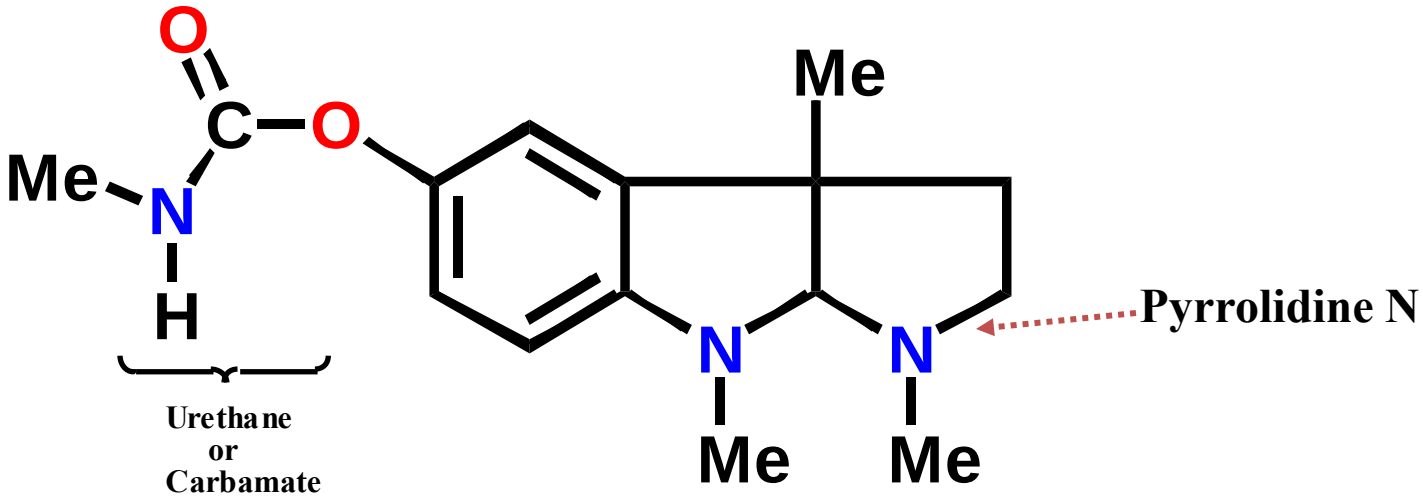
# Anticholinesterases

## Physostigmine



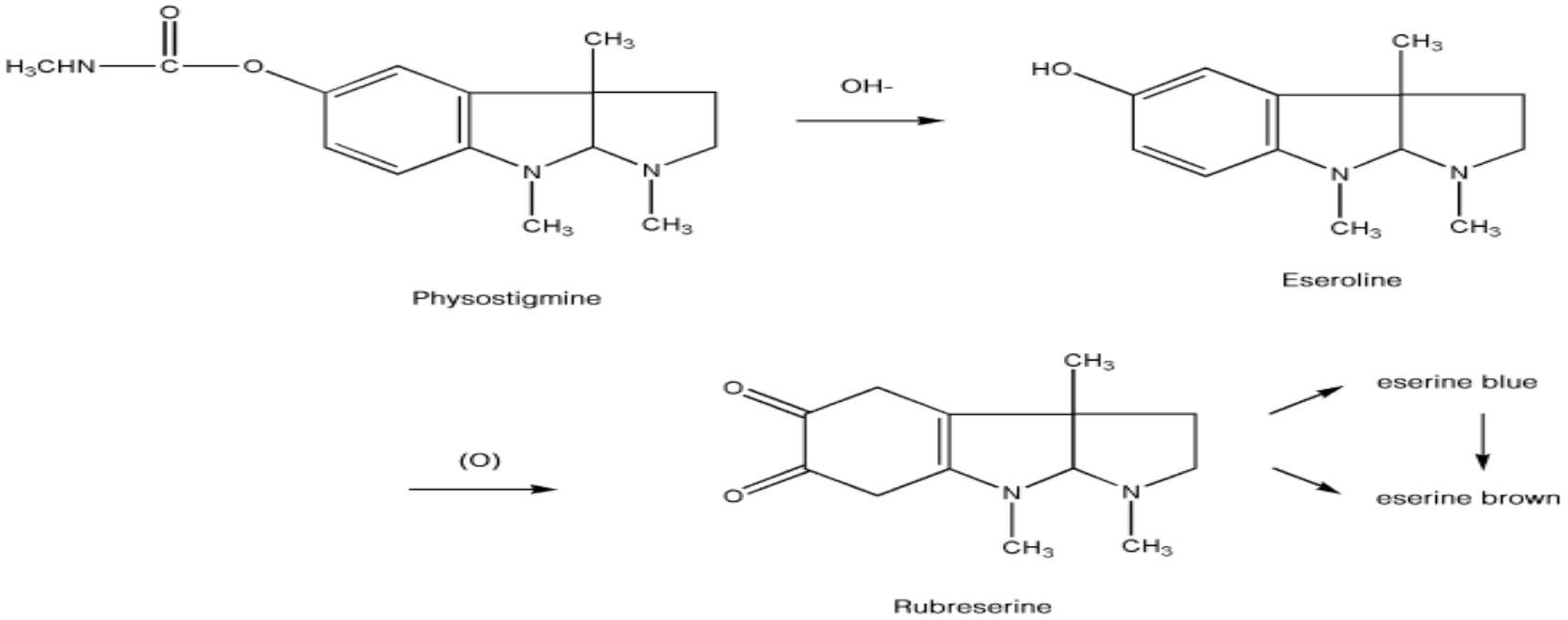

- Natural product (alkaloid)
- Carbamate is essential (equivalent to ester of Ach)
- Aromatic ring is important
- Pyrrolidine N is important (ionised at blood pH)
- Pyrrolidine N is equivalent to the quaternary nitrogen of Ach

**It occurs as a white, odorless, microcrystalline powder that is slightly soluble in water and freely soluble in alcohol, chloroform, and the fixed oils**

**The alkaloid, as the free base, is quite sensitive to heat, light, moisture, and bases, undergoing rapid decomposition.**

**In solution, it is hydrolyzed to methyl carbamic acid and eseroline, neither of which inhibits AChE.**

**Eseroline is oxidized to a red compound, rubreserine, and then further decomposed to eserine blue and eserine brown. Addition of sulfite or ascorbic acid prevents oxidation of the phenol, eseroline, to rubreserine.**

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**Physostigmine is a relatively poor carbamylating agent of AChE and is often considered a reversible inhibitor of the enzyme.**

**Its cholinesterase-inhibiting properties vary with the pH of the medium . The conjugate acid of physostigmine has a pKa of about 8, and as the pH of the solution is lowered, more is present in the protonated form. Inhibition of cholinesterase is greater in acid media, suggesting that the protonated form makes a contribution to the inhibitory activity well as its carbamylation of the enzyme.