

GLYCOLYSIS
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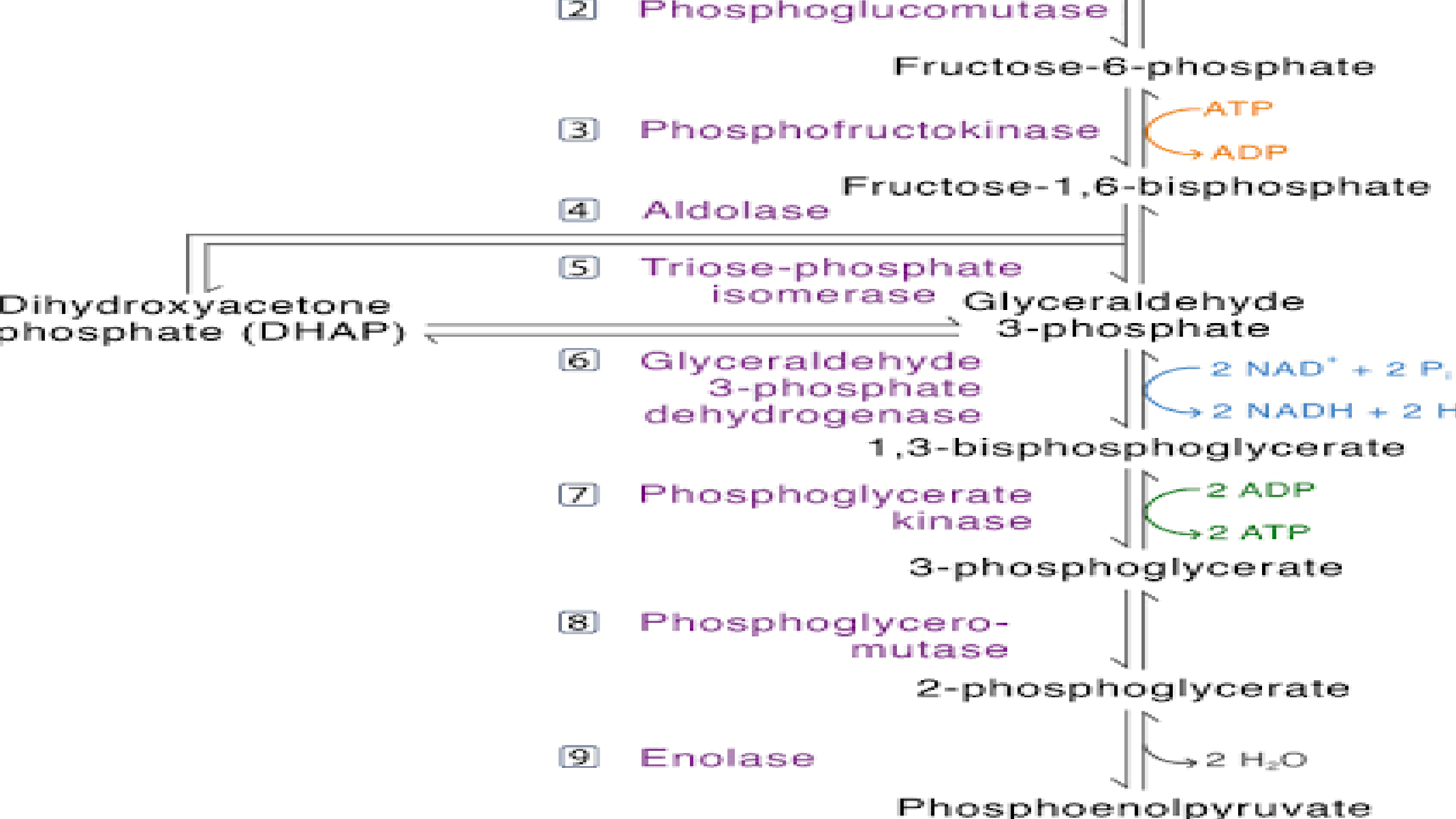
Glycolysis is derived from the Greek words (glycose – sweet or sugar; lysis – dissolution).

