

# PYRIDINE AND PIPERIDINE ALKALOIDS

-Folia Nicotianae - PYRIDINE / PYRROLIDINE

-Nicotine and Its Derivatives

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-Herba Lobeliae - PIPERIDIN

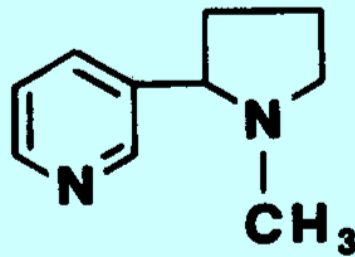
-Cortex Radicis granati

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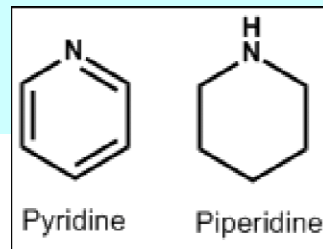
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-Pyrrolizidine-derived alkaloids

# Piperidine/Pyridine alkaloids

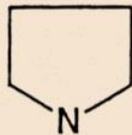


Tobacco (*Nicotiana*)  
Horsetail (*Equisetum*)



Nicotine

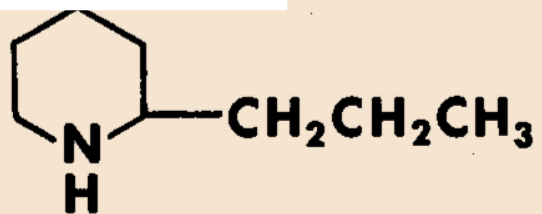
Pyrrolidine



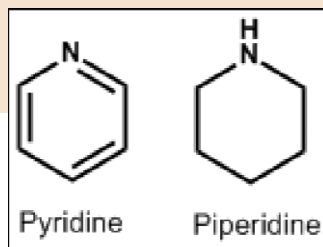
Ornithine

Nicotine

# Piperidine alkaloids

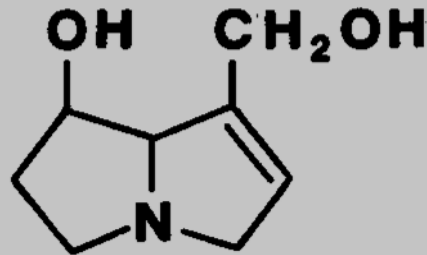


Poison hemlock (*Conium*)  
Indian tobacco (*Lobelia*)



Coniine

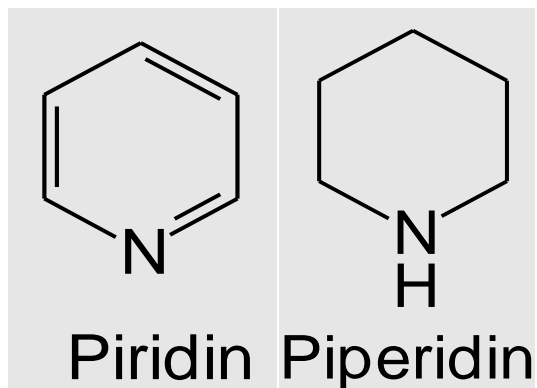
# Pyrrolizidine alkaloids



Groundsel (*Senecio*)  
Blue devil (*Echium*)  
Heliotrope (*Heliotropium*)

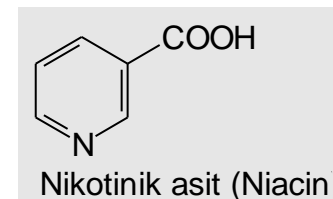
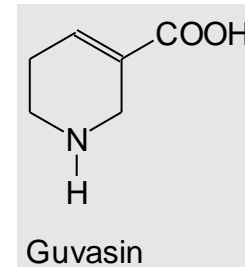
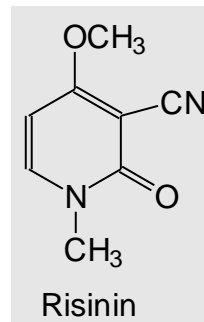
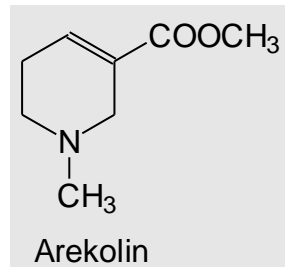
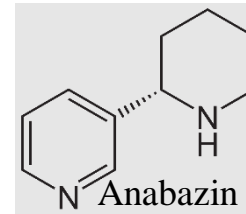
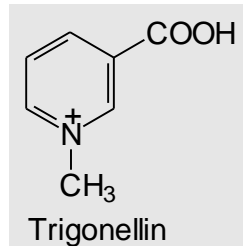
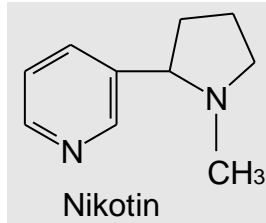
Figure 3–2 Retronecine

