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ALKALOIDS (UG)

B.Sc-IInd Year

Unit-04

ALKALOIDS

- First introduced by German Chemist **Carl F. W. Meissnerin** (1819).
- Derived from the word Alkali.
- Group of naturally occurring organic compound which are basic in nature contain one or more nitrogen atoms normally of heterocyclic nature is known as alkaloids.
- Posses physiological action on human or animal body.

Distribution of Alkaloids

- ✓ Abundant in higher plants (Angiosperm)
- ✓ Present in different families like Apocynaceae, Rubiaceae, Solanaceae etc..
- ✓ Present in any parts of plants:
 - a) Aerial parts (Ephedrine)
 - b) Entire plants (vincristine, vinblastine)
 - c) Leaves (Caffeine)
 - d) Root (Reserpine)
 - e) Bark (Quinine)
 - f) Fruits (Piperine)
 - g) Latex (Morphine, Codeine)

PROPERTIES OF ALKALOIDS

Physical properties

- 1) **Crystalline Solids** (some are amorphous solid- Emetine. Some are liquid- Nicotine, coniine, Pilocarpine)
- 2) **Colourless** (Berberine and Colchicine- Yellow, Betanidine- Orange)
- 3) Solubility (Free alkaloids are soluble in organic solvents and salt form are soluble in water)
Exception:- Caffeine and ephedrine (Soluble in water), Morphine (insoluble in ether)
- 4) Optically Active
- 5) Bitter in taste

Chemical properties

- 1) **Basic** in nature (due to presence of L.P. of electrons on N-atom)
- 2) Nitrogen exists as:
 - **Primary**- Nor ephedrine
 - **Secondary**- Ephedrine
 - **Tertiary**- Atropine
 - **Quaternary ammonium**- Tubocurarine
- 3) Basicity
 $2^\circ > 1^\circ > 3^\circ$
Weak base –Caffeine, **Strong base**- Atropine,
Amphoteric- Morphine, **Neutral alkaloid**- Colchicine