The pathway of glycolysis was elucidated in 1940 .This pathway often referred as Embden-Meyerhof pathway (E.M. pathway).

Glycolysis is defined as the sequence of reactions converting glucose or glycogen to pyruvate or lactate, with the production of ATP.

SALIENT FEATURES:

- **Glycolysis takes place in all cells of the body. Glycolysis occurs in the presence or absence of the oxygen .**
- **Lactate is the end product under anaerobic condition. Pyruvate is the end product under aerobic conditions .**
- **It is the major pathway for ATP synthesis in tissues lacking mitochondria, example: erythrocytes, cornea etc. Glycolysis is very essential for brain which is dependent on glucose for energy**
- **Glycolysis may be summarized by the net reaction.**
- **Glucose + 2ADP + 2P_i -----> 2 lactate + 2ATP**



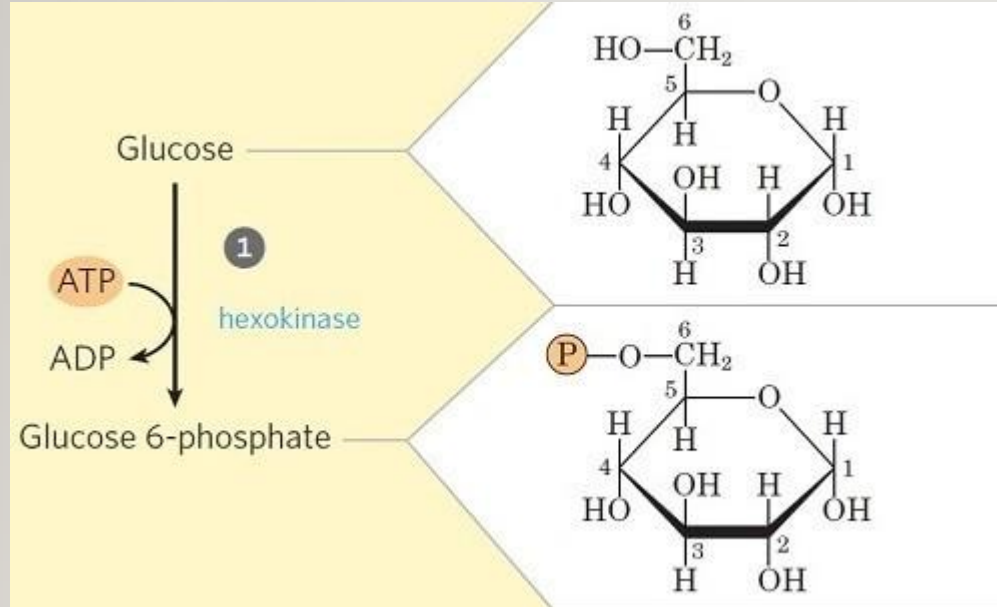
Glycolysis enzymes:

- **In most kinds of cells, the enzymes that catalyze glycolytic reactions are present in the extra-mitochondrial fraction of the cell in the cytosol.**
- **One common characteristic in all the enzymes involved in glycolysis is that nearly all of them require Mg^{2+} . The following are the enzymes that catalyze different steps throughout the process of glycolysis:**
 - **Hexokinase**
 - **Phosphoglucosomerase**
 - **Phosphofructokinase**
 - **Aldolase**
 - **Phosphotriose isomerase**
 - **Glyceraldehyde 3-phosphate dehydrogenase**
 - **Phosphoglycerate kinase**
 - **Phosphoglycerate mutase**
 - **Enolase**
 - **Pyruvate kinase**

- During glycolysis, a single mole of 6-carbon glucose is broken down into two moles of 3-carbon pyruvate by a sequence of 10 enzyme-catalyzed sequential reactions. These reactions are grouped under 2 phases, phase I and II.
- Stage I comprises “preparatory” reactions which are not redox reactions and do not release energy but instead lead to the production of a critical intermediate of the pathway.
- Stage I consists of the first five steps of the glycolysis process.
- Similarly, in Stage II, redox reactions occur, energy is conserved in the form of ATP, and two molecules of pyruvate are formed.
- The last five reactions of glycolysis constitute phase II.

