College of Pharmacy
Organic Pharmaceutical Chemistry II

Lec4: Synthetic Cholinergic Blocking Agents and Products; Ganglionic Blocking Agents (Neuromuscular Blocking Agents).

SYNTHETIC CHOLINERGIC BLOCKING AGENTS

A. Aminoalcohol Esters

B. Aminoalcohol Ethers

C. Aminoalcohols

D. Aminoamides

E. Miscellaneous

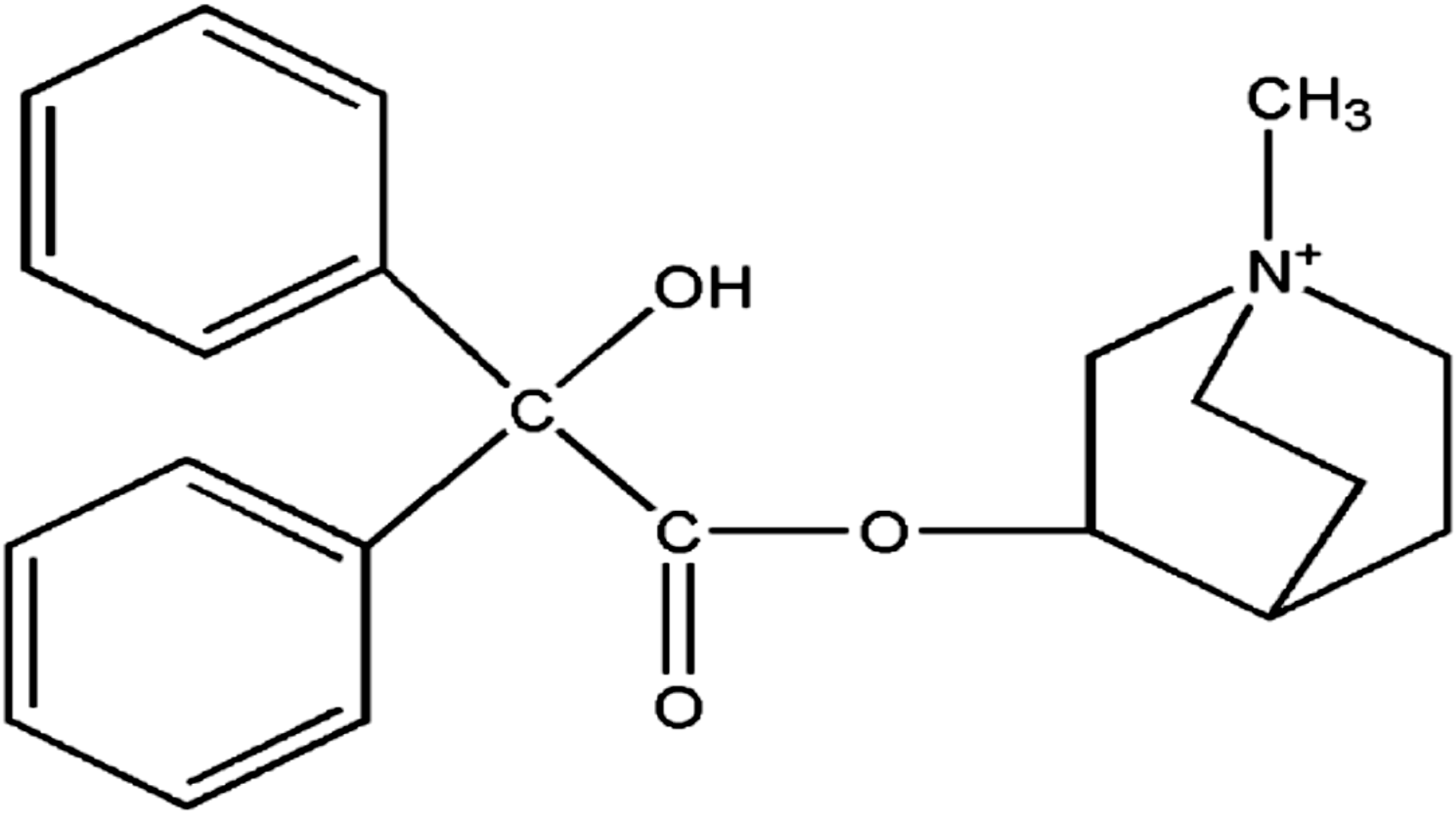
Aminoalcohol Esters

- ***Clidinium Bromide, USP:***

➢Clidinium bromide is combined with the anxiolytic drug chlorodiazepoxide in “Librax”.

