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Regulation of enzyme activity

Regulation of enzyme activity is important to coordinate the different metabolic processes.
It is also important for homeostasis i.e. to maintain the internal environment of the organism constant.
Regulation of enzyme activity can be achieved by two general mechanisms:

1- Control of enzyme quantity

Enzyme quantity is affected by:

A- Altering the rate of enzyme synthesis and degradation,

B- Induction

C- Repression

2- Altering the catalytic efficiency of the enzyme by

Catalytic efficiency of enzymes is affected by:

A- Allosteric regulation

B- Feedback inhibition

C- Proenzyme (zymogen)

D- Covalent modification

E- Protein – Protein interaction

1.Control of enzyme quantity

A- Control of the rates of enzyme synthesis and degradation.

As enzymes are protein in nature, they are synthesized from amino acids under gene control and degraded again to amino acids after doing its work.

Enzyme quantity depends on the rate of enzyme synthesis and the rate of its degradation.

- **Increased enzyme quantity** may be due to an increase in the rate of synthesis, a decrease in the rate of degradation or both.
- **Decreased enzyme quantity** may be due to a decrease in the rate of synthesis, an increase in the rate of degradation or both.
- For example, the quantity of liver arginase enzyme increases after protein rich meal due to an increase in the rate of its synthesis; also it increases in starved animals due to a decrease in the rate of its degradation.

B- Induction

Induction means an increase in the rate of enzyme synthesis by substances called inducers

According to the response to inducers, enzymes are classified into:

Constitutive enzymes, the concentration of these enzymes does not depend on inducers.

Inducible enzymes, the concentration of these enzymes depends on the presence of inducers

For example, induction of lactase enzyme in bacteria grown on glucose media.

C- Repression

Repression means a decrease in the rate of enzyme synthesis by substances called repressors.

Repressors are low molecular weight substances that decrease the rate of enzyme synthesis at the level of gene expression.

Repressors are usually end products of biosynthetic reaction, so repression is sometimes called feedback regulation.

For example, dietary cholesterol decreases the rate of synthesis of HMG CoA reductase (β-hydroxy β-methyl glutaryl CoA reductase), which is a key enzyme in cholesterol biosynthesis.

D- De repression

Following removal of the repressor or its exhaustion, enzyme synthesis retains its normal rate.

E- Concentration of substrates, coenzymes and metal ion activator The susceptibility of the enzyme to degradation depends on its conformation. Presence of substrate, coenzyme or metal ion activator causes changes in the enzyme conformation decreasing its rate of degradation.

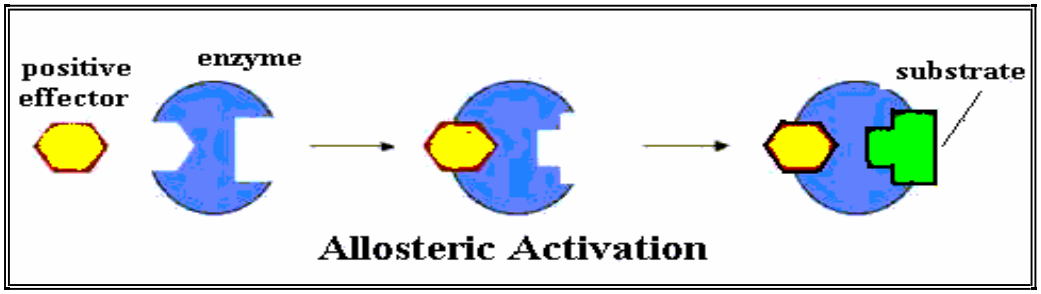
2. Control of catalytic efficiency of enzymes

A- Allosteric Regulation

Allosteric enzyme is formed of more than one protein subunit. It has two sites; a catalytic site for substrate binding and another site (allosteric site), that is the regulatory site, to which an effector binds.

Allosteric means another site

If binding of the effector to the enzyme increases it activity, it is called positive effector or allosteric activator e.g. ADP is allosteric activator for phosphofructokinase enzyme.



If binding of the effector to the enzyme causes a decrease in its activity, it is called negative effector or allosteric inhibitor e.g.

- ATP and citrate are allosteric inhibitors for phosphofructokinase enzyme.
- Glucose-6-phosphate is allosteric inhibitor for hexokinase enzyme.

Mechanism of allosteric regulation

Binding of the allosteric effector to the regulatory site causes conformational changes in the catalytic site, which becomes more fit for substrate binding in positive effector (allosteric activator), and becomes unfit for substrate binding in negative effector (allosteric inhibitor) as shown in the following diagram.

Catalytic site ^ **Allosteric Enzyme**	 **Positive effector** It gives the catalytic site of the enzyme a conformation, which is more fit for substrate binding.	 **Negative effector** It gives the catalytic site of the enzyme a conformation, which is unfit for substrate binding.

A representative diagram for the mechanisms of allosteric regulation

Kinetics of allosteric enzymes

- One of the common characteristics of an allosteric enzyme is that it shows a sigmoid plot when velocity is plotted against substrate concentration
- Allosteric enzymes generally do not follow the Michaelis-Menten equation.The Lineweaver-Burk plot is concave upward.