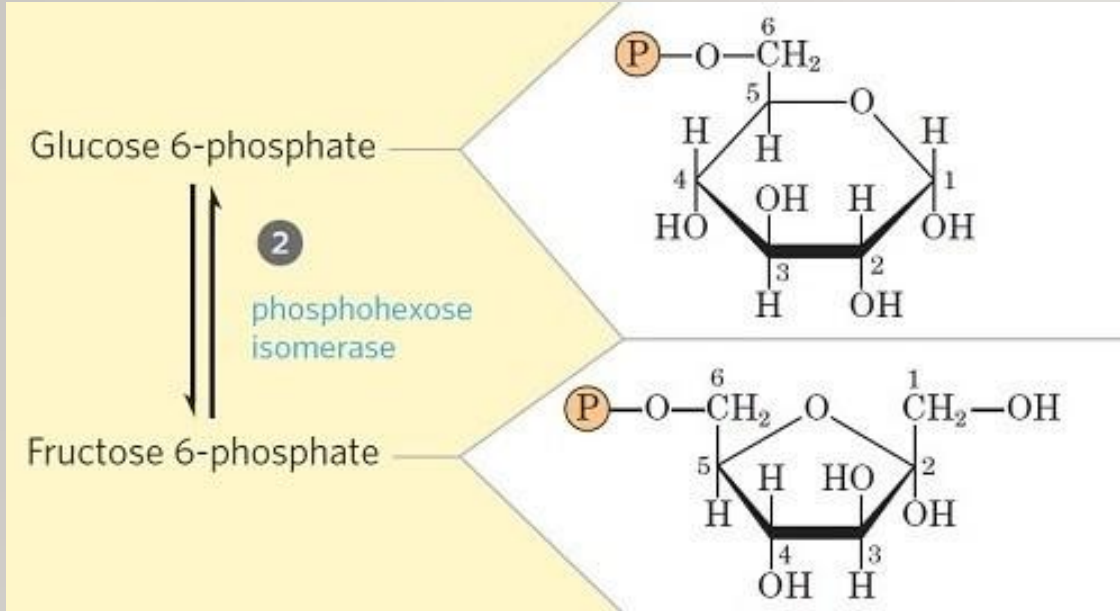
The ten steps of glycolysis occur in the following sequence:

Step 1- Phosphorylation of glucose



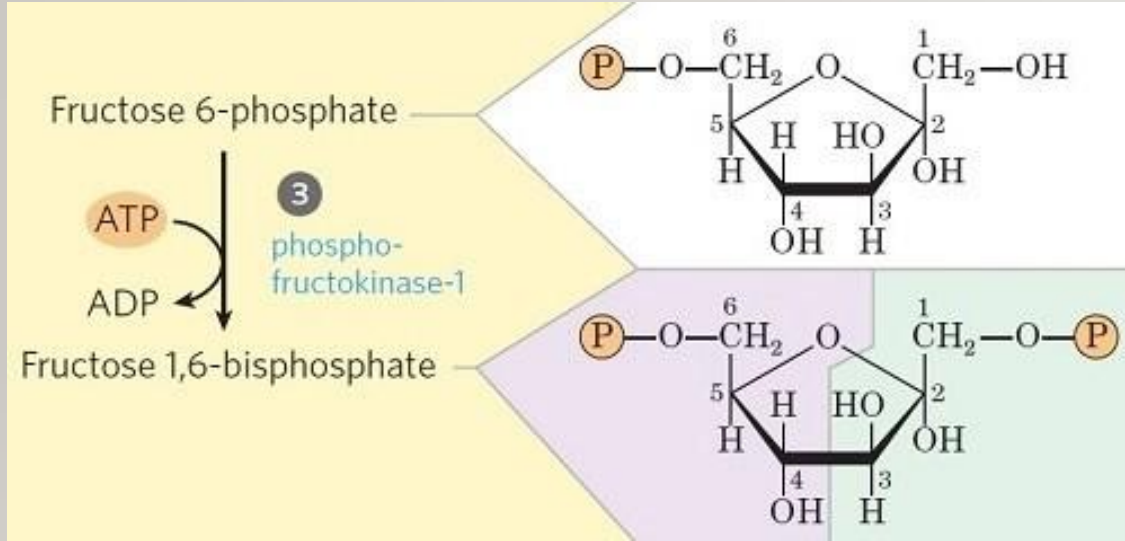
- In the first step of glycolysis, the glucose is initiated or primed for the subsequent steps by phosphorylation at the C₆ carbon.
- The process involves the transfer of phosphate from the ATP to glucose forming Glucose-6-phosphate in the presence of the enzyme hexokinase and glucokinase (in animals and microbes).
- This step is also accompanied by considerable loss of energy as heat.

