Unit-III (BOP-474)

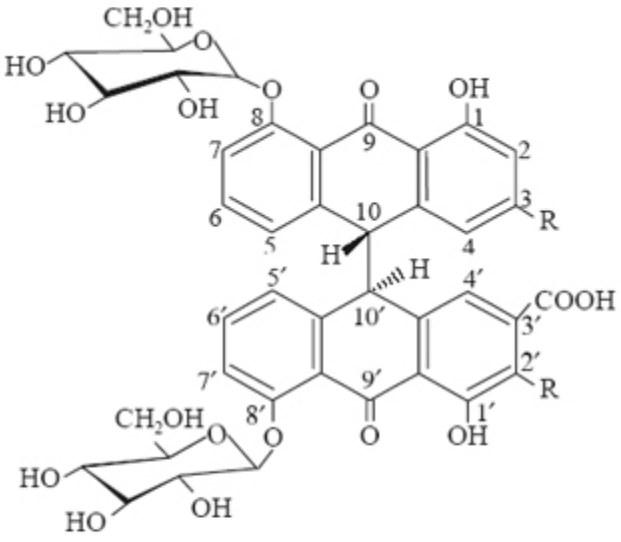
Sennosides

Senna was first used in the European medicine as early as the 9th or 10th century by the Arabs. An Egyptian native Issae Judaeus (850 to 900 A.D.) was reported to be the pioneer in bringing and introducing the drug to Egypt from Mecca,

Synonyms Senna leaf; Sennae folium; Tinnevelley Senna; Indian Senna;

Biological Sources Senna is the dried leaflets of *Cassia senna* L. (*Cassia acutifolia* Delile, (Alexandria senna), or of *Cassia angustifolia* Vahl (Indian or Tinnevelley Senna) belonging to the family *Leguminoseae*.

Chemical Constituents The principle active constituents of senna are *four* sennosides A, B, C and D, which are the dimeric glycosides having their aglycones composed of either *rhein* and/or aloe-emodin moieties *i.e.*; 10, 10'-*bis* (9, 10-dihydro-1, 8-dihydroxy-9-oxoanthracene-3-carboxylic acid). The structure of the above *four* glycosides are as given below:



Glycosides	R	C-10 & C-10'	Characteristics
Sennoside-A	—COOH	*trans-*	Optically active, a levoratory isomer present in large concs; water insoluble
Sennoside-B	—COOH	*meso-*	Intramolecularly compensated present in large concs; more water soluble
Sennoside-C	—CH_2OH	*trans-*	Aglycone (–) isomer; present in small concs;
Sennoside-D	—CH_2OH	*meso-*	Aglycone (+) isomer; present in small concs.

Besides, relatively small quantities of monomeric glycosides and free anthraquinones are also present in senna pods, such as: **rhein–8-glucosides, rhein-8-diglucoside, aloe emodin-8-glucoside,aloe-emodin anthrone diglycoside, rhein, aloe-emodin and isorhamnetin.**

It also contains **kaempterol** (a phytosterol), mucilage, resins, myricyl alcohol, chrysophanic acid, calcium oxalate and salicylic acid.

Specific method of extraction for the sennosides: Exclusively for commercial purposes, the sennosides are extracted as their corresponding calcium sennosides in varying strengths because of its enhanced stability.

Methodology: The drug powder (about 80-100 mesh size) is duly macerated with either 80% acetone or 90% methanol for a period of 6 hours, followed by 2 hours with cold water. This process helps to achieve an extract that contains between 17-18% sennosides and enables to extract about 65% of sennosides from the crude drug.

The sennosides and other anthracene derivatives may be extracted by the help of a mixture of polyethylene glycols (in 70% v/v ethanol) and solutions of non-ionic surfectants.

However, the isolation of individual sennosides may be achieved by employing non-polar synthetic resins having porous structural features. *Alternatively,* the drug powder is macerated with citric acid in methanol which is followed by a repeated extraction with a mixture of methanol, toluene and ammonia. The resulting extract is treated with a concerntrated solution of calcium chloride to salt out the sennosides as their respective calcium salts.

Chemical Tests

1. **Modified Borntrager's Test:** It gives a pink to red colouration for the presence of anthraquinone glycosides.

2. The mucilage of senna gives a distinct red colouration with Ruthenium Red solution.

Substituents and Adulterants Tinnevelley senna is invariably found to be adulterated with the

following *three* cheaper varities of senna namely:

(*a*) Dog senna ie; *Cassia abovata,*

(*b*) Palthe senna ie; *Cassia auriculatad,* and

(*c*) Arabian Senna or Mecea senna or Bombay senna *i.e.*; wild variety of *Cassia angustifolia* Vahl. from Southern Arabia.

Utilization:

1. Senna and its branded preparations, are usually employed as purgative in habitual constipation. The glycosides are first absorbed in the small intestinal canal after which the aglycone portion gets separated and ultimately excreted in the large intentine (colon). The released anthraquinones irritate and stimulate the colon thereby enhancing its peristaltic movements causing bulky and soft excretion of faces.

2. The inherent action of senna is associated with appreciable griping , and therefore, it is generally dispensed along with carminatives so as to counteract the undesired effect.