**

**Physostigmine was used first as a topical application in the treatment of glaucoma.**

**Its lipid solubility properties permit adequate absorption from ointment bases. It is used systemically as an antidote for atropine poisoning and other anticholinergic drugs by increasing the duration of action of ACh at cholinergic sites through inhibition of AChE. Physostigmine, along with other cholinomimetic drugs acting**

**Physostigmine, along with other cholinomimetic drugs acting in the CNS, has been studied for use in the treatment of Alzheimer disease.**

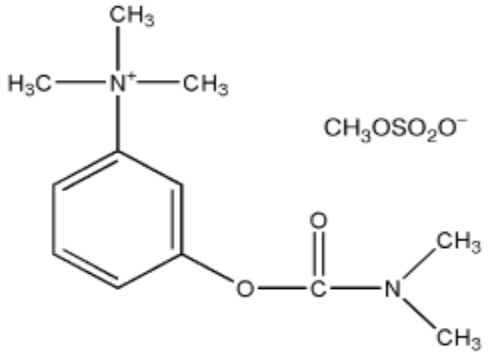
## *Physostigmine Salicylate,* USP

**The salicylate of physostigmine (eserine salicylate) may be prepared by neutralizing an ethereal solution (a solution of any substance in ether) of the alkaloid with an ethereal solution of salicylic acid.**

## *Physostigmine Sulfate, USP.*

**Physostigmine sulfate occurs as a white, odorless, microcrystalline powder that is deliquescent in moist air.**

# Neostigmine Bromide.



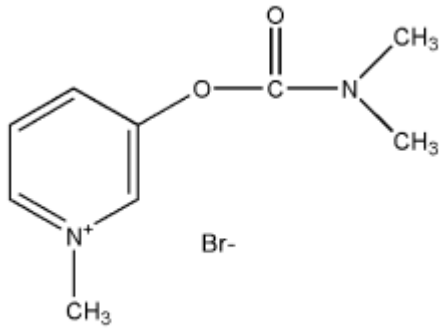

Neostigmine Methylsulfate

**Neostigmine bromide,**
**(m-hydroxyphenyl)**
**trimethylammonium bromide dimethylcarbamate**
**or the dimethylcarbamic ester of 3-hydroxyphenyltrimethylammonium bromide**
**(Prostigmin bromide)**

**It is a synthetic anticholinesterase based on Physostigmine.**
**It resembles the aromatic features of Physostigmin and also the distance between The ester and ammoinum ion is same. But since it has charge on Nitrigen, it cannot cross the CNS like Physostigmine does. Also its half-life is shorter than Physostigmine.**

