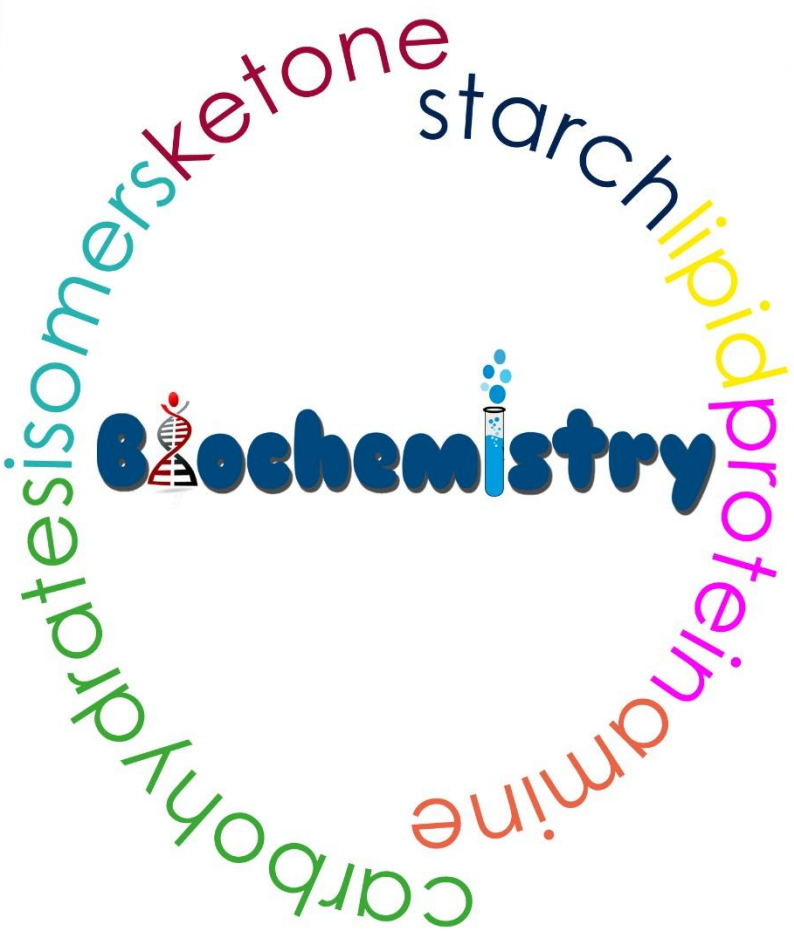


◉Sheet ○Slides

Subject :	Enzyme classification and Co-factors
Done by :	Qusai Zureikat
Corrected by :	عبدالله الزبده
Number :	12

Naming of enzymes.

-Most enzymes are named scientifically according to the substrate they are dealing with. In general, the name of the enzyme should indicate the name of the substrate acted upon, followed by the type of reaction catalyzed, followed by the suffix –(ase).

For example:

ATPase is the enzyme that breaks down ATP.

ATP Synthase is the enzyme that synthesizes ATP.

-Most enzymes follow this rule except a few that have non-scientific common names that are in no relation to the mechanism of the reaction and don't indicate the action of the enzyme, such as

Trypsin, Pepsin and Renin

-Another method of naming enzymes is using **The Enzyme Commission number (EC number)**, which consists of the letters "EC" followed by four numbers separated by periods. Those numbers represent a progressively finer classification of the enzyme.

The first digit indicates the major class of the enzyme

The second digit indicates the minor class of the enzyme

The third and fourth digits indicate a further sub-classification

For example, *(Do not memorize)* the tripeptide aminopeptidases have the code

"EC 3.4.11.4", whose components indicate the following groups of enzymes:

- EC 3 enzymes are hydrolases (enzymes that use water to break up some other molecule)
- EC 3.4 are hydrolases that act on peptide bonds
- EC 3.4.11 are those hydrolases that cleave off the amino-terminal amino acid from a polypeptide
- EC 3.4.11.4 are those that cleave off the amino-terminal end from a tripeptide.

