1. The Alkaloids derived from Ornithine and Lysine

A- Tropane alkaloids

-*Folia Stramonii*

-*Folia Hyoscyami*

-*Herba ve Radix Belladonnae*

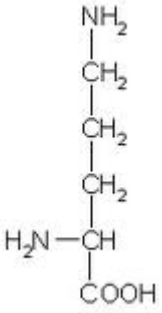
-*Duboisia myoporoides*

-*Withania Somnifera*

-*Atropinum*

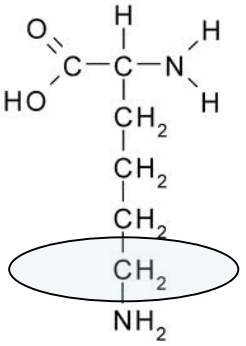
-*Folia Cocae*

1. The Alkaloids and drogs derived from Ornithine and Lysine



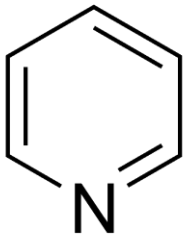
Ornithine 4 C

A- Tropane alkaloids
-Folia Stramonii
-Folia Hyoscyami
-Herba ve Radix Belladonnae
-Duboisia myoporoides
-Withania Somnifera
-Atropinum
-Folia Cocae

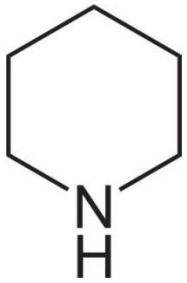


Lysine 5 C

B-Pyridine and Piperidine alkaloids
-*Folia Nicotianae*
-Nikotin ve Türevleri



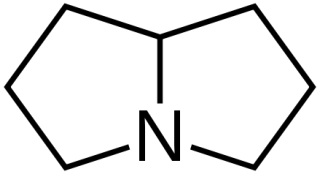
pyridine



piperidine

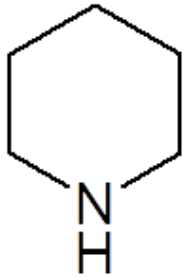
C- Pyrrolizidine-derived alkaloids

-Herba Lobeliae
-Cortex Radicis granatii

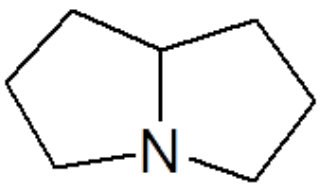


Ornithine-pyrrolidine (hygrin) and Lysine-piperidine (pelletierins) are a sources of complex alkaloids. The amino acids are transformed into polycyclic structure, then, the pyrrolizidines, quinolizidines, indolizidines alkaloids are formed. They also occur with the participation of different precursors in this structure (such as nicotinic acid: nicotine; acetate: tropane).

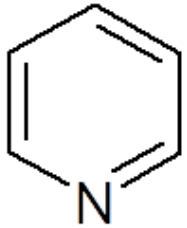
Ornithine and Lysine derivative alkaloids have very different therapeutic and pharmacological interests. Some of them are still used in treatment, such as atropine, scopolamine, cocaine, some of them have limited usages such as spartein, some of them have only historical values, such as lobelin, arekolin. Many of them are also known for their toxic effects.