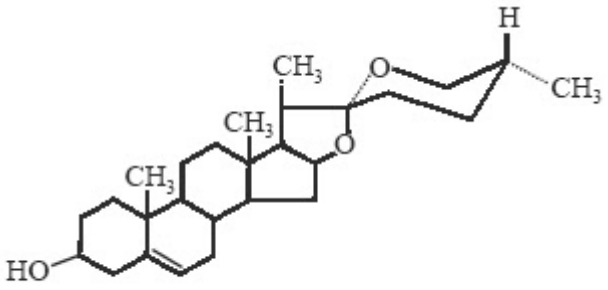
Dioscorea

Synonyms Rheumatism root; Yam.

Biological Source It essentially comprises of the dried tubers of *Dioscorea delitoidea* Wall.,*Dioscorea tokora* Makino, and *Dioscorea composita* and other species of *Dioscorea* belonging to the family *Dioscoreaceae.*

Neutral Saponin : Basic lead acetate is used to precipitate the neutral steroidal saponins from aqueus extract. Nevertheless, a few saponins are also precipitated from their aqueous solutions either by the addition of $Ba(OH)_2$ solution or by the addition of $(NH_4)_2.SO_4$ solution.

Chemical Constituents The major active constituent of **dioscorea** is *diosgenin* usually present in the range of 4-6%. **Diosgenin** is the *aglycone* of saponoin **dioscin.**



Diosgenin

Besides, the rhizomes contain starch to the extent of 75% but it has no edible utility because of its bitter taste. They also contain phenolic compounds and an enzyme *sapogenase.*

Uses

1. **Dioscorea** is mostly employed in the treatment of rheumatic arthritis.

2. **Dioscorea** has a tremendous potential as a commercial product because of its high content of diosgenin, which in turn is invariably employed as a starting material for the synthesis of a host of important therapeutic drugs, for instance: *sex-hormones, oral contraceptives* and several*corticosteroids*.

Solanum Alkaloids

Biological Source It consist of the dried and full grown berries of *Solanum khasianum* belonging to the family *Solanaceae.*

Geographical Source The plant grows indigenously on the *Khasia Mountains* in Assam (India).

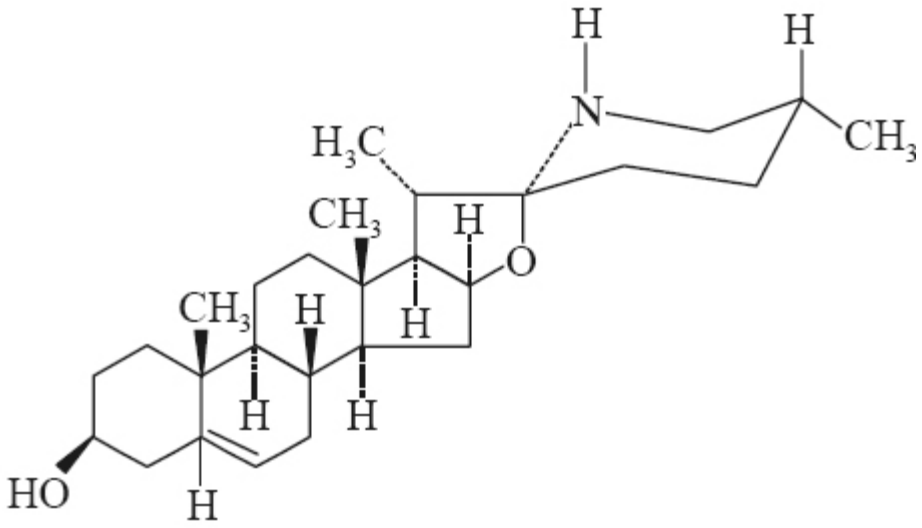
Preparation The plant usually grows in various climatic and agricultural conditions. Almost after a duration of six months the plants are normally harvested for the collection of berries. They are dried immediately either in an artificial environment at low temperature (50-60°C) or dried preferably in shade so as to bring down the initial large moisture content to enable its prolonged storage life. The dried berries are powdered by mechanical grinders and the oil is removed by solvent extraction. The defatted material (marc) is then extracted in a soxhlet assembly with ethanol (95% v/v) The resulting alcoholic extract is filtered, concentrated under

vacuo, treated with HCl (12N) and refluxed for at least six hours. The alcoholic extract thus obtained is made alkaline by the

addition of ammonia and the eontents are again refluxed for a duration of 1 hour. The contents of the flask is filtered and the residue is washed, dried and taken up in chloroform. The resulting mixture is fltered and the steroidal alkaloid solasodine is obtained as a solid residue soonafter evaporating the solvent.

Unlike, their *oxygen* counterparts, all these N-containing alkaloids exhibit the same stereochemistry at C-25 (methyl being equatorial always), but C-22 isomers do exist, such as: solasodine and tomatidine.