Step 2- Isomerization of Glucose-6-phosphate



- Glucose 6-phosphate is reversibly isomerized to fructose 6-phosphate by the enzyme phosphohexoisomerase/phosphoglucosomerase.
- This reaction involves a shift of the carbonyl oxygen from C1 to C2, thus converting an aldose into a ketose.

Step 3- Phosphorylation of fructose-6-phosphate



- This step is the second priming step of glycolysis, where fructose-6-phosphate is converted into fructose-1,6-bisphosphate in the presence of the enzyme phosphofructokinase.
- Like in Step 1, the phosphate is transferred from ATP while some amount of energy is lost in the form of heat as well.

Step 4- Cleavage of fructose 1, 6-diphosphate

This step involves the unique cleavage of the C-C bond in the fructose 1, 6-bisphosphate.

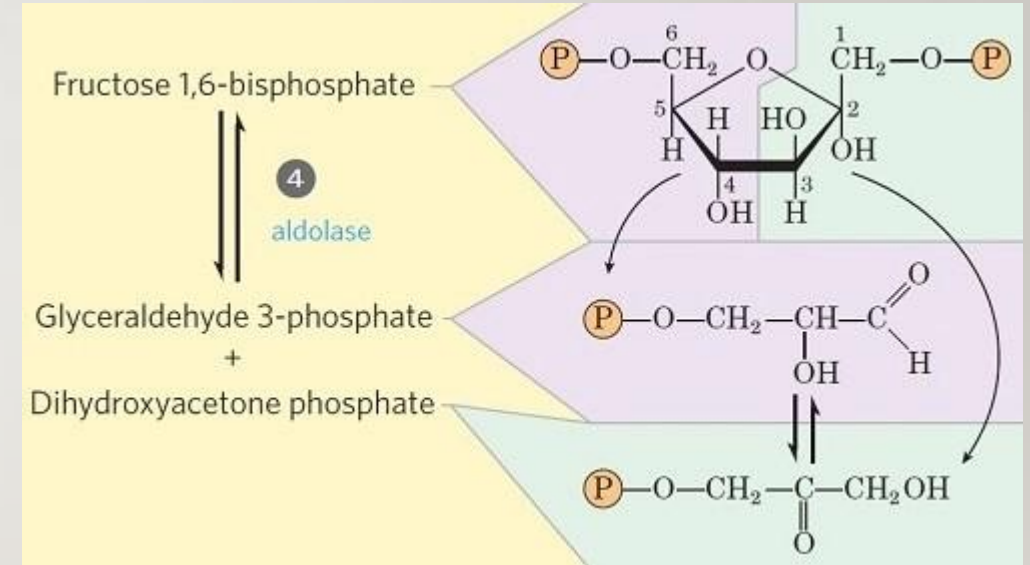
The enzyme fructose diphosphate aldolase catalyzes the cleavage of fructose 1,6-bisphosphate between C₃ and C₄ resulting in two different triose phosphates: glyceraldehyde 3-phosphate (an aldose) and dihydroxyacetone phosphate (a ketose).

