vasopressors and cardiac monitoring are also a key treatment for seriously ill animals . If diarrhea is present , survival is good ; the body is actively flushing the toxin out. In humans , emesis or vomiting will be induced at the hospital and supportive treatment will be given . Without medical advice from a physician or the Poison Control Center , vomiting should not be induced . This poisoning is very serious and should only be treated by a medical professional .

Interesting facts about Solanine :

Tomatoes are prized by humans for their cancer -fighting antioxidants . People eat these to gain their benefits and may try to extend this benefit to their pets . A cat can be fatally poisoned by just 100 g of ripe tomato . that someone carelessly left out or if unknowing of the danger , tries to feed their animal . Even though cats will not normally eat tomatoes, bored animals or young animals will . This cat was in the hospital for two weeks, excessively vomiting , continuous diarrhea , dehydration , and the inability to move . The cat barely recovered even after such a small dose .

Potato farmers harvest their crop before ripening to prevent the spread of viruses . The green vines are often used as animal feed . Yet if cattle or pigs are fed the peeling of unripe or spoiled potatoes, the poisoning and death rates will increase dramatically . This is because the toxin is more concentrated in the fruit (or the reproductive portion of the plant , such as the eye of the potato) .

In the 1960's , the search for a new potato was completed. The United States has interested in producing a potato strictly for French fry production . Lenape was an excellent candidate . This crossbred potato had all the qualities of a great French fry potato . After commercial production , it was found that Lenape had very high levels of solanine . Fourteen mg / 100g causes a bitter taste and above twenty mg / 100g causes a burning in the mouth and throat. Lenape was

found to have 30mg / 100g . This created a new standard that all potatoes had to be tested for levels of solanine prior to production .

Your mom was right ; don't eat green potatoes or old potatoes! Exposure to light or stress (or even aging) causes trans formation of a potato ' s amylo plasts to chloro plasts , followed by the synthesis of the green pigment , chlorophyll . Light , stress , and aging also cause the potato to produce chaconine and solanine . The appearance of chlorophyll is thus a warning that something is wrong with the potato . About 30 % to 80 % of the glycol alkaloid content of a potato is in its peel with the remainder in the flesh of the tuber . And don't think that just cooking the green potato will deactivate the toxin . Boiling , micro waving , or freezing as no effect on the toxin. Deep - frying (my favorite) has been shown to reduce the levels of toxin .

Points to Ponder :

The Night shade family members make two distinctly different categories of toxins . No one plant has a both kinds of toxins since the toxins have opposite effects . The Atropine side of the family makes cholinergic antagonists causing depression of the parasympathetic system , while the Solanine producers make cholinesterase inhibitors , causing stimulation of the para sympathetic branch of the central nervous system . Nowhere in the literature mentioned that possibly one member of the family could be used (carefully!!!) to treat the poisoning from another type of nightshade . Night shade can be the family that honestly has both the poison and the cure (depending on the circumstances) .

One question remains; why does the plant produce these toxins in the first place , These toxins could be serving as a defense mechanism . Since the alkaloids cause the plant to be bitter tasting and the effects of low dose consumption are uncomfortable to an animal , these poisons could prevent the plants from being grazed on and destroyed . They could also serve as a fungicide or an insecticide to prevent damage to the plant .

Nerium Oleander



Nerium Oleander in flower

Contents :

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- 5 Trunk oil
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- 8 Popular culture

1 – Introduction :

Oleander (*Nerium oleander* , (pronounced / ' nɪəriəm ' ɔʊli : . ændər /) , is an evergreen shrub or small tree in the dogbane family Apocynaceae and is one of the most poisonous plants known. It is the only species currently classified in the genus *Nerium*. Other names include Adelfa , Alheli Extranjero , Baladre , Espirradeira , Flor de São Jose , Laurel de jardín , Laurel rosa , Laurier rose , Flourier rose , Olean , Aiwa , Rosa Francesca , Rosa Laurel , and Rose - bay (Inchem 2005) , закым [zakum] (Bulgarian) , leander (Hungarian), leandru (Romanian), zakum, zakkum, zakhum (Turkish) , zaqqum (Arabic) ; harduf (Hebrew :) ; Kaneru (Sinhalese) ; a rali (Tamil and Malayalam - South Indian languages) ; kanagillu (Kannada - South Indian language) ; kaner (in Hindi , and , also , in Punjabi - the language from North Indian state of Punjab) ; and in Chinese it is known as jia zhu tao (Chinese : 夹竹桃) . The ancient

city of Volubilis in Morocco took its name from the old Latin name for the flower .

