# Alkaloids

## (Part I)

# Alkaloids

## Definition

**Alkaloids, which mean alkali-like substances, are basic nitrogenous heterocyclic compounds of plant origin generally possessing a marked physiological action.**

## Deviation from Definition

1) Some alkaloids are not basic e.g. Colchicine, Piperine, quaternary alkaloids

2) Few alkaloids contain nitrogen in a non-ring system
   e.g. Ephedrine, Colchicine. Mescaline

3) Plant origin:
   Some alkaloids are derived from bacteria, fungi, insects, frogs, animals.

# Alkaloids

## Classification

**1- True alkaloids**

- Derived from amino acid
- Nitrogen atom is a part of heterocyclic ring

**2- Protoalkaloids**

- Derived from amino acid
- Nitrogem atom is not a part of heterocyclic ring

**3- Pseudo alkaoids**

- Not derived from amino acid
- nitrogen atom is a part of hetrocyclic ring

**4- False alkaloids**

-non alkaloids give false positive reaction with alkaloidal reagents

# Alkaloids

## Distribution and occurrence:

- Rare in lower plants.
- Dicots are more rich in alkaloids than Monocots.
- Families rich in Alkaloids: Apocynaceae, Rubiaceae, Solanaceae and Papaveracea.
- Families free from Alkaloids: Rosaceae, Labiatae

## Function in Plants

- They may act as protective against insects and herbivores due to their bitterness and toxicity.
- They are, in certain cases, the final products of detoxification (waste products).
- Source of nitrogen in case of nitrogen deficiency.
- They, sometimes, act as growth regulators in certain metabolic systems.
- They may be utilized as a source of energy in case of deficiency in carbon dioxide assimilation.

# Alkaloids

## FORMS OF ALKALOIDS:

- Free bases
- Salts with Organic acids e.g. Oxalic, acetic acids
- Salts with inorganic acids e.g. HCl, $H_2SO_4$.
- Salts with special acids:

  e.g. Meconic acid in Opium, Quinic acid in *Cinchona*
- Glycosidal form e.g. Solanine in *Solanum*.

# Alkaloids

## Nomenclature

- **Trivial names of alkaloids should terminate with the suffix: (ine)**
- **Their names may be derived from:**

**Genus name e.g. Atropine from *Atropa***

**Species name e.g. Cocaine from *Coca***

**Common name e.g. Ergotamine from Ergot**

**Physiological activity e.g. Emetine emetic**

**Discoverer e.g. Pelletierine from Pelletier**

# Alkaloids

## PREFIXES AND SUFFIXES:

- **Prefixes:**
  - **"Nor-" designates N-demethylation or N-demethoxylation, e.g. norpseudoephedrine and nornicotine.**
  - **"Apo-" designates dehydration e.g. apomorphine.**
  - **"Iso-, pseudo-, neo-, and epi-" indicate different types of isomers.**
- **Suffixes:**
  - **"-dine" designates isomerism as quinidine and cinchonidine.**
  - **"-ine" indicates, in case of ergot alkaloids, a lower pharmacological activity e.g. ergotaminine is less potent than ergotamine.**

# PHYSICAL PROPERTIES:

## I- Condition:

**Most alkaloids are crystalline solids.**

**Few alkaloids are amorphous solids e.g. emetine.**

**Some are liquids that are either:**

**Volatile e.g. nicotine and coniine, or**

**Non-volatile e.g. pilocarpine and hyoscine.**

## II- Color:

**The majority of alkaloids are colorless but some are colored e.g.:**

**Colchicine and berberine are yellow.**

**Canadine is orange.**

**The salts of sanguinarine are copper-red.**

# PHYSICAL PROPERTIES:

## III- Solubility:

**Both alkaloidal bases and their salts are soluble in alcohol.**

**Generally, the bases are soluble in organic solvents and insoluble in water**

**Exceptions:**

**Bases soluble in water: caffeine, ephedrine, codeine, colchicine, pilocarpine and quaternary ammonium bases.**

**Bases insoluble or sparingly soluble in certain organic solvents: morphine in ether, theobromine and theophylline in benzene.**