The remaining steps in glycolysis involve three-carbon units, rather than six carbon units.

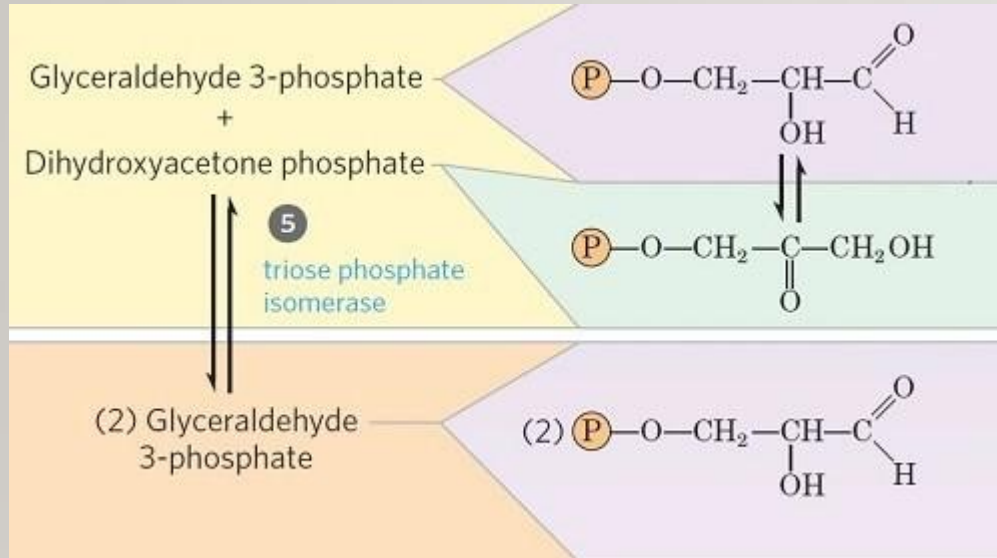
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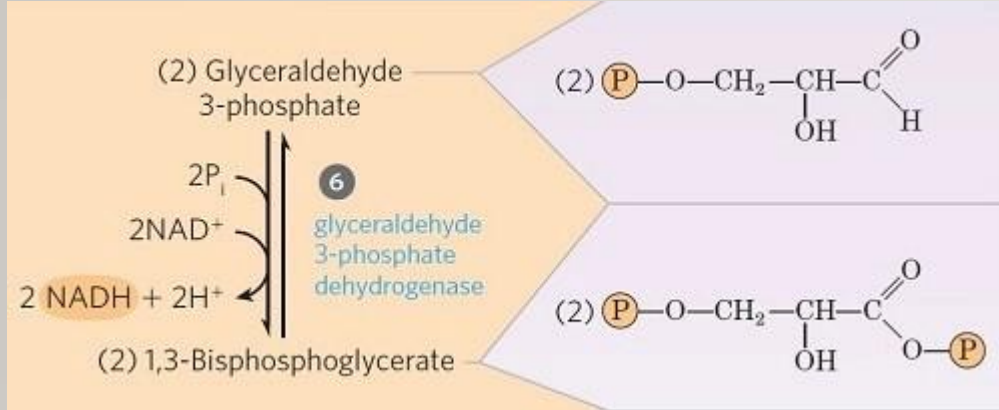


