

3. GLYCOLYSIS

Glycolysis or Embden- Meyerhoff pathway is the major pathway for the utilization of glucose for the production of energy and is found in the cytosol of all cells.

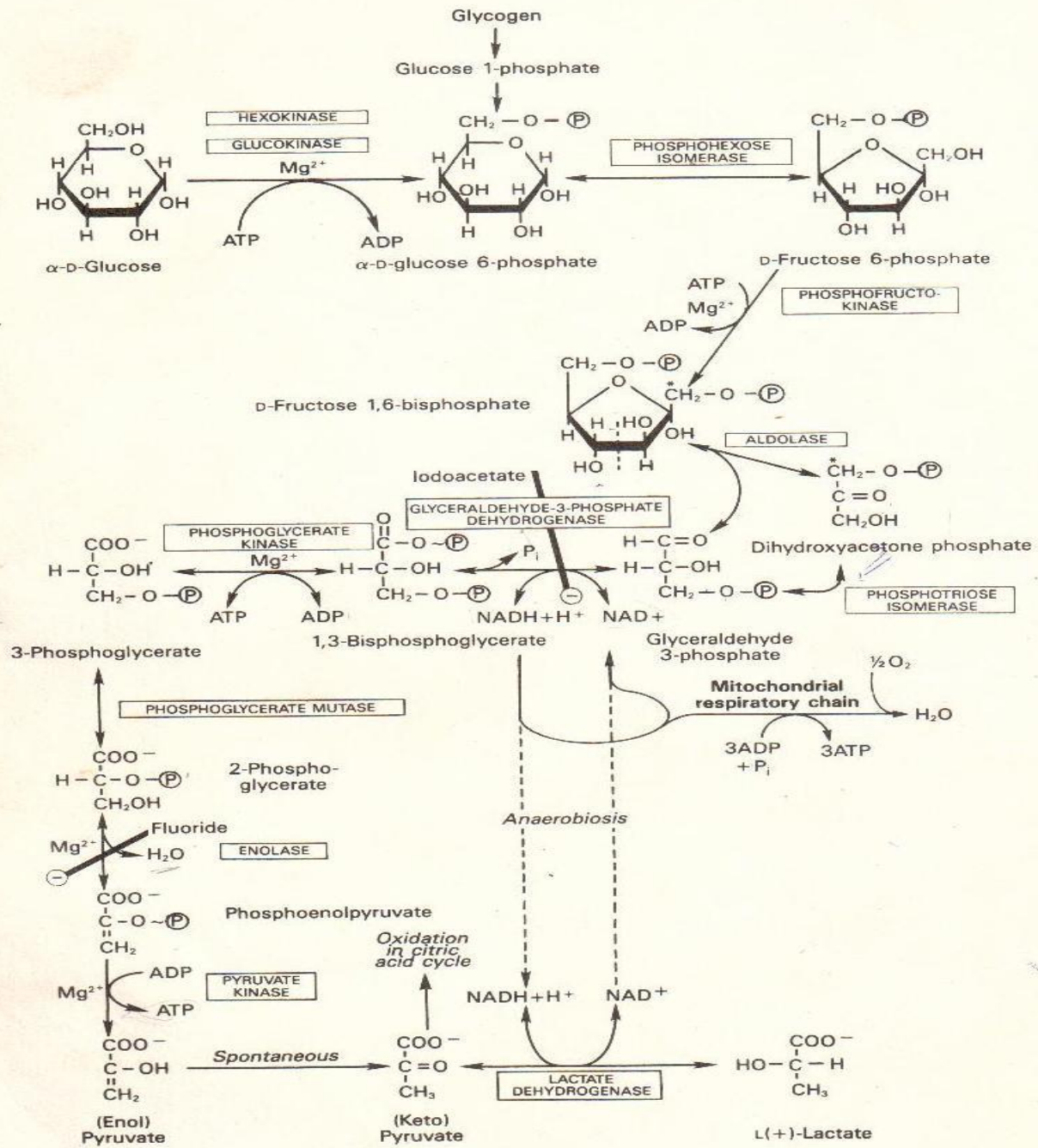
Glycolysis can function under aerobic and anaerobic conditions.

It is then converted to acetyl CoA and further oxidized to CO₂ and H₂O via Citric acid cycle in mitochondria.

All of the enzymes of the glycolysis pathway are found in the extramitochondrial soluble fraction of the cell, the cytosol.

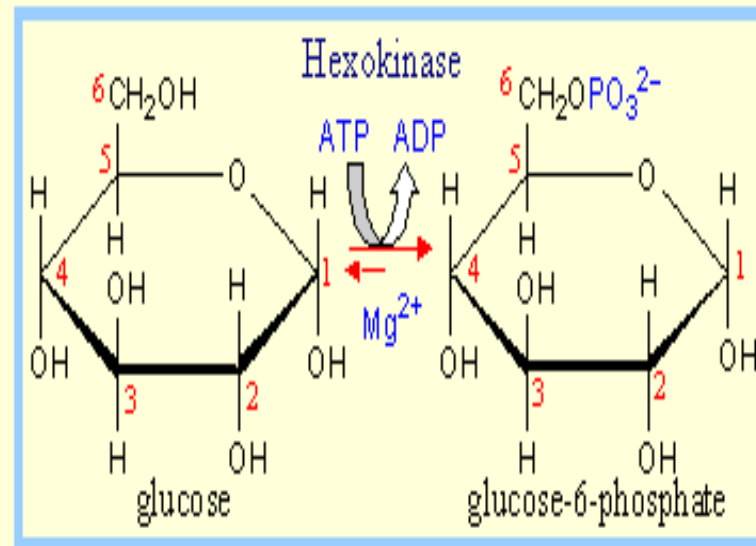
They catalyze the reactions involved in the glycolysis of glucose to pyruvate under aerobic condition and lactate or alcohol under anaerobic condition.