# PYRIDINE - PIPERIDINE ALKALOIDS

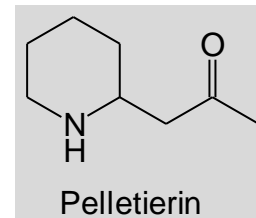
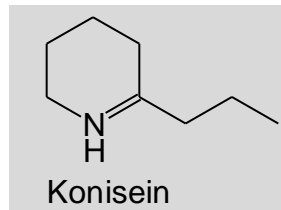
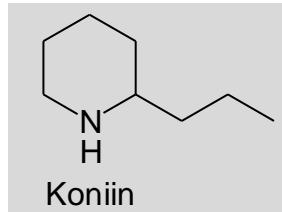


- 1- NICOTINE AND NICOTINIC ACID DERIVATIVES**
- 2- Piperidine and Pyridine Dimer Alkaloids
- 3- 2-ALKYL PIPERIDINE DERIVATIVES**
- 4- 2,6-DIALKYL PIPERIDINE AND PYRIDINE DERIVATIVES**
- 5- Monoterpenic Piperidine and Pyridine Alkaloids
- 6- Piperidine Amide Alkaloids

# 1- NICOTINE AND NICOTINIC ACID DERIVATIVES

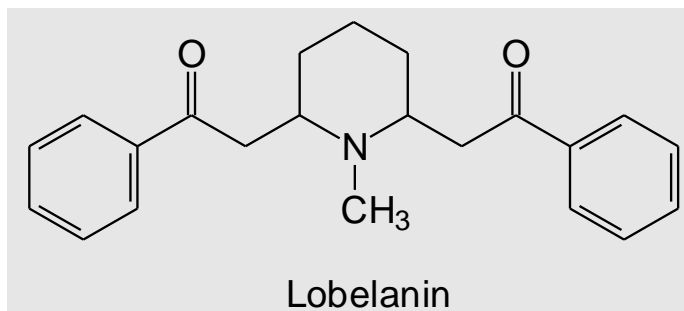
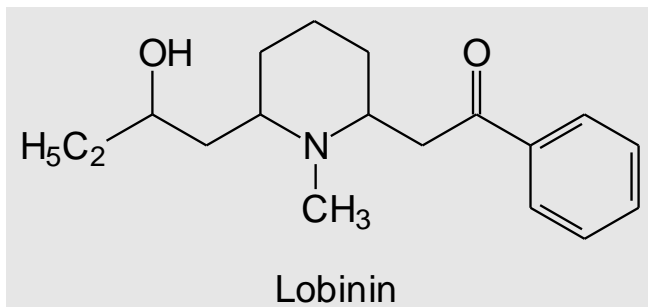


### 3- 2-ALKYL PIPERIDINE DERIVATIVES



4-

## 2,6-DIALKYL PIPERIDINE AND PYRIDINE DERIVATIVES





# *Nicotiana tabacum* L.

**60 *Nicotiana* Species Naturally**

**found in the World**

**America, Australia and the South Pacific Islands**

**3 species of *Nicotiana* are found in Turkey.**

- |                                  |                                |
|----------------------------------|--------------------------------|
| • <i>Nicotiana tabacum</i> L.    | Corolla pinkish-red            |
| • <i>Nicotiana rustica</i> L.    | Corolla greenish-yellow        |
| • <i>Nicotiana glauca</i> Graham | Corolla yellow-wax in the stem |