Step 5- Isomerization of dihydroxyacetone phosphate



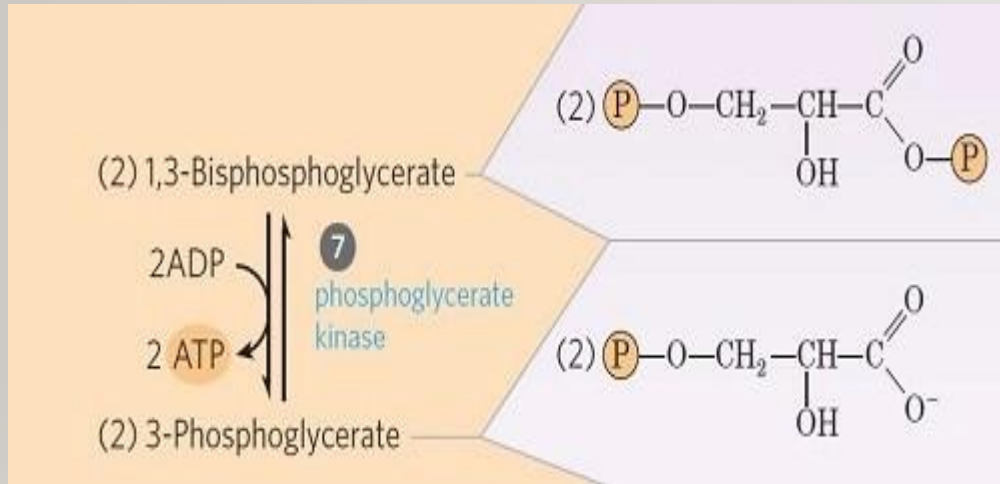
- Glyceraldehyde 3-phosphate can be readily degraded in the subsequent steps of glycolysis, but dihydroxyacetone phosphate cannot be. Thus, it is isomerized into glyceraldehyde 3-phosphate instead.
- In this step, dihydroxyacetone phosphate is isomerized into glyceraldehyde 3-phosphate in the presence of the enzyme triose phosphate isomerase.
- This reaction completes the first phase of glycolysis.

Step 6- Oxidative Phosphorylation of Glyceraldehyde 3-phosphate



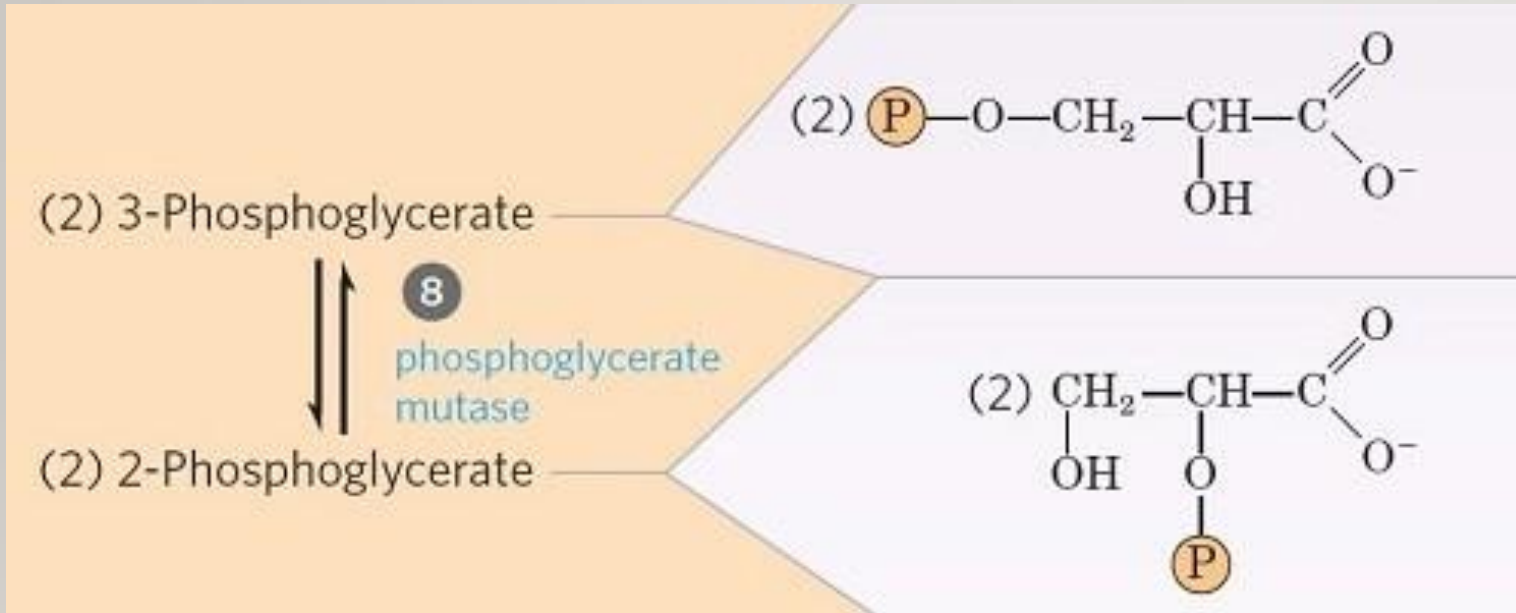
- **Step 6 is one of the three energy-conserving or forming steps of glycolysis.**
- **The glyceraldehyde 3-phosphate is converted into 1,3-bisphosphoglycerate by the enzyme glyceraldehyde 3-phosphate dehydrogenase (phosphoglyceraldehyde dehydrogenase).**
- **In this process, NAD^+ is reduced to coenzyme NADH by the H^- from glyceraldehydes 3-phosphate.**
- **Since two moles of glyceraldehyde 3-phosphate are formed from one mole of glucose, two NADH are generated in this step.**