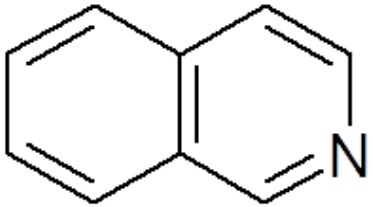
Pipiridin



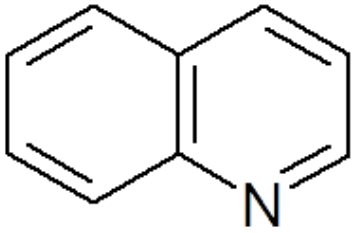
Pirolizidin



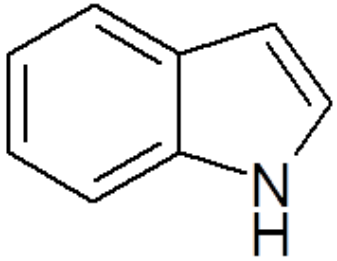
Piridin



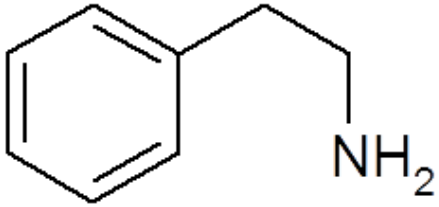
Isokuinolin



Kuinolin



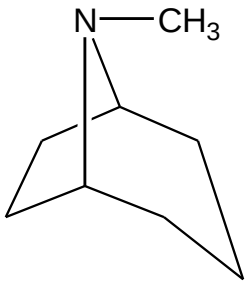
Indol



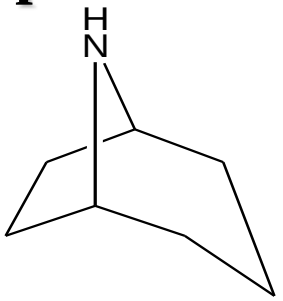
Feniletilamin

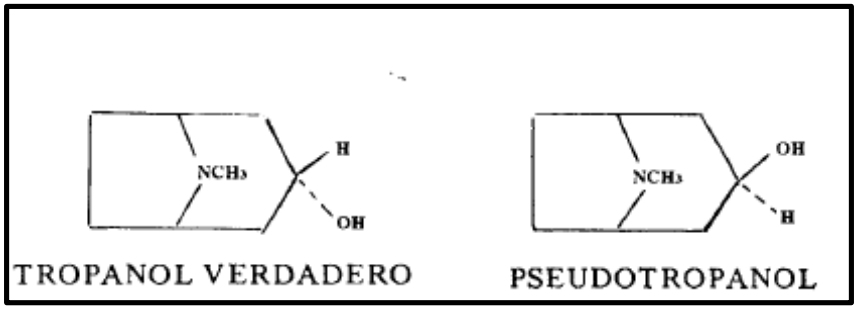
Tropane alkaloids

TROPANE
N-metil pyrolidine+ piperidine



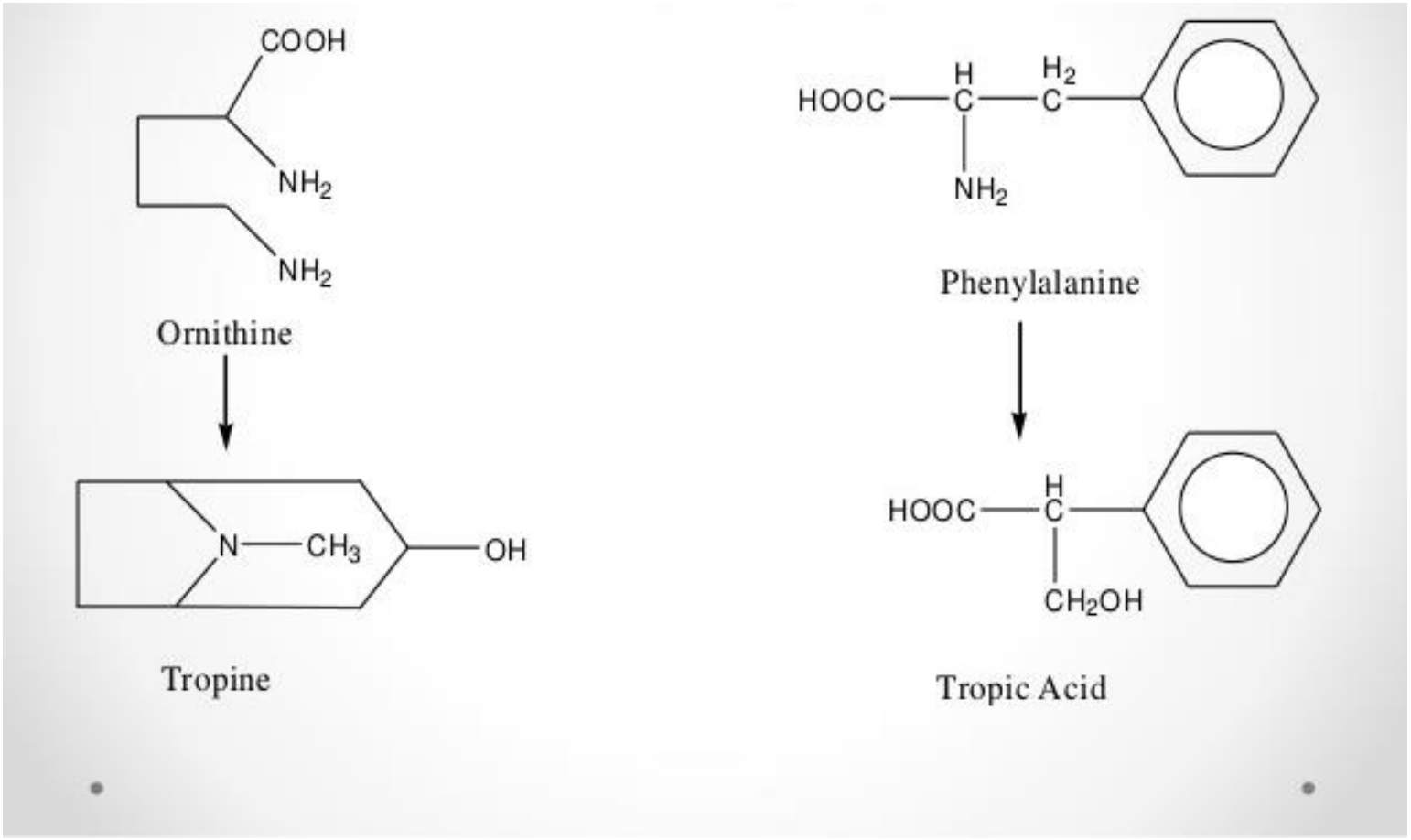
NORTROPANE
Pyrrolidin+Piperidine





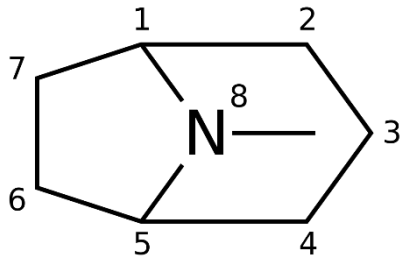
The basic skeleton of tropan alkaloids are tropane and nortropane rings. The alkaloids in this group are esters of alcohols formed by the addition of --OH groups to the tropane and nortropane skeleton with various acids.

