



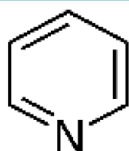
Pharmacognesy III

*From textbooks: (Trease and Evans
Pharmacognosy, 16th Ed.)
Pharmacognesy and
Pharmacobiotechnology, 9th ed,
Robbers JE, Speedie MK, Tyler VE.)*

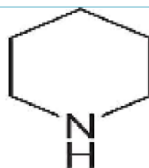
م. د. شيرين محمد مكي الحسيني

Pyridine – piperidine- pyrrolidine alkaloids

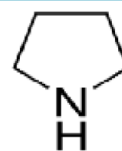
The amino acid ornithine, its decarboxylation product, putrescine, and proline constitute the basic unit of the tropane, ecgonine, nicotine (pyrrolidine ring).



pyridine



piperidine



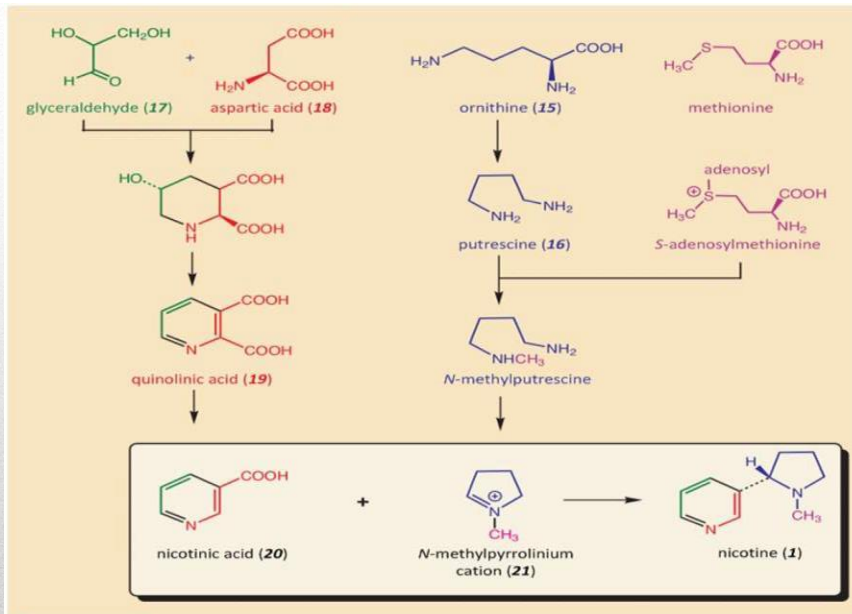
pyrrolidine

- Upon reduction, the tertiary base, pyridine is converted into the secondary base piperidine.
- **These two nuclei form the basis for this group which sometimes is divided into three subgroups:**
 - 1- Derivatives of **piperidine** e.g. lobeline from lobelia.
 - 2- Derivatives of **nicotinic acid** e.g. arecoline from areca.
 - 3- Derivatives of **both pyridine-pyrrolidine** e.g. nicotine from tobacco.

BIOSYNTHESIS OF PYRIDINE- PIPERIDINE ALKALOIDS

The biosynthetic pathway leading to this compound is summarized as follows:

- 1- Ornithine is incorporated into nicotine in tobacco plants.
- 2- This incorporation result in a symmetric labeling pattern of nicotine.
- 3- Putrescine, N- methylputrescine, and N- methylaminobutanal are all incorporated.
- 4- The N-methylpyrrolinium ion is the key intermediate which, through electrophilic aromatic substitution attached to C-3 of the pyridine ring of nicotinic acid.
- 5- Nicotinic acid is formed in higher plants and certain microorganisms via quinolinic acid by the condensation of glyceraldehyde-3-phosphate and aspartic acid.

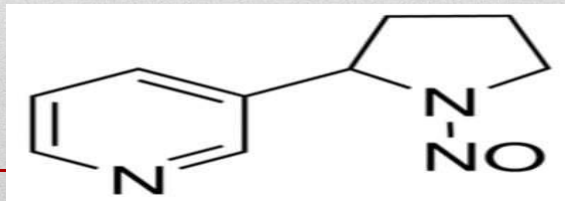


Biosynthetic pathway of nicotine

1- Tobacco:

- It is the dried leaves of *Nicotiana tobacco* F: Solanaceae.
- It is cultivated for smoking, it contains alkaloids from 0.6-0.9%, the main one is nicotine which is an oily liquid alkaloid, it is colorless liquid but when oxidized convert to yellow color.
- nicotine has pronounced effects on the cardio vascular system, where peripheral vasoconstriction, atrial tachycardia & an increase in both systolic & diastolic blood pressure are observed.
- It is worth noting that 50% of all smokers die of heart disease & 20% of lung cancer.

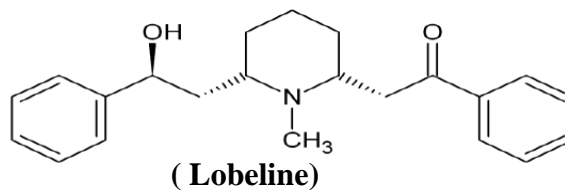
- The carcinogenicity of tobacco is probably not due to nicotine but rather to a far more potent carcinogen (**N-nitroso nor nicotine**)
- It is found in cigarettes, cigars & chewing tobacco.
- levels in the range of (2-90)pp (parts per billion) concentrations of N nitrosamines are considered hazardous to health.



N-nitroso nor nicotine

2- Lobelia or (Indian tobacco)

- It is the dried leaves & tops of *Lobelia inflata*
F: Lobeliaceae (Campanulaceae).
- The drug contains 14 alkaloids, of which lobeline is the major & most important.

