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Enzymes and coenzymes (1)

Color index :

Main text

IMPORTANT

Extra Info

Drs Notes

Foundation Block - Biochemistry Team

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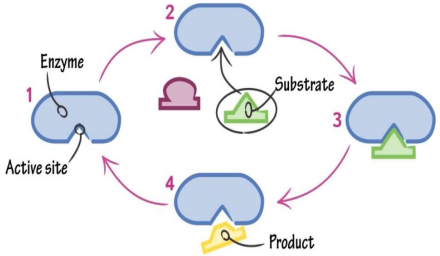
MED439

Objectives:

- Understand the peptide bonding between amino acids.
- Identify classes of enzymes based on the type of reactions they catalyze.
- Comprehend the basic terms of coenzymes, isoenzymes, enzyme activity and specificity along with factors affecting their activity.
- Understand the enzyme kinetics, types of inhibition and regulation of enzyme activity.
- Discuss the clinical role enzymes play in the diagnosis of diseases.

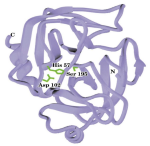
What are enzymes ?

- Enzymes are biological catalysts that speed up the rate of a reaction without being -consumed- changed in the reaction.
- Enzyme is a catalyst, a catalyst is a facilitator, it speeds up the reaction rate.
- Enzymes are non-consumable molecules.
- All enzymes are protein in nature, but not all proteins are enzymes.
- Some enzymes have both active and regulatory sites.
- Substances upon which the enzymes act are called substrates.
- Enzymes bind to their specific substrates to convert them to product(s).

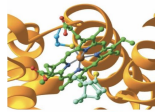


Properties of enzymes

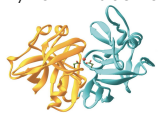
1. **Active site** :
   a. It's the region of enzyme that binds with the substrate and where catalysis occurs.
   b. All enzymes have one or more active sites.
   c. Once the substrate is bound, catalysis takes place.
2. **Specificity** :
   a. Enzymes bind to their specific substrates in the active site to convert them to product(s).
   b. Enzymes are Highly specific, Interact with only one or a few of the substrate.
   c. Catalyze only one type of reaction.
3. **Regulation** :
   a. Enzymes can be activated or inhibited so that the rate of product formation responds to the need of the cell .



Structure of trypsin enzyme.
Trypsin is a digestive enzyme



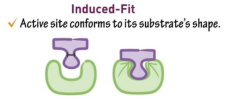
An enzyme with its active site .



Structure of pepsin enzyme

Models of enzyme substrate binding

Induced fit binding



- After the binding of substrate the enzyme changes its shape to fit more perfectly with substrate "not fully complementary" زي القفاز ياخذ شكل اليد بعد ما ينلبس

Lock and key binding

- The enzyme has an active site that fits the exact dimensions of the substrate " Active site is complementary to the substrate ".

Classification of enzymes

A helpful video

★ **Dr:** You should memorize them

Classification	Type of reaction catalyzed
1.**oxidoreduct**ases	Oxidation – Reduction reaction
2.**transfer**ases	Transfer of functional groups
3. **hydrol**ases	Hydrolysis reactions means bond breaking Group elimination means double or triple bond formation .
4. **ly**ases	Group elimination to form double bonds
5. **isomer**ases	isomerization if you have a molecule, isomerase will change a group position in the same molecule"
6.**liga**ses	Bond formation coupled with ATP hydrolysis

Omar
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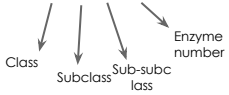
Hard
Learning
International
Languages

-ase suffix indicates that it is an enzyme.

Enzyme nomenclature (naming)

- It is based on the rules given by IUBMB (international union of biochemistry and molecular biology).
- EC 3.4.17.1 , EC means Enzyme Commission (classification).
- EC Class.Subclass.Sub-subclass.Enzyme number.

Example:
EC: 3.4.17.1 (carboxypeptidase A)



Example for a better understanding about EC 3.4.17.1
3 = (hydrolysis, break a bond)
4 = (break which bond? A peptide bond for example)
17 = (which peptide bond? alanine and serine for example)
1 = (there are many enzymes which can do this function so eventually we need to mention the enzyme number, hypothetically its enzyme number 1 in this example)

Cofactors and Coenzymes.

