GLYCOLYSIS

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Glycolysis is derived from Greek word, **Glykys = sweet, Lysis = to breakdown or splitting. Glycolysis which literally means breakdown of sugars.** So in this process one molecule of glucose (**6C)** oxidized and broken down into two molecules of pyruvate or Pyruvic acid **(3C)**. The entire process takes place in 10 steps. Glycolysis is also called **Embeden-Meyerhof Pathway**. Glycolysis is **anaerobic oxidation occurring in the cytoplasm of the cells.**

10 step of glycolysis can be subdivided into two phases.

1. **The prepratory phase (steps 1- 5) – spend ATP**
2. **The Payoff Phase (steps 6- 10) - generates ATP & NADH.**

The 10 step of glycolysis are as follows.

1. **Phosphorylation of glucose and interconversion of glucose 6 phosphate and Fructose 6 phosphate –** In glycolysis first of all a molecule of glucose is phosphorylated to glucose 6 phosphate by the enzyme glucokinase (in liver) or hexokinase (occurring in all other tissue) using ATP as phosphate Donor. **The reaction is generally called as phosphorylation.**

$$\textbf{Glucose + ATP} \xrightarrow{glucokinase/hexokinase,\ Mg^{2+}} \textbf{glucose-6-phosphate + ADP}$$

2. The second step in this the enzyme; phosphohexose isomerase catalyzes the transformation of glucose -6- phosphate to its structural isomer Fructose -6- phosphate.

3. **Conversion of fructose 6 phosphate into Fructose 1,6 diphosphate –** Fructose 6 phosphate is converted in this step to diphosphate derivative by the transfer of the terminal phosphate group of another ATP to the number 1 carbon of fructose -6- phosphate to form Fructose 1,6 diphosphate. Phosphofructokinase is the main allosteric enzyme for this reaction. This enzyme is responsible for the transfer of phosphate group (from ATP) at C1 position.

   The activity of **phosphofructokinase** enzyme accelerates whenever the cell is deficient in ATP but it is inhibited when sufficient ATP molecules are present in the cell which lowers the affinity of enzyme for Fructose -6- phosphate, due to this reason **phosphofructokinase is said to be as pacemaker of glycolysis**.

$$\textbf{Fructose-6-phosphate + ATP} \xrightarrow{Phosphorfructokinase,\ Mg^{2+}} \textbf{fructose 1,6diphosphate + ADP}$$

4. **Cleavage of FDP to phosphate –** Fructose 1,6 diphosphate is split between carbon 3 and 4 into two essentially similar molecules i.e. dihydroxyacetone phosphat (a ketoses) and glyceraldehyde 3 phosphate (an aldose). This reaction is catalyzed by enzyme aldolase. The resulting two triose phosphate are not identical but isomers of each other. They are interconvertible by means of an isomerizing reaction catalysed by the enzyme phosphotriose isomerase.

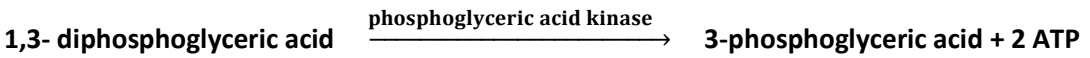
5. **Isomerisation of dihydroxyacetone phosphate –** Enzyme triose phosphate isomerase catalyzes the reversible conversion of dihydroxyacetone phosphate to glyceraldehyde -3- phosphate. Thus from one molecule of fructose 1,6 di phosphate, two molecules of glyceraldehyde 3 phosphate are formed.

6. **Oxidation of glyceraldehyde -3- phosphate –** Oxidation of glyceraldehyde -3- phosphate takes place forming 1,3- diphosphoglyceric acid. The reaction occurs in the presence of inorganic phosphate (Pi) and coenzyme NAD^+.

   Enzyme 3 phosphoglyceraldehyde dehydrogenase catalyzes the reaction which yields two hydrogen atoms from each phosphoglyceraldehyde or glyceraldehyde -3- phosphate (PGAL) molecules. **Nicotinamide adenine dinucleotide (NAD^+) becomes reduced by accepting two electrons and one Proton to NADH.**

7. **Phosphorylation of 1,3- diphosphoglyceraic acid and formation of ATP–**

   1,3 diphosphoglyceraic acid releases a phosphate which combines with ADP to form ATP and 3 phosphoglyceric acid by an enzyme phosphoglyceric acid kinase. In this reaction ATP formation takes place without the involvement of hydrogen transfer system and thus it is popularly called as **substrate level phosphorylation.**



8. **Formation of 2-phosphoglyceric acid –** In this step of glycolysis phosphate group recovers from 3 phosphoglyceric acid to form 2 phosphoglyceric acid by the help of an enzyme **phospho glyceromutase,** which shifted the phosphate from C_3 to C_2.

