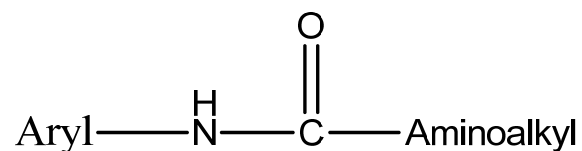
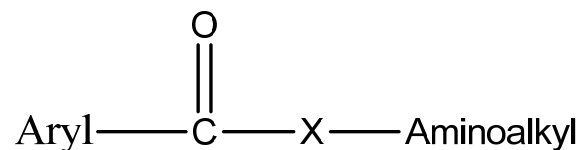


SAR of Antihistamines

The basic structural requirements for the first generation antihistaminics is



Lipophilic portion

- The lipophilic portion of the molecule is essential for local anaesthetic activity.
- This portion of the molecule consists either of the phenyl ring or a 2,6-dimethylphenyl group attached to a carbonyl function through an amino group.

■ In p-aminobenzoic acid derivatives, an electron donating substituent at the ortho or para position increases the activity.

e.g. amino group in tetracaine.

■ Electron withdrawing substituent such as (NO_2 , CO, CN) reduces the local anaesthetic activity.

■ Substitution of amino function present at para position by butyl group increases lipid solubility.

The intermediate chain

* The intermediate chain always contains short alkylene chain of 1- 3 carbons in length linked to the aromatic ring via several functional groups.

* The nature of the intermediate chain determines the chemical stability and duration of action of the drug.

* The anilides are more resistance to metabolic inactivation hence have longer duration of action.

* The placement of alkyl group in ester function e.g. in meprylcaine or amide function e.g. in prilocaine hinders hydrolysis by metabolic enzymes thus prolongs duration of action however it increases systemic toxicity.