Unit – I (BOP-474)

Alkaloids,

Occurrence and Distribution in Different Organ's of Plant:

McKee* (1962) reported that about 1000 **alkaloids,** which are known, belong to almost 100 families, 500 genera and spread over 1200 species. However, it has been observed beyond reasonable doubt that the **alkaloids** are not evenly distributed amongst the plant kingdom. They have been found to be absent in *Algae* and in the lower groups of plants with the exception of one or two families of the fungi. The glaring examples of fungal alkaloids include those of ergot alkaloids.

Classification of alkaloids.

Classifies **alkaloids** in the following *four* heads, namely:

(a) **Biosynthetic Classification**

Examples

(*i*) Indole alkaloids derived from *tryptophan*.

(*ii*) Piperidine alkaloids derived from *lysine*.

(*iii*) Pyrrolidine alkaloids derived from *ornithine*.

(*iv*) Phenylethylamine alkaloids derived from *tyrosine*.

(*v*) Imidazole alkaloids derived from *histidine*.

(*b*) Chemical Classification

Examples

(*i*) Pyrrolidine alkaloids *e.g.*, **Hygrine;**

(*ii*) Piperidine alkaloids *e.g.*, **Lobeline;**

(*iii*) Pyrrolizidine alkaloids *e.g.*, **Senecionine;**

(*iv*) Tropane alkaloids *e.g.*, **Atropine;**

(*v*) Quinoline alkaloids *e.g.*, **Quinine;**

(*vi*) Isoquinoline alkaloids *e.g.*, **Morphine;**

(*vii*) Aporphine alkaloids *e.g.*, **Boldine;**

(*viii*) Indole alkaloids *e.g.*, **Ergometrine;**

(*ix*) Imidazole alkaloids *e.g.*, **Pilocarpine;**

(*x*) Diazocin alkaloids *e.g.*, **Lupanine;**

(*xi*) Purine alkaloids *e.g.*, **Caffeine;**

(*xii*) Steroidal alkaloids *e.g.*, **Solanidine;**

(*xiii*) Amino alkaloids *e.g.*, **Ephedrine;**

(*xiv*) Diterpene alkaloids *e.g.*, **Aconitine.**

(c)Pharmacological Classification

Examples

(*i*) **Morphine** as Narcotic analgesic;

(*ii*) **Quinine** as Antimalarial;

(*iii*) **Strychnine** as Reflex excitability;

(*iv*) **Lobeline** as Respiratory stimulant;

(*v*) **Boldine** as Choleretics and laxatives;

(*vi*) **Aconitine** as Neuralgia;

(*vii*) **Pilocarpine** as Antiglaucoma agent and miotic;

(*viii*) **Ergonovine** as Oxytocic;

(*ix*) **Ephedrine** as Bronchodilator;

(*x*) **Narceine** as Analgesic (narcotic) and antitussive.

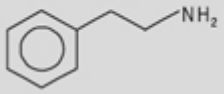
(*d*) Taxonomic Classification

(*i*) **Cannabinaceous Alkaloids:** *e.g.*, *Cannabis sativa* Linn., (**Hemp, Marijuana**).

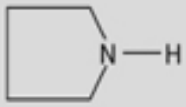
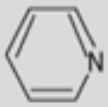
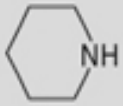
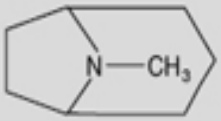
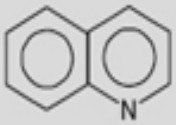
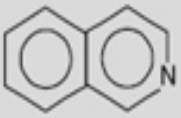
(*ii*) **RubiaceousAlkaloids:** *e.g.*, *Cinchona Sp.* (**Quinine**); *Mitragyna speciosa* Korth (**Katum, Kratum, Kutum**); *Pausinystalia johimbe* (K. Schum) (**Yohimbe**).

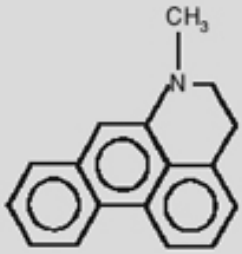
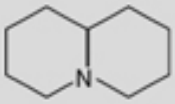
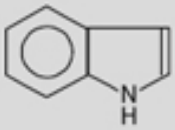
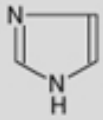
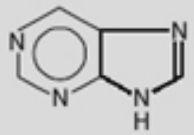
(*iii*) **SolanaceousAlkaloids:** *e.g.*, *Atropa belladona* L., (**Deadly Nightshade, Belladona**); *Hyoscyamus niger* L. (**Henbane, Henblain, Jusquaime**); *Mandragora officinarum* L..

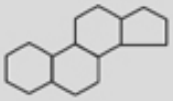
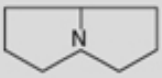
(*a*) Non-heterocyclic Alkaloids A few typical **alkaloids** having non-heterocyclic nucleus are erumerated below:

S.No.	Basic Ring Structure	Alkaloid	Botanical Origin	Family
1	**Phenylethylamine** 	Ephedrine	*Ephedra vulgaris*	*Gnetaceae*
		Hordenine	*Hordeum vulgare*	*Graminae*
		Capsaicin	*Capsicum annunum*	*Solanaceae*
		Mescaline	*Laphophora williamsii*	*Cactaceae*
		Narceine	*Papaver somniferum*	*Papaveraceae*

(*b*) Heterocyclic Alkaloids A large number of specific **alkaloids** possessing heterocyclic nucleus are stated below:

S.No.	Basic Ring Structure	Alkaloid	Botanical Origin	Family
1	**Pyrrolidine** 	Hygrine Stachydrine	*Erythroxylon coca* *Stachys tuberifera*	*Erythroxylaceae* *Labiatae*
2	**Pyrindine** 	Arecoline Ricinine Trigenelline	*Areca catchu* *Ricinus communis* *Trigonella foenumgraecum*	*Palmaceae* *Euphorbiaceae* *Leguminosae*
3	**Piperidine** 	Connine Lobeline Pelletierine	*Conium maculatum* *Lobelia inflata* *Punica granatum*	*Umbelliferae* *Lobeliaceae* *Punicaceae*
4	**Tropane [Piperidine-Pyrrolidine (N-Methyl)]** 	Atropine Cocaine Hyoscyamine	*Atropa belladone* Datura stramonium *Erythroxylon coca* *Atropa belladona*	*Solanaceae* *Solanaceae* *Erythroxylaceae* *Solanaceae*
5	**Quinoline** 	Quinine, Quinidine Cuspareine	*Cinchona officinalis* *Cusparia trifoliata*	*Rubiaceae* *Rutaceae*
6	**Isoquinoline** 	Papaverine Berberine Emetine Corydaline Tubocurarine	*Papaver somniferum* *Hydrastis canadensis* *Uragoga ipecacuanha* *Corydalis aurea* *Corydalis solida* *Chondodendron tomentosum*	*Papaveraceae* *Berberidaceae* *Rubiaceae* *Fumariaceae* *Fumariaceae* *Menispermaceae*

7	**Aporphine Isoquinoline Phenanthrene** 	Boldine	*Peumus boldus*	*Monimiaceae*
8	**Norlupinane** 	Sparteine	*Lupinus lutens, Lupinus niger, Cytisus scoparius, Anagyris boetida*	*Leguminosae*
		Lupinine	*Lupinus luteus*	*Leguminosae*
			Anabasis aphylla	*Chenopodiaceae*
9	**Indole (Benzopyrrole)** 	Ergotamine, Ergometrine	*Claviceps purpurea*	*Hypocreales*
		Physostigmine	*Physostigma Venenosum*	*Leguminosae*
		Reserpine	*Rauwolfia serpentina*	*Apocynaceae*
		Yohimbine	*Coryanthe johimbe*	*Rubiaceae*
			Rauwolfia serpentina	*Apocynaceae*
		Vinblastine (Vincaleukoblastine)	*Vince rosea*	*Apocynaceae*
		Strychnine	*Strychnos nux-vomica*	*Loganiaceae*
10	**Imidazole (Glyoxaline)** 	Pilocarpine	*Pilocarpus jaborandi*	*Rutaceae*
11	**Purine (Pyrimidine-Imidazole)** 	Caffeine	*Thea sinensis Camellia sinensis*	*Ternstroemiaceae*
			Coffea arabica	Rubiaceae
			Theobroma cacao	Sterculiaceae

12	**Tropolone** 	Colchicine	*Colchicum autumnale*	*Liliaceae*
13	**Steroid** 	Connesine	*Holarrhena anti-dysenterica*	*Apocynaceae*
		Funtumine	*Funtumia latifolia*	*Apocynaceae*
		Solanidine	*Solanum spp.*	*Solanaceae*
		Veratramine	*Veratrum grandiflorum, Veratrum viride*	*Liliaceae*
14	**Terpenoid (Diterpene)**	Aconine	*Aconitum napellus*	*Ranunculaceae*
		Aconitine (Glycoside)	–do–	–do–
		Atisine	*Aconitum heterophyllum, Aconitum anthora,*	*Ranunculaceae*
		Lycoetonine	*Aconitum lycoctonum,*	*Ranunculaceae*
15	**Pyrrolizidine** 	Sennecionine	*Senecio vulgaris*	*Compositae*
		Senneciphylline	*Senecio platyphllus*	*Compositae*

The various reagents that are invariably used either for the testing of **alkaloids** by precipitation or by the formation of microcrystalline complexes (salts) are as stated below along with their individual compositions, namely:

(*i*) **Mayer's Reagent (Potassium-Mercuric Iodide Test Solution):**

Mercuric chloride = 1.36 g, Potassium Iodide = 3.00 g ,Distilled water to make = 100.00 ml

(*ii*) **Wagner's Reagent (Potassium Triiodide):**

Iodine = 1.3 g ,Potassium = 2.0 g,Distilled water to make = 100.00 ml

(*iii*) **Kraut's Reagent (Modified Dragendorff's Reagent or Potassium Bismuth Iodide):**

Bismuth Nitrate = 8.0 g ,Nitric Acid = 20.0 ml ,Potassium Iodide = 27.2 g

Distilled water to make = 100.00 ml

(*iv*) **Marme's Reagent (Potassium-Cadmium Iodide Reagent):**

Cadmium Iodide = 10.0 g ,Potassium Iodide = 20.0 g ,Distilled water to make = 100.00 ml

(*v*) **Scheibler's Reagent (Phosphotungstic Acid Reagent):**

Sodium Tungstate = 20.0 g ,Disodium Phosphate = 70.0 g,Distilled water to make = 100.00 ml

Note: Acidify with nitric acid to litmus paper.

(*vi*) **Hager's Reagent:** A saturated solution of *Picric Acid.*

(*vii*) **Sonnenschein's Reagent (Phosphomolybdic Acid):**

A 1% (w/v) solution of phosphomolybdic acid in ethanol.

(*viii*) **Bertrand's Reagent (Silicotungstic Acid):**

A 1% (w/v) solution of silicotungstic acid in distilled water.

Note: Filter and store in a refrigerator.

[E] Colour Reactions with Specific Reagents : A number of such **specific reagents** shall be described in the section that follows:

(*a*) **Froehd's reagent:** Dissolve 5 mg of molybdic acid or sodium molybdate in 5 ml of pure concentrated H_2SO_4.

Note: The reagent should be freshly prepared before use.

(*b*) **Erdmann's reagent:** A mixture of 10 drops of concentrates HNO_3, and 100 ml of water are added to 20 ml of pure concentrated H_2SO_4.

(*c*) **Marqui's reagent:** A mixture of 2-3 drops of formaldehyde solution (40%) with 3 ml of concentrated H_2SO_4.

(*d*) **Mandalin's reagent:** Dissolve 1 g of finely powdered ammonium vanadate in 200 g of pure conc. H_2SO_4.