Enzyme Classification

A) Enzymes can be classified according to their *structure* to:

1) **Simple Enzymes:** They consist of proteins only (An amino acid sequence with no attachments)
2) **Conjugated Enzymes (Holoenzyme):** They consist of a proteinous part called *apoenzyme* and non-proteinous part called *co-factor*. (Example: Myoglobin/Hemoglobin require Heme to function)

-**Cofactors**, mostly metal ions or coenzymes, are inorganic and organic chemicals that assist enzymes during the catalysis of reactions. **Coenzymes** are non-protein organic molecules that are mostly derivatives of vitamins soluble in water by phosphorylation; they bind apoenzyme to proteins to produce an active *holoenzyme*.

B) Enzymes can be classified according to their *function* into 6 major groups:

- Oxidoreductases
- Transferases
- Hydrolases
- Lyases
- Isomerases
- Ligases

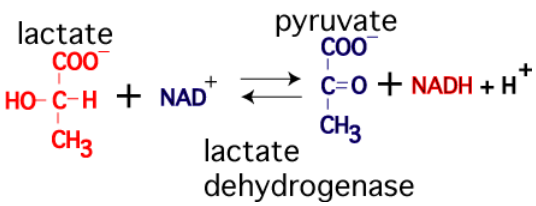
1) Oxidoreductases: are enzymes that catalyze the transfer of hydrogen or electrons from one molecule (the reductant, also called the electron donor) to another (the oxidant, also called the electron acceptor). This means that those enzymes act on -at least- 2 substrates "redox couple".

-This group can be further divided into 4 main classes:

a. Dehydrogenases
b. Oxidases
c. Peroxidases
d. Oxygenases

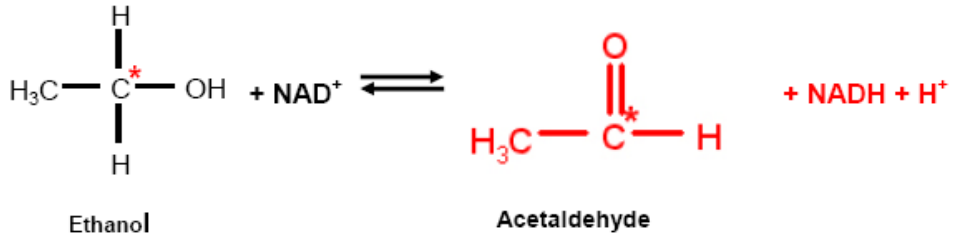
-**Dehydrogenases:** Catalyze hydrogen transfer from the substrate to a molecule known as nicotinamide adenine dinucleotide (NAD+)

-An example of this is lactate dehydrogenase which catalyzes the following reaction:



-Lactate + NAD+ ⇆ Pyruvate + NADH + H+

Another example is Alcohol dehydrogenase



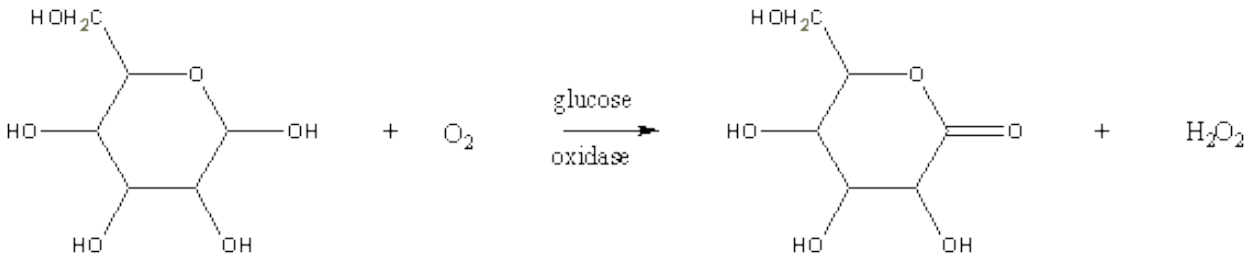
Ethanol

Acetaldehyde

-Oxidases: Catalyze hydrogen transfer from the substrate to molecular oxygen producing hydrogen peroxide as a by-product. Hydrogen Peroxide (H2O2) is also a well-known oxidizing agent but in this case, molecular oxygen is the only one that carries out oxidation, H2O2 is only a by-product.