**Uses**
**1-Myasthenia gravis**
**2-To counter urinary retention**
**3-Antidote to non-depolarization neuromuscular blocking drugs**

***Pyridostigmine Bromide,* USP.**

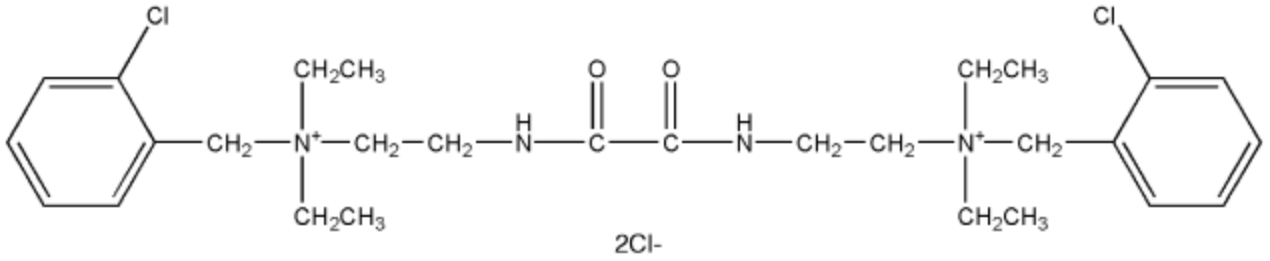



Pyridostigmine Bromide

**Pyridostigmine bromide,**
**3-hydroxy-1-methylpyridinium bromide dimethylcarbamate**
**or pyridostigmine bromide (Mestinon)**

**Pyridostigmine bromide is about one fifth as toxic as neostigmine. It appears to function in a manner similar to that of neostigmine and is the most widely used anticholinesterase agent for treating myasthenia gravis.**

# ***Ambenonium Chloride.***




Ambenonium Chloride

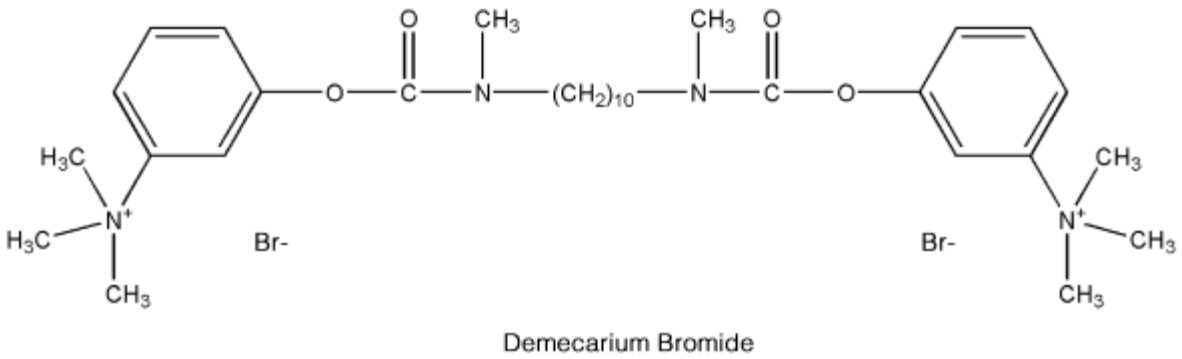
**Ambenonium chloride, [oxalylbis(iminoethylene)]bis[(*o*-chlorobenzyl)diethylammonium]dichloride (Mytelase chloride)**

**Ambenonium chloride is used for the treatment of myasthenia gravis in patients who do not respond satisfactorily to neostigmine or pyridostigmine.**

**This drug acts by suppressing the activity of AChE. It possesses a relatively prolonged duration of action and causes fewer side effects in the GI tract than the other anticholinesterase agents.**

**Because of its quaternary ammonium structure, ambenonium chloride is absorbed poorly from the GI tract. In moderate doses, the drug does not cross the blood-brain barrier. Ambenonium chloride is not hydrolyzed by cholinesterases.**

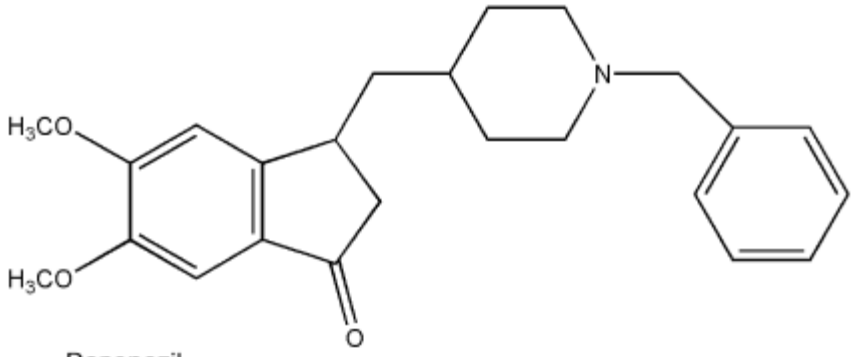
# ***Demecarium Bromide***




Demecarium Bromide

**Its efficacy and toxicity are comparable to those of other potent anticholinesterase inhibitor drugs. It is a long-acting miotic used to treat wide-angle glaucoma and accommodative esotropia.**

