**DEFINITION**

“Alkaloids are basic nitrogenous compounds of plant origin having definite pharmacological activities”.

Alkaloids are derived from plant sources, basic in nature, have one or more nitrogen atom (usually in heterocyclic ring), have marked physiological action on man and other animals. So they are very close in properties to amines.

**HISTORY OF ALKALOIDS**

1. Narcotine (first alkaloid) isolated in 1803 by French Apothecary (pharmacist) Darosne.

2. Morphine 1816

3. Strychnine 1817

4. Emetine 1817

5. Brucine 1819

6. Caffeine 1819

7. Quinine 1820 (first alkaloid whose structure was synthesized & established)

8. Coniine 1826

**DISTRIBUTION OF ALKALOIDS IN PLANTS KINGDOM**

**1. Among angiosperms:**

They are present in the plants of the solanaceae e.g. Atropine, ranunculaceae, papaveraceae, leguminosae, berberidaceae.

**2. Among gymnosperms:**

Alkaloids are rarely present but some families has taxaceae family contain alkaloids e.g. taxus (anticancer drug is obtained i.e. taxol).

**DISTRIBUTION OF ALKALOIDS AMONG PLANT PARTS**

Alkaloids are present in different parts having different examples:

Seeds of nux vomica (physostigmine)

Fruit of black pepper (piperine)

Beans of coffee (caffeine)

Leaves of belladonna (atropine)

Leaves of hyoscyamus (hyoscine)

Roots of aconite (aconitine)

Rhizomes of ipecac (emetine)

Rhizomes of sanguinaria (sanguinirine)

Exudates of opium (morphine)

Bark of cinchona (quinine)

**NOMENCLATURE OF ALKALOIDS**

Alkaloids are named by different ways:

**1)** According to generic name e.g. atropine from atropa belladonna, physostigmine from physostigmine venenosum.

**2)** Specific species name e.g. belladonine from belladonna, serpentine from rauwolfia serpentine.

**3)** According to general name of drug e.g. ergotamine from ergot.

**4)** According to pharmacological activities e.g. emetine from ipecacuanha.

**5)** According to name of discoverer e.g. ajmaline from rauwulfia.

**TYPES OF ALKALOIDS**

 Alkaloids are the plant metabolic by-product of amino acids.

 Amino acids are precursors of alkaloids. They can be synthesized from amino acids by deamination and carboxylation of amino acids.

 Alkaloids can be classified into 3 types

**1)** True Alkaloids

**2)** Proto Alkaloids

**3)** Pseudo Alkaloids

**1) True Alkaloids:**

These are the alkaloids which have nitrogen atom in their heterocyclic ring and they are derived from amino acids e.g. quinine, morphine, codeine.

**2) Proto Alkaloids:**

Which do not have nitrogen atom in heterocyclic ring but derived from amino acids. They are considered as biological amines e.g. ephedrine, cholchicine.

**3) Pseudo Alkaloids:**

Which have nitrogen atom in their heterocyclic ring but nit derived from amino acids e.g. pinidine, steroidal alkaloids etc.

**SALIENT FEATURES**

 They have one or more nitrogen atom in a molecule. It may have up to five nitrogen atom e.g. ergotamine.

 Alkaloids have nitrogen atom inside the heterocyclic ring but outside the ring. They are also called non-heterocyclic alkaloids.

 Nitrogen present in alkaloids occurs as primary, secondary, tertiary or quaternary ammonium ions.

**Primary amines**

R NH2

**Secondary amines**

R NH

R

**Tertiary amines**

R N R

R

**Nature of alkaloids:**

 Many alkaloids are crystalline in nature and some are amorphous, only few are liquid in nature e.g. nicotine.

 Alkaloids contain carbon, nitrogen, hydrogen and oxygen, when they become oxygen free they become iquid.

 Crystalline nature of alkaloids is useful mean rapid microscopic identification.

 Alkaloids are bitter in taste, basic in nature because they have one lone pair of electrons on nitrogen atom.

 A few alkaloids are coloured in nature such as berbarine is yellow in colour and sanguinarine HCl is copper red in colour.

**Solubility of alkaloids:**

 Solubility of alkaloids is pharmaceutically important. This factor is important for separating alkaloids from non alkaloidal contents from plants. Alkaloids occur in plants in free state or in salt from or as oxide.

 Free alkaloids are insoluble in water but soluble in organic solvents. When alkaloids react with acids they form salts and these salts are soluble in water but insoluble in organic solvents.

**EXTRACTION OF ALKALOIDS:**

There are two main processes for the extraction of alkaloids

**1. Process A:-**

If alkaloids are in salt form

**2. Process B:-**

If alkaloids in free form

**1. Process A:-**

Powder drug + Water (moisten it)

Mix with lime, diluted with dilute acid

(salt of drug is formed)

Dissolved in acid

Treated with organic solvents

(impurities are removed)

Add diluted acid and separate it

**2. Process B:-**

Crude drug + water or aqueous alcohol or dilute acid

Shaken with organic layer (may be chloroform)

(to remove all impurities)

Excess of sodium bicarbonate or ammonia is added to aq. Layer

Alkaloids are precipitated

Filtration (to take residue)

**IDENTIFICATION TEST**

The different qualitative tests can be performed for establishing profile of given extract for its chemical compostion. The following tests may be performed on extracts to detect various phyto-constituents present in them.