**Salts are usually soluble in water and, insoluble or sparingly soluble in organic solvents.**

**Exceptions:**

**Salts insoluble in water: quinine monosulphate.**

**Salts soluble in organic solvents: lobeline and apoatropine hydrochlorides are soluble in chloroform.**

# IV-ISOMERIZATION:

**Optically active isomers may show different physiological activities.**

***l*-ephedrine is 3.5 times more active than *d*-ephedrine.**

***l*-ergotamine is 3-4 times more active than *d*-ergotamine.**

***d*- Tubocurarine is more active than the corresponding *l*- form.**

**Quinine (*l*-form) is antimalarial and its *d*- isomer quinidine is antiarrythmic.**

**The racemic (optically inactive) *dl*-atropine is physiologically active.**

# CHEMICAL PROPERTIES:

## I- Nitrogen:

**Primary amines** $R\text{-}NH_2$ **e.g. Norephedrine**

**Secondary amines** $R_2\text{-}NH$ **e.g. Ephedrine**

**Tertiary amines** $R_3\text{-}N$ **e.g. Atropine**

**Quaternary ammonium salts** $R_4\text{-}N$ **e.g** ***d*-Tubocurarine**

## II- Basicity:

$R_2\text{-}NH > R\text{-}NH_2 > R_3\text{-}N$

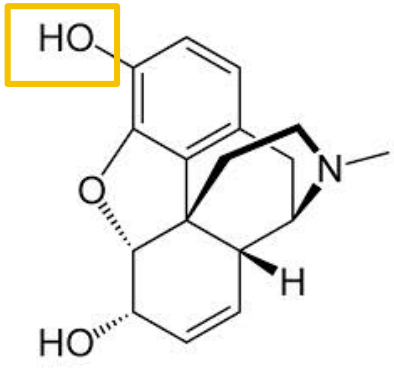
**Saturated hexacyclic amines is more basic than aromatic amines.**

# ACCORDING TO BASICITY ALKALOIDS ARE CLASSIFIED INTO:

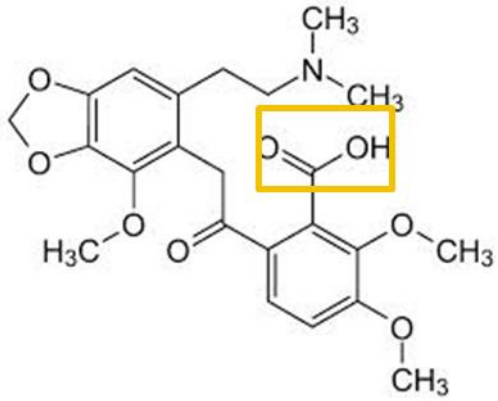
- ❑ **Weak bases** **e.g. Caffeine**
- ❑ **Strong bases** **e.g. Atropine**
- ❑ **Amphoteric → due to the presence of acidic group(s)**

• **Phenolic Alkaloids** ***Alkaloids with Carboxylic groups**

**e.g. Morphine**




**e.g. Narceine**




- ❑ **Neutral alkaloids** **e.g. Colchicine**

# Detection and characterization:

## A- Precipitation by certain reagents

1- Mayer's reagent (potassium-mercuric iodide) yellowish-white precipitate.

2- Dragendorff's reagent (potassium-bismuth iodide) gives orange red recipitate.

3- Wagner's reagent (potassium triiodide) forms red flocculent precipitate.

## B- Color reactions with certain reagents

1- Froehd's reagent (sulphomolybdic acid)

2- Marqui's reagent (formaldehyde + $H_2SO_4$)

3- Mandalin's reagent (sulphovanadic acid)

4- Mecke's reagent (selenic acid + $H_2SO_4$)

5- Erdmann's reagent ($HNO_3$ + $H_2SO_4$)

