PharmacognosyIII

Lec. 3 **3rd stage 2nd semester** **Year 23-24**

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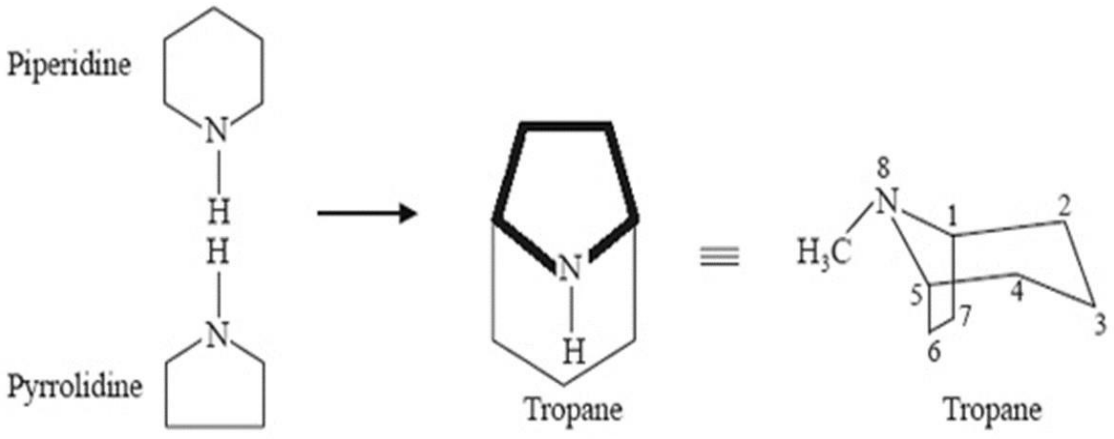
ALKALOIDS

Tropane alkaloids

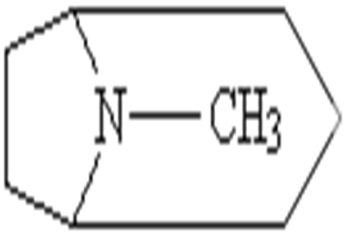
- The principal alkaloids of medicinal interest in this group are (−)-hyoscyamine, a racemic mixture of atropine which is more stable and hyoscine (scopolamine). The compounds are esters and are hydrolyzed by heating at 60°C with baryta water. Atropine yields tropic acid and tropine. Hyoscine gives tropic acid and oscine (scopine is actually formed by enzymatic hydrolysis but the chemical treatment converts it to the more stable geometric isomer, oscine).
- They are extremely poisonous.

Tropane is a dicyclic compound found by the condensation of a pyrrolidine precursor (ornithine) with three carbon atoms derived from acetate.

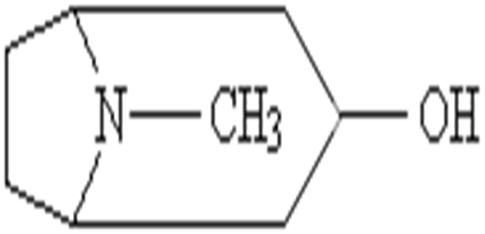
Both pyrrolidine and piperidine ring systems can be recognized in the molecule.



The 3-hydroxy derivative of tropane is known as tropine.

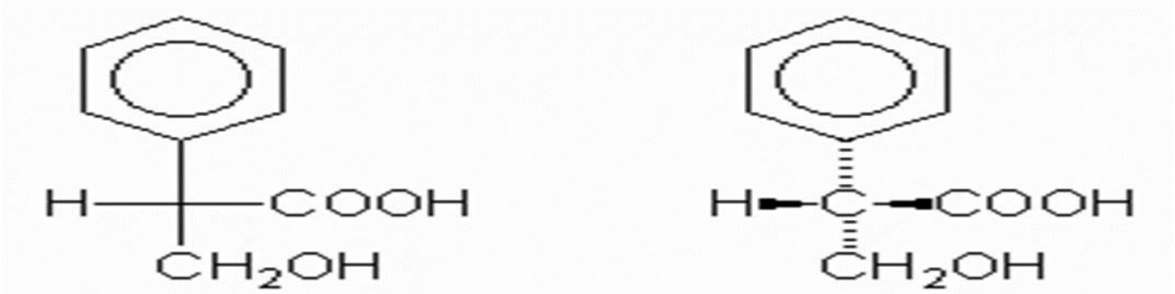


Tropane



Tropine

Its esterification with (-)-tropic acid yields hyoscyamine (tropine-tropate) ester, which may be racemized to form atropine.

