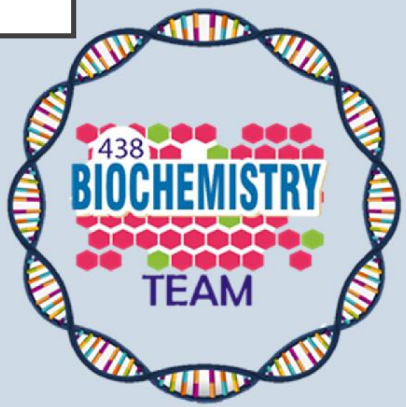
ENZYMES AND COENZYMES II

- **Color Index:**
  - **Original slides.**
  - Important.
  - 436 Notes
  - **438 notes**
  - **Extra information**



Biochemistry team 438

Enzyme inhibition

Inhibition a process in which the enzyme activity is regulated or controlled

To inhibit to stop the enzyme activity

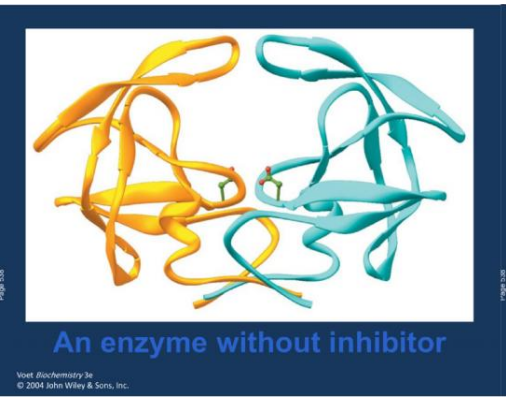
Main Types of enzyme inhibition

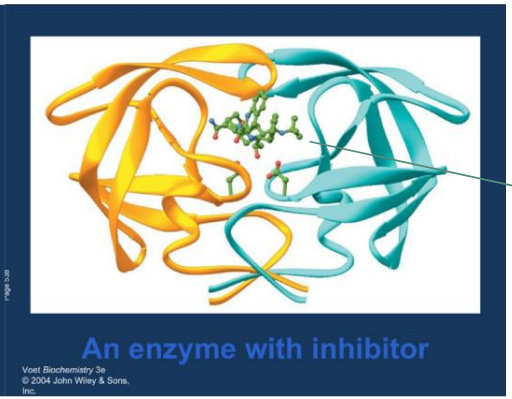
Competitive

inhibitor and substrate have to be structurally similar(same shape) because they're competing for the same site(the active site).

Noncompetitive

inhibitor binds to enzyme in a site OTHER than the active site.

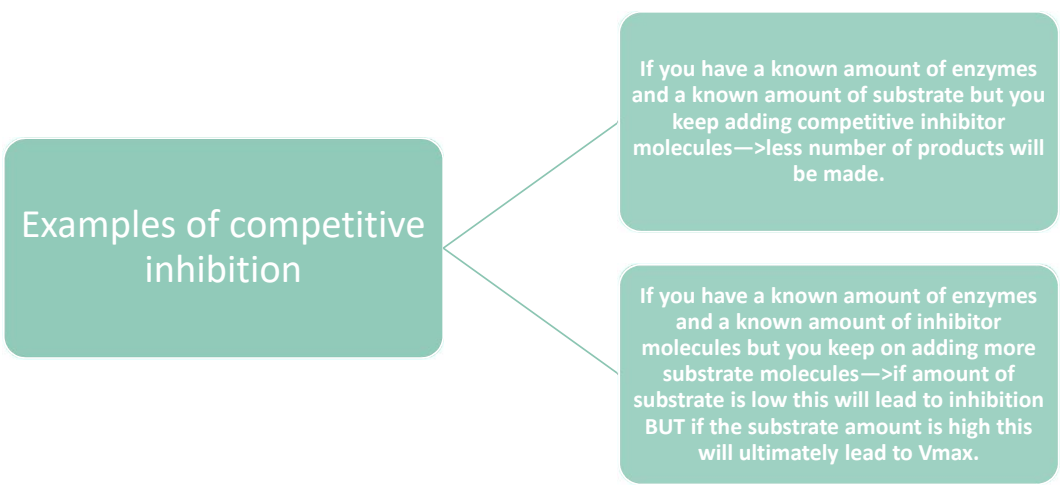




Notice where the inhibitor is located; it's probably sitting in the active site

Notes:

- Activation: increasing the activity of enzymes
- Inhibition: decreasing/stopping the activity of enzymes
- Inhibition could be **partial** (25% or 50% or 75% and so on) or **complete**(100%)
- (there are actually 3 types of enzyme inhibition the 3rd one is uncompetitive but it's not discussed)



Competitive inhibition

The inhibitor is a structural analogue that competes with the substrate for binding at the active site of enzyme.

Two equilibria are possible:
E + S —>ES —>E + P
And
E + I—> EI

this enzyme inhibitor complex is in active because the inhibitor blocked the active site.

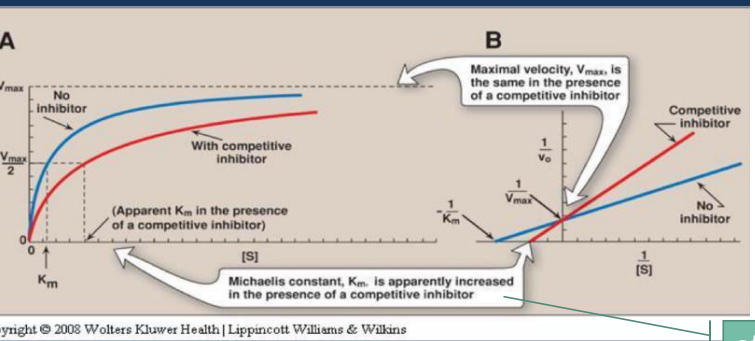
- In competitive inhibition, Vmax is unchanged in the presence and the absence of inhibitor.

- The value of Km increases because substrate and inhibitor compete for binding at the same site.(thus preventing enzymatic reactions)

- A higher concentration of substrate is required to achieve half-maximal velocity

Inhibitor is a molecule that INHIBITS

Activator is a molecule that ACTIVATES



In A you can't pinpoint the exact point of Vmax

In B you can

affinity decreases

Competitive inhibition is always a reversible reaction.
Affinity:
Vmax: تعني الحد الذي يصل عنده المركب للتشبع

Non-competitive inhibition

- The inhibitor does not have structural similarity to the substrate
- The inhibitor binds to the enzyme at a site away from the substrate binding site(active site)
- No competition exists between the inhibitor and the substrate
- The inhibitor can bind to a free enzyme or to an enzyme-substrate complex
- In both cases the complex is catalytically inactive

- The value of Vmax is decreased by the inhibitor, but Km remains the same because the affinity of S for E is unchanged.

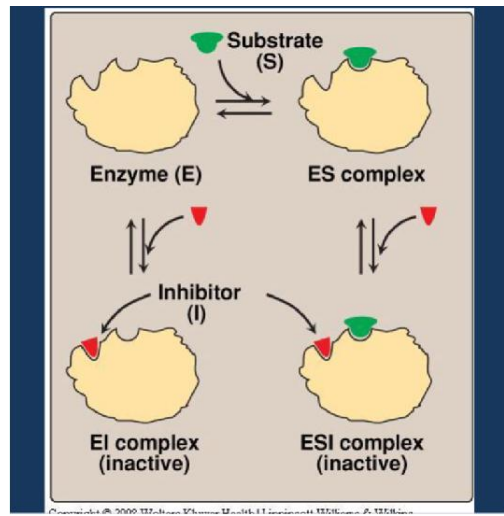
(because substrate and inhibitor aren't competing for the same site)