The reactions are given in Fig.9.6.



1. Phosphorylation of Glucose

- Glucose enters into the glycolytic pathway by phosphorylation to glucose 6-phosphate, accomplished by the enzyme hexokinase.



However, in liver parenchyma cells and in pancreatic islet cells, this function is carried out by glucokinase.

ATP is required as phosphate donor, and it reacts as the Mg-ATP complex.

The terminal high-energy phosphate of ATP is utilized, and ADP is produced.

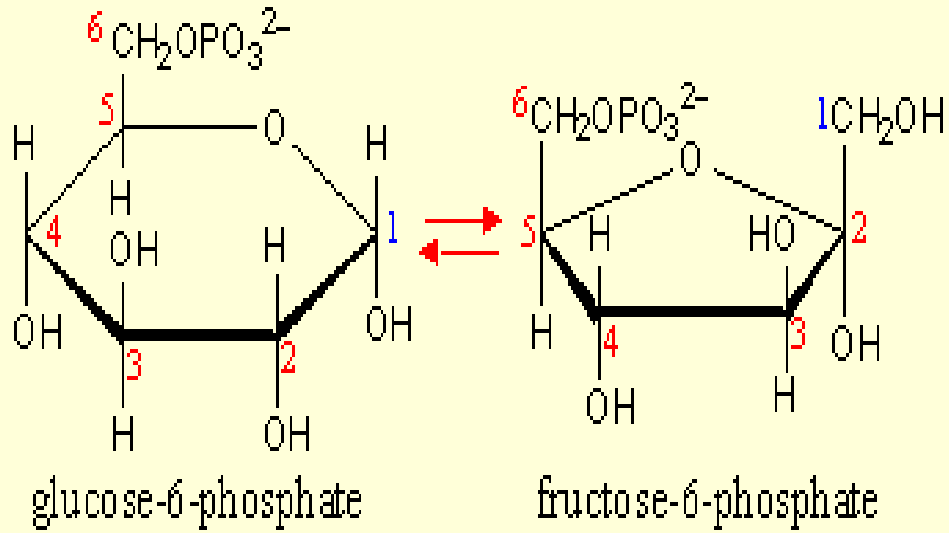
The reaction is accompanied by considerable loss of free energy as heat and therefore, under physiologic conditions, may be regarded as irreversible.

Hexokinase is inhibited in a allosteric manner by the product, glucose 6- phosphate. The function of glucokinase is to remove glucose from the blood following digestion and absorption. It is specific for glucose.

- **2. Conversion of Glucose 6 phosphate to fructose 6-phosphate**

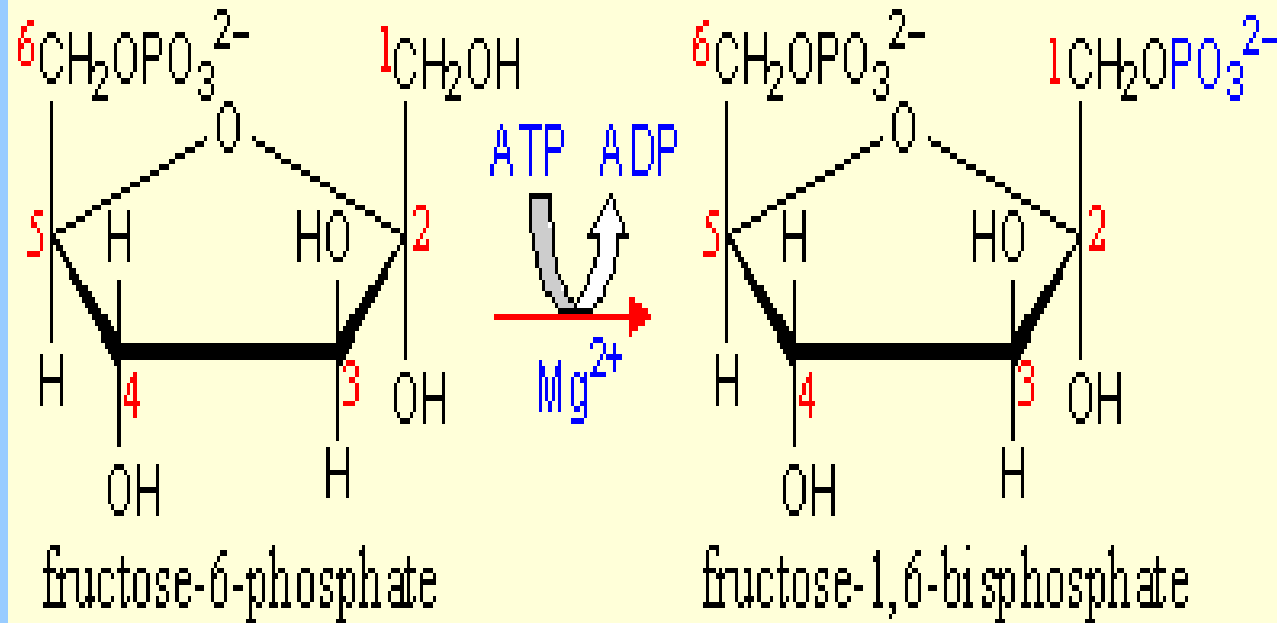
Glucose 6 phosphate is converted to fructose 6-phosphate by phosphohexose isomerase, which involves an aldose-ketose isomerization.