An example is glucose oxidase which catalyzes the following reaction:

β-D-glucose + O2 ⇆ gluconolactone + H2O2



Glucose oxidase is used in monitoring sugar levels for diabetics

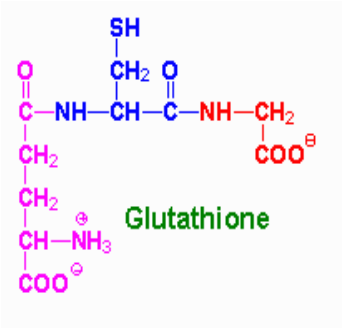
-Peroxides: catalyze oxidation of a substrate by hydrogen peroxide producing water.

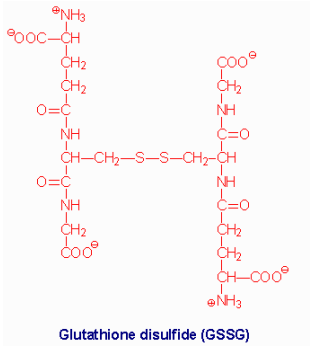
In *Oxidases*, H2O2 is produced as *a by-product*

In *Peroxides*, H2O2 is used as *a reactant.*

An example is the oxidation of two molecules of glutathione (GSH) in the presence of hydrogen peroxide:

2 GSH + H2O2 + 2H+ ⇆ G-S-S-G + 2 H2O





-Oxygenases: catalyze substrate oxidation by molecular oxygen

-The reduced product of the reaction in this case is water and not hydrogen peroxide

An example of this is the oxidation of lactate to acetate catalyzed by lactate-2-monooxygenase

CH3-CH(OH)-COOH + O2 ⇆ CH3COOH + CO2 + H2O

Both Oxidases and Oxygenases use molecular oxygen but:

Only Oxygenases take the oxygen atom and incorporate it into the substrate. In Oxidases, the oxygen is not taken and placed within the substrate.

There are two types of Oxygenases

Monooxygenases, transfer one oxygen atom to the substrate, and reduce the other oxygen atom to water.

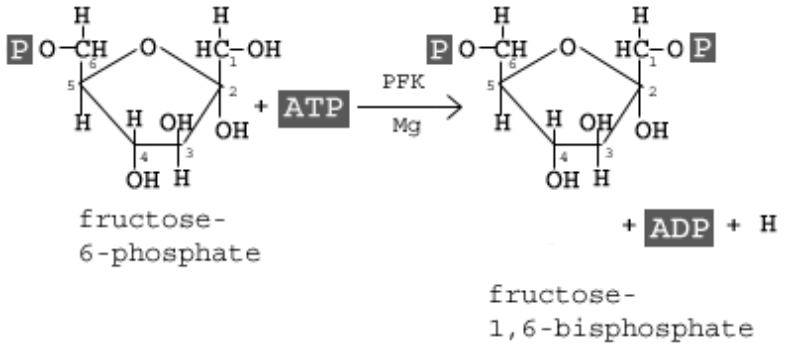
Dioxygenases, incorporate both atoms of molecular oxygen (O_2) into the product(s) of the reaction.

2) Transferases: These enzymes transfer a functional group (C, N, P or S) from one substrate to an acceptor molecule. They have –at least- 2 substrates.