Detection of Alkaloids

The powdered drug is stirred with few ml of dilute hydrochloric acid and filtered. The filtrate is tested carefully with various alkaloidal reagents as follows:

**1) Mayer’s test:**

A general presumptive test for cocaine, morphine, heroin, and other alkaloids.

**Mayer's reagent**

Mayer’s reagent is a solution of potassium mercury iodide in water.

**Procedure**

To 1mL of the extract, add 2-3 drops of the Mayer’s reagent.

**Indication**

A positive result is indicated by a cream precipitate.

**Principle Behind the Tests**

Halogenation followed by Complex reaction mechanism.

**2) Wagner’s Test:**

It is an analytical method used to detect the presence of alkaloids.

**Wagner’s Reagent**

An aqueous solution of iodine and potassium iodide **Procedure**

To 1 mL of extract few drops of of wager’s reagent.

**Indication**

Brown or reddish brown precipitates are formed.

**Principle Behind the Tests**

Halogenation followed by Complex reaction mechanism.

**3) Hager’s Test:**

Hager’s test in another qualitative method of analysis.

**Hager’s reagent**

Saturated solution of picric acid in water.

**Procedure**

To 1mL of the extract, add 2-3 drops of the Hager’s reagent.

**Indication**

Yellow precipitates are formed.

**Principle Behind the Tests**

Nitration followed by Complex reaction mechanism

**4) Dragendorff’s test:**

**Reagent**

Consists of bismuth carbonate, sodium iodide, glacial acetic acid, ethyl acetate and water.

**Procedure**

To few ml of filtrate add 1 or 2 ml of dragendorff’s reagent.

**Indication**

Yellow to reddish brown precipitates are formed.

**Principles Behind the Tests**

Complex formation

**CLASSIFICATION OF ALKALOIDS**

**1) Pyridine and Piperidine Alkaloids:**

Pyridine Piperidine

**Example:**

Nicotine, Lobeline and Arecholine.

**2) Tropane Alkaloids:**

Tropane Ring

**Example:**

Atropine, hyoscine

**3) Quinoline Alkaloids:**

Quinoline

**Example:**

Quinine, Quinidine, Cinchonine and Iso-cinchonine

**4) Iso-quinoline Alkaloids:**

Iso-quinoline

**Example:**

Morphine, ipecac and codeine.

**5) Indole Alkaloids:**

Indole

**Example:**

Strychnine, brucine, vinchristine vinblastine, physostigmine, ergotamine and reserpine.

6) **Imidazole Alkaloids:**

Imidazole

**Example:**

Pilocarpine.

7) **Alkaloidal Amine:**

Protoalkaloids, N-atom is outside the ring so no structure

**Example:**

Ephedrine, colchicines.

**8) Purine Bases Containing Drugs:**

Purine Base

**Example:**

Caffeine, theophylline, theobromine.

**9) Steroidal Alkaloids:**

Steroidal Ring

**Example:**

Veratridine.

**Pyridine-Piperidine alkaloids**

Nicotine

**Botanical Origin:**

*Nicotiana tabacum*

**Family:**

Solanaceae

**Part Used:**

Dried leaves

**Habit & Habitat:**

 Plant is a herb

 Indigenous: North America.

**Collection**:

It is obtained from curing process but it is now commercially cultivated worldwide. Other varieties are cultivated as ornamental plants or grow as a weed. After curing it is meant for chewing, smoking etc.

Nicotine is used as insecticide. Plant is collected and dried.

**Constituents:**

Main constituents is

 Nicotine 2-8%

 Nor-nicotine (obtained by demethylation of nicotine)

 Campharine

 Anabasine

**Structure:**

Nicotine Nor-nicotine

**Uses:**

1. As CNS stimulant (at low doses)

2. As CNS depressant (at high doses)

3. As insecticide (It functions as an anti-herbivore chemical with particular specificity to insects; therefore nicotine was widely used as an insecticide in the past)

4. Heart rate decreases

5. Nicotine chewing gum is used as substitute of smoking

6. Transdermal patches are used

Lobeline

**Synonyms:**

 Indian tobacco

 Devil's tobacco

 Cardinal Flower

 Great Lobelia

**Botanical Origin:**

*Lobelia inflata*

**Family:**

Lobeliaceae

**Part Used:**

Dried leaves & flowering tops or aerial parts.

**Habit & Habitat:**

 It is an erect annual or biennial herb, 1 to 2 feet high; lower leaves and also flowers are stalked, the latter being pale violet-blue in colour, tinted pale yellow within.

 Plant is indigenous to eastern & central United States and Canada

 Cultivated in USA & Holand.

**Collection:**

 Plant is cultivated in autumn or in March or April

 Ovary develops into inflated capsules then plant is cut in August or September

 When it produce numerous capsules then they are collected and dried.

 Inflated capsules indicate the maximum concentration of active constituents.

**Constituents:**

Lobelia contains about 14 major alkaloids & they are 0.24-0.4%.

 Major one is lobeline and other are the isomeric derivatives such as lobelidine.

 Also contain some volatile oils, resins, lipids and gums (lipid contain some fixed oils).

**Structure:**

**Uses:**

Lobeline, an active constituent in the lobelia plant, is very similar to nicotine in its effect on the central nervous system. Lobeline acts as a relaxant overall while also dilating the bronchioles (air passages), thereby increasing respiration and possibly helping the lungs.