➢Clidinium bromide works in IBS by decreasing gastrointestinal motility. Chlordiazepoxide is an anti-anxiety medication.

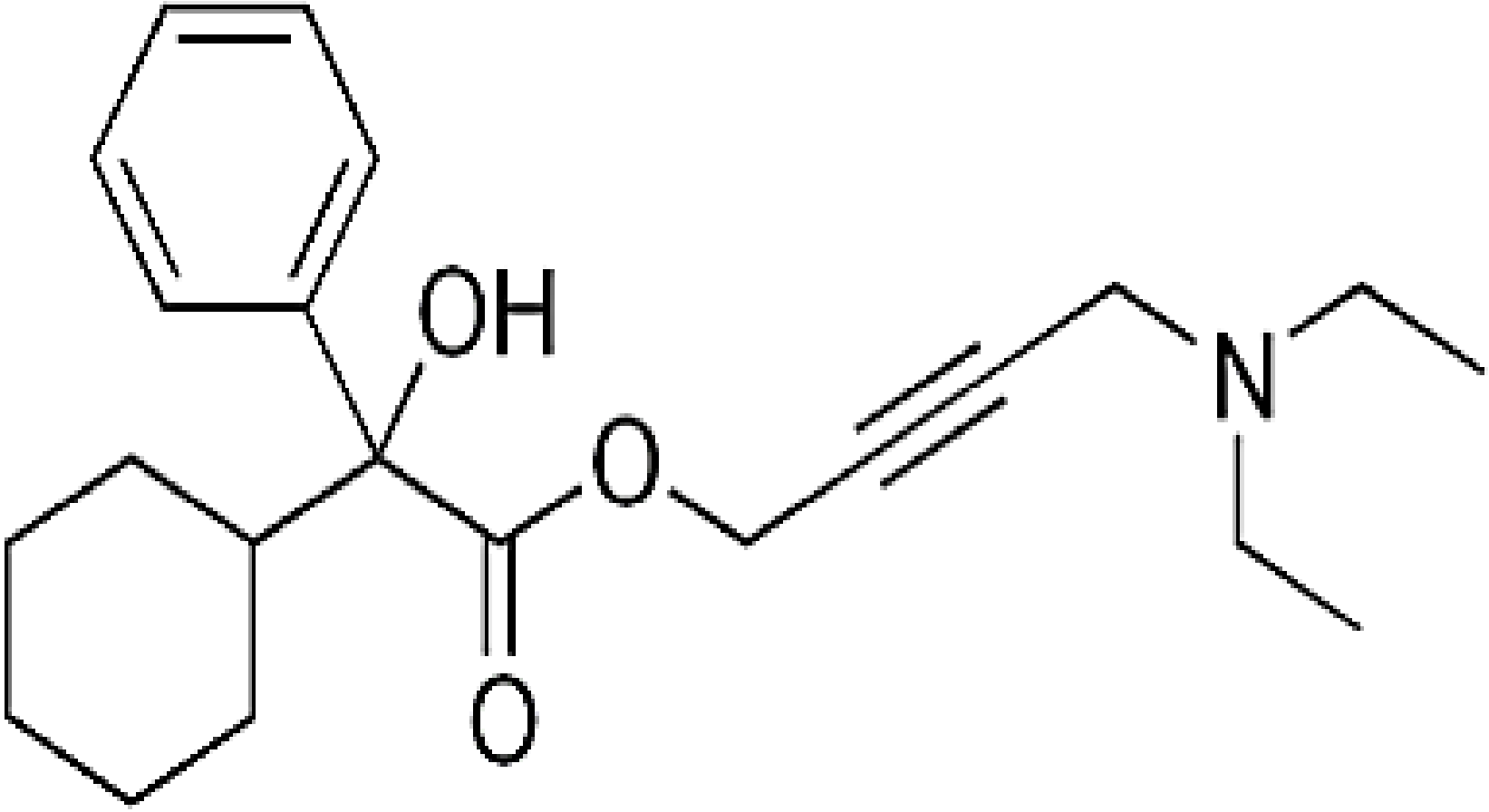
➢Chlordiazepoxide’s use in IBS is thought to be due to its calming ability for patients that have IBS symptoms that are worsened by anxiety.