- Some enzymes require **non-protein** groups to become active:

Non-protein part + Apoenzyme (Inactive) = Holoenzymes (Active)

- Non-protein part :
  - Cofactor : are small molecules or metal ions such as Cu2+, Fe3+, Zn2+, etc. which help an enzyme to catalyze a reaction.
  - Coenzymes is small organic molecules such as NAD+ " Small organic molecules " .
    a. prosthetic Group : Coenzymes that are permanently associated with an enzyme e.g. FAD.
    b. Co-substrate : Coenzymes that only temporarily associate with an enzyme e.g. NAD.
- Apoenzyme (Inactive) :
  - The inactive form of enzyme without its non- protein part .

Imagine that the substrate is food, the enzyme is the mouth and the cofactor/coenzyme/isoenzymes are the teeth of the mouth (the enzyme itself)

original pic

Ribozymes , zymogens and Isoenzymes

- Isoenzymes : are enzymes that catalyze the same chemical reaction but they have slightly different structures
- isoenzymes have the same function (catalyze the same reaction) but different structures .
- Ribozymes : are RNAs (Ribonucleic acids) with enzymatic activity.
- Zymogens : are inactive enzyme precursors that require a biochemical change to become active e.g. cleavage of a peptide blocking the active site and they are activated when needed.

Activation energy

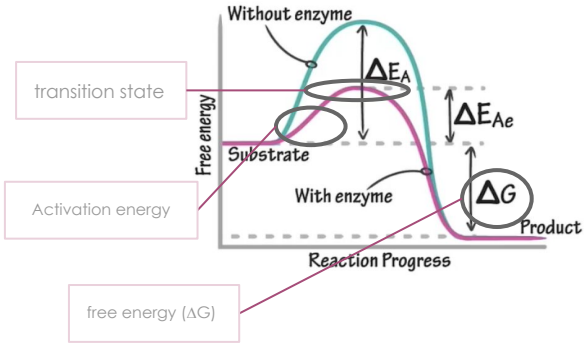
A helpful video

How do enzymes work?

- In every chemical reaction, the reactants pass through a transition state that has greater energy than that of the reactants or products alone (the highest point as shown in the figure, it's also called high-energy intermediate).
- Activation energy (E_A): The difference in energy between the reactants and the transition state. In the figure you can see E_A without the enzyme and E_{Ae} with the enzyme .
- If the activation energy is available then the reaction can proceed forming products.
  - For molecules to react, they must contain sufficient energy to overcome the energy barrier of the transition state. In the absence of of enzyme, only a small amount of molecules may passes enough energy to achieve the transition state between reactants and products.
  - So, the lower the activation energy, the more molecules have sufficient energy to pass through the transition state, and therefore, the faster the rate of the reaction.
- An enzyme reduces the activation energy required for a reaction:

1. It provides an alternative transition state of lower energy called the enzyme-substrate complex
2. Speeds up the reaction.
3. Enzymes decrease the activation energy .

- they do not alter the free energy (ΔG) (available energy).
  - ΔG remains the same, while E_A is reduced i.e. enzymes do not change the equilibrium of the reaction. However, they accelerate the rate by which equilibrium is reached.



Enzymes activity or velocity

A helpful video

- Velocity is the rate of a reaction catalyzed by an enzyme .
- Enzyme activity is expressed as: m moles of product formed/min/mg enzyme
- Activity of an enzyme is expressed as: m moles / min / mg (milli moles "of substrate" per minute per milligram "of the enzyme")

Factors that affect the enzyme activity

1

temperature:

- Every enzyme has an optimal temp. for catalyzing a reaction
- The rate of an enzyme reaction initially increases with rise in temperature (increase in velocity).
- At high temp. enzymes are denatured and become inactive.
  (In humans most enzyme have an optimal temp. of 37C)

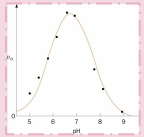
كل أنزيم له درجة حراره محدده يعمل فيها وكل ما زادت درجة الحراره يزداد معدل التفاعل ولكن اذا وصلت درجة حراره عاليه مره راح يتأثر الانزيم وبالتالي ما راح يشتغل

2

pH :

- Effect of pH on the ionizable groups in the active site of enzyme or in the substrate affect catalysis
- Every enzyme has an optimal pH for catalyzing a reaction.
- Most enzymes have highest activity between pH 6 and pH 8.
- Pepsin (digestive enzyme in the stomach) has highest activity at pH 2.

