pharmacognosy

3rd stage/2nd term

Quinoline Alkaloids

Dr. Zahraa Shubber

Lec .4

Quinoline Alkaloids

- Consist of alkaloids and alkaloidal salts obtained from the bark of certain Cinchona species **(Quinine, Quinidine, Cinchonine, Cinchonidine).**
- The amount of alkaloids present depend on **species, environment of the tree, age and method of bark collection.**
- Quinine; Anti-malarial Synthetic alkaloids are now used as substitute for quinine for malaria.
- Cinchona and its alkaloids are only members of this group that are therapeutically important at present.

Cinchona bark

- Is the dried bark of the stem or the root of ***cinchona succirrubra*** (red cinchona) or other species of cinchona (yellow cinchona). F. Rubiaceae)
- cinchona contains about 25 closely related alkaloids, the most important of which quinine, quinidine, cinchonine and cinchonidine.
- Derived from tryptophan amino acid.

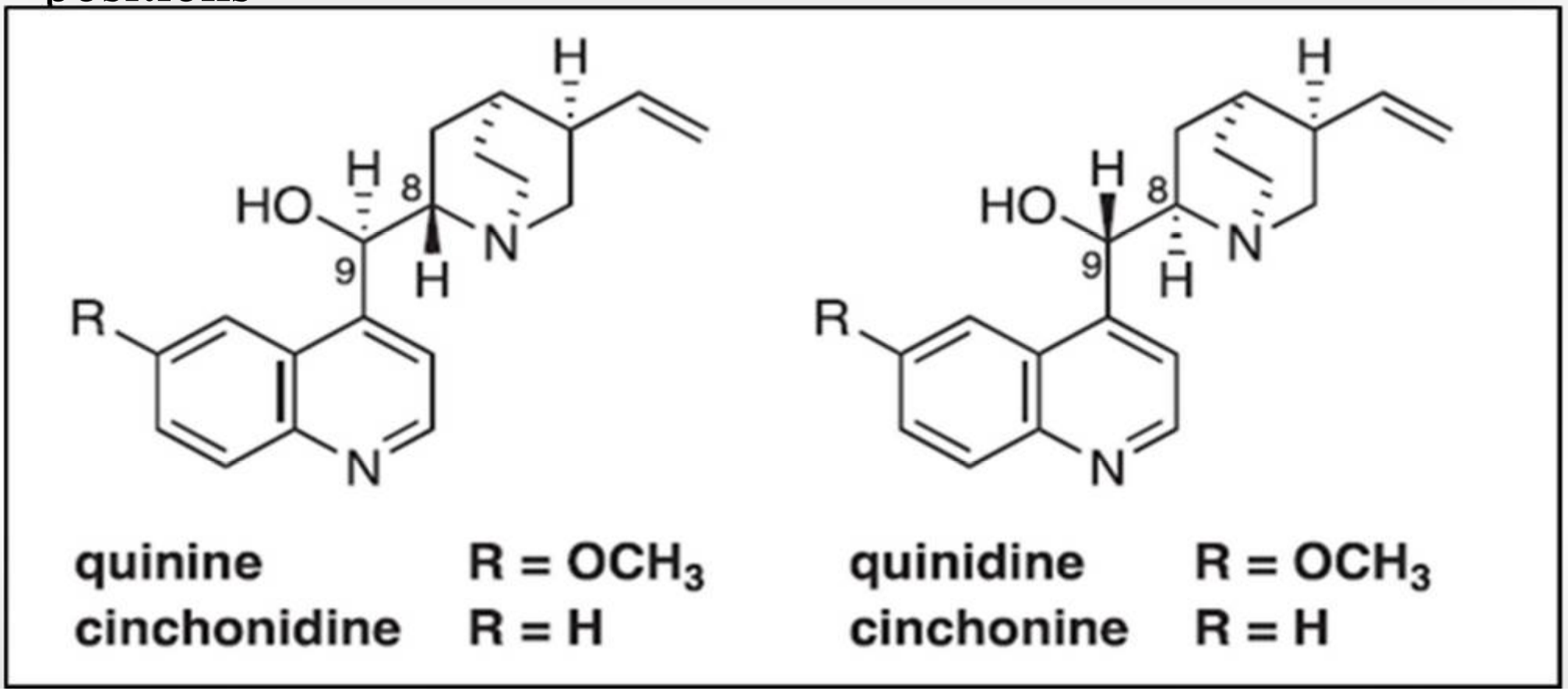
Uses of cinchona

- Cinchona and its alkaloids have been used in the treatment of **malaria fever** for many years.
- **Quinine** continues to be used in the treatment of malarial in many part of the world but in U.S.A. this alkaloids is utilized primarily in the preparation of effervescent tonic water.
- quinidine is now principle cinchona alkaloids employed therapeutically.
- **Over doses of cinchona products results in**

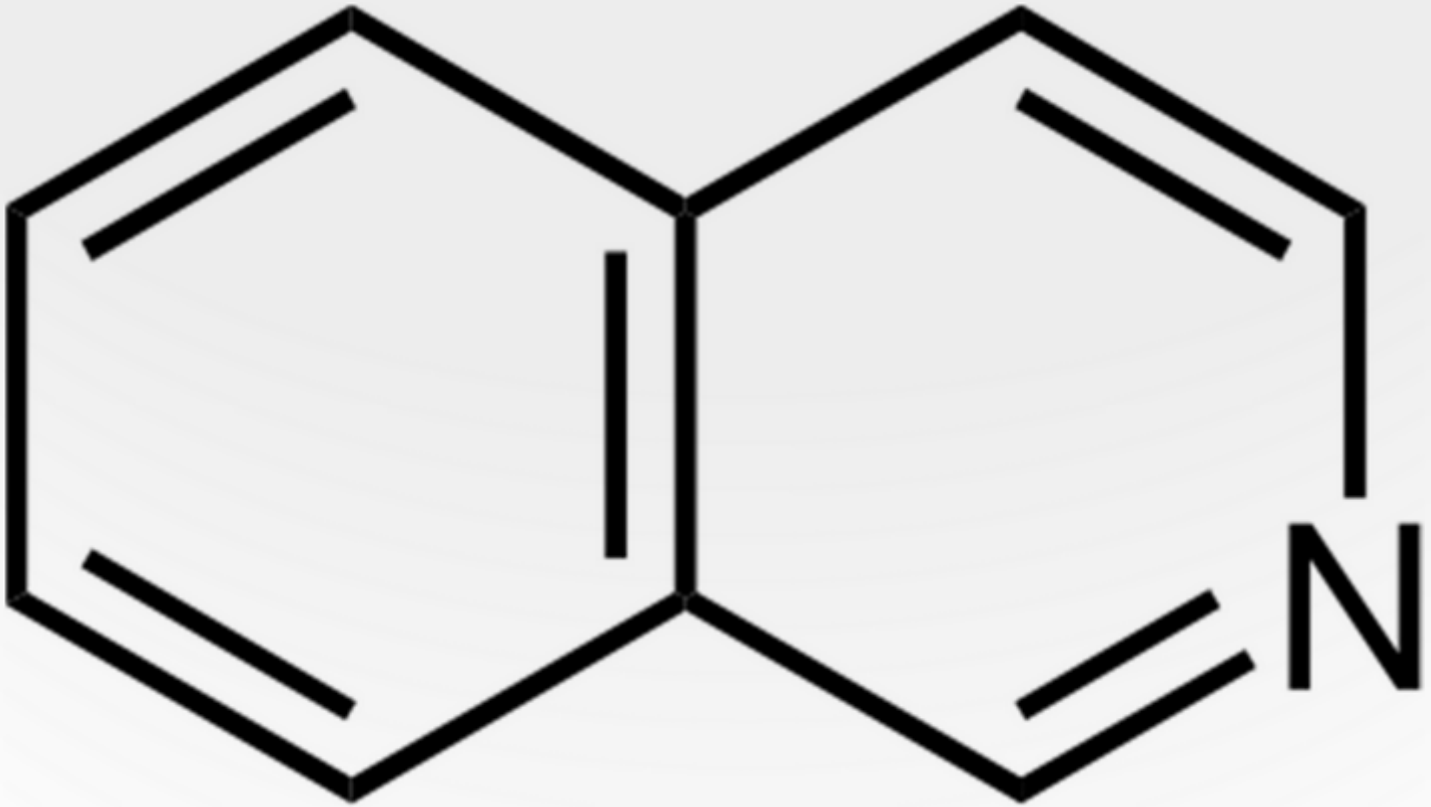
1. Temporary loss of hearing.
2. In impaired sight.
3. Ringing of the ear (Tinnitus)