The Byosynthesis of Tropane Alkaloids



Tropane alkaloids

Tropan or Nortropan ring could have 1, 2 or 3 -OH groups, and it is esterified with various acids.
*** There are those that contain epoxide group.**
Tropan alkaloids generally show distribution in the Solanaceae family, as well as Erythroxylaceae etc..
Thus, one hydroxyl, two hydroxyl containing groups, etc. as follows,
1-Monohydroxy Alkamine and Esters
2-Dihydroxy Alkamine and Esters
3-Trihydroxy Alkamine and Esters
4-Epoxytropanol Esters are formed.



1-Monohydroxy Alkamine and Esters

1) Monohydroxy Alkamine ve Esters

A-Tropanol (**trans**)

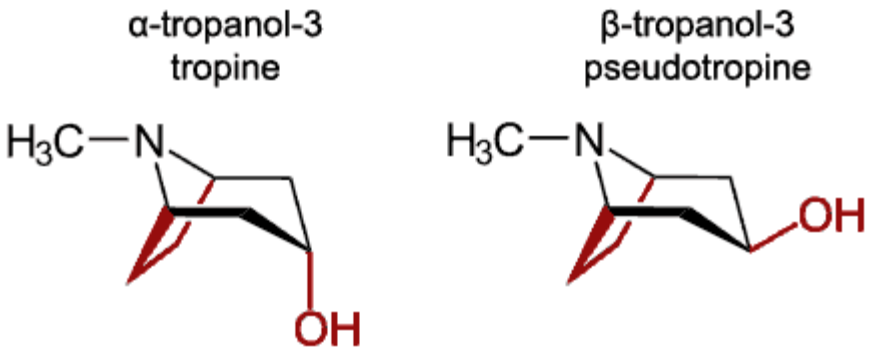
B-Psödotropanol (**cis**) (Tropane alcohols)

Tropanol ve psödotropanol are tropane alcohols.