# CLASSIFICATION OF ALKALOIDS

**Biogenetic.**

**Based on the biogenetic pathway that form the alkaloids.**

**Botanical Source.**

**According to the plant source of alkaloids.**

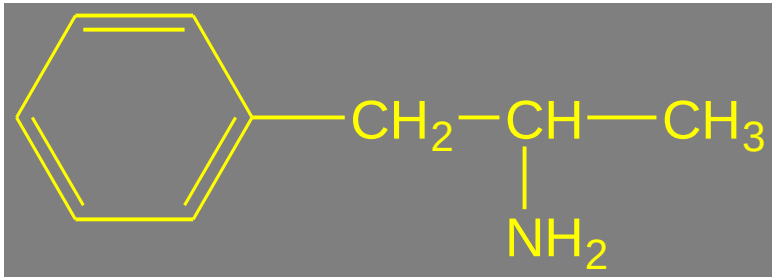
**Type of Amines.**

**Primary, Secondary, Tertiary alkaloids.**

**Basic Chemical Skeleton**

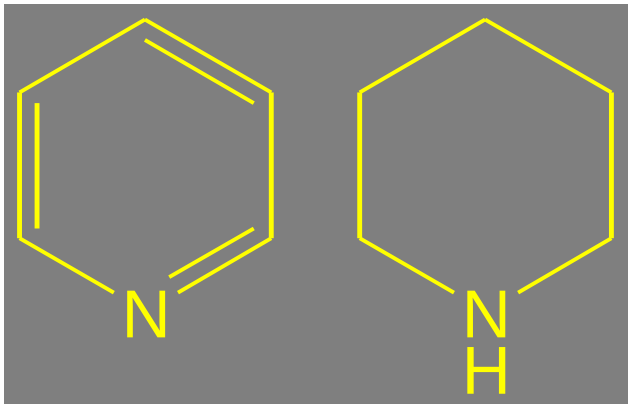
## Phenylalkylamines:

e.g. Ephedrine



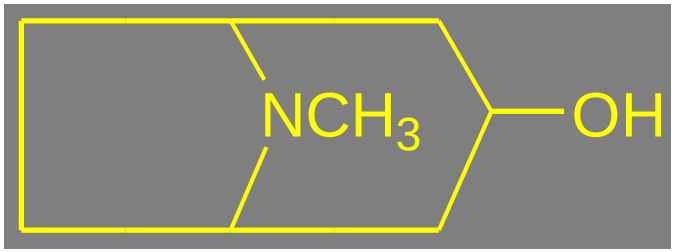

## Pyridine and piperidine

e.g. lobeline, nicotine



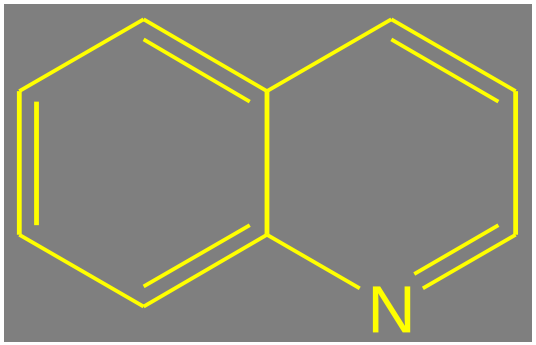

## Tropane

e.g. Atropine.