# **Maya Inscriptions AD, 6th - 7th Century**

**In Religious Rites**

**In traditional ceremonies**

**Pleasurable**

**For medical purposes**

# Tobacco

- **Smoking and other forms of inhalation of tobacco smoke creates an addiction psychologically and physically. It is accepted that nicotine is the most important addictive factor in tobacco smokers. Nicotine affects both the CNS and the peripheral autonomic nervous system.**
- **Psychological addiction is very strong.**
- **The rate of re-use is very high for those who stop using it.**
- **Nicotine is a very toxic alkaloid and 40-60 mg (50 mg toxic dose) causes a human death.**
- **The amount of nicotine in a cigarette generally contains is 1-2 mg.**

# Pharmaceutical Products Developed For Those Who Want To Get Rid Of Smoking Addiction

Nicotine Containing Gums

Nicotine Containing TTS (transdermal treatment system)

Nicotine Nasal Spray

Nicotine Inhaler

Nicotine Pastilles

## **CHRONOLOGICAL HISTORY OF TOBACCO**

1828 - Nicotine isolation and experiments on animals

(Karl Ludwig Reinmann and Wilhelm Henrich Posselt)

1843 – Express te Nicotine's Closed formula (Melsens)

1893 - Proof of the chemical formula of Nicotine (Adolf Pinner)

1895 - Nicotine synthesis (Pictet and Crepieux)

1901 - Isolation of 3 nicotine-like alkaloids (Pictet and Rotschy)

## **Pharmacological Effects of Tobacco Alkaloids**

Since tobacco alkaloids are small molecules and lipophilic, they are easily absorbed from the skin and mucosa.

It is oxidized in the liver and tissues to form the main metabolites as Nicotine-N-Oxide and Cotinine.

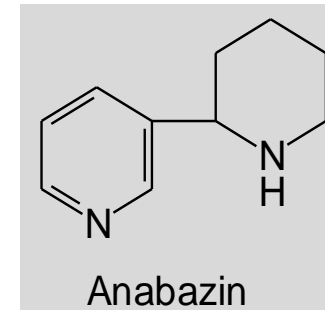
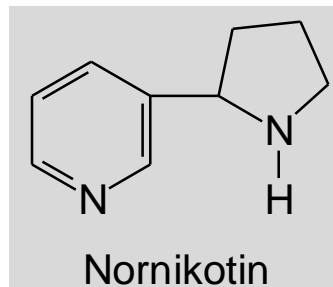
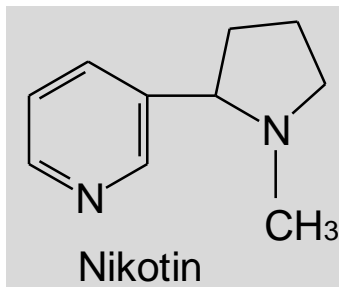
Since nicotinic receptors are present in different cholinergic structures, nicotine can pass easily to the central nervous system, so its pharmacological effects are numerous and complex.

- 1- Effects on the Central Nervous System
- 2- Effects on the Neuromuscular Junction
- 3- Effects on the Autonomic Ganglia

# FOLIA NICOTIANAE

## TÜTÜN YAPRAĞI/Tobacco Leaf

It is a drug obtained from the varieties of *Nicotiana tabacum* L. (Solanaceae) and contain about 0.5 - 10% alkaloids.



When Folia Nicotianae is mentioned, the first thing that comes to mind is the smoking tobacco leaves obtained from *N. tabacum* and its varieties.

These alkaloids are formed by the condensation of pyridine and pyrrolidine rings and are oxygen-free alkaloids. Nicotine has a methyl attached to nitrogen in the pyrrolidine ring. There is no methyl group in nornicotine, and in anabasine, the second ring is not the pyrrolidine but the piperidine ring.

- The Anabazin was named after it was first isolated from *Anabasis* species from the Chenopodiaceae family.
- Anabasine is also present in *N. tabacum* leaves, but the amount is not large.
- ANABASINE is mostly found in *N. glauca* and this plant is a species that wild-growing in Anatolia. *N. glauca* (Antalya, İçel), naturalized in Western Anatolia (İzmir)
- When a seed that does not contain any alkaloids, after germinations, alkaloid synthesis can begin. For example: tobacco and poppy seeds do not contain alkaloids. nicotine; it is primarily a product of root metabolism, but subsequent reactions (demethylation, oxidation) occur in the leaves of the plant.