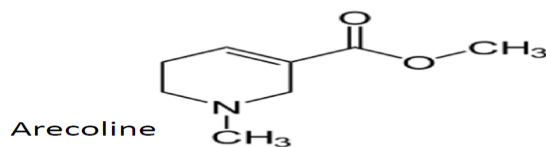


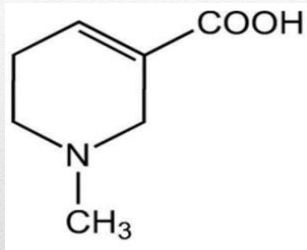
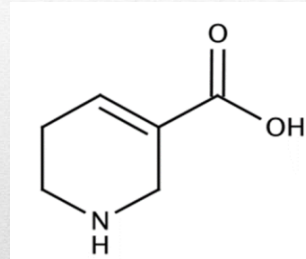
(Lobeline)

- **Lobeline** occurs in colorless crystals very slightly soluble in water, but readily soluble in hot alcohol.
- **Uses and Dose.** Galenical preparations of Lobelia were formerly used for expectorant purposes.
- Lobeline is a respiratory stimulant, but its action is somewhat unreliable and of brief duration.
- Other effects resemble those of nicotine. For this reason, 0.5 to 1.5 mg doses of lobeline sulfate are incorporated in tablets or lozenges which are intended to aid in breaking the tobacco habit.

3- **Areca:**

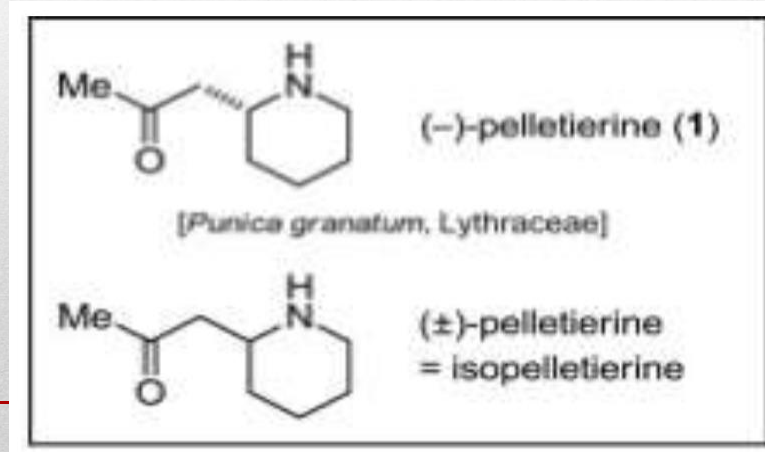
- Is the dried, ripe seed of *Areca catechu* (Fam. Palmae).
- Areca contains several alkaloids which are reduced pyridine derivatives.
- Among them are arecoline (arecaidine methyl ester), arecaidine (N-methyl guvacine), guvacine (tetrahydronicotinic acid), and guvacoline (guvacine methyl ester). The content of total alkaloids ranges up to 0.45%.



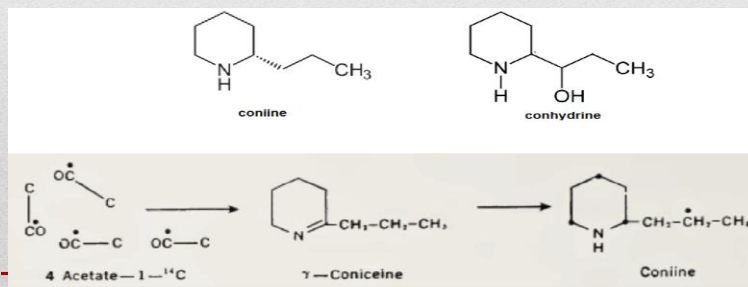
**Arecoline****Guvacine (tetrahydroisocotinic acid)**

- **Use.** Arecoline Hydrobromide is used in veterinary medicine as an anthelmintic drug against parasitic worms especially tenea.
- **4- POMEGRANATE:**
- Pomegranate Root and Stem Bark or Granatum is derived from *Punica granatum* (Fam. Punicaceae).
- They contain about 0.5–0.9% of volatile liquid alkaloids, the chief of which are pelletierine and pseudopelletierine, together with about 22% of tannin.

- Pelletierine tannate, a mixture of the tannates of the alkaloids, was included in the BP 1948 and was used as an anthelmintic with a specific action on tapeworms.



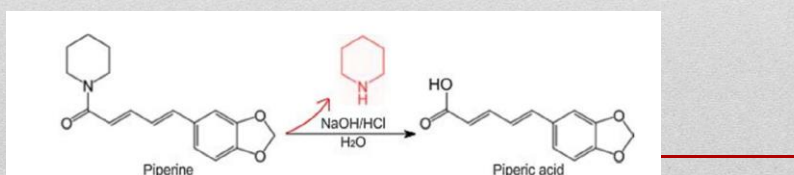
- **4- Conium (poison hemlock):**
- It is the full grown but unripe fruit of *Conium maculatum* (F:Umbelliferae).
- It contains number of alkaloids the important of which is coniine & conhydrine.



Biosynthesis of coniine

5- Piper:

- It is the dried full grown unripe fruit of *Piper nigrum* (F: Piperaceae).
- It contains up to 4.5-8% of piperine.
- Mainly used as a condiment.
- It has an irritant, stimulant & febrifuge activity (decrease body temperature).
- On hydrolysis of piperine we get another alkaloid piperidine which is a liquid alkaloid.



THANK UUUU