- The symptoms of toxicity condition has been called **(Cinchonism).**

- **Quinidine** is stereoisomer of **quinine** and present in 0.25-1.25% in cinchona barks.
- Quinidine is used to treat various **cardiac arrhythmias**.
- Quinine is the stereoisomer of quinidine.
- cinchonine and cinchonidine are stereoisomers at the C-8 and C-9 positions



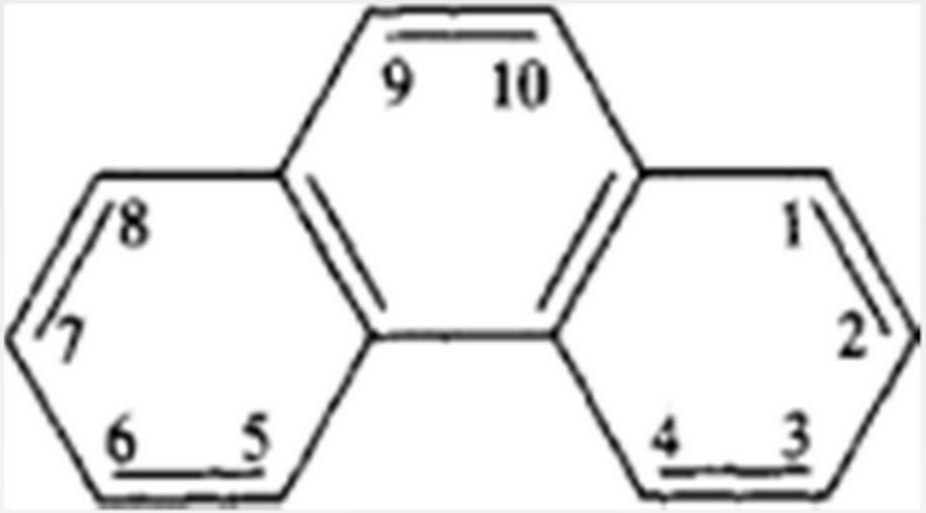
Isoquinoline



Isoquinoline

- Isoquinoline structure occurs in a considerable member of alkaloids, widely distributed in plant families.
- The important drugs and their alkaloids in this group **are ipecac and emetine, curare (tubocurarine) and opium and its alkaloids.**
- the more **important opium alkaloids as morphine, codeine and thebaine** which exhibit a phenanthrene nucleus, the majority of alkaloids have the isoquinoline ring structure and these phenanthrene alkaloids are derived biosnthetically from benzylisoquinoline intermediate.

Phenanthrene nucleus



Isoquinoline Alkaloids

- Drugs: opium and ipecac.
- Alkaloids of both these herbs are the same group, yet they **differ chemically and also in their pharmaceutical actions.**