Phosphoglucose Isomerase



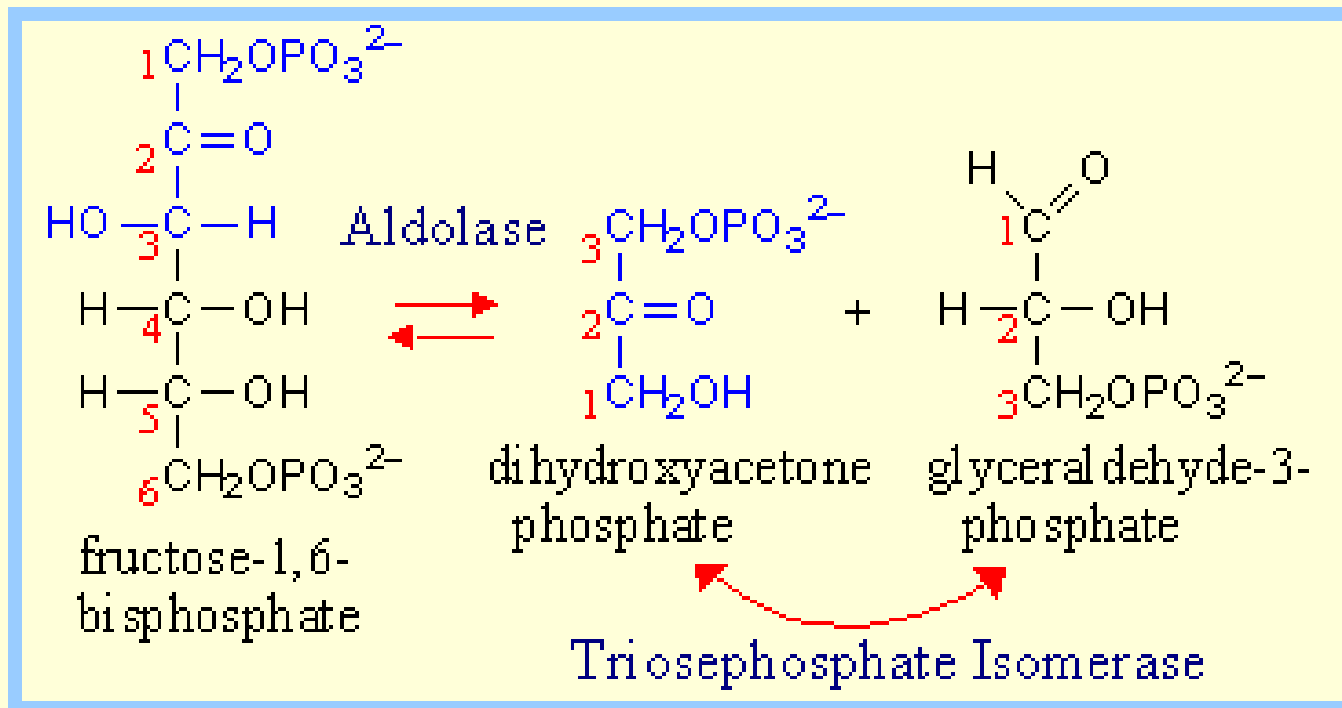
- **3. Phosphorylation of fructose 6-phosphate to fructose 1, 6-bisphosphate**
- This reaction is catalyzed by the enzyme phosphofructokinase to produce fructose 1, 6-bisphosphate.
- The phosphofructokinase reaction is irreversible under physiologic conditions.

