Pyrrolizidine Alkaloids

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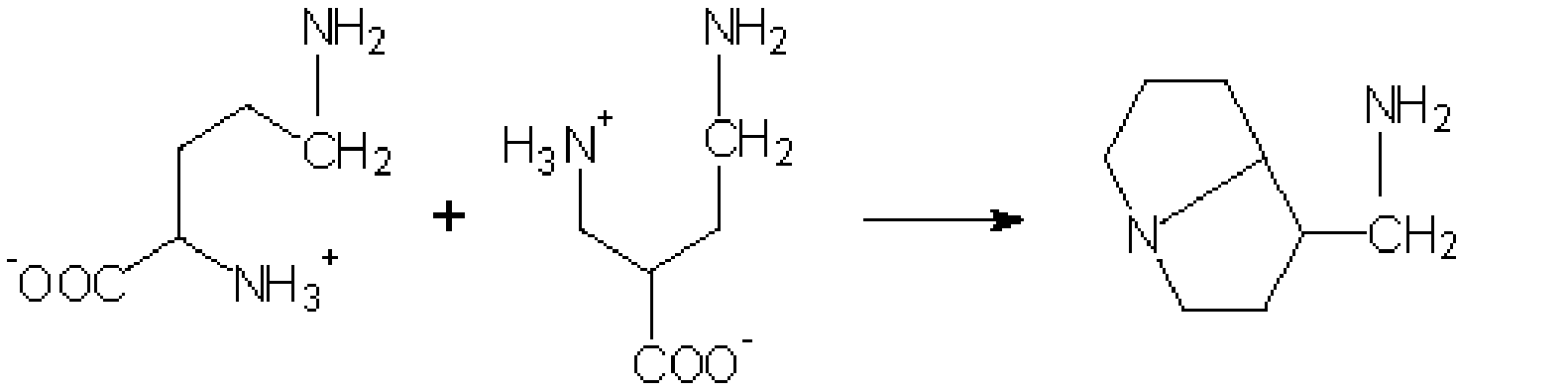
- Pyrrolizidine alkaloids have mainly been found in the (Only) families Asteraceae and Boraginaceae.
- Asteraceae: Doronicum, Eupatorium, Petasites, Senecio, Tussilago and
- Boraginaceae: Alkanna, Anchusa, Cynoglossum, Echium, Heliotropium, Symphytum.
- Drugs containing these alkaloids, Senecio and Symphytum species stand out.
- Their toxicity is more important because several species have no therapeutic value other than their cytotoxic (in vitro) effect.

Although pyrrolizidine alkaloids are not medically important, they are important because they contain toxic hepatotoxic compounds against livestock, such as Senecio (Asteraceae/Compositae) species. Some of the alkaloids also have carcinogenic and mutagenic properties (such as Symphytum species (Boraginaceae), they are found in very small quantities in vegetable crops.

These alkaloids are also known to have an ecological role in protecting butterflies.
Also for humans, chronically; Loss of appetite, causes toxicity with abdominal pain and cirrhosis. They rarely cause acute poisoning. This happens when the plants carrying these alkaloids contaminate the grains (toxicity of pyrrole).

Pyrrolizidine Alkaloids

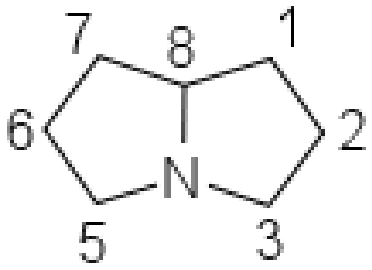
- Alkaloids often exist in the form of esters, so-called «Nesins, nesic acids», these esters are formed with characteristic mono- or dibasic acids.
- These are also biosynthesized from ornithine.
- It is believed that the hepatotoxic effect of senecionine is through the degradation of alkaloids in the liver to strongly alkylated pyrrole esters.