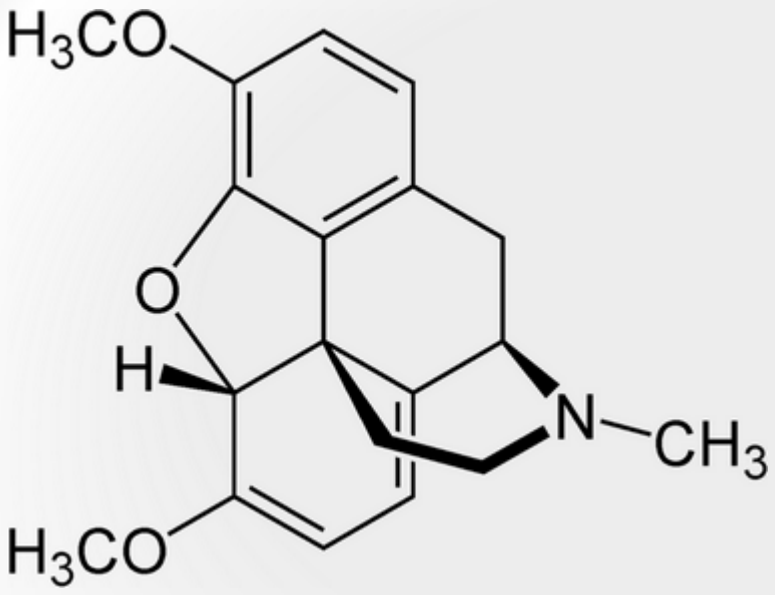
- **Opium alkaloids: morphine, codeine, ethylmorphine, thebaine, heroin and papverine.**

- **Ipecac alkaloids**: **emetine, cephaeline, psychtrine, methylpsychotrine.**

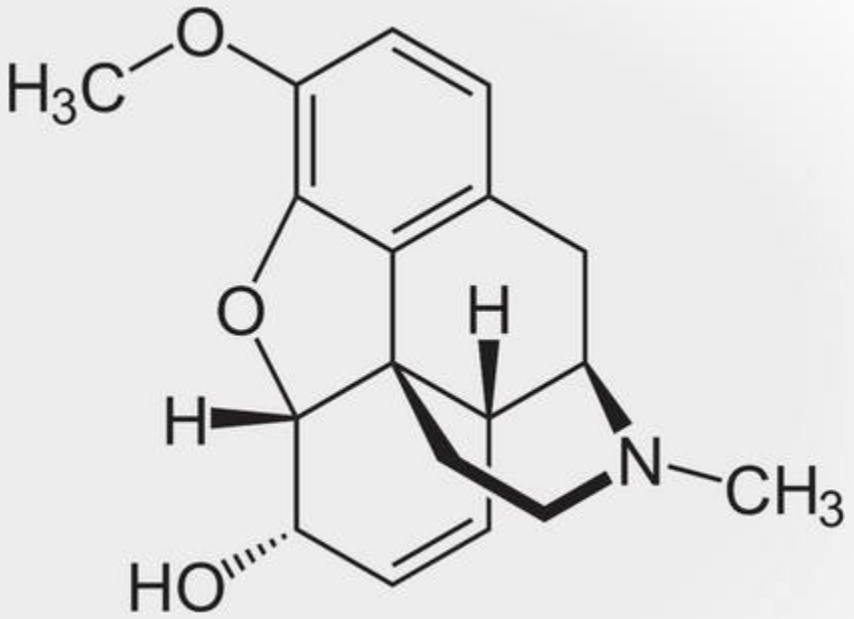
Biosynthesis of Isoquinoline alkaloids

- These compound result from condensation of phenyethyl amine derivative with a phenyl acetaldehyde derivative. Both of these moieties are derived from phenylalanine and tyrosine.
- Administration of tyrosine to papver somniferum resulted in the formation of papaverine.