There are 60 *Nicotiana* species in the world.

If the natural distribution of this genus is examined, 75% is found in the American continent and 25% in Australia and the South Pacific.

- *Why has the distribution of Nicotiana species in the world been so widespread and widespread?* We can give the following answers for this question.
- 1. The use in different ways *Nicotiana* species are continue, due to the delightful effects
- 2. The fact that most of the species are suitable for growing in different soil and climatic conditions

- **3 Nicotiana species LOCATED IN TURKEY.**
- *N. tabacum*; It is mainly used in the preparation of cigarettes, cigars, pipe tobacco, rarely chewing tobacco or snuff.
- Aegean region (grown in Uşak and Manisa on the shores of the Aegean sea extending from Ayvalık to Fethiye)
- Marmara region (especially grown in Düzce and Hendek)
- Black Sea region (in a wide region stretching from Zonguldak to Hopa)
- It is also growing in the Eastern Anatolia Region (Malatya, Elazığ, Muş, Bitlis, Mardin and Gaziantep).

- *N. rustica* (mad tobacco, hasankeyf tobacco-deli tütün) (cultivated in Gaziantep and K. Maraş regions.)
- 
- Use of *N. rustica* as Maraş otu:
- In Gaziantep and Kahramanmaraş, district markets and spice shops sell a mixture called marachotu or herb in nylon bags, and in this mixture, 2 parts of mad tobacco, 1 part of oak, walnut or vine ash is mixed, it is prepared by sprinkling water lightly on it and kneading.
- This mixture is taken as an average teaspoon and placed between cotton or thin cigarette paper and placed between the gum and the lower lip and kept there for 5-10 minutes and then discarded.
- In this way, Maraş otu, is a tobacco use in which nicotine is taken through the oral mucosa. The amount of nicotine taken with Maraş powder at one time is about **7-10 mg**, this amount is quite high compared to nicotine taken with cigarettes. Therefore, its pleasurable and calming effect is higher than the nicotine.

# Nicotine Salts and Derivatives

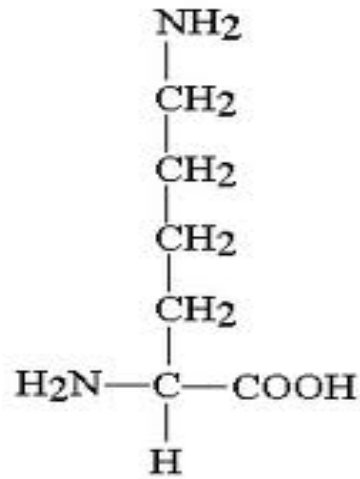
- **Isoniazid**, which is also a nicotinic acid derivative, is used in tuberculosis.
- **Nicotinyl alcohol tartrate** is used as a vasodilator at a dose of 25-50 mg 4 times a day in peripheral vascular diseases and hyperlipidemia.
- **Niacin and Niacinamid** participate in the formation of the coenzyme Nicotinamide Adenine Dinucleotide and Nicotinamide Adenine Dinucleotide phosphate (these coenzymes take in or give off hydrogen in aerobic respiration in all body cells.)
- **Niacin** deficiency is characterized by skin lesions called pellagra (hyperpigmentation and hyperkeratinization, as well as neurological changes in the skin areas exposed to the sun; mild tremor, depression and peripheral neuropathy occur). In addition, the symptoms of other B complex vitamins are observed.
- **Niacin**; In addition to lowering the cholesterol level, it also has a vasodilator effect.

- To obtain nicotine from the leaves, the tobacco are wetted with an alkaline solution and distilled. The distillate is either collected in dilute sulfuric acid or absorbed into active coal. After that, nicotine is obtained, then it is cleaned by crystallizing.
- **Nicotine;** it has been used in agriculture as a contact insecticide with paralysis and irritant effect on crop pests as 40% nicotine sulphate (black leaf 40) solution or its derivatives (oleate, laurate and naphthenate) which are the soap form of nicotine.