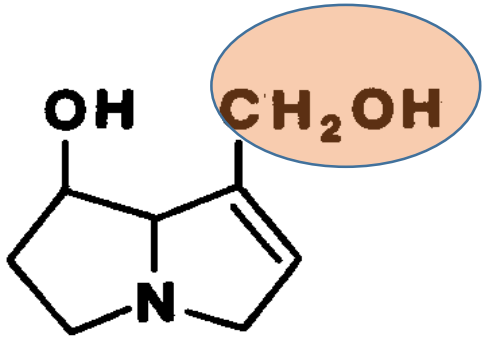
2 x ornithine

pyrrolizidine alkaloid

Pyrrolizidine Alkaloids

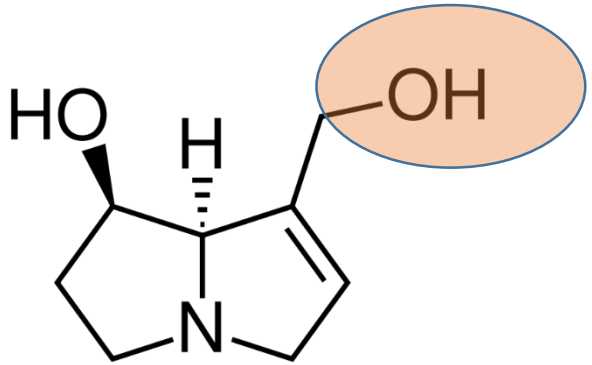


Pyrrolizidine



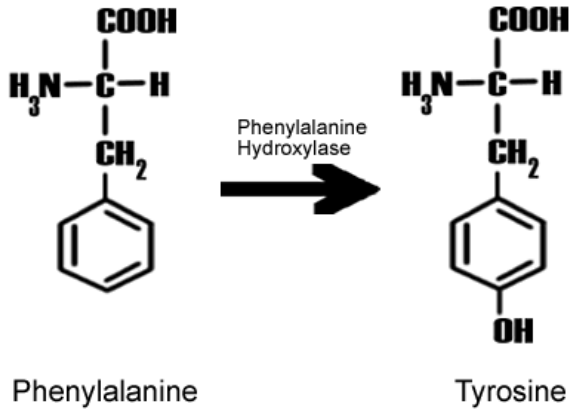
Retronesin

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



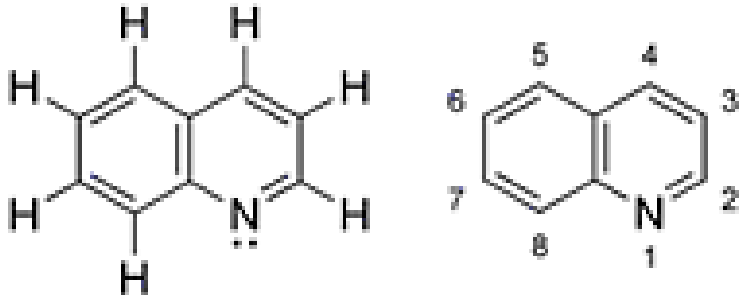
There are many combinations of amino alcohols and nesic acids. There is a hydroxymethyl group at the carbon.

3. Phenylalanine, Tyrosine and Dihydro Phenylalanine Derivative Alkaloids

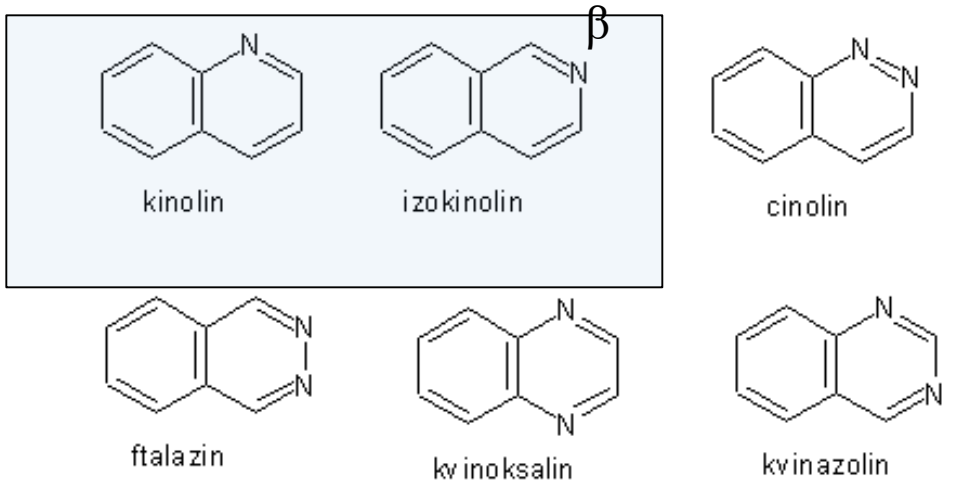


Alkaloids derived from tyrosine (Quinolein and isoquinolein

- ***Herba Ephedra***
- ***Catha***
- ***Rhizoma Sanguinariae***
- ***Papaver* ler....**
- ***Rhizoma Hydrastis***
- ***Radix Colombo***
- ***Curare***
- ***Radix Ipecacuanhae***
- ***Semen Colchici***
- ***Folia Boldo***



- Quinolein; It is one of the benzopyridine isomers. It carries nitrogen in alfa position. The isomer carrying the position beta is called isoquinolein.
- The quinolein ring system is in the structure of many alkaloids.
- (But in Chincona alkaloids, the quinoleine ring is independent).