Chemical Structure

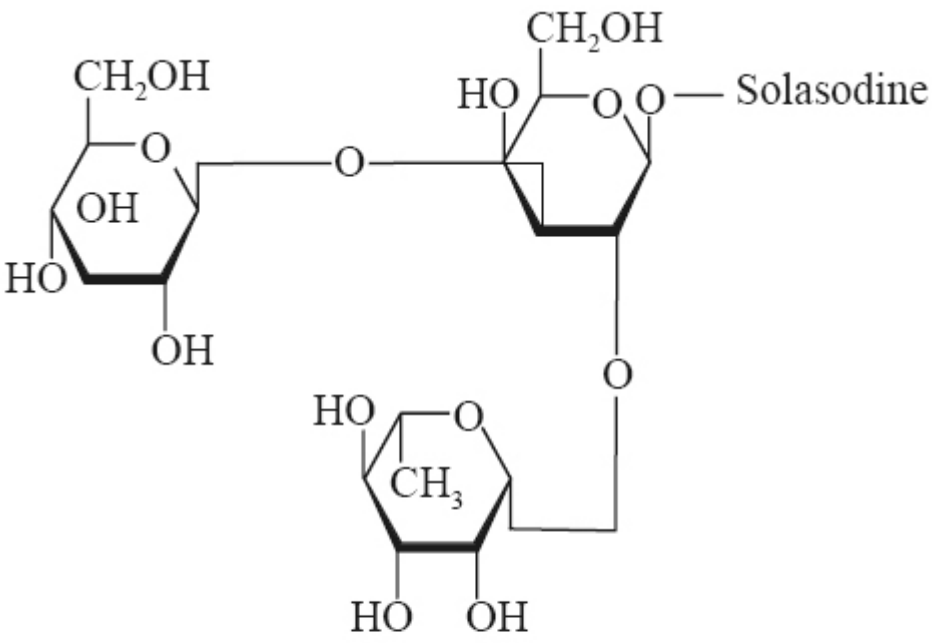


Solasodine

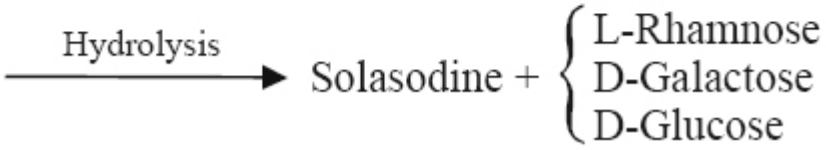
Isolation It is obtained by the hydrolysis of **solasonine** which yields **solasodine**, L-rhamnose, Dgalactose and D-glucose respectively. It is the dehydrated product.

Characteristic Features

(*i*) It is obtained as hexagonal plates from methanol or by sublimation under high vacuum.



Solasonine



(*ii)* It is freely soluble in benzene, pyridine, and chloroform; moderately soluble in ethanol, methanol, and acetone; slightly soluble in water and practically insoluble in ether.

Identification Tests (for Solanum Alkaloids)

1. Dissolve 5-10 mg of the alkaloid in a few drops of hot amyl alcohol or ethanol and allow it cool gradually. The appearance of jelly-like product gives the characteristic test of the solanum alkaloids.

2. When a few mg of the alkaloids is treated with antimony trichloride solution in dry chloroform, it gives rise to a distinct red colouration.

3. The **solanum alkaloids**, in general, produces an instant red-violet colour with formaldehyde (HCHO) and sulphuric acid (H_2SO_4). This particular test is so distinct and sensitive that it is used for the quantitative estimation of these alkaloids colorimetrically.

Uses

Solasodine is the hydrolysed product of **solasonine** which is mostly used as a starting material for the synthesis of steroidal drugs, such as: **19-NOR steroids, pregnane** etc.

However, the two species of *Solanum*, namely: *S. laciniatum* and *S. aviculare* are considered to be a rich source of alkaloids (*i.e.*, the aglycone moieties) that are employed exclusively as the starting materials for the synthesis of several hormones and adreno-cortical steroids.

The **solanum alkaloids**, stated above are essentially the nitrogen-analogues of steroidal saponins.

It is invariably used as a starting material for steroidal drugs.

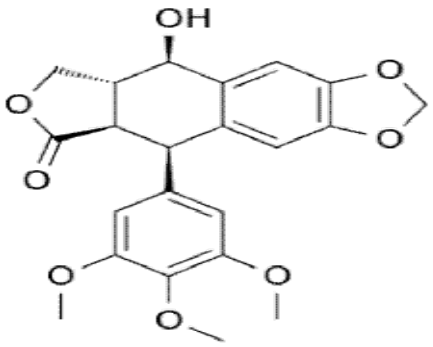
Podophyllotoxin

It is present at concentrations of 0.3 to 1.0% by mass in the rhizome of American Mayapple (*Podophyllum peltatum*).Another common source of podophyllotoxin is the rhizomes of *Sinopodophyllum hexandrum* (Berberidaceae).

It is biosynthesized from two molecules of coniferyl alcohol by phenolic oxidative coupling and a series of oxidations, reductions and methylations.

Podophyllotoxin extraction :

: The resin (50 g) of P. peltatum was extracted with hot CHCl3 over a day. The soluble fraction was chromatographed on neutral alumina (activity II), and eluted with CHCl3 to yield 20.4 g (40.8 %) of podophyllotoxin. The main lignan compounds of the rest of extract are: deoxypodophyllotoxin (1 %), β-peltatin (9 %) , α- -peltatin (7 %).