C-Nor-tropanol ring

All of them contain a hydroxyl group at C 4th.

They are optically inactive, meaning the molecule does not change the polarized light.



A-Tropanol Esters

- **Tropanol + atropic acid ..... Atropamine**
- Tropanol + veratric acid ..... Convolamine
- Tropanol + 2-OH-3-Phenyl Propionic acid ..... Littorin
- Tropanol + vanilic acid ..... Fillabin
- Tropanol + acetic acid
- Tropanol + propionic acid
- Tropanol + butyric acid
- Tropanol + benzoic acid
- Tropanol + isobutyric acid
- Tropanol + isovalerianic acid

While the alkaloids, which are tropanol esters, have dilating effects, namely mydriatic effects, those containing pseudotropanol ring are local anesthetics like cocaine.

In other words, the effect differs according to the state of the hydroxyl group in location of space.

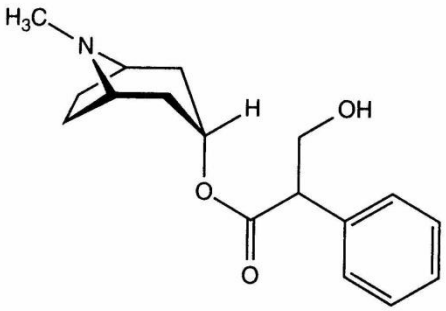
The Most Important Tropanol Esters Are Tropic Acid Esters

Optically active !!! Esters formed by these alkamines with organic acids are optically active.

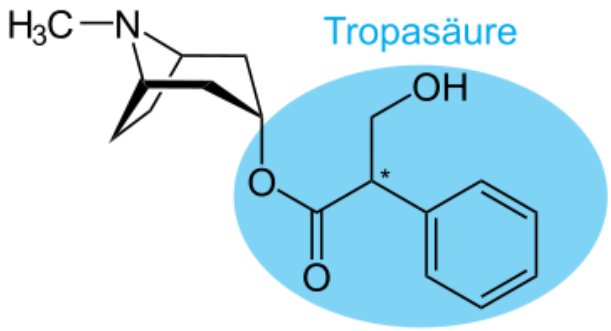
(l) Tropic acid (l-levojir) + Tropanol : Hyoscyamine (l)

(dl) Tropic acid (dl-racemic) + Tropanol : Atropine (dl)

They show parasympatholytic effects and are mydriatic.



Atropine

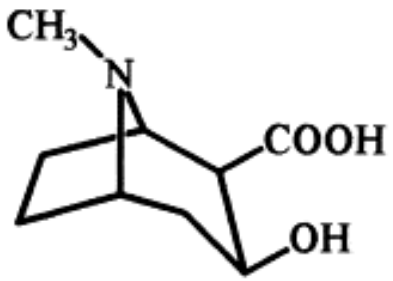


Hyoscyamin

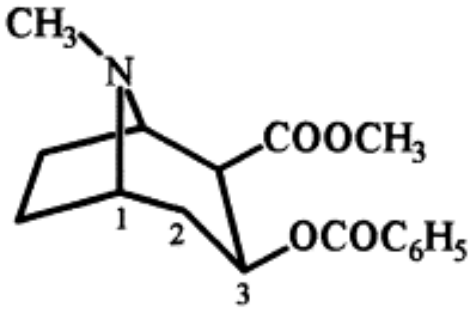
B-Pseudotropanol ve Ecgonine Esters

Pseudotropanol + benzoic acid …… ..TROPACOCAINE
Pseudotropanol + tiglic acid.....TIGLOIDIN
In pseudotropanol, ecgonine is formed by the attachment of a –COOH group to the 3rd carbon.
Therefore, ecgonine can do 2 different esters.