Clidinium Bromide

Oxybutynin:

- Acts on bladder smooth muscles.
- This reduction in smooth muscle tone allows for greater volumes of urine to be stored in the bladder, which results in less urinary incontinence, urgency, and frequency.
- Oxybutynin acts as a competitive antagonist on M1, M2, and M3 receptor subtypes.

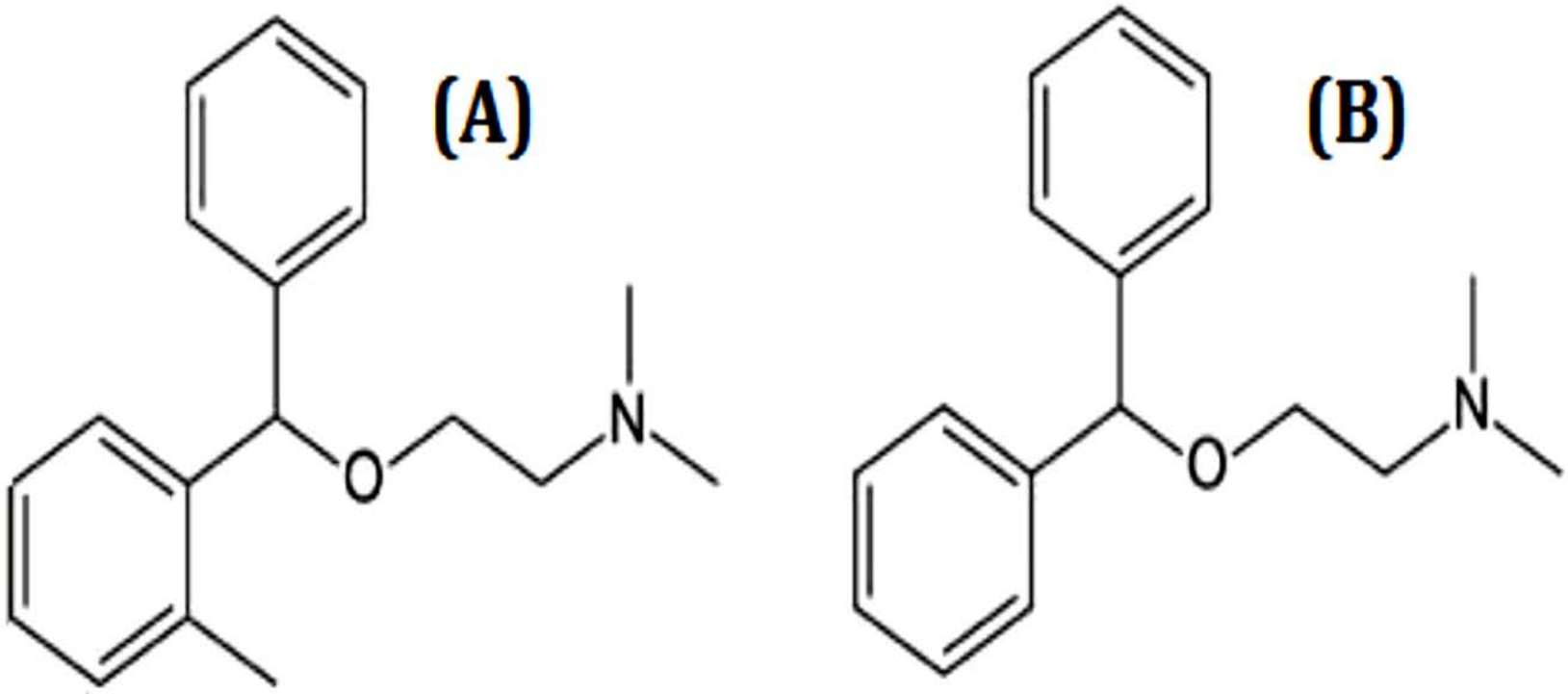


Oxybutynin

Aminoalcohol Ethers

- ***Orphenadrine Citrate:***

  - It does reduce voluntary muscle spasm, however, by a central inhibitory action on cerebral motor areas, a central effect similar to that of atropine.
  - Is closely related to diphenhydramine structurally but has much lower antihistaminic activity and much higher anticholinergic action.



Similarity of structural formulae of (A) orphenadrine, (B) diphenhydramine.

Aminoalcohols

- Several of the drugs in this class of antimuscarinic agents possess bulky groups in the vicinity of hydroxyl and cyclic amino functional groups.
- These compounds are similar to the classic aminoester anticholinergic compounds derived from atropine.

Aminoalcohols

- All of the aminoalcohols used for paralysis agitans are tertiary amines. Because the desired locus of action is central, formation of a quaternary ammonium moiety destroys the antiparkinsonian properties.
- These aminoalcohols have been quaternized, however, to enhance the anticholinergic activity to produce an antispasmodic and antisecretory compound, such as tridihexethyl chloride.