Scientific classification

Kingdom : Plantae
(unranked) : Angiosperms
(unranked) : Eudicots
(unranked) : Asterids
Order : Gentianales
Family : Apocynaceae
Genus : **Nerium L .**
Species : N . oleander

Binomial name

Nerium Oleander

L .

2 - Growth

It is native to a broad area from Morocco and Portugal eastward through the Mediterranean region and southern Asia to Yunnan in southern parts of China . It typically occurs around dry stream beds. It grows to 2 - 6 m tall , with spreading to erect branches. The leaves are in pairs or whorls of three, thick and leathery, dark green, narrow lanceolate , 5 - 21 cm long and 1-3.5 cm broad , and with an entire margin . The flowers grow in clusters at the end of each branch; they are white, pink, red or yellow , 2.5 - 5 cm diameter, with a deeply 5 - lobed corolla with a fringe round the central corolla tube . They are often, but not always, sweetly scented. The fruit is a long narrow capsule 5 - 23 cm long , which splits open at maturity to release numerous downy seeds .

In the past , scented plants were sometimes treated as a distinct species *N. odorum*, but the character is not constant and it is no longer regarded as a separate taxon .

3 - Cultivation and use :

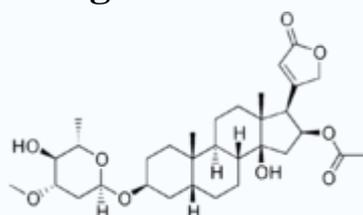
Oleander grows well in warm subtropical regions, where it is extensively used as an ornamental plant in landscapes , parks , and along roadsides. It is drought tolerant and will tolerate occasional light frost down to - 10° C . It is commonly used as in landscaping freeway medians in California and other mild-winter states in the Continental United States because it is easily maintained — it is deer resistant and tolerant of poor soils and drought . Oleander can also be grown in cooler climates in greenhouses and conservatories, or as indoor plants that can be kept outside in the summer . Oleander flowers are showy and fragrant and are grown for these reasons. Over 400 cultivars have been named, with several additional flower colors not found in wild plants having been selected, including red, purple, pink and orange ; white and a variety of pinks are the most common. Many cultivars also have double flowers. Young plants grow best in spaces where they do not have to compete with other plants for nutrients .

4 - Toxicity :

Oleander is one of the most poisonous plants in the world and contains numerous toxic compounds, many of which can be deadly to people, especially young children. Despite this fact, it is sometimes grown in school yards.^[6] The toxicity of Oleander is considered extremely high and it has been reported that in some cases only a small amount had lethal or near lethal effects. The most significant of these toxins are oleandrin and neriine , which are cardiac glycosides They are present in all parts of the plant, but are most concentrated in the sap, which can block out receptors in the skin causing numbness. It is thought that Oleander may contain many other unknown or un - researched compounds that may have dangerous effects . Oleander bark contains rosagenin which is known for its strychnine - like effects. The entire plant , including the sap, is toxic, and any part can cause an adverse reaction . Oleander is also known to hold its toxicity even after drying. It is thought that a handful or 10 - 20 leaves consumed by an adult can cause an adverse reaction, and a single leaf could be lethal to an infant or child. According to the Toxic Exposure Surveillance System (TESS) in 2002 there were 847 known human

poisonings in the United States related to Oleander . There are innumerable reported suicidal cases of consuming mashed oleander seeds in southern India. Around 0.5 mg per kilogram of body weight is lethal to many animals, and various other doses will affect other animals. Most animals can suffer a reaction or death from this plant .