Podophyllotoxin

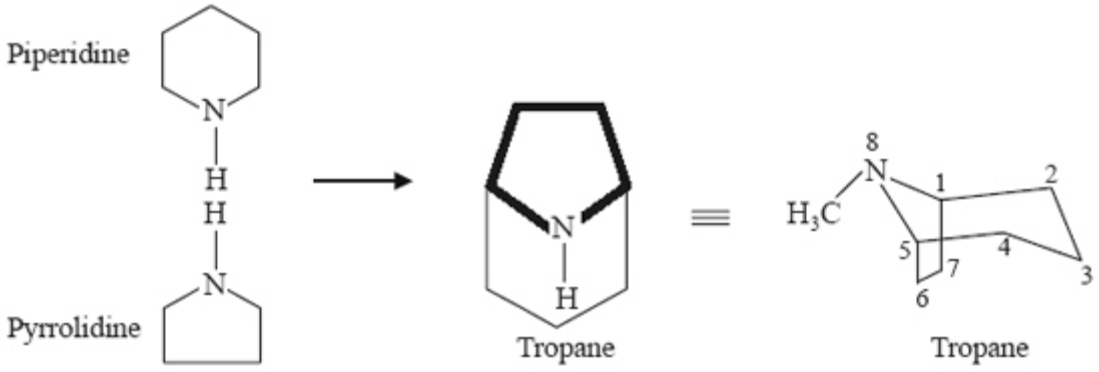
Podophyllotoxin and its derivatives display binding activity to the enzyme topoisomerase II during the late S and early G2 stage. For instance, etoposide binds and stabilizes the temporary DNA break caused by the enzyme, disrupts the reparation of the break through which the double-stranded DNA passes, and consequently stops DNA unwinding and replication. Mutants resistant to either podophyllotoxin, or to its topoisomerase II inhibitory derivatives such as etoposide (VP-16), have been described in Chinese hamster cells. The mutually exclusive cross-resistance patterns of these mutants provide a highly specific mean to distinguish the two kinds of podophyllotoxin derivatives.Mutant Chinese hamster cells resistant to podophyllotoxin are affected in a protein P1 that was later identified as the mammalian HSP60 or chaperonin protein

Uses

- It is used as anti-cancer agent.
- Podophyllotoxin possesses a large number of medical applications and can be used as a cathartic, purgative, antiviralagent, vesicant, and antihelminthic.
- Additionally, podophyllotoxin and its derivatives are leads for anti-tumor agents .

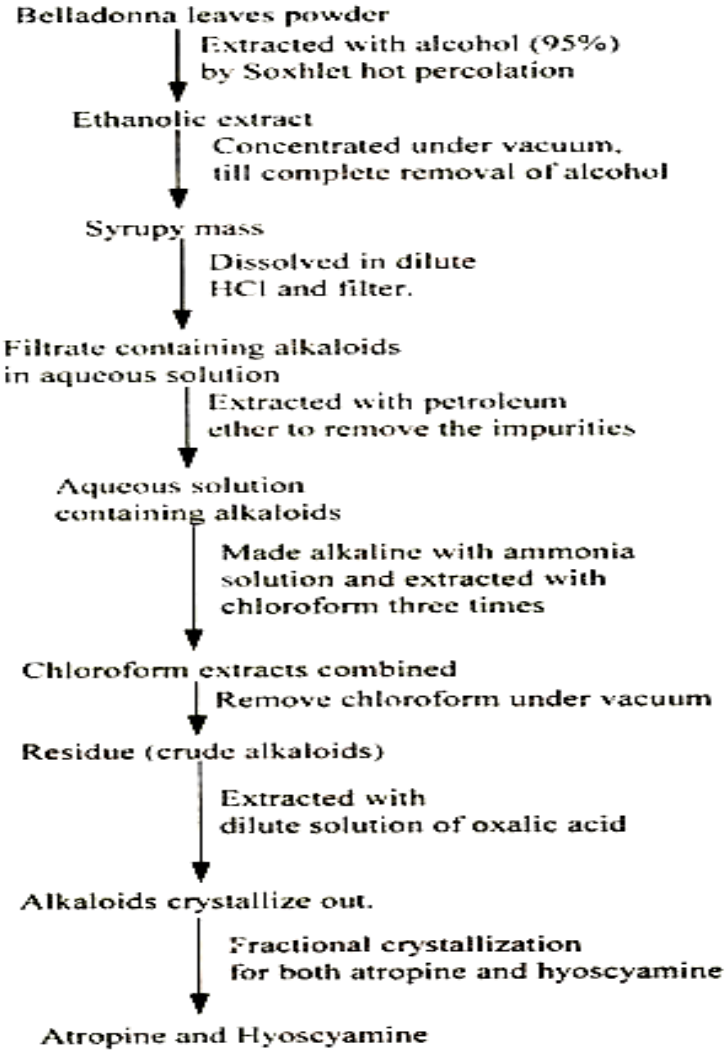
Tropane Alkaloids

Tropane is a bicyclic compound obtained by the condensation of one mole each of **pyrrolidine** and **piperidine** as shown below.