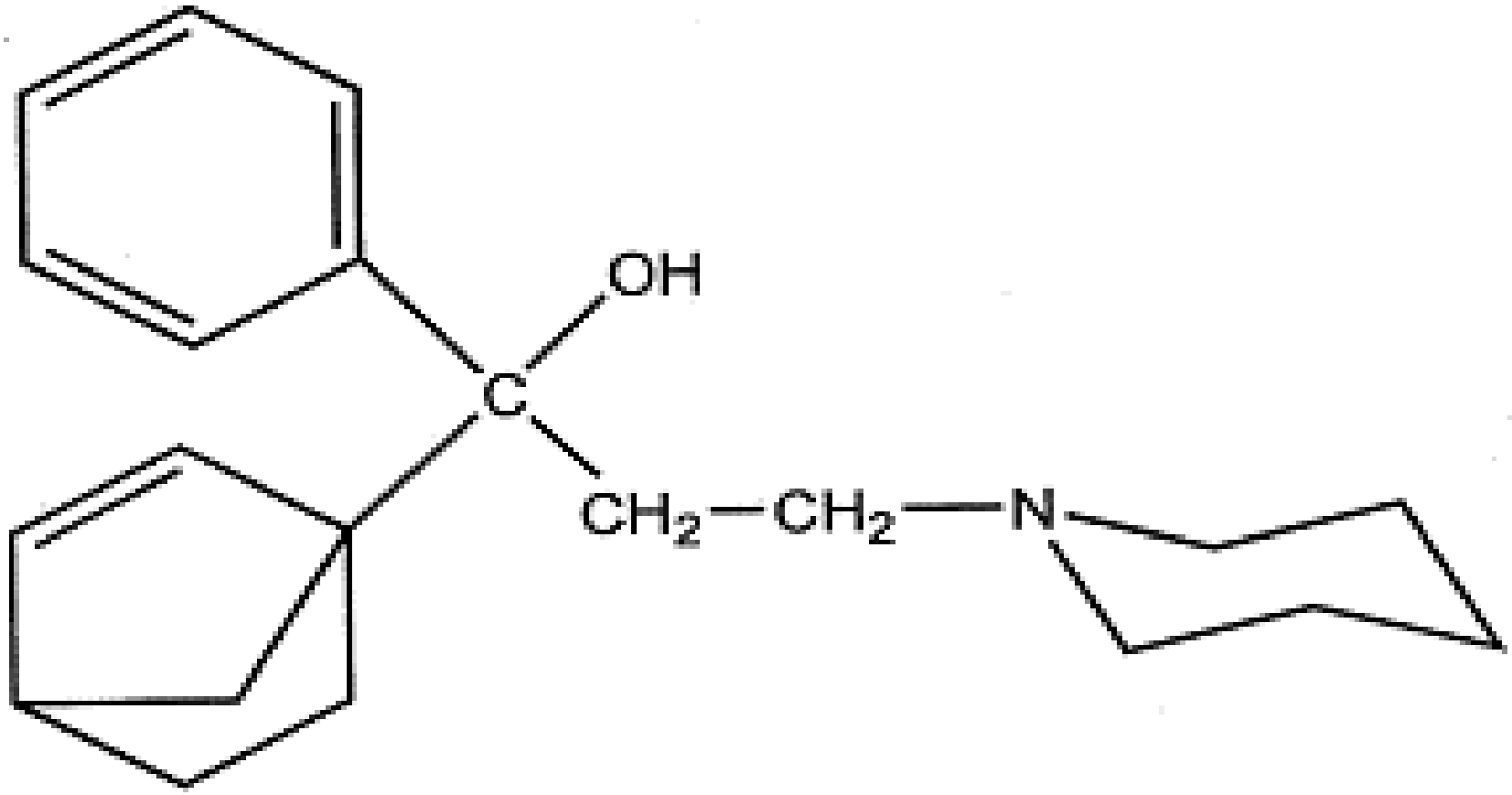
Aminoalcohols

- ***Biperiden Hydrochloride, USP:***
- Biperiden hydrochloride (Akineton®) is used in all types of Parkinson disease and helps to eliminate akinesia, rigidity, and tremor.
- It is also used in drug-induced extrapyramidal disorders to eliminate symptoms and permit continued use of tranquilizers.

Aminoalcohols

- ***Biperiden Hydrochloride, USP:***
- Biperiden is also of value in spastic disorders not related to Parkinsonism, such as multiple sclerosis, spinal cord injury, and cerebral palsy.

- It is contraindicated in all forms of epilepsy.