1. Used in spasmodic asthma & chronic bronchitis

2. As substitute of tobacco

3. As respiratory stimulant

4. To give up smoking habit

5. Used as emetic

6. Muscle spasms

7. To induce vomiting

ARECOLINE

**Synonyms:**

Betal nut

**Botanical Origin:**

*Areca catechu*

**Family:**

Palmae

**Part Used:**

Dried seeds.

**Habit & Habitat:**

 Plant is a tall palm about 15-17m in height

 Indigenous to south Eastern Asia (India, Malaysia, Srilanka), South China, East Indies, East Africa, Zanzibar, Tanzania.

**Collection:**

 Fruits are collected

 Fruit contains a single seed within thin seed coat and large endosperm

 Seeds are removed from the fruit and they are treated with lime and dried.

**Constituents:**

Major principle constituent is

 Arecoline.

Other constituents are

 Arecaine

 Guvacine

 Arecaidine

Arecoline is in abundant form/ high concentration and physiologically active.

It also contain small amount of volatile oils, lipids tannins and gums.

**Structure:**

**Uses:**

1. Used as anti-helminthic in veterinary medicines

2. As vermicide

3. As taenifuge (to expel thread worms in dogs)

4. Possess vasoconstrictive property

**Tropane Alkaloids**

Atropine

**Synonyms:**

 Belladonna

 Devil's Berries

 Death Cherries

 Deadly Nightshade

 Beautiful death

**Botanical Origin:**

*Atropa belladonna*

**Family:**

Solanaceae

**Part Used:**

Dried leaves & flowering tops.

**Meaning of Words:**

 Atropine is derived from “Atropos” meaning inflexible which indicates the poisonous symptoms or nature of the plant.

 Belladonna is an Italian word “Bella” means beautiful and “Donna” means lady (Princess Coleptra caused mydriasis by this).

**Habit & Habitat:**

 Plant is a branching herbaceous perennial, often growing as a subshrub, from a fleshy rootstock.

 Indigenous to U.S. & Canada

 Cultivated in France, Germany, India, U.K (England) and in Kashmir valley (in Pakistan).

**Collection:**

 Leaves and flowering tops are collected during flowering season and are collected from 3years old plant.

 Dried immediately after collection at 600C, otherwise they become deteriorate.

 Roots are dugout from 4years old plant and dried at 40-500C.

**Constituents:**

Major alkaloid is

 Atropine

 Scopolamine (Hyoscine)

 Hyoscyamine

Others are

 Apoatropine

 Belladonine

**Structure:**

**Uses:**

1. Anticholinergic

2. Lowers the parasympathomimetic activity of muscles and glands, so in this way used in surgery to check the nasal secretions and salivary secretions

3. Antiasthmatic

4. Spasmolytic

5. Analgesic

6. Cycloplegic & mydriatic in Ophthalmology (causes mydriasis in Ophthalmology as cycloplegic)

7. Antidote for mushroom and heavy metal poisoning

8. As an antidote to organophosphate and carbamate poisoning

9. Used to treat colitis, spastic bladder, renal and biliary colic, ulcers and irritable bowel syndrome

Hyoscine

**Botanical Origin:**

*Hyoscyamus niger*

**Family:**

Solanaceae

**Part Used:**

Dried leaves and flowering tops

**Habit & Habitat:**

 Plant is a biennial herb/ annual herb

 Indigenous to Europe, Asia, Africa

 Cultivated in Soviet union, USA, Canada, Germany

**Collection:**

 Leaves and flowering tops are collected during flowering season and are collected from 3years old plant.

 Dried immediately after collection at 600C, otherwise they become deteriorate.

 Roots are dugout from 4years old plant and dried at 40-500C.

**Constituents:**

Major alkaloid is

 Atropine

 Scopolamine (Hyoscine)

 Hyoscyamine

**Structure:**

**Uses:**

1. As antiemetic to prevent nausea and vomiting associated with motion sickness.

2. As anticholinergic

3. As antispasmodic

4. As mydriatic

5. For ophthalmic purposes.

6. As a general depressant and adjunct to narcotic painkillers.

Stramonium

**Synonyms:**

 Jimson weed

 Thorn apple

 Datura

 Hell's bells

 Moonflower

 Mad seeds

**Botanical Origin:**

*Datura stramonium*

*Datura alba*

**Family:**

Solanaceae

**Part Used:**

Dried leaves and flowering tops

**Habit & Habitat:**

 Plant is an annual herb forming a bush up to 1–1.5 m tall

 Indigenous to America, Europe.

**Collection:**

Leaves and flowering tops are collected and dried in flowering season.

**Constituents:**

 Atropine

 Scopolamine

**Structure:**

**Uses:**

1. As antiemetic to prevent nausea and vomiting associated with motion sickness.

2. As anticholinergic

3. As antispasmodic

4. As mydriatic

5. It is considered slightly more sedative to the central nervous system than is belladonna.

**QUINOLINE ALKALOIDS**

Cinchona

**Botanical Origin**:

*Cinchona succirubra* (red cinchona)

*Cinchona ledgeriana* (yellow cinchona)

*Cinchona calisaya* (yellow cinchona )

**Family**:

Rubiaceae.

**Part Used** :

Dried bark of stem & roots.

**Habit & Habitat :**

 The plant is a tree

 Indigenous to Peruvian Andes & South America

 Cultivated in Indonesia , Java , Zaire and India at altitude of 1000 – 3000 m

**Cultivation & Collection :**

 The drug collection is replace by cultivation as it is collected from wild plant .

