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Organic Pharmaceutical Chemistry II

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SOLANACEOUS ALKALOIDS AND ANALOGS

The solanaceous alkaloids, represented by:

- (-)-hyoscyamine
- Atropine [(±)-hyoscyamine], and
- Scopolamine (hyoscine).

What are the differences?

Structural Considerations

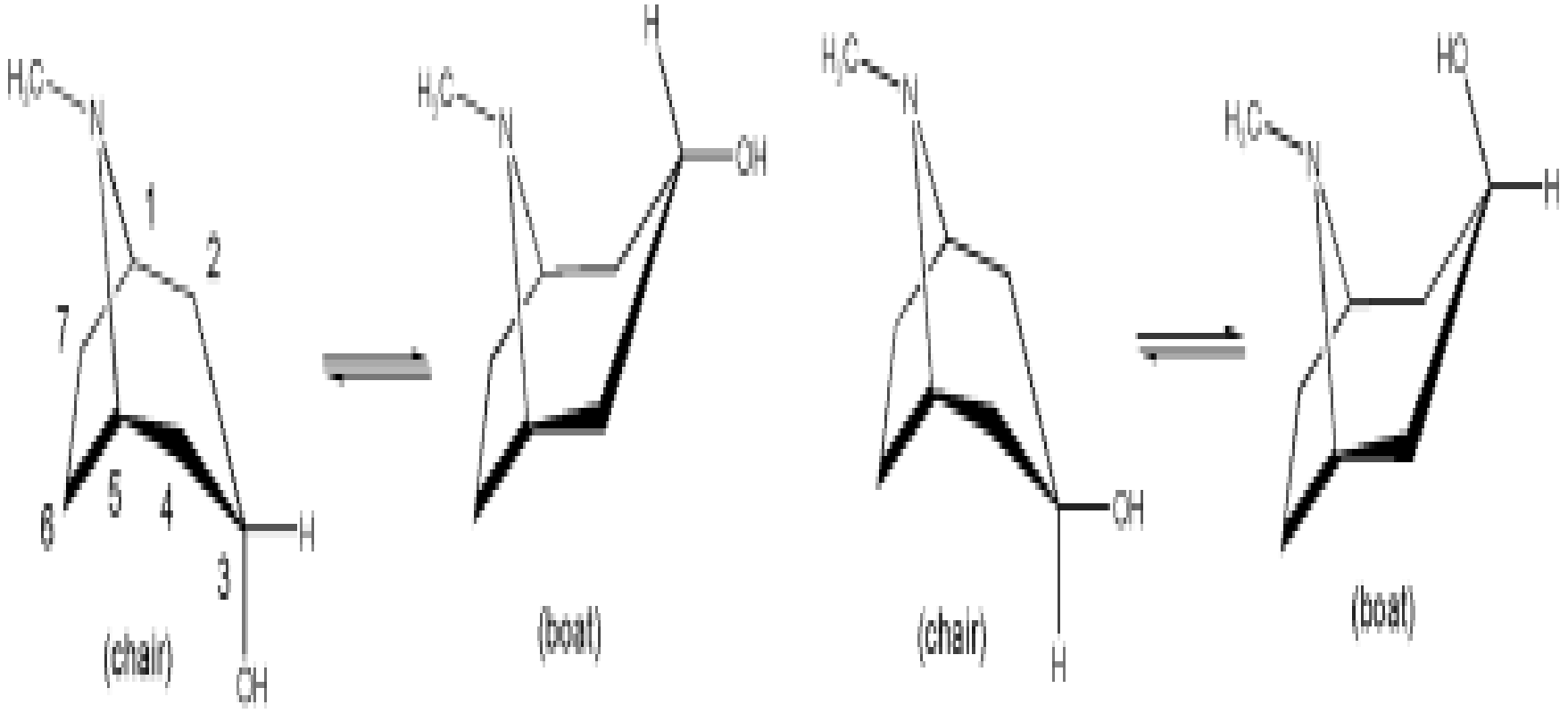
- All of the solanaceous alkaloids are esters of the bicyclic aminoalcohol 3-hydroxytropane or of related aminoalcohols.

- The chair conformation is accepted because this form has the lowest energy requirement.

Structural Considerations

- Quaternization of the tertiary amine produces variable effects in terms of increasing potency.