- Kinase: an enzyme that catalyzes the transfer of phosphate groups from high-energy, phosphate-donating molecules (Most commonly ATP) to specific substrates.
  (Naming of kinases: Name of substrate followed by Kinase)

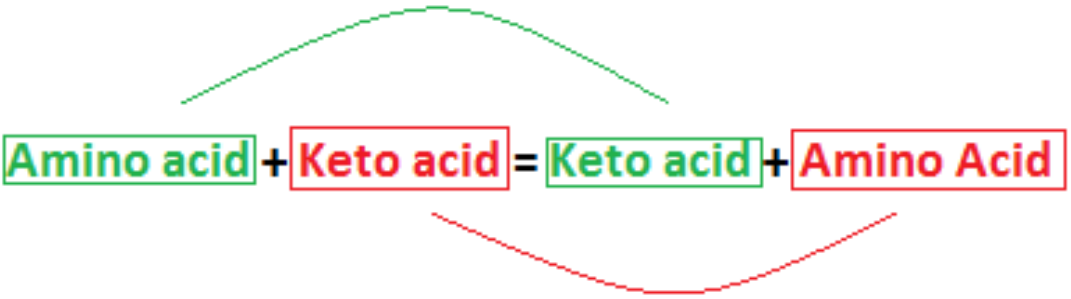
An example is Phosphofructokinase, which catalyzes transfer of phosphate from ATP to fructose-6-phosphate:

Fructose 6-P + ATP $\leftrightarrow$ F 1,6 bisphosphate + ADP



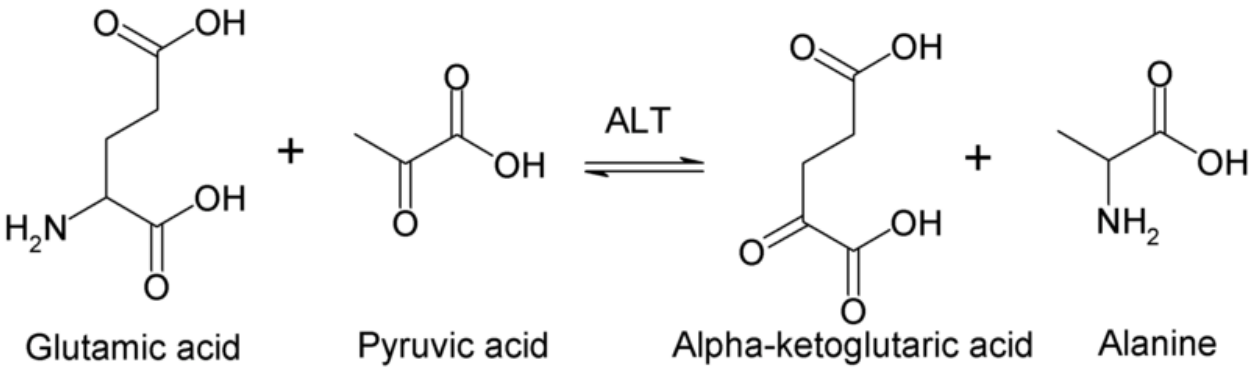
Transaminase/Aminotransferase: A transaminase transfers an amino functional group from one amino acid to a keto acid, converting the amino acid to a keto acid and the keto acid to an

amino acid. This allows for the interconversion of certain amino acids.



