Enzymes Introduction and Mechanism of Action

Learning Objectives

- Characteristics of Enzymes
- Classification of Enzymes
- Nomenclature of Enzymes
- Active site and Transition state
- Mechanism of enzyme actions

Clinical Importance

Diagnosis and prognosis of diseases.

Disorders: genetic, nutritional, tissue damage

Pharmacologic agents and **Gene Therapy**

Drugs /Antibiotics.

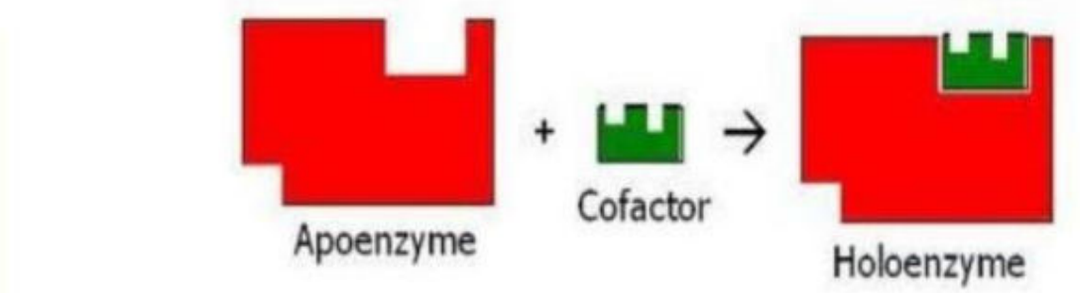
Enzymes

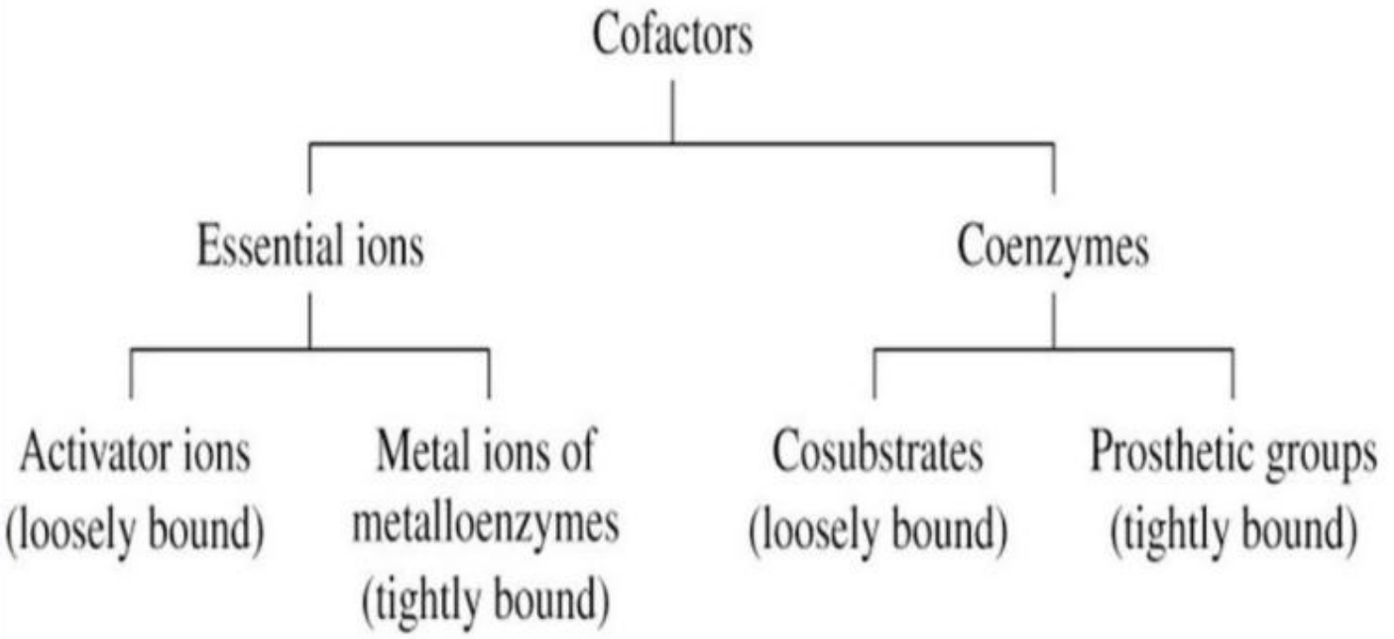
- **Enzymes** are specialized proteins that function in the acceleration of chemical reactions
- Exception?
- Ribozymes