A few typical pharmacological actions of some **alkaloids** are stated below showing their broadspectrum of activities, namely:

S.No.	Alkaloid	Pharmacological Action
1	**Morphine**	Narcotic analgesic
2	**Codeine**	Expectorant, analgesic
3	**Brucine**	CNS-Stimulants
4	**Strychnine**	CNS-Stimulants
5	**Ergotamine**	Uterine muscle contractions
6	**Atropine**	Mydriatics
7	**Homotropine**	Mydriatics
8	**Pilocarpine**	Myotics
9	**Physostigmine**	Myotics
10	**Ephedrine**	Hypertensive
11	**Reserpine**	Hypotensive
12	**Quinine**	Antimalarial
13	**Caffeine**	CNS-stimulant
14	**Tubocurarine**	Neuromuscular blocking action
15	**Emetine**	Antiprotozoal action
16	**Hyoscyamine**	Relief of spasms of urinary tract
17	**Cocaine**	CNS-stimulant
18	**Colchicine**	Anti-gout
19	**Lobeline**	Treatment of asthma
20	**Arecoline**	Parasympathomimetic action
21	**Protoveratrine A**	For management of hypertension in pregnancy
22	**Conessine**	Antiprotozoal and antiamoebic
23	**Vasicine**	Expectorant and bronchodilator
24	**Vinblastine**	Antineoplastic
25	**Vincristine**	Antineoplastic
26	**Piperine**	Carminative, stomachic
27	**Heroin**	Narcotic analgesic
28	**Hyoscine**	Motion sickness (sedation)
29	**Theophylline**	Smooth musele relaxant
30	**Aconitine**	Treatment of neuralgia, sciatica, rheumatism and inflammation.

Pyridine Alkaloids

The *three* above mentioned **pyridine alkaloids,** *viz*., **nicotine, anabasine** and **niacin,** shall now be discussed individually in the sections that follows:

Tobacco

Synonym: *Nicotiana chinensis* American tobacco, Nicotania tabacum, Nicotiana tabacum L, Nicotiana tabacum var. Samsun, tobacco.

Biological Source :

It is obtained from the dried leaves of *Nicotiana tabacum* Linn., (*Solanaceae*)

Geographic Information

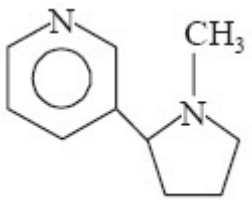
Plant or plant parts used in or around the home.Tobacco is cultivated in some areas of Canada as a commercial crop for the tobacco industry.

Description:

Herbs viscid, annual or short-lived perennial, 0.7-2 m tall, glandular hairy overall. leaf blade ovate to elliptic or lanceolate, membranous, glandular hairy, base narrowed, nearly half clasping, apex acuminate.

Chemical Constituent: Nicotine, nornicotine & anabasine.

Chemical Structure



Nicotine

Characteristic Features

1) It is a colourless to pale yellow oily liquid, very hygroscopic in nature, and turns brown on exposure to air and light.
2) It has an inherent acrid burning taste.
3) It develops the odour of pyridine.
4) It has a bp 247°C with partial decomposition..
5) It is a steam-volatile product.
6) It readily forms salts with almost any acid; and double salts with many metals and acids.
7) **Solubility:** It is miscible with water below 60°C; and on mixing nicotine with water the volume contracts. However, it is found to be very soluble in chloroform, ethanol, ether, petroleum ether and kerosene oils.

Identification Tests

1. **Nicotine Hydrochloride ($C_{10}H_{14}N_2$.HCl):** It is obtained as deliquescent crystals having specific rotation $[\alpha]_D^{20}$ $+104^0$.

2. **Nicotine Dihydrochloride ($C_{10}H_{14}N_2$.2HCl):** The deliquescent crystals are extremely soluble in water and ethanol.

Uses

1. It is used extensively as an insecticide and fumigant.

2. It finds its application as a **'<u>contact poison</u>'** in the form of soap *i.e.*, as its oleate, laurate and naphthenate salts.

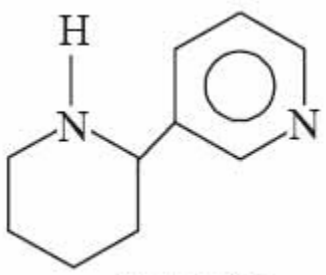
3. It is also used as a **'stomach poison'** in combination with bentonite.

4. One of its recent applications nicotine is employed as chewable tablets of lozenges for the treatment of smoking withdrawl syndrome.

5. It possesses a unique action on the autonomic ganglia which it first stimulates and subsequently depresses ultimately leading to *paralysis.*

Anabasine

Synonym Neonicotine;



Anabasine

Chemical Structure

Characteristic Features

1) It is a liquid freezing at 9°C; and boiling at 270-272°C.
2) It is soluble in most organic solvents and water.

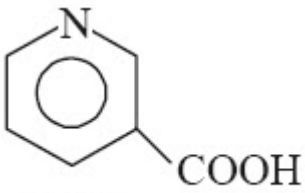
Identification Tests

1. Being a secondary amine it can form a nitroso derivative.

Uses It is invariably employed as an effective insecticide.

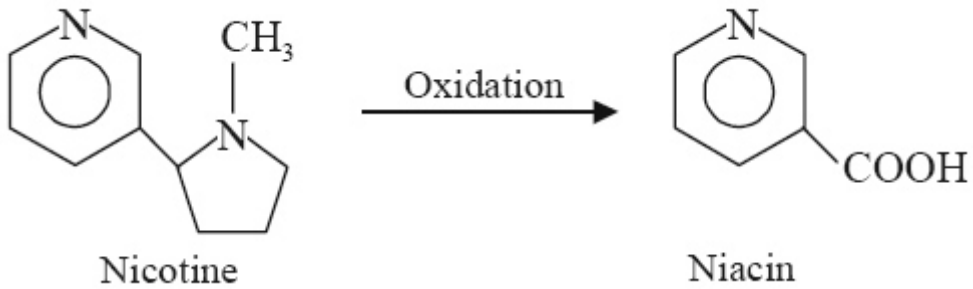
Niacin

Chemical Structure



Niacin

Preparation It may be prepared by the **oxidation of nicotine*** as given below.



Nicotine Niacin

Characteristic Features:

1. It sublimes without any decomposition.
2. It is a nonhygroscopic substance and fairly stable in air.
3. It shows uv_{max} : 263 nm; and pH 2-7 of a saturated solution.
4. *Solubility:* 1 g dissolves in 60 ml water; freely soluble in boiling water and ethanol; soluble in propylene glycol; and insoluble in ether.

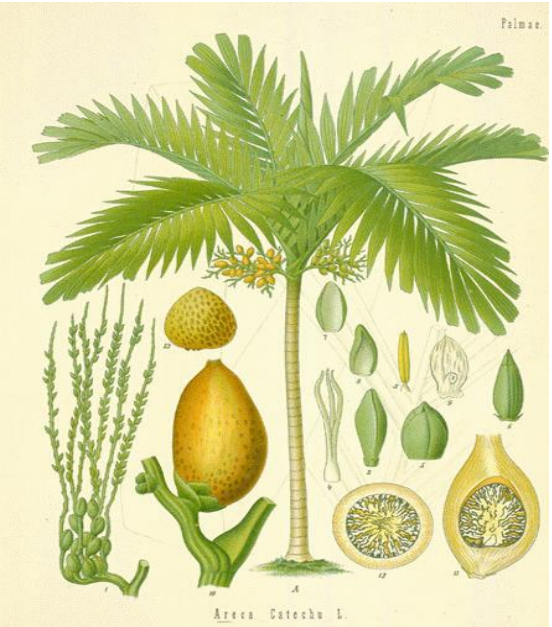
Uses

1. It is used as antihyperlipoproteinemic agent.
2. It is a vital vitamin (enzyme cofactor).

Areca

Common Name: Areca seed, Betel nut.

BotanicalName: *Areca catechu* L., Family –Palmae.



Description---A handsome tree cultivated in all the warmer parts of Asia for its yellowish-red fruits, conical shape with flattened base and brownish in colour externally; internally mottled like a nutmeg.

The seeds are cut into narrow pieces and rolled inside Betel Pepper leaf, rubbed over with lime and chewed by the natives.

They stain the lips and teeth red and also the excrement, they are hot and acrid when chewed.

Part Used & Method for Pharmaceutical Preparations: The seeds from the ripe fruit are collected in winter or spring. They are dried in the sun, soaked in water and cut into slices.

Properties & Taste: Pungent, bitter and warm.

Chemical composition:

The seed contains alkaloids such as arecaidine and arecoline, which, when chewed, are intoxicating and slightly addictive. The seed also contains condensed tannins (procyanidins) called arecatannins which are carcinogenic.

Use:

1. To kill parasites.

2. To promote circulation.

3. To promote water metabolism.

Other Species---In Malabar *Areca Dicksoni* is found growing wild and is used by the poor as a substitute for the true Betel Nut (*A. aleraceae*).

Piperidine Alkaloids

The various important alkaloids that essentially have the *piperidine nucleus* are, namely: **Coniine, Lobeline, Lobelanine** and **Piperine,** which shall be discussed individually in the sections that follows:

Lobelia

Nomenclature:

Scientific Name: *Lobelia inflata* L.

Vernacular name(s): Indian-tobacco

Scientific family name: *Campanulaceae*

Vernacular family name: bellflower

Geographic Information

British Columbia, New Brunswick, Nova Scotia, Ontario, Prince Edward Island, Quebec.

General symptoms of poisoning:

Collapse, coma, death, pain, paralysis, sweating, vomiting.

Notes on poisoning:

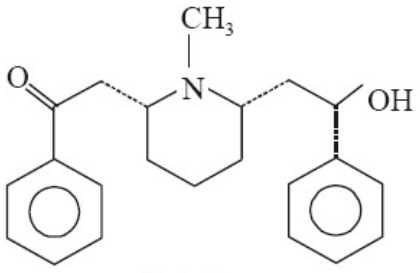
In overdoses of the plant extract, symptoms included vomiting, sweating, pain, paralysis, depressed temperature, rapid but feeble pulse, coma, and death.

Chemical Constituents :

Lobeline

Synonyms α-Lobeline; Inflatine;

Chemical Structure



Lobeline

Characteristic Features

1. Lobeline is obtained as needles from ethanol, ether and benzene having mp 130-131°C.

2. It is freely soluble in chloroform, ether, benzene and hot ethanol; and very slightly soluble in water and petroleum ether.

Identification Tests

1. **Colour Test: Lobeline** on the addition of a few drops of concentrated sulphuric acid followed by a drop of formalin solution gives rise to a distinct red colouration.

2. **Froehd's Test:** It produces an instant rose red colouration with **Froehd's Reagent** that ultimately changes to blue.

3. **Erdmann's Reagent:** It develops a faint green colour which intensifies on slight warming.

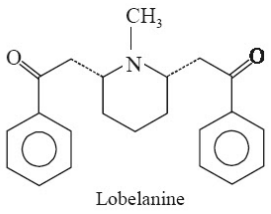
Uses:

1. It is widely used as a respiratory stimulant.

2. Its effects resemble those of **nicotine** and hence used in lozenges or chewing tablets, containing 0.5-1.5 mg of **Lobeline Sulphate,** to help in breaking the tobacco habit, otherwise known as **'smoking deterrants'.**

Lobelanine

Chemical Structure



Lobelanine

Characteristic Features

1. It is obtained as rosettes of needles from ether or petroleum ether having mp 99°C.

2. It is freely soluble in acetone, benzene, ethanol, chloroform; and slightly soluble in water and ether.

Identification Tests

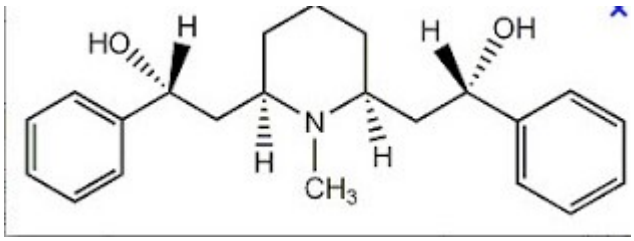
1. **Lobelanine Hydrochloride ($C_{22}H_{25}NO_2$.HCl):** The crystals obtained from dilute ethanol decomposes at 188°C; it is soluble in chloroform; and slightly soluble in absolute ethanol and cold water.

