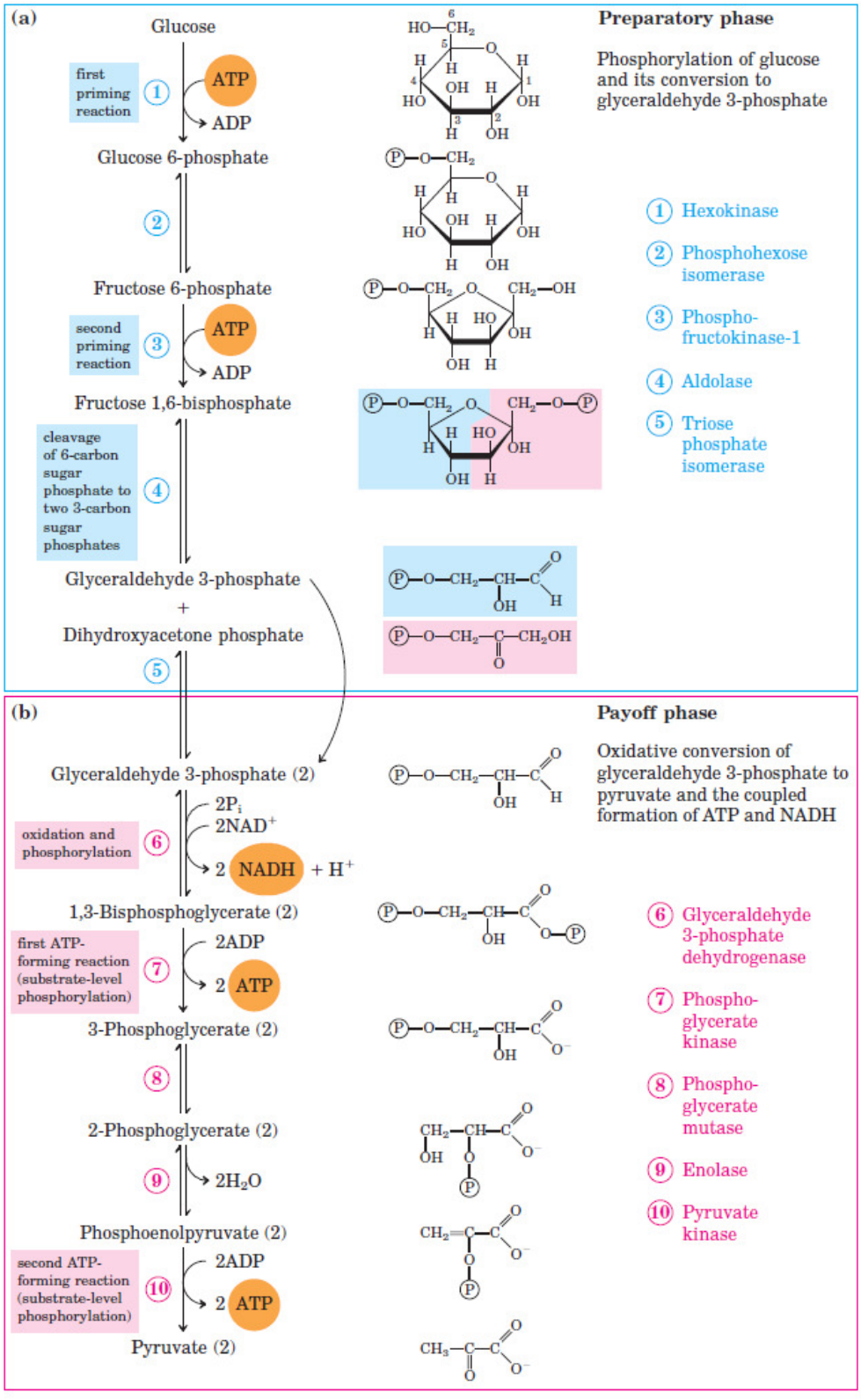
## Glycolysis : All Steps with Diagram, Enzymes, Products, Energy Yield and Significance

Glycolysis is derived from the Greek words (*glykys = sweet and lysis = splitting*). It is a universal catabolic pathway in the living cells.

**Glycolysis can be defined as** the sequence of reactions for the breakdown of Glucose (6-carbon molecule) to two molecules of pyruvic acid (3-carbon molecule) under aerobic conditions; or lactate under anaerobic conditions along with the production of small amount of energy.

This pathway was described by Embden, Meyerhof and Parnas. Hence, it is also called as **Embden-Meyerhof pathway** (EM pathway).