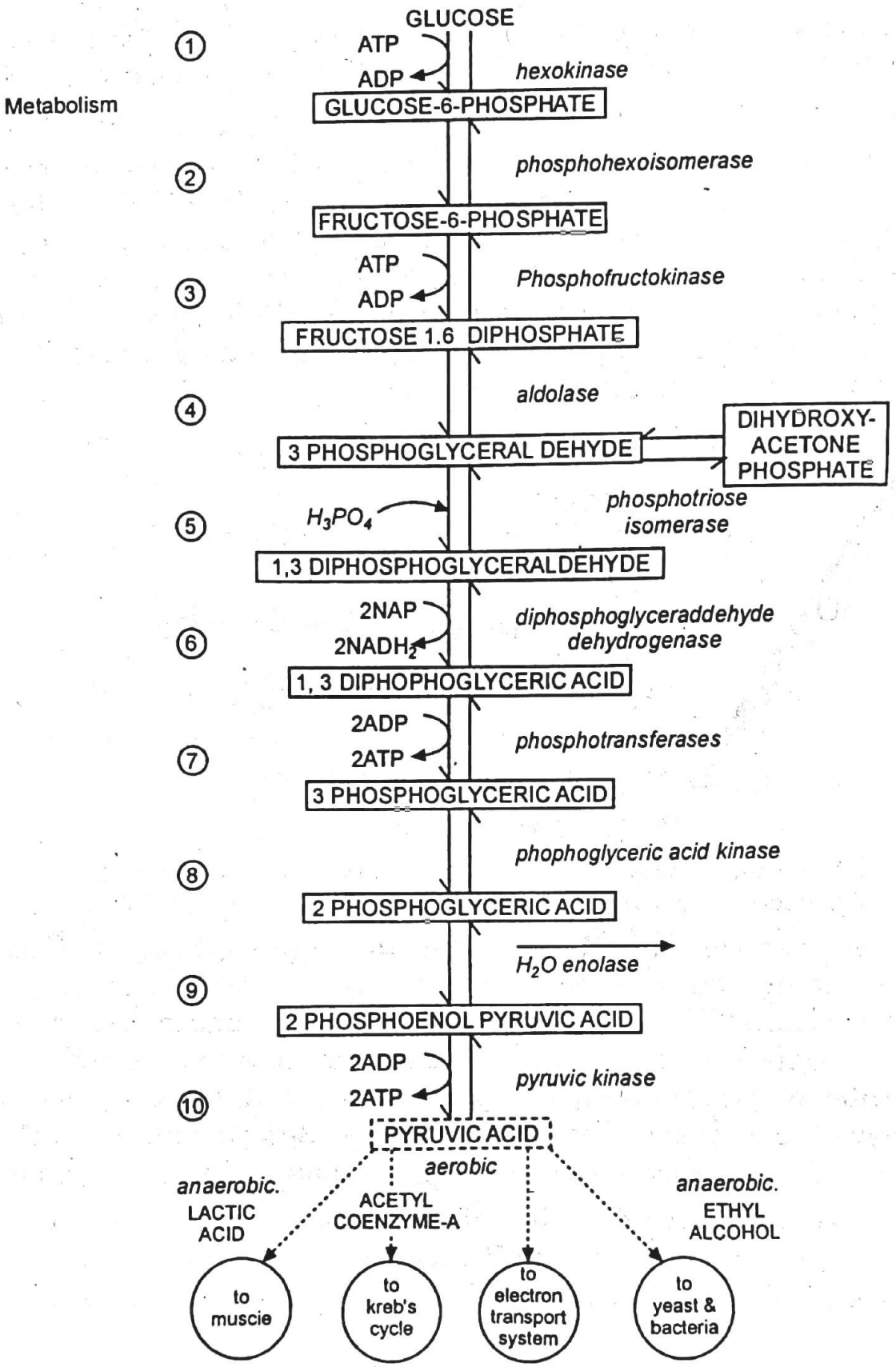
9. **Formation of phosphoenol pyruvic acid and pyruvic acid** – This is the ninth step in the process of glycolysis which involves the conversion of 2 phosphoenol pyruvic acid by an enzyme enolase. In this step 2 phosphoglycerate is dehydrated by the action of enzyme phosphopyruvate hydratase (**enolase**) forming phospho enol pyruvate (phosphoenol pyruvic acid).