2. **Lobelanine Hydrobromide ($C_{22}H_{25}NO_2$.HBr):** The crystals do not give a sharp mp, but gets decomposed at 188°C.

3.

Lobelanidine

Chemical Structure



Lobelanidine

Characteristic Features

1. It is obtained as scales from ethanol with mp 150°C.

2. It is freely soluble in benzene, chloroform, acetone; slightly soluble in ether, petroleum ether; and almost insoluble in water.

Identification Tests

1. **Lobelanidine Hydrochloride ($C_{22}H_{29}NO_2$. HCl)*:*** It is obtained as needles from ethanol having mp 135-138°C.

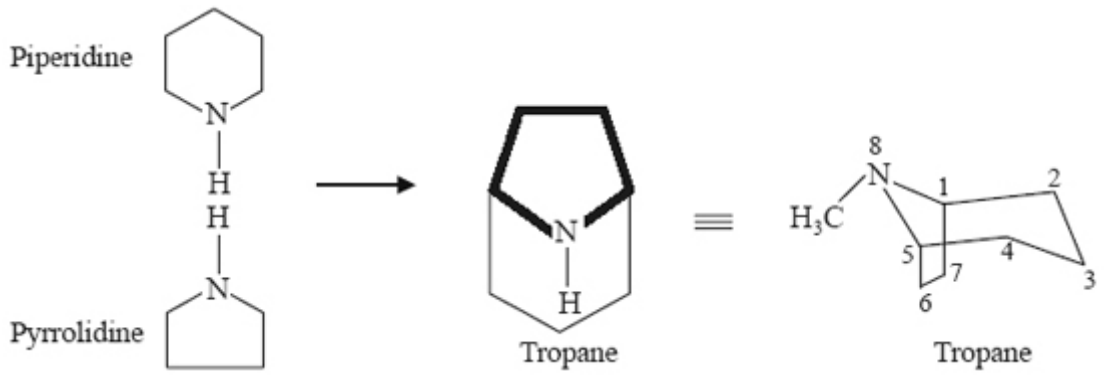
2. **Lobelanidine Hydrobromide ($C_{22}H_{29}NO_2$.HBr)*:*** Its crystals have a mp 189°C.

Uses.

Lobelia is used in spasmodic asthma and chronic bronchitis.

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 essentially consists of a 7-carbon bicyclic ring with a N-atom strategically bridged between C-1 and C-5 and providing a C_7N unit. It is, however, pertinent to mention here that the tropane base contains two chiral centres (*i.e.*, asymmetric C-atoms), namely: C-1 and C-5, but surprisingly it does not exhibit any optical activity (an exception) by virtue of the fact that *intramolecular compensation* prevails. 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:

Belladonna

Synonyms:

Folia belladonnae, Belladonna herb, Belladonna leaves, deadly nightshade leaves, Sag-angur Patti (Hindi).

Botanical source: It consists of dried leaves and flowering tops of *Atropa belladonna* Linn.

Family: Solanaceae

Geographical source: Plant is a native of Central and Southern Europe. It is cultivated in England, Germany, Balkan countries, America and in India also.

Macroscopical characters:

Leaves:

(i) Type- Simple;

(ii) Form-Broadly ovate;

(iii) Color- yellowish-green;

(iv) Arrangement – alternate, arranged in pairs on the upper stems, each pair with a large and a small leaf;

(v) Size- 5-25 cm length, 2, 5-12 cm broad;

(vi) Margin- acuminate;

(vii) Surface- slightly hairy; Petiolate, petiole 4cm length

Flower:

(i) Colour- purple;

(ii) Size- 2.5 cm length, 1.2 cm wide;;

(iii) Arrangement of flower- born singly upon short, drooping pedicels arising in

(iv) the axils of the pairs of leaves;

(v) Corolla- campanilate;

(vi) Calyx- 5 lobed, stemns-5, epipetalous;

(vii) Ovary- superior, bilocular with numerous ovules and axile Placentation.

Atropa belladonna L.

Fruits:

(i) Colour- green to dark purplish black,

(ii) Type- berry.

Microscopical characters of belladonna root:

Periderm:

Periderm is distinguishable into Phellem and Phellodenn.

Cork:

Cork few layers, cells tangentially elongated and arranged in radial rows.

Phellogen:

Phellogen is not distinguishable through a faint layer can be made out.

Phelloderm:

Phelloderm few layers, cells tangentially elongated and contain starch and yellowish matter.

Secondary Phloem:

Several layers of starch bearing parenchyma with groups of sieve elements. Phloem fibres absent. Numerous sandy bails, a characteristics feature of belladonna root and leaf, are seen scattered throughout in the phloem tissue.

Cambium:

It is represented in the form of a ring containing 4 to 5 layers of rectangular cells arranged in radial rows.

Secondary xylem:

Secondary xylem forms the bulk of the root and occupied a large area. Secondary xylem consists of largely starch bearing parenchyma with several scattered groups of vessels (3 to 10), associated with tracheids, fibres and Cellulosic parenchyma. The groups of vessels are more towards the cambium. Primary xylem forming the central mass shows distinct diarch nature.

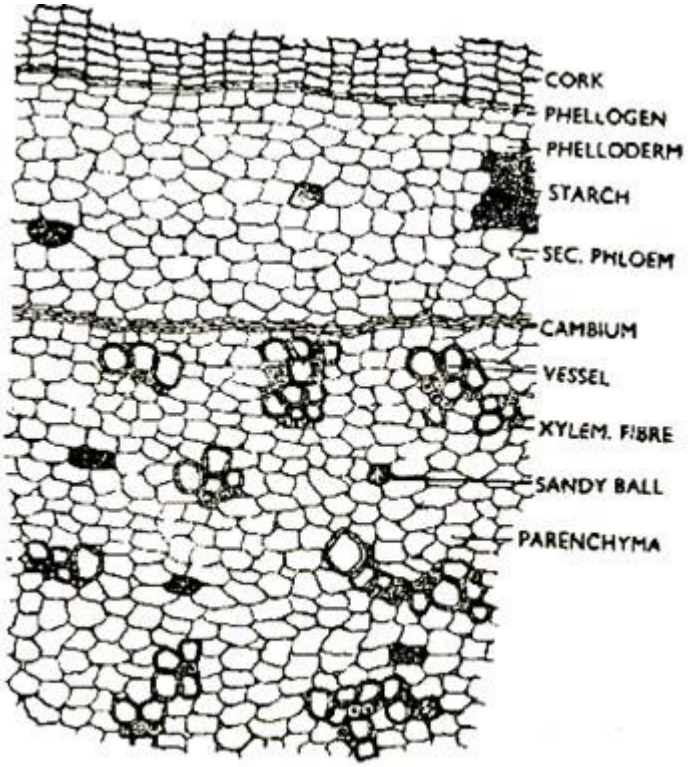


Fig. 3: T. S. of belladonna root

Chemical constituents:

1. Tropane alkaloids (0.2-0.5%):

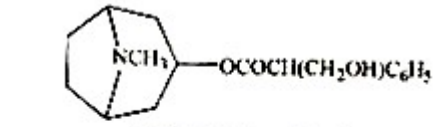
i. L-hyoscyamine (90%),

ii.D, L- hyoscyamine(Atropine)

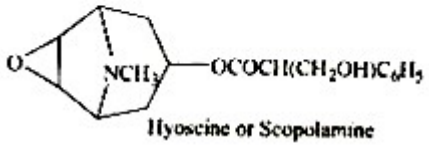
iii. Scopolamine (10%),

iv. Apoatropine,

iv. Belladonnine (+).



Hyoscyamine or Atropine



Hyoscine or Scopolamine

Uses:

1) Mydriatic (dilation of the pupil).
2) Antispasmodic (a drug that counteracts a sudden, violent, involuntary muscular contraction)
3) Antimuscarinic effect (acts peripherally to produce parasympathetic inhibition).
4) Antisialagogue (a drug that arrest the flow of excess of saliva)
5) Cerebral sedative (reduce excitement)

Chemical Test:

Vitali Test:

A drop of fuming HNO_3 is added it a small portion of a extract of any Solanaceous drug like species of Atropa, Hyoscyamus and Datura or the Tropane alkaloids themselves and then evaporated to dryness on a water bath. Thereafter it is cooled and on addition of 2 drops of 5% alcoholic potassium hydroxide solution, purple colour is formed indicating the presence of Tropane alkaloids.

Datura

Botanical source: It consists of dried leaves and flowering tops of Datura metal Linn. And Datura stramonium.

Family: Solanaceae

Macroscopical characters:

Leaves:

(i) Sub glabrous spreading herb with cylindrical stem.

(ii) Shape single triangular ovate.

(iii) Base unequal

(iv) Margin toothed.

Flower:

(i) Solitary, funnel shaped large and tubular, 7.5 to 9 cm length.

(ii) Corolla 15 to 18 cm length, 10-12.5 cm across at the mouth

Fruit:

Sub-globose capsule covered with short and blunt spines, 2.5 to 3.2 cm diameter nodding or sub erect.

Microscopical characters:

Lamina:

Upper epidermis:

They are single layered, cells rectangular with cuticularized outer walls. Trichomes, both covering and glandular are seen. Covering trichomes are uniseriate, multicellular, warty and blunt at the apex. Glandular trichomes are made up to a stalk of one cell and a 2 to 4 celled glandular head.

Mesophyll:

It is differentiated into palisade and spongy parenchyma.

Palisade:

It is a single layered, compact and cells radially elongated

Spongy parenchyma:

They are many layered, loosely arranged with intercellular spaces. Sphaeraphides, microsphenoidal crystals and vascular strands are found in the upper layers of spongy parenchyma.

Lower epidermis:

It is identical to upper epidermis. Stomata and numerous trichomes are seen on the lower epidermis.

Midrib:

The epidermis layers of lamina are continuous in the midrib region also. Strips of collenchymas appear below the upper and above the lower epidermis. This is followed by cortical parenchyma containing prisms of calcium oxalate and microsphenoidal crystals. Embedded in the central region of the cortical parenchyma is a bicollateral bundle.

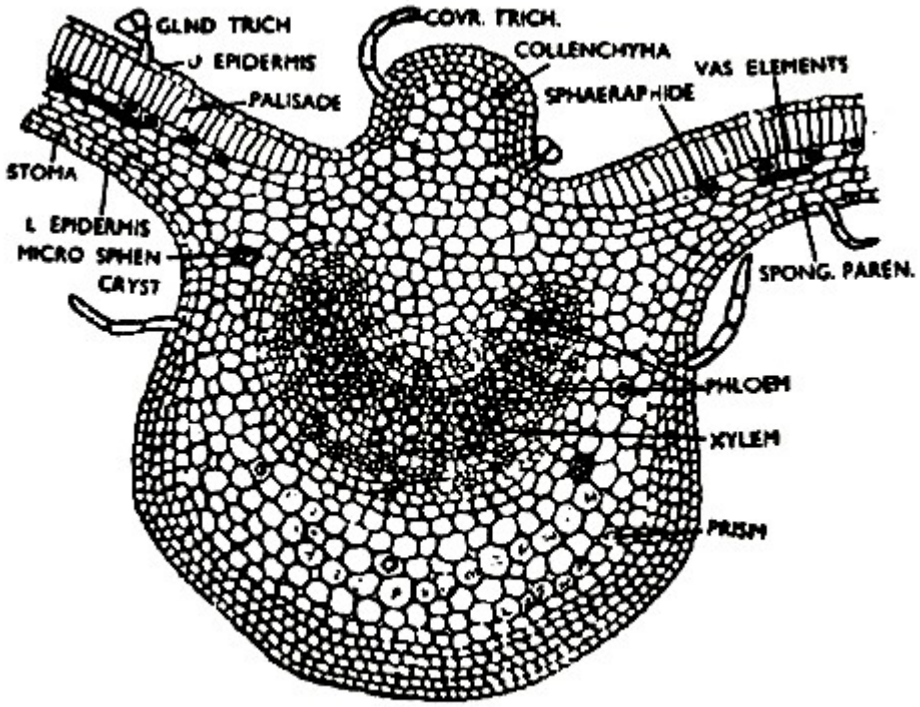


Fig. 5: T. S. of datura leaf

Chemical constituents:

1. Tropane alkaloids-

a. Hyoscyamine

b. Scopolamine (hyoscine)

2. Fastudine and fastunine,

3. Fastusic acid, alantoin.

4. Ascorbic acid, etc.

Hyoscyamine or Atropine

Hyoscine or Scopolamine

Uses:

1. Mydriatic (dilation of the pupil).

2. Antispasmodic (a drug that counteracts a sudden, violent, involuntary muscular contraction)

3. Antimuscarinic effect (acts peripherally to produce parasympathetic inhibition).

4. Antisialagogue (a drug that arrest the flow of excess of saliva)

5. Cerebral sedative (reduce excitement)

Chemical Test:

1. Vitali- Morin reactions:

The drug is treated concentrated nitric acid, filtered and solution is evaporated to dryness. To the residue, add acetone and methanolic potassium hydroxide solution, violet colour is produced due to Tropane derivative.

