Enzymes and coenzymes II

Foundation block..

Important definitions

Enzyme inhibition

Inhibition is a process in which the enzyme activity is regulated or controlled (this means enzyme activity will stop)

K_i (Inhibitor constant)

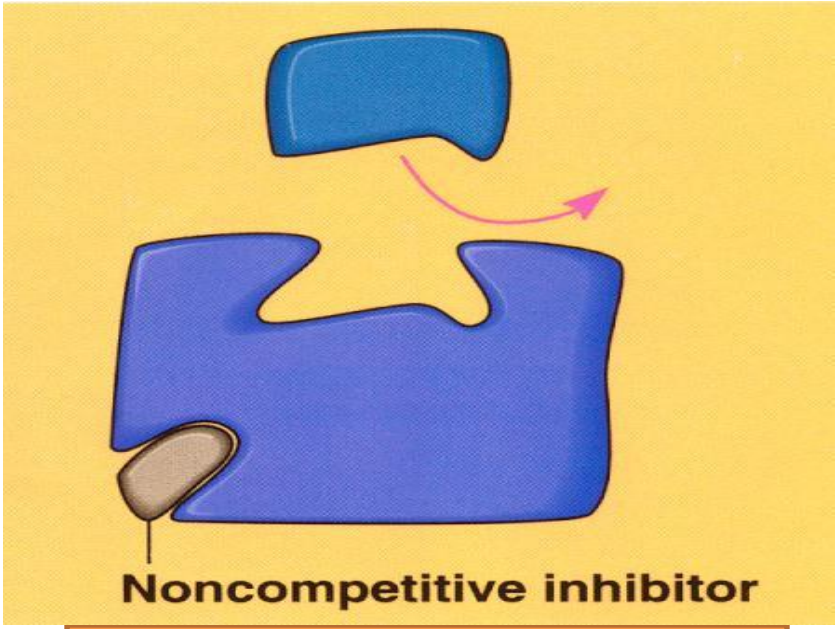
The inhibitor constant, Ki, is an indication of how potent(having great power), an inhibitor is; it is the concentration required to produce half maximum inhibition.

Plotting 1/v against concentration of inhibitor at each concentration of substrate (the Dixon plot) gives a family of intersecting lines