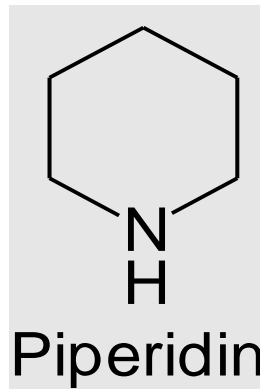
# Piperidine alkaloids

Piperidine alkaloids

**Lysine Derived Alkaloids**



lysine



Piperidin

- Among those containing the pyridine and piperidine ring, **Herba Lobelia and Cortex Granati** drugs will be examined.
- Lysine and related compounds, which are homologues of ornithine, also yield many alkaloids.
- **Lycopodium** alkaloids are also derived from lysine.

# *Cortex Radicis Granati* (Nar Kök Kabuğu)

- The drug contains the roots and stem barks of the *Punica granatum* (Punicaceae). The cortex are smooth and yellowish in color.
- It contains 0.5-0.7% volatile liquid alkaloids.
- Major alkaloids are pelletierine and isopelletierine (pseudopelletierine). The pelletierine contain propanone in the 2nd position.



- Pelletierine and isopelletierine have anthelmintic effect. There are 22% tannins in the cortex. It has been used as an anthelmintic since the time of Dioscorides. It is mentioned that in the Ebers papyri around 1550 BC, the shell was used in the treatment of worms.
- It is used to obtain pelletierin-sulphate. Some patients experience nausea, vomiting against pelletierine sulfate. If given together with (complex) tannins, this sensitivity decreases.
- The use of drugs and salts obtained is leaved due to their harmful effects.

## **Seed Oil - Seed Oil**

Increases skin elasticity.

It has moisturizing properties.

It contains punisic acid.

It is effective in dry skin, eczema, sunburn, psoriasis.

It has a powerful anti-inflammatory and antioxidant effects.

It has been proven topically to kill the cancer cells.

Pomegranate Preparations

Seed Extract, Hull Extract and Juice

# Pelletierin Tannat

It is a mixture of tannic acid salts of alkaloids obtained from the root and stem bark of the *Punica granatum* (Punicaceae).

Tannic acid is added to the aqueous solution of this mixture and neutralized with ammonia, and the pelletierine tannate precipitates.

It is a yellowish, odorless, amorphous powder and has an astringent taste in the mouth.

It has a special effect against tapeworms. It is ineffective for other parasites. Since it is highly toxic, it is only given to adults.

# Herba Lobelia

## Indian Tobacco, Puke weed

*Lobelia inflata* (Campanulaceae) are the aerial parts of the plant collected and dried at the end of flowering time. This plant grows wild in the east of US and Canada. It is cultured in America and Holland.

It was used by the North American Indians. (Indian Tobacco). It was recommended in asthma in 1813.

The amount of alkaloids in the drug varies between 0.2-0.5%.

Indian Lobelia is actually *L. nicotianaefolia*, an officially recognized species in India. The alkaloid is localized within the milk tubes found in the phloem. The amount of alkaloids is highest at the time of flowering.

These alkaloids, bearing substituents on both sides, can be symmetrical or non-symmetrical.

Symmetrical Lobelidiol (alcohol group), Lobelidion (ketone group)

Non-symmetrical Lobelin (2-cis-8,10-diphenillobelionol)

There are 3 asymmetric C atoms in the molecule. It is optically active and levogir.

### ***Herba Lobelia preparations;***

**It is used in spasmodic asthma and chronic bronchitis.**

**It is included in the preparations used to discourage smoking (similar to nicotine but weaker pharmacological effects).**

**Controlled studies revealed that lobeline and alkaloids exhibited placebo effects in stop-smoking (No effect).**

## **Lobelin HCl; (-) Lobelin**

It is obtained by applying several extraction methods.

It is colorless crystals, slightly soluble in water and very soluble in hot alcohol.

Lobelin is a respiratory stimulant that increases and accelerates the respiratory movement.

Lobelin HCl; is a respiratory stimulant in injectable forms. It is used in cases in narcosis asphyxia and breathing difficulties in newborn babies.