-3 examples of amino acids that interconvert with corresponding keto acids are:

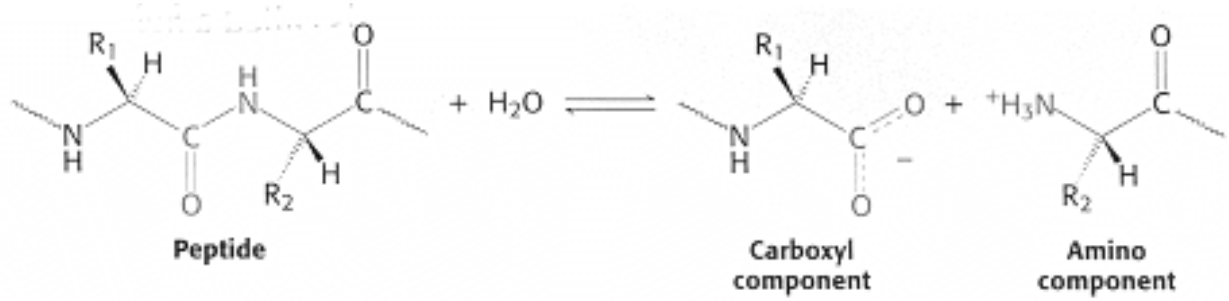
AMINO ACID	KETO ACID
Alanine	*Pyruvate*
Glutamic acid	*Alpha-ketoglutarate*
Aspartic acid	*Oxaloacetate*



3) Hydrolases: These enzymes catalyze cleavage reactions while using water across the bond being broken or the fragment condensations. Peptidases, esterases, lipases, glycosidases, phosphatases, Proteases, nucleases are all

examples of hydrolases named depending on the type of bond cleaved

- Proteases: catalyze proteolysis, the hydrolysis of a peptide bond within proteins

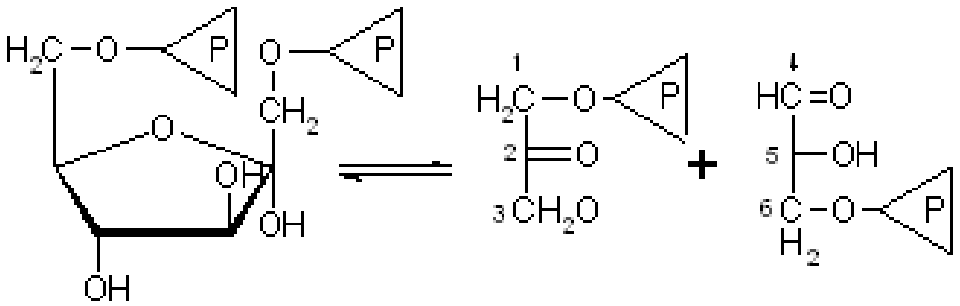


- ✓ Trypsin, a digestive enzyme, is quite specific and catalyzes the splitting of peptide bonds only on the carboxyl side of lysine and arginine residues
- ✓ Thrombin, an enzyme that participates in blood clotting, catalyzes the hydrolysis of Arg-Gly bonds in particular peptide sequences only

4) Lyases: These enzymes remove groups from their substrates with the associated formation or removal of double bonds between C-C, C-O and C-N by a means other than hydrolysis.

An example is aldolase, which breaks down fructose-1,6-bisphosphate into dihydroxyacetone phosphate and glyceraldehydes-3-phosphate.

F 1,6 bisphosphate ⇆ DHAP + GAP



the substrate splits when water is added, then you are dealing with a hydrolase, if not, then it's a lyase.

5) Isomerase: These enzymes catalyze intramolecular rearrangements. They act on 1 substrate.

- Mutase: an enzyme of the isomerase class that catalyzes the shifting of a functional group from one position to another within the same molecule.

6) Ligases: Ligases join C-C, C-O, C-N, C-S and C-halogen bonds The reaction is usually accompanied by the consumption of a high energy compound such as ATP and other nucleoside triphosphates.

- Carboxylases: an enzyme which catalyses the addition of a carboxyl group to a specified substrate. (Pyruvate Carboxylases)

The number of carbon units is increasing (The chain becomes longer "*anabolism*"), ATP is required and this addition doesn't initiate the addition or breakdown of a double bond unlike in Lyases.