(the bell-shaped curve)
Effect of pH on the initial rate of the reaction catalyzed by most enzymes



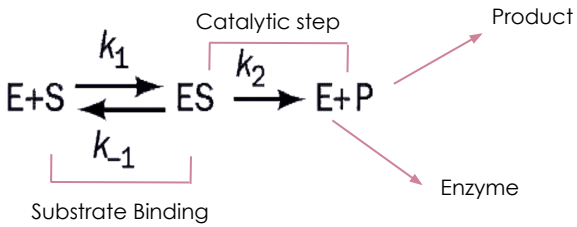
3

[E] & [S] concentrations :

- The rate of an enzyme reaction [E] is directly proportional to the conc. of enzyme , if the substrate concentration [S] is higher than enzyme.
- The reaction velocity increases initially with increasing [S] .
- Further addition of substrate has no effect on enzyme velocity (v).
- At low [S], the reaction rate is proportional to [S] .

Enzymes kinetics

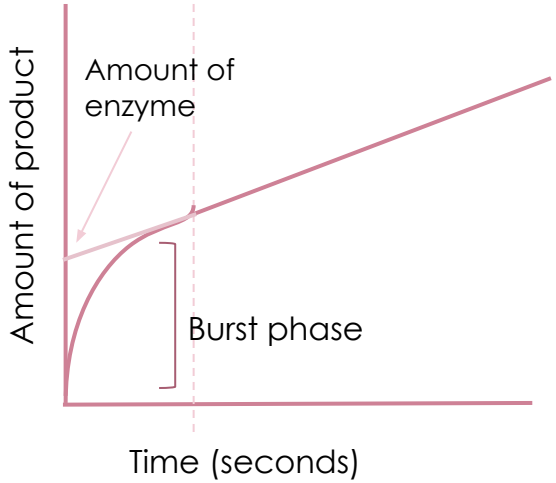
- The model of enzyme kinetics was first proposed by Michaelis and Menten in 1913 and later modified by Briggs and Haldane.
- The Michaelis Menten equation describes the relationship of initial rate of an enzyme reaction to the [S].



Initial rate of enzyme reaction

1. Pre- steady state (The time they take to get arranged):
   - Enzyme + high concentration of substrate = an initial short period of time (a few hundred microseconds) during which intermediates of products gradually build up.
   - NO PRODUCT DURING THIS PHASE. (Enzyme-substrate complex formation only) .
2. Steady state :
   - occurs after initial state, when the reaction rate and the concentration of intermediates changes slowly with time.An intermediate changes into steady state when the rate of its synthesis becomes equal to its rate of degradation.

★ explanation
Thanks to 436 team



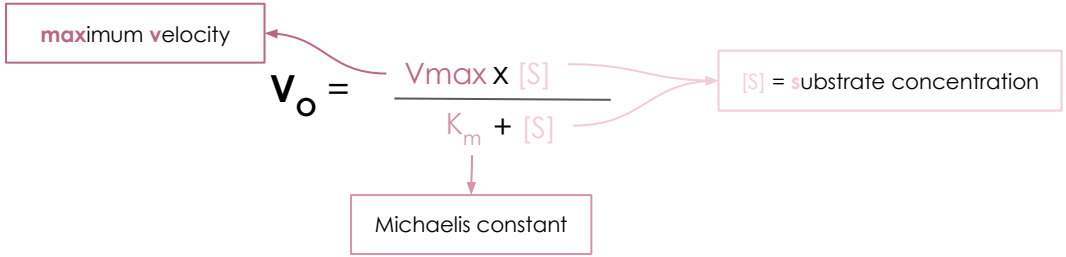
- Pre-steady state kinetics
  - مرحلة إرتباط الإنزايم بالـ substrate عشان يتكون لي ال ES وهو ليس product إنما إنزايم مرتبط مع substrate
  - (Enzyme-substrate complex)
  - هذه الخطوة تعتبر قصيرة جدا لأن كمية المادة اكبر بكثير من كمية الإنزايم فبالتالي تصبح نسبة ارتباط هذه المادة بالانزايم قليلة.