4 – 1 : Effects of poisoning :



Oleandrin , one of the toxins present in Oleander

Reactions to this plant are as follows : Ingestion can cause both gastrointestinal and cardiac effects. The gastrointestinal effects can consist of nausea and vomiting , excess salivation, abdominal pain, diarrhea that may or may not contain blood, and especially in horses , colic . Cardiac reactions consist of irregular heart rate, sometimes characterized by a racing heart at first that then slows to below normal further along in the reaction . The heart may also beat erratically with no sign of a specific rhythm. Extremities may become pale and cold due to poor or irregular circulation. Reactions to poisonings from this plant can also affect the central nervous system. These symptoms can include drowsiness, tremors or shaking of the muscles , seizures , collapse , and even coma that can lead to death . Oleander sap can cause skin irritations, severe eye inflammation and irritation , and allergy reactions characterized by dermatitis .

4 – 2 : Medical treatment required :

Poisoning and reactions to Oleander plants are evident quickly, requiring immediate medical care in suspected or known poisonings of both humans and animals . Induced vomiting and gastric lavage are protective measures to reduce absorption of the toxic compounds . Charcoal may also be administered to help absorb any remaining toxins. ^[4] Further medical attention may be required and will depend on the severity of the poisoning and symptoms .

Digoxin Immune Fab is the best way to cure an oleander poisoning if inducing vomiting has no or minimal success, although it is usually only used for life - threatening conditions due to side effects .

Drying of plant materials does not eliminate the toxins. It is also hazardous for animals such as sheep , horses , cattle , and other grazing animals, with as little as 100 g being enough to kill an adult horse . Plant clippings are especially dangerous to horses, as they are sweet . In July 2009 , several horses were poisoned in this manner from the leaves of the plant . Symptoms of a poisoned horse include severe diarrhea and abnormal heartbeat . There are a wide range of toxins and secondary compounds within Oleander , and care should be taken around this plant due to its toxic nature. Different names for Oleander are used around the world in different locations, so when encountering a plant with this appearance, regardless of the name used for it , exercise great care and caution to avoid ingestion of any part of the plant, including its sap and dried leaves or twigs. Do not use the dried or fresh branches for spearing food, in preparing a cooking fire, or as a food skewer. Many of the Oleander relatives, such as the Desert Rose (*Adenium obesum*) found in East Africa, have similar leaves and flowers and are equally toxic .

5 - Trunk oil :

While the reasons are unknown , some visibly healthy oleander shrubs that have become sick or other wise diseased may generate a type of oil from the trunk and shallow roots . Depending upon the size of the shrub, the oil quantity can vary greatly and has the capability to saturate the soil in its vicinity as the shrub's sickness progresses . This is possibly an explanation for the plant's name of " Olea " , whose Latin translation is "oil". The oil is light - brown colored and possesses a rancid scent. The toxicity of the oil is unknown , because the neuro-toxic chemicals in the rest of the tree come from the leaves vein -system and not from the pulp surrounding these veins .

6 - Larval host plant

Some invertebrates are known to be unaffected by oleander toxins, and feed on the plants. Caterpillars of the Oleander or Polka-dot Wasp Moth (*Syntomeida epilais*) feed specifically on oleanders and survive by eating only the pulp surrounding the leaf-veins, avoiding the fibers. Larvae of the Oleander or Common Crow Butterfly (*Euploea core*) also feed on Oleanders. The Common Crow larvae retain or modify toxins, making them unpalatable to would-be predators such as birds, but apparently not to other invertebrates such as spiders and wasps .

7 - Potential medicinal use :

Pliny the Elder in his *Naturalis Historia* written circa AD 77 claimed that despite its toxicity Oleander was an effective snakebite cure: "...if taken in wine with rue..." .

Despite a lack of any proven benefits , a range of Oleander-based treatments are being promoted on the Internet and in some alternative medicine circles, drawing a warning letter from the U.S. Food and Drug Administration (FDA) .

8 - Popular culture :

In the novel *Dragonwyck* , the plant and its poisonous effect are essential to the plot. The plant can be seen in the film by the same name .

White Oleander is a 1999 book by Janet Fitch that was made into a 2002 drama film with the same name directed by Peter Kosminsky ; poisoning using the oleander plant is central to the plot.

The legend of Chloe is possibly the most well known of the Myrtles Plantation's supposed ghosts; Chloe was a slave who was reputed to have killed her mistress and the mistress' two daughters by cooking a birthday cake poisoned with oleander .