Enzyme Co-Factors

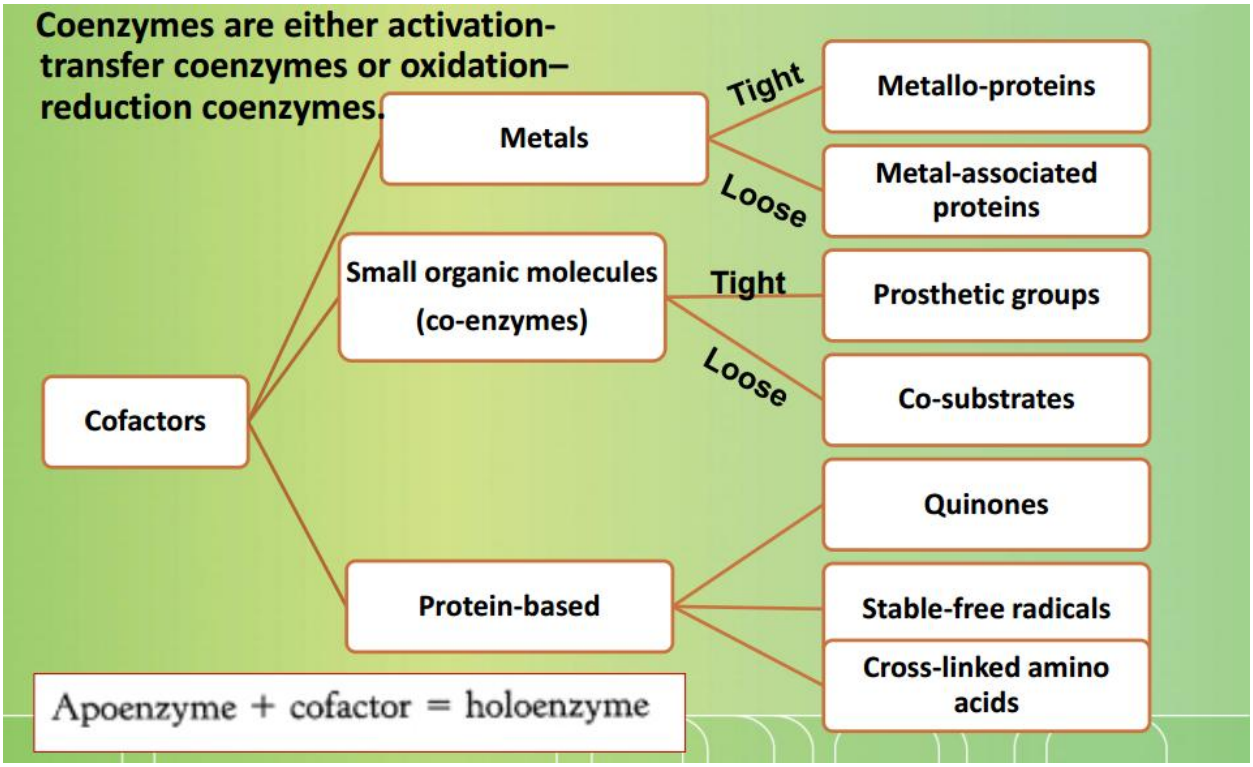
For many enzymes the functional groups of the amino acids within the active site are responsible for the catalysis.

Within the active site, *Hydrophobic* amino acids are responsible for the binding of the active site to the substrate

and *Polar amino* acids cause the binding regardless of the nature of the substrate. Histidine is most commonly found within the active sites of enzymes because it's pKa is very close to physiological one which means it can donate and accept protons within physiological ranges of pH.

Coenzymes are divided into two groups:

1) Activation-transfer coenzymes
2) Oxidation–reduction coenzymes



-Heme group which is an organic structure with iron embedded in it is an example of Metallo-protein (Organometallic)

-Protein-based cofactors are catalytic centers found in proteins formed by the modification of one or more amino acid residues "modified AAs from within the enzyme itself".

-Coenzymes are derived from water-soluble **Vitamins.**

-Vitamins are organic structures, needed in small amounts, cannot be synthesized within the body and have to be obtained from outside.