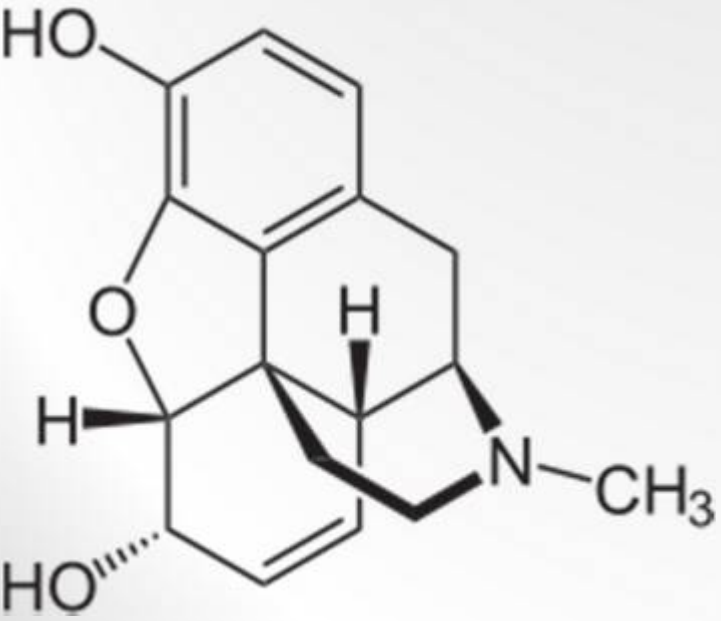
- A key feature of this morphine way is enzymatically controlled methylation pattern, that gives rise – reticuline then salutaridine which is the first intermediate with a phenanthrene nucleus.
- Another interesting aspect of this pathway is the biosynthetic relationship of thebaine, codeine and morphine stepwise demethylation of thebaine leads first to relatively mild analgesic codeine and then to potent narcotic morphine.



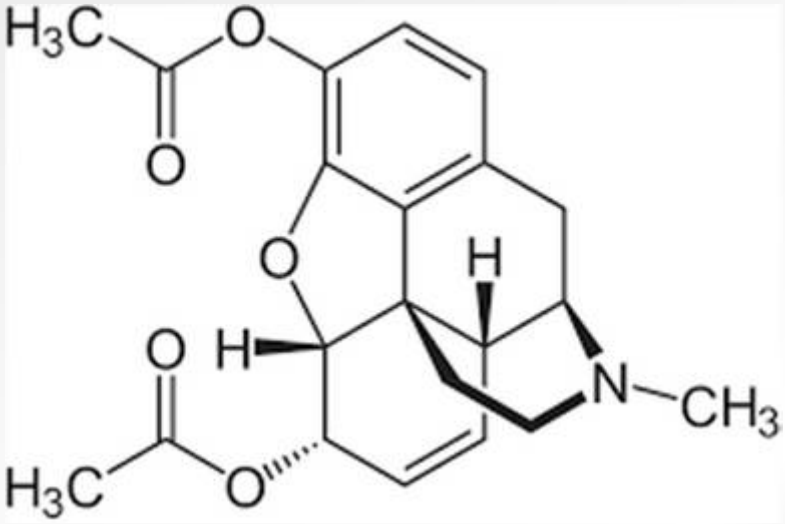
Thebaine



Codeine



Morphine



Heroin

Opium

- **Opium** is the air dried milky exudates obtained by incising the unripe capsules of **papver somniferum** or its variety **album** (F. Papveraceae).
- Active constituent, More than 30 different alakloids have been obtained from opium and its extracts.
- The most important of these are morphine, codeine, noscapine (formerly narcotine), papverine and thebaine, other alkaloid narceine, protopine, laudanine, codamaine, cryptopine, lanthopine and meconidine.

- Opium is a pharmaceutics necessity, it act chiefly on **CNS, its action first stimulates and then depresses nerve response.**
- It serves as

- **an analgesic,**
- **hypnotic and**
- **narcotic,**

- Side effects are **contracts the pupil of the eye and constipation**.