## Site of Glycolysis

Glycolysis occurs in the cytoplasm of virtually all the cells of the body.

## Types of Glycolysis

There are two types of glycolysis.

- **Aerobic Glycolysis**: It occurs when oxygen is plentiful. Final product is **pyruvate** along with the production of Eight ATP molecules.
- **Anaerobic Glycolysis**: It occurs when oxygen is scarce. Final product is **lactate** along with the production of two ATP molecules.

## Steps of Glycolysis

Glycolysis is an extramitochondrial pathway and is carried by a group of eleven enzymes. Glucose is converted to pyruvate in 10 steps by glycolysis.

***The glycolytic patway can be divided into two phases:***

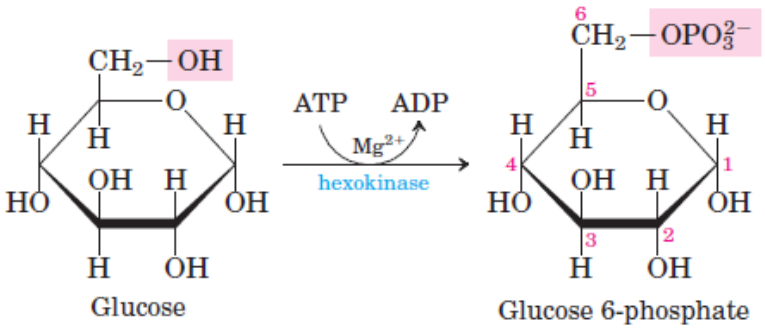
### Preparatory Phase :

This phase is also called **glucose activation phase**. In the preparatory phase of glycolysis, two molecules of ATP are invested and the hexose chain is cleaved into two triose phosphates. During this, phosphorylation of glucose and it's conversion to glyceraldehyde-3-phosphate take place. The steps 1, 2, 3, 4 and 5 together are called as the preparatory phase.

### Payoff Phase :

This phase is also called **energy extraction phase**. During this phase, conversion of glyceraldehyde-3-phophate to pyruvate and the coupled formation of ATP take place.
Because Glucose is split to yield two molecules of D-Glyceraldehyde-3-phosphate, each step in the payoff phase occurs twice per molecule of glucose. The steps after 5 constitute payoff phase.

### Step 1 : Uptake and Phosphorylation of Glucose




- Glucose is phosphorylated to form glucose-6-phosphate.

- The reaction is catalysed by the specific enzyme **glucokinase** in liver cells and by non specific enzyme **hexokinase** in liver and extrahepatic tissue. The enzyme splits the ATP into ADP, and the Pi is added onto the glucose.
- Hexokinase is a **key glycolytic enzyme**. Hexokinase catalyses a regulatory step in glycolysis that is irreversible.
- Hexokinase, like many other kinases, requires Mg2+ for its activity.

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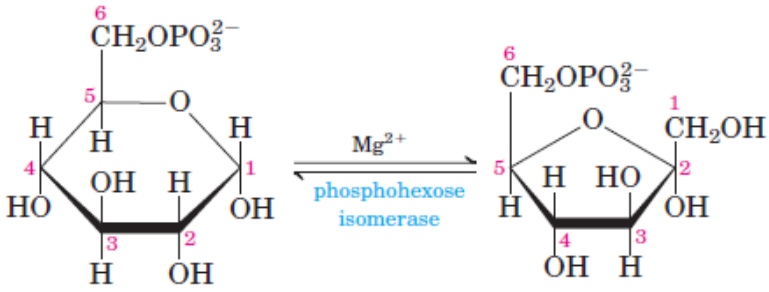
## Step 2 : Isomerization of Glucose-6-Phsphate to Fructose-6-Phosphate




Glucose 6-phosphate  Fructose 6-phosphate

- Glucose-6-phosphate is isomerised to fructose-6-phosphate by **phosphohexose isomerase**.
- This reaction involves an aldose-ketose isomerisastion catalysed by phosphohexose isomerase. There is opening of the glucopyranose ring of glucose-6-phosphate to a linear structure which then changes to the furanose ring structure of fructose-6-phosphate.