Phosphofructokinase



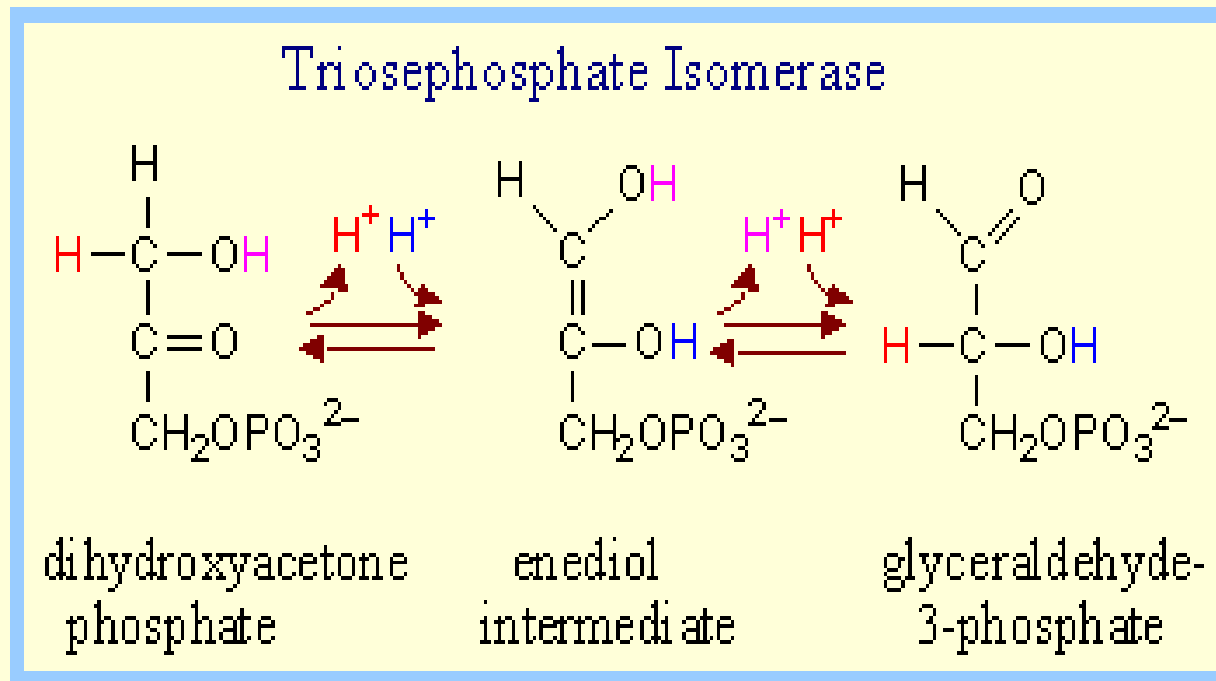
- **4. Cleavage of Fructose 1,6-bisphosphate**

- Fructose 1,6-bisphosphate is split by aldolase (fructose 1,6-bisphosphate aldolase) into two triose phosphates, glyceraldehyde 3-phosphate and dihydroxyacetone phosphate.



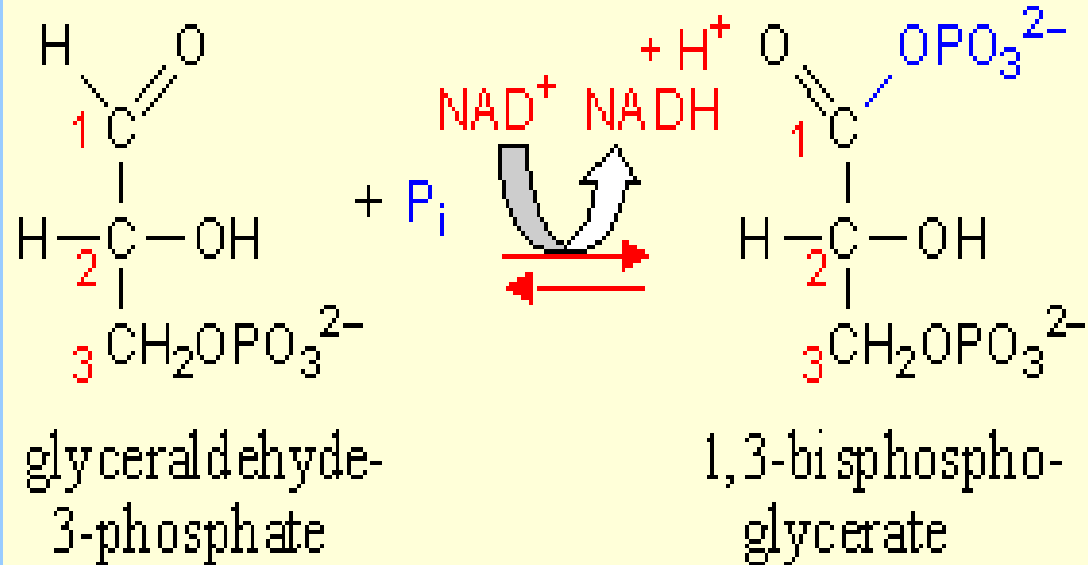
5. Inter conversion of triose phosphates

Glyceraldehyde3-phosphate and dihydroxy acetone phosphate are interconverted by the enzyme phosphotriose isomerase. At this stage 2 molecules glyceraldehyde 3-phosphate are formed.