 The cultivation of plant give opportunity to collect seed from plant producing high quality bark.

 Seedlings are planted in the seed beds at a distance of 1 m in rich, porous and well-drained soil in slops.

 When the plant is 2 years old the plants are protected from wind by growing banana tree in them.

 Shade favours the high production of active constituents (quinine) of the bark.

 Tree grown provide shade to the trunk as stem grow tall and lower branches die and drop of and plant crown grow very closely.

 The bark is collected manually from the stem of 6 to 9 years old plant.

 The bark of trunk as well as of roots are also collected.

**Constituents:**

The cinchona bark contain about 35 alkaloids (6.5%).

The cultivated bark contain 7 to 10 % total alkaloids.

The main alkaloids are:

 Quinine (70%)

 Quinidine

 Cinchonine

 Cinchonidine.

The alkaloids are present in combination with

 Quinic acid (5to 8%)

 Quinovic acid

 Cinchotannic acid.

**Structure:**

**Uses:**

1. Glanicals of cinchona have long been used as bitter tonic & stomachic.

2. On account of astringent action ,a decoction &acid infusion .

3. Suitable for treatment of plasmodium falciparum infection(falciparum malaria).

4. Use as antimalarial and antipyretic agent.

5. Quinidine is employed for prophylaxis of cardiac arrhythmias & for treatment of atrial fibrillation.

6. Cinchona is used in eye lotions to numb pain, kill germs, and as an astringent. Cinchona extract is also applied to the skin for hemorrhoids, stimulating hair growth, and managing varicose veins.

7. Quinine is sometimes used as a cutting agent in street drugs such as cocaine and heroin.

8. Quinine is used as a treatment for *Cryptocaryon irritans* (commonly referred to as white spot, crypto or marine ich) infection of marine aquarium fish

9. Because of its relatively constant and well-known fluorescence quantum yield, quinine is also used in photo chemistry as a common fluorescence standard.

10. Quinine (and quinidine) are used as the chiral moiety for the ligands used in sharpless asymmetric dihydroxylation.

**ISO-QUINOLINE ALKALOIDS**

IPECAC

**Botanical Origin**:

*Cephaelis ipecacuanha*

*Cephaelis acuminata*

**Family**:

Rubiaceae

**Part Used** :

Dried roots & Rhizomes.

**Habit & Habitat:**

 Plant is a shrub with cylinder rhizomes.

 Cephalis ipecacuanha is indigenous to Brazil

 Cultivated in India , Malaysia.

 Cephalis acuminate is indigenous to Columbia and Panama .

**Collection:**

 Drug is collected in dry season.

 During dry season they are dried under sun for 2-3 days.

**Constituents:**

Drug contain major alkaloids (non-phenolic)

 Emetine (ipecacuanha) 60-75%

 Emetine (accuminata) 30-50%

Minor Alkaloids are (phenolic)

 Cephaeline

 Psychotrine

**Structure:**

**Mechanism Of Action :**

 Irritate GIT

 Stimulate CTZ

 Medullary or central effect

**Uses:**

1. In large doses cause emesis

2. Anti-amoebic drug

3. Antiprotozoal drug in amoebic dysentery

4. Expectorant property

5. Pediatricians once recommended ipecac be kept in the home as a ready emetic for use in cases of accidental poisoning

6. Ipecac may also delay the administration or reduce the effectiveness of other treatments, such as activated charcoal, whole bowel irrigation, or oral antidotes.

OPIUM

**Botanical origin**:

*Papaver somniferum*

**Varieties**:

Album

Nigrum

**Family**:

Papaveraceae

**Part used**:

Raw opium or latex obtained by the incision from the unripe capsules.

**Habit & Habitat:**

 Opium poppy is an annual herb grow in Medietarean countries & India.

 The variety album is cultivated in India and it is indigenous to America and produce whitish flower variety.

 Nigrum is indigenous to Europe and produce violet colour flowers.

**Collection:**

 Seeds are sown in winter or in spring season, when plant attain height of 15cm, fields are cultivated

 In April or May poppy blossoms

 In June or July produce capsules

 There are 5-8 capsules in each plant

 When capsules change in colour from bluish-green to yellow, this is the critical time for collection because alkaloids concentration is maximum at this time

 Capsules are incised around the circumference with 3 blades knife called *Nushtur* (1mm deep)

 Incisions are not very deep into the endocarp otherwise latex will moved inside and lost

 All the latex tubes open into one another so, it is not necessary to cut all the tubes.

 At first latex is milky white in colour which is then coagulate and turn brown to blackish in colour.

 In the next morning the dried latex is scrapped off with scraper then raped in poppy leaves

**Constituents:**

Opium contains some 30 alkaloids which are largely combined with the organic acid i.e. “Meconic acid”.

Drug also contains principle alkaloids like:

 Morphine 4-21%

 Codeine 0.5-2.5%

 Papaverine 0.5-2%

 Thebaine 0.5-2.5%

 Noscapine 4-8%

 Narceine

 Codamine

**Structures:**

**Uses:**

1. Opium and morphine are widely used to relieve pain and particularly valuable as hypnotic.

2. It is useful for allaying cough.

3. It acts as sedative.

4. Morphine and codeine decrease metabolism particularly before the introduction of insulin, used for the treatment of diabetes.

