BIO TEAM 429

إعداد:

بدور القدره محمد الوطيان

سميه العمري

إيمان الرشيدي

تم إعداد وتنسيق المذكره على أساس تبسيط المعلومات وترتيبها بوضع الجداول والرسوم التخطيطيه على قدر المستطاع

ووضعها على هيئة أسئله مع الأجوبه من أجل سهولة المذاكره والإستفاده القصوى

مع ذلك....هذا لايمنع من الرجوع إلى الكتاب كمصدر أساسي للمذاكره

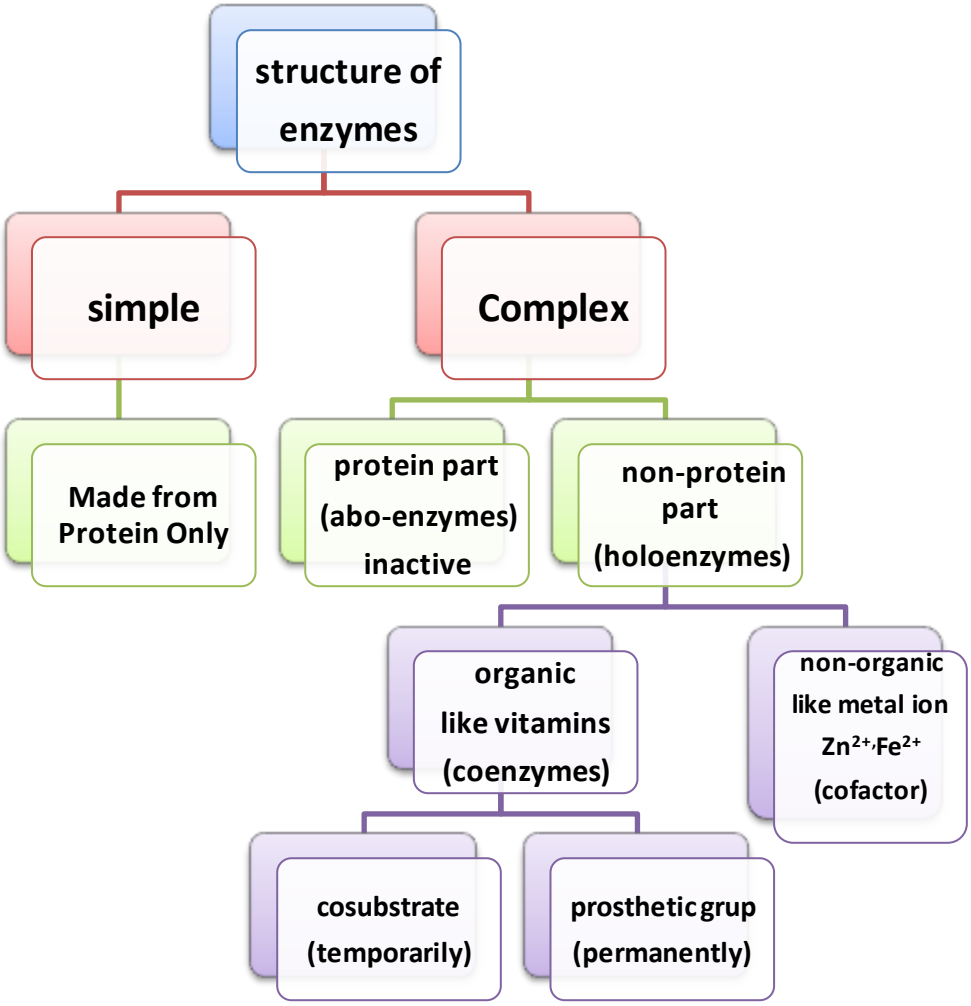
مع تمنياتنا للجميع بالتوفيق والنجاح

ولا نرجوا من عملنا هذا إلا الدعاء لنا بالتوفيق

Enzymes

- Enzymes are biological catalysts that speed up the reaction without being changed in the reaction, and are not consumed
- RNA with catalytic activity are called ribosome
- All enzymes have active site
  - What is the components in active site that create 3-D Surface complementary to the substrate?
  - Amino acid chains

- the active site binds to substrate ⇒ forming an enzyme-sub-strate (ES) complex ⇒ converted to an enzyme-product (EP)
  Complex ⇒ enzyme + product
  - What is the turnover number or k_{cat} ?
  - It's the number of molecules of substrate that converted to product per enzyme molecule per second
  - True or false?
  - Enzymes are highly specific ( )
  - True
  - Enzymes catalyzing many type of chemical reaction ( )
  - False , just catalyze one type
- **Zymogene** : is inactive enzyme (be active when the body need it)
  - Why?
  - To avoid organs destroy
- **Isoenzymes**: tow enzymes have the same function but the different in structure