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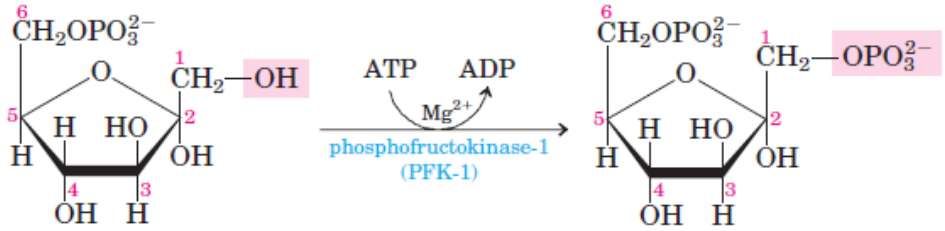
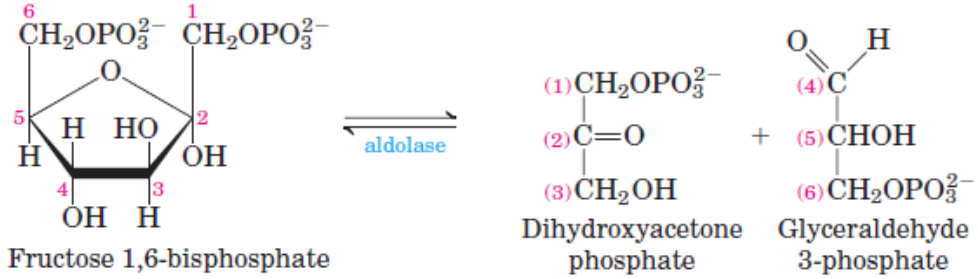
## Step 3 : Phosphorylation of F-6-P to Fructose 1,6-Biphosphate




Fructose 6-phosphate  Fructose 1,6-bisphosphate

- Fructose-6-phosphate is further phosphorylated to fructose 1,6-bisphosphate.
- The enzyme is **phosphofructokinase-1**. It catalyses the transfer of a phosphate group from ATP to fructose-6-phosphate.
- The reaction is irreversible.
- One ATP is utilised for phosphorylation.
- Phosphofructokinase-1 is the **key enzyme** in glycolysis which regulates breakdown of glucose.

## Step 4 : Cleavage of Fructose 1,6-Biphosphate




Fructose 1,6-bisphosphate  Dihydroxyacetone phosphate  Glyceraldehyde 3-phosphate

- The 6 carbon fructose-1,6-bisphosphate is cleaved into two 3 carbon units; one glyceraldehyde-3-phosphate (GAP) and another molecule of dihydroxy acetone phosphate (DHAP).
- The enzyme which catalyses the reaction is **aldolase**. Since the backward reaction is an aldol condensation, the enzyme is called aldolase.
- The reaction is reversible.

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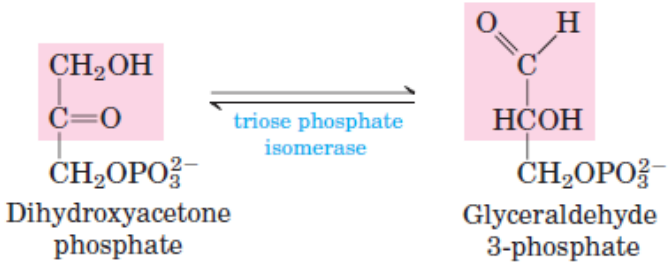
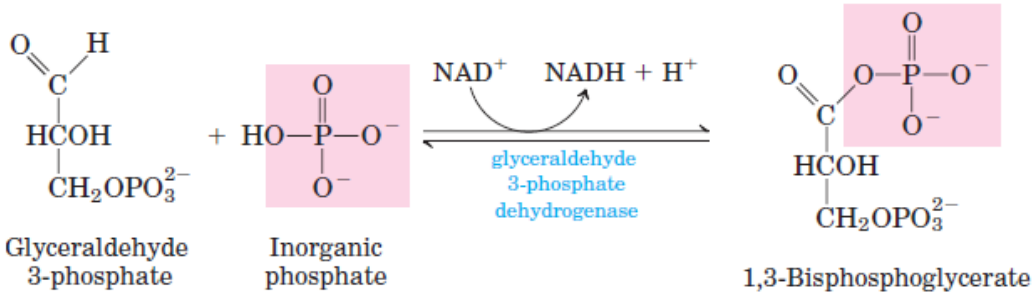
**Step 5 : Interconversion of the Triose Phosphates**