5. In the treatment of diarrhea.

6. Opium is also used as diaphoretic.

7. Miosis pin size pupil

8. It is used as preanesthetic medication sub-cutaneous about one hour before general anesthesia.

9. It is used pulmonary oedema.

10. It is muscle relaxant (papverine)

11. It control excessive peristalsis (apomorphine)

12. It is used as ant-tussive (narcotine)

**Identification Test:**

 Drug contain 3.5% meconic acid present free and in combination with morphine and other alkaloids.

 It form rhombic crystals soluble in water and alcohol and give red colour with the solution of ferric chloride which is not alter by adding dilute HCl

**INDOLE ALKALOIDS**

Indole consists of a benzene ring fuse with ∞ & β position of pyrol ring.

A number of important alkaloids possessing indole as a part of their structure. The important drugs and their **alkaloid of indole group** are:

 Rauwolfia

 Reserpine

 Catharanthus

 Physostigmine

 Ergot

 Nux vomica

RAUWOLFIA

**Synonyms**:

Snake root ,

Choti chandan (urdu)

**Botanical origin**:

*Rauvolfia serpentina*

**Family**:

Apocynaceae

**Part used** :

Dried fragment of the rhizome and dried tap root .

**History:**

 The genus name was selected in the honour of Dr. Leonhard Rauwolf a German botanist, physician and explorer

 Serpentina long , tapering , snake like root of plant

**Habit & Habitat:**

 Plant is a shrub

 Native: India & Burma

 Cultivated: Pakistan, Indonesia, Malaysia, Philippine, Witham, Java, Thailand

**Collection:**

 Collection is occur from wild plant which is now replaced by cultivation.

 Roots and rhizomes are dug out in October and November.

 When the plant roots are 2 to 4 years.

 The aerial parts and roots are separated and cut transversally and then washed and dried in air, containing moisture up to 2%, should be protected from light .

**Constituents:**

It contain a series of alkaloids about 30 to 80 types, have been isolated.

There are 3 series of alkaloids has been reported .

**1. Weakly basic indole alkaloids**

Reserpine , rescinnamine , deserpidine , yohimbine .

**2. Indoline alkaloid of intermediate basicity**

Ajmaline , isoajmaline , ajmalicine ,rauvofinine, corynanthine

**3. Strong anhydronium bases**

Serpentine, Serpentinine

**Structure:**

**Pharmacological Actions:**

**1. Hypnotic and sedative :**

It acts as hypnotic agent by depleting amines in cns .

**2. Antihypertensive:**

Reserpine acts as antihypertensive agent by depleting nor-epinephrine through the inhibition of catecholamine storage in post-ganglionic adrenergic nerve ending.

**3. Tranquilizer:**

Rauwolfia alkaloids also used as tranquilizer due to its sedative activity.

**4. Circulatotr diseases:**

Yohimbine is important alkaloid that is used in the treatment of impotence in circulatory disorder.

**5. Antipsychotic :**

Reserpine is used as antipsychotic agent to relief the symptoms in agitated psychotic state.

**6. Antidiabetic:**

Yohimbine has successfully used in diabetic problems .

**7. Cardiac arrhythmias:**

Ajmaline is used to treat cardiac arrhythmias.

In peripheral autonomic nervous system, effects of cholinergic system is increased and adrenergic is decreased .

**Uses:**

1. Anti-hypertensive drug

2. Nervousness and insomnia

3. Anti-psychotic drug

4. In mild to moderate hypertension it is used in combination for lowering BP.

5. In psychotic state i.e. schizophrenic patients that are unable to tolerate other antipsychotic agent, reserpine is used.

6. It has been used for millennia as an antidote against bites of venomous reptiles

7. Extracts of the roots are valued for the treatment of intestinal disorders, particularly diarrhea and dysentery and also an anthelmintic. Mixed with other plant extracts, they have been used in the treatment of cholera, colic and fever.

8. Rauwolfia root has proven highly effective (89%) in cases of chronic hives.

9. Rauwolfia root has occasionally proven effective in cases of malnutrition that were unresponsive to high protein or high-energy diets.

CATHARANTHUS

**Synonym:**

*Vinca rosea*

**Botanical origin**:

*Catharanthus roseus*

**Family:**

Apocynaceae

**Part used:**

Dried whole herb.

**Habit & Habitat:**

 Plant is an erect perennial herb

 Native to Madagascar but it is Cosmopolitan (present all over the world).

 Cultivated as ornamental plant in Southern Florida, Africa, Europe, Thailand, Taiwan, Australia.

**Collection:**

 It is dried under shade as it contains petal and volatile oil.

 These are collected when contain maximum amount of constituents.

**Production:** 500kg of plant will produce 1gm of vinblastin.

**Constituents:**

It contain about 70 alkaloids.

They are basically bisindole (Indole + Indoline) which are obtain for anticancerous activity.

Major alkaloids having neuroplastic activity is:

 Vinblastin (vinica leukoblastin)

 Vincristine (leurocristine) 0.0002% in plant

 Vincasidine

 Vinrosidine

 Vincaleurosine

 Vindesine (semi-synthetic derivative of Vinblastine)

 Vinorelbin (newer semi-synthetic drug with broader anti-tumour activity and less neurotoxic effect)

**Mechanism Of Action:**

 Vinblastine at very low concentrations they suppress microtubule dynamics and at higher concentrations they reduce microtubule polymer mass. Recent findings indicate that they also produce microtubule fragments by stimulating microtubule minus-end detachment from their organizing centres.