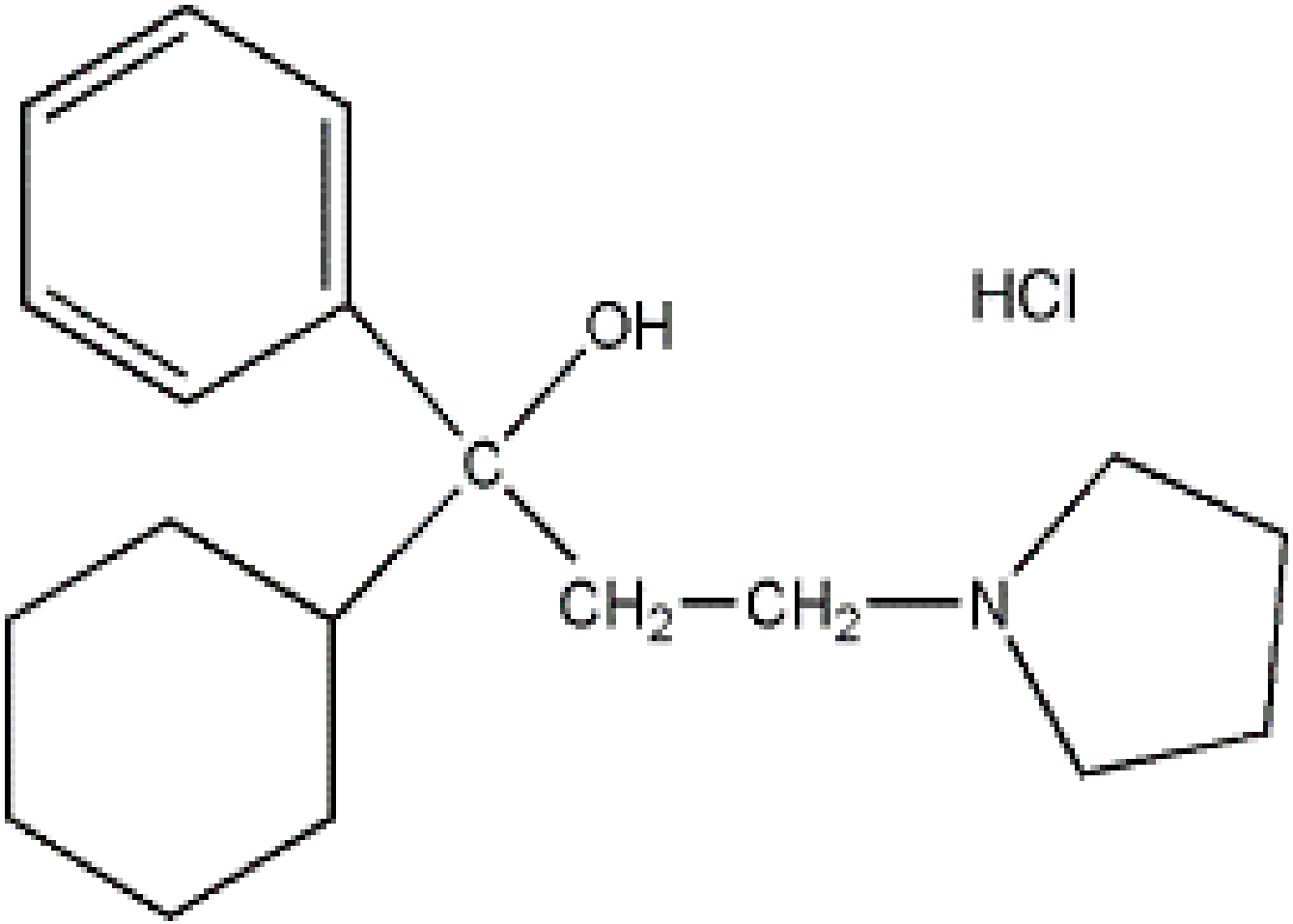
Biperiden

Aminoalcohols

- ***Procyclidine Hydrochloride, USP:***

Procyclidine hydrochloride, (Kemadrin), is an effective peripheral anticholinergic and, indeed, has been used for peripheral effects, its clinical usefulness lies in its ability to relieve voluntary muscle spasticity by its central action.

Therefore, it has been used with success in the treatment of Parkinson syndrome.



Procyclidine Hydrochloride