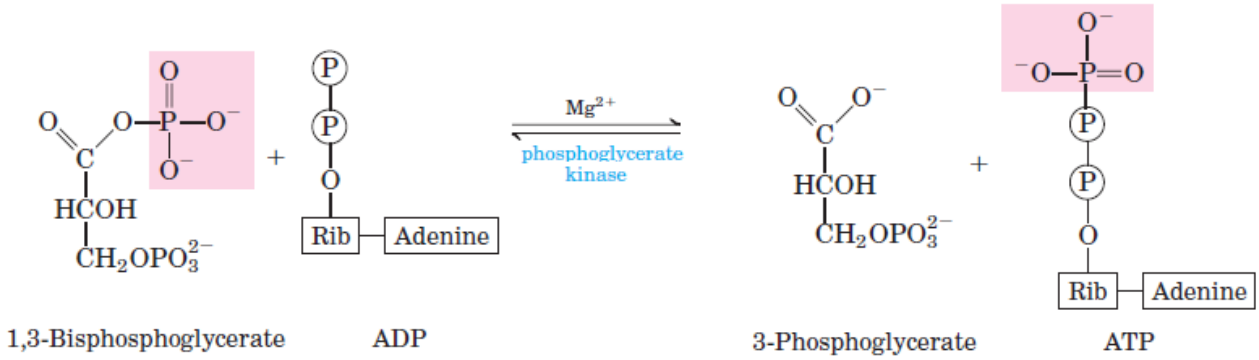

- GAP is on the direct pathway of glycolysis, whereas DHAP is not. Hence **Triose-phosphate isomerase** converts DHAP into GAP useful for generating ATP. Thus net result
- is that glucose is now cleaved into 2 molecules of glyceraldehyde-3-phosphate.
- This reaction is rapid and reversible.

**Step 6 : Oxidative phosphorylation of GAP to 1,3-Bisphosphoglycerate**




- The first step in the payoff phase is the oxidation of glyceraldehyde 3-phosphate to 1,3-bisphosphoglycerate.
- This reaction is catalyzed by **glyceraldehyde 3-phosphate dehydrogenase**.
- It is the energy-yielding reaction. Reactions of this type in which an aldehyde group is oxidised to an acid are accompanied by liberation of large amounts of potentially useful energy. During this reaction, NAD+ is reduced to NADH.
- This is a reversible reaction.

**Step 7 : Conversion of 1,3-Biphosphoglycerate to 3-Phosphoglycerate**



- The enzyme **phosphoglycerate kinase** transfers the high-energy phosphoryl group from the carboxyl group of 1,3-bisphosphoglycerate to ADP, forming ATP and 3-phosphoglycerate.
- This is a unique example where ATP can be produced at substrate level without participating in electron transport chain. This type of reaction where ATP is formed at substrate level is called as Substrate level phosphorylation.

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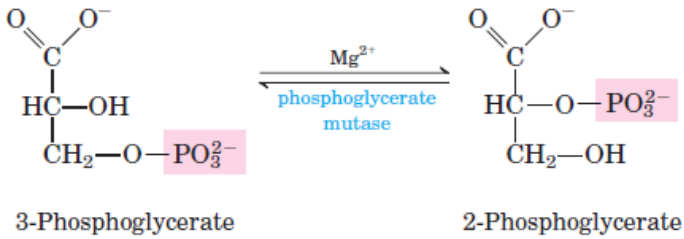
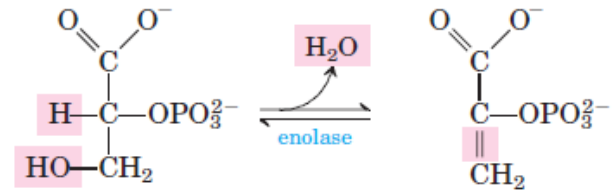
**Step 8 : Conversion of 3-Phosphoglycerate to 2-Phosphoglycerate**




3-Phosphoglycerate 2-Phosphoglycerate

- 3-phospho glycerate is isomerized to 2-phospho glycerate by shifting the phosphate group from 3rd to 2nd carbon atom.
- The enzyme is **phosphogluco mutase**.
- This is a readily reversible reaction.
- Mg2+ is essential for this reaction.

