SEC CHEMISTRY SEM IV

ENZYMES

Definition: Enzymes are biological catalysts composed of protein molecules. Proteins are polymers of amino acids. They enhance the rate of biological reactions without itself being altered.

Characteristics of enzyme catalysis:

(i) Very high reaction rate
(ii) Mild reaction conditions (i.e. high pressure, temperature or pH not required)
(iii) High specificity
(iv) Allostericity (Capacity for regulation)

Structure of enzyme: Enzyme consists of an active site , which binds the substate (reactant) and results in catalysis.

Characteristics of active site:

(i) Active site is very small as compared to total size of enzyme.
(ii) It is a three dimensional structure, which binds to the substrate forming enzyme substrate complex.
(iii) The enzyme- substrate complex is held together by multiple weak interactions like vander waals forces, hydrophobic force, electrostatic force, H-bonding etc.
(iv) Active site is a cleft which binds substrate by geometric or chemical complementarity.

Classification and Nomemclature of enzymes:

Enzymes are usually named according to the chemical reaction they catalyze. This is known as enzyme's **systematic** name. Most enzyme names end with **'ase'.**

Each enzyme is also given a code by the Enzyme Commission to help denote its function. The nomenclature was determined by the **Enzyme Commission** in 1961 (with the latest update having occurred in 1992), hence all enzymes are assigned an "EC" number. Enzymes are classified into six different groups and the classification does not consider the enzyme structure.

EC numbers are four digits, for example a.b.c.d, where "a" is the class, "b" is the subclass, "c" is the sub-subclass, and "d" is the sub-sub-subclass. The "b" and "c" digits describe the reaction, while the "d" digit is used to distinguish between different enzymes of the same function based on the actual substrate in the reaction

EC.1. OXIDOREDUCTASE
Function : Catalyzes redox reactions through electron transfer
Example: Dehydrogenase

EC.2. TRANSFERASE
Function: Transfers chemical groups like methyl, aldehydic, ketonic, phosphoryl, amino etc. from one substrate to another. $A\text{-}X + B \rightleftharpoons BX + A$
Example: Aminotransferse

EC.3. HYDROLASES
Function: catalyze hydrolytic cleavage of C-O, C-N, C-C, P-O bonds. $A\text{-}X + H_2O \rightleftharpoons X\text{-}OH + HA$
Example : peptidases

EC.4. LYASES
Function: Addition of groups to double bonds, or formation of double bonds by removal of groups
Example : Decarboxylase

EC.5. ISOMERASES

Function: Transfer a group within a molecule to form an isomer

Example: Cis-trans isomerase

EC.6. LIGASES

Function: Join molecules by the help of ATP hydrolysis

Example: RNA synthetase

Example :

(i) Enzyme **tripeptide aminopeptidases** (systemic name) has the code **EC.3.4.11.4.**

EC.3. denotes hydrolases (ie enzymes using water to break bonds)

EC.3.4 denotes hydrolases that act on peptide bonds (ie bonds joining amino acids)

EC.3.4.11 denotes hydrolases that breaks of amino terminal amino acid from polypeptide

EC.3.4.11.4 denotes hydrolases breaking amino terminal amino acid from a tripeptide

(ii) Enzyme **glucose ATP phosphotransferase** (hexokinase) (systemic name) has the code **EC.2.7.1.1**

EC.2. denotes transferase (ie enzymes catalyzing transfer of chemical groups)

EC.2.7 denotes a transferase transferring phosphate group

EC.2.7.1 denotes acceptor has a hydroxy group

EC.2.7.1.1 denotes the hydroxyl group acceptor as D-glucose

General mechanism of enzyme catalysis:

$$E + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ES$$

$$ES \xrightarrow{k_2} E + P$$

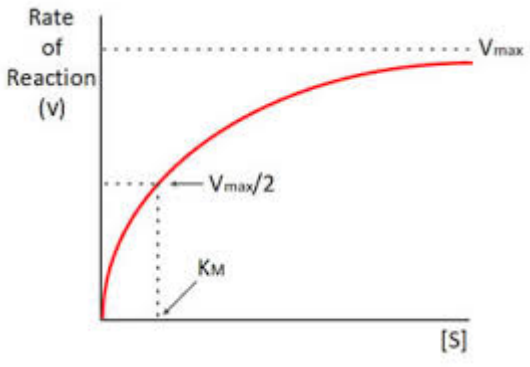
[E = enzyme, S= substrate, ES = Enzyme substrate complex, P = product]