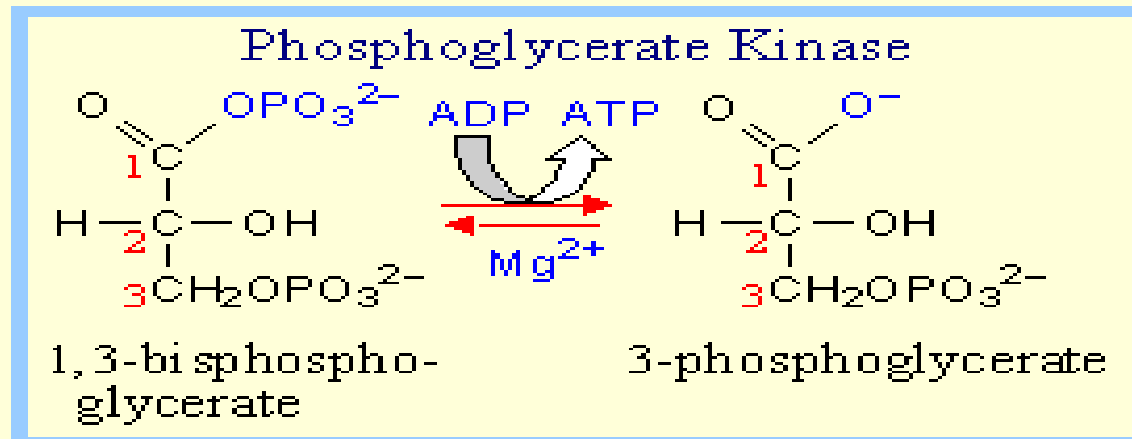


- **6. Oxidation of glyceraldehyde 3-phosphate to 1,3 bisphosphoglycerate**
- Glyceraldehyde 3-phosphate is converted to 1,3 bisphosphoglycerate by glyceraldehyde 3-phosphate dehydrogenase using NAD⁺ as the coenzyme.
- Finally, by phosphorolysis, inorganic phosphate (pi) is added, forming 1,3 bisphosphoglycerate, and the free enzyme.
- Energy released during the oxidation is conserved by the formation of a high-energy sulfur group that becomes, after phosphorolysis, a high-energy phosphate group in position 1 of 1,3 bisphosphoglycerate.

Glyceraldehyde-3-phosphate Dehydrogenase

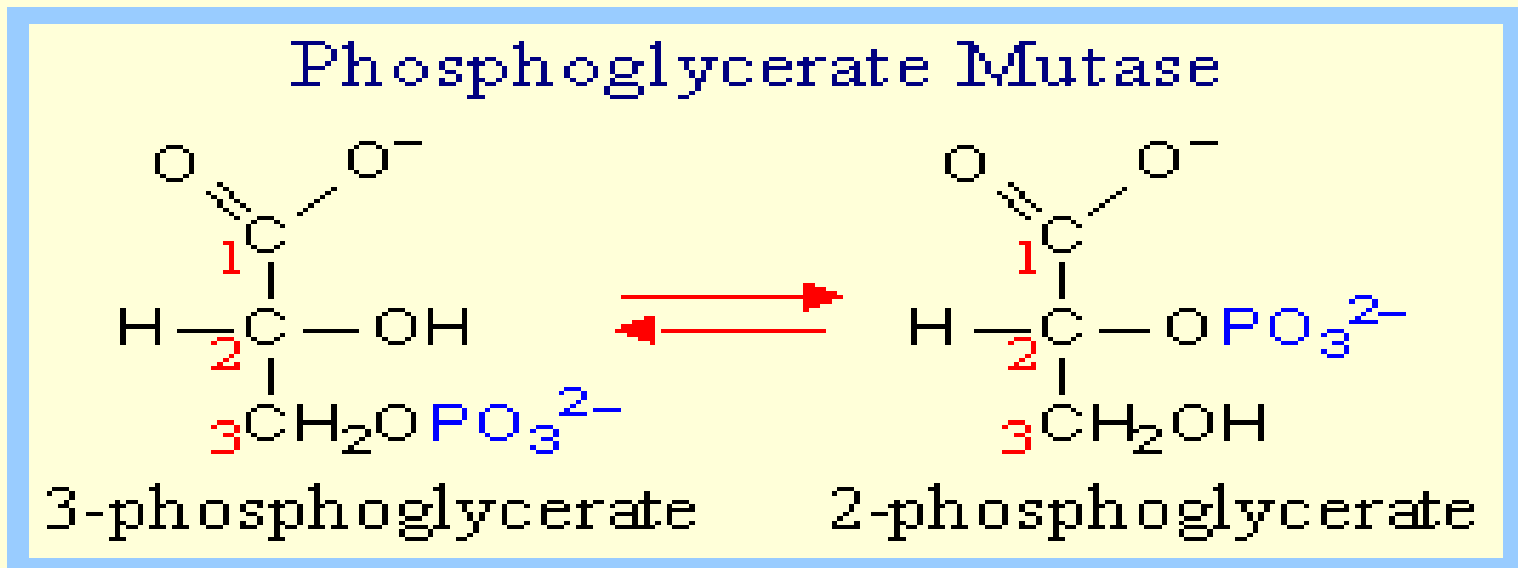


- 7. Transfer of phosphate group from 1,3 bisphosphoglycerate
- 1,3-diphosphoglycerate is oxidized to 3-phosphoglycerate by phosphoglycerate kinase.
- This high-energy phosphate is captured as ATP in a further reaction with ADP.
-
- Since two molecules of triose phosphate are formed per molecule of glucose undergoing glycolysis, two molecules of ATP are generated at this stage per molecule of glucose.