- Activation transfer coenzymes are initiating a covalent bond with the substrate through the mechanism of their action.

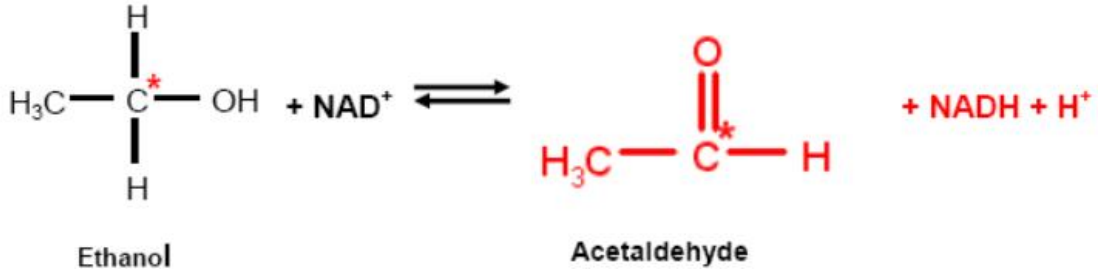
Questions Time!

1- Which one of the following is the reducing agent in this enzyme-catalyzed reaction?

Lactate + NAD+ ⇆ Pyruvate + NADH + H+

a- Lactate b- NAD+ c- dehydrogenase d- Pyruvate

2- Which one of the following is oxidized in this enzyme-catalyzed reaction?



a- Ethanol b- NAD+ c-dehydrogenase d-H+

3- Choose the correct answer regarding the following enzyme-catalyzed reaction:

$$\underline{X} + H_2O_2 \rightarrow \underline{Y} + H_2O$$

a- X is the reducing agent
b- Catalyzed by oxidase enzyme
c- H_2O_2 is reduced to H_2O
d- More than one of the above

4- Peroxidases and oxygenases:
a- Both produce H_2O as a reduced product
b- Oxidize the substrate
c- Molecular oxygen is used by one of them ant not the other
d- All of the above

5- This reaction is catalyzed by:

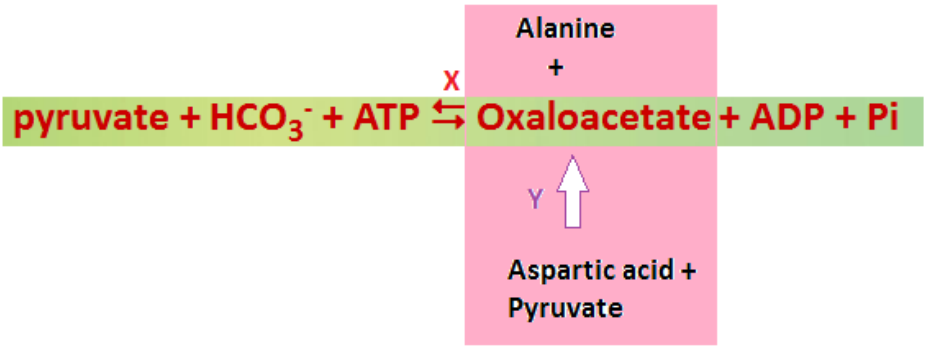
$$CH3\text{-}CH(OH)\text{-}COOH + O2 \leftrightarrows CH3COOH + CO2 + H2O$$

a- Peroxidase b- monooxygenase c- dioxygenase
d-oxidase

6- Splitting polymers into monomers is catalyzed by:

a- Isomerase b- Lyase c- Ligase d- Hydrolase

7- Choose the best answer regarding these two reactions:



	X	Y
A	Carboxylase	Oxidase
B	Lyase	Oxidase
C	Carboxylase	Transaminase
D	Lyase	Transaminase

Answers:

1	2	3	4	5	6	7
a	a	d	d	b	D	c