Step 7- Transfer of phosphate from 1, 3-diphosphoglycerate to ADP



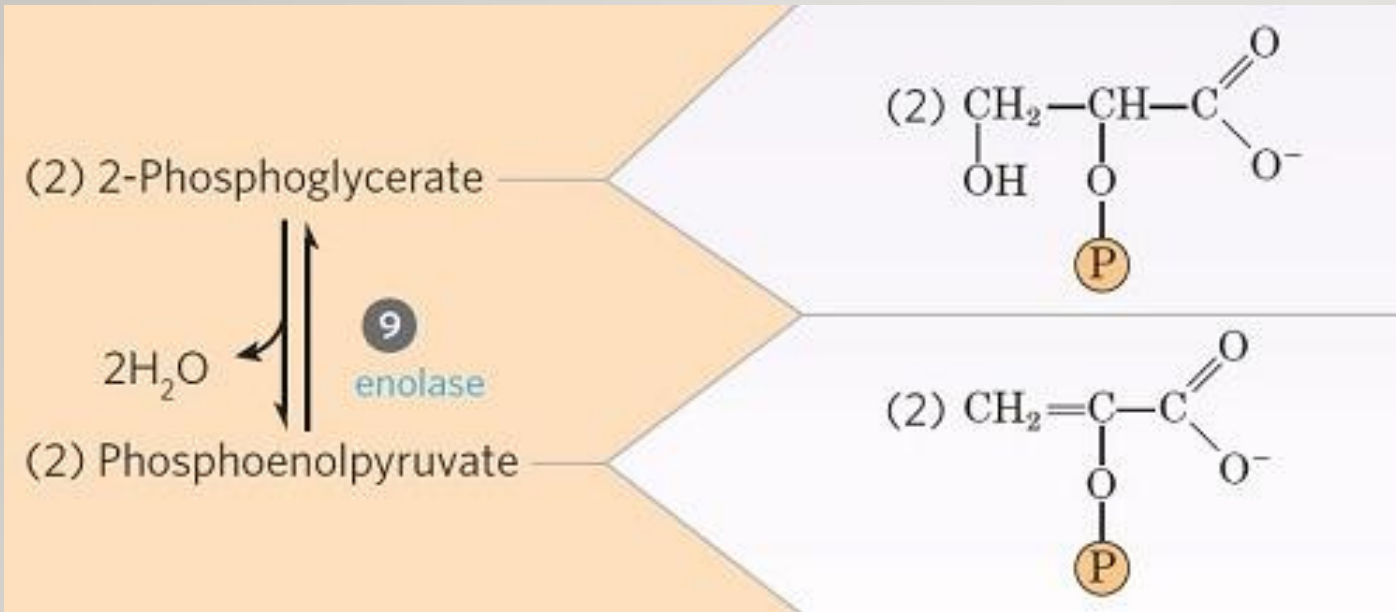
- This step is the **ATP-generating step** of glycolysis.
- It involves the transfer of phosphate group from the 1, 3-bisphosphoglycerate to ADP by the enzyme phosphoglycerate kinase, thus producing ATP and 3-phosphoglycerate.
- Since two moles of 1, 3-bisphosphoglycerate are formed from one mole of glucose, two ATPs are generated in this step.