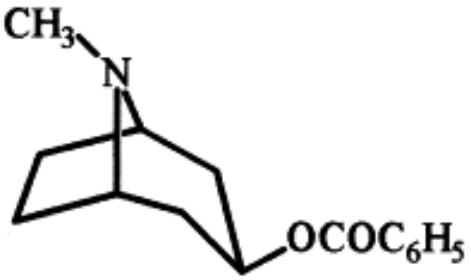
Ecgonine + Methanol + Benzoic Acid : COCAINE
Ecgonine-methyl ester + Cinnamic acid : Cinnamyl Cocaine
Ecgonine-methyl ester + Truxylic acid : α-Truksillin
Ecgonine-methyl ester + isotroxylic acid : β-Truksillin



Ecgonine



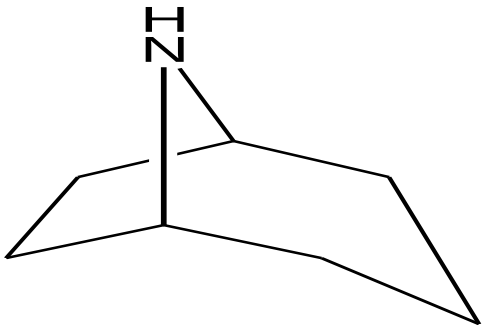
Cocaine



Tropacocaine

C-Nortropanol Esters

- The best known ones are,
- **Nor-Tropanol + l-tropic acid: Norhiocyamine**
- **Nor-Tropanol + 3-methyl butyric acid: Poroidin**
- **Nor-Tropanol + 2-methyl butyric acid: Isoporoidin**
- Nor-Tropanol + veratric acid. Convolvin

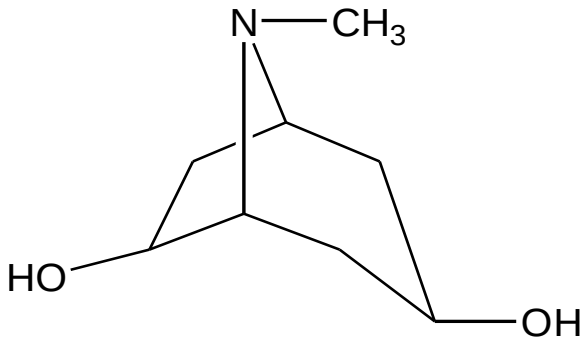


2-Dihydroxy Alkamine and Esters

Dihydroxytropane + 3-methylbutyric acid : Valeroidin

Duboisia myoporoides

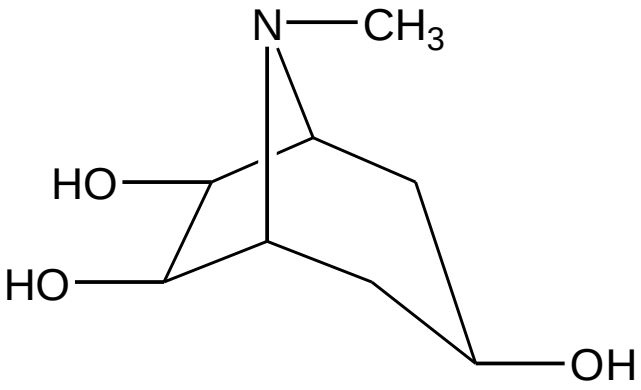
Obtain from such species as *Datura sanguinea*, such as the valeroidine



3-Trihydroxy Alkamine Esters

- Trihydroxytropane (Teloidine) + Tiglic acid : Meteloidine

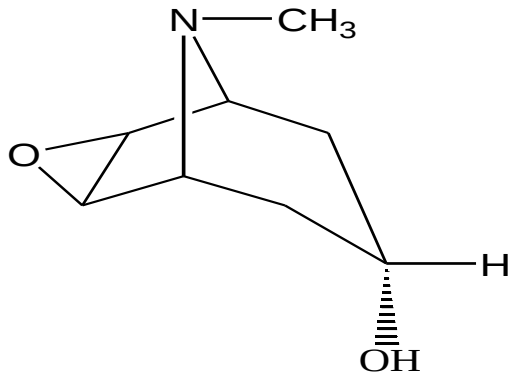
- *Datura ferox*
- *Datura innoxia*



4-Epoxytropanol Esters

- If an oxygen bridge is formed between the 7. and 8. carbons, then epoxitropanol, or scopanol, is formed as a different ring structure.