Stramonium

Botanical source: leaves & flowering tops of datura stramonium **Family:**solanaceae .

Morphology:

Leaves are grayish green with a crenate margin & unequal base

Microscopic Characters:

- Dorsiventral leaf.
- Collenchyma above & below the mid rib .
- Unicellular covering & glandular trichomes .
- Xylem surrounded by phloem .
- Anisocytic stomata

Chemistry: Hyoscine, atropine, belladonine

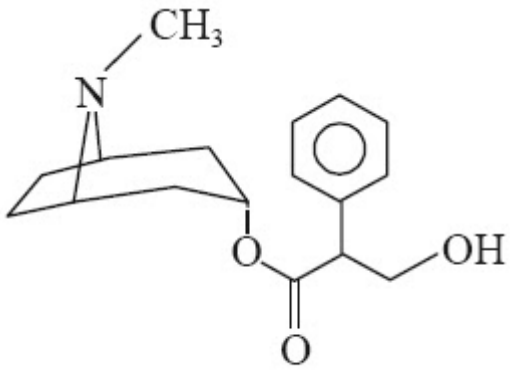
Use: Hyoscine is an antiemetic.

Chemical Test: Vitali morin test.

Atropine

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

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.

3. **Solubility:** 1 g dissolves in 455 ml water; 90 ml water at 80°C; 2 ml ethanol; 27 ml glycerol; 25 ml ether, 1 ml chloroform; and in benzene.

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.

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.

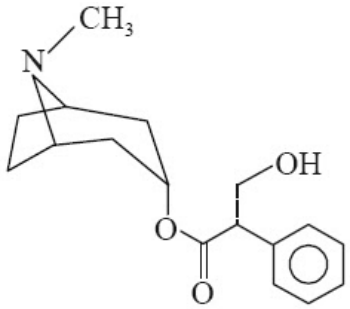
6. It also find its applications to reduce such secretions as: saliva, sweat, and gastric juice.

Hyoscyamine

Synonyms *l*-Tropine Tropate; Daturine; Duboisine; *l*-Hyoscyamine;

Biological Sources It is obtained from the roots and leaves of *Atropa bella*dona L. (*Solanaceae*) (0.21%) (**Thorn Apple**); fruits, roots and leaves of *Datura metel* L. (*Solanaceae*) (**Unmatal, Metel, Hindu Datura**); leaves and seeds of *Datura stramonium* L. (*Solanaceae*) (**Jimson Weed, Thorn Apple, Stramonium**); root bark of *Duboisia myoporoides* R. Br. (*Solanaceae*) (**Pituri, Corkwood Tree**); young plants of *Hyoscyamus niger* L. (*Solanaceae*) (**Henbane, Henblain Jusquaime**);

Chemical Structure



Hyoscyamine

Characteristic Features:

1. **Hyoscyamine** is obtained as silky tetragonal needles from evaporating ethanol having mp 108.5°C.

2. **Solubility Profile:** 1 g dissolves in 281 ml water , 69 ml ether, 150 ml benzene, and 1ml chloroform. It is freely soluble in dilute mineral acids and ethanol.

Identification Tests The various identification tests for **hyoscyamine** are, namely:

1. **Gerrard Reaction: Hyoscyamine** (and also **atropine**) responds to the **Gerrard Reaction** wherein about 5-10 mg of it reacts with mereuric chloride solution (2% w/v) in 50% ethanol to give rise to an instant red colouration without warming.

2. **Schaer's Reagent:** A few mg of **hyoscyamine** when made to react with a few drops of the **Schaer's Reagent** *i.e.*, 1 volume of 30% H_2O_2 mixed with 10 volumes of concentrated sulphuric acid, produces a distinct green colouration.

3. **Vitali-Morin Colour Reaction:** A few mg of **hyoscyamine** (and also atropine) is treated with about 0.2 ml of fuming HNO_3, evaporated to dryness on the water-bath. To the residue is then added 0.5 ml of a 3% (w/v) solution of KOH in methanol, it gives a bright purple colouration, that changes to red and finally fades to colourless.

4. ***para*-Dimethylaminobenzaldehyde Reagent:** [Prepared by dissolving 2 g of-Dimethylaminobenzaldehyde in 6 g of H_2SO_4 to which 0.4 ml of water is added previously]. Add to 5-10 mg of **hyoscyamine** in an evaporating dish 2-3 drops of this reagent and heat on a boiling water-bath for several minutes. A distinct red colouration is produced that ultimately gets changed to permanent cherry red upon cooling.

5. **Hyoscyamine Hydrobromide ($C_{17}H_{23}NO_3$.HBr):** It is obtained as deliquescent crystals having mp 152°C; very soluble in water; 1 g dissolves in 3 ml ethanol; 1.2 ml chloroform and 2260 ml ether.

6. **Hyoscyamine Hydrochloride ($C1_7H_{23}NO_3$.HCl):** The crystals have mp 149-151°C; and freely soluble in water and ethanol.

Uses

1. It is mostly employed as an anticholinergic drug.
2. It exerts relaxation of bronchial and intestinal smooth museles (*i.e.*, antispasmodic action).
3. It also inhibits contraction of the iris muscle of the eye to produce mydriasis.
4. It decreases significantly decreases the sweat gland and salivary gland secretions.

Coca

Synonyms: Coca, Folium cocae

Botanical source:

It consists of the dried leaves of Erythroxylon coca var. coca (Huanco or Bolivian coca) and Erythroxylon coca var. spruceanum (Java, Peruvian, Truxillo).**Family:**Erythoxylaceae.

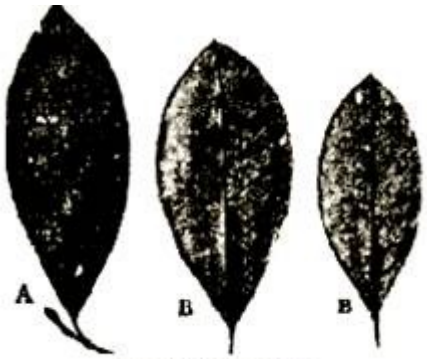


Fig. 6: Coca leaves

Geographical source: Bolivia, Peru, Indonesia and India.

Microscopical characters:

Upper Epidermis: The upper epidermis with straight anticlinal walls.

Stomata: The paracytic stomata are present in only lower epidermis.

Lower epidermis:

- It contain papillose cells and 6-7 rows of parenchymatous cells giving raised curved lines on the surface.
- Mucilage in few epidermal cells.
- Calcium oxalate prisms in the cells of both the epidermis.
- Palisade in a single layer of the cells with calcium oxalate clusters or prisms.
- Meristele in the midrib shows an arc of xylem, phloem with pericyclic fibres below and sclerenchymatous mass above.
- Lignified idioblasts under the surface.

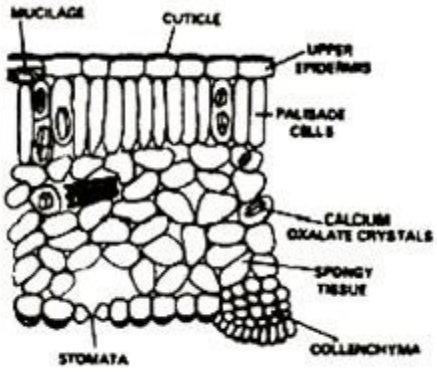
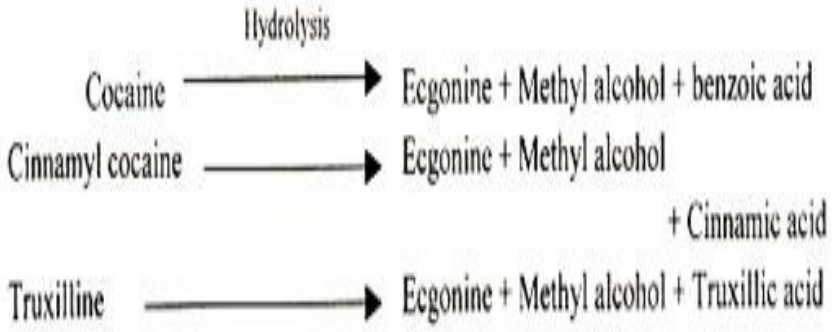


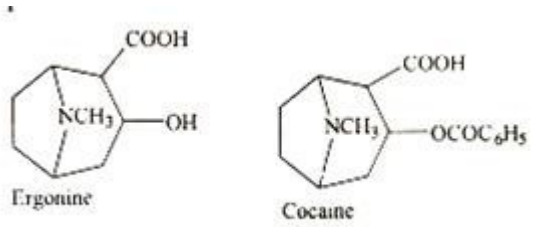
Fig. 7: T. S. of Coca leaf

Chemical constituents:

1 to 1.5% alkaloids cocaine, cinnamyl cocaine and a and β-truxilline. Coca alkaloids in contrast to alkaloids of hyoscyamine group are derived from pseudotropine. All the alkaloids are derivatives of ecgonine and can be easily hydrolysed. Cocaine is methyl benzoyl ecgonine.



Bolivian leaves contain cocaine and cuscohygrine; while truxilo coca contains cocaine and cinnamyl cocaine and truxilline. From Java coca, tropacocaine or benzoyl pseudoatropine has been isolated.



Chemical test:

Cocaine powder is treated with sulphuric acid, heated, followed by addition and mixing of water. It gives the characteristics smell of methyl benzoate.

Uses:

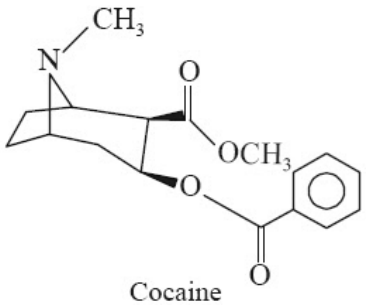
1. Cocaine is a local anesthetic.

2. Coca leaves are used asumulant, restorative and also in convulsions.

3. Cocaine reduces the sensitive and respiratory depressant effects of morphine and allied drugs, due to CNS stimulant properties.

4. Owing to hallucinogenic and additive effects of cocaine, it has become the drug of abuse and hence, its uses are limited to ophthalmic surgery and surgery of ear, nose and throat.

Chemical Structure



Cocaine

Characteristic Features:

1. **Cocaine** is obtained as the monoclinic tablets from ethanol having mp 98°C.

2. It usually becomes volatile above 90°C; however, the resulting sublimate is *not* crystalline in nature.

3. **Solubility Profile:** 1 g of cocaine dissolves in 600 ml of water; 270 ml of water . It is also soluble in acetone, carbon disulphide and ethyl acetate.

Identification Tests:

1. **Cocaine Hydrochloride ($C_{17}H_{21}NO_4.HCl$) (Cocaine Muriate):** It is obtained as granules, crystals, or powder. It has a slightly bitter taste and usually numbs lips and tongue. Its physical characteristics are: mp ~ 195°C.