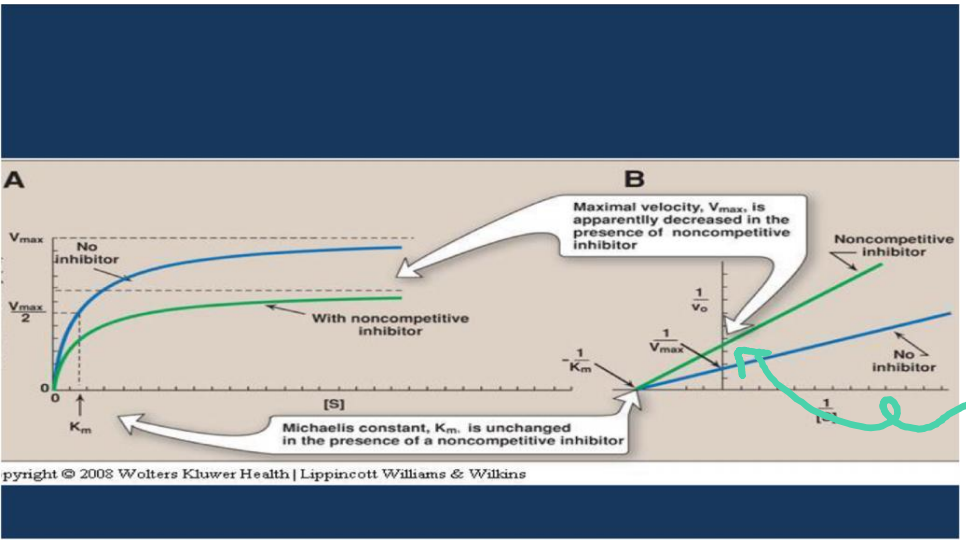
Two possibilities:

ES + I —>ESI (inactive)

E + I —>EI (inactive)

Once the enzyme is bound to the inhibitor the complex becomes inactive even if the substrate comes later.





لاحظوا انه فوق اصغر

ليش؟ لانه مقلوب

:مثلا

½is bigger than ¼

➢ Ki(inhibitor constant):

Ki is a measure of the affinity of the inhibitor for the enzyme. Also known as dissociation constant.

Km is for SUBSTRATE + enzyme

Ki is for INHIBITOR + enzyme

Regulation of enzyme activity

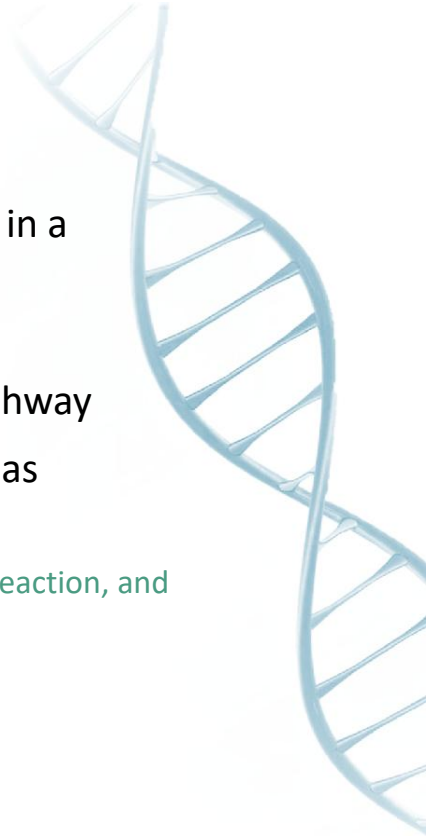
- Regulatory enzymes usually catalyze the **first** or an **early reaction** in a metabolic pathway

(if you don't want the end-product, why do all the work?)

- They catalyze a rate-limiting reaction that controls the overall pathway
- They may also catalyze a reaction unique to that pathway known as "committed step"

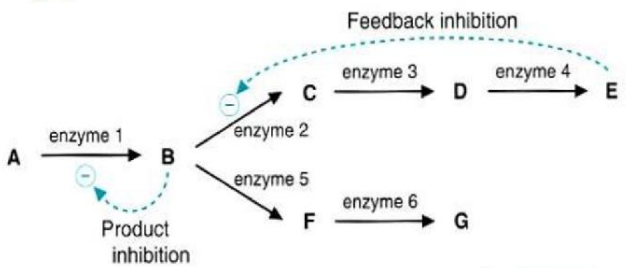
(If I want to stop Glucose breakdown, I will try to find a step that will only affect this reaction, and won't affect the breakdown of another molecule.)