- How enzyme activity can be regulated?
- By activate or inhabited of enzyme ,and that depending On the needs of cell
  - True or false :
  - Many enzymes are localized in specific organelles Within the cell ( )
  - True

The functional classes

classification	Type of reaction catalyzed
1. **Oxidoreductase**	Oxidation-reduction reaction
2. **Transferases**	Transfer of functional groups
3. **Hydrolases**	Hydrolysis (It is oxidation by H2O)
4. **Lyases**	It breaks the bonds without Oxidation, Reduction, nor Hydrolyses.
5. **Isomerases**	Isomerization (Change its appearance. It changes from D ----> L)
6. **Ligases**	Attach or (يعمل كخياط) with need for ATP.

- All chemical reactions have an energy barrier separating
  The reactants and the products
  - What is called this barrier?
  - It's called the free energy of activation
- By stabilizing the substrat in the transition state.....
  The enzyme greatly increase the concentration of the reactive intermediate that can convert to product
  - What is maximal velocity (v_{max})?
  - It's the number of substrate molecules converted to product per unit time
- If the substrate concentration is high ...then the rate of enzyme-catalyzed reaction increase until saturation
  So adding more substrate will be ineffective
- The reaction velocity increase with temperature until a peak velocity is reached
  - Why?
  - Because it's result of increased number of molecules having sufficient energy to pass over the energy barrier And form products of the reaction

- Enzymes are affected by changes in pH.
- The most favorable pH value is the point where the enzyme is most active, is known as the optimum pH.

- PH is also a factor in the stability of enzymes. As with activity, for each enzyme there is also a region of pH optimal stability.
  - Why?
  - Because active site has functional group that has charges, the active site and the substrate must have the same charge.

- The PH optimum varies from different enzymes:
  - Pepsin PH= 2
  - Amylase PH = 7
  - Alkaline phosphates PH= 9t
- Extremes of pH can lead to denaturation of the enzyme.

Michaelis-Menten Equation

- It is a relationship between the enzyme and it's substrate

Michaelis-Menten Equation:

$$\nu_0 = \frac{V_{max}\,[S]}{K_M + [S]}$$

- It represents the effect of substrate concentration on the reaction rate of the enzyme.

  - V_o= Initial reaction velocity.
  - V_{max}= Maximal Velocity.
  - Km= Michaelis Constant = (K_1 + K2) / K1
  - [S]= Substrate concentration.

- *What is The Steady State assumption?*
- The Rate of synthesis of ES complex = the rate of its degradation. (يتكون -يتكسر-يتكون-يتكسر .. وهكذا)
- What is The Initial Velocity?
- It is used in the analysis of enzyme reactions. We can measure the rate of reaction as soon as the enzyme is mixed with its substrate. In this state the concentration of the product is very small so it can be ignored.
- What is K_m?
- It is the substrate concentration at which the velocity of reaction =half of V_{max}. …Which mean half of Active sites are saturated.

❖ If ...

- Km (Low) = the Affinity between the S and E (Increase).
- Km (High) = the Affinity between S and E (Decrease).

- What is the *Order of Reaction?*
- *The First Order = When [S] is less than Km.*
- *The Zero Order = When [S] is greater than Km*.

- *What is inhibitor?*
- Any substance that can diminish the velocity of an enzyme-catalyzed reaction

❖ There are two type of enzyme inhibition :

1. Reversible: bind to enzyme through non-covalent bond
2. Irreversible: bind to enzyme through covalent bond

- Competitive Inhibitor :
  - Here there is a competition between the Substrate and the Inhibitor on the active site...
  - Why?
  - Because the Inhibitor has a Structure Analog that make the active site unable to determine if this is an Inhibitor or a Substrate.

- *The Stain Drugs as examples of Competitive Inhibitors:*
  - The Reaction of Cholesterol Synthesis is catalyzed by *hydroxymethylglutaryl-CoA reductase (HMG-CoA reductase).*
  - The Stain drug atrovastatin (Lipitor), Simvastain (Zocor) are structure analogs to HMGCoA reductase.
  - They inhibit de novo (anew) cholesterol synthesis. That's why they are used to lower the cholesterol level.