2. **Cocaine Nitrate Dihydrate ($C_{17}H_{22}N_2O_7.2H_2O$):** Its crystals have mp 58-63°C. It is freely soluble in water or ethanol; and slightly soluble in ether.

3. **Cocaine Sulphate ($C_{17}H_{21}NO_4.H_2SO_4$):** It is obtained as white, crystalline or granular powder, which is soluble in ethanol and water.

Uses

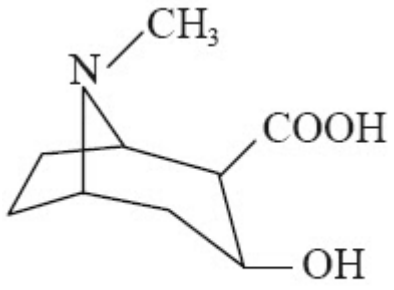
1. It is used as a local anaesthetic as it causes numbness.

2. Its main action is a CNS-stimulant and, therefore, categorized as '*narcotic drugs*'. It is a highly habit-forming drug.

Ecgonine

Biological Source It is also obtained from the leaves of *Erythroxylum coca* Lam. (*Erythroxylaceae*) (**Coca**) as its *l*-form.

Chemical Structure



Ecgonine

Isolation Ecgonine may be obtained by the hydrolysis of **cocaine** as given below:

Cocaine -------Hydrolysis----à Ecgonine + Benzoic acid + Methanol

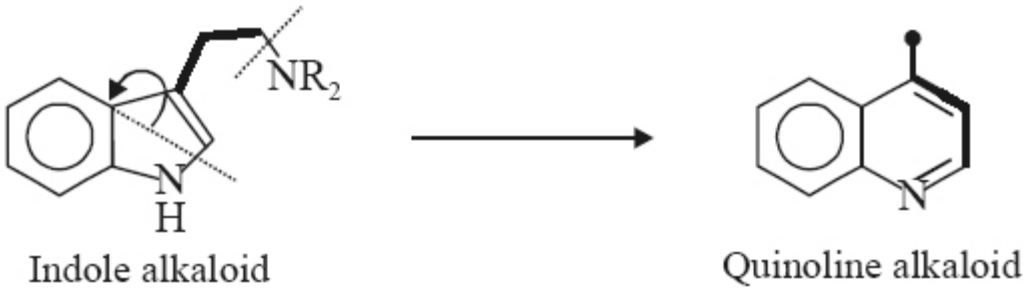
Uses It is mostly used as a topical anaesthetic.

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

Cinchona bark / jesuit's bark / peruvian bark

Biological source: dried bark of cultivated trees of-

Cinchona calisaya
Cinchona officinalis
Cinchona ledgeriana
Cinchona succirubra
Family: rubiaceae
Geographical source: India, Bolivia, srilanka.

Morphology:

Stem bark is rough with transverse fissures . Outer surface is grey & inner surface is pale yellowish brown to deep reddish brown. Root bark is curved, outer surface is scaly, outer & inner surface with same colour.

Microscopic\Characters:

Cork cells are thin walled. Cortex has phloem fibres . Medullary rays with radially arranged cells. Idioblast of calcium oxalate is a specific characteristic. Starch grains in parenchymatous tissues. Stone cells rarely present.

Chemical constituents:

Contains quinine, quinidine, cinchonine & cinchonidine .

Also contains quinic acid & cinchotannic acid.

Chemical Test:

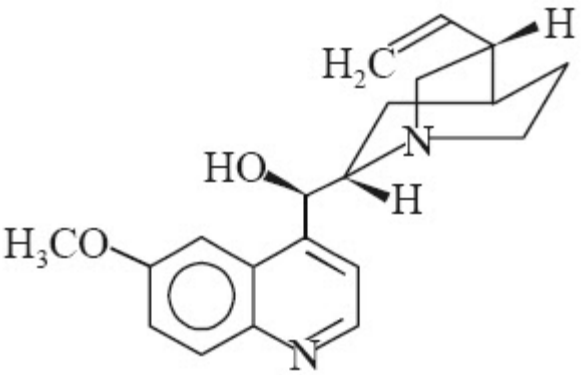
1. On heating the drug in a dry test tube with glacial acetic acid, purple vapours are produced
2. Thalleoquin test: drug + bromine water + dilute ammonia gives an emerald green colour
3. Drug when treated with quinidine solution gives a white precipitate with silver nitrate which is soluble in nitric acid.

Uses:

Anti malarial, anti pyretic, quinine is used in arrythmias against atrial fibrillation.

A. Quinine

Chemical Structure



Quinine

Characteristic Features

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

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

5. The pH of its saturated solution in 8.8.

6. 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.

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.

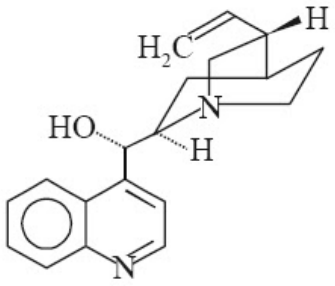
4. It has been used to treat hemorrhoids and varicose veins.

5. **Quinine** is also used as a oxytocic agent.

6. **Quinine** is supposed to be prophylactic for flu.

B. Cinchonine

Chemical Structure



Cinchonine

Uses

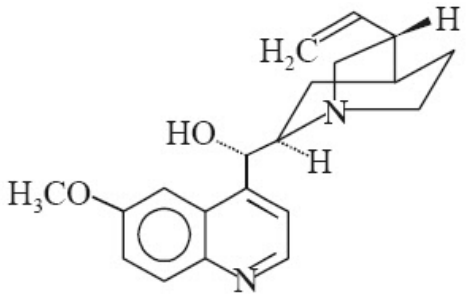
1.It is used as an antimalarial agent.

2. It is employed as a tonic in waters, bitters and liqueurs.

3. It is broadly used for febrifuge, schizonticide, stomachic, amebiasis, dysentry, flu, fever, and as a mild stimulant of gastric mucosa.

C. Quinidine

Chemical Structure It is the dextrorotatory *stereoisonter* of **quinine**



Quinidine

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Characteristic Features

1. **Quinidine** is obtained as triboluminescent crystals having mp 174-175°C after drying of the solvated crystals.

4. It gives a distinct and characteristic blue fluorescence in dilute sulphuric acid (2N).

5. The uv absorption spectrum is identical with that of **quinine.**

6. **Solubility Profile:** 1 g gets dissolved in 2000 ml cold water, 800 ml boiling water, 36 ml ethanol, 56 ml ether, 1.6 ml chloroform; very soluble in methanol; and practically insoluble in petroleum ether.

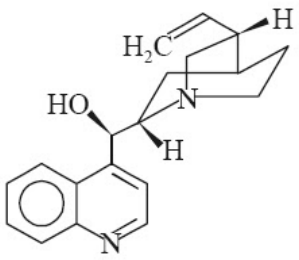
Uses

1. It is used as an antiarrhythmic agent.

2. It finds its applications as an antimalarial drug.

D. Cinchonidine

Chemical Structure



Cinchonidine

Characteristic Features

1. It is obtained as orthorhombic prisms or plates from ethanol having mp 210°C.

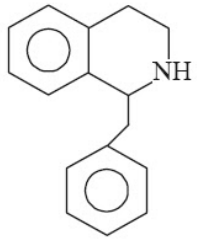
2.**Solubility Profile:** It is found to be freely soluble in chloroform and ethanol; moderately soluble in ether; and practically insoluble in water.

Differences Among Four Major Cinchona Alkaloids

S. No.	Characteristics	Quinine	Quinidine	Cinchonine	Cinchonidine
1	Chemical Formula	Methoxy Vinyl rubanol	Methoxy Vinyl rubanol	Vinyl rubanol	Vinyl rubanol
2	Rotation of Alcoholic solution	(–)	(+)	(+)	(–)
3	Fluorescence in oxy-genated acids	Blue	Blue	–	–
4	Thallaioquin Test	+ve	+ve	–ve	–ve
5	Erythroquinine Test	+ve	+ve	–ve	–ve
6	Herrpathite Test	+ve	–ve	+ve	–ve
7	Solubility in (ml):				
	Water	1900	2000	–	–
	Chloroform	1.2	1.6	110	++
	Ethanol	0.8	36.0	60	++
	Glycerol	20.0	–	–	–
	Ether	250	56.0	500	+

Modified Benzyltetrahydroisoquinoline Alkaloids

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



Benzyltetrahydroisoquinoline

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

Opium / poppy plant

Biological source: dried latex obtained from capsules of papaver somniferum
Family:papaveraceae .
geographical source: India (MP), turkey, Pakistan, Afghanistan

Morphology:

The dried latex is dark brown, extremely bitter to taste & has a strong odour.

Chemical constituents:

Contains phenanthrene type of alkaloids such as morphine & codeine & benzyl isoquinoline type of alkaloids such as papaverine & noscapine .These occur as salts of meconic acid.

Use:
Morphine is a narcotic analgesic & stimulant .
Codeine is an anti tussive .
Papverine is a smooth muscle relaxant.

ChemicalTest:

1. aqueous solution of meconic acid shows a deep reddish purple colour with ferric chloride
2. morphine when sprinkled with concentrated HNO3 shows an orange red colour. This is not

allowedbycodeine

3. morphine solution when treated with ferric chloride & potassium ferricyanide gives a bluish greencolour

4. papaverine solution in HCl & potassium ferricyanide develops a lemon yellow colour

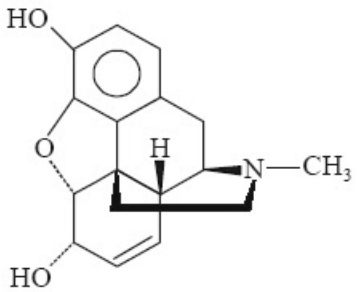
Varietiesofopium:

Indian, Turkish, Persian, European, manipulated Persian & European.

A. Morphine

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

Chemical Structure



Morphine

Characteristic Features

1. **Morphine** is occurs in its metastable phase having mp 197°C. However, the high melting form sublimes at 190-200°C .

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.

Note: Morphine reduces iodic acid and potassium iodate.

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Uses

1. It is used as a potent narcotic analgesic.

2. It is usually given in severe pains and also in such instances where patient fails to show positive response to other analgesics.

3. It exerts a biphasic action on the CNS.

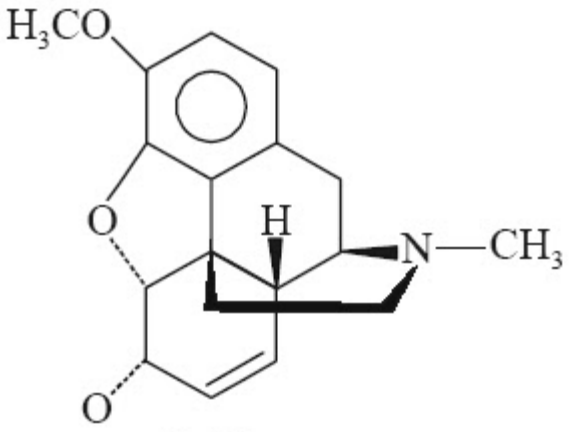
4. It is found to sedate the respiratory centre, emetic centre and the cough centre through its action in the medulla.

5. It stimulates the chemoreceptor-trigger-zone located in the medulla that ultimately causes nausea and vomilting; and this is perhaps regarded as a side-effect.

6. It also exerts sedative and hypnotic actions.

B. Codeine

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 (octahedral) 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.