 Vincristine binds to tubulin dimers, inhibiting assembly of microtubule structures. Disruption of the microtubules arrests mitosis in metaphase. Therefore, the *vinca* alkaloids affect all rapidly dividing cell types including cancer cells, but also those of intestinal epithelium and bone marrow. *Tubulin* is a structural protein that polymerizes to microtubules.

**Clinical Uses:**

**1. Hodgkin’s disease:**

Vinblastin is used to treat hodgkin’s disease.

**2. Non-Hodgkin’s disease:**

Vincristine is used to treat non-hodgkin’s disease.

**3. Neuroplasm:**

Vinblastin sulphate and vincristine sulphate i.e, obtain from catharanthus is used to treat neuroplasm.

**4. Lung cancer:**

Vinorelbin Tatarate semisynthetic derivative of vinblastin given as single agent or in combination with cisplastin for 1st line treatment of small cell lung cancer.

**5. Chemotherapy regimens:**

Vincristine is delivered via intravenous infusion for use in various types of chemotherapy regimens.

**6. Acute Lymphoid Leukaemia:**

Vindesine is used in acute lymphoid leukaemia in children.

**7. Vinblastine is used to treat:**

i. Histolytic lymphoma

ii. Renal cell carcinoma

iii. Testicular cancer

iv. Breast cancer

v. Carcinoma of testis

**8. Vincristine is used to treat:**

i. Breast cancer

ii. Lymphosarcoma

iii. Neuroblastoma

iv. Lung cancer

v. Cervical cancer

vi. Acute lymphocytic leukaemia in children.

NUX VOMICA

**Synonyms:**

Poison Nut, Semen strychnos, Quaker Buttons, dogs Button, Button seed.

**Botanical name:**

*Strychnos nux-vomica*

 Strychnous is Greek word refers to a number of poisonous plants.

 Nux-vomica is from two Latin words that means a nut causing vomiting.

**Family:**

Loganiaceae.

**Part used:**

Dried ripe seeds.

**History:**

The drug was introduced in Europe in 16th cetury although it was used for poisoning animals.

In 1640, its use began in medicines.

Brucine was isolated in 1819 and strychnine in 1817.

**Habit & Habitat:**

 Plant is a small tree.

 They are native to Srilanka, East Indies, Nothern Australia, on the Malabar Coast.

 Most of the commercial supply comes from Cambodia and Srilanka, East Bengal, Barma, England, Thailand.

**Collection:**

Fruit is collected from November to February.

Fruit is a berry having 1-5 seeds that are freed from the bitter pulp by exportation.

The size of fruit is almost small range size.

When fruit ripes it becomes greenish yellow colour epicarp with whitish pulp inside, in which 1-5 seeds are embedded.

These seeds are washed after removing pulp.

Then they are dried out.

Seeds contain testa and endospore.

Strychnine is abundatly present in inner side of endosperm.

Brucine is present in the outer layer of endosperm.

**Constituents:** Nux Vomica contains the alkaloids about 1.8-5.3%,

The major principle constituents are

 Strychnine

 Brucine

Other minor alkaloids are

 Protostrychnine

 Pseudostrychnine

 Oxistrychnine

 Isostrychnine

 Chlorogenic acid

 Fixed oil 3%

**Structure:**

**Mechanism Of Action:**

Strychnine is extremely toxic and function as a central stimulant.

Alkaloid produce excitation of all parts of CNS and block the inhibitory spinal impulses at post synaptic level that leads to exaggeration in reflexes resulting in toxic convulsions.

Strychnine also interfere with agonist binding site of nicotinic Ach receptors.

**Uses of Strychnine:**

**1. Central Stimulant**

The most direct symptom caused by strychnine is violent convulsions due to a simultaneous stimulation of the motor or sensory ganglia of the spinal cord.

**2. Rodenticides**

It also used as rodenticides.

**3. Indigestion:** The powder made from the strychnine seeds was used to alleviate indigestion.

**4. Stimulant:**

Mixtures of Nux Vomica were also used as a stimulant on the gastro-intestinal tract. In the mouth it acts as a bitter dietary, increasing appetite by stimulating peristalsis.

**5. Laxative:**

It was formerly combined with cascara and other laxatives to treat chronic constipation

**6. Digestant:**

It increase flow of gastric juice that help in digestion.

**7. Appetizer:**

By stimulating peristalsis increase appetite.

**8. Respiratory Stimulant:**

Used as respiratory stimulant in very minute quantity in case of respiratory blockage.

**9. Circulatory Stimulant:**

It is used as circulatory stimulant in surgical shocks. The most direct symptom caused by strychnine is violent convulsions due to a simultaneous stimulation of the motor or sensory ganglia of the spinal cord. During the convulsions there is a rise in blood pressure.

**Uses of Brucine:**

**1.** Brucine closely resembles strychnine in its action, but is slightly less poisonous as it only causes paralysis of the peripheral motor nerves. It is said that the convulsive action of strychnine is absent in Brucine.

**2.** It was used in pruritus and as a local anodyne in inflammations of the external ear.

**3.** Commercially used as alcohol denaturant.

PHYSOSTIGMA

**Synonyms:**

Ordeal Bean, Chop Nut , Calabar beans.

