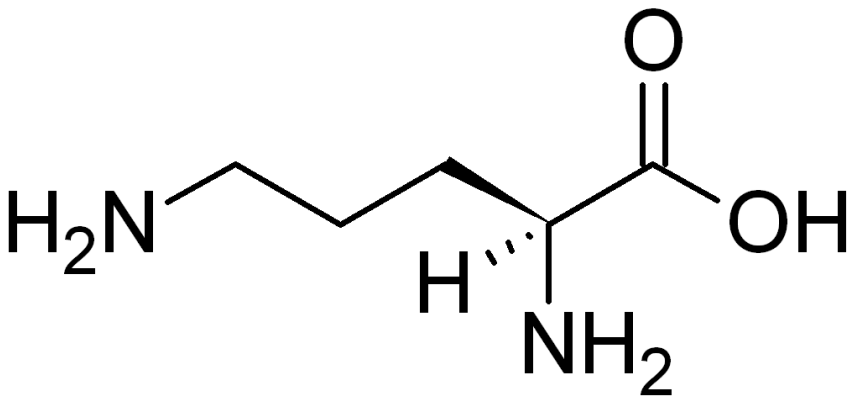
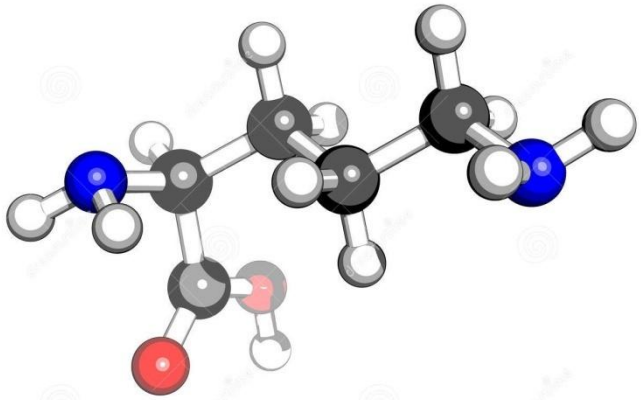
# Alkaloids Derived from Ornithine and Lysine

Prof . Dr. Ali H. Meriçli

Two amino acids with four or five carbon atoms - ornithine and lysine – are at the origin of many alkaloids whose structure may be simple (pyrrolidines, such as hygrine from coca leaves, piperidines, such as pelletierine from the pomagranate tree). Structural complexity, in this group, translates into the formation from several molecules of the amino acid, of polycyclic edifices : pyrrolizidines, indolizidines, quinolizidines (bi-, tri-, tetra-, and pentacyclic).

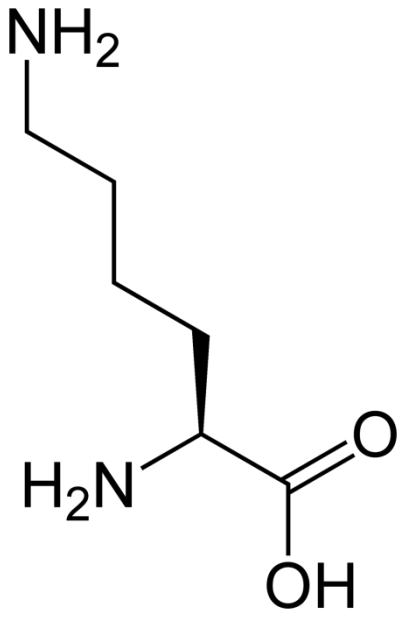
The complexity may also arise from the partipitation of other precursors : acetate (tropanes, homotropanes), phenylalanine (phenantroinindozolidine), tryphophan (elaocarpidine), nicotinic acid (nicotine, anabasine), or phenylpropanoic acid (alkaloids of the Lythraceae).