- In general, quaternization reduces parasympathomimetic action much more than parasympatholytic action.



TROPINE
(3α-Hydroxytropane or
3α-Tropanol)

PSEUDOTROPINE
(3β-Hydroxytropane or
3β-Tropanol)

- Can quaternary ammonium compounds be absorbed? Explain how?

Quaternary ammonium compounds

- Quaternary ammonium compounds combine reversibly with endogenous substances in the gut, such as mucin, to form neutral ionpair complexes.
- These complexes penetrate the lipid membrane by passive diffusion.

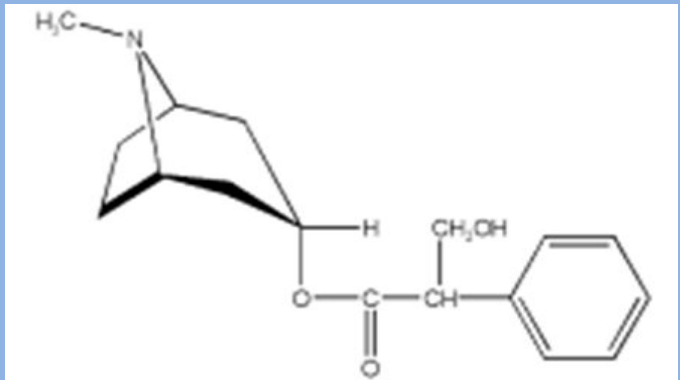
Products

Atropine Sulfate , USP:

- Atropine is administered in small doses before general anesthesia to lessen oral and air passage secretions and, when administered with morphine, to lessen the respiratory depression induced by morphine.

Atropine Sulfate , USP

- Atropine is a specific antidote to prevent the muscarinic effects of ACh accumulation
- Atropine does not protect against respiratory failure caused by depression of the respiratory center and the muscles of respiration.



ATROPINE
(or hyoscyamine)

Hyoscyamine, USP:

- Hyoscyamine is the levo form of the racemic mixture known as atropine.

- By comparing the activities of (-)-hyoscyamine, (+)-hyoscyamine, and the racemate (atropine).

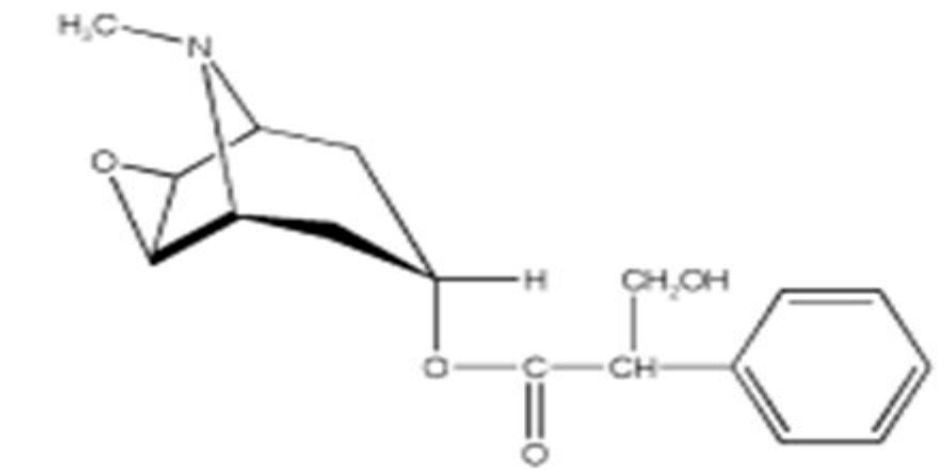
Hyoscyamine, USP:

- The greater peripheral potency for the (-) isomer and twice the potency of the racemate.

- What does this mean? Why not to use the (-) isomer in stead of the racemate mixture?

Scopolamine (hyoscine):

- Scopolamine is the levo component of the racemic mixture that is known as atroscine.
- The alkaloid is racemized readily in the presence of dilute alkali.