Michaelis Menten equation

$$v_i = \frac{v_{max}[S]_0}{K_M + [S]_0} \text{-------(1)}$$

where v_i = initial rate of enzyme catalyzed reaction, $v_{max} = k_2[E]_0$ = maximum rate of the enzyme catalyzed reaction, $[S]_0$ = initial substrate concentration, $K_M = \frac{k_2 + k_{-1}}{k_1}$ = **Michaelis Menten constant.**

Michaelis Menten plot:



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Michaelis Menten constant (K_M)

Definition: It is the substrate concentration required to achieve half the maximum velocity.

Unit: moles/litre
Significance: Smaller the K_M greater is the affinity of enzyme for substrate, ie lower K_M better enzyme for the substrate

Turnover number (k_2)

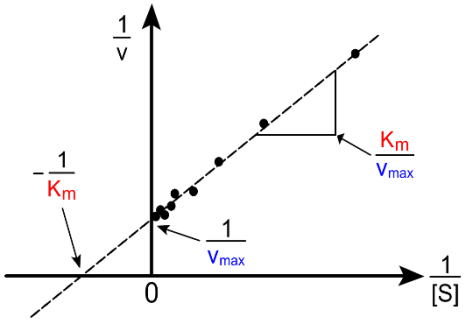
Definition: The number of times an enzyme regenerates itself to react with substrate molecules per unit time.
Unit : sec^{-1}
Significance: Larger the turnover number more evolved the enzyme.

Line weaver Burk equation:

Reciprocating equation (1)

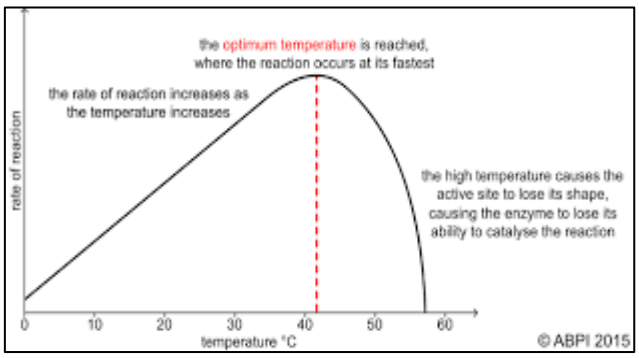
$$\frac{1}{v_i} = \frac{1}{v_{max}} + \frac{K_M}{v_{max}[S]_0}$$

Line weaver Burk Plot:

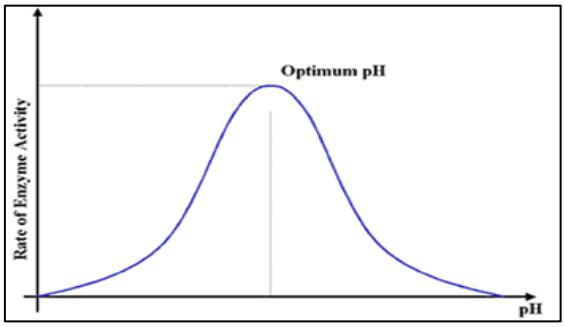


Effect of temperature and pH on enzyme activity

High temperature and high and low pH alters the folded structure of proteins, the biomolecule of which enzyme is composed. At low temperature the rate of the catalytic reaction is very low. Hence enzymes act only at optimum pH and temperature.



Temperature Effect



pH effect

Enzyme Inhibition

Definition: An enzyme inhibitor is a molecule which binds to the enzyme and decreases its catalytic activity.