Tropane is regarded as the principle base of a plethora of alkaloids obtained from various members of the natural order, viz., *Solanaceae*, *Erythroxylaceae*, *Convolvulaceae*, and *Dioscoreaceae.* It It happens to be a *meso*-compound. A few important members belonging to the **tropane alkaloids** are, namely: **atropine, cocaine, cinnamoyl cocaine, ecgonine** and **hyoscyamine.** These alkaloids shall now be treated individually in the sections that follows:

Isolation of Tropane alkaloids:



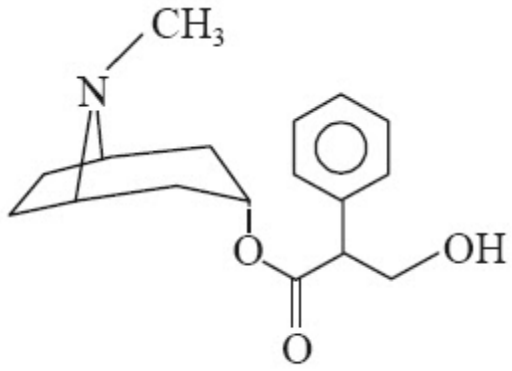
Isolation of tropane alkaloids (Atropine and Hyoscyamine)

Atropine

Synonyms Tropine tropate; *dl*-Hyoscyamine; *dl*-Tropyl Tropate; Tropic acid ester with Tropine.

Biological Sources It is obtained from the roots and leaves of *Atropa belladona* Linn. (*Solanaceae*) (**Belladona**); and the seeds and leaves of *Datura stramonium* Linn. (*Syn.: Datura tatula* Linn.) (*Solanaceae*) (**Jimson Weed, Thorn Apple, Stramonium**), besides other species of *Solanaceae*, such as: *D. metel* Linn.; *D. innoxia* Mill., *D. alba* Nees.; and *D. fastuosa* Linn.

Chemical Structure



Atropine

Characteristic Features

1. **Atropine** is obtained as long orthorhombic prisms from acetone having mp 114-116°C.

2. It usually sublimes in high vacuum at 93-110°C.

Identification Tests It forms various types of salts, namely:

1. **Atropine Hydrochloride ($C_{17}H_{23}NO_3.CH_3NO_3$):** The granular crystals have mp 165°C. It is soluble in water and ethanol. The pH of 0.05 molar solution is 5.8.

2. **Atropine Methyl Bromide ($C_{17}H_{23}NO_3.CH_3Br$) (Tropin):** Its crystals have mp 222-223°C. It is soluble in 1 part of water, slightly soluble in ethanol, and practically insoluble in ether and chloroform.

Uses

1. It is used in preanaesthetic medication.

2. It is employed as an anticholinergic agent.

3. It is also used as a mydriatic.

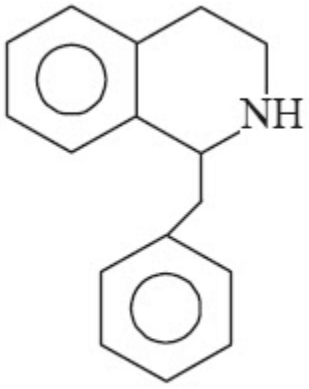
4. It is employed as an antidote in opium and chloral hydrate poisoning.

5. It is frequently employed to minimize spasm in cases of intestinal gripping caused due to strong purgatives.

6. It also find its applications to reduce such secretions as: saliva, sweat, and gastric juice.

Isoquinoline Alkaloids

The modification of *benzyltetrahydroisoquinoline* nucleus to certain other types of alkaloid(s) could be accomplished by virtue of phenolic oxidative coupling.



Benzyltetrahydroisoquinoline

Interestingly, the coupling of two benzyltetrahydroisoquinoline molecules *via* ether bridges result into the formation of two important alkaloids, namely: **tetrandrine** and **tubocurarine,** as given below.

It is, however, pertinent to mention here that the aforesaid mode of coupling is perhaps less frequently found than that involving carbon-carbon bonding between aromatic rings. The major **opium alkaloids** *viz.*, **morphine, codeine** and **thebaine** are obtained through this mode of coupling. (R)-*Reticuline* has been established beyond any reasonable doubt as the precursor of the above *three* **morphinan alkaloids.** Interestingly, there exist an ample evidence to show that the later stages of the proposed biosynthetic pathway undergo *modifications* in certain strains of *opium poppy*. Thus, in such modified strains of opium poppy **thebaine** is being converted to **oripavine** and **morphinone,** whereby the phenolic O-methyl moiety is removed before that of the ether, *i.e.*, the same steps are carried out but in an altogether different order.

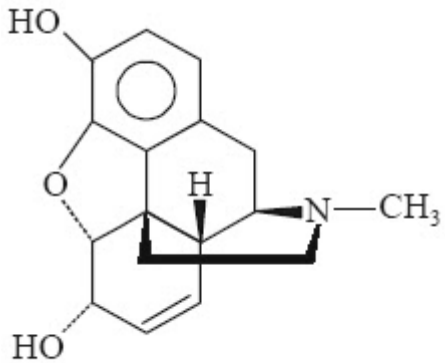
The various alkaloids belonging to this category, namely: **morphine, codeine, thebaine, reticuline, oripavine** and **morphinone** shall be discussed separately in the following sections:

A. Morphine

Synonyms Morphium; Morphia; Dolcontin; Duromorph; Morphina; Nepenthe.