SCOPOLAMINE
(or hyoscine)

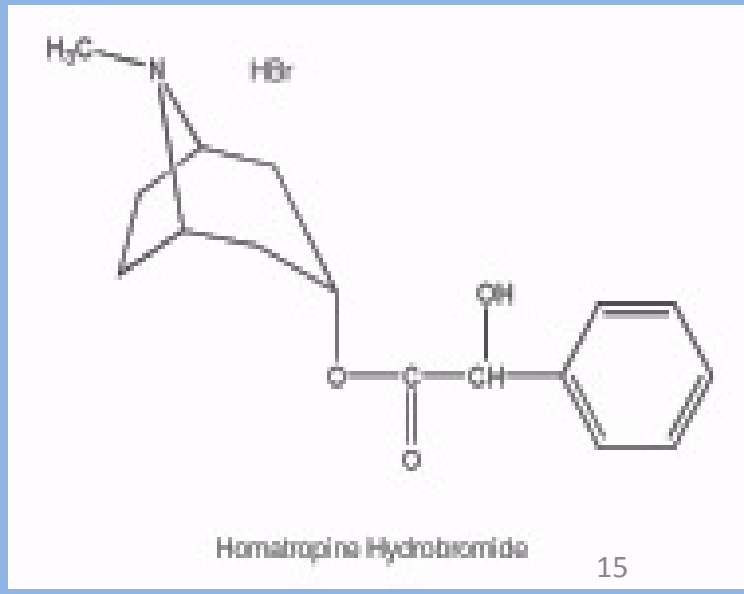
Scopolamine (hyoscine):

- Scopolamine differs markedly from atropine in its action on the higher nerve centers.

- A sufficiently large dose of scopolamine will cause an individual to sink into a restful, dreamless sleep for about 8 hours.

Homatropine hydrobromide:

- Homatropine hydrobromide is used topically to paralyze the ciliary structure of the eye (cycloplegia) and to effect mydriasis.
- In the eye, it acts more rapidly but less persistently than atropine.



Homatropine Hydrobromide

Ipratropium bromide:

- Ipratropium bromide is used in inhalation therapy to produce dilation of bronchial smooth muscle for acute asthmatic attacks.
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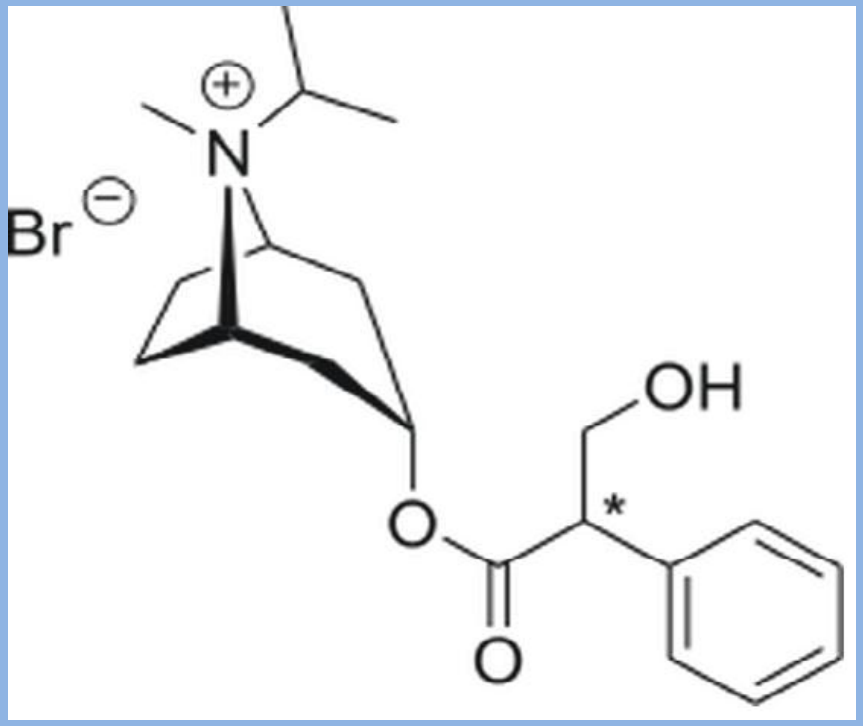

Ipratropium bromide:

- The drug produces bronchodilation by competitive inhibition of cholinergic receptors bound to smooth muscle of the bronchioles.
- Ipratropium may also act on the surface of mast cells to inhibit ACh-enhanced release of chemical mediators.

References:

- **Reference text**: Wilson and Gisvold Textbook of Organic Medicinal and Pharmaceutical Chemistry; Delgado JN, Remers WA, (Eds.); 12th ed., 2011.