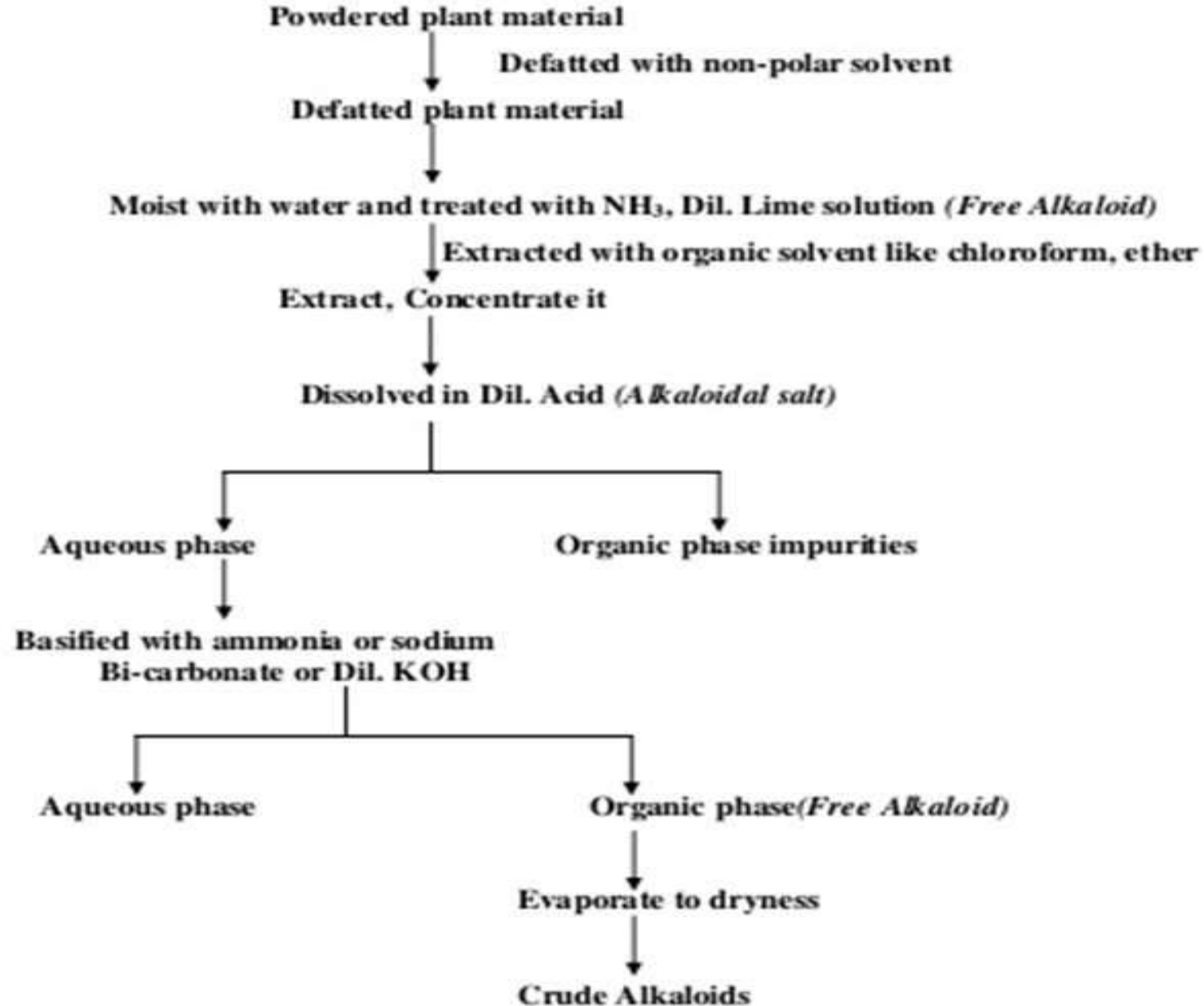
ISOLATION OF ALKALOIDS

Stas Otto Method

The extraction of alkaloids is based on their basic character and solubility pattern. Extraction is usually served by one of the following general method, i.e., Stas Otto Method:

- 1) The plants are defatted with petroleum ether, especially in case of seeds and leaves to remove the fat soluble constituents and then with polar solvents. The extract is concentrated under reduced pressure and treated with alkali so that the free bases convert in their salts and separated with organic solvents. This process is known as Stas-Otto process.
- 2) The powdered material is moistened with water and mixed with lime, which combines with acids, tannins and other phenolic substances and sets free the alkaloid salts. Extraction is then carried out with organic solvents such as ether or petroleum spirit. The concentrated organic liquid is then shaken with aqueous acid and allowed to separate. Alkaloid salts are now in aqueous liquid, while many impurities remain behind in the organic liquid.
- 3) The powdered material is extracted with polar solvents such as water or aqueous alcohol containing dilute acid. Pigments and other unwanted materials are removed by shaking with chloroform or other organic solvents. The free alkaloids are then precipitated by the addition of excess sodium bicarbonate or ammonia and then separated by filtration or by extraction with organic solvents.
- 4) The extract is treated with ammonia so as to convert the alkaloid salts into their free bases. Such liberated alkaloids in free base form are conveniently extracted with organic solvents like ether, benzene, chloroform etc. This method is not useful for the isolation of alkaloids of quaternary nitrogen. The product is then dissolves in acetone and then passed this solution through an ion exchange column which afforded the alkaloids in a high state of purity.