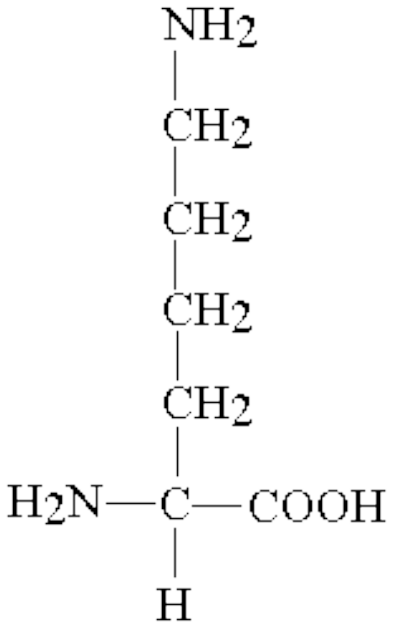


$$H_2N-CH_2CH_2CH_2-\underset{\displaystyle NH_2}{\underset{|}{CH}}-COOH$$

# Ornithine

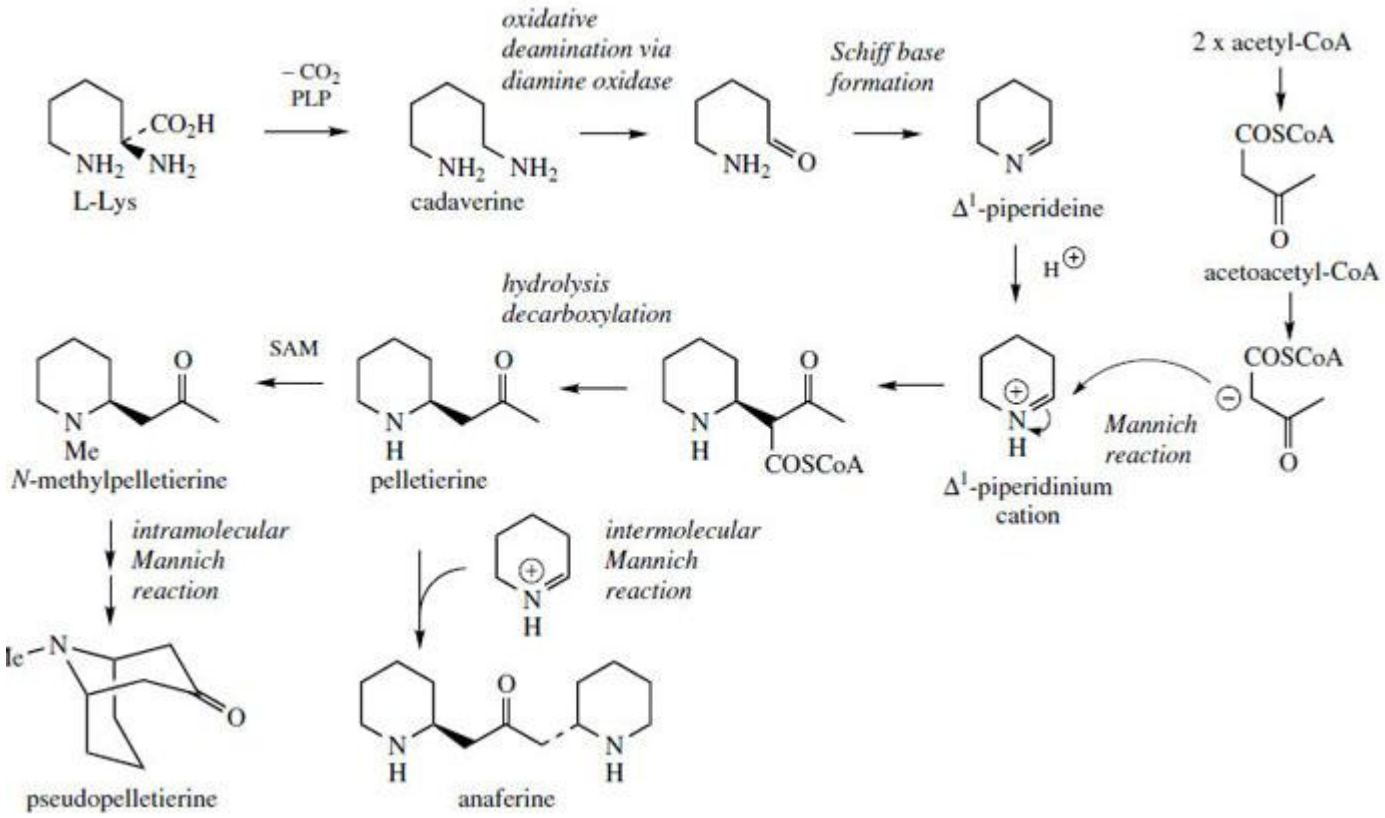


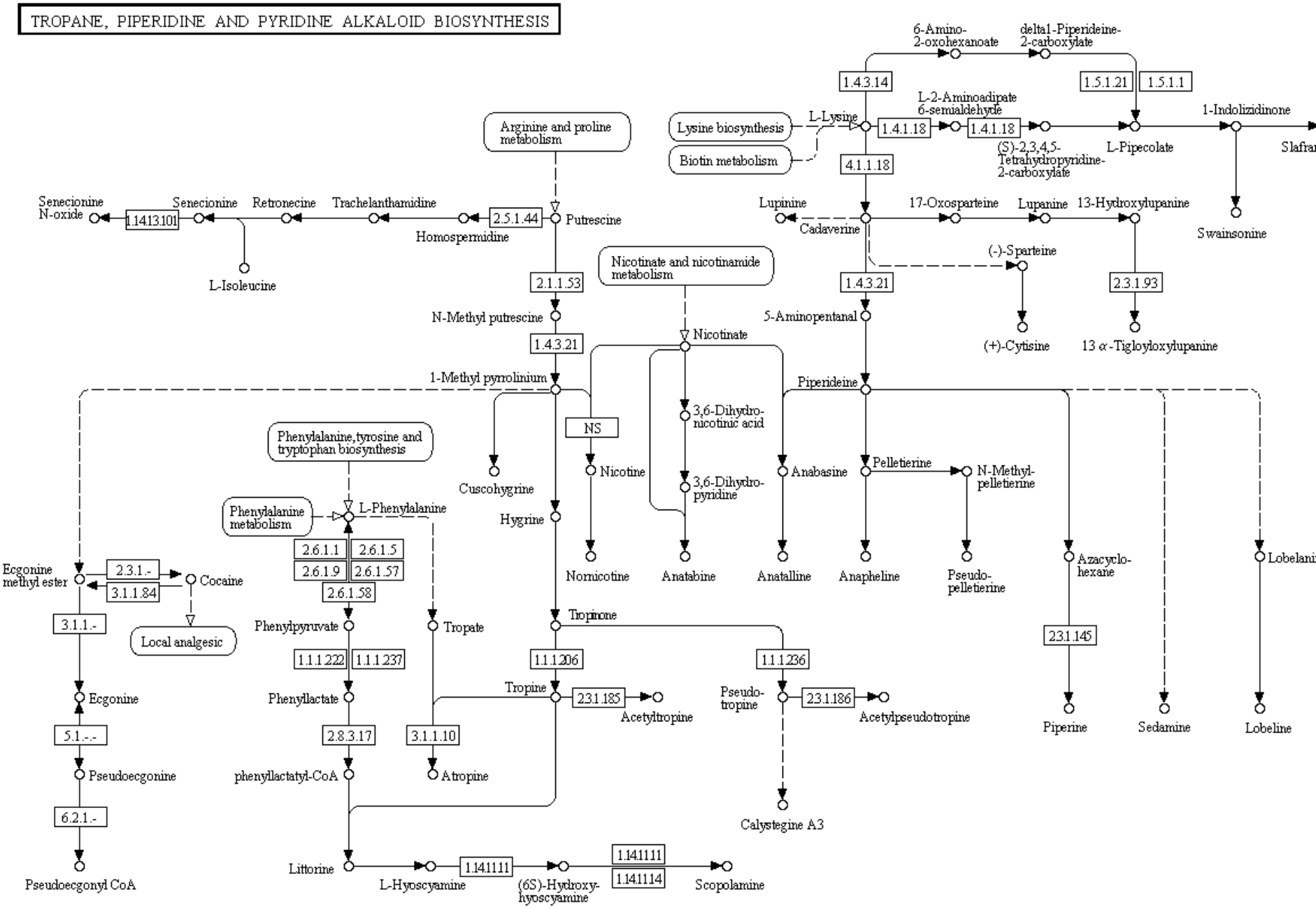

# lysine

Also known are compounds in which a ring arising from ornithine (pyrrolidine) or lysine (piperidine) is combined with complex structures of the flavone, benzylisoquinoline, or harmane.

In the biosynthesis the enzymes whose coenzyme is pyridoxal phosphate have the most important role .

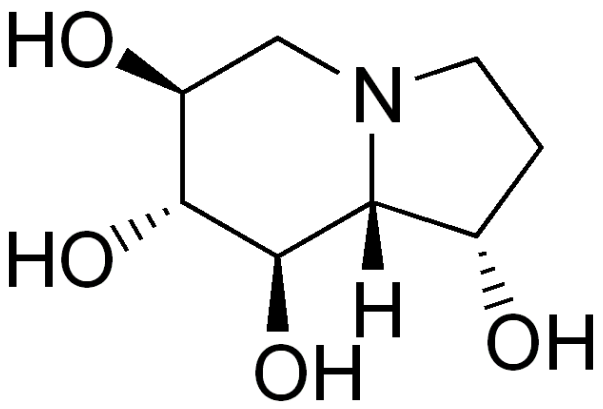



# Biosynthesis pathway of piperidines

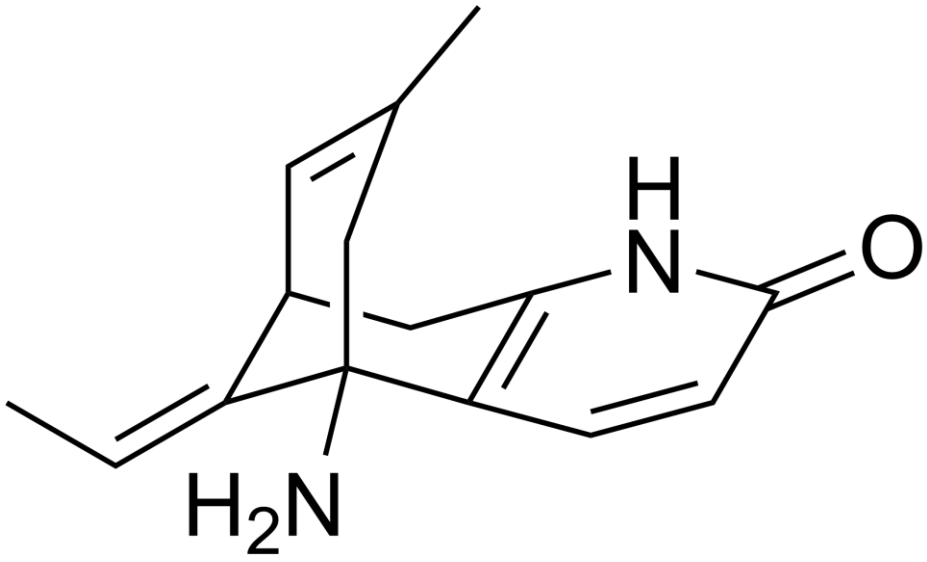

TROPANE, PIPERIDINE AND PYRIDINE ALKALOID BIOSYNTHESIS
Arginine and proline metabolism
Lysine biosynthesis
Biotin metabolism
L-Lysine
6-Amino-2-oxohexanoate
delta1-Piperideine-2-carboxylate
1.4.3.14
1.5.1.21
1.5.1.1
L-2-Aminoadipate 6-semialdehyde
1.4.1.18
1.4.1.18
4.1.1.18
(S)-2,3,4,5-Tetrahydropyridine-2-carboxylate
L-Pipecolate
1-Indolizidinone
Slafra
Senecionine N-oxide
1.14.13.101
Senecionine
Retronecine
Trachelanthamidine
2.5.1.44
Homospermidine
Putrescine
L-Isoleucine
Lupinine
Cadaverine
17-Oxosparteine
Lupanine
13-Hydroxylupanine
Swainsonine
(-)-Sparteine
Nicotinate and nicotinamide metabolism
2.1.1.53
1.4.3.21
2.3.1.93
N-Methyl putrescine
5-Aminopentanal
Nicotinate
(+)-Cytisine
13α-Tigloyloxylupanine
1.4.3.21
1-Methyl pyrrolinium
Piperideine
3,6-Dihydro-nicotinic acid
NS
Phenylalanine,tyrosine and tryptophan biosynthesis
Cuscohygrine
Nicotine
3,6-Dihydro-pyridine
Anabasine
Pelletierine
N-Methyl-pelletierine
Phenylalanine metabolism
L-Phenylalanine
Hygrine
2.6.1.1
2.6.1.5
2.6.1.9
2.6.1.57
2.6.1.58
Nornicotine
Anatabine
Anatalline
Anapheline
Pseudo-pelletierine
Azacyclo-hexane
Lobelani
Ecgonine methyl ester
2.3.1.-
3.1.1.84
Cocaine
Local analgesic
3.1.1.-
Phenylpyruvate
Tropate
Tropinone
1.1.1.222
1.1.1.237
1.1.1.206
1.1.1.236
23.1.145
Ecgonine
Phenyllactate
Tropine
23.1.185
Acetyltropine
Pseudo-tropine
23.1.186
Acetylpseudotropine
Piperine
Sedamine
Lobeline
5.1.-.-
2.8.3.17
3.1.1.10
Pseudoecgonine
phenyllactatyl-CoA
Atropine
6.2.1.-
Calystegine A3
Pseudoecgonyl CoA
Littorine
1.14.1111
L-Hyoscyamine
(6S)-Hydroxy-hyoscyamine
1.14.11.11
1.14.11.14
Scopolamine

The pharmacological and therapeutic interst of the alkaloids derived from ornithine and lysine is very uneven. Some are currently used in therapy (atropine, scopolamine), while others are now of limited use (sparteine) or only of histological interest (lobeline, arecoline). Many ought to be known only because of their toxicity : pyrrolizidine alkaloids from Boraginaceae and Asteraceae that are often gifted with medicinal virtues (senecionine etc.), quinolizidine alkaloids of Fabaceae that are common in our environment because of their ornamental character, not forgetting nicotine in tobacco.

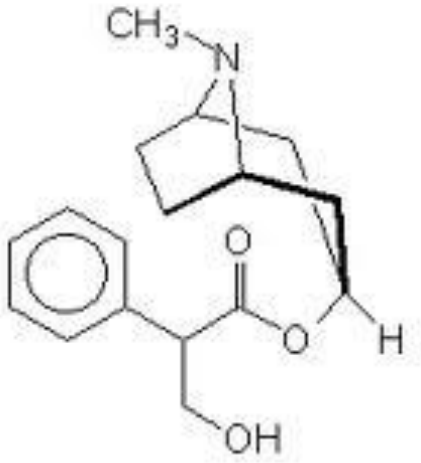
A small number have interesting potential, for example, some indolizidines (castanospermine) which are efficacious against retroviruses, or huperzine, which has been tested in the context of Alzheimer's disease.