Aminoamides

- From a structural standpoint, the aminoamide type of anticholinergic represents the same type of molecule as the aminoalcohol group, with the important exception that the polar amide group replaces the corresponding polar hydroxyl group.

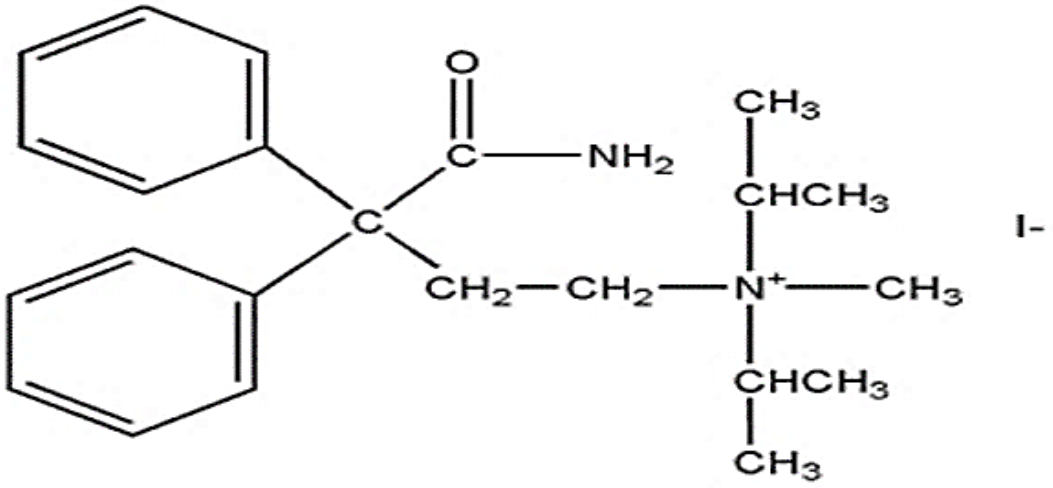
- Aminoamides retain the same bulky structural features found at one end of the molecule or the other in all of the active anticholinergics.