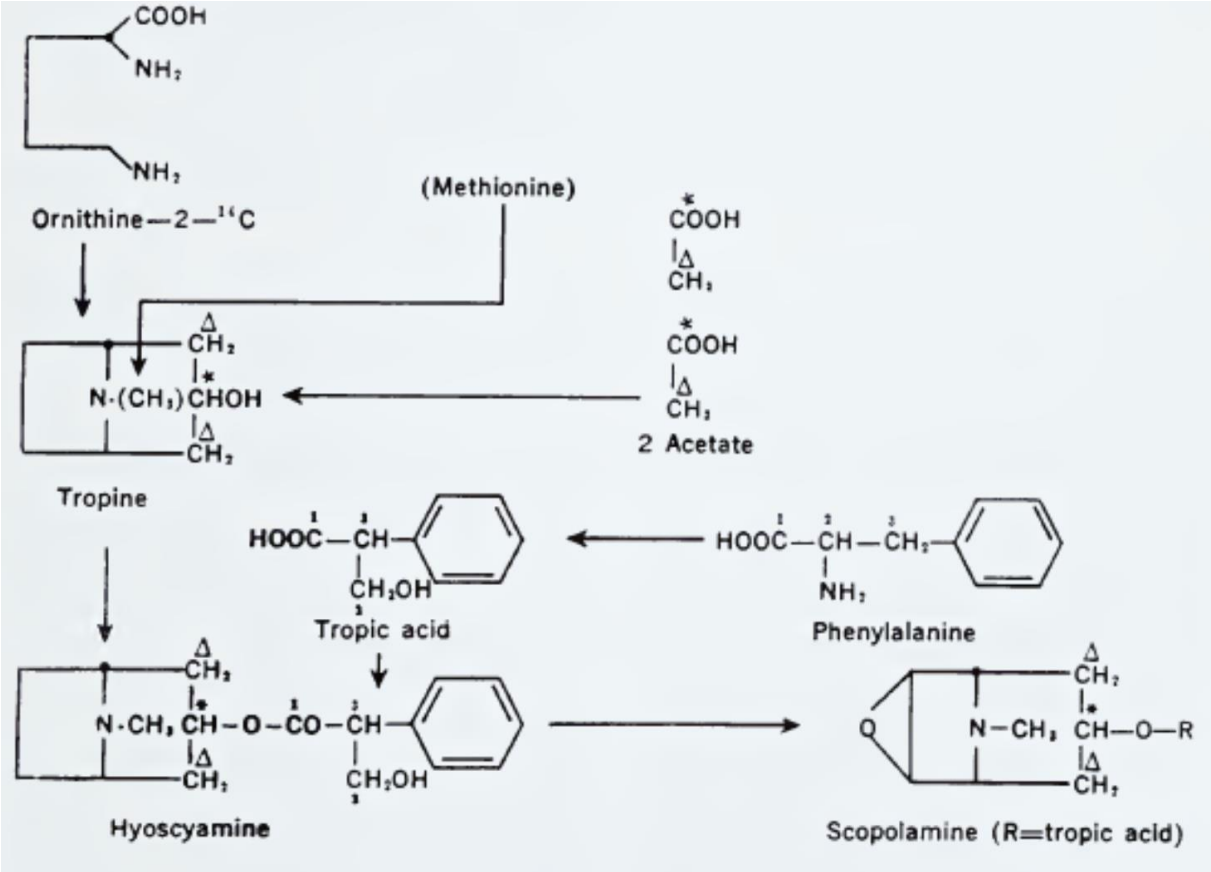


(S)-(-)-tropic acid
(S)-(-)-3-hydroxy-2-phenylpropanoic acid

Biosynthesis of tropane alkaloids:

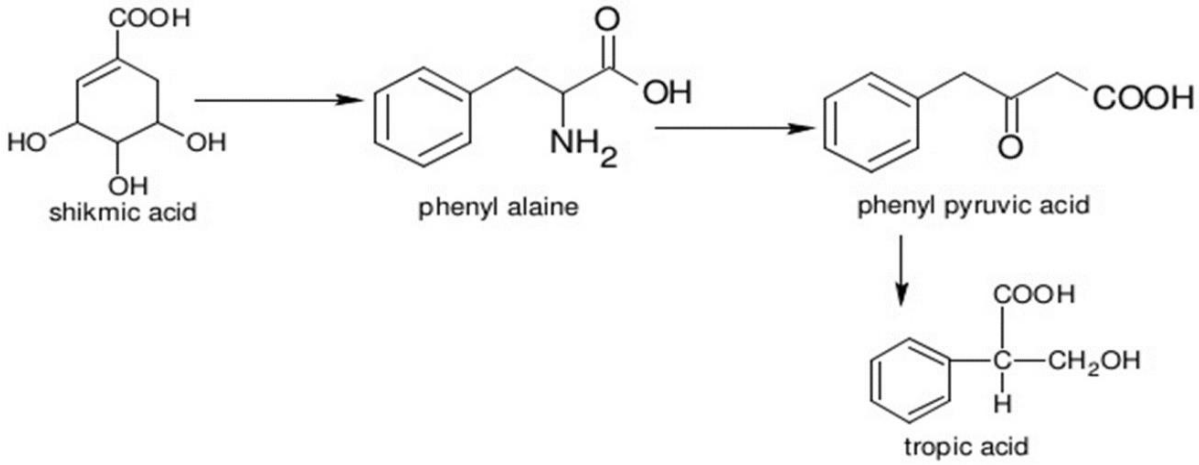
Hyoscyamine and Scopolamine.

Feeding studies with labeled ornithine have revealed that this amino acid is incorporated stereospecifically to form the pyrrolidine ring of tropine. The remaining three carbon atoms derive from acetate, thus completing the piperidine moiety. Methylation results via transmethylation front a suitable donor, e.g., methionine, to complete the tropine nucleus. Esterification of tropic acid with tropine produces hyoscyamine.



Biosynthesis of hyoscyamine and scopolamine

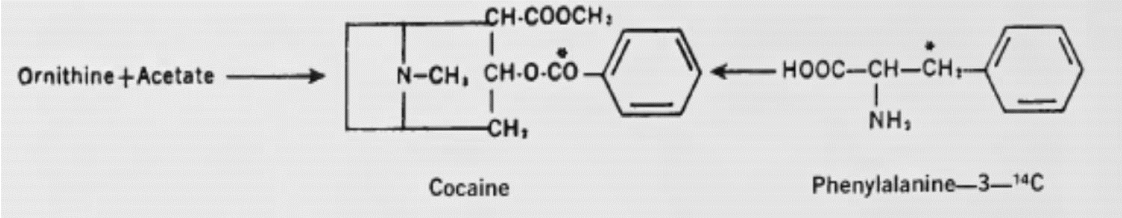
Tropic acid is formed by an intramolecular rearrangement of phenyllactate.



- The (-)-isomer is hyoscyamine, the (+)-isomer is not found in the plant, and the (±) isomer is atropine.

- Hyoscyamine is more active than atropine.
- Hyoscine (scopolamine) is an epoxide of atropine and it is the (-)-isomer.
- The (±)-isomer of scopolamine is atropine.
- All together over 200 tropane alkaloids have now been recorded. Semisynthetic derivatives e.g. N-butyl bromide (buscopan), which have medicinal importance.

Cocaine: Feeding experiments with Erythroxylon coca have shown that phenylalanine-3-14C is incorporated into cocaine, the radioactivity being located in the benzoyl group. Presumably, the ecgonine moiety derives from ornithine and acetate in a manner analogous to tropine biosynthesis.