Step 8- Isomerization of 3-phosphoglycerate



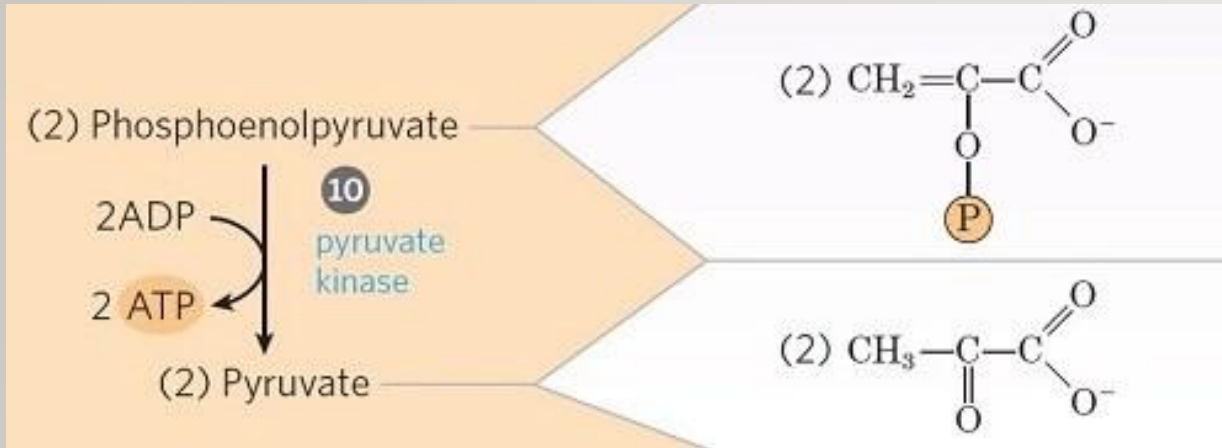
- The 3-phosphoglycerate is converted into 2-phosphoglycerate due to the shift of phosphoryl group from C3 to C2, by the enzyme phosphoglycerate mutase.
- This is a reversible isomerization reaction

Step 9- Dehydration 2-phosphoglycerate



- In this step, the 2-phosphoglycerate is dehydrated by the action of enolase (phosphopyruvate hydratase) to phosphoenolpyruvate.
- This is also an irreversible reaction where two moles of water are lost.

Step 10- Transfer of phosphate from phosphoenolpyruvate



- This is the second energy-generating step of glycolysis.
- Phosphoenolpyruvate is converted into an enol form of pyruvate by the enzyme pyruvate kinase.
- The enol pyruvate, however, rearranges rapidly and non-enzymatically to yield the keto form of pyruvate (i.e. ketopyruvate). The keto form predominates at pH 7.0.
- The enzyme catalyzes the transfer of a phosphoryl group from phosphoenolpyruvate to ADP, thus forming ATP.

Result of Glycolysis

The overall process of glycolysis results in the following events:

- 1. Glucose is oxidized into pyruvate.**
- 2. NAD^+ is reduced to NADH.**
- 3. ADP is phosphorylated into ATP.**

THANK YOU