Biological Sources Morphine is obtained from a variety of medicinal plants, such as: *Argemone mexicana* L. (*Papaveraceae*) (**Prickly Poppy**); *Eschscholzia californica* Cham. (*Papaveraceae*) (**California Poppy**); *Papaver bracteatum* Lindl. (*Papaveraceae*) (**Great Scarlet Poppy;** Thebaine Poppy); *Papaver somniferum* L. (*Papaveraceae*) (**Opium Poppy;** and Poppyseed Poppy Keshi).

Chemical Structure



Morphine

Isolation The latex obtained by incision on the unripe capsule of opium poppy is first collected in clean, plastic containers, and the process of incision is repeated at least four times on the same capsule after an interval of two days. Care must be taken to make the incisions on the superficial surface only so as to collect exclusively the external exudation of latex. Subsequently, the latex is dried carefully either by exposing to air on metallic shallow plates or by passing a stream of hot air.

Thus the '*opium*' or the dried latex is stored for the isolation of **morphine.** It is found to contain usually 9.5% **morphine** when calculated as anhydrous morphine.

The morphine may be isolated form **'Powdered Opium'** by adopting the following steps sequentially:

Step-1: The powdered opium is shaken with calcium chloride solution and filtered.

Step-2: The resulting filtrate is concentrated and to it is added 10% w/v sodium hydroxide solution carefully *i.e.*, to solubilize morphine, codeine and narceine. It is now filtered.

Step-3: The filtrate containing morphine, codeine and narceine is extracted with chloroform. The resulting mixture is separated.

Step-4: The lower chloroform layer contains codeine, whereas the upper aqueous layer comprises of **morphine** and **narceine.**

Step-5: The aqueous layer is first acidified and subsequently made alkaline with ammonia, whereby morphine gets precipitated and collected as a while solid residue (Yield = 9.5%).

Characteristic Features

1. **Morphine** is obtained as short, orthorhombic, columnar prisms from anisole that gets decomposed at 254°C. It also occurs in its metastable phase having mp 197°C. However, the high melting form sublimes at 190-200°C (0.2 mm pressure at 2 mm distance).

2. It has a bitter taste.

3. **Morphine** (free-base) unlike most other alkaloids in their free-base forms is found to be sparingly soluble in chloroform and nearly insoluble in ether or benzene.

4. **Morphine** gets dissolved in caustic alkalies by virtue of the fact that the OH moiety at C-3 is phenolic in nature and the other OH function at C-6 is a secondary alcoholic group.

5. **Morphine** is a monoacidic base and hence, forms salts that crystallizes rapidly. These are found to be neutral to litmus and methyl orange.

6. The average pH of a saturated solution of morphine salt is found to be 4.68.

Note: Morphine reduces iodic acid and potassium iodate.

Derivatives of Morphine A number of derivatives of morphine are produced that essentially have distinct characteristic features as enumerated below:

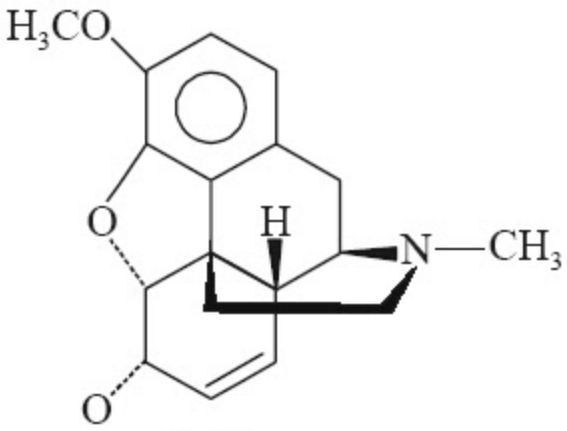
(*iv*) **Solubility Profile:** 1 g dissolves in about 5000 ml of water, 1100 of boiling water, 210 ml of ethanol, 98 ml of boiling ethanol, 1220 ml of chloroform, 6250 ml of ether, 114 ml of amyl alcohol, 10 ml of boiling methanol, 525 ml of ethyl acetate; freely soluble in solutions of fixed alkali and other alkaline earth hydroxides, in phenols, cresols; moderately soluble in mixtures of chloroform with alcohols; and slightly soluble in ammonia benzene.

B. Codeine

Synonyms Codicept; Morphine monomethyl ether; Morphine 3-methyl ether; Methylmorphine.

Biological Sources It is obtained from the plant *Argemone mexicana* L. (*Papaveraceae*) **(Prickly Poppy);** *Eschscholzia california* Cham. (*Papaveraceae*) **(California Poppy);** *Papaver bracteatum* Lindl. (*Papaveraceae*) **(Great scarlet poppy, Thebaine Poppy);** and *Papaver somniferum* L. (*Papaveraceae*) **(Opium Poppy, Poppyseed Poppy Keshi).**

Chemical Structure



Codeine

Preparation It is invariably present in opium from 0.7 to 2.5% depending on the sources of plant substances. However, mostly it is prepared by carrying out the methylation of **morphine.**

Characteristic Features

1. It is obtained as monohydrate orthorhombic sphenoidal rods or tablets (octahedra) from water or dilute ethanol having mp 154-156°C (after drying at 80°C).