Aminoamides

- ***Isopropamide Iodide, USP:***
- ***Stelabid® (Isopropamide Iodide/Trifluoperazine HCI)***
- Isopropamide iodide is a potent anticholinergic, producing atropine-like effects peripherally.
- Even with its quaternary nature, it does not cause sympathetic blockade at the ganglionic level except at high dosages.
- Its principal distinguishing feature is its long duration of action.
- A single dose can provide antispasmodic and antisecretory effects for as long as 12 hours.

Aminoamides

- ***Isopropamide Iodide, USP:***
- It is used as adjunctive therapy in the treatment of peptic ulcer and other conditions of the GI tract associated with hypermotility and hyperacidity.



Isopropamide Iodide

Aminoamides

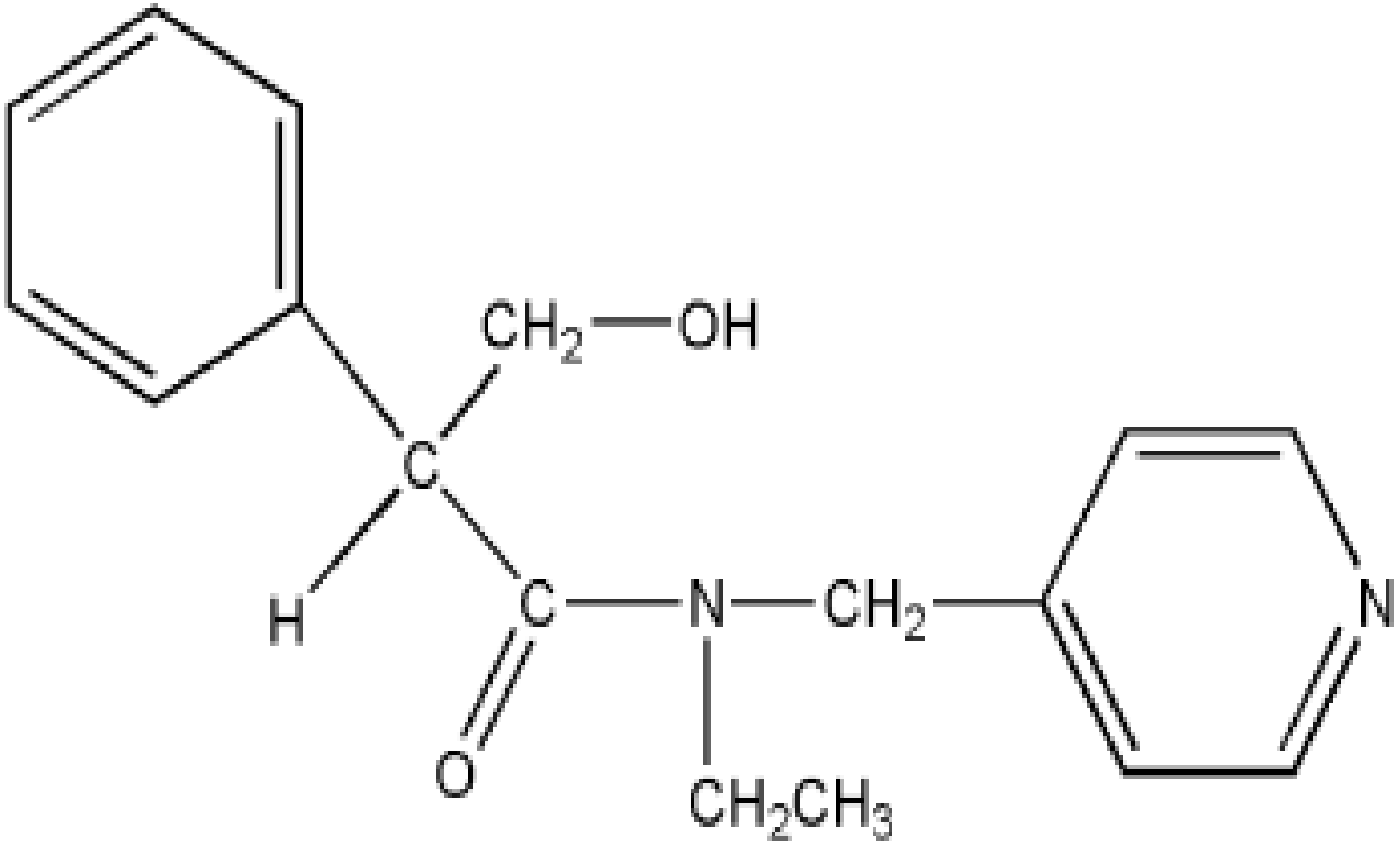
- ***Tropicamide, USP:***

- Tropicamide, (Mydriacyl), is an effective anticholinergic for ophthalmic use when mydriasis is produced by relaxation of the sphincter muscle of the iris, allowing adrenergic innervation of the radial muscle to dilate the pupil.

Aminoamides

- ***Tropicamide, USP:***

- Its maximum effect is achieved in about 20 to 25 minutes and lasts for about 20 minutes, with complete recovery in about 6 hours.