- *Non-Competitive Inhibitor :*
  - The inhibitor and substrate bin to different site

- Example of enzyme inhibitor as drug:
  - B-lactam antibiotics, such penicillin, act by inhibiting enzymes involved in bactererialbcell wall synthesis
  - (ACE) inhibitors, the lower blood pressure

Competitive	Non Competitive
Here V_{max} is constant.	V_{max} Decrease
K_m Increase because S increased to breakdown the bond between I and E.	K_m Constant
The reaction Reversible	Some of them Irreversible

- **Regulation of Enzymes Activity By:**

1. Substrate Availability
2. Allosteric Binding Sites.
3. Regulation of enzymes by covalent modification.
4. Induction and repression of enzyme synthesis.

❖ The rates of most enzymes are responsive to changes in substrate concentration
  - Why?
  - Because the intracellular level of many substrates is in the range of the K_m

- True or false:
- Increase in substrate concentration prompts an decrease in reaction rate( )
- False (an increase in reaction rate)

- The regulation maybe :

- *Short Term:*
  Allosteric Binding Sites + Covalent modification
- *Long Term:*
  Synthesis of enzymes.

- *Allosteric Binding Sites* :

❖ Occupy another space, other than the substrate
❖ Usually contains multiple sub-units.
❖ It is regulated by molecules called effectors or modifiers.
❖ The substrate that binds on the Allosteric. They attached to it with non-covalently which mean Reversible

- What's function of *Allosteric Binding Sites*?
  1. Change the affinity of the enzyme for its substrate.
  2. Modify the maximal catalytic activity of enzyme.

  Or do both of them in the same time.
  BUT doesn't change the enzyme specificity...
  ((يعني اليوم ما يشتغل على شئ وبكره شئ ثاني!))

❖ + effectors: increase enzyme activity
❖ - effectors: inhibit enzyme activity

- Division of Allosteric Binding Sites:

1. Homotropic effector: They are molecules that are the same type of substrate, act as the effector, but they are not the substrate itself. Usually it's (+).
2. Heterotropic effector: They are molecules different then the substrate. Sometime they are (+) and other time they are (-) depending of the substrate. Feedback Inhibition is an example for it.

- *.Regulation of enzymes by covalent modification:*

Change in action of the enzyme by making the enzyme attach to a phosphate group.

- Phosphorylation and dephosphorelation :
- The enzyme either takes the phosphate group from the ATP. Or reattach it to make the enzyme back.all of that depends on whether the enzyme is active or inactive.

❖ The enzymes that help building are mostly in the dephosphorelation form.
❖ The enzymes that break are mostly active in the phosphorelation form.

- *Induction and repression of enzyme synthesis.*
- Change in the amount of enzyme leads to change in the amount of active sites.
  - ❖ Enzyme Repression= Decreasing the amount of enzyme.
  - ❖ Enzyme Induction= Increase the amount of enzyme.
  - ❖ The enzyme in the plasma should be in the inactive condition until stimulation come along and activate it.

- **Enzymes In clinical Diagnosis:**
- Enzymes In Plasma :

❖ Functional = they are found in the plasma and their substrate also found in plasma.They are released into the plasma in an inactive condition until stimulation comes and activate it. Most of the functional are Zymogens.
❖ Nonfunctional= they are found inside the cells. But they leak to the plasma because of the cell turnover which means they don't have substrates in the plasma. And you can find a large amount of them in the plasma. Also, they have no physiologic use in plasma

- *Alteration of plasma enzyme levels in diseases states:*

❖ Diseases are caused by increase release of intracellular enzymes into the plasma.
❖ The diagnosis of disease for heart, liver, skeletal muscle and other tissues are determined by the activity of its enzymes.

- *Plasma enzymes as diagnostic tools:*

❖ Specific enzymes= If we knew each enzyme and what tissue it come from it help a lot in diagnosis

- For example: ALT enzyme is secreted from liver. So, if we found a high level of this enzyme in plasma, this is signal of a possible damage in hepatic tissue

❖ Non specific enzymes= some enzyme are not specific for only one tissue some of them are secreted from more than one tissue.

- For example: AST enzyme is secreted from liver, red blood cells, cardiac muscle, skeletal muscle, and Kidney. So if we see an increase level of this enzyme in the plasma it is hard to determine which tissue is the damaged one. So the lack of tissue specificity limits the diagnostic value of many plasma enzymes

- *Isoenzymes and diseases of the hear:*

❖ They are enzymes that catalyze the same reaction. But they don't have the same physical properties because of the differences in the amino acid sequence.

❖ Their level in the plasma may determine the presence of a disease of damage. For example, the plasma levels of creatine kinase (CK) are commonly determining the myocardial infarction.

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