ISOLATION OF ALKALOIDS

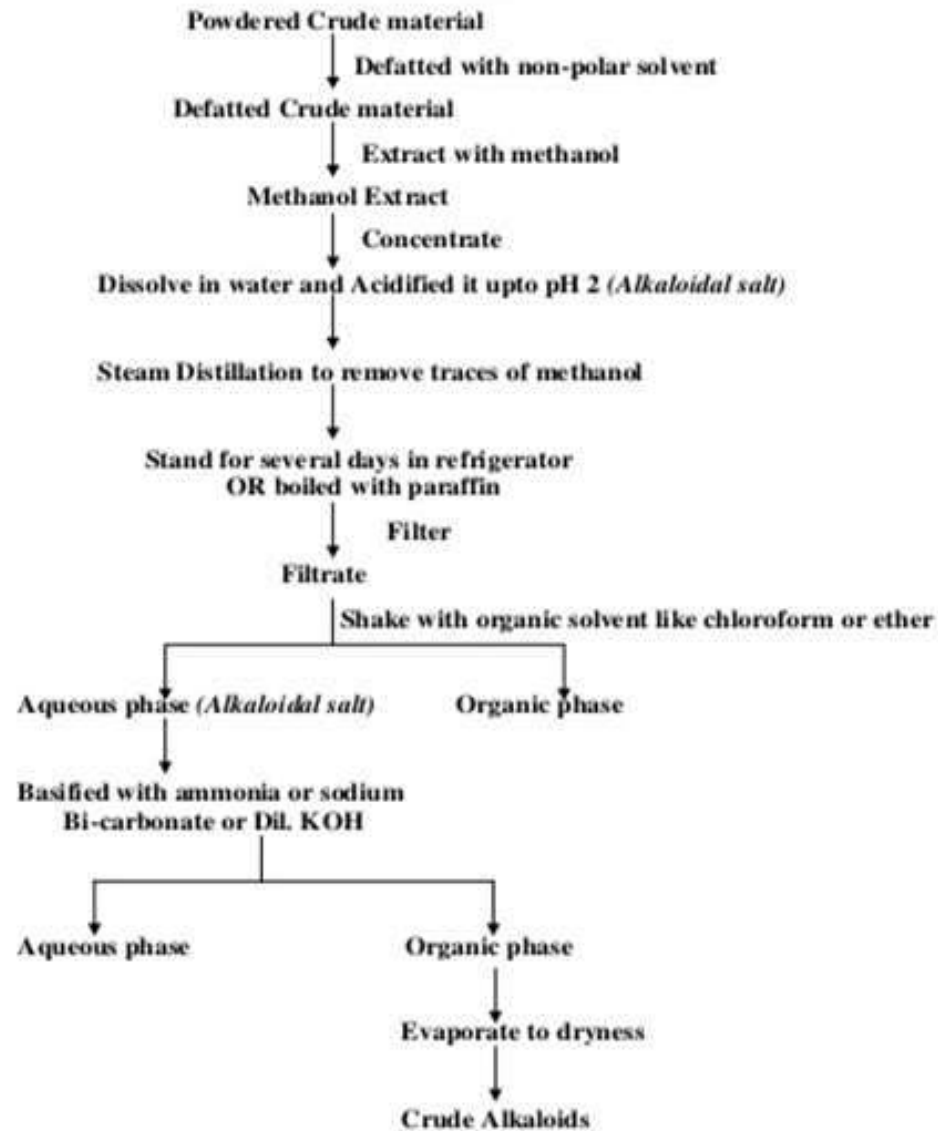


Stas Otto Method

Stas Otto Method

ISOLATION OF ALKALOIDS

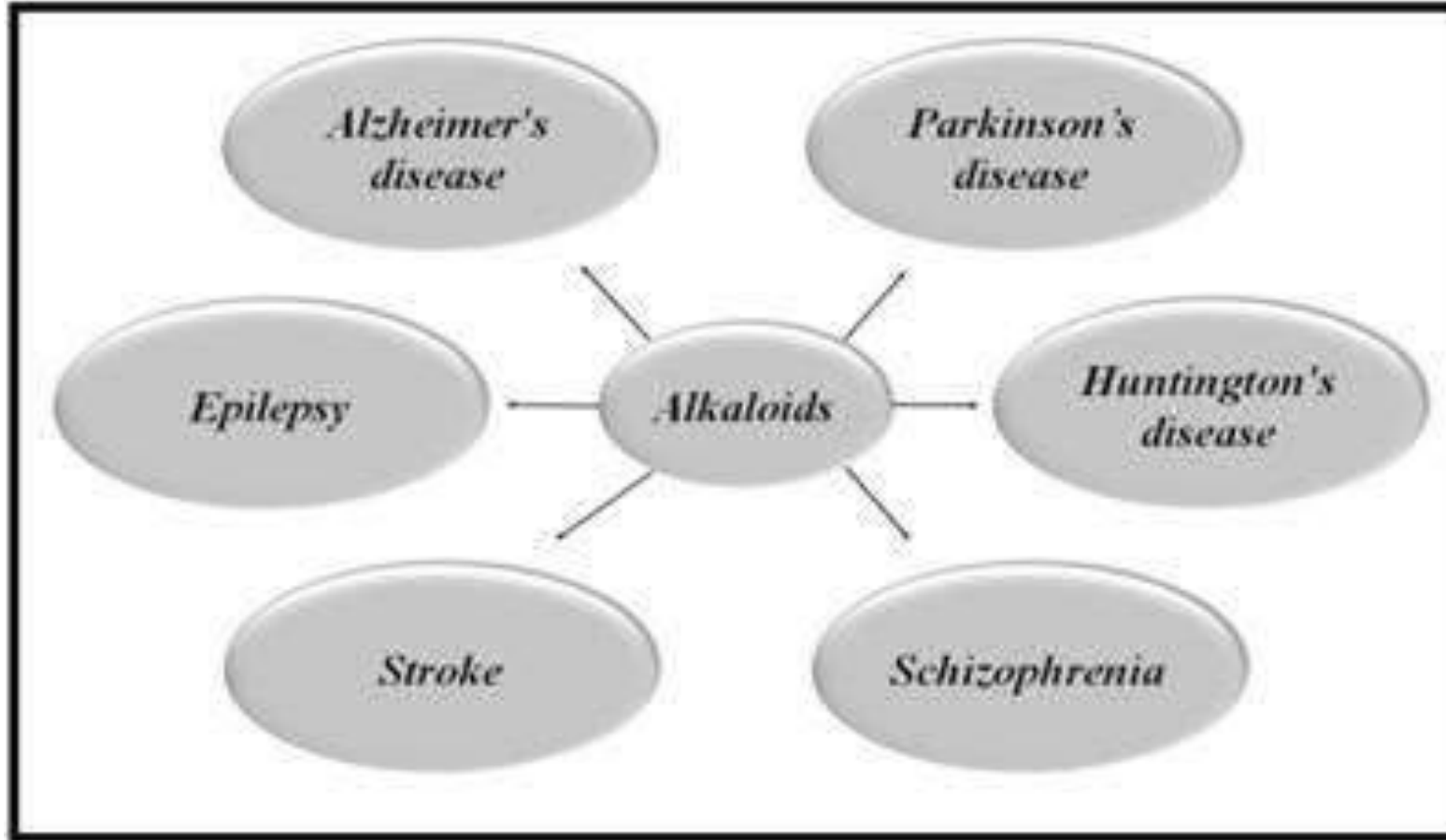
This is another Method



Manske's Method

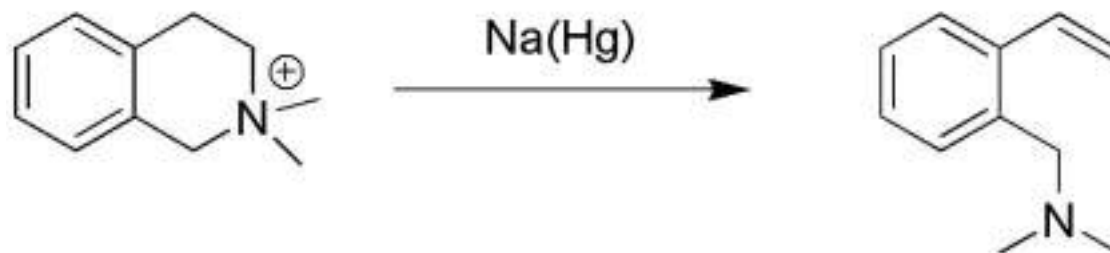
Manske's Method