**Botanical Origin:**

*Physostigma venenosum*

 Physostigma is Greek word which means an “inflated or bladder like stigma”

 Venenosum is a Latin word which means “full of poison.”

**Family:**

Leguminosae

**Part Used:**

The dried ripe seeds.

**Habit & Habitat:**

 Plant is a perennial woody climber.

 Grow in West Africa(Guinea)

 Introduced into India and Brazil.

**Collection:**

 Fruit is a legume containing 2-5 seeds.

 The seeds ripen at all seasons, but are best and most abundant during the rainy season in Africa, June till September.

 Collect the seeds and dried.

**Constituents:**

The chief constituent is:

Physostigmine (0.5%) also called Eserine

It also include:

Isophysostigmine

Eseramine

Geneserine

Physovenine

Calabatine

Calabacine.

**Mechanism Of Action:**

Physostigmine is reversible inhibitor of cholinestase enzyme which are degrading enzymes of Acetylcholine.

Acetylcholine is neurotransmitter that is parasympathatomimetic agent.

Thus, the effects of endogenous acetylcholine increases.

**Clinical Uses:**

**1. Ophthalmic use:**

Chiefly used for diseases of the eye, it causes rapid contraction of the pupil and disturbed vision.

**2. In Glaucoma:**

Increase intraocular pressure and decrease lacrimation so used in glaucoma.

**3. As stimulant:**

Used as a stimulant to the unstriped muscles of the intestines in chronic constipation.

**4. In B.P:**

Its action on the circulation is to slow the pulse and raise blood-pressure.

**5. In CNS:**

It depresses the central nervous system, it has been employed internally for its depressant action in epilepsy.

**6. In Acute Tetanus:**

It is given hypodermically in acute tetanus.

ERGOT

**ERGOT**

**Botanical origin**:

*Cleviceps purpurea*

**Family:**

Clevicipitaceae

**Part used:**

Sclerotium developed on rye plant.

**RYE**

**Botanical origin:**

Secale cereale

**Family:**

Graminae

**Habit & Habitat:**

 Hard mycelium grow on rye plant

 Commercial supply from Eastern countries, Russia, Germany, France, Portugal, Hungry, Switzerland, U.S.A.

 Cultivated in Spain.

**Collection:**

**Stage I**

 In spring season fungus produced some sexual spores named as ***Ascospores*** which may come in contact with the ovary of rye plant where they penetrate in the tissue then they germinate into hyphal strands.

 Mass of hypae is named as “***Mycelium***”.

 Some of hyphae is may produce asexual spores which is ***Conidiospores*** and this conidiospores may attach with the viscous sugary secretions named as ***Honey dew***, insects are attracted toward honey dew and carry spores to the ovary of other plants where it germinate and produce fungus and cycle is repeated named as ***Asexual cycle*** or ***Sphacelial stage***.

**Stage II**

Mycellium replaced entire ovary and become purple hard mass which is actually the desired product sclerotium then it is collected and dried and if not collected they fall on ground and germinate a ascospores.This stage is named as ***Ascigerous stage*** or ***Sexual stage***.

Collection may be carried out with hands or machines before harvesting the rye plant. When it turn to purple immediately collect and let it dry and store it in air tight container because ergot is liable to attack by insects and bacteria.

**Ergotism**

Rye flour made from the contaminated rye grains was subsequently made into rye bread and ingested. Thus, the fungus was responsible for severe outbreaks of poisoning in human and in cattle which is today known as “***Ergotism***”.

**Costituents:** Some are water soluble and mostly they are water insoluble alkaloids are present.

Water soluble alkaloids are:

Ergonovine & its derivative Ergometrine

Water insoluble alkaloids are:

Ergotamine & its derivative Ergotaminine

**Structure:**

**Mechanism Of Action:**

Mechanism of action is probably vasoconstriction of the dilated carotid artery bed with a concomitant decrease in the amplitude of pulsation.

It may inhibit receptor uptake of norepinephrine at sympathetic nerve endings, increasing the vasoconstrictive action.

The drug is also an antagonist of serotonin activity.

**Clinical Uses:**

**1. Quick delivery**

Ergonovine stimulate the uterine muscles and increase the frequency and amplitude of uterine contraction and help in quick delivery.

**2. Treatment of migraine:**

It is used medicinally for treatment of acute migraine attacks (sometimes in combination with caffeine and Ergotamine tartrate.

It is categorised as specific analgesic in treatment of migraine. By decreasing the extra cranial blood flow and reduce the amplitude of pulsation in cranial atrious that are associated with migraine.

**3. As vasoconstrictor:**

Ergotamine produces vasoconstriction peripherally as well as damages the peripheral epithelium.

**4. Use in uterine contractility:**

It can increase uterine contractility and occasionally is used therapeutically immediately post-partum to decrease uterine bleeding.

**5. During delivery:**

Ergometrine is used to facilitate delivery of the placenta and to prevent bleeding after childbirth by causing smooth muscle tissue in the blood vessel walls to narrow, thereby reducing blood flow.

**IMIDAZOLE ALKALOIDS**

PILOCARPINE

**Botanical Origin:**

*Pilocarpus jaborandi*

**Family:**

Rutaceae

**Part Used:**

Dried leaflets

**Habit & Habitat:**

 Plant is a shrub

 Indigenous to Brazil

 Cultivated in Westindies and Central America.

**Collection:**

 Leaves are collected from wild sources.