And it is also known as dissociation constant

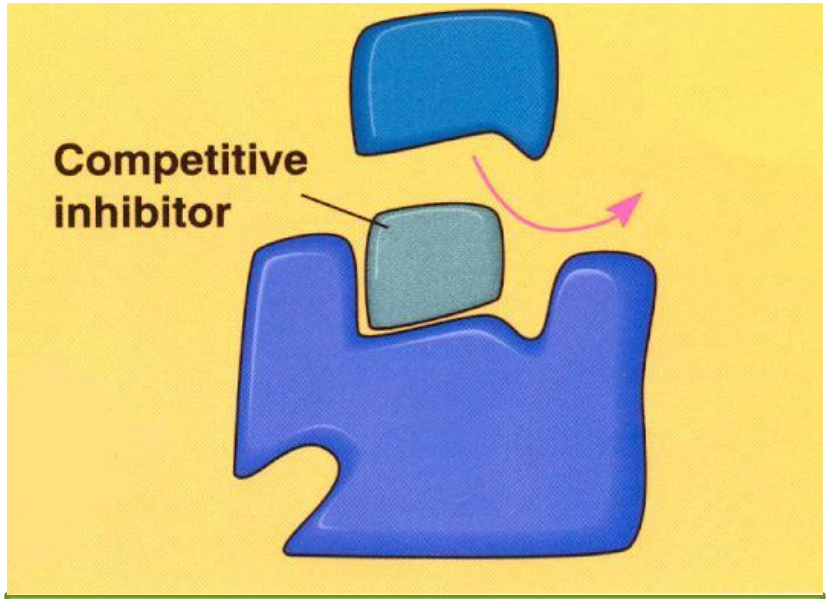
Enzyme inhibition

Noncompetitive inhibition



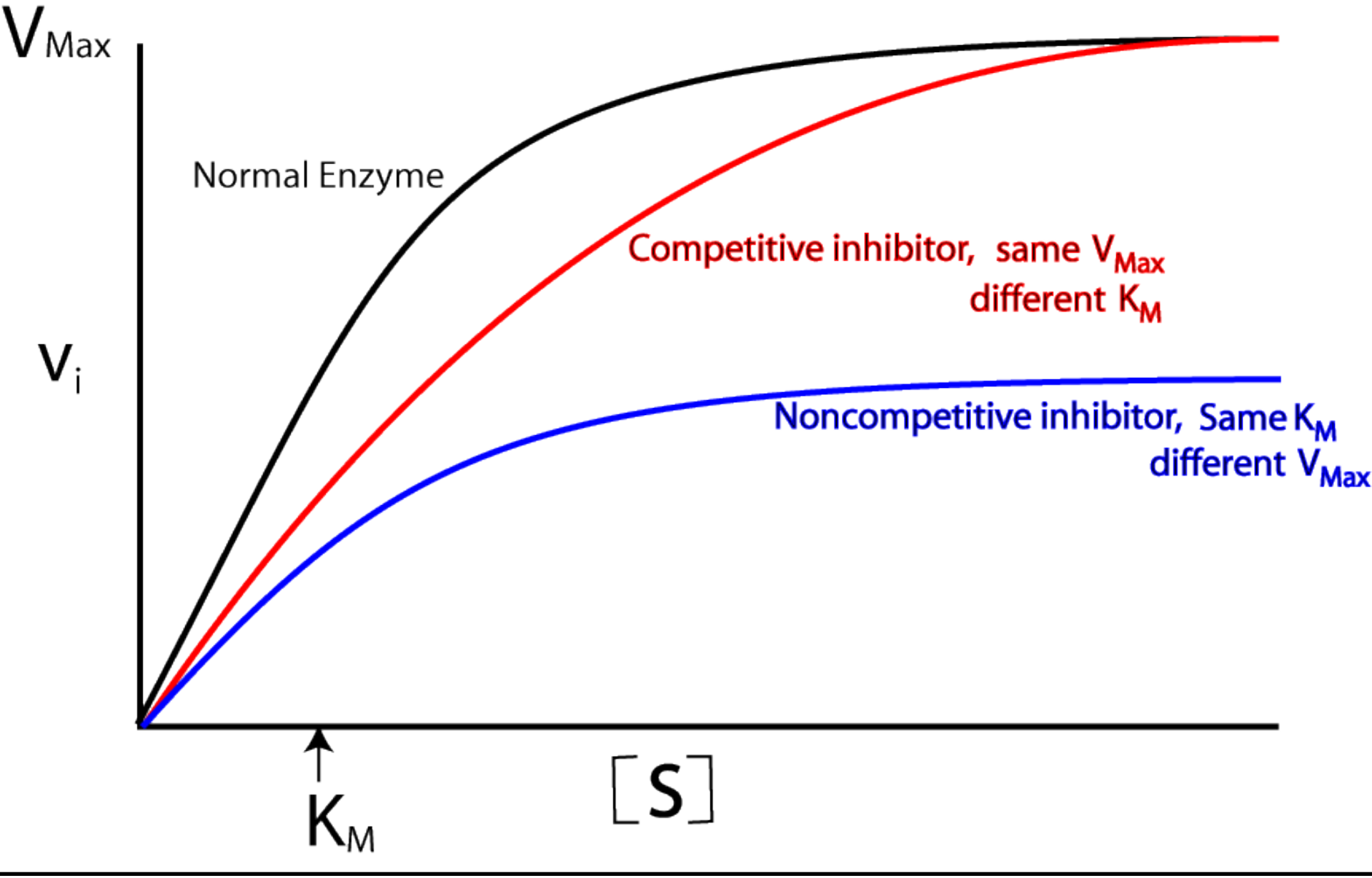
***The inhibitor binds to different site = No competition exists between the inhibitor and the substrate .**

Competitive inhibition



***Where the inhibitor compete with the substrate for the same binding site .**

Competitive inhibition	Noncompetitive inhibition
Competes for the active site	Does not compete for the active site (binds to a site away from it ⟶ No competition exists
Two equilibria are possible: $E + S \leftrightarrow ES \rightarrow E + P$ (still active) and $E + I \leftrightarrow EI$ (inactive)	The inhibitor can bind to a free enzyme or to an enzyme-substrate complex $ES + I \leftrightarrow ESI$ (inactive) $E + I \leftrightarrow EI$ (inactive)
In competitive inhibition, Vmax is unchanged in the presence and the absence of inhibitor	The value of Vmax is decreased by the inhibitor.
The value of Km is increased because substrate and inhibitor compete for binding at the same site.(where : Km=the greatest rate of reaction that an enzyme can achieve.)	Km is unchanged because the affinity of S for E is unchanged. (where : Km=the greatest rate of reaction that an enzyme can achieve.)
A higher concentration of substrate is required to achieve half-maximal velocity	With noncompetitive inhibition, enzyme molecules that have been bound by the inhibitor are taken out of the game
The inhibitor is a structural analogue (similar)	The inhibitor does not have structural similarity to the substrate


V_{Max}
Normal Enzyme
Competitive inhibitor, same V_{Max}
different K_M
V_i
Noncompetitive inhibitor, Same K_M
different V_{Max}
K_M
[S]

Regulation of enzyme activity

Enzymes catalyze :

1- first or early reactions

2- rate limiting reactions that affect the whole pathway

3- a committed step: (a reaction unique to a particular pathway)

Feedback inhibition	Feed positive activation
When the product of reaction exceeds the conc. limit → inhibits the regulatory enzyme	When the end product is below conc. limit it activates the regulatory enzyme

Allosteric enzyme regulation : it is an enzyme that can be regulated in a pathway by the binding of certain substances to a site **other than** the catalytic site

*هي الانزيمات التي تنظم من خلال ارتباط بعض المواد في موقع يختلف عن الموقع المحفز

***Most allosteric enzymes are oligomers (2 or more polypeptide chains or subunits [protomers])**

Cooperative binding : The process by which binding of a ligand to a regulatory site affects binding of the same or of another ligand to the enzyme.