Characteristics of enzyme catalysts

- Increase rate of reaction by factor of 10^6
- Highly selective and specific
- Not changed as a result of catalysis
- Does not change the equilibrium constant
- **Enzymes Alter Only the Reaction Rate and Not the Reaction Equilibrium**

Cofactor containing enzymes





Examples of coenzymes and cofactors

Vitamin	Coenzyme	Enzymes	Enzymes	Cofactors
Thiamine	TPP	Transketolase, pyruvate Dehydrogenase	Ferroxidase	Copper
Riboflavin	FAD, FMN	Succinate dehydrogenase	Carbonic anhydrase	Zinc
Niacin	NAD,NADP	Malate dehydrogenase	Cytochrome oxidase	Copper, Iron
Pyridoxine	PLP	transaminases	Hexokinase	Magnesium
Folic acid	THF	One carbon metabolism	Glutathione peroxidase	Selenium
Pantothenic acid	Coenzyme A	Pyruvate dehydrogenase	Arginase	Manganese
			Xanthine Oxidase	Molybeden

Classification of Enzymes

Class	Subclass
I *Oxidoreductases*	*Dehydrogenases, oxidases, peroxidases, catalase, oxygenases, hydroxylases, reductases*
II *Transferases*	*Transaldolase, transketolase, kinases,* etc.
III *Hydrolases*	*Esterases, glycosidases, peptidases, phosphatases, thiolases, amidases,* etc.
IV *Lyases*	*Decarboxylases, aldolases, hydratases, dehydratases synthases*
V *Isomerases*	*Racemases, epimerases, mutases*
VI *Ligases*	*Synthetases, carboxylases*