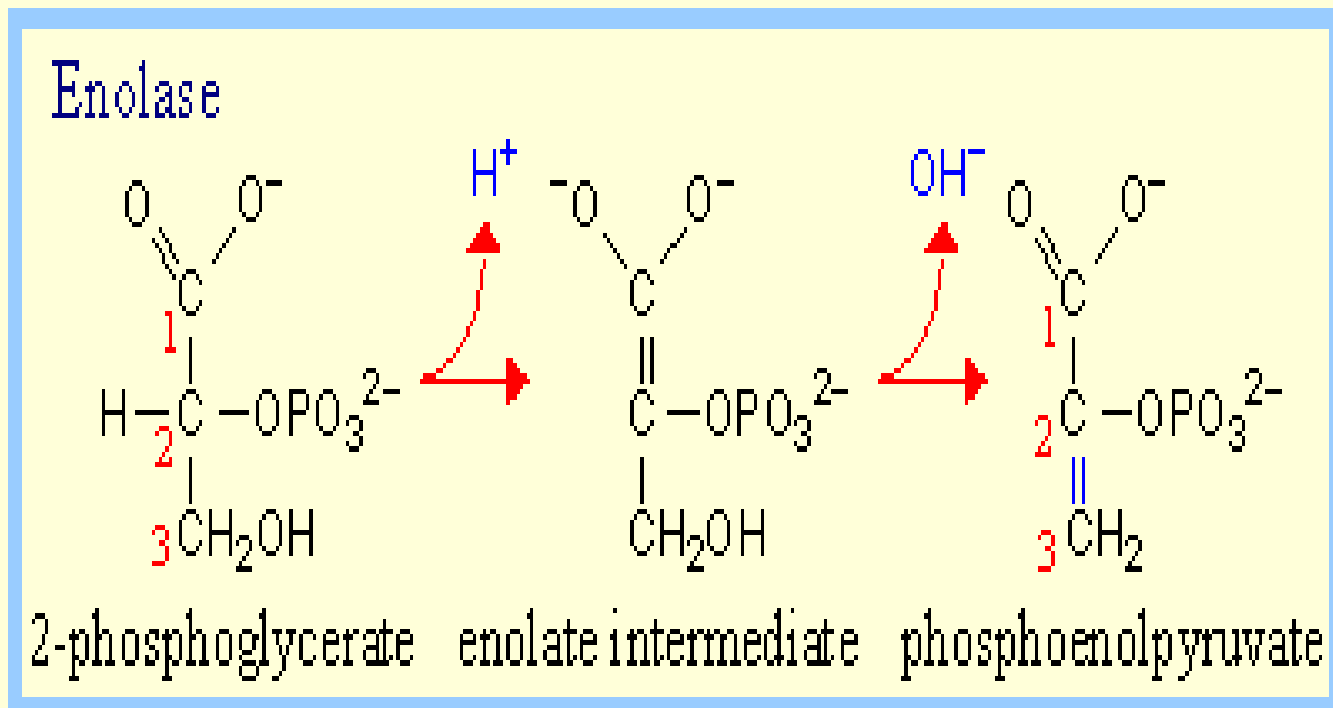
- **8. Conversion of 3-phosphoglycerate to 2-phosphoglycerate**

In the next reaction 3-phosphoglycerate is converted to 2-phosphoglycerate by the enzyme phosphoglycerate mutase.



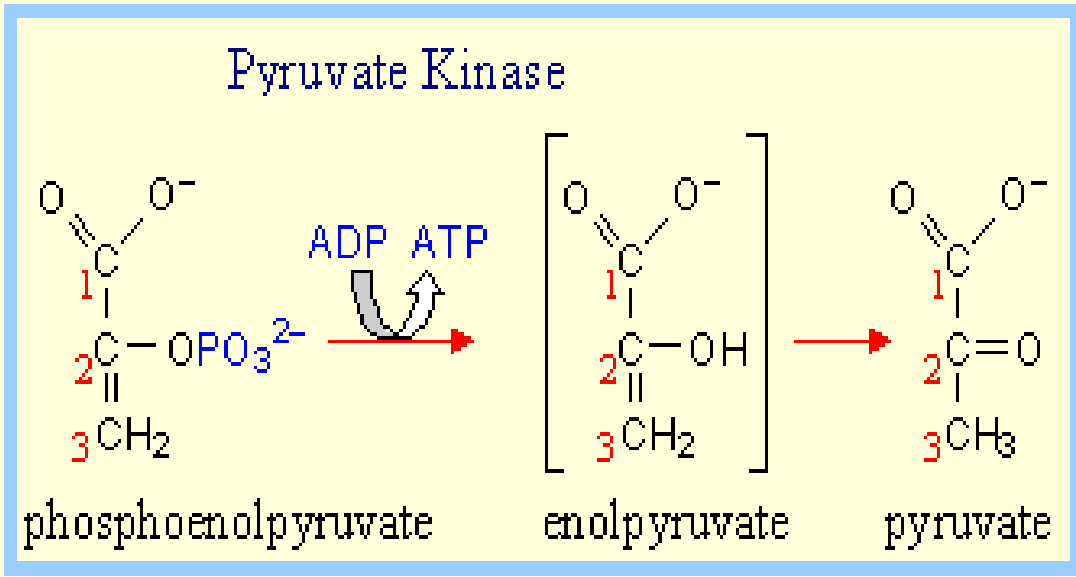
9. Dehydration of 2-phosphoglycerate to phosphoenolpyruvate

The subsequent step is catalyzed by enolase that promotes the reversible removal of a water molecule to form phosphoenolpyruvate.