* هي العمليه التي ترتبط فيها المادة في المكان المنظم و بالتالي يؤثر في ارتباط المواد نفسها او مواد اخرى في هذا لانزيم

Binding of an **allosteric modulator** → change in the **conformation** of the enzyme
→a change in the **binding affinity** of enzyme for the substrate

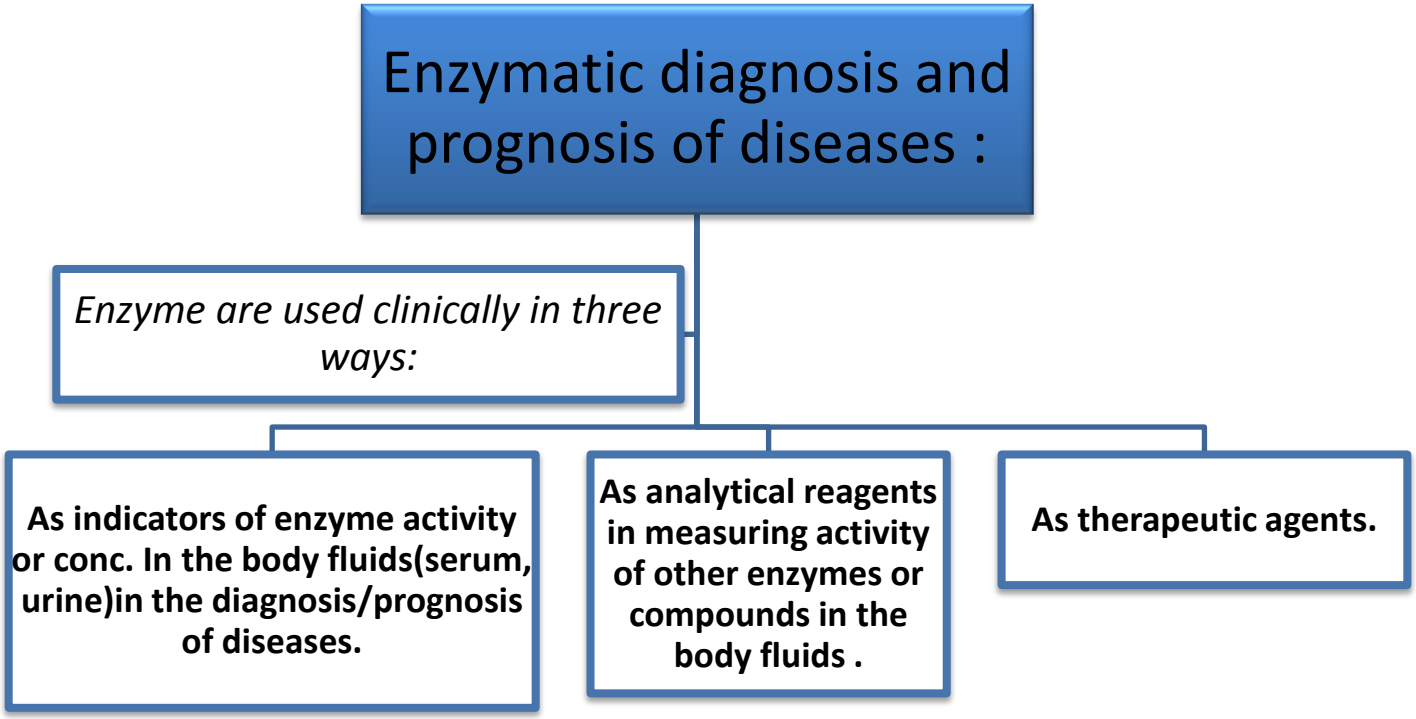
This affect can be :

Positive (activation):
increased E, S affinity

Negative (inhibition):
decreased E, S affinity

Two types that occur in allosteric enzymes :

Homotropic	Heterotropic
Effect of one ligand on the binding of the **same** ligand (a regulatory enzyme modulated by its own substrate)	Effect of one ligand on the binding of a **different** ligand



The most commonly used body fluids for measuring enzyme activity are :

- serum
  - Serum markers in the diagnosis of disease:
    - Pancreatic disease
    - Heart disease
    - Liver disease
- Plasma
  - There are
    - Plasma-specific enzymes
    - Non-plasma-specific enzymes

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