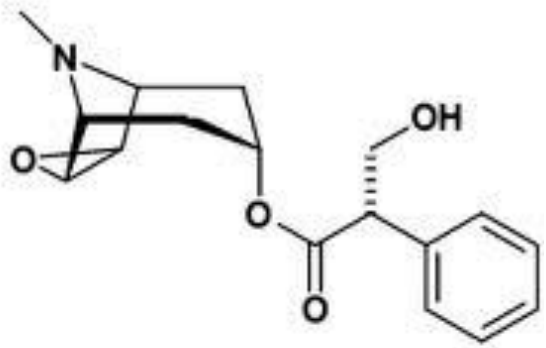

castanospermine



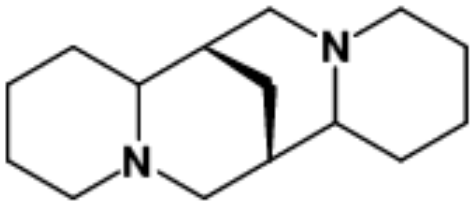

huperzine



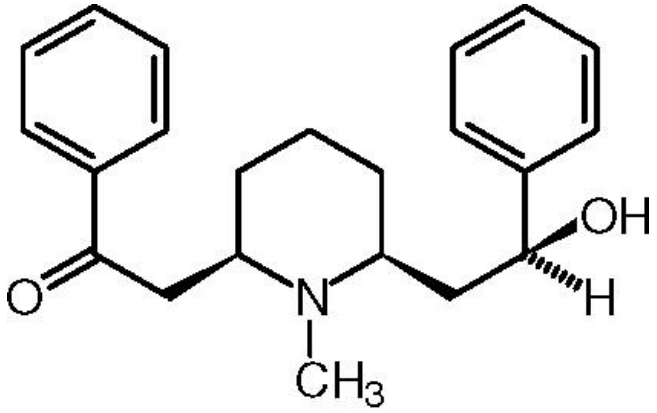

Atropine



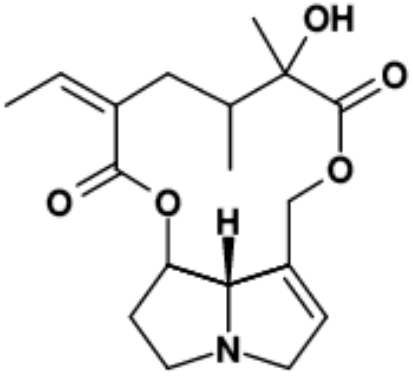

Scopolamine



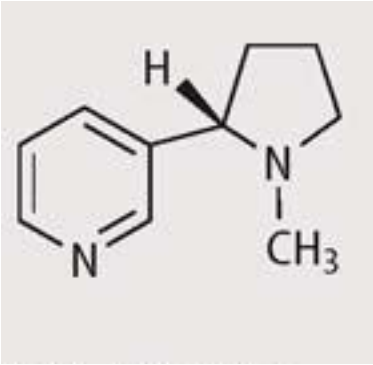

Sparteine




(–)-lobeline




Senecionine




**Nicotine**

# Tropane Alkaloids

Tropane alkaloids have common a nitrogen containing bicyclic structural element, namely azabicyclo[3, 2, 1] octane : they are 8-methyl-8-azabicyclo[3, 2, 1] octanes.

Approximately 200 alkaloids are known in this group, and they are distributed in a small number of Angiosperm families especially **Solanaceae** (they are found in about twenty genera like *Atropa, Datura, Mandragora, Physalis, Scopolia, Hyoscyamus, Withania*), Erythroxylaceae (*Erythroxylum*), Convolvulaceae (*Convolvulus, Calystegia*).

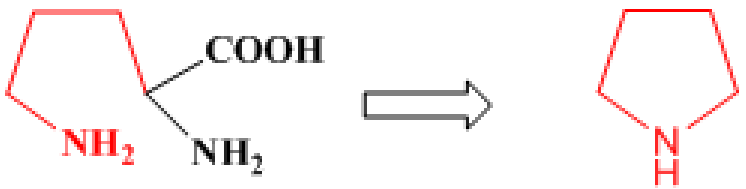
**From a pharmacological point of wiev, (-)-hyoscyamine and its racemate (±)-atropine**, are substances of considerable interest : they have parasymphatolytic properties, and they are also the starting point from which synthetic organic chemistry created, among others, most of the anticholinergics. Similarly, cocaine was the origin of the synthetic local anesthetics.

# STRUCTURE OF TROPANE ALKALOIDS

With only few exceptions the pyrano- and dihydropyranotropanes of the Proteaceae and calystegines, tropane alkaloids are esters of tropane alcohols and of acids of various structures, either aliphatic or aromatic.

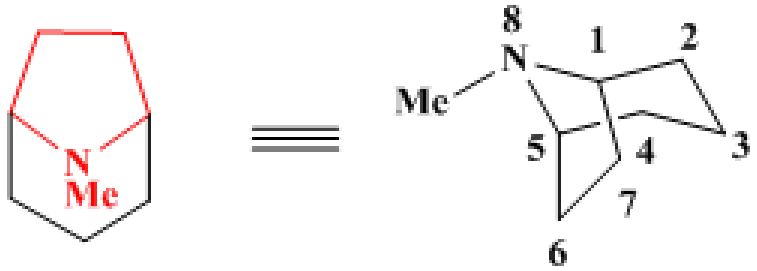
# A- Tropanols

These alcohols fall into two series depending on the orientation of the hydroxy group at C-3. Derivatives of tropan-3α-ol (tropanol) are by far the most common, and those of are essentially specific to the **Solanaceae**. The tropanols are optically inactive. They are often hydroxylated at C-6 or C-7 or both, and sometimes 6,7-epoxidized. Almost all of the alkaloids of the Erythroxylaceae are esters of ecgonine, which is tropan-3β-ol substituted at C-2 and in the β configuration by a carbonyl group.



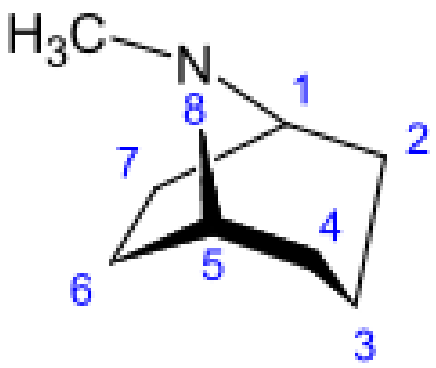

L.Ornithine

Pyrrolidine ($C_4N$)



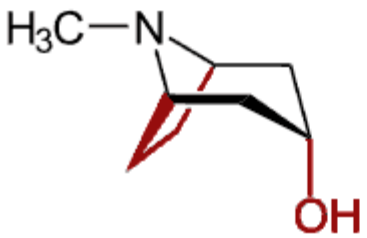

Tropane

**Structure of L-ornithine and Tropane**




**Tropane**

α-tropanol-3
tropine



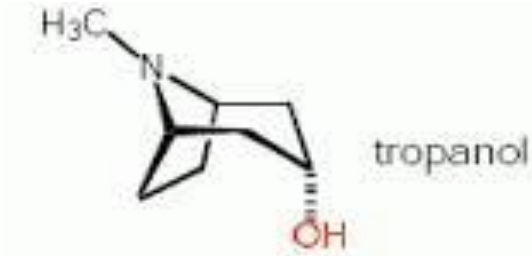

endo

**Tropanol**
**(3α-hydroxytropane)**

β-tropanol-3
pseudotropine

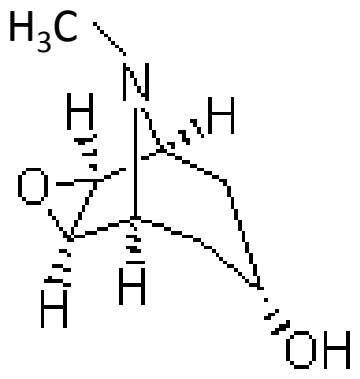

exo

**Pseudo-tropanol**
**(3β-hydroxytropane)**

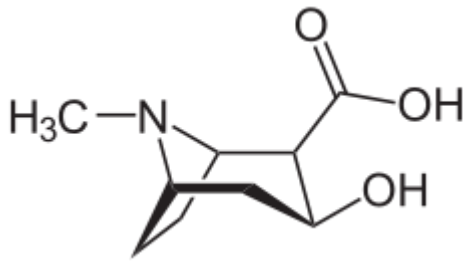



tropanol

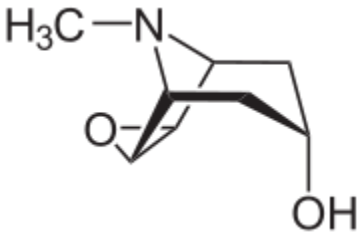

pseudotropanol




**Scopanol**

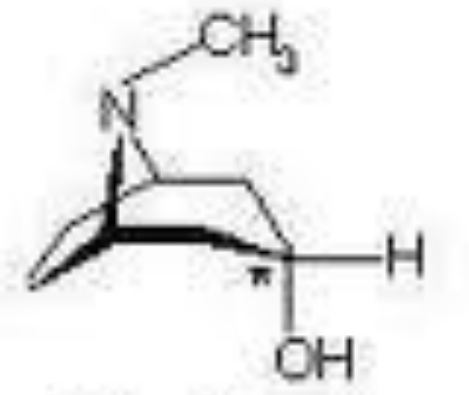



Ecgonine

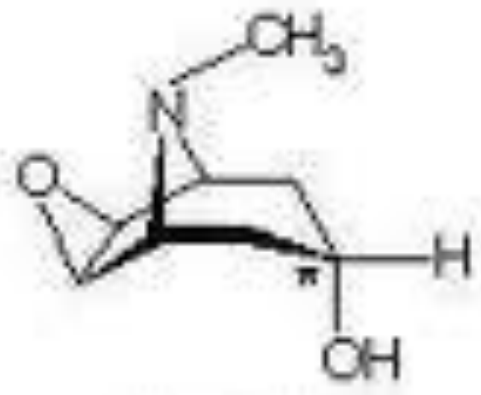


## B.Acids

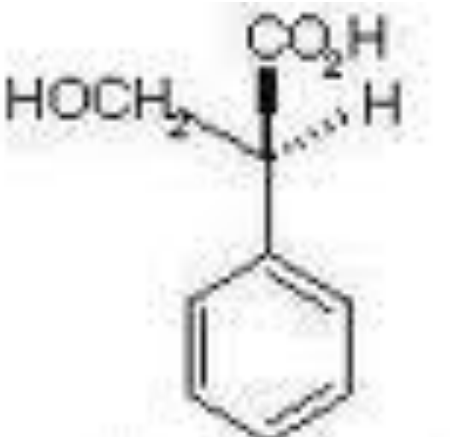
The acids may be aliphatic (acetic, butyric, isovaleric, tiglic, angelic acid) or aromatic. In the latter case, the acid may be specific like (S)-(-)-tropic acid, or may be more widely distributed in the plant kingdom like benzoic, phenylacetic, cinnamic acid and their derivatives. The acides are rarely heterocyclic.