Papver somniferum

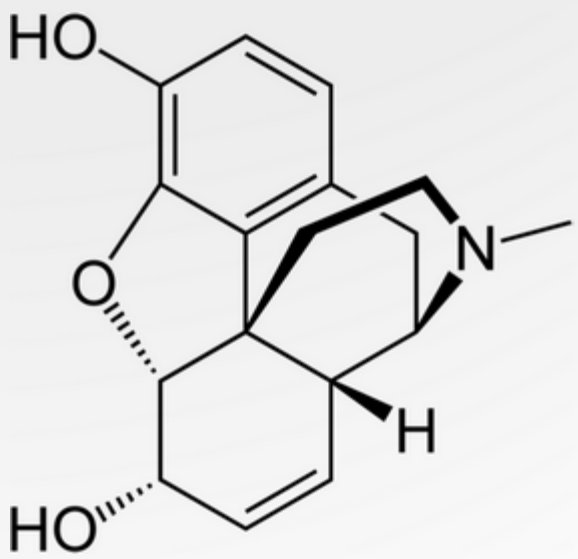
- 30 Alkaloids, mainly 6 alkaloids **morphine, codeine, thebaine, Noscapine, Narceine and papverine.**

1. Morphine

- Is the most important of the opium alkaloids, morphine and related alkaloids are morphinan isoquinoline derivatives.
- The molecule contains **a phenolic and an alcoholic hydroxyl group.**
- Morphine and its salts are classed as narcotic analgesic they are strongly hypnotic.
- Their use tends to induce nausea, vomiting, constipation and habit formation.

- Morphine and related opium alkaloids have analgesic activity features of centrally acting analgesics. These are

1. Cenral C atom with no hydrogen substitution (Quaternary).
2. Phenyl group or isostere attached this C atom.
3. A 2-carbon bridge separating the tertiary nitrogen atom and central C atom.
4. Tertiary N atom.



-Codeine

- Is the most widely used opium alkaloid obtained from opium (0.2-0.7%) or prepared from morphine by methylation (of phenolic hydroxyl group) or from thebaine reduction and demethylation.
- It is **methyl morphine** (replace the phenolic hydroxyl group).

Codeine and salt has **narcotic analgesics and antitussives, they are used as sedatives, especially in allaying coughs, and its action is similar to morphine, but less toxic and less danger of habit of formation.**

. Milder sedative

. Relieve cough

. Habitual use many cause constipation

Both morphine and codeine decrease metabolism.

3-Heroin (Diacetyl morphine)

- Is formed by acetylation of morphine, heroin's action is similar to morphine **but more potent and dangerous of habit formation.**

4-Pavaverine occurs naturally in opium (1%), it is a **smooth muscle relaxant.**

5-Noscapine or narcotine exists in opium as free base (3-10%), it posses **narcotic properties and as antitussive**.

Opioids

- Refer to synthetic morphine like compounds, many of opioids offer the same narcotic and pain relieving properties as morphine but not as habit- forming, other **posses the cough relieving activity of codeine but are not addictive.**

Ipecac Alkaloids - Ipecacuanha

- Ipecacuanha root is the dried root or rhizome and root of **Cephaelis**
- Family Rubiaceae
- It should contain at least 2% alkaloids
- Isoquinoline alkaloids mainly **Emetine, psychotrine and cephaeline**

Uses:

1. Expectorant
2. Emetic
3. Amoebic Dysentry

- Emetine is **more expectorant and less emetic** in action that cephaeline
- Psychotrine: selective HIV inhibitors (study could lead to therapeuticall useful agent)

Cephaelis

Ipecac

- Consist of the dried rhizome and roots F. Rubiaceae
- Ipecac contains 5 alkaloids (2-2.5%), the principle alkaloids are emetine, cephaline and psychotrine which contained chiefly in the bark.

Uses:

- Ipecac in the form of syrup us used in the treatment of **drug overdose and in cases of poisoning.**
- It produces **emesis through a local irritation** effect on GI mucosa and a **central medullary effect, by stimulation** of the chemoreceptor trigger zone.

Emetine

- Emetine (methyl cephaleine) is an alkaloid from ipecac or prepared synthetically by methylation of cephaeline.

Uses: Emetine HCl is

1. Antiamebic
2. possesses expectorant and emetic properties.

Curare

- Tubocurarine the most important alkaloid in curare
- It uses **as muscle relaxant in surgical procedure**
- It is also act as a template of other muscle relaxant such as atracurium.


Thank You.