2. It is found to sublime (when anhydrous) at 140-145°C under 1.5 mm reduced pressure.

3. It is observed to melt to oily drops when heated in an amount of water is sufficient for complete solution, and subsequently crystallizes on cooling.

5. **Solubility Profile:** 1 g dissolves in 120 ml water, 60 ml water at 80°C, 2 ml ethanol, 1.2 ml hot ethanol, 13 ml benzene, 18 ml ether, 0.5 ml chloroform; freely soluble in methanol, dilute acids and amyl alcohol; and almost insoluble in solutions of alkali hydroxides and in petroleum ether.

Identification Test It forms various types of salts, namely:

1. **Codeine Acetate ($C_{20}H_{25}NO_5$):** The dihydrate is obtained as crystals having an acetic acid odour. It is found to be soluble in water and ethanol. It loses acetic acid on keeping and subsequently turns into a product which is incompletely soluble in water.

2. **Codeine Hydrobromide ($C_{18}H_{21}NO_3$.HBr):** The dihydrate is obtained as crystals and the anhydrous product shows a mp 190-192°C; $[\alpha]_D^{22} - 96.6^0$; 1 g dissolves in 60 ml water, 110 ml ethanol; and pH about 5.

Uses

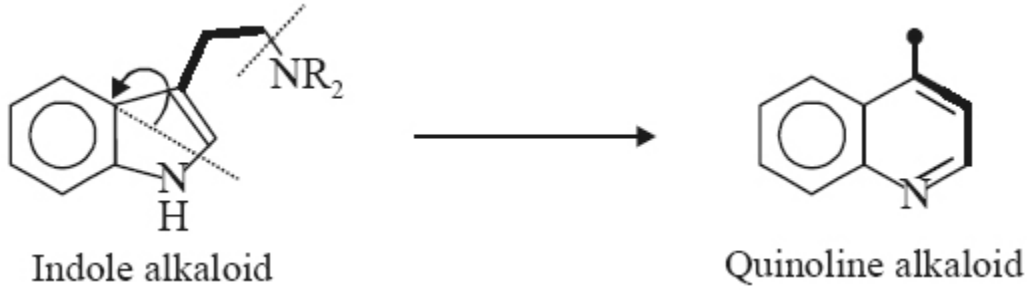
1. It is mostly used as a narcotic analgesic.

2. It is invariably employed as an antitussive.

Quinoline Alkaloids

A good number of very prominent and remarkable examples of the **'quinoline-alkaloids'** derived from *tryphphan* are nothing but the modifications of the terpenoid indole alkaloids commonly found in the genus *Cinchona* belonging to the natural order *Rubiaceae*.

Interestingly, more than twenty alkaloids have been isolated and characterized from the bark of *Cinchona calisaya* and *Cinchona ledgeriana*, very commonly known across the globe as the **Yellow Cinchona;** besides the other equally well-known species *Cinchona succirubra*, popularly known in trade as the **Red Cinchona.** However, the four long prized and most popular **quinoline alkaloids** known for their antimalarial activities are namely: **quinine, cinchonine, quinidine,** and **cinchonidine.** These alkaloids shall now be described individually in the sections that follow. It is worthwhile to state here that these structures are not only unique but also remarkable wherein the indole nucleus is replaced by a quinoline system through an intramolecular rearrangement as given below:

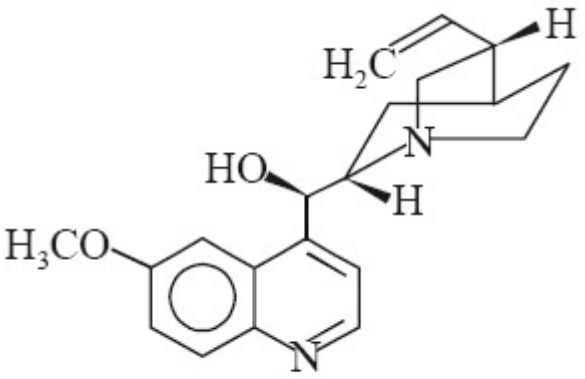


Indole alkaloid Quinoline alkaloid

A. Quinine

Biological Sources The *cinchona* species (*Rubiaceae*) specifically contains **quinine** in the bark upto 16% (mostly 6-10%) in a variety of its species, namely: *Cinchona calisaya* Wedd.; *C. ledgeriana* Moens ex Trimen; *C. officinalis* Linn. f.; *C. robusta* How.; and C. *succirubra* Pavon ex Klotzsch. The representative samples of dried **cinchona, cinchona bark** or **peruvian bark** is found to contain nearly 0.4 to 4% **quinine.**

Chemical Structure



Quinine

Isolation of Quinine, Cinchonine, Cinchonidine and Quinidine The isolation of all the *four* important quinoline alkaloid, such as: **quine, cinchonine; cinchonidine** and **quinidine** may be accomplished by adopting the following steps carefully and sequentially.