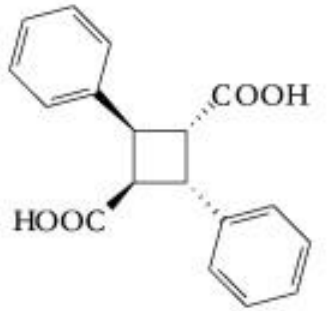

**Tropanol**



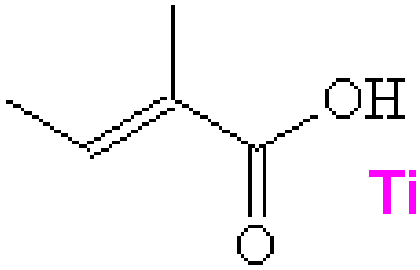

**Scopanol**



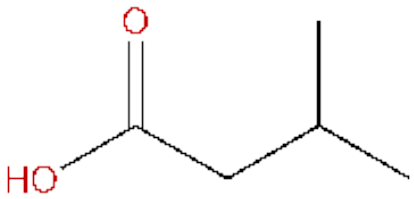

**(S)-Tropic acid**



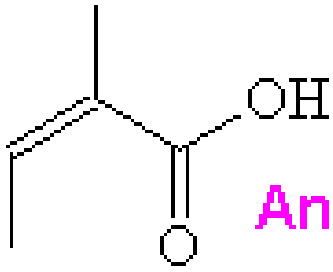

**α-Truxillic acid**




**Tiglic Acid**



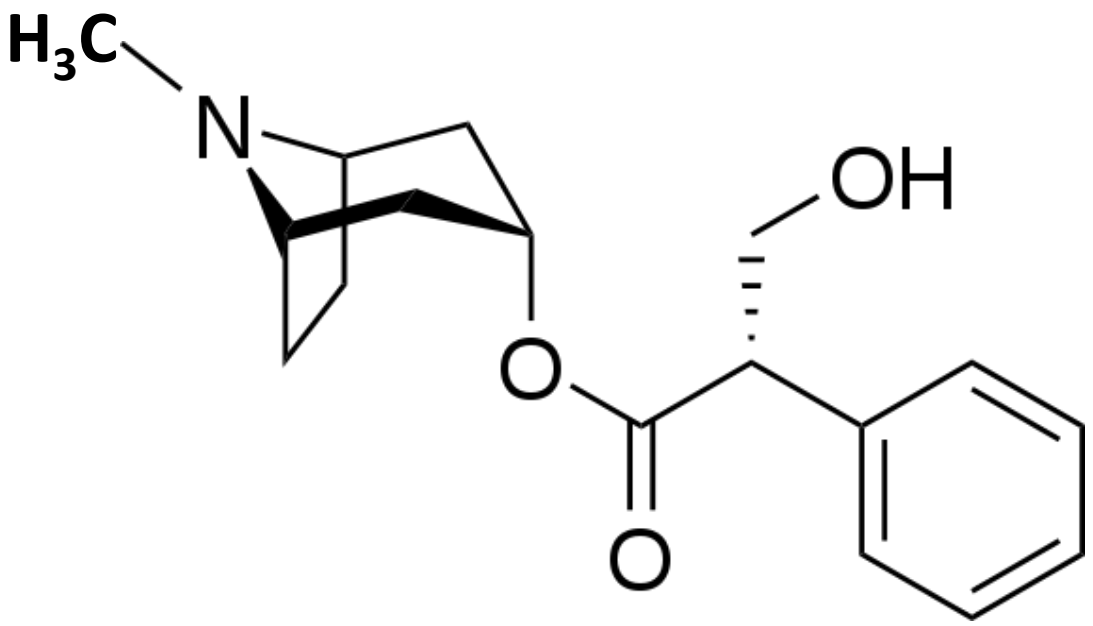

**Isovaleric acid**



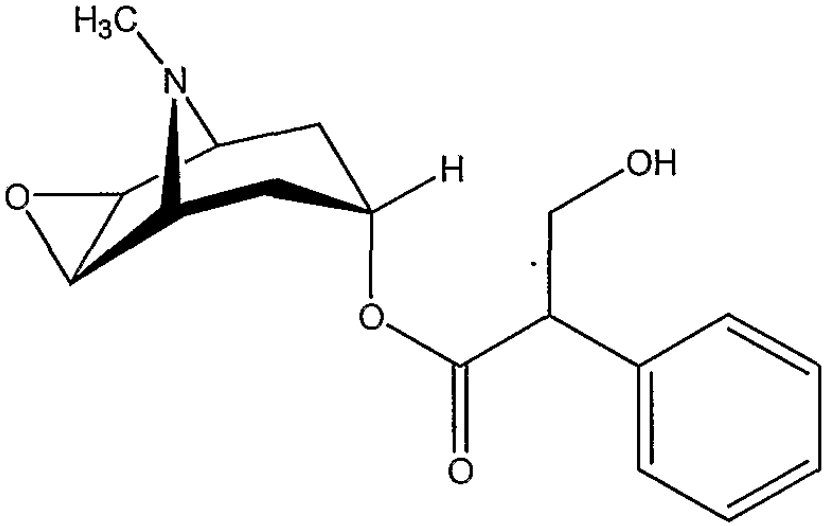

**Angelic Acid**

# C-Alkaloids

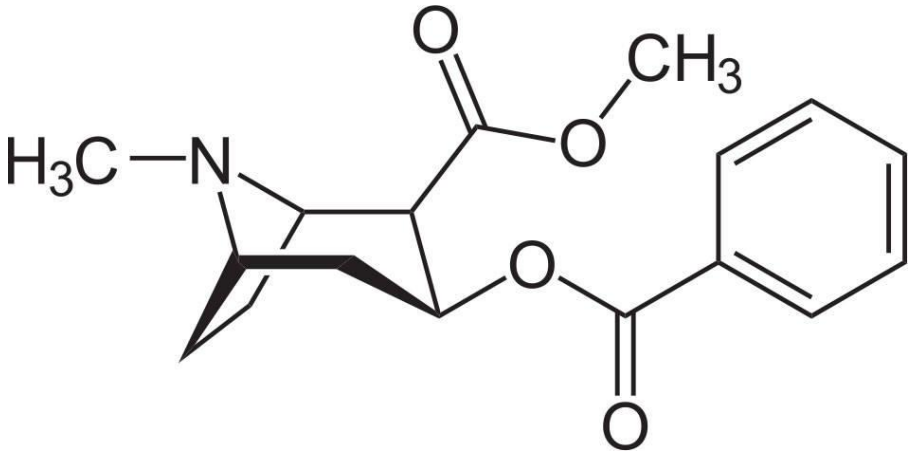
The most representative structures are shown below




**Hyoscyamine**




**Scopolamine**




**Cocaine**

# BIOSYNTHETIC ORIGIN

Several precursors are involved in the elaboration of tropane alkaloids

-Phenylalanine is at the origin of the $C_6$-$C_3$ aromatic acids as well as of tropic acid

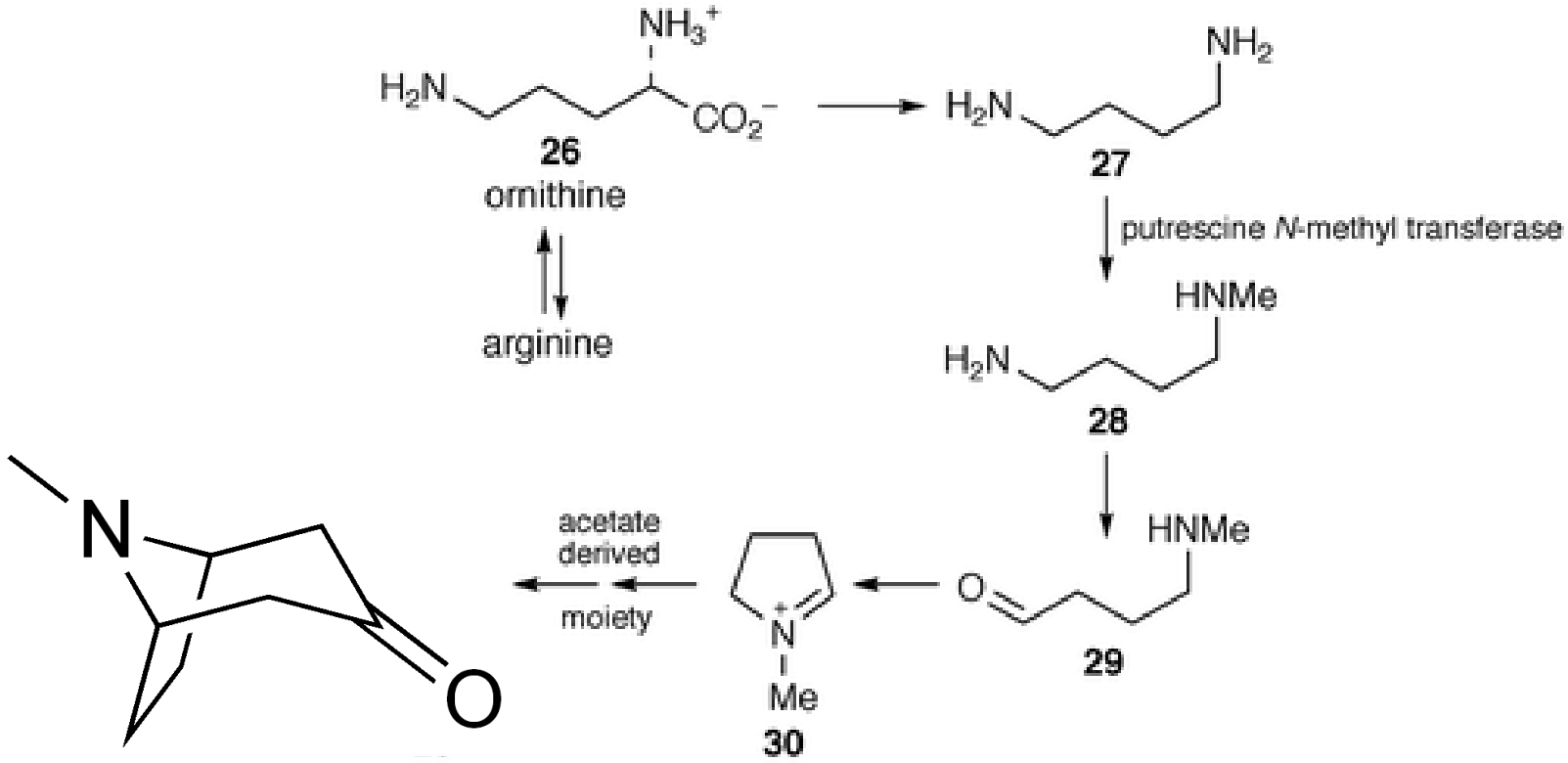
-Isoleucine is the precursor of $C_5$ aliphatic acids such as tiglic acid