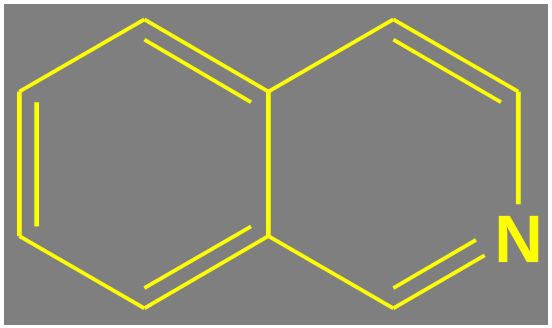
## Quinoline

e.g. quinine and quinidine



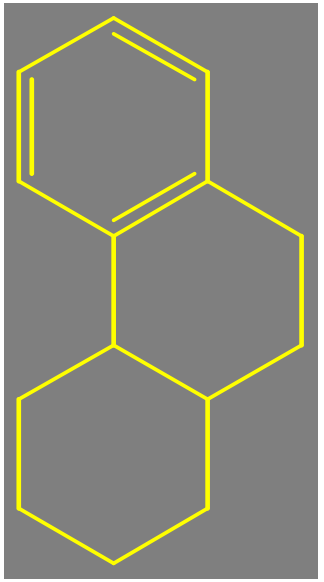

## Isoquinoline

e.g. papaverine



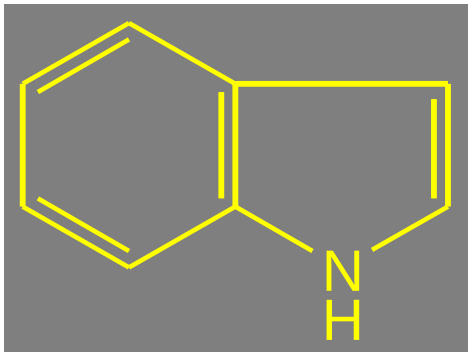

## Phenantheren

e.g. Morphine



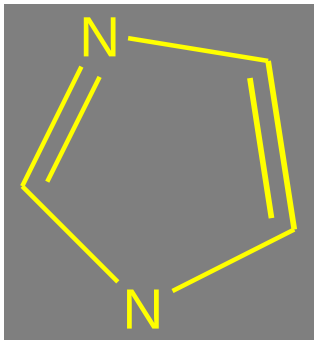
## Indole

e.g.ergometrine



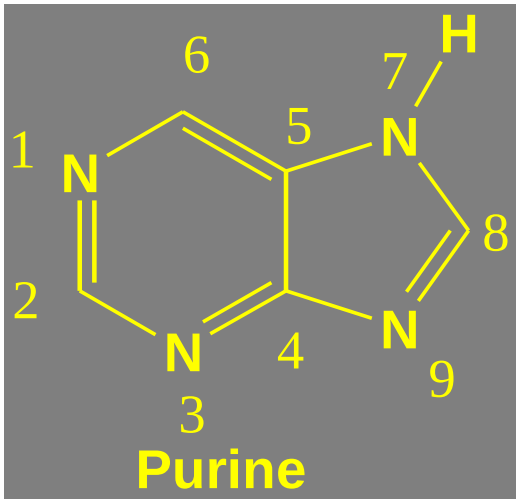

## Imidazole

e.g. pilocarpine



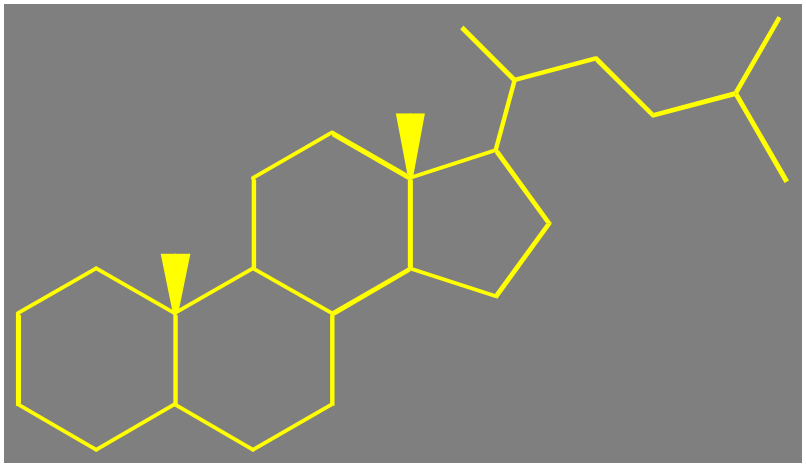

## Purine

e.g. caffeine



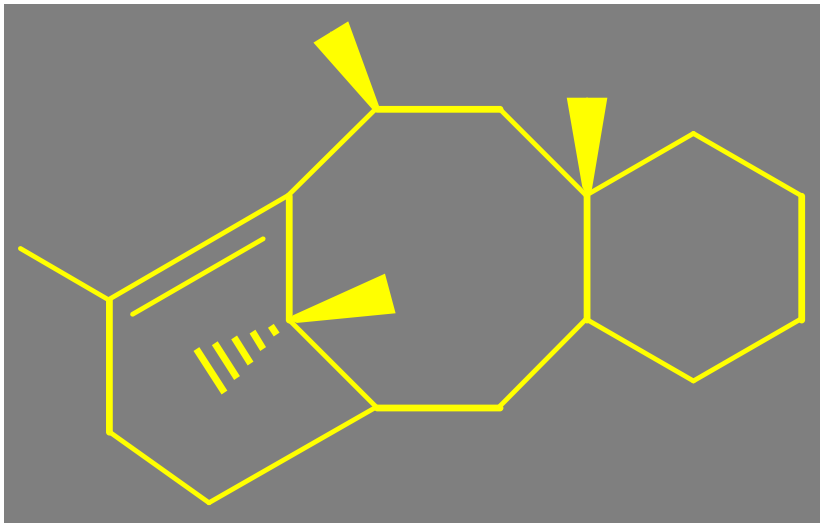
## Steroidal

**e.g. *Solanum* and *Veratrum* alkaloids**

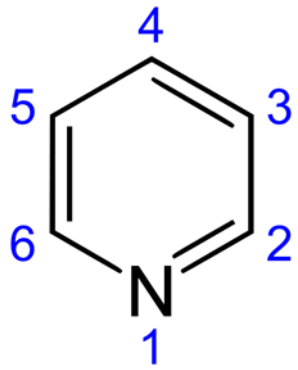


## Terpenoid

**e.g. Taxol**



# 1- Drugs containing pyridine alkaloids



# Drugs containing pyridine alkaloids

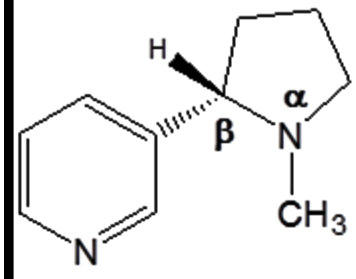
► **Tobaccos**

The leaves of the tobacco plant

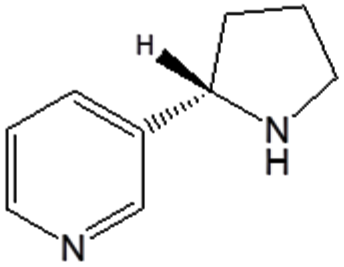
***Nicotiana tabacum*** **(Fam: Solanaceae)**

are used for production of Cigarettes.

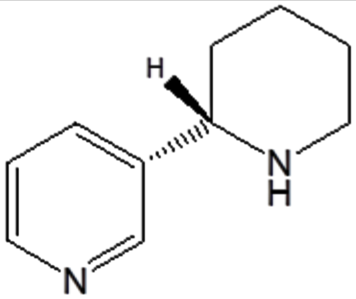
► They are toxic plants which contain alkaloids, chiefly represented by nicotine (75%) in addition to nor-nicotine, and anabasine




Nicotine (β-pyridyl-α-methyl pyrorolidine)




Nornicotine




Anabasine (β-pyridyl-α piperdine)

## Properties:

1- The 3 alkaloids are volatile liquids.

2- Nicotine is tertiary alkaloid while the others are secondary.

3- Nicotine has some miscibility with water.

# Identification

1- Nicotine + p-dimethylaminobenzaldehyd + HCl gives rose-red color.

2- aq. Solution of nicotine + acidic vanillin gives red color.

3- aq. Solution of nicotine + formaldehyde + $HNO_3$ gives red colo

**Uses:**

**1-It has a unique action on autonomic ganglia which it first stimulates and then depresses leading to paralysis action on skeletal muscle**

**2- Insecticide & Pesticide.**

**3- No medicinal use due to toxicity.**

**4- It is used in the form of chewing gum or transdermal system for relieving the symptoms of withdrawal of cigarettes.**

## Pharmacology

► Nicotine possesses a high affinity to the gangionic-cholinergic (nicotinic) receptors.

► So, it stimulates all autonomic ganglia.

► it acts on the CNS causing tremors and convulsions.

► it also stimulates the respiratory and vomiting centers.

► It acts on the smooth muscle of the intestine, by increasing tone and motor activity.

