ENZYME REGULATION

Allosteric Regulation

Allosteric enzyme: Some enzymes possess additional sites, besides the active site, known as allosteric sites. Such enzymes are known as allosteric enzymes.

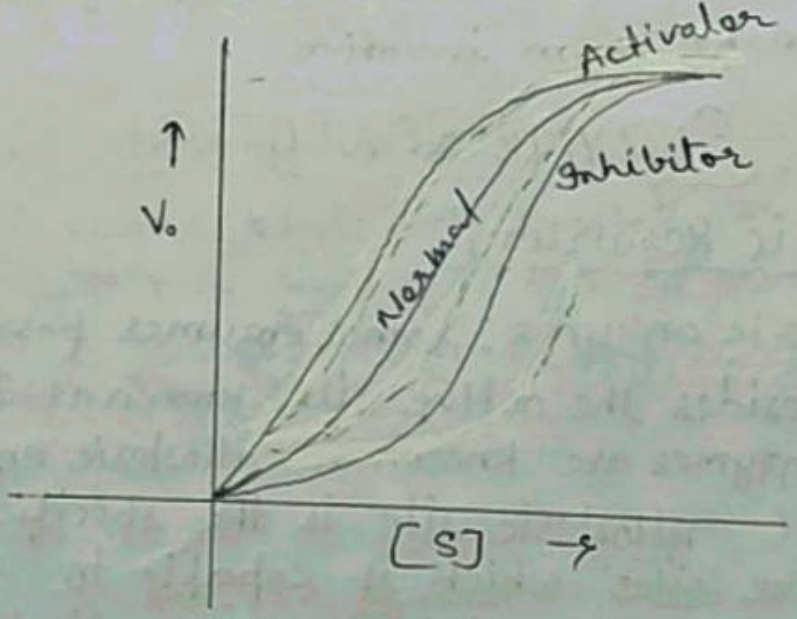
Allosteric site is the specific site other than the active site which is capable to change the substrate binding affinity of particular enzyme.

Allosteric effectors: Certain substances referred to as allosteric modulators (effectors or modifiers) bind at the allosteric site and regulate the enzyme activity. The enzyme activity is increased when a positive (+) allosteric effector binds at the allosteric site known as activator site. On the other hand, a negative (−) allosteric effector binds at the allosteric site called inhibitor site and inhibits the enzyme activity.

Homotropic effect : Substrate molecule is used as effector molecule ie. the substrate influences the substrate binding through allosteric mechanism, their effect is always positive. e.g Haemoglobin (O_2 binding to Hb).

Heterotropic effect : Substrate and effectors are different. ie. allosteric modulator affects the binding of substrate to the enzyme. Heterotropic interactions are either positive or negative.

- Allosteric enzymes give a sigmoidal curve instead of hyperbola when the velocity (v) versus substrate (s) concentration are plotted..



* There are two models to explain the kinetics of allosteric enzyme —
  a) Symmetrical model b) Sequential model

a) Concerted Transition model or Symmetrical model.

- Given by Monod, Wayman & changeux (MWC).

It has following features —

- Allosteric enzymes are oligomers (Polymeric) containing identical unit called Protomer or Monomer.
- They are arranged in the symmetrical model.

- Each monomer binds to only one ligand (S or I or A) or having only one binding site for one ligand.
- The oligomeric protein can exist in two conformation T and R. The different conformation can arise from the rearrangement of quaternary structure or from change in the tertiary structure.

$$T \rightleftharpoons R$$

- Transformation between one-conformation to other is all or none event that means at a given point of time all the unit of enzyme exist in either T (Taut or tight) or R (Relaxed) state or conformation.
- Affinity of a binding site is depends on conformation of the protomer. The binding of ligand to a particular conformation will cause the equilibrium shift towards itself (i.e. where ligand binds). $nT \rightleftharpoons R$
  - * when ligand binds with R state

$$T \rightleftharpoons nR$$

  - * when ligand binds with T state

$$nT \rightleftharpoons nR$$

- T represents the conformation with lower affinity for ligand (Activator or substrate) and high affinity for inhibitor.
- R-state represents the conformation with higher affinity for ligand (Activator)
- I binds to T state & causes $R \rightarrow T$ transition and & make velocity curve more sigmoidal.
- Activator bind to the R-state and causes $T \rightarrow R$ transition and make velocity curve more hyperbolic.
- Change in curve is due to the change in the initial velocity in the presence of A or I.

Equilibrium Constant (L) = $\frac{[T_o]}{[R_o]}$

$[T_o]$ = Initial concentration of T state.

$[R_o]$ = Initial concentration of R state.

Non-Exclusive Bonding constant or Co-efficient (C)

$C = \frac{K_{SR}}{K_{ST}}$

K_{SR} = Intrinsic dissociation constant for the substrate binding site on a protomer in R state.

K_{ST} = Intrinsic dissociation constant for the S binding site on a monomer in T state.

Problem with Symmetrical Model -

It does not explain progressive +ve or -ve co-operativity.

b) Sequential Model:

- Given by Koshland, Nemetty and Filmer.
- When ligand bind to enzymes ie. allosteric molecule there is a significant change in the conformation of enzyme.
- These conformation changes result into the altered affinity of vacant site for its ligand. In effect, either increases or decreases affinity for next substrate or ligand to bind, depends on +ve or -ve co-operativity respectively, that means next ligand bind with altered affinity or modified site of subunit which is sequential.