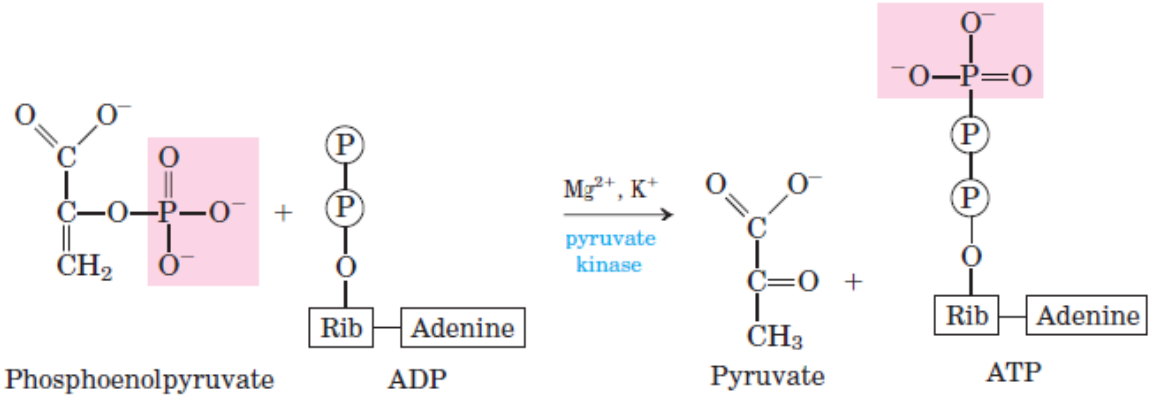
**Step 9 : Dehydration of 2-Phosphoglycerate to Phosphoenolpyruvate**




2-Phosphoglycerate Phosphoenolpyruvate

- 2-phosphoglycerate is converted to phosphoenol pyruvate by the enzyme **enolase**.
- One water molecule is removed.
- A high energy phosphate bond is produced. The reaction is reversible.
- Enolase requires Mg++.

**Step 10 : Conversion of Phosphoenol Pyruvate to Pyruvate**




Phosphoenolpyruvate ADP Pyruvate ATP

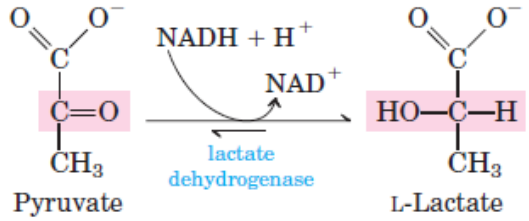
- Phosphoenol pyruvate (PEP) is dephosphorylated to pyruvate, by **pyruvate kinase**.
- First PEP is made into a transient intermediary of enol pyruvate; which is spontaneously isomerized into keto pyruvate, the stable form of pyruvate.
- One mole of ATP is generated during this reaction. This is again an example of substrate level phosphorylation.

## Additional Step in Anaerobic Condition

When animal tissues cannot be supplied with sufficient oxygen to support aerobic oxidation of the pyruvate and NADH produced in glycolysis, NAD+ is regenerated from NADH by the reduction of pyruvate to lactate.

Some tissues and cell types (such as erythrocytes, which have no mitochondria and thus cannot oxidize pyruvate to CO2) produce lactate from glucose even under aerobic conditions.

The reduction of pyruvate is catalyzed by **lactate dehydrogenase**.




## Net energy (ATP) yield per molecule of Glucose in Glycolysis

## Energy Yield in Aerobic Glycolysis

| Step | Enzyme | Source | No. of ATP |
|---|---|---|---|
| 1 | Hexokinase | – | -1 |
| 3 | Phosphofructokinase | – | -1 |
| 6 | Glyceraldehyde-3-phosphate dehydrogenase | NADH | (+3) x 2 = +6 |
| 7 | Phosphoglycerate kinase | ATP | (+1) x 2 = +2 |
| 10 | Pyruvate kinase | ATP | (+1) x 2 = +2 |
| **Net Yield** | | | **8 ATPs** |

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## Energy Yield in Anaerobic Glycolysis

| Step | Enzyme | Source | No. of ATP Formed/consumed |
|---|---|---|---|
| 1 | Hexokinase | – | -1 |
| 3 | Phosphofructokinase | – | -1 |
| 7 | Phosphoglycerate kinase | ATP | (+1) x 2 = +2 |
| 10 | Pyruvate kinase | ATP | (+1) x 2 = +2 |
| **Net Yield** | | | **2 ATPs** |

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## Significance of the Glycolysis Pathway

1. Glycolysis is the only pathway that is taking place in all the cells of the body.
2. Glycolysis is the only source of energy in erythrocytes.
3. In strenuous exercise, when muscle tissue lacks enough oxygen, anaerobic glycolysis forms the major source of energy for muscles.
4. The glycolytic pathway may be considered as the preliminary step before complete oxidation.
5. The glycolytic pathway provides carbon skeletons for synthesis of non-essential amino acids as well as glycerol part of fat.
6. Most of the reactions of the glycolytic pathway are reversible, which are also used for gluconeogenesis.