PHYSIOLOGICAL ACTION OF ALKALOIDS

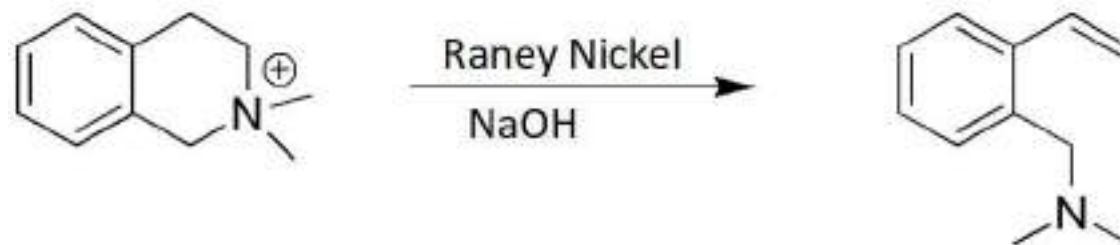


EMDE MODIFICATION

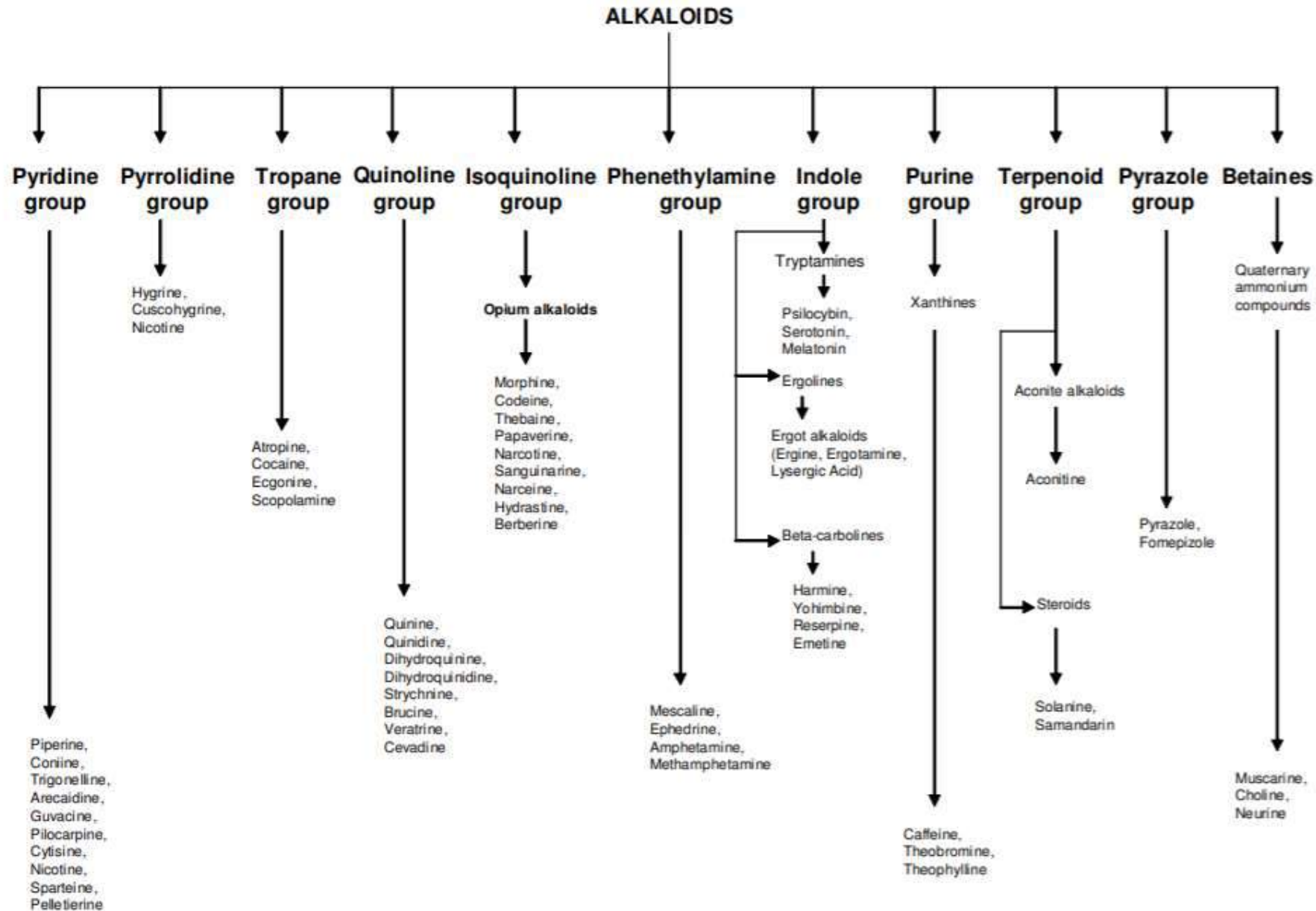
- **Emde Reaction:** Method for the reduction of a quaternary ammonium cation to a tertiary amine with sodium amalgam.