10. **Formation of ATP from phospho enol pyruvic acid –** In the tenth and the last step of glycolysis the phosphoenol pyruvic acid is converted into the enolpyruvate, form by an allosteric enzyme pyruvate kinase or pyruvic acid kinase. The enzyme transfers a phosphoryl group from phospho enol pyruvic acid to ADP, thus producing ATP and pyruvic acid. This phosphorylation is a non-oxidative reaction and **enolpyruvate** rapidly changes into **ketopyruvate** form.

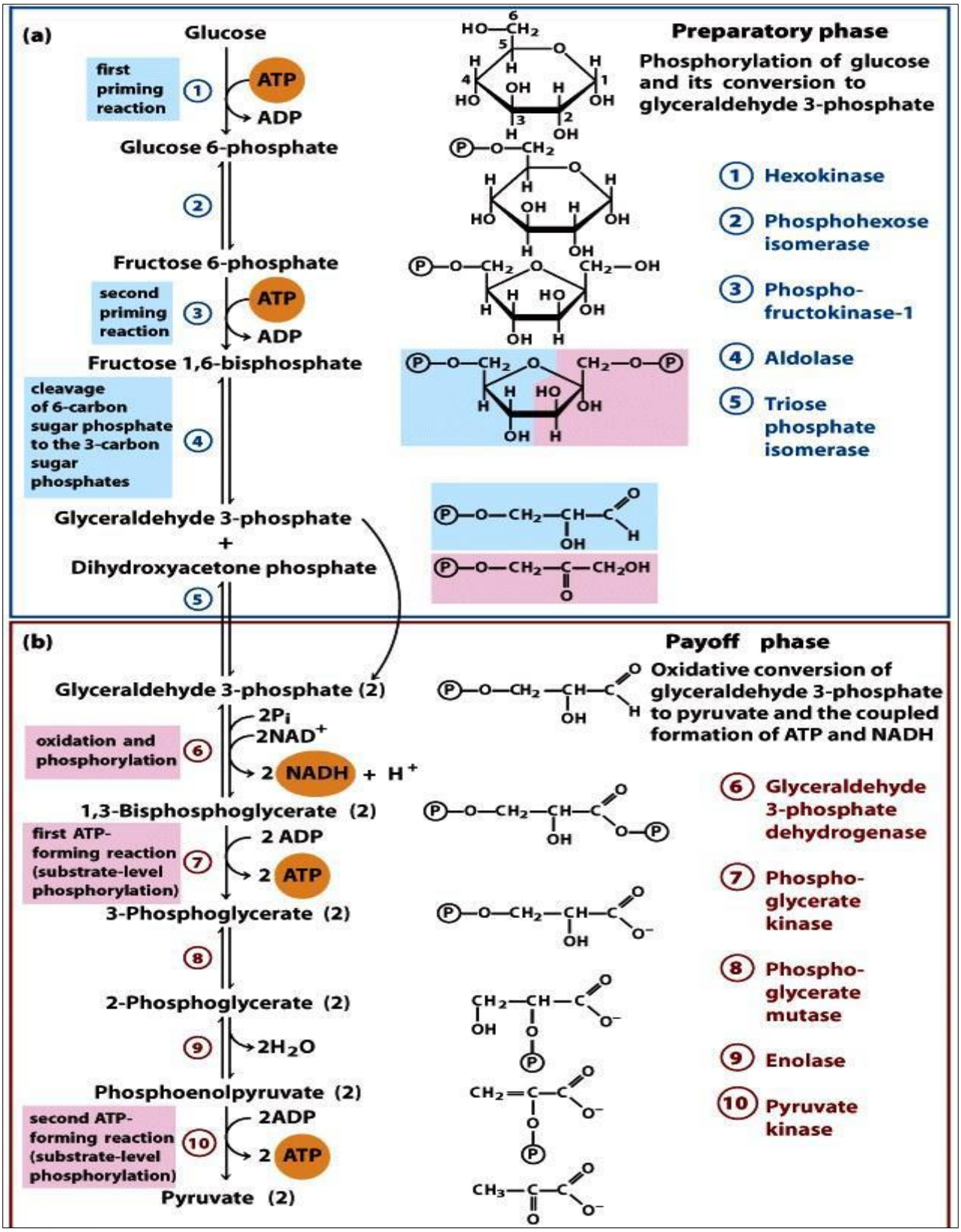
Important –

- **In the yeast cells the pyruvic acid produces ethyl alcohol and in muscles, enzyme lactate dehydrogenase changes it into the lactic acid.**

- **In the entire process of glycolysis 4 molecules of ATP are formed while 2 molecules of ATP are used in activation of glucose hence the net gain of 2 ATP molecules.**



Embeden Meyerhof pathway and fate of pyruvic acid



Flow chart of glycolsis (Taken from Lehninger, Principles of Biochemistry)

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