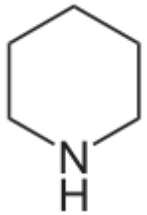
► It acts on the cardiovascular system, by inducing vasoconstriction and an increase in arterial blood pressure.

► In the long run, nicotine is responsible for the genesis of cardiovascular, pulmonary diseases.

► It is used in the form of chewing gum or transdermal system for relieving the symptoms of withdrawal of cigarettes.

► It is also used as insecticide.

# Piperidine Alkaloids



## Conium alkaloids

► Source: poison Hemlock fruits *Conium maculatum* family umbeliferae

►Constituents: Coniine.

►Properties:

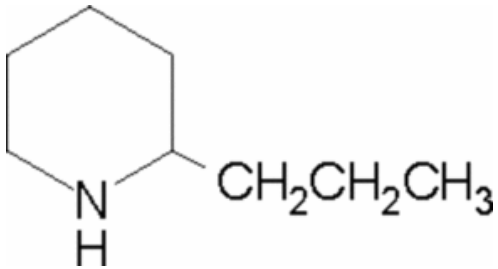
1- Volatile liquid.

2- Free from Oxygen

►uses:

Local analgesic so used for Hemorrhoids and anal fissures.

The drug has to be administered with care, as narcotic poisoning may result from internal use, and overdoses produce paralysis