- **Emde Modification:** Combination of Raney nickel alloy and sodium hydroxide solution was used as the reduction agent in place of sodium amalgam in the original Emde reaction.

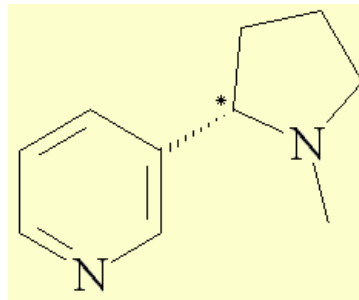


CLASSIFICATION OF ALKALOIDS



STRUCTURE OF NICOTINE

- Nicotine is also called 3-(1-methyl-2-pyrrolidinyl)pyridine according to the IUPAC nomenclature.
- It is a bicyclic compound with a pyridine cycle and a pyrrolidine cycle.
- The molecule possesses an asymmetric carbon which has S-configuration.
- It exists in two enantiomeric compounds i.e. (R) and (S). The naturally occurring and most active enantiomer of nicotine, isolated from *Nicotiana tabacum*. It is an enantiomer of a (R)-nicotine.
- Representation of the S molecule in 2D:



- Representation of the R molecule in 3D:

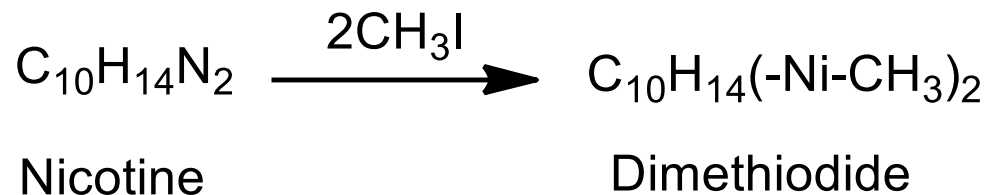


STRUCTURE ELUCIDATION OF NICOTINE

1) The molecular formula has been found to be $C_{10}H_{14}N_2$.

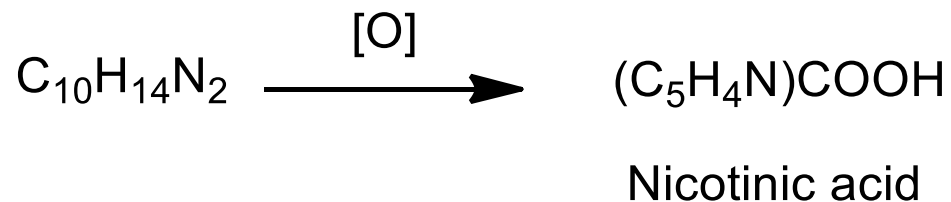
2) Presence of two 3° N-atoms

When treated with methyl iodide, it forms dimethiodide showing that both N-atoms of nicotine are tertiary in character.



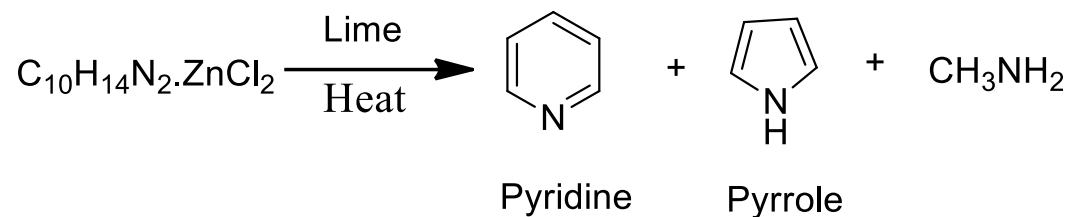
3) Presence of a Pyridine ring

On oxidation with chromic acid or nitric acid, it gives nicotinic acid. This shows that it contains a pyridine ring with a side chain.