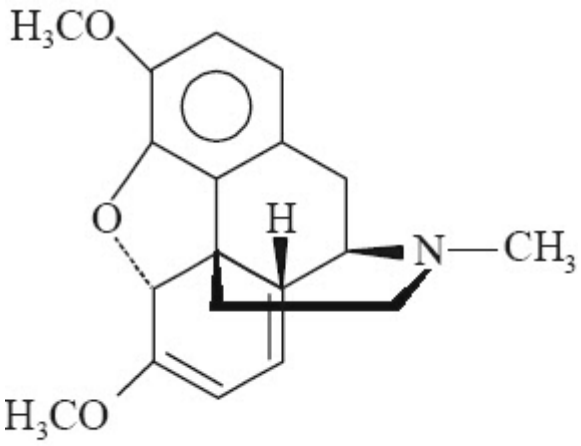
4. **Solubility Profile:** 1 g dissolves in 120 ml water, 60 ml water at 80°C, 2 ml ethanol, 1.2 ml hot ethanol, 13 ml benzene, 18 ml ether, 0.5 ml chloroform; freely soluble in methanol, dilute acids and amyl alcohol; and almost insoluble in solutions of alkali hydroxides and in petroleum ether.

Uses

1. It is mostly used as a narcotic analgesic.
2. It is invariably employed as an antitussive.

C. Thebaine

Chemical Structure



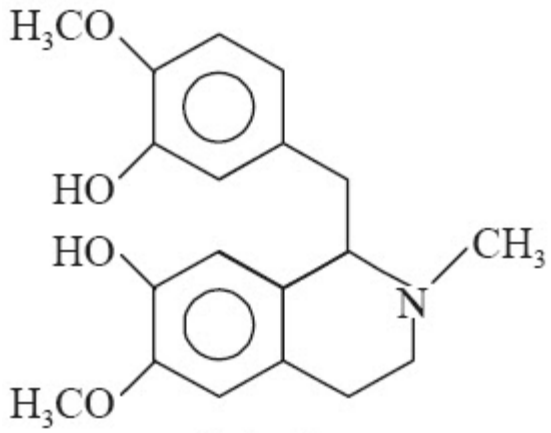
Thebaine

Characteristic Features

1. It is obtained as orthorhombic, rectangular plates by sublimation at 170-180°C under atmospheric pressure.
2. **Solubility Profile:** 1 g dissolves in 1460 ml water at 15°C, in about 15 ml hot ethanol, 13 ml chloroform, 200 ml ether, 25 ml benzene, 12 ml pyridine; and not very soluble in petroleum ether.

D. Reticuline

Chemical Structure



Reticuline

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Characteristic Features

1. The *dl*-form of **reticuline** is obtained as pink crystals having mp 146°C.

2. *Solubility Profile:* It is soluble in aqueous buffer of pH < 7.5 or > 11; and is practically insoluble in water at pH 8-10.

Ipeac

Synonyms:

Radix ipecacuanhae, Ipecacuanha root, Ipecac Rio, Brazilian or Johore ipecac.

Botanical source:

Ipecacuanha consists of dried root or rhizome and roots of Cephaelis ipecacuanha (Brot.) A Rich. (Rio or Brazilian ipecac) or of Cephaelis acuminata Karsten. (Cartagena, Nicaragua or Panama ipecac). **Family:** Rubiaceae.

Geographical source: Brazil, Forests of Mattogrossa and Minas, Malaya States (Johore), Burma and Bengal.

Macroscopical characters:

(i) Rio Ipecac

(ii) Size Length 5-15 cm, diameter 3 to 5 mm (usually 4mm)

(iii) Shape cylindrical, slightly tortuous

(iv) Surface annulated, each emulation or annulated ring encircles the root from half to three quarter; annulations are broad and round; sometime attached rhizome or its free pieces and lateral roots or their scars are seen.

(v) Colour Brick red to brown

(vi) Odour Slight, powder irritant and Sternulatory.

(vii) Taste Bitter and acrid

(viii) Fracture Short and starchy in the bark, splintery in the xylem.

(ix) Fracture surface Wide greyish barks occupying two-third. Diameter and central yellowish - white wood occupying one-third diameter.

Microscopical characters:

Cork: 3-5 layered, tangentially elongated cells filled with brown matter.

Phellogen: 2 layered, immediately below the cork, shining and cells tangentially elongated.

Cortex: Several layered with thin walled polyhedral parenchyma with small intercellular spaces. The cortical parenchyma contains acicular raphides either in bundles or scattered all over.

Phloem: Several thin patches around the well developed xylem and consists of perforated sieve tubes.

Xylem: Cells are lignified. Because of their lignifications, it is difficult to differentiate medullary rays from other wood elements in a cross section. Each rays cell, is radially elongated and contains starch. The dense secondary xylem consists of tracheids, tracheidal vessels, fibres and parenchyma. Starch grains are also seen in the xylem parenchyma.

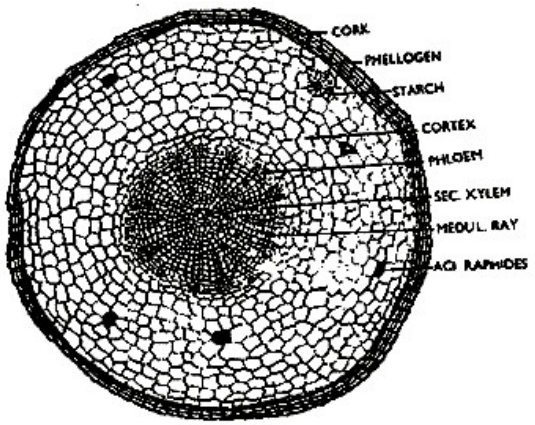


Fig. 10: T. S. of Ipecac (*Cephaelis ipecacuanha*) root

Chemical constituents:

Isoquinoline alkaloids (2 to6%)

i. Emetine (1.4-1.7%)

ii. Cephaeline (0.5-1.2%)

iii. Psychotrine (0.05%)

iv. Psychotrine methyl ether and

v. Emetamine

Uses:

1. In cases of amoebic dysentery.

2. Expectorant in dry bronchitis

3. Emetic (causes vomiting)

Test for emetine:

Add 5 ml hydrochloric acid to 0.1 gm of powdered drug, heat and filter. To the filtrate add small crystals of potassium chlorate or cholamine T. the colour of the filtrate become yellow-orange and then red.

Substitutes and adulterants:.

Naregamia alata (Goanase Ipecac) Meliaceae and contains naregamine.

Cryptocoryne spirallis (Araceae).

Tylophora asthmatica (Asclepiadaceae) contains tylophorine and tylophorinine.

Bastard Ipecac or wild Ipecac- Asclepias curassavica, (Asclepiadaceae) and contains a glycoside asclepin.

Indole Alkaloids

Ergot

Ergot is a fungal disease very commonly and widely observed on a good number of wild as well as cultivated grasses, and is produced by different species of **claviceps.** This particular disease is usually characterized by the formation of hard and seed like **'ergots'** in place of the normal seeds. However, these specific structures are frequently termed as **sclerotia,** which represent the **'resting stage'** of the fungus.

The generic name, **'claviceps'**, usually refers to the club-like nature of the **sclerotium*,** whereas *purpurea* signifies its purple colour.

Medicinal ***ergot*** is the dried sclerotium of the fungus *Claviceps purpurea* (Fries) belonging to the natural order *Clavicipitaceae* developed in the ovary of rye, *Secale cereale* (*Germinae/Poaceae*).

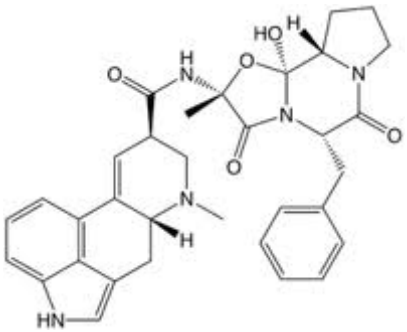
There are certain other species of *Claviceps* which have been found to produce ergots in the ovaries of other member of *Graminae* and *Cyperaceae*.

In fact, there exist *four* main categories of **ergot alkaloids** which may be distinguished, namely:

(*a*) **clavine alkaloids,** (*b*) **lysergic acids,** (*c*) **lysergic acid amides,** and (*d*) **ergot peptide alkaloids.**

There are, in fact, *ten* **ergot peptide alkaloids** which are: **ergotamine, ergosine, ergocristine, ergocryptine, ergocornine, ergotaminine, ergosinine, ergocristinine, ergocryptinine,** and **ergocorninine;** however, the *last five* alkaloids being isomers of the *first five.*

Biological Source	Ergot is the dried sclerotium of a fungus, *Claviceps puprea*, arising in the ovary of the rye, *Secale cereale*.
Family	The fungus belongs to family Clavicipitaceae and the rye-plant belongs to the family Graminae.
Geographical Source	Germany and Switzerland, substitutes found in France, Algeria, USA and Canada.
Morphology/Macroscopical Characters	The sclerotia is hard, violet, characteristic odor with an unpleasant taste.
Microscopic Characters	Shows an outer zone of purplish-brown rectangular cells while the pseudoparenchyma consists of oval and rounded cells with fixed oil and protein.
Chemistry	The ergot alkaloids (ergolines) are indole alkaloids and can be divided into two classes:1) The clavine-type alkaloids, which are derivatives of 6,8-dimethylergoline 2) The lysergic acid derivatives: a) Water soluble ones such as ergometrine and (b) Water insoluble ones such as ergotamine.

	 Ergotamine – An indole alkaloid obtained from the Ergot
Chemical Tests	1. gives a blue colour with Van Curk's reagent (para dimethylamino benzaldehyde)2. gives blue fluorescence in water 3. when treated with ether, H_2SO_4 followed by sodium bicarbonate, aqueous layer shows a red violet colour 4. ergotamine + glacial acetic acid + ethyl acetate + H_2SO_4gives a blue solution with a red tinge. When further treated with $FeCl_3$ the red tinge disappears and blue colour becomes more prominent 5. powdered ergot when treate with NaOH solution develops a strong odor of trimethylamine.
Adulterants/Allied drugs/ Substitutes	Substitutes: Ergot of wheat, Ergot of barley, Ergot of oats, and Ergot of diss.
Uses	Ergometrine is used as an oxytocic drug to assist in labor and delivery and reduce post-partum haemorrhage. Ergotamine is used as an analgesic for treatment of migraines.

	Lysergic acid diethylamide (LSD-25) is a semi-synthetic preparation of lysergic aci with potent pyschotomimetic activity.

Identification Tests :

(*i*) **Van Urk Test:** When a solution containing an **ergot alkaloid** is mixed with **Van Urk Reagent**, it gives rise to a characteristic deep blue colouration.

(*ii*) **Glyoxylic Acid Reagent Test: Ergot alkaloids** gives a blue colouration with the addition of Glyoxylic acid reagent and a few drops of concentrated H_2SO_4.

(*iii*) **Fluorescence Test:** The aqueous solution of the salts of ergot alkaloids produce a distinct blue fluorescence.

Uses:

1.Ergometrine is used as an oxytocic.

2.Ergometrine maleate also acts as an oxytocic and produces much faster stimulation of the uterine muscles as compared to other ergot alkaloids.

Sclerotium A hardened mass formed by the growth of certain fungi. the sclerotium formed by ergot on rye is of medical importance due to its toxicity.

Ergotamine

Characteristic Features

1. It is obtained as elongated prisms from benzene that get decomposed at 212-214°C.

2. It usually becomes totally solvent-free only after prolonged heating in a high vacuum.

3. It is found to be highly hygroscopic in nature; and darkens and decomposes on exposure to air, heat and light.

Identification Tests :

Ergotamine Hydrochloride [$C_{33}H_{35}N_5O_5$.HCl]: It is obtained as rectangular plates from 90% (v/v) ethanol which get decomposed at 212°C. It is found to be soluble in water-ethanol mixtures; and sparingly in water or ethanol alone.

Uses:

1. It is employed as a potent antimigraine drug.

2. **Ergotamine tartrate** is used invariably to prevent or abort vascular headaches, including *migraine* and *cluster headaches.* The mechanism of action is perhaps due to direct vasoconstriction of the dilated carotid artery bed with concomitant lowering in the amplitude of pulsations.

3. **Ergotamine tartrate** is also an antagonist of the serotonin activity.

