

Chemical Degradation Pathways in Drug Substances - Study Material

1. Introduction to Chemical Degradation

Chemical degradation refers to the breakdown of drug substances due to chemical reactions, leading to loss of potency, formation of toxic products, reduced shelf life, and altered safety and efficacy.

2. Oxidation

Oxidation involves gain of oxygen, loss of hydrogen, or loss of electrons. Types include auto-oxidation and free radical oxidation.

Factors: Oxygen, light, metals, temperature, pH.

Prevention: Antioxidants, chelating agents, cool/dark storage, nitrogen flushing.

3. Hydrolysis

Hydrolysis is the cleavage of chemical bonds by water. Common in esters and amides.

Prevention: pH adjustment, buffers, co-solvents, surfactants, salt formation.

4. Racemization

Conversion of one enantiomer into another forming a racemic mixture, leading to loss of activity.

Factors: Temperature, light, solvent, catalysts.

Example: L-epinephrine is more active than D-form.

5. Polymerization

Combination of monomers to form polymers.

Factors: Heat, light, oxygen, metal ions, pH.

Consequences: Reduced efficacy, viscosity increase, color change.

Prevention: Controlled temperature, stabilizers, proper packaging.

6. Factors Affecting Degradation

Environmental: Temperature, light, humidity, oxygen.

Formulation: pH, solvent, concentration, excipients.

7. Analytical Techniques

HPLC, UV Spectroscopy, FT-IR are used to detect degradation and stability.

8. Prevention Strategies

Formulation: antioxidants, buffers.

Packaging: amber bottles, airtight containers.

Storage: cool, dry, protected from light.

9. Importance

Ensures safety, efficacy, shelf life, and regulatory compliance.

10. Exam-Oriented Points

Oxidation: electron loss

Hydrolysis: water cleavage

Racemization: optical inactivity

Polymerization: large molecule formation