- **Skopanol + l-tropic acid : HYOSCINE**
- **Skopanol + dl-tropic acid : SCOPOLAMINE**



General principles of the Tropane Alkaloids

- They react with common alkaloid reagents. Even diluted concentrations, they can precipitate with these reagents.
- Mayer, Dragendorff are most used reagents
- Atropine, hyoscyamine and scopolamine have strong mydriatic effect.
- Cocaine (pseudo-tropanol) causes numbness (Anesthetic effect) in the tongue, but mydriatic effect lasts for a short time.
- They can also be recognized that way.

Determination of Tropane Alkaloids

-Paper Chromatography

- **TLC**

<u>Quantification;</u>

Titrimetric

Colorimetric

-Methods based on the Vitali-Morin Reaction

-Precipitation of alkaloids with ammonium raynekate

-The compounds formed with some dyestuffs (Bromkresol purpur)

Vitali Morin reaction
Identification of tropane structure bearing alkaloids
Generally these alkaloids are tropic acid esters. They are easily identified by the Vitali Morin reaction.

Dark purple color

Physiological Effects of Tropan Alkaloids

- Have many physiological effects....
- Relaxes smooth muscles
- Dilates the pupil in the eye - mydriasis
- It dilates the blood vessels
- There is an increase in heart rate and body temperature.
- It reduces pain and induces sleep
- It stimulates the central nervous system first, then depresses.
- Some induce hallucinations

The Usages of Tropane Alkaloids

-Used in eye exams to dilate the pupil (tropanol esters)

- Prevents blockage of digital heterosites (antidote)

- For narcosis preparation

-Used against vehicle (in the bus) / seasickness (epoxitropanol esters)

-Used in asthma attacks

-Antidote in morphine and lead (Pb) poisoning

-Psödo-tropanol esters (cocaine) local anesthetic

Drugs Containing Tropane Alkaloids
MEDICINAL SOLANACEAE PLANTS
parasympatholytics

Solanaceae Alkaloids

- ***Folia Stramoni*; Datura leaf**
- ***Folia Hyoscyami*-Banotu leaf**
- ***Herba ve Radix Belladonnae*-Belladon herb ve root**
  - **Atropinum**
- ***Duboisia myoporoides***
- ***Radix Mandragorae-Adam otu root-Mandrake***
- ***Withania somnifera***
- ***Folia Cocae-Koka lrsf***
  - ***Cocainum***

RESULT

- **Tropane alkaloids are common in the Solanaceae family.**
- **The number of herbs used in therapeutics is not so much.**
- **The pharmaceutical industry obtains atropine and scopolamine for this, uses some species such as, different species of *Datura, Hyoscyamus* and *Dubosia.***

- **They are described in the 10th edition of the French Pharmacopoeia.**

Folia Stramoni; Datura leaf, Stramonium Leaf
Tatula, Boru çiçeği, Şeytan elması, Ayı çiçeği

Drog; The dry leaves or flowers of *Datura stramonium* and its varieties (Solanaceae) gives the drog.

Drog; When calculated in terms of hyoscyamine, it should contain more than 0.25% alkaloids.

It could not find Europe until the 16th century.

But now, it is widely grown in Europe.

It is a strong-hard, annual plant in the roadside and fields in Anatolia.

Datura stramonium; it is an annual plant. It has large leaves with 5-7 lobes, highly branched. The fruit is a **septicide capsule** and **spiny**. Leaves are petiolate, 15-25 cm tall, with little indented or lobed edges; lobes pointed, deep toothed tips. Especially **the lower face is hairy, the upper face is almost nude**. The flowers are solitary and large. Leaves are blue-green in color (due to anthocyanosides).