- ❑ Any molecule that will bind to enzyme & change its activity is called a **ligand** or a **modulator**
- ❑ Regulatory enzymes are enzymes which are modulated; activated or inhibited



Feedback Inhibition	Feed positive activation
the end-product of a metabolic pathway **exceeds** its concentration limit	the end product of a metabolic pathway is **below** its concentration limit
inhibits the regulatory enzyme to normalize the pathway	activates the regulatory enzyme to normalize the pathway

Feedback Inhibition



Why didn't E inhibit enzyme 1?

Because then it will inhibit the production of G.

We call the B→ C step the **committed step**

Types of regulation

Allosteric Enzyme Regulation

- The enzymes in metabolic pathways whose activities can be regulated by certain compounds that bind to enzyme **other** than the catalytic site are known as allosteric enzymes

- The term “allosteric” came from Greek word “allos” meaning “other”

Modulator binds somewhere other than the active site

Cooperative binding

- It is the process by which binding of a ligand to a regulatory site affects binding of the same or of another ligand to the enzyme
- Binding of an allosteric modulator causes a change in the conformation of the enzyme
- This causes a change in the binding affinity of enzyme for the substrate
- The effect of a modulator may be positive (activation) or negative (inhibition)

-- Positive: increased E, S affinity

-- Negative: decreased E, S affinity

Most allosteric enzymes are oligomers (two or more polypeptide chains or subunits)

The subunits are known as protomers

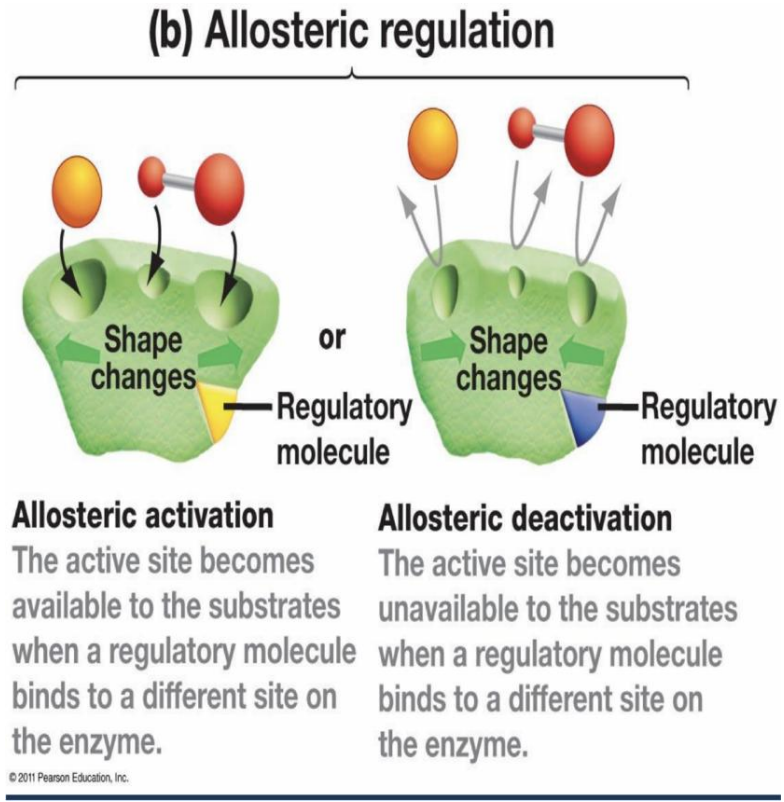
Two types of interactions occur in allosteric enzymes:

– Homotropic:

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

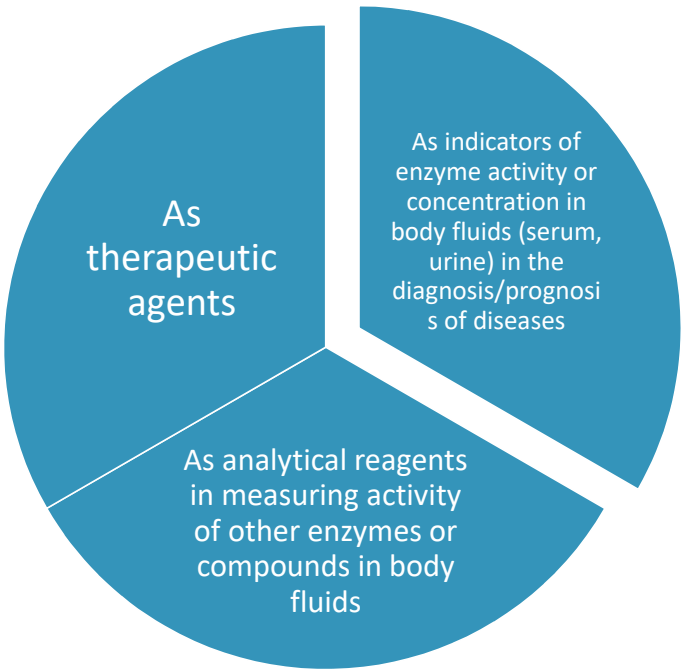
– Heterotropic:

Effect of one ligand on the binding of a different ligand



Enzymatic diagnosis and prognosis of diseases

Enzymes are used clinically in three ways:



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

serum and **plasma**

- There are:

1. Plasma-specific enzymes
2. Nonplasma-specific enzymes

❖ Serum markers in the diagnosis of diseases:

- Heart disease
- Pancreatic diseases
- Liver diseases

Review

Med436

Regulatory enzymes usually catalyze the first or an early reaction in a metabolic pathway

Two types of interactions occur in allosteric enzymes:

- Homotropic: Effect of one ligand on the binding of the same ligand

- Heterotropic: Effect of one ligand on the binding of a different ligand.

Enzymes are used clinically in three ways

	Competitive inhibition	Noncompetitive
meaning	similar to the structural of the substrate and competes with it for binding at the active site	The inhibitor does not have structural similarity to the substrate. The inhibitor binds to the enzyme at a site away from the substrate binding site
V_{max}	V_{max} is unchanged in the presence and the absence of inhibitor	The value of V_{max} is decreased by the inhibitor
K_m	K_m is increased because substrate and inhibitor compete for binding at the same site	K_m is unchanged because the affinity of S for E is unchanged

MCQs

Q1; Inhibition could be :

A- partial
B- complete
C- competitive or non competitive
D- all of the above

Q2; Regulatory enzymes are

A- always activated
B- always inhibited
C- modulated
D- none of the above

Q3; What does the positive modulator do?

A- Increase E,S affinity
B- Decrease E,S affinity
C- Doesn't change E,S affinity

Q4; Feed Positive Activation happens when the end product of a metabolic pathway:

A- Exceeds its concentration limit
B- Is below its concentration limit
C- both A&B

Answer key:

1) D
2) C
3) A
4) B

SAQs

Q1: What happens to Km in case of competitive inhibition?

Increases

Q2: What happens to Vmax in case of non competitive inhibition ?

Decreases

Q3:Which types of diseases can serum markers diagnose?

Heart, liver, pancreatic diseases

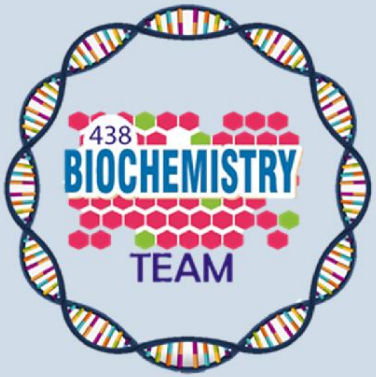
Q4:What is the name of the molecule that modulates enzyme activity?

Ligand or modulator

Q5: In homotropic interactions, the regulatory enzyme is modulated by ……

its own substrate

➢ Special thanks to:



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