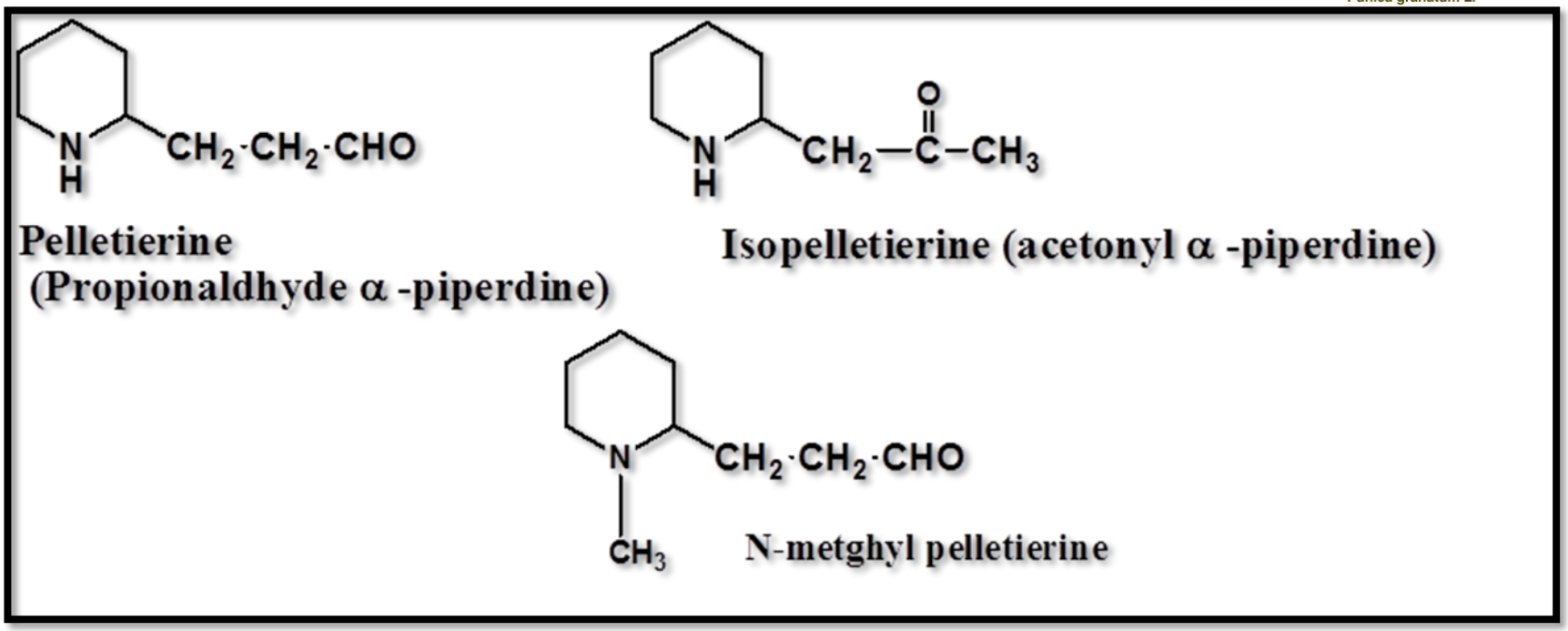
# Pomegranate alkaloids

- Source: Pomegranate barks.(root bark), *Punica granatum* family Lythraceae
- Constituents:

1- Pelletierine. 2- Isopelletierine.

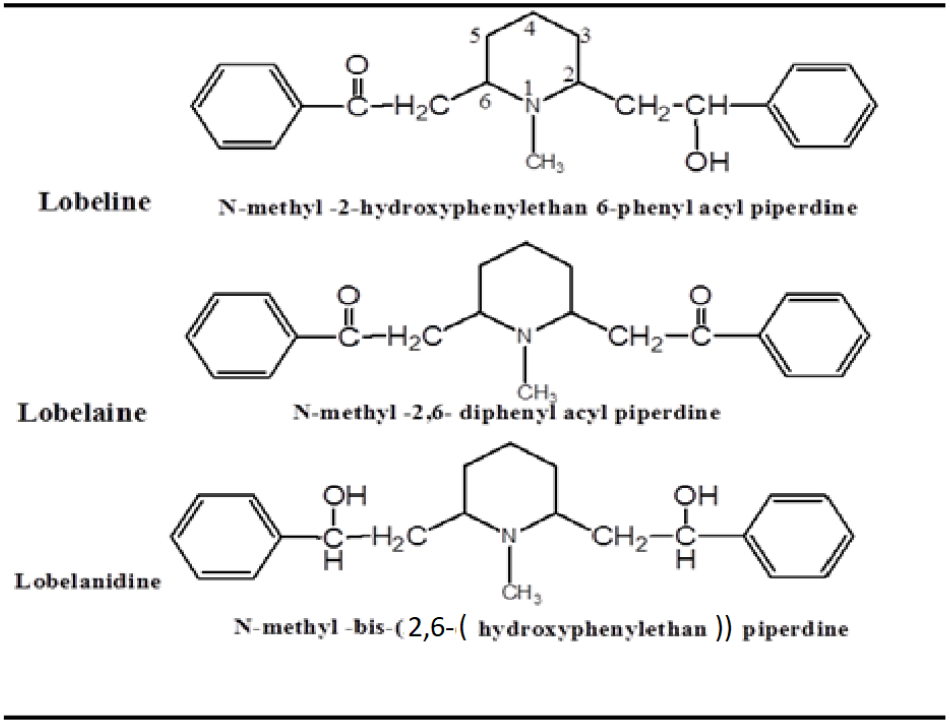
3- Methylpelletierine.

- Volatile liquid Alkaloids
  - The plant was used as Taeniafuge and Vermifuge **(anthelmintic).**

# *Lobelia* Alkaloids

- **Source: *Lobelia* Herb (Indian Tobacco). From *Lobelia inflata* family campanulaceae**
- **Constituents: 1- Lobeline (50%). 2- Lobelanine. 3- Lobelanidine.**




# Properties:

1- Lobeline is sparingly soluble in water.

2- Lobeline HCl is soluble in $CHCl_3$.

- Test:

1- Lobeline + Marqui's reagent → Red colour

2- Lobeline + Froehd's reagent → Red colour → Blue

- Uses:

1- Lobelia extract is used as expectorant Tincture of Lobelia

2- Lobeline is respiratory stimulant.

3- Lobeline is used to break tobacco habits in the form of tablets or lozenges.

4- treatment of CNS disorders like Alzheimer disease.

5- lobeline has been reported as a useful agent to treat dependency on drugs such as cocaine, ampheteamine, caffeine, opiates, barbiturate, benzodiazepines, cannabinoids, alcohol, hallucinogen and nicotine