The glandular hair on the epidermis is a Solanaceae type glandular hair with a short stems and a multicellular head. There are druses in the mesophyl.

- It is stated that there are about 24 species of *Datura* (Datura stramonium L.) genus, except *Datura ferox* and *Datura metel*, originating from Central America and especially Mexico.
- *Datura* is common in the flora of Turkey as a wild plant. Since it is not very selective in terms of soil properties, it grows as a weed (Wild plant) on roadsides, abandoned areas and fields.
- The total amount of alkaloids in the leaves has been reported as 0.20-0.45%. Although it is known that most of these alkaloids carrying tropane ring are composed of l-**hyoscyamine** (2/3) and **scopolamine** (hyoscine) (1/3), there is also **atropine** formed as a result of partial racemization of l-hyoscyamine in the plant.

Many drugs are obtained from another type of *Datura* species, one of them is *Datura metel*. It grows in Mediterranean countries and is cultured in America. It is included in the Indian pharmacopoeia.

Datura species has been cultivated in America and some European countries. The Development in *Datura* agriculture in the world are under the control of Germany, and the amount of alkaloids has been increased from 0.3% to 2%, especially with the developed seeds, in recent years.

***Datura stramonium*, has antispasmodic, pain relieving and narcotic properties. These properties are due to hyoscyamine.** The species acts similar to belladonna leaves, in the same way it enlarges the pupil. **It is a central nervous system sedative, this effect is stronger than Belladonna.**

In small and large doses; general physiological and therapeutic effects and toxicities are practically similar. It can be used in the same doses as belladon and interchangeably.

It is used in the form of cigarettes in spasmodic asthma. **Stramonium cigarettes** paralyze the ends of the bronchi, thus relieving bronchial spasm.

All parts of the plant contain atropine and scopolamine, the highest amount of these compounds are found in the seeds.

Usually used as a tea. The seeds, leaves, and flower nectar are edible and smoked.

Delirium, obsession, hallucinations, disorientation and inconsistent speaking have been observed in the users. Often users do not remember what they are doing/they did...

Herba Hyoscyami; Banotu

Drog; *Hyoscyamus niger* (Solanaceae) dry leaves or flowers form a drug. Drog; when calculated in terms of hyoscyamine, it should contain more than 0.05% alkaloids.

The plant has annual and perennial varieties. The leaves of annual varieties 30-50 cm high are more sticky and hairy leaves. Two-year varieties are higher, reaching up to 80 cm.

Since two-year varieties have more leaves, so, this variety is cultivated more.

The flowers of the plant are pale yellow with purple veins,

The fruit is a pixidium

The leaves used in pharmacy are stemless. These leaves, up to 15-20, even 25 cm, are 5-7 cm wide. Gray-green leaves are pointed and deeply lobed and the lobes are not equal to each other. There are plenty of trichomes on both surfaces. It is sticky due to the feathers.

Trichomes are single-row and multi-celled. In the glandular hairs, the stem and head are multi-celled. There are simple crystals and twin crystals in mesophyll.

Its effects are similar to Belladon and Stramonium but weaker, due to the higher content of scopolamine in the alkaloid mixture, its effects on the brain are higher than Belladon.

- ***Hyoscyamus niger*** **leaves** usually carry 0.045-0.14% alkaloids. Major alkaloids; **hyoscyamine and scopolamine**.
- Usage:
- It is used as a sedative and pain reliever.
- It is used especially for kidney stones and pain affecting the urinary system. Its sedative and antispasmodic effects have a positive effect on the reduction of tremors and their intensity in Parkinson's disease.
- It is used internally in the treatment of asthma, motion sickness, Menier syndrome (inner ear tension; a disease with dizziness, a feeling of fullness in the ear, tinnitus and hearing loss).

- The herba (aerial parts of plant) of *H. muticus* is also used as a drug.
- The plant grown in North Africa-Egypt has a total of 0.5-1% alkaloids.
- This plant is used to obtain alkaloids.