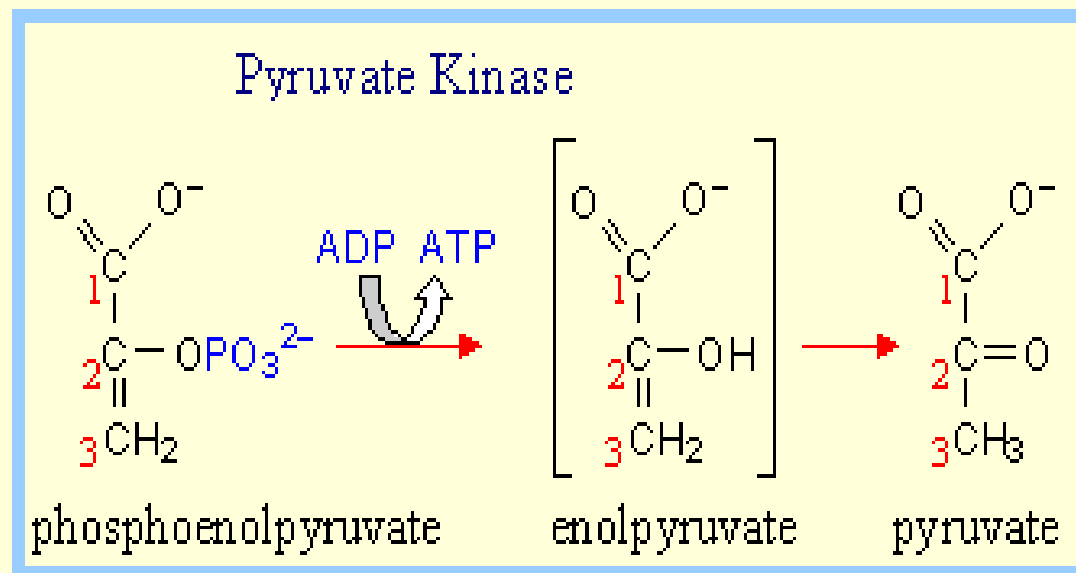
- 10. Transfer of phosphate group from phosphoenol pyruvate to ADP**

The high-energy phosphate of phosphoenol pyruvate is transferred to ADP by the enzyme pyruvate kinase to generate, at this stage, two molecules of ATP per molecule of glucose oxidized.



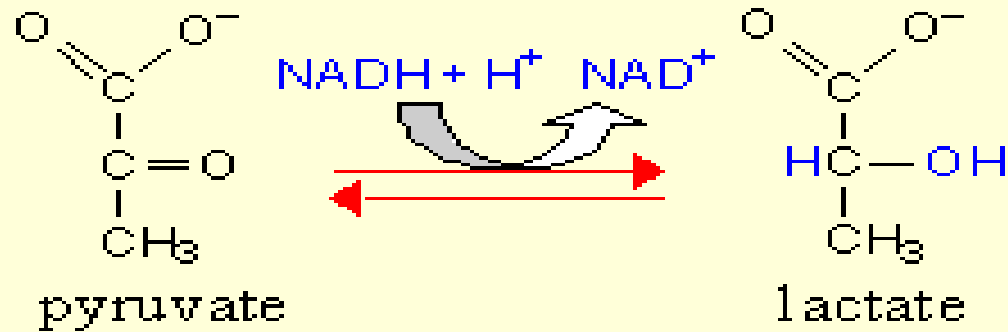
11. Conversion of phosphoenol pyruvate to enolpyruvate

Enol pyruvate formed is converted spontaneously to the pyruvate.

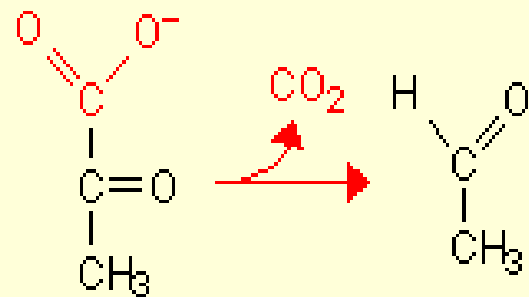


- **Under anaerobic condition.**
- If anaerobic conditions prevail, the reoxidation of NADH by transfer of reducing equivalents through the respiratory chain to oxygen is prevented.
- Then, pyruvate is reduced by the NADH to lactate, the reaction being catalyzed by lactate dehydrogenase.
- The reoxidation of NADH via lactate formation allows glycolysis to proceed in the absence of oxygen by regenerating sufficient NAD⁺ for another cycle of the reaction catalyzed by glyceraldehyde-3 phosphate.
- During fermentation, pyruvate is reduced by NADH to ethyl alcohol being catalysed by alcohol dehydrogenase.

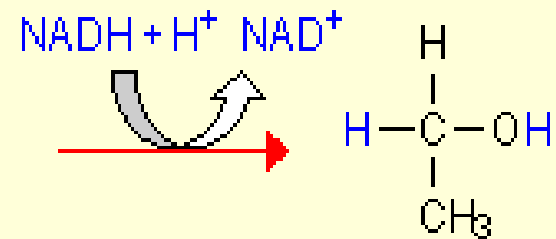
Lactate Dehydrogenase



Pyruvate Decarboxylase



Alcohol Dehydrogenase



- **Under aerobic condition**
- Under aerobic condition, pyruvate is taken up into mitochondria, and after conversion to acety-CoA is oxidized to CO₂ by the citric acid cycle.
- The reducing equivalents from the NADH+H⁺ formed in glycolysis are taken up into mitochondria for oxidation.