4.**Ergotamine tartrate** is frequently used along with caffeine for the management and control of migraine headache. Both serve as cerebral vasoconstrictors; while the latter is considered to increase the action of the former.

Rauwolfia

Synonyms and vernacular name:
Bengali – Sarpagandha; Tamil – Chinanmdpodi; Hindi – Chandrika; Bihar- Pagla ki dawa.

Biological source: Rauwolfia consists of the dried roots and rhizomes of Rauwolfia serpentina . It contains not less than 0.15% of reserpine. **Family:**Apocynaceae

Geographical source:
It is widely distributed in West land and in shady forests in Punjab eastward to Nepal, Sikkim, and Assam in India; Bhutan, Pakistan, Java and Thailand, etc.

Macroscopical characters:
(i) External features of roots and rhizomes are nearly similar but rhizomes can be made out by the presence of small central pith.

(ii) Drug consists of mostly small pieces, which are 2 to 15 cm long and 3 to 22 mm diameter.

(iii) Pieces are cylindrical, slightly tapering and tortuous.

(iv) Outer surface is greyish yellow, pale brown or brown.

(v) Fracture short.

(vi) Fracture surface show yellowish to brown bark and dense pale yellow radiating wood with 2 to 8 annular rings occupying nearly three fourth of the diameter.

(vii) Odour- Odourless

(viii) Taste -bitter.

Microscopical characters (T.S.):

T. S. of the root presents a circular outline with typical stratified cork and other secondary features. Following are the tissues seen from the periphery to the center.

1. Periderm:

a. Cork (Phellum):

Stratified, consists of alternating bands- of smaller, suberized and un-lignified cell up to 8 to 10 raw in radial depth- larger, suberized but lignified cell upto 5 to 7 raw in radial depth.

b. Phellogen:

Indistinct but is seen as a narrow layer of thin walled cells,

c. Phelloderm:

5 to 7 layers, immediately below the phloem, cell is arranged in the radial rows whereas away from phloem, cell is oval and has intercullar spaces. Phelloderm contains abundant starch grains (with triradiate hilum) and typical twin prisms of calcium oxalate.

2. Secondary phloem:

Is transverse by conspicuous medullary rays. Phloem consists of sieve tubes, companion cells and phloem parenchyma. Starch grains and calcium oxalate prism occurs throughout the phloem tissue.

3. Secondary xylem:

It is also transverse by well develop medullary rays. Xylem consists of vessels, wood fibres and lignified parenchyma. The vessels appear rounded, polygonal or at times radially elongated and

occurs inner single or in pairs. Xylem fibres appear as rounded and polygonal structure with thick lignified walls. Typical oxalate prism and starch grains resembling those of the phelloderm and phloem occur freely in the wood parenchyma.

4. Medullary rays:

It runs radially from the center to the cortex through the phloem. Rays in the xylem region are lignified, pitted and are 1 to 5 cells wide although uniseriate rays are prominent. In the phloem region the ray cells are not lignified. Starch and typical oxalate prisms are in the medullary ray cells.

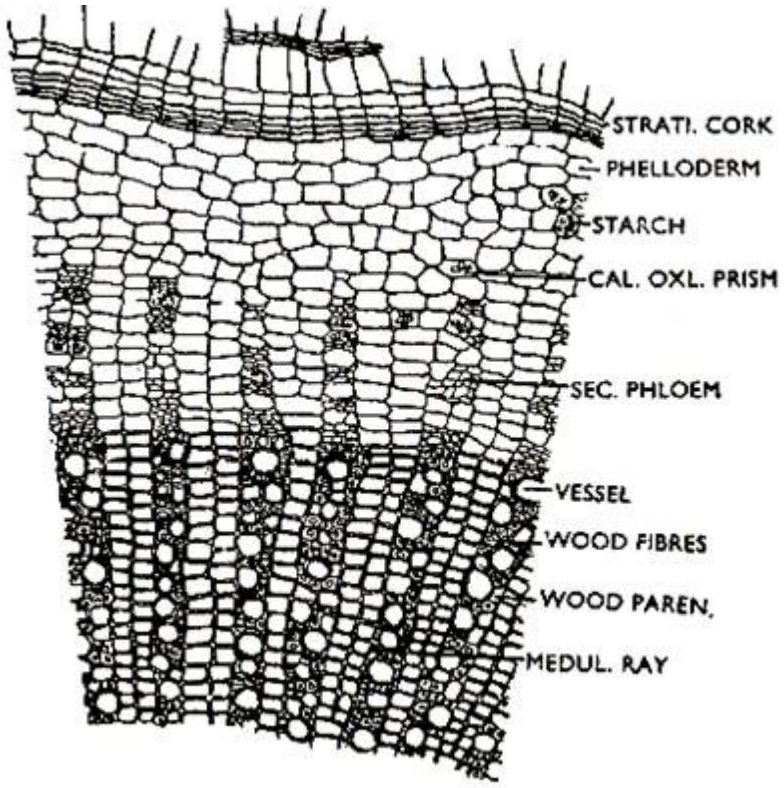


Fig. 12: T. S. of Rauwolfia root

Chemical constituents:

i. Alkaloids- Indole alkaloids (1.5 or 3%) present.

ii. Weakly basic Indole type (pH 7 to 7.5)

iii. Reserpine group – Reserpine, Rescinnamine, deserpidine.

iv. Tertiary indoline alkaloids (pH-8). Ajmaline group- Ajmaline and Ajmalicine.

v. Strongly basic anhydronium bases (pH-11).

vi. Serpentine group – Serpentine, Serpentinine and Alsotonine.

Uses:

- Rauwolfia is used as hypotensive and tranquillizer.
- Reserpine being the main alkaloid is responsible for the activity and is used in anxiety condition and other neuropsychoiatric diseases.
- Sedative – calm down activities and excitement (reserpine group).
- Stimulates the central of peripheral nervous systems (Ajmaline group).
- The decoction of root is used to increase uterine contraction in difficult cases.
- The extract is used for intestinal disorders and as anthelmintic bitter tonic and febrifuge.

Substitutes and adulterants:

The following species of rauwolfia are substituted for genuine drug.

R. vomitoria- this can be distinguished from the official drug on the basis of Sclereids which are present here in abundance.

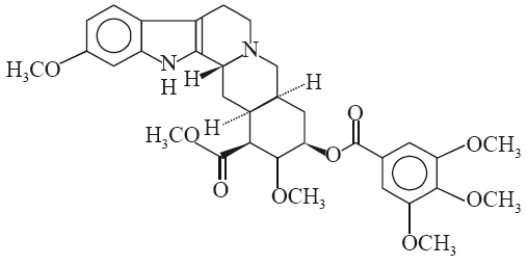
R. canescens: Here again the stone cells are present but the characteristic stratified cork is totally absent.R micrantha: show both stratified cork and stone cells.

All these do contain reserpine and other less important alkaloids in small quantities.

Adulterants:

R. densitiflora and R. perakensis do not contain reserpine. They do have stratified cork and stone cell.

Chemical Structure



Reserpine

Characteristic Features

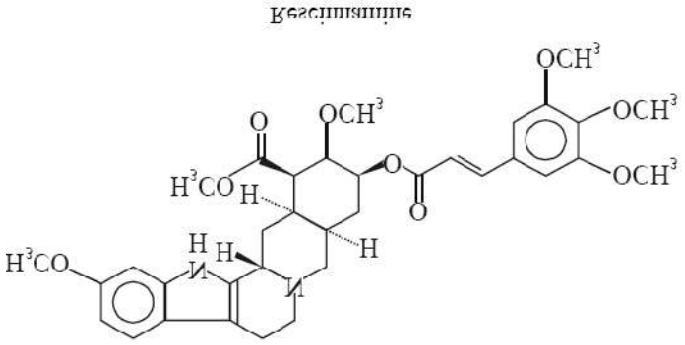
1. It is obtained as long prisms from dilute acetone which get decomposed at 264-265°C.

2. **Reserpine** is weakly basic in nature.

5. It is found to be freely soluble in chloroform (~ 1g/6 ml), glacial acetic acid, methylene chloride; soluble in benzene, ethyl acetate; slightly soluble in acetone, methanol, ether, in aqueous solutions of citric and acetic acids; and very sparingly soluble in water..

Rescinnamine

Chemical Structure



Characteristic Features

1. It is obtained as fine needles from benzene having mp 238-239°C (under vacuum).

2.**Solubility Profile:** It is moderately soluble in methanol, benzene, chloroform and other organic solvents; and practically insoluble in water.

Uses It is mostly used as an antihypertensive.

Alkaloids Derived from Tryptophan

L-Tryptophan is a neutral heterocyclic amino acid containing essentially an indole ring system. It has been observed that it serves as a precursor for a wide spectrum of indole alkaloids. The various alkaloids derived from tryptophan are conveniently classified into the following categories, namely: (*i*) **Simple Indole Alkaloids;** (*ii*) **Simple** b**-Carboline Alkaloids;** (*iii*) **Terpenoid Indole Alkaloids;** (*iv*) **Quinoline Alkaloids;** (*v*) **Pyrroloindole Alkaloids;** (*vi*) **Ergot Alkaloids.**

Vinca

Synonyms and Regional name:

Vinca rosea, Lochnera rosea, Sadaphuli, Rattanjot Billaganneru; Hindi- Sadabahar; Beng.- Nayantara.

Biological source: It is dried whole plant of Catharanthus roseus.**Family:** Apocynaceae

Geographical source:

It is indigenous to Madagascar. This plant is cultivated as an ornamental plant and found in tropical regions like Africa, Australia, Eastern Europe, South Florida, India, Taiwan and Thailand.

Macroscopical characters:

(i) Type – Annular or perennial herb;

(ii) Size – 0.5 to 1 meter length;

(iii) Leaves – Ovate, oblong, glossy above glaucous below;

(iv) Flowers – 2 to 3 in cymes, axillary and terminal clusters. Bases on flower colour, three varieties are known namely – alba-white, ocillata-white with pink or carmine red eyes and roseus -with rose coloured flowers.

(v) Fruit- a follicle, cylindrical and many seeded.

(vi) Taste – Bitter;

(vii) Odour – slight.

Fig. 14: *Catharanthus roseus*

Microscopical characters:

Lamina:

Upper epidermis:

Single layered with more or less rectangular cells, the outer walls of which are circularized. Only covering trichomes are unicellular, long and dagger shaped, warty and with a bulbous base. Sometimes very short trichomes are also seen. A few stomata are seen on the upper epidermis.

Mesophyll:

Mesophyll is differentiated into palisade and spongy parenchyma.

Palisade: Single layered cells elongated and compact.

Spongy parenchyma:

5-9 layered, loosely arranged with intercellular spaces. Calcium oxalate crystals of any kind are totally absent. Vascular strands are seen here at times.

Lower epidermis: Same as upper epidermis but the number of stomata are more.

Midrib:

Epidermal layers of lamina are continuous in the midrib region also. Strips of collenchyma appear below the upper epidermis and above the lower epidermis. This is followed by cortical parenchyma. A well developed vascular bundle is seen in the centre of midrib.