- Its action is more rapid in onset and wears off more rapidly than that of most other mydriatics.
- To achieve mydriasis, either 0.5% or 1% concentration may be used, although cycloplegia is achieved only with the stronger solution.



Tropicamide

Miscellaneous

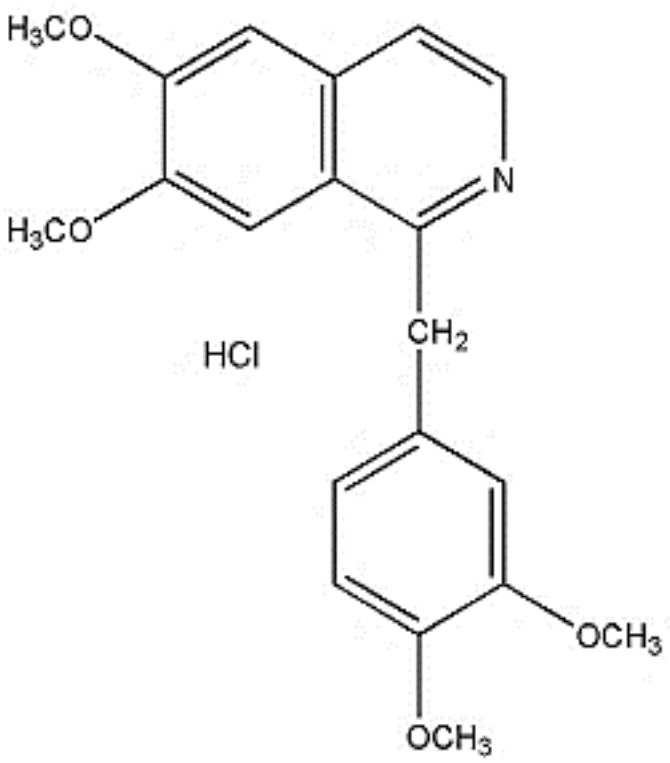
- ***Papaverine Hydrochloride, USP:***
- Papaverine hydrochloride has a main effect on smooth muscle as a spasmolytic.
- It is acting as a direct, nonspecific relaxant on vascular, cardiac, and other smooth muscle.
- Because of its broad antispasmodic action on ACh muscarinic receptors, it is often called a nonspecific antagonist.

Miscellaneous

- ***Papaverine Hydrochloride, USP:***
- Papaverine hydrochloride has been used in the treatment of peripheral vascular disorders, but its use is limited by lack of potency.
- Papaverine hydrochloride interferes with the mechanism of muscle contraction by inhibiting the cyclic nucleotide phosphodiesterases in smooth muscle cells.

Miscellaneous

- ***Papaverine Hydrochloride, USP:***
- The increased levels of cAMP and cGMP are associated with muscle relaxation through their phosphorylation of myosin light-chain kinase.



Papaverine Hydrochloride

References:

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