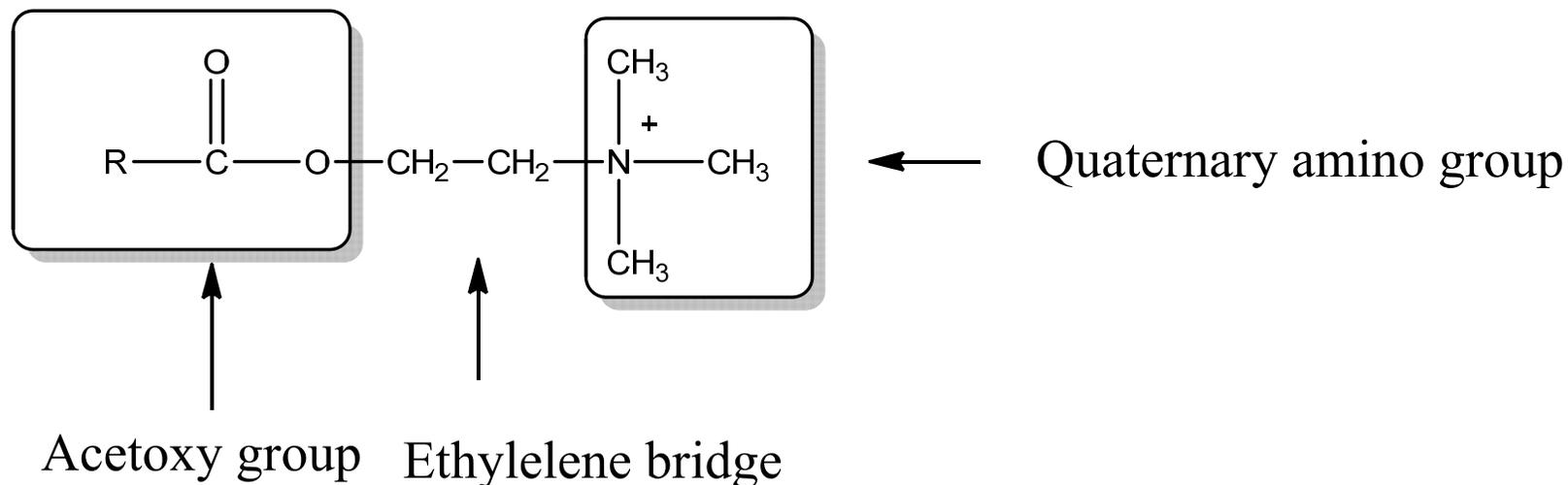


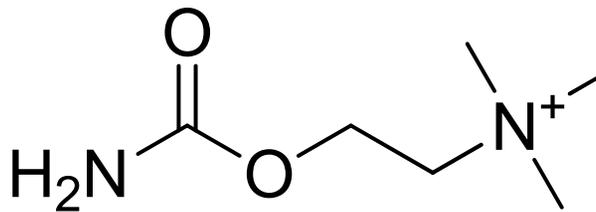
SAR (Structure activity relationship) of directly acting cholinergic Drugs

The general structure of directly acting cholinergic drugs is represented below

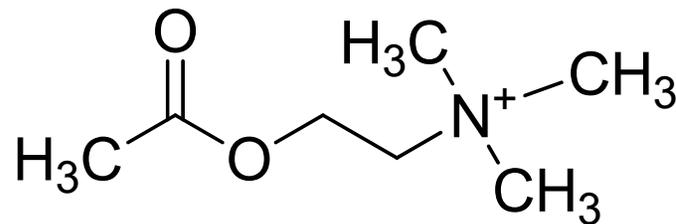


The acetoxy group

- ❖ The higher analog of methyl group i.e. propionyl or butyryl groups are less active than acetyl group.
- ❖ Choline ester of aromatic or higher molecular weight carboxylic acid possess anticholinergic activity.
- ❖ Carboxylate esters are susceptible to hydrolysis by cholinesterase. However, carbamate esters of choline are more stable to hydrolysis e.g. In carbachol.

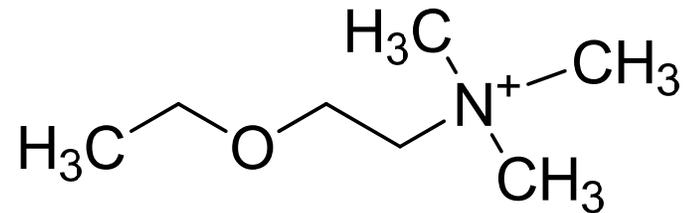


Carbachol (Stable to hydrolysis)



Acetylcholine (susceptible to hydrolysis)

- ❖ Replacement of ester group either by ether or ketone group produce chemically stable and potent compound. Hence neither the ester group or carbonyl group is required for activity.

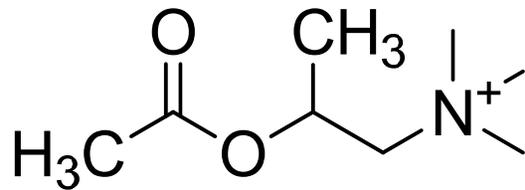


Choline ethyl ether possess cholinergic activity

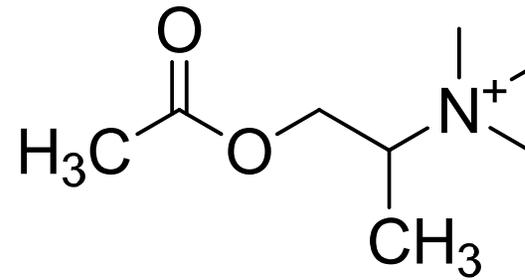
The ethylene bridge

- ❖ Increasing the carbon chain length from 2-C to more than 2 carbons i.e. 3/4/5 decreases the activity.
- ❖ Replacement of the hydrogen atom from the ethylene bridge by methyl group leads to equal or greater cholinergic activity. Presence of groups larger than methyl decrease the activity.

- ❖ The α and β methyl substituted derivatives offers receptor selectivity towards muscarinic receptor.
e.g. β -methyl choline (methacholine) acts selectively on muscarinic receptor while α -methyl choline acts on nicotinic receptor.



β -methyl choline



α -methyl choline

- ❖ The S (+) enantiomer of methacholine is equipotent with acetylcholine while R (+) enantiomer is 20 time less potent.

Quaternary ammonium group

- ❖ The quaternary ammonium group is essential for muscarinic activity.
- ❖ Replacement of nitrogen atom from quaternary ammonium group by Sulphur or arsenic or selenium decrease the activity.
- ❖ Compound containing primary or secondary or tertiary amino groups are less active than the compound containing quaternary ammonium group.
- ❖ Replacement of methyl group by ethyl or larger alkyl group produce inactive compounds.