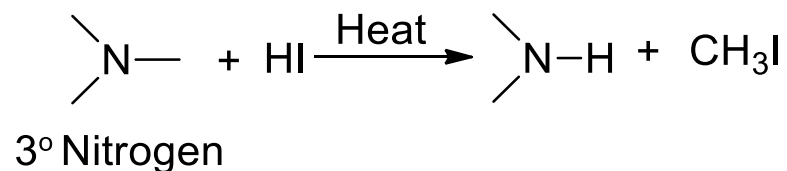


4) Structure of the Side Chain

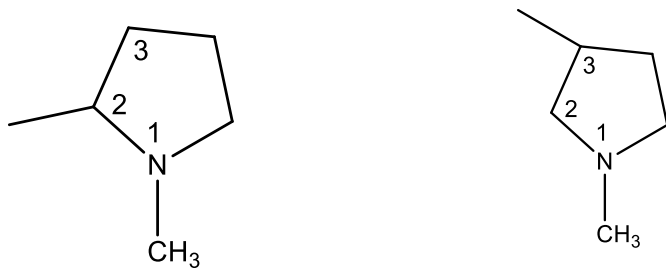
- i) Nicotine zinc chloride complex on distillation with lime gives (a) pyridine (b) pyrrole (c) methylamine. This indicates that the side chain is a pyrrole derivative.



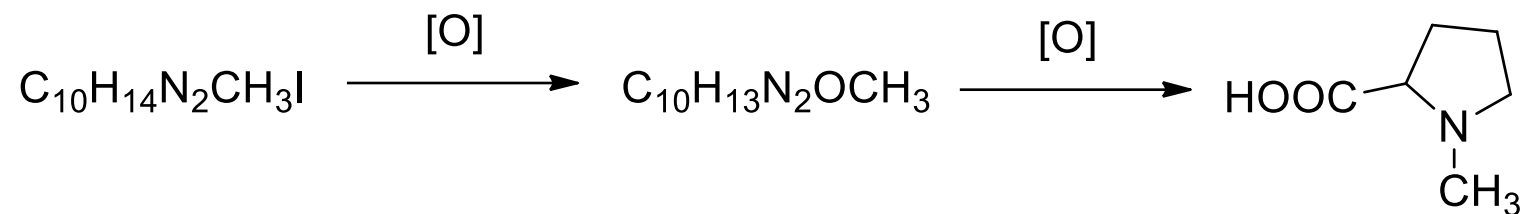
- ii) When heated with conc. HI at 200-300°C, nicotine forms methyl iodide. This proves that CH₃ group in the side chain is attached to N-atom.



- iii) To account for the side chain, (C₄H₇)N-CH₃, It may be written as N-methylpyrrolidine group.

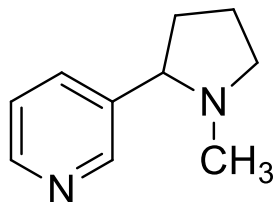


iv) Nicotine hydroiodide when treated with methyl iodide, forms nicotine isomethiodide which on oxidation with potassium ferricyanide yields nicotine. Nicotone on oxidation with chromium trioxide produces hygrinic acid. Therefore, the pyrrolidine ring is bonded to pyridine ring through 2-position.



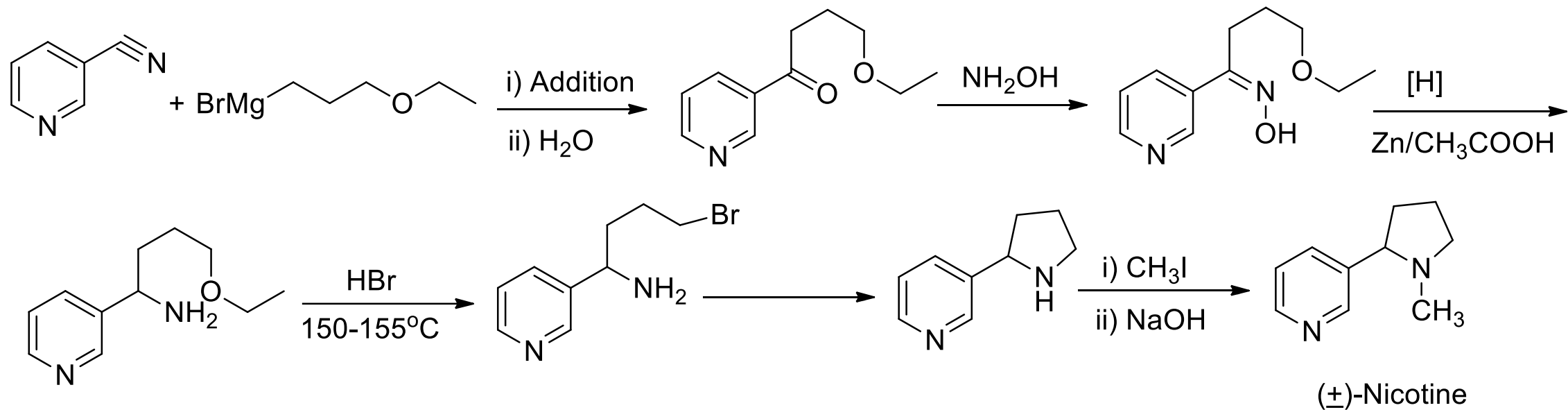
5) Structural formula

From (3) and (4), the structural formula of nicotine may be considered as:



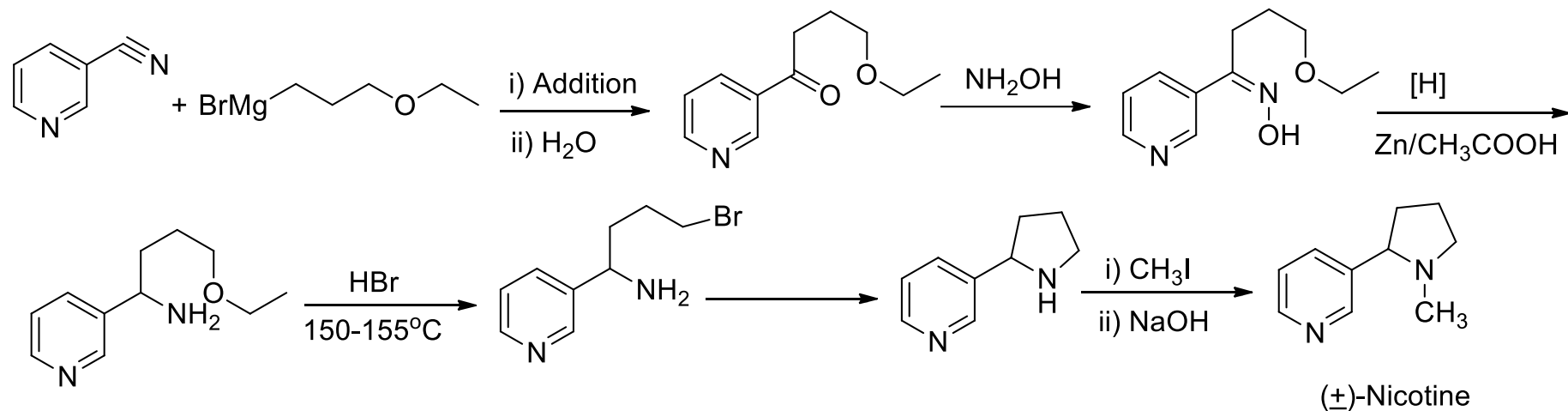
6) Synthesis

The structure of nicotine has been confirmed by the following synthesis:

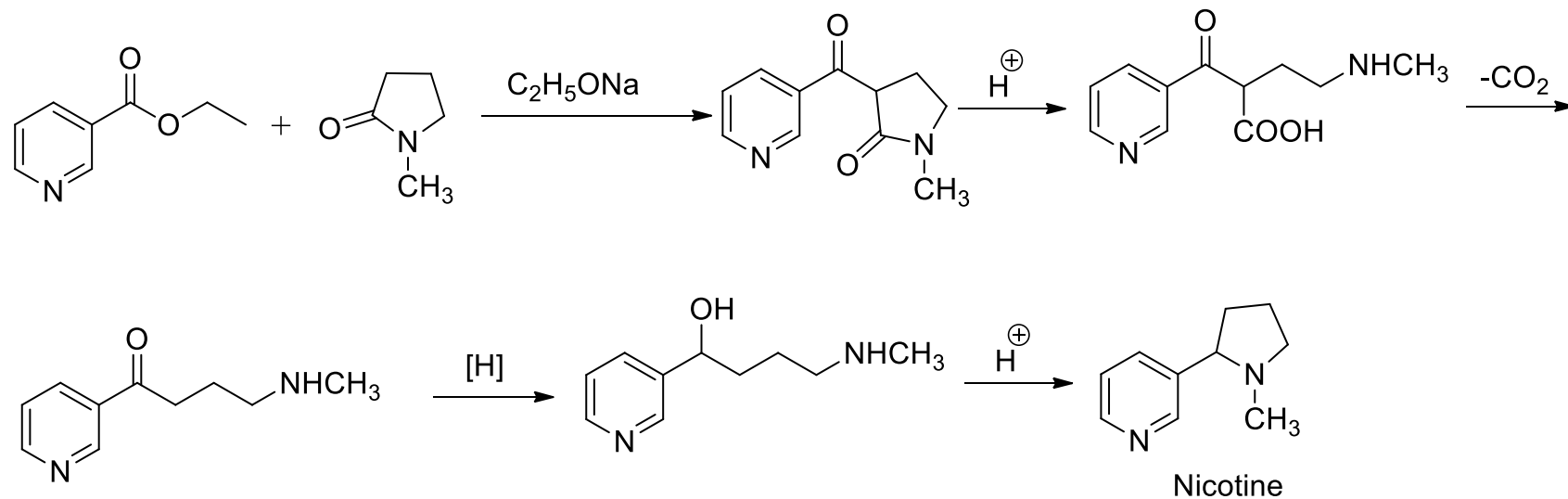


SYNTHESIS OF NICOTINE

(1) From Nicotinonitrile

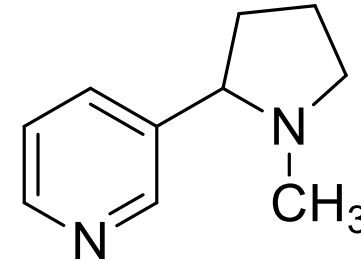


(2) Laboratory Synthesis



MEDICINAL IMPORTANCE OF NICOTINE

- Naturally occurs in large amounts in the leaves of tobacco plants, *Nicotiana tabacum*.
- Bitter-tasting compound, hygroscopic and oily liquid that is miscible with water
- Useful in treating Parkinson's and Alzheimer's disease
- Leads to increased heart rate and blood pressure
- Enhance Brain Function in People With Cognitive Decline

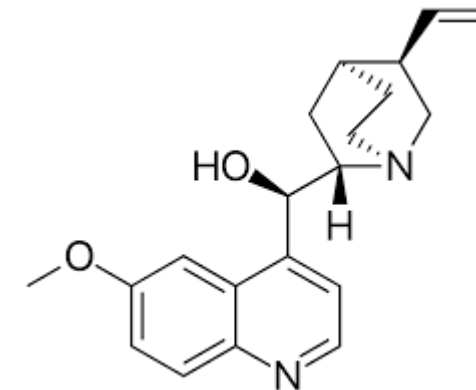


- Increased acetylcholine release may contribute to enhanced cognition and attention
- Increased dopamine release may contribute to rewarding/addictive qualities
- Increased nor epinephrine release may contribute to stimulation and arousal.
- Involves in multiple neurotransmitter systems

Note: It high doses cause nicotine poisoning

MEDICINAL IMPORTANCE OF QUININE

- Naturally occurs in bark of cinchona tree.
- Used in treatment of malaria.
- Used in treatment of malaria like parasitic disease known as Babesiosis
- Stimulates hair growth.
- Used for the prophylaxis from cardiac arrhythmias and for treatment of arterial fibrillation
- Used as anti-rheumatic.
- Treatment of gall bladder problems.
- Treatment of gastro-enteritis



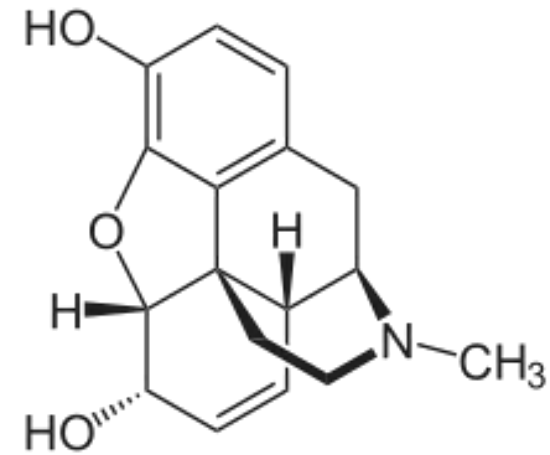
Note: It high doses cause poisoning

MEDICINAL IMPORTANCE OF MORPHINE

➤ Naturally occurs in capsule of the poppy plants, known as papaverum somniferum.

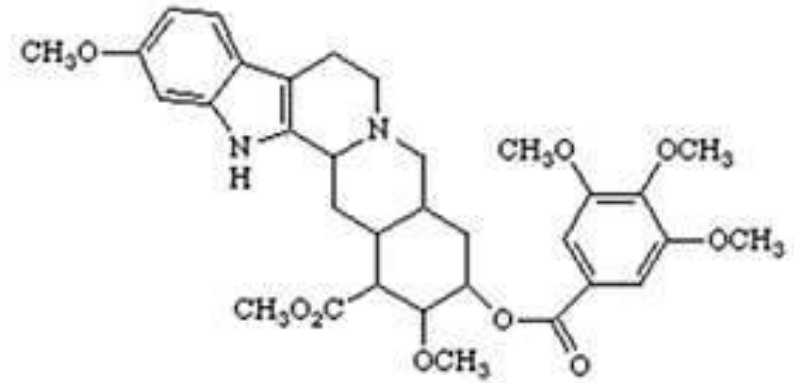
➤ **Uses of Morphine:**

- Analgesia
- General anesthetic
- Cough suppressant
- Anti-diarrheal
- Pre-operative medication
- Post-operative medication



MEDICINAL IMPORTANCE OF RESERPINE

- Naturally occurs in *Rauvolfia serpentina* plant.
- Treatment of high blood pressure (Hypertension).
- Control heart rate and force of cardiac contraction.
- Treatment of gastric ulcer and Asthama.
- Prevent strokes, heart attacks and kidney problems
- Treatment of cardiac arrhythmia and bronchitis
- Used for relief of psychotic (abnormal condition of the mind) symptoms.



Note: It high doses cause poisoning