- **Energy conservation**

- Two triosephosphates are produced from each molecule of hexose metabolized.
- Dihydroxyacetone phosphate can be isomerized by isomerase to glyceraldehyde 3 phosphate which is then converted to 1, 3 diphosphoglyceric acid by glyceraldehyde 3 phosphate dehydrogenase system requiring NAD^+ and inorganic phosphate.
- From this high-energy compound and from phosphoenol pyruvate another high energy compound derived from it, two ATP molecules can be obtained from ADP present in the cell.

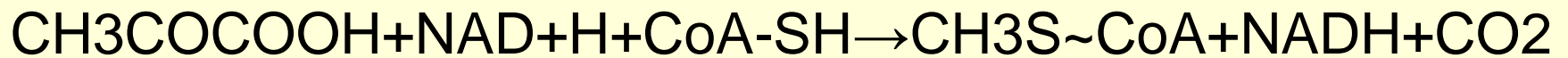
- Under aerobic conditions, pyruvate is the product of glycolysis, and the NADH formed by the dehydrogenation of glyceraldehyde 3 phosphate is then reoxidised to NAD⁺ by O₂ and produce 3ATP molecules.
-
- Thus the energy conserved from 2 molecule of glyceraldehyde 3 phosphate via electron transport chain reoxidation is 6 ATP molecules.
- Hence under aerobic glycolysis, the total number of ATP molecules produced is 10.
- Out of this 2 ATP molecules are used during the initial reactions. The net ATP molecules produced is 8.

- The conversion of two triose phosphates to lactic acid (or ethanol) yields four molecules of ATP.
- However, two ATP molecules are used up in the production of glucose-6-phosphate from glucose and fructose-1, 6-disphosphate from fructose-6-phosphate.
- The net production of ATP is thus only two ATP molecules per mole of glucose during anaerobic glycolysis or fermentation.

- **Oxidation of Pyruvate to Acetyl CoA**

- Pyruvate derived from glucose by glycolysis, is dehydrogenated to yield acetyl-CoA and CO₂ by pyruvate dehydrogenase, located in the mitochondria.

- The reaction is as follows:

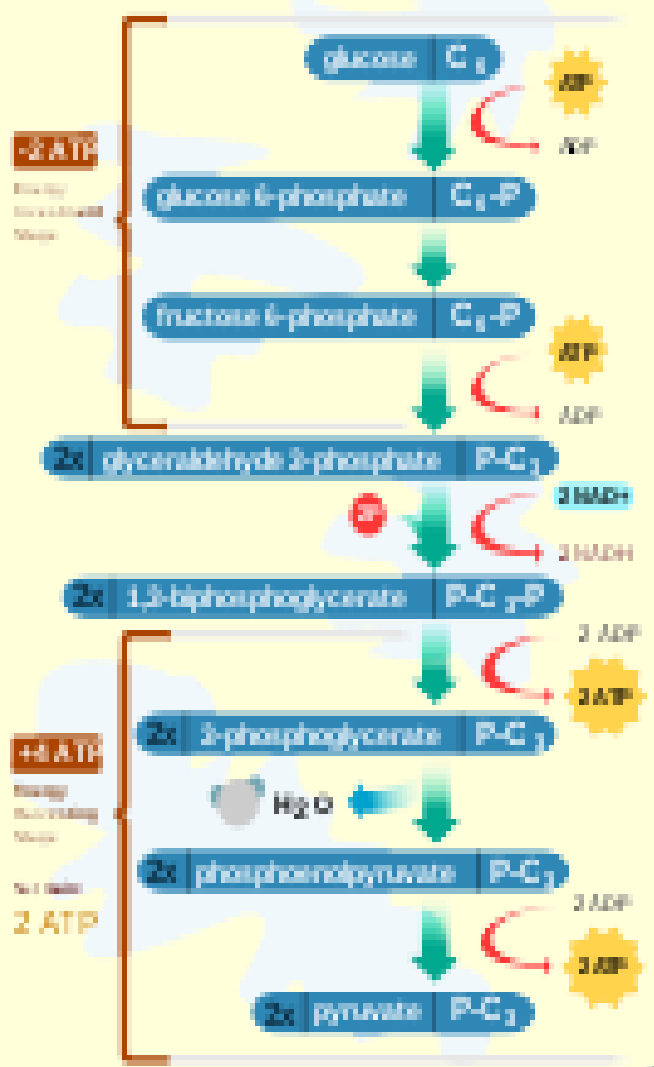


- Pyruvate Acetyl CoA

- Thiamine pyrophosphate, coenzyme A, lipoic acid and NAD⁺ are coenzymes needed for the reaction.

- The acetyl CoA is fed into citric acid cycle and oxidized to CO₂ in citric acid cycle.

Glycolysis in the Cytoplasm



Citric Acid Cycle in the Mitochondria