-Ornithine is the origin of the pyrrolidine ring of the tropane nucleus

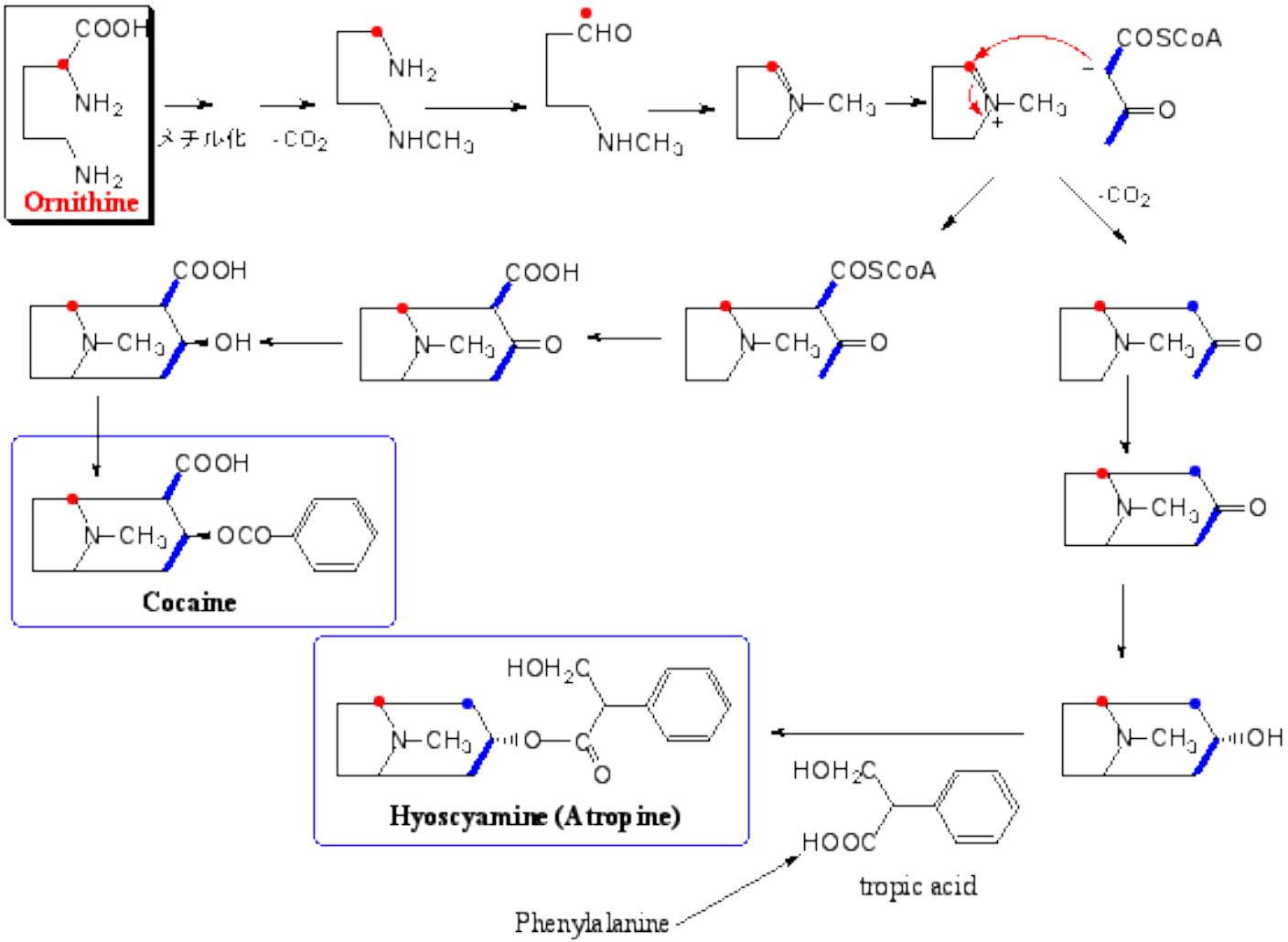
-Acetate (in the form of acetoacetyl coenzyme A or malonyl coenzyme A) contributes the additional carbon atoms needed to built the piperidine ring of the tropane nucleus

Ornithine, the precursor of the trophane nucleus, is rapidly dacarboxylated to putrescine, which is then methylated. Putrescine can also be formed from arginine.

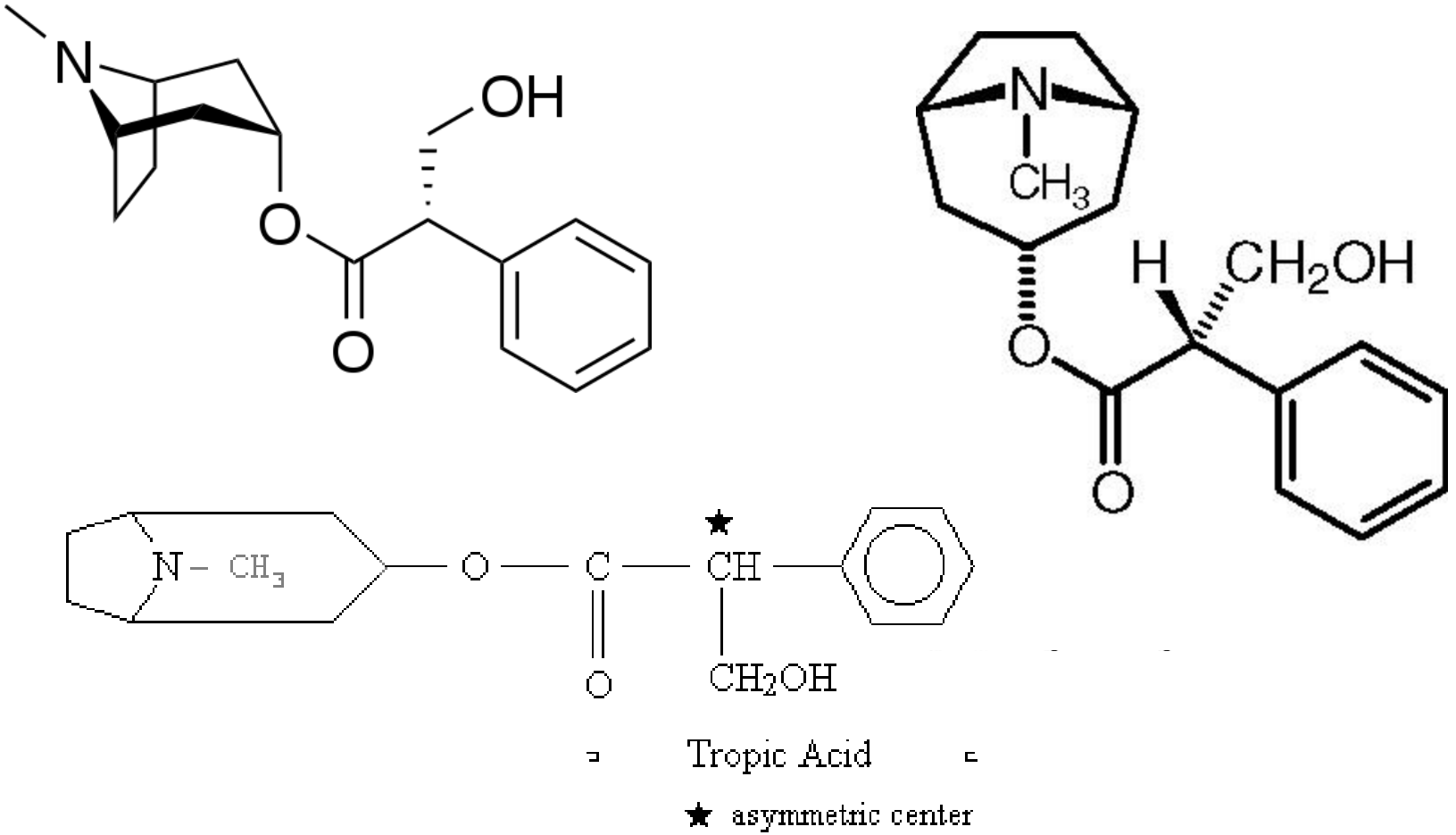
Origin of tropic acid : The precursor of tropic acid is (S)-phenylalanine.