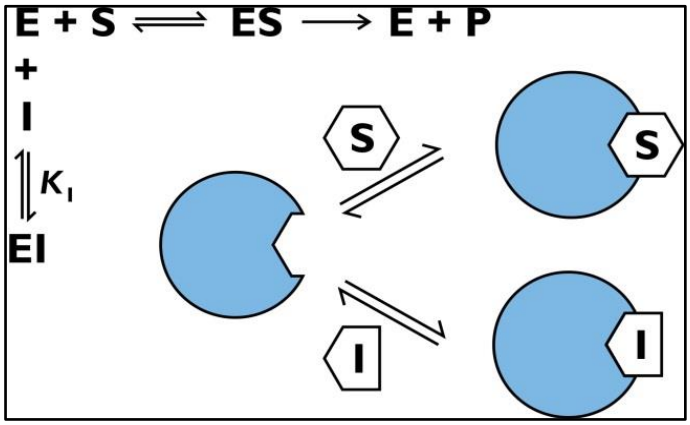
Significance: (i) Used in the manufacture of drugs to stop enzymatic reactions in pathogens
(ii) Used in manufacture of pesticides (iii) Used to control metabolic reactions in our body, which lead to disease conditions.

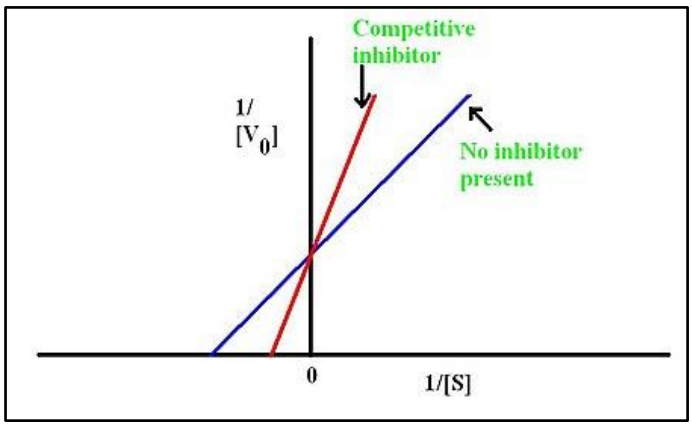
Types of Inhibitors: (i) Competitive(ii) Non-competitive (iii) Uncompetitive

	COMPETITIVE	NON- COMPETITIVE	UN-COMPETITIVE
1.	Inhibitor(I) and substrate (S) similar to one another and compete for the same active site of enzyme	I and S dissimilar, bind at different sites of enzyme. Binding of I affects conformation of active site, which stops the catalysis reaction but does not affect the binding of S to E.	I and S dissimilar, bind at different sites of enzyme. Binding site of I opens only after S binds to the enzyme.
2.	v_{max} same	v_{max} decreases	v_{max} decreases
3.	K_M increases	K_M same	K_M decreases
4.	Reversible	Irreversible	Irreversible

$K_M = \frac{k_2+k_{-1}}{k_1} = \frac{k_{-1}}{k_1}$, **when** $k_2 \ll k_{-1}$, thus K_M can be considered as the dissociation constant of the E-S complex.