# Donepezil

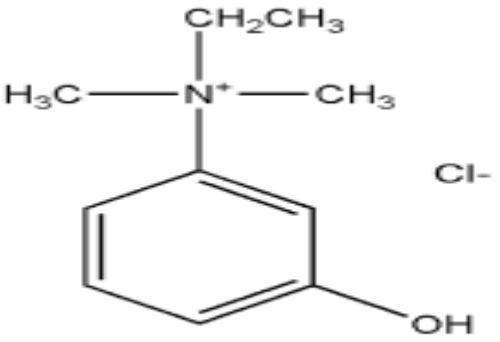


Donepezil

**It is indicated for the treatment of symptoms of mild-to-moderate Alzheimer disease.**

**Its 1000x more selective for ACHE than BuChE. It has greater affinity for AChE in brain than the periphery**

# ***Edrophonium Chloride,*** **USP.**

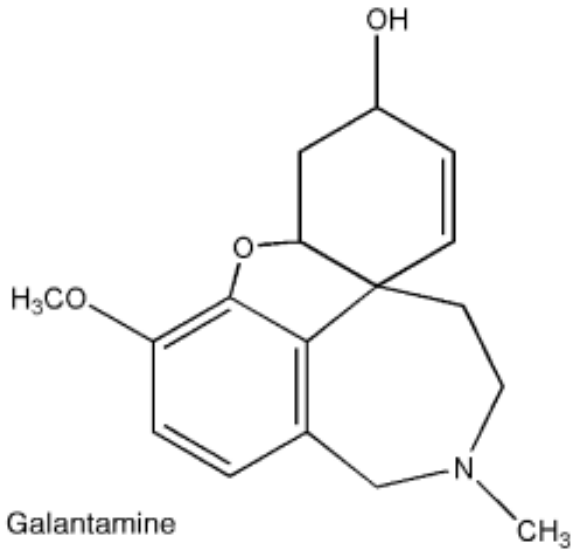



Edrophonium Chloride

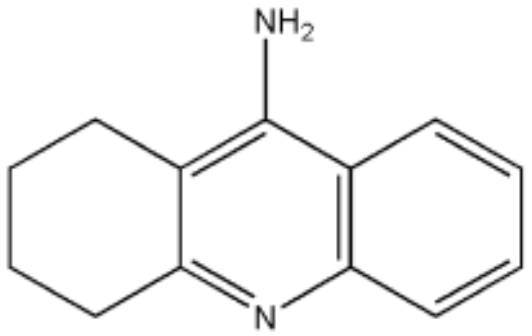
**Edrophonium chloride,**
**ethyl(*m*-hydroxyphenyl)dimethylammonium chloride**
**(Tensilon)**

**On parenteral administration, edrophonium has a more rapid onset and shorter duration of action than neostigmine, pyridostigmine, or ambenonium.**

**It is a specific anticurare agent and acts within 1 minute to alleviate overdose of d-tubocurarine, dimethyl d-tubocurarine, or gallamine triethiodide. The drug is also used to terminate the action of any one of these drugs when the physician so desires.**

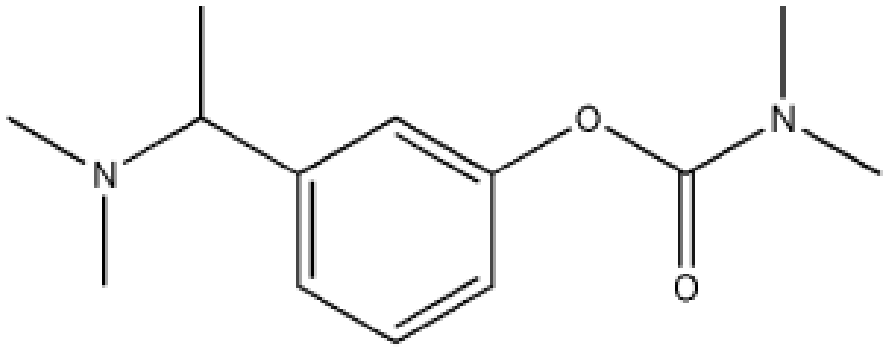



Galantamine




Tacrine Hydrochloride

HCl




Rivastigmine