UG - Semester - VI
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Mechanism of Enzyme action

Enzymes accelerate reactions by providing a reaction pathway which involves lesser activation energy. our knowledge about the mechanisms involved in the enzyme catalysis is very little. However, as long ago as 1894, Fisher suggested the Lock and key hypothesis to explain the action of enzymes in enzyme-catalysed reactions. This hypothesis is still acceptable but in the modified way as induced fit hypothesis. These theories assume the existence of active sites or cavities on the surface of the enzyme molecules.

'Trypsin' is a proteolytic enzyme that hydrolyses peptide bonds in proteins, especially at the carboxyl side of lysin and arginine.

The mechanism follows the Lock and key and covalent catalysis mechanism and involves formation of an enzyme – substrate complex and an acyl-enzyme intermediate.

step-wise mechanism:

Step-1: Formation of Enzyme-substrate (ES) complex.

- The substrate (protein/peptide) enters the active site of trypsin.
- The positively charged amino acid (Lys or Arg) fits into the specificity pocket.
- weak bonds form between enzyme and substrate.

$$E + S \rightleftharpoons [ES]$$

Step-2: Nucleophilic attack and Acyl-enzyme formation.

- The -OH group of serine (ser-195) in ~~trypsin~~ trypsin attacks the carbonyl carbon of the peptide bond.
- peptide bond breaks.
- one part of peptide is released.
- The other part remains attached to enzyme → Acyl-enzyme intermediate.

$$ES \longrightarrow \text{Acyl-enzyme} + \text{Product}_1$$

Step-3: Hydrolysis of Acyl-enzyme.

- water molecule attacks the acyl-enzyme complex.
- The bond between enzyme and substrate breaks.

Step-4: Release of product and Regeneration of Enzyme.

$$\text{Acyl-enzyme} + H_2O \longrightarrow E + \text{Product}_2.$$

- second product is released
- Enzyme becomes free again.

$$\text{Protein} + \text{Trypsin} \longrightarrow \text{Peptides} + \text{Trypsin}$$