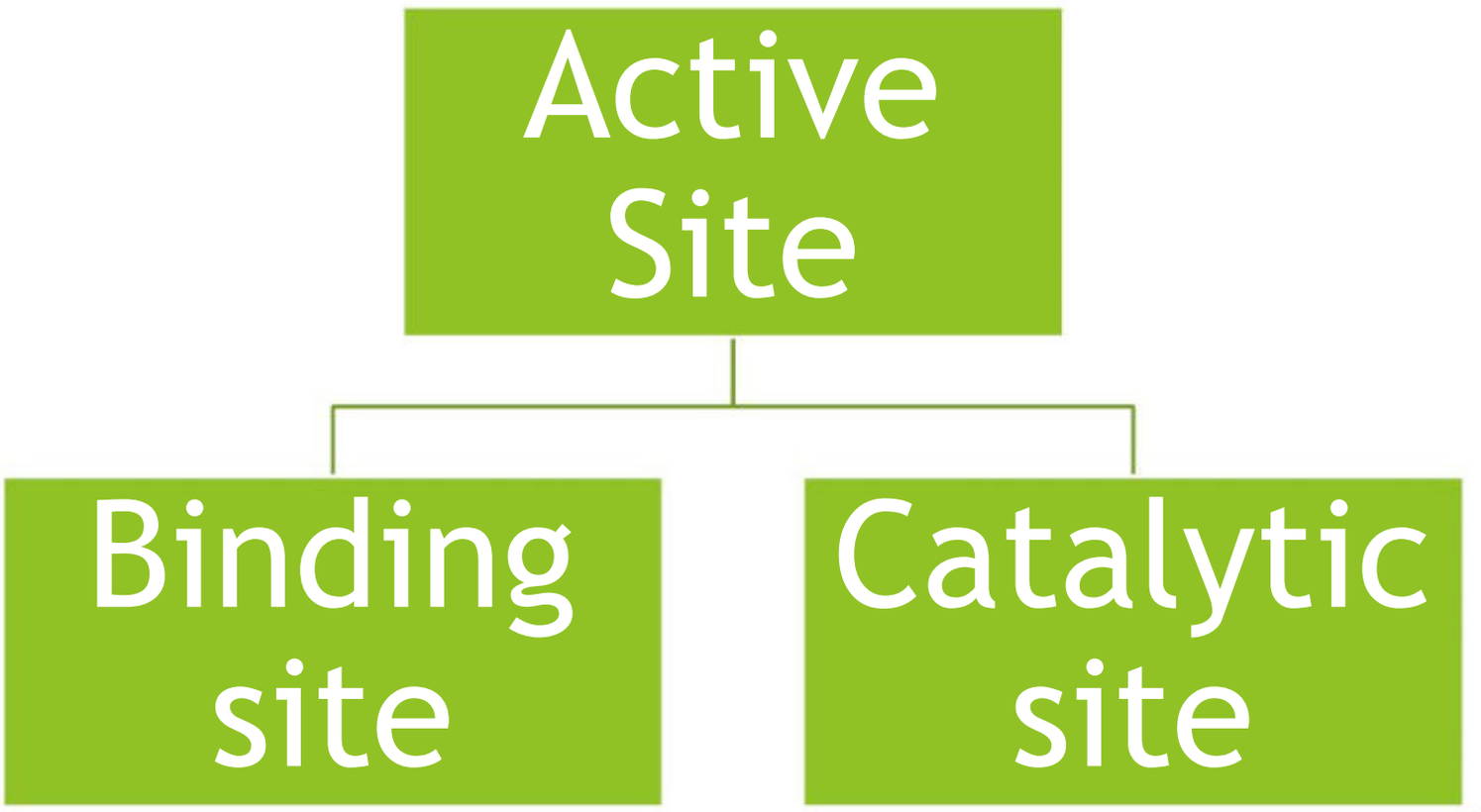
Nomenclature of Enzymes

- International Union of Biochemistry and Molecular Biology (IUBMB)
- **Recommended name**
- **Systematic name** EC1.1.1.27 (Lactate Dehydrogenase)

Special names

- Phosphatase vs Phosphorylase
- Synthetase vs Synthase
- Dehydrogenase vs Oxidase vs Oxygenase

Active site



Features of Active Site

- *3D cleft formed by groups that come from different parts of the amino acid sequence*
- *takes up a relatively small part of the total volume of an enzyme*
- *clefts or crevices*
- *Substrates are bound to enzymes by multiple weak attractions*

Transition state

- Enzymes lower activation energy by stabilizing transition state
- The active site can provide catalytic groups that enhance the probability that the transition state is formed
- 1. **LOCK-AND-KEY MODEL FOR SUBSTRATE BINDING: Emil Fisher**
- **2. “INDUCED FIT” MODEL FOR SUBSTRATE BINDING: Daniel E koshland**

Mechanism of catalysis

1. Catalysis by Proximity
2. Catalysis by strain
3. Acid Base Catalysis

Chymotrypsin

4. Covalent Catalysis
5. Metal ion catalysis

Metal ion catalysis

- Assist in binding of the substrate,
- Stabilize developing anions in the reaction.
- Accept and donate electrons in oxidation-reduction reactions.

- Serine protease like chymotrypsin : acid base catalysis as well as covalent catalysis
- RNAase : covalent catalysis
- Metal ion: carbonic anhydrase

Clinical scenario 1

- Vitamin B6 responsive and unresponsive cystathionuria: two variant molecular forms

Clinical Scenario 2

- A child was born with inherited mutation in an enzyme, so that it is unable to bind its coenzyme.

As a result,

(A) the enzyme doesnot bind to its subtrate

(B) the enzyme will not be able to form transition state complex

(C) the reaction will proceed with free coenzyme

(D) the enzyme will use some other coenzyme

References

- Victor W. Rodwell, David A. Bender, Kathleen M. Botham, Peter J. Kennelly, P. Anthony Weil. Harper's Illustrated Biochemistry, 30th Edition
- Denise R. Ferrier; Lippincott Illustrated Reviews Biochemistry, 7th Edition

Thank You!