NH3+
H2N
CO2−
26
ornithine
arginine
NH2
H2N
27
putrescine N-methyl transferase
HNMe
H2N
28
HNMe
O
29
acetate
derived
moiety
N+
Me
30
N
O

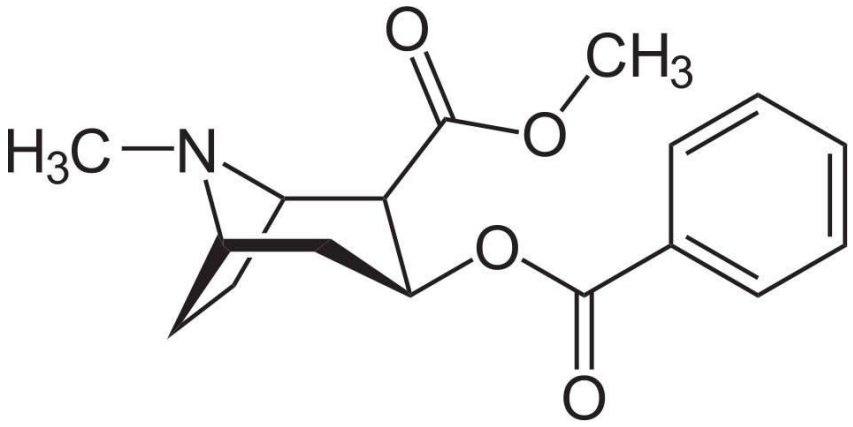
**tropinone**

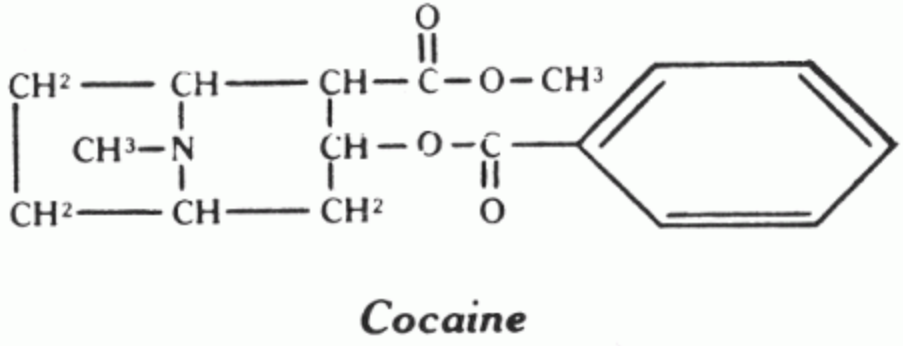



# Trophane alkaloid-Biosynthesis

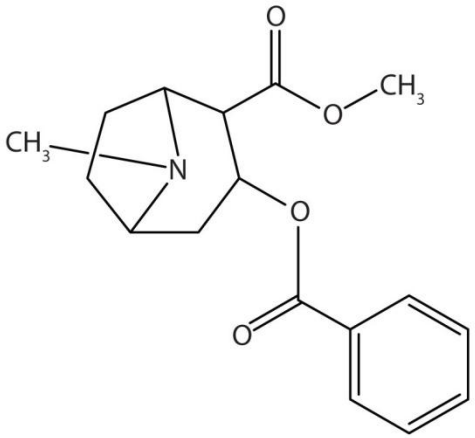



# Hyoscyamine structures in different forms




*Cocaine*




# Cocaine structures in different forms

# Characterization of Alkaloids Containing a Tropane Nucleus

Alkaloids that are esters of tropic acid are easy to characterize by the Vitali-Morin reaction; after fuming nitric acid and redissolving the residue with acetone, a **dark purple** color develops in the presence of an ethanol solution of potassium hydroxide.

Tropane alkaloids are easy to detect by TLC. HPLC gives good resolution (reverse phase and ion pair). GC can also be used, particularly to analyze coca leaves, after extraction, to analyze products suspected cocaine. In the case of Solanaceae alkaloids, hyoscyamine and scopolamine are partially dehydrated to apo derivatives (apoatropine, aposcopolamine) on the chromatography columns. For purposes of quantitation, preliminary silylation prevets dehydration.

# OFFICIAL SOLANACEAE CONTAINING TROPANE ALKALOIDS

**Deadly nightshade** ***Atropa belladonna***

**Belladonnae folium**

**Thorn apple** ***Datura stramonium***

**Stramonii folium**

**Henbane** ***Hyoscyamus niger***

**Hyoscyami herba**

***Atropa belladonna***
**(güzelavratotu)**

***Datura stramonium***
**(grows in Cyprus)**
**Tatula, şeytan elması**

*Hyoscyamus niger*

**Banotu, gavur haşhaşı**

For each of the three drugs, the Pharmacopoeia indicates in addition the minimum concentration of total alkaloids expressed as hyoscyamine relative to the drug dried at 100-105 $^{0}$C as well as the approximate propertions of the chief alkaloids. They are all very known medicinal and also toxic drogs.

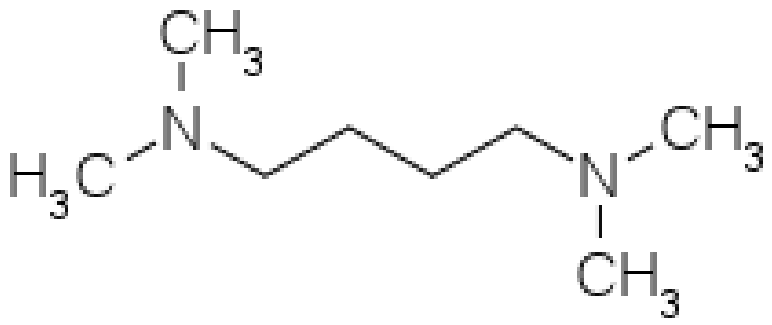
All the plants grow widespread in Europe and Turkey. Only *Datura stramonium* grows wildly in Cyprus, but other species like *Hyoscyamus aureus* and *H. albus* grow wildly in Cyprus.

***Hyoscyamus aureus***

The three official species are cultivated chiefly in the eastern European countries. Different breeds and varieties are cultivated. The harvest normally occurs at the beginning of the floration, and the drying must be at low temperature; in the case of belladonna, another harvest at the end of the season is possible.

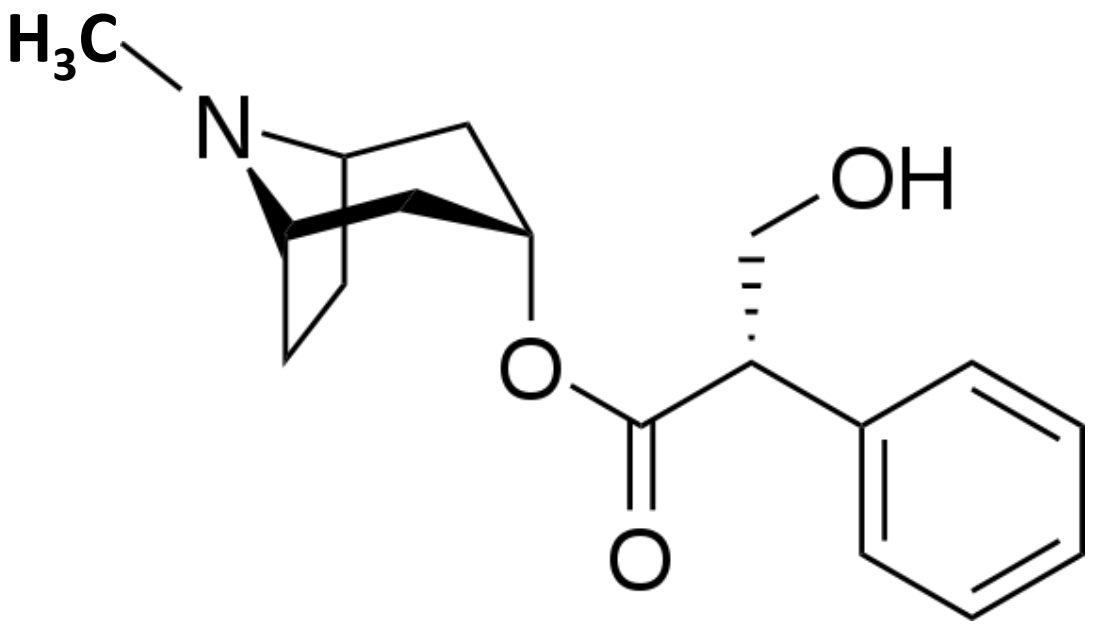
**Chemical Composition :** All the three drugs are rich in minerals: 12-15% Belladonnae folium, 15-18% Stramonii folium, 18-20% Hyoscyami herba). The belladonna leaf contains a small quantity of a coumarin, namely scopoletin. The foul odor of hyoscyami herba is due to tetramethylputrescine.


scopoletin
(7-hydroxy-6-methoxycoumarin)



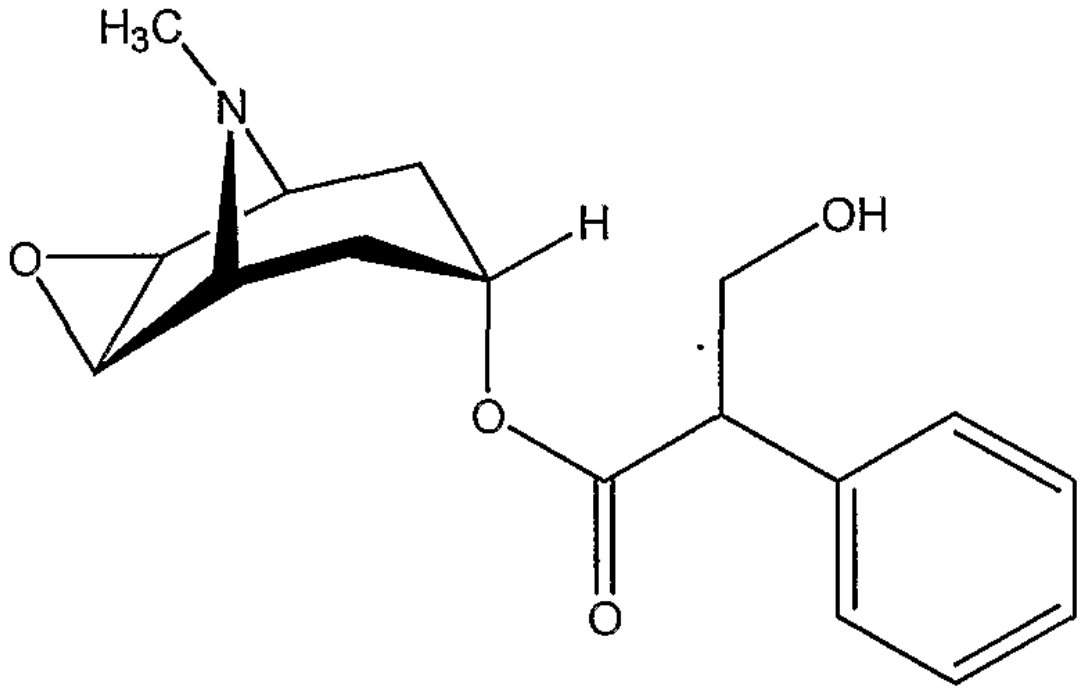

tetramethylputrescine

# Main alkaloids




**(-)-Hyoscyamine**

Atropine is(±)-racemate of (-)-hyoscyamine.




**Scopolamine**

**Belladonnae folium:** The concentration of the total alkaloids in the leaf ranges from 0.3 to 0.6% (1% in cultivated clones). Hyoscyamine is by far the chief constituent (90%) and occurs alongside small quantities of scopolamine.