 Now demand of leaves transfer into cultivation.

 Leaves are collected and dried.

**Constituents:**

Drug contains about 0.5-1% alkaloids:

1. Pilocarpine (occur as oily syrupy liquid)

2. Isopilocarpine

3. Pilocarpidine

4. Pilosine

5. Isopilosine

**Structure**

**Mechanism Of Action:**

Pilocarpine is reversible inhibitor of cholinestase enzyme which are degrading enzymes of Acetylcholine.

Acetylcholine is neurotransmitter that is parasympathatomimetic agent.

Thus, the effects of endogenous acetylcholine increases.

**Clinical Uses:**

**1. Ophthalmic use:**

Chiefly used for diseases of the eye, it causes rapid contraction of the pupil and disturbed vision.

**2. In Glaucoma:**

It is used in glaucoma

**3. Increase secretions**

It increase the lacrimation and act as eye protectant.

**4. Antidote**

It act as antagonist of Atropine.

**ALKALOIDAL AMINE**

EPHEDRA

**Synonyms:**

Ma huang

Ma mean astringent

Huang mean yellow

In china this drug has been used as medicines for 5000 years.

**Botanical Origin:**

*Ephedra sinica*

**Family**

Gnetaceae

**Part Used:**

Entire plant or over ground portion of plant

**Habit & Habitat**

 Plant is a low shrub

 Grow in Pakistan, China & India.

**Collection**

Over-ground portion is cut and dried.

**Constituents:**

Drug contains about 0.5-2% alkaloids:

1. Ephedrine 30-90% (occur as white rosettes or needle like crystals)

2. Pseudoephedrine

**Structure:**

**Mechanism of Action**

It act on α1, β1 and β2 adrenergic receptors and stimulate the sympathetic system

**Uses:**

1. In cough preparations due to antitussive properties

2. Used in Hypotension because it is vasoconstrictor and cause increase blood pressure.

3. Used in bronchial asthma because it is bronchodilator.

4. Pseudoephedrine act as nasal decongestant.

COLCHICINE

**Botanical Origin:**

*Colchicum autumnale*

**Family:**

Liliaceae

**Part Used:**

Dried seeds & corms

**Habit & Habitat:**

 Plant is a herb

 Cultivated in England, Central Europe & Northern Africa

 Commercial supply comes from Yugoslavia & Italy.

**Collection:**

 Seeds are collected in July or August.

 Corms are collected in Spring season before the leaves development.

 Corms are dried at temperature not exceeding 65 oC.

**Constituents:**

Drug contains about 0.6-1.2% alkaloids in which major alkaloid is Colchicine.

**Structure:**

**Mechanism of Action:**

 Exact mechanism is not known.

 It is believed that it inhibit leukocytes migration and reduce the lactic acid production by the leukocytes and decrease the deposition of Uric acid which cause inflammation and pain.

**Uses:**

1. Treatment of Gout

2. Anti-inflammatory in gouty inflammation.

3. It produce polyploidy (doubling of chromosomes) experimentally antineoplastic properties have been reported.

4. In large doses cause GIT irritation.

**PURINE BASES**

COFFEE

**Botanical origin:**

*Coffea arabica*

*Coffea liberica*

**Family:**

Rubiaceae

**Part used:**

Dries seeds & coffee beans

**Habit & Habitat:**

 Evergreen tree

 Indigenous to Ethiopia & eastern Africa

 Cultivated in Indonesia, Srilanka, America & Brazil.

**Collection:**

 Fruit is a spheroidal drupe (peach like fruit with thin outer layer having single seed).

 Seeds are collected and roasted.

 When seeds are roasted, they swell and change its colour into dark brown and attain characteristics odour and flavour.

 The aroma of seeds is due to the presence of oil named as ***Caffeol*** produced during the roasted process.

**Constituents:**

Seeds contain following alkaloids:

1. Caffeine 1-2%

2. Chlorogenic acid (caffeotannic acid)

3. Pentose sugar, Glucose, Proteins & Fatty acids

**Structure:**

**Uses:**

1. CNS stimulant

2. Diuretic

3. Dietic

TEA OR BLACK TEA

**Botanical Origin:**

*Camellia sinensis*

*Thea sinensis*

**Family:**

Theaceae

**Part Used:**

Dried leaves

**Habit & Habitat:**

 Evergreen tree or shrub

 Indigenous to Eastern Asia

 Cultivated in China, Japan, Indonesia, Srilanka & Asia

**Collection:**

**1. Black tea**

Black tea is prepared in Srilanka and India by heaping the fresh leaves until the fermentation has started.

Leaves are then rapidly dried by using artificial heat.

**2. Green tea**

Green tea is prepared in China and Japan by rapidly drying the freshly picked leaves in copper pan over a mild artificial heat .

Leaves are rolled in the palm of hand when dried.

**Constituents:**

Leaves contain following alkaloids:

1. Caffeine

2. Theophylline

3. Theobromine

4. Tannins in the form of gallotannic acid

5. Yellow colouring matter

**Mechanism of action:**

 Increase sodium efflux

 Increase water excretion

 CNS stimulant

 Smooth muscle relaxant (theophylline)

 Astringent action (tannins)

**Uses:**

1. Diuretic

2. CNS stimulant

3. Theophylline used as bronchodilator in asthma

4. Cardiac oedema (diuretic)

5. Astringent action due to tannins