Drugs containing tropane alkaloids:

Belladonna (Deadly night shade leaf)

- Two parts of belladonna are official, the root and the leaf.
- It is the dried leaf or root of *Atropa belladonna,* F: Solanaceae.
- The root is richer than the leaf in alkaloids. The root contains 0.6% while the leaves 0.4%.
- Most of the alkaloids found in the leaf are: (-) hyoscymine, and traces of atropine in fresh plants. Atropine is formed by racemization during the extraction process. Small amount of other bases are found in the root but not in the leaf; these include the anhydride of atropine

(apoatropine) and it's stereoisomer belladonnine and scopolamine (hyoscine).

Uses

Belladonna acts as a parasympathetic depressant which accounts for its use as a spasmolytic agent. It possesses anticholinergic properties and is used to control excess motor activity of the gastrointestinal tract and spasm of the urinary tract.

Hyoscyamus or Henbane

- The dried leaves and flowering tops of *Hyoscyamus niger*, F: Solanaceae.
- It contains 0.04% of total alkaloids calculated as hyscyamine, the drug also contains hyoscine and traces of atropine.

Uses: Hyoscyamus is a parasympatholytic, but the crude drug is rarely employed in medicine today.

Egyptian Henbane

- It is the dried leaves and flowering tops of *Hyoscyamus muticus*, yield about 1.5% of total alkaloids consisting largely of hyoscyamine.
- The plant is indigenous to and cultivated in Egypt.
- The plant is used perhaps entirely for the extraction of its alkaloids.

Stramonium

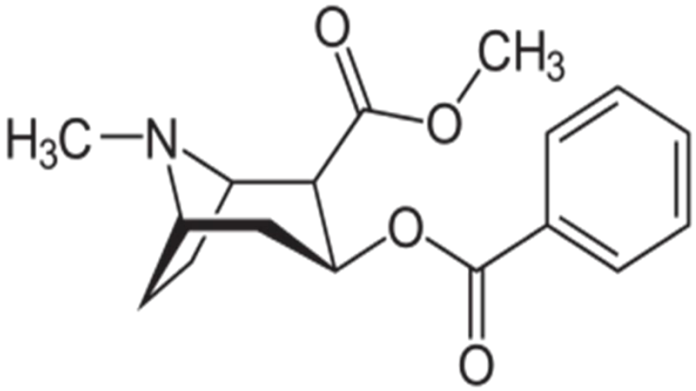
- It is the dried leaves and flowering tops of *Datura stramonium*, F: Solanaceae.
- It contains up to 0.4% of total alkaloids calculated as hyoscyamine.

Use:

- Stramonium is an anticholinergic having an action like that of belladonna.
- Powdered Stramonium is an ingredient in preparations that are intended to be burned and the vapor inhaled for the relief of asthma. These so-called asthma powders. Food and Drug Administration placed Stramonium-containing asthma powders in the category of drugs that could be dispensed only on prescription.

- All these drugs are used as mydriatic (dilate the pupils of the eyes) and as antispasmodic, and as parasympatholytic or anticolinergic and to decrease all the secretions (sweat, saliva, milk etc…).
- It is used as adjunctive therapy in the treatment of peptic ulcer, functional digestive disorder, and diarrhea.

Cocaine



- It is a habit-forming drug from the leaves of *Erythroxylum coca*, F: Erythroxylaceae.
- The plant is also called coca or coca leaves.
- Coca leaves contain 3 basic types of alkaloids:

1. Derivatives of ecgonine (cocaine, cinnamyl cocaine, α and β truxilline).
2. Tropine (tropacocaine, valerine).
3. Hygrine (Hygroline, cuscohygrine).

- Only the ecgonine derivatives are commercially important.
- The most important of these is cocaine.
- Cocaine is the methyl ester of benzoyl ecgonine.
- Cocaine and cocaine hydrochloride, are agents of abuse, are generally inhaled or sniffed and are rapidly absorbed across the pharyngeal mucosa, resulting in cerebral stimulation and euphoria.
- Cocaine hydrochloride is a local anesthetic.
- It is applied topically to mucous membrane as 2-5% solution.