**Stramonii folium:** The concentration of the total alkaloids is between 0.2 and 0.5%, and at the time of the harvest, hyoscyamine and scopolamine represent two-third and one-third of the total alkaloids respectively.

**Hyoscyami herba:** This is the species containing the least total alkaloids: 0.04-0.15%. Hyoscyamine is the chief constituent, and the percentage of scopolamine can be high (25% and more).

**Assay:** The identification is based for all three drugs, on the characterization of the tropic esters by the Vitali-Morin reaction: extraction of the alkaloids in dilute sulfuric acid, back-extraction ($Et_2O$) after alkalinization ($NH_4OH$), solvent evaporation, nitration of the residue at high temperature ($HNO_3$), and color development in an acetone solution of the nitrated product in the presence of an ethanol solution of NaOH. A purple color develops.

Also required is a TLC analysis of a methanol solution of the total alkaloids. The plates are visualized with potassium iodobismutate, followed by sodium nitrite. Under these conditions, the spots or bands corresponding to **hyoscyamine** turn from brown to **reddish-brown**, but not to **bluish-gray**, which is characteristic of **atropine**.

The quantitation method is classic: extraction (ethanol + diethyl ether in the presence of ammonia), dilution (diethyl ether), formation of salts ($H_2SO_4$), return to the bases ($NH_4OH$, $CHCl_3$), and quantitation of the total alkaloid residue by back-titration (acidimetry). The concentration of the total alkaloids, calculated as hyoscyamine must not less than 0.3% (Belladonnae folium), 0.25% (Stramonii folium) and 0.05% (Hyoscyami herba).

**Pharmacological Activity:** The activity of the alkaloids must be distinguished from that of the drugs, and the substantial toxicity of the drugs must be emphasized.

**Pharmacological Activity of the Alkaloids:**
**Atropine:** Atropine and hyoscyamine have the same activity: they are parasympatholytics; hyoscyamine has a stronger activity than rasemic atropine, but it is the latter that is commonly prepared and used.

Atropine is an inhibitor of the muscarinic receptors of the peripheral organs innervated by the parasympathetic post-ganglionic fibers, and of the central nervous system. It acts by competitive and reversible inhibition of acetylcholine binding onto its receptors, and this antagonism leads, in the organs in question, to symphatomimetic-like effects.

- In the heart and after temporary bradycardia, atropine increases the heart rate by supressing vagal inhibition.

-In the blood vessels, the effects on blood pressure are not marked (but with toxic doses, a vasodilatation of cutaneous capillaries is observed, especially on the face).
- In the smooth fibers, atropine induces relaxation and motor inhibition: it decreases intestinal tone as well as the amplitude and frequency of peristaltic contractions, paralyzes the ureters, increases bladder pressure, decreases biliary duct tone, and blocks the bronchoconstricting effect of acetylcholine.

-Secretions are effected: saliva, sweat, gastric, pancreatic, bronchial, and lachrymal secrections are all decreased (toxic doses inhibit sweat production and cause high fever).
- In the eyes, the alkaloid induces a passive mydriasis, by paralyzis of the sphincter pupillae. There is also a paralysis of the accommodation consecutive to the loss of ciliary muscle tone (the eye remains adjusted for distant vision) and an increase in intra-ocular pressure.

In addition to the effects on the autonomic nervous system, atropine has effects resulting from its interaction with central muscarinic receptors. Toxic doses cause substantial excitation: agitation, disorientation, exaggerated reflexes, hallucinations, delirium, mental confusion and insomnia; at low doses, the action is less clear, and tends to be depressant and sedative.

**Scopolamine:** The parasymphatholytic activity of scopolamine is identical to that of atropine, but much less marked, especially on the myocardium. Its effects on the CNS are clear different: sedative, depressant, hypnotic, with amnesia. It potentiates neuroleptics, improves parkinsonism, and its “incapacitating” at high doses. Scopolamine also can be used against motion sickness.

**Pharmacological Activity of the Drugs: Toxicity**

*Atropa belladonna* (fruits, roots, leaves) and *Datura stramonium* (seeds, leaves, roots) are toxic. The ingestion of these plants induce characteristic symptoms, just like drug overdosage : after a brief delay, the face turns red, the mouth and mucosal membranes turn dry, and an intense thirst and muscular weakness develop. The heart rate increases substantially (120-150 beats/min), and mydriasis and hyperthermia are always observed. Hallucinations and delirium follow, accompanied by agitation, loss of motor coordination, sometimes convulsions; sleepiness or a coma is next

Recovery takes time (1-3 days). The altered mental status can drive the patient to random acts with threat to life. The patient must be monitored and maybe treated (charcoal, sedatives). Adminstration of physostigmine (a cholinesterase inhibitor,an alkaloid obtained from *Physostigma venenosum*) is justified in a few special cases.

*Hyoscyamus niger* intoxications are exceptional and not serious. The whole plant has little alkaloidal content and its repulsive odor deters inadverted consumers.

**Uses of the drugs** : The three official drugs are exculively directed to the preparation of galenicals, since the industrial extraction of alkaloids is done from Solanaceae with higher concentrations of total alkaloids. All medicines based on Solanaceae containing tropane alkaloids can induce non-negligible adverse effects. Such medicines contain atropine, therefore they have the corresponding contraindications.

**Belladonna** : The galenicals- tincture, powder, extract- are ingredients of various combinations. Most combinations are proposed for the symptomatic treatment of unproductive coughs, and sometimes for acute congestion of the thoroat and larynx. Other combinations are a short-term symptomatic treatment for constipation : in this case belladonna drugs are combined with Frangulae cortex, Cascara sagrada or Aloe.

**Stramonium** : Official stramonium has practically been abandoned : it is no longer found except in one syrup proposed for thr symptomatic treatment of unproductive coughs.

**Henbane** : Henbane is not used much more than stramonium.

**Uses of the alkaloids** :

**Atropine :** Mostly used as atropine sulfate
Therapeutic indications : The indications for the injectable solutions of atropin sulfate are currently the following :

- A-V block or atrioventicular heart block
- in case of myocardial infarction
- in preanesthesia
- for the symptomatic treatment of acute pain due to functional problems of the gastrointestinal and biliary tracks

- as an antispasmodic for ureteral colic and spasmodic anuria
- as a spesific antidote to treat anticholinesterase poisoning or by parasymphatomimetic or cholinergic medications
- to treat Parkinson's disease

Atropin sulphate in eye drops has the following indications

- to treat uveal inflammations
- to induce cyploplegia for refraction examinations

**Contraindications :**

The activity of the eye prohibits the use of atropine in the case of narrow (closed) angle glaucoma, in which the iris tissue comes in contact with the posterior surface of the cornea, thereby preventing the outflow of the aqueous humor. Other contraindications are a risk of urinary retention of urethro-prostatic origin, gastroesophageal reflux, paralytic ileus, intestinal atony.

Atropine must be used with with caution in case of prostatic hyperplasia, as well as renal, hepatic, or coronary insufficiency, cardiac rhythm abnormalities, chronic bronchitis, or pregnancy. The side effects of atropine limits its use : dryness of the mouth difficulties of accomodation (with eye drops) reddening of the face, constipation, and less frequently tachycardia and palpitations, urinary retention, decrease in broncial secretions etc.

**Hyoscyamine** : It is practically not used in Europe, still used sometimes in U.S.A.

**Scopolamine** : Mostly used as scopolamine hydrobromide.

Scopolamine has been used in the treatment of parkinsonism and of painful spasms. It can be used as a component of preanesthetic medication.

Currently the chief use of scopolamine is for the prevention of motion sickness. The delivery system is a skin patch to be applied behind the ear. This form is contraindicated in case of narrow (closed) angle glaucoma, in the case of urinary retention of urethroprostatic origin, and in the children under 12 years of age.

Scopolamine can induce atropine-like side effects (dryness of the mouth, blurred vision) and potentially, drowsiness. The simultaneous absorption of the alcoholic beverages is to be strictly avoided. Mental confusion is possibly in the elderly.

# Other Solanaceae drugs containing tropane alkaloids

*Duboisia myoporoides* **Duboisiae folium**

**Corkwood tree**

*Duboisia* tree grows wildly in Australia. The leaves are rich in alkaloids (up to 3%) and scopolamine is as by far the chief constituent. The trees are cultivated in Australia. Since the beginning of the 1980's, the leaves of *Duboisia* produced in Australia have been exported toward Europe, mainly to Germany, for extraction. Thus, in 1988-89, about 500 metric tons of leaves were exported.

*Duboisia leichardtii* is another Australian tree which also contains in the leaves in high amounts scopolamine.

# *Mandragora officinarum* Mandragorae radix

## Mandrake root adam otu

The plant is growing in the southern part of Turkey and also in Cyprus.

The roots contain approxymately 0.3% tropane alkaloids with hyoscyamine as by far the chief constituent.

**This plant is known as “manroot plant” because its roots look like a man, and in some districts it is believed that digging up the roots brings unluckiness.**

## *Datura metel* — Daturae meteli folium

This is an annual species native to India and naturalized around the Mediterranean rim. The leaves contain approxymately 0.5% total alkaloids with scopolamine as by far the chief constituent. They can be used for the extraction of alkaloids.

## *Datura innoxia* — Daturae innoxiae fructus

This species is native to Mexico and naturalized around the Mediterranean rim. The leaves are traditionally used forthe hallucinogenic properties.

***Brugmansia sanguinea = Datura sanguinea = Datura arborea***

**Brugmansiae (Daturae) sanguinae folium**

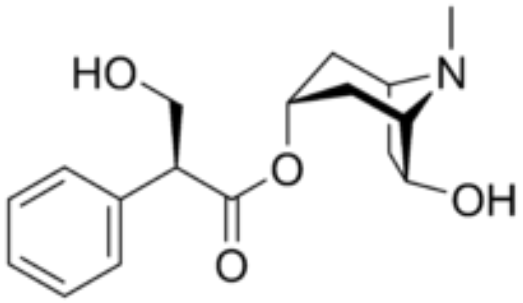
This tree-datura grows wildly in South America. The leaves contain about 0.8% alkaloids, with scopolamine as by far the chief constituent. They can be used for the extraction of alkaloids.

# *Hyoscyamus muticus* Hyoscyami mutici folium
# Egyptian henbane

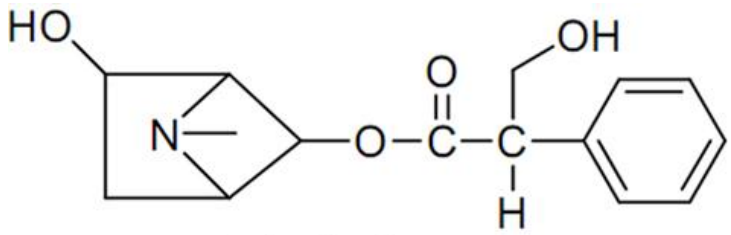
This species, widespread from Egypt to Iran is very closed to *Hyoscyamus niger*. Its leaves, which can be used for the extraction of alkaloids, contain more than 1% total alkaloids, with the hyoscyamine-atropine group dominating.

## *Anisodus tanguticus* **Anisodi radix**

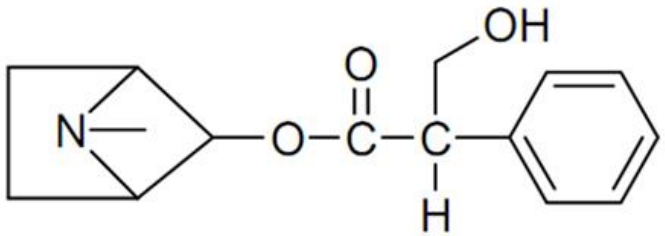
This Chinese plant (zang qie) is an ingredient of traditional anesthetic preparations. Its roots contain alkaloids, namely anisodine and anisodamine, which are structurally related to those of the officinal Solanaceae



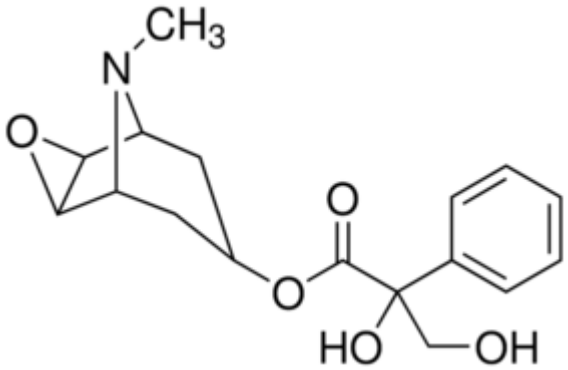

anisodamine




Anisodamine




Atropine




anisodine

Anisodamine, a CNS stimulant, an anticholinergic and an antispasmodic, is used to treat acute enteritis and septic shock (bacillary dysenthery); by dilating the capillaries, it impruves microcirculation. Anisodine is a CNS depressant, it is antagonized by physostigmine, and chiefly used to treat migraine headaches.

# ALKALOID-CONTAINING ERYTHROXYLACEAE : COCA

The use of coca in South America predates the Incan empire : it was nearly 5000 years ago that the natives of the Andes began cultivating, optimizing, and using coca for the production of its leaves. These are traditionally used as a masticatory to abolish hunger and fatigue. The Incas believed that it had a divine origin, and reserved it for religious ceremonies and privileged social classes. Today coca leaves continue to be chewed by thousands of people of the Andes; it is a source of cocaine, an alkaloid without any therapeutic interest today, but whose traffic and illicit use keep growing endlessly.

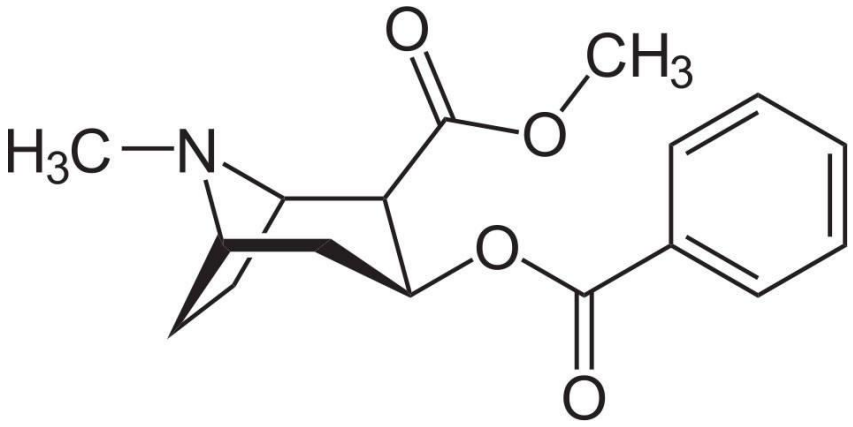
The history of coca cannot be told, even briefly, without mentioning that in 1885, an American pharmacist by the name J. S. Pemberton concocted a «French wine of coca, ideal tonic», an imitation of a preparation marketed in France since 1863 and internationally renowned, namely «vin Mariani». Soon, Pemberton modified his formula, replacing the alcohol with cola extract and the plain water with fizzy water , Coca-Cola was born (A. G. Candler, 1892), and has been used as «brain tonic». At the beginning of the twentieth century (1903) cocaine was removed from the original formula.

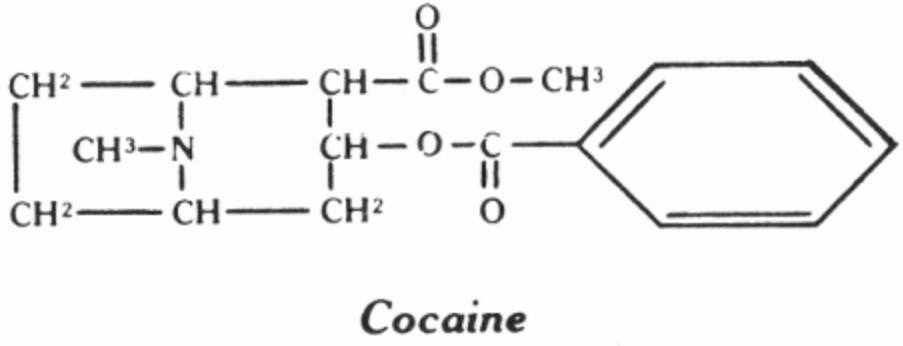
**COCA** ***Eryhroxylum coca***

**Cocae folium**

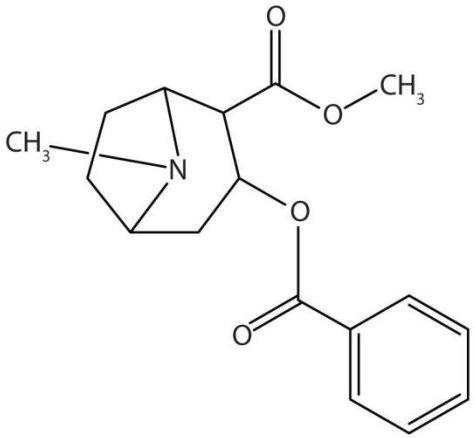
**Chemical Composition** :The drug contains variable quantities of an essential oil which includes methyl salicilate, flavonoids and tannins.

The alkaloid concentration ranges from 0.5 and 1.5% depending on the species, the variety, the geographical origin, and other factors. The chief alkaloid (30 to 50%) is the ester, volatile as a free base, namely cocaine (= methylbenzoylecgonine). It occurs alongside other derivatives of ecgonine : cinnamylcocaine (= methylcinnamylcocaine), truxillines (esters of cinnamic acid), and several pyrrolidines (hygrine, cuscohygrine).




*Cocaine*




# Cocaine structures in different forms

**Pharmacological Properties** : Cocaine is a local anesthetic. As a contact anesthetic, it blocks ion channels in neutronal membranes, and interrupts the propagation of action potentials corresponding to the sensory message. Cocaine is also a parasymphatomimetic : it acts as an adrenergic stimulant by blocking the reuptake of dopamine and noradrenaline at the presynaptic neuron by binding to their transporters.

This adrenergic stimulation causes hyperthermia, mydriasis, and vasconstriction of most of the blood vessels, which increases resistance and contributes to increasing blood pressure. The heart rate increases. Centrally, the stimulation results in a sensation of euphoria with intellectual stimulation, decreased hyperactivity and other effects sought by drug addicts.

**Uses**: Neither coca leaf nor its galenicals are used any more, but the leaves still used to extract cocaine. In the United States, cocaine is sometimes used im combinations for local anesthesia, for example to stitch small wounds.

**Traditional Uses of the Coca Leaf** : The use of the coca leaf as a masticatory is very ancient. Proved by statuettes found in archeological digs, this use predates the Inca domination by a very long time. Traditionally, the coca leaf is chewed, and added alkalis facilitate the release of cocaine. The coca leaf is also used in countries such as Bolivia, in infusion, the common form is the tea bag which yields a stringly aromatic infusion, consumed like coffee or tea (mate de coca).

**Illicit Use of Cocaine** : Cocaine hydrochloride is generally «snorted» by the internasal route, and less often by IV injection. During IV use, the dysphoria which follows the brief euphoria is substantial, and leads some users to stimultaneously consume heroin. Cocaine intake causes euphoria, intellectual stimulation, hyperactivity, a feeling of hyperlucidity, and an accleration in the elaboration of ideas. Cocaine use commonly causes severe headaches and sometimes causes convulsions, delusions and hallucinations suggesting a serios paranoid psychosis are also described.

**Reference Books :**

**Main Book**

**Bruneton, J., Pharmacognosy, Phytochemistry, Medicinal Plants, TEC & DOC Editions, Paris 1999**

**Other Books**


- Hänsel, R., Sticher, O., Pharmakognosie – Phytopaharmazie, Springer Medizin Verlag, Heidelberg 2010
- Evans, W.C., Trease and Evans Pharmacognosy, Elsevier Limited, Edinburgh, London 2002
- Baytop, T., Farmakognozi I-II, İstanbul Üniv. Yay. No. 2783, Eczacılık Fak. No.29, İstanbul 1980
- Tanker, M., Tanker N., Farmakognozi I-II, Ankara Üniv. Eczacılık Fak. Yay. No. 63, Ankara 1990