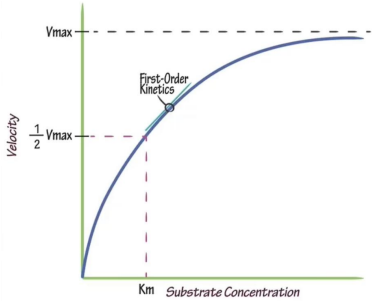
- Steady state kinetics
  - بعد ما تكون عندي (Enzyme-substrate complex) ES سيصبح تركيزه يزداد بشكل ثابت مع الوقت (نلاحظ إن الميل في الصورة يزداد بثبات)

original pic

Michaelis Menten Equation

- It measures the initial velocity (V_o) of an reaction enzyme .
  - Michaelis Menten model Examines the reaction of single substrate with a single enzyme to create a product.
  - First order kinetics : reaction rate is proportionally related to substrate concentration .
  - the plateau " V max " is zero order kinetics which means change in substrate concentration does not change the velocity of the reaction





Initial velocity vo of a simple Michaelis–Menten reaction versus the substrate concentration[S]

K_m (Michaelis Constant)

- K_m is the substrate concentration at which the initial rate is one-half of the maximum rate (1/2 Vmax) .
- It is the [S] (substrate concentration) required to saturate half of all of the active sites of an enzyme .
- The K_m value of a substrate depends on its affinity with the enzyme.
  - High K_m means low affinity with enzyme (more substrate needed to saturate the enzyme) .
  - Low K_m means high affinity with enzyme (less substrate needed to saturate the enzyme) .

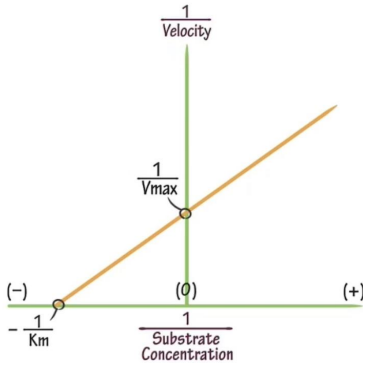
original pic

Lineweaver - Burk plot

A helpful video

- Also called the double-reciprocal plot, obtained by taking reciprocals of the Michaelis menten equation Usage " it represents Michaelis menten equation in straight line and it uses inverse of the variable in Michaelis menten equation".
- It is plotted to

a. calculate the K_m and Vmax values .
b. determine the mechanism of action of enzyme inhibitors .



Quiz

Q1 : When classifying enzymes, which class functions to eliminate groups ?			
A) Oxidoreductases	B) Transferases	C) Lyases	D) Ligases
Q2 : Some enzymes require ……. groups such as …… to become active enzymes.			
A) Non-protein - FAD	B) Non-protein-Na	C) Binding site-Transferase	D) Binding site-Ribozymes
Q3 : Which phase contains the highest energy ?			
A) Reactants	B) Products	C) Transition	D) A and B
Q4 : The KM value of a substrate depends on:			
A) it's affinity with the enzyme	B) Activation energy of the reaction	C) Number of substrates involved	D) No correct answer
Q5 : K_m is the substrate concentration at which :			
A) initial rate is one half the maximum rate	B) initial rate is one third the maximum rate	C) initial rate is one quarter the maximum rate	D) initial rate is one fifth the maximum rate
Q6 : Enzymes that are having slightly different molecular structures but performing identical activity are:			
A) Holoenzymes	B) Apoenzymes	C) Coenzymes	D) Isoenzymes

SAQs :

Q1: Mention one difference between the pre-steady state and the steady state.

Q2: Enumerate 3 types of enzymes

★ **MCQs Answer key:**

1) C 2) A 3) C 4) A 5) A 6) D

★ **SAQs Answer key:**

1) Chick **slide 8**

2) transferases, ligases, hydrolases

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Learn from yesterday,live for today,hope for tomorrow,The important thing is not to stop questioning.

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