# PHYSICAL PHARMACEUTICS II BP(403T)

## UNIT V (DRUG STABILITY)

## CLASS 46

**Topic:Stability of pharmaceuticals**

Decomposition and stabilization of medicinal agents

Pharmaceutical decomposition can be classified as different types

- Hydrolysis
- Oxidation
- Isomerization
- Epimerization
- Photolysis

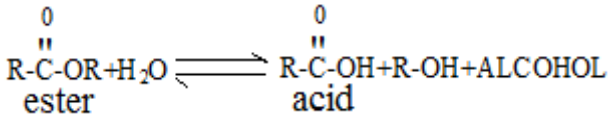
The above process effects the stability of drugs in liquid, solid and semisolid products.

**1.Hydrolysis:**

- This problem is most common in systems containing water such as emulsions, suspensions, solutions etc
- Also for drugs which are affected by traces of moisture in the form of water vapour form atmosphere.
- Main classes of drugs that undergo hydrolysis are esters, amides and lactams
- Hydrolysis is usually catalysed by hydrogen ion (specific acid hydrolysis) or hydroxyl ions (specific base catalysis) and also by other acidic or basic species i.e general acid-base catalysis due to components of buffers.

**A. Ester hydrolysis:**

- The most common type of ester hydrolysis reactions involve acyl-oxygen cleavage.
- Ester hydrolysis whether acid or base is given as



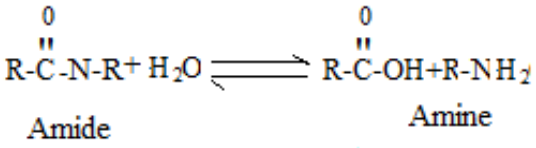
Although it seen like second order reaction, but it is treated as psedo-first order reaction, because the concentration of $H^+$ or $OH^-$ is kept sufficiently high or constant by use of buffers.

Eg drugs which undergo ester hydrolysis like Procaine, Tetracaine, Atropine, Physostigmine, Aspirin.

**B. Amide hydrolysis**:

Although amides are more stable than esters, they also undergo specific and general acid-base hydrolysis.

Upon hydrolysis amides cleave into amine instead of alcohol as in case of esters.




Eg drugs which undergo amide hydrolysis like Dibucaine, Ergometrine, Chloramphenicol, Niacinamide and Barbiturates.

**Ring hydrolysis:**

Hydrolytic reactions also cleavage drugs with ring by subsequent attack by hydrogen or hydroxyl ions.

Drugs undergo ring hydrolysis are Benzodiazipines, Nitrzepam, Penicillins, Cephalosporins.

**Protection against hydrolysis:**

Hydrolytic or soluolytic reactions are retarded by following approaches.

- **In solid dosage forms** like tablets, capsules, powders and granules, hydrolysis is prevented by avoiding their contact with moisture at the time of manufacture, packaging in suitable moisture resistant packs such as strippacles and storage in controlled humidity and temperature conditions.
- Extra protection can be achieved by incorporating a suitable desicant in pack such as silica gel bags.
- **In liquid dosage forms** such as solutions, suspensions, emulsion the main problem is hydrolysis, so the decomposition by hydrolysis due to either specific or general acid-base catalysis can be minimized by adjusting the $P^H$ for maximum stability, and also by adding suitable buffering agents.

- hydrolysis can also be minimized by altering the dielectric constant either by complete or partial replacement of water with non-aqueous solvents eg are Alcohol, Glycerin, Propylene glycol.
- Hydrolysis of certain drugs like Benzocaine, Procaine can be decreased by the addition of complexing agents like caffeine.
- Micellar solubilisation of drugs by use of surfactants protects them from hydrolysis.
- Refrigeration of drugs and drug solution also retard hydrolytic reactions.