M.Sc. Botany

Semester-II (2018-20)

MBOTCC-7: Physiology & Biochemistry

Unit –V

BIOCHEMICAL ENERGETICS

GLYOLYSIS

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