COMPETITIVE INHIBITION Scheme and Line weaver Burk Plot

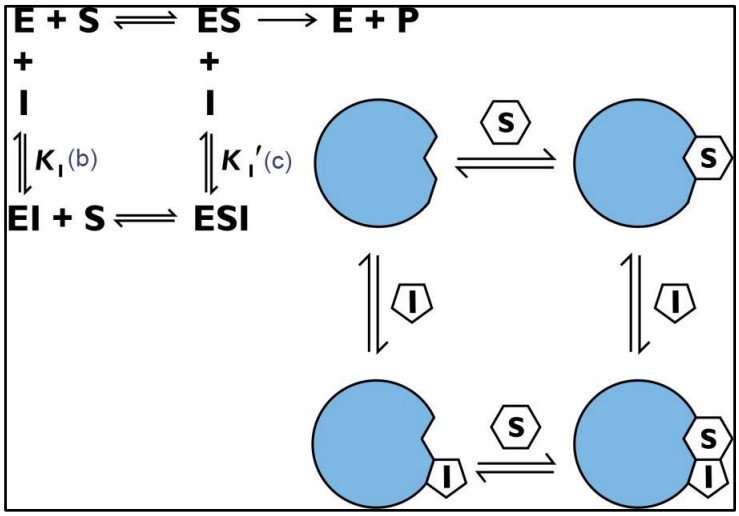


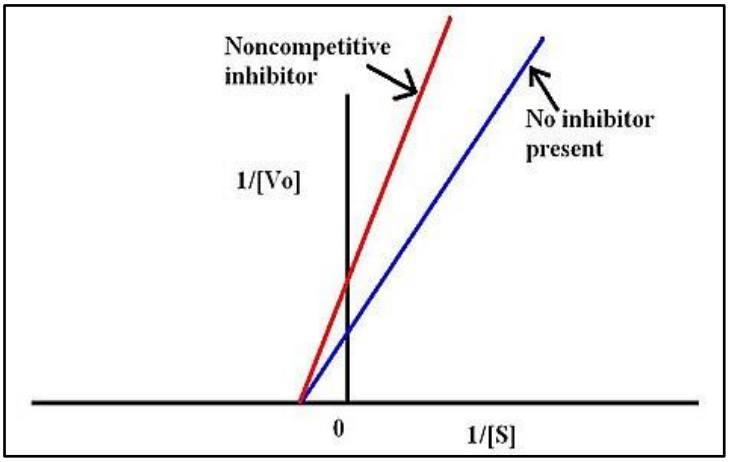


(i) As S increases it removes I from the active site , therefore v_{max} same.

(ii) But addition of I drags the E+S ⇌ES equilibrium towards LHS, therefore ES concentration decreases, dissociation of ES increases and K_M increases.

NONCOMPETITIVE INHIBITION Scheme and Line weaver Burk Plot

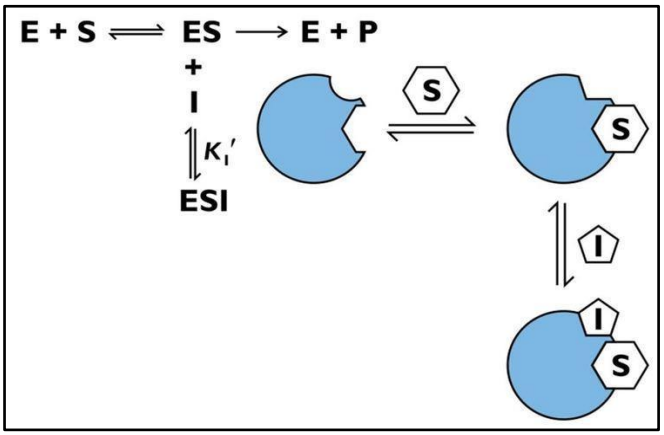


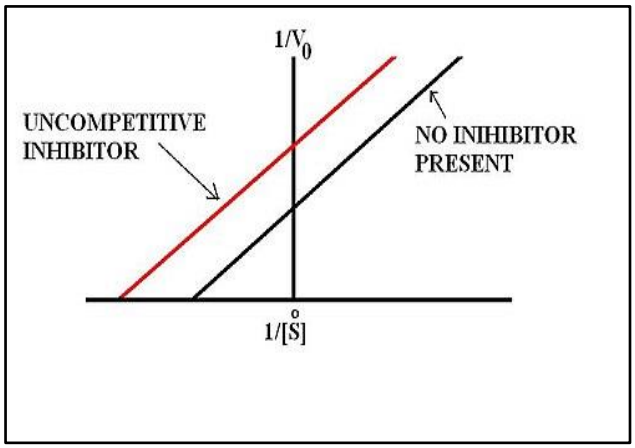


(i) Binding of Substrate with Enzyme is independent of the presence of Inhibitor. Hence K_M remains same in spite of Inhibitor addition.

(ii) Formation of EI or ESI stops enzyme from catalyzing substrate reaction, and since I sits at site different from active site, addition of more S cannot remove I, therefore v_{max} decreases.

UNCOMPETITIVE INHIBITION Scheme And Line weaver Burk Plot





(i) Addition of I moves the equilibrium E+S ⇌ ES towards RHS, thus more ES formed, dissociation of ES decreases and K_M decreases.

(ii) Formation of ESI stops enzyme from catalyzing substrate reaction, and since I sits at site different from active site, addition of more S cannot remove I, therefore $\boldsymbol{v_{max}}$ decreases.