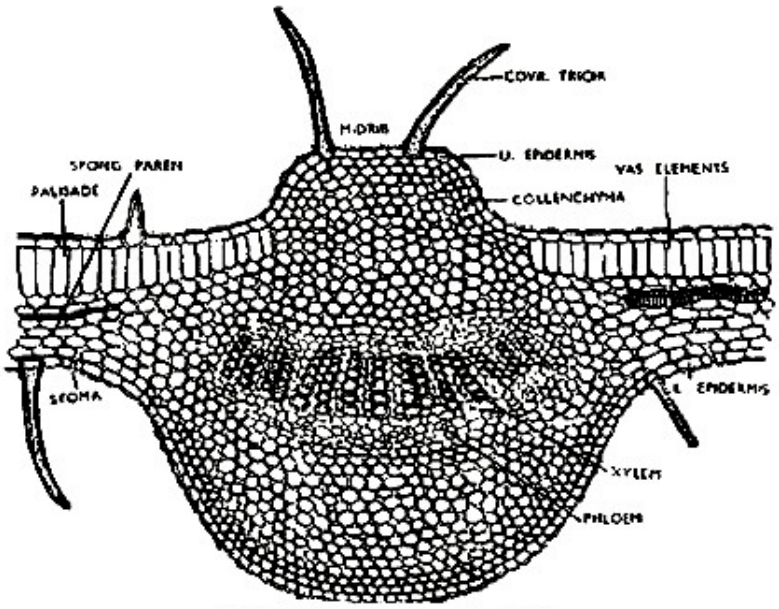


Fig. 15: T. S. of Catharanthus leaf

Chemical constituents:

1. Indole and indoline alkaloids:

(i) Ajmalicine

(ii) Lochnerine

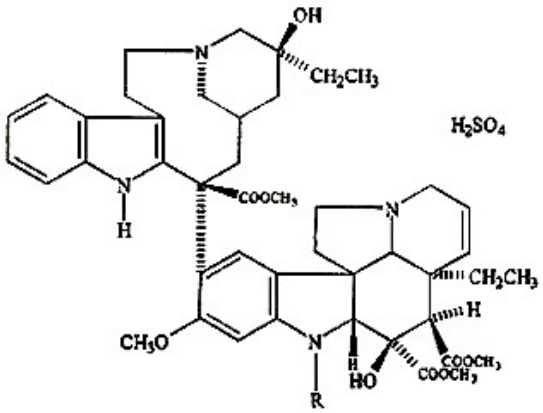
(iii) Serpentine and

2. Tetrahydroalstonine:

(i) Dimeric Indole bases of monoterpene type

(ii) Vinblastin

(iii) Vincristin.



R= CH_3 Vinblastine sulphate
R= CHO Vincristinesulphate

Uses:

- Antineoplastic (antimitotic= Cytostatic = anticancer antitumour).
- In the treatment of Hodgkin's disease.
- In the treatment of leukemia in children.
- Vinca is used in hypertension.

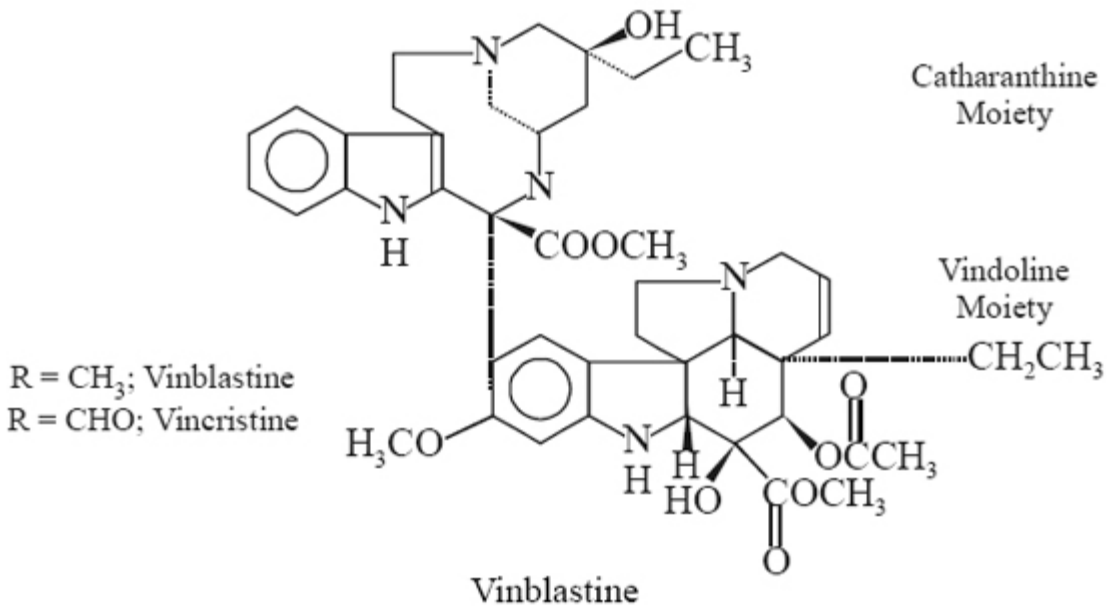
((*iv*) **Vinblastine:** The nucleophilie vindoline, C-5 of the indole nucleous is being activated adequately by the OMe at C-6, besides the N-atom of the indole moiety. The resulting adduct is subsequently reduced in the dihydropyridinium ring by the NADH-dependent 1, 4-addition, giving the substrate for hydroxylation. Its ultimate reduction gives rise to vinblastine.

(*v*) **Vincristine:** It is the oxidized product of vinblastine whereby the inherent N-formyl group on the indoline fragment is transformed.

Vinblastine

Biological Source It is obtained from *Vinca rosea* Lin.. (*Apocynaceae*).

Chemical Structure



Characteristic Features:

1. It is obtained as solvated needles from methanol having mp 211-216°C.

4. It is soluble in alcohols, chloroform, acetone, ethyl acetate and is practically insoluble in water and petroleum ether.

Uses:

1. The alkaloid is used for the treatment of a wide variety of neoplasms.

2. It is also recommended for generated Hodgkin's disease, lymphocytic lymphoma, hystiocytic hymphoma, mycosis fungoides, advanced testicular carcinoma, Kaposi's sarcoma, and choriocarcinoma and lastly the breast cancer unresponsive to other therapies.

3. It is effective as a single entity, however, it is normally given along with other neoplastic agents in combination therapy for the increased therapeutic effect without any noticeable additive toxicity.

4. It arrests mitosis at the metaphase.

5. It is found to be effective in the acute leukemia of children.

Vincristine.

Characteristic Features

It is obtained as blades from methanol having mp 218-220°C.

Uses 1. **Vincristine sulphate** is recommended for the treatment of acute lymphocytic leukemia, and in combination therapy in Hodgkin's disease, lymphosarcoma, reticulum cell sarcoma, neuroblastoma, Wilm's tumour and rhabdomyosarcoma.

2. It is broadly used as an antineoplastic agent.

Note: Viucristine sulphate being highly unstable; therefore, its refregerated storage in sealed ampules is absolutely essential.

Nux-vomica

Synonyms: Semen strychni, Nux-vomica seeds, Kuchla (Hindi), Zer Kachuro (Guj.)

Botanical source: Nux vomica consists of the dried ripe seeds of Strychnos nux- vomica L.

Family: Loganiaceae

Geographical source:

South India, Malabar Coast, Kerala, Eastern Ghats, Bengal, Ceylon and North Australia

Fig. 16: *Strychnos nux-vomica L.*

Macroscopical characters:

(i) Size: 10-30 mm in diameter and 4 to 6 mm thick;

(ii) Shape: Disc shaped, some time flat, little depressed on one side and arched on the other, some time irregularly bent.

(iii) Margin: More or less rounded

(iv) Outer surface: Ash grey or greyish grey covered with numerous closely appressed silky hairs, radiating from the center. Hilum is present in the center of one of the flat surfaces. Micropyle is seen as a small projecting point on the margin. Hilum and micropyle are connected by a ridge;

(v) Endosperm: It is present below the testa and is grey and horny. Below the endosperm in the center is a narrow slit like cavity.

(vi) Embryo: It is seen at the micropyle end with a cylindrical, radicle and two cordate cotyledons.

(vii) Odour: None.

(viii) Taste: Very bitter.

Microscopical characters:

1. Testa:

Hairy epidermis:

Single layered; each epidermal cell forms a lignified trichomes comprising of a pitted bulbous base and a projection which is narrowly elongated and slightly bent beyond the base. The trichomes of all epidermal cells run parallel in one direction giving the testa of the seed a silky appearance. Collapsed parenchyma: Two layered collapsed parenchymatous cells with yellowish brown contents.

2. Endosperm:

They form the bulk of the seed. Outermost layers of the endosperm below the collapsed parenchyma appear palisade like whereas the inner layers contain cells which are polyhedral. The cells of endosperm also contain aleurone grains and oil droplets.

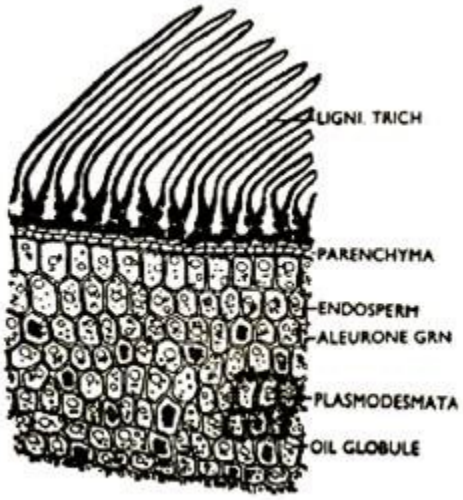


Fig. 17: T. S. of Nux vomica seed

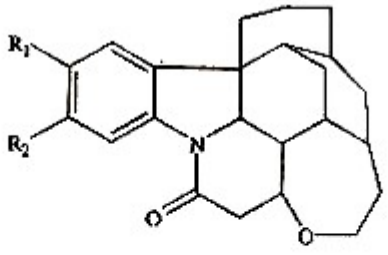
Chemical constituents:

i. Alkaloids (2.5 to 5%): Indole -strychnine and brucine.

ii. Miner-Vomicine and pseudo strychnine.

iii. Glycoside: Monoterpene glycoside- Loganin.

iv. Fixed oil (2 to 4%).



Strychnine

	R_1	R_2
Strychnine	H	H
Brucine	OCH3	OCH3

Uses:

- *Spinal cord stimulant.*
- In cases of neurasthenia (excessive fatigue of neurotic origin).
- As a circulatory stimulant.
- Nerve and sex tonic
- Bitter stomachic (strengthening of stomach and promoting its action).

Chemical test:

1. Strychnine test:

To a thick section of endosperm add ammonium vanadate and sulphuric acid. Middle portion of endosperm is strained purple because of strychnine.

2. Strychnine test:

Strychnine also gives violet colour with potassium dichromate and conc. Sulphuric acid.

3. Brucine test:

To a thick section add concentrated nitric acid. Outer part of endosperm is strained yellow to orange because of brucine.

4. Hemicelluloses test:

To a thick section add iodine and sulphuric acid. The cell walls are strained blue.

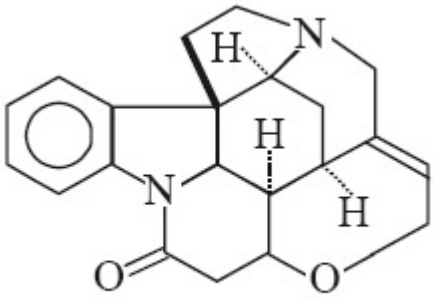
5. Organoleptic test:

Put a little drug at the tip of the tongue. It tastes bitter.

Substitutes and adulterants: S. potatorum and S. nux-blanda are the common adulterants

Strychnine

Chemical Structure



Strychnine

Salient Features:

1. **Strychnine** contains *two* N-atoms even then it happens to be a mono-acidic base.

2. **Strychnine** readily forms a variety of salts, such as: nitrate, N6-oxide, phosphate and sulphate. Interestingly, the N-atom which is specifically involved in the salt formation is the one that is located *farthest* from the aromatic benzene ring.

3. The second N-atom is strategically positioned as an amide nitrogen; and, therefore, it does not exhibit any basic characteristics.

Characteristic Features

1. It is obtained as brilliant, colourless cubes from a mixture of chloroform and ether having mp 275-285°C.

2. **Solubility Profile:** 1g dissolves in 182 ml ethanol, 6.5 ml chloroform, 150 ml benzene, 250 ml methanol, 83 ml pyridine; and very slightly soluble in water and ether.

Uses 1. **Strychinine** is extremely interesting pharmacologically and is regarded as a valuable tool in both physiologic and neuroanatomic research.

2. It is extremely toxic, and functioning as a central stimulant.

4. The drug is rarely used in modern medical practice but is utilized as a *vermin killer i.e.*, animal or insect killer.

5. It is used chiefly in poison baits for rodents.