Step 1: The cinchona bark is dried, powdered, sieved and treated with calcium oxide (slaked lime), NaOH solution (10% w/v) and water and kept as such for 6-8 hours.

Step II: The resulting mixture is treated with benzene in sufficient quantity and refluxed for 12-16 hours. The mixture is then filtered while it is hot.

Step III: The hot filtrate is extracted successively with 6N. sulphuric acid. The mixture of alkaloidal bisulphate is heated upto 90°C and maintained at this temperature upto 20-30 minutes.

Step IV: The resulting solution is cooled to room temperature and made alkaline by the addition of solid pure sodium carbonate till a pH 6.5 is attained.

Step V: The alkaloidal sulphate solution thus obtained is treated with sufficient quantity of activated charcoal powder (1g per 1L), boil, shake vigorously and filter.

Step VI: Cool the hot filtrate slowly in a refrigerator (2-10°C) overnight and again filter. Collect the residue and the filtrate separately.

Step VII: The residue (or precipitate) of quinine sulphate is boiled with water and made alkaline by adding cautiously solid sodium carbonate. The resulting precipitate is that of **quinine.**

Step VIII: The filtrate obtained from step-VI comprises of **cinchonine, cinchonidine** and **quinidine;** which is treated with NaOH solution (10% w/v) very carefully to render it *just alkaline*. It is successively extracted with adequate quantity of ether. The lower (aqueous layer) and the upper(ethereal layer) are collected separately.

Step IX: The aqueous layer contains **cinchonine.** It is evaporated to dryness in a Rotary Film Evaporator, extracted with absolute ethanol, decolourized with activated charcoal powder and allow it to crystallize slowly in a refrigerator (2-10°C) overnight. The crystals of **cinchonine** are obtained.

Step X: The ethereal layer obtained in step-VIII contains **quinidine** and **cinchonidine.** It is extracted with dilute HCl (2N) several times till a drop of the extract on evaporation does not give a positive test for alkaloids. Neutralize the combined acidic extract by adding solid sodium potassium tartrate *carefully.* Filter the resulting mixture and collect the *precipitate* and the *filtrate* separately.

Step XI: The precipitate of **cinchonidine tartrate** is treated with dilute HCl carefully. The resulting solution of alkaloid hydrochloride is made alkaline by the addition of dilute ammonium hydroxide when **cinchonidine** is obtained as a precipitate.

Step XII: The filtrate obtained from Step-X contains quinidine tartrate which is treated with solid potassium iodide powder carefully till the whole of quinidine gets precipitated as quinidine

hydroiodide salt. It is filtered and the solid residue is finally treated with dilute NH_4OH to obtain the precipitate of **quinidine.**

Characteristic Features

1. It is obtained as orthorhombic needles from absolute ethanol having mp 177° (with some decomposition).

2. It sublimes in high vacuum at 170-180°C.

3. The pH of its saturated solution in 8.8.

4. It gives a distinct and characteristic blue fluorescence which is especially strong in dilute sulphuric acid.

7. **Solubility Profile:** 1 g dissolves in 1900 ml water; 760 ml boiling water; 0.8 ml ethanol; 80 ml benzene; 18 ml benzene at 50°; 1.2 ml chloroform; 250 ml by ether; 20 ml glycerol; 1900 ml of 10% ammonia water; and almost insoluble in petroleum ether.

Identification Tests Quinine may be identified either by a series of **Colour Tests** or by the formation of several known derivatives having characteristic features; and these shall be discussed separately as under:

(*a*) Colour Tests: These are, namely

1. **Oxygenated Acids:** Oxygenated acids, such as: sulphuric acid or acetic acid gives a strong blue fluorescence with quinine. This test is very sensitive even in extremely dilute solutions.

2. **Herpathite Test:** To a boiling mixture of quinine (0.3g) in 7.5 ml glacial acetic acid, 3 ml ethanol (90% v/v) and 5 drops of concentrated H2SO4, add 3.5 ml of I2 solution (1% w/v) in ethanol, crystals of *iodosulphate of quinine* or **Herpathite*** separates out on cooling. The crystals thus obtained exhibit metallic lustre, appears dark in reflected light and alive-green in transmitted light.

3. **Thalleioquin Test:** When a few drops of bromine water are added to 2 or 3 ml of a weakly acidic solution of quinine salt, followed by the addition of 0.5-1.0 ml of strong ammonia solution, it produces a distinct characteristic emerald green colouration. It is an extremely

sensitive colour test which may detect quinine even upto a strength as low as 0.005% (w/v). The end coloured product is known as **thalleioquin** for which the exact chemical composition is not yet known.

(*b*) Both cinchonine and cinchonidine do not respond to the Thalleioquin Test.

Uses

1. It is frequently employed as a flavour in carbonated beverages.
2. It is used as an antimalarial agent.
3. It is also employed as a skeletal muscle relaxant.
4. It has been used to treat hemorrhoids and varicose veins.
5. **Quinine** is also used as a oxytocic agent.
6. **Quinine** is supposed to be prophylactic for flu.