Herba Ephedra

•Ephedra "Ma Huang"

•Ma: Astringent

•Huang: Yellow (determines the taste and color of the drug)

•** It has been used as a medicine for 5000 years in China.

•** However, in 1923, Ephedrine began to be used in modern medicine.

•** China, Pakistan and India; Ephedra obtained countries

The species growing in China are

•*E. sinica*

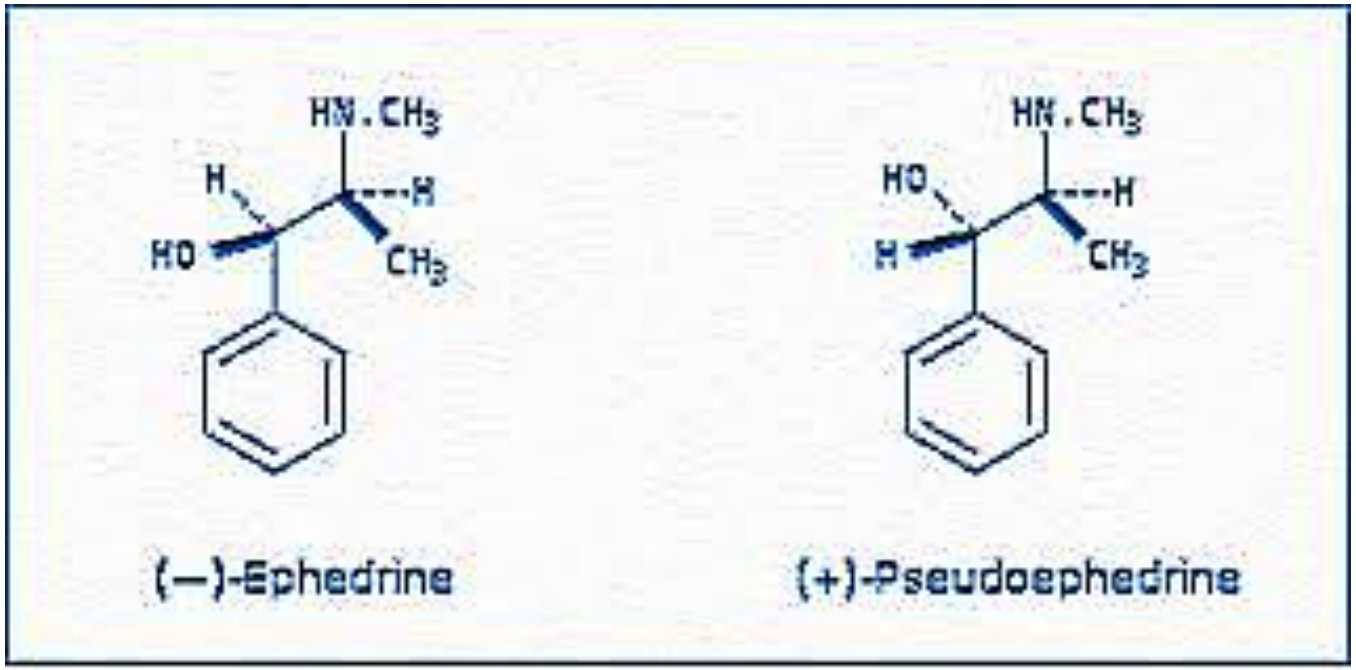
•*E. equisetina*

•*E. gerardiana*

•*E. intermedia*

•*E. major*, which are species grown in India-Pakistan, are used to obtain ephedrine and pseudoephedrine.

•The amount of alkaloids collected in the fall is the highest.


HN.CH3
H
HO
H
CH3
(−)-Ephedrine
HN.CH3
HO
H
H
CH3
(+)-Pseudoephedrine

Ephedrine HCl

•Ephedrine is obtained either by extraction from *Ephedra* species or by chemical synthesis.

•It is obtained from brewer's yeast by fermentation of carbinol used as synthesis starting material.

•Ephedrine; is white, acicular crystals.

•Soluble in water, alcohol, chloroform, ether and petroleum ether.

•Ephedrine; When used orally or parenterally it relaxes bronchial smooth muscle (-adrenergic receptor stimulation)

•It causes vasoconstriction in skin and mucous membranes.

•If taken in high doses, it increases blood pressure, causes headache, dizziness, palpitations and vomiting. It causes nervousness and insomnia by stimulating the central nervous system.

•It is found in preparations used to get rid of excess weight (effects on cardiovascular system and CNS)

Isolation of Ephedrine

Powdered drug

- Na_2CO_3 + Organic solvent (Benzen)
- Extraction

Evaporation (Crude Benzene Extract)

- Diluted acid-- Extraction (Liquid -Liquid)

Aqueos-Acid phase (Benzene phase)

Alkaline base

Organic phase (Chlorophorm)

Ephedrine ve Pseudoephedrine can be separate each other due to their different solubility

- It is used in preparations in the form of
- Ephedrine HCl or
- Ephedrine Sulphate salt.

- It is included in combined preparations in the treatment of cold, flu, high fever, dry cough and bronchitis with shortness of breath.
- Included in asthma preparations (Bronchodilator)

- Pseudoephedrine HCl
- Nasal decongestant; It is used for symptomatic treatment of allergic rhinitis, vasomotor rhinitis, cold and flu.

Catha edulis
Khat veya Abyssinian Tea
Bushmans Tea - Indigenous Medicinal Tree

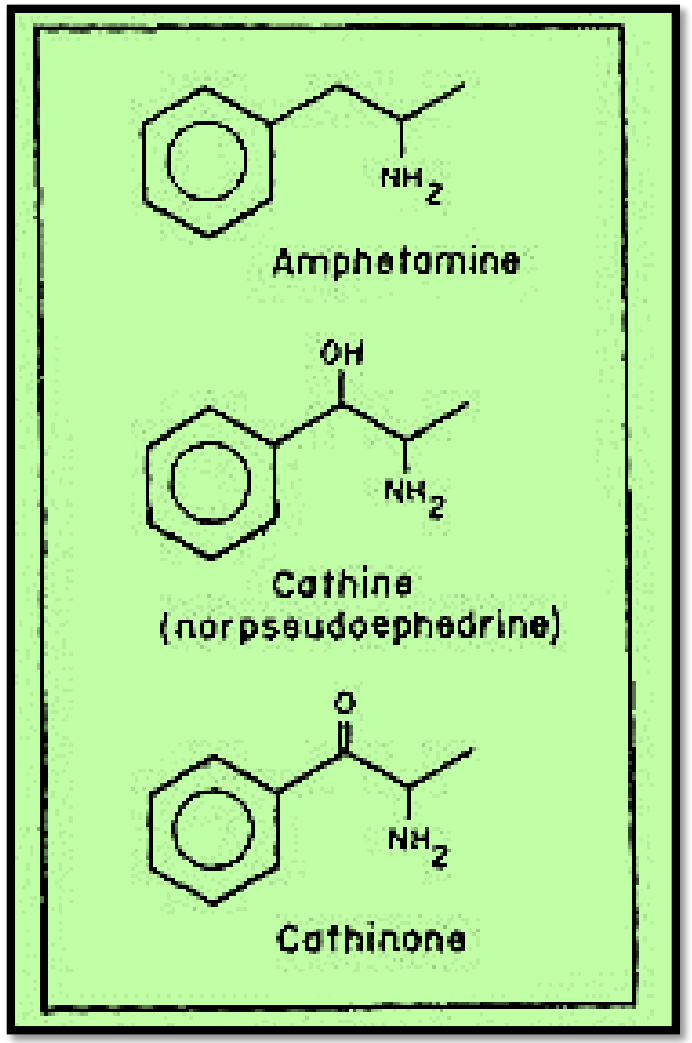
- *Catha edulis* (Celastraceae)
- Growing tropical East Africa
- It is cultured in Ethiopia and Yemen.
- The major substance in fresh and young leaves is cathinone.
- In dry drug and old leaf, cathinone turns into norpseudoephedin and norephedrine.

It is used against hunger and fatigue and as a pleasure (just like Coca).

In African and Arabic countries, fresh leaves are used by people by chewing, chewing is a normal habit.

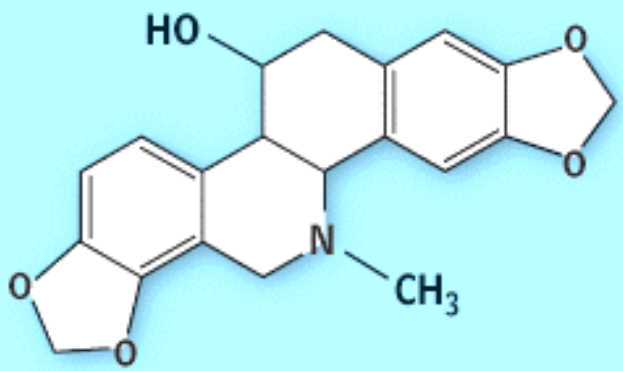
- Cathinon; pharmacologically similar to D-amphetamine. It causes loss of appetite, increase in body temperature, respiratory stimulant, mydriasis, arrhythmia and hypertension.

- 50-200 g leaves of the plant are used by chewing and keeping in the mouth for a while.

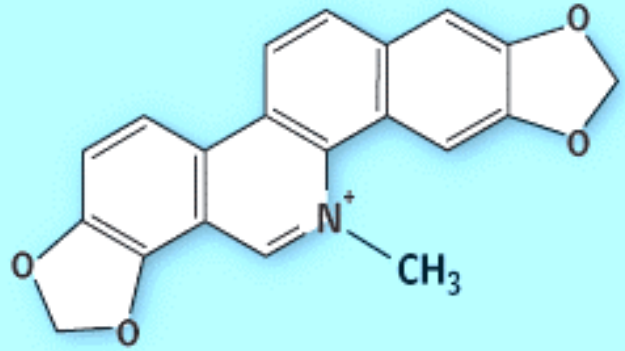


Sangunaria canadensis-Bloodroot

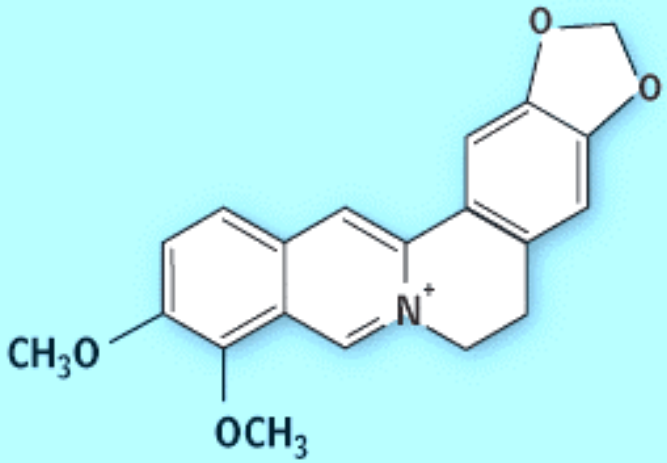
- Papaveraceae family
- A perennial, red latex-producing plant
- It grows widely in North America, stretching from Florida to Mississippi.
- Usually alkaloids located in the rhizome. 4-7%.
- Main components: Sangunarin-benzophenanthridine alkaloid (50%) causes mating in chromosomes just like colchicine.
- In America, this herb is added to syrups as an additive. It is red in color.
- There is also a red resin and starch.



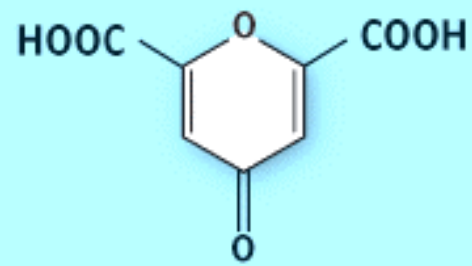
chelidonin



sanguinarin

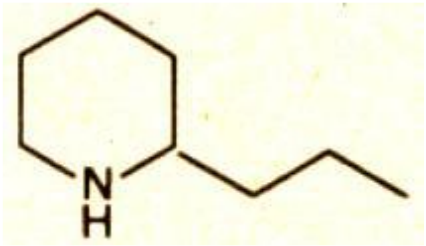


berberin



kyselina chelidonová

Conium maculatum
Poison Hemlock



koniin

Unripe fruits contain 1.5% alkaloids. Like Major alkaloids, Coniine, Conisein, Conhydrin.

Although the use of the plant is now abandoned, it must be known due to its toxicity. The fruit of the plant of the Apiaceae family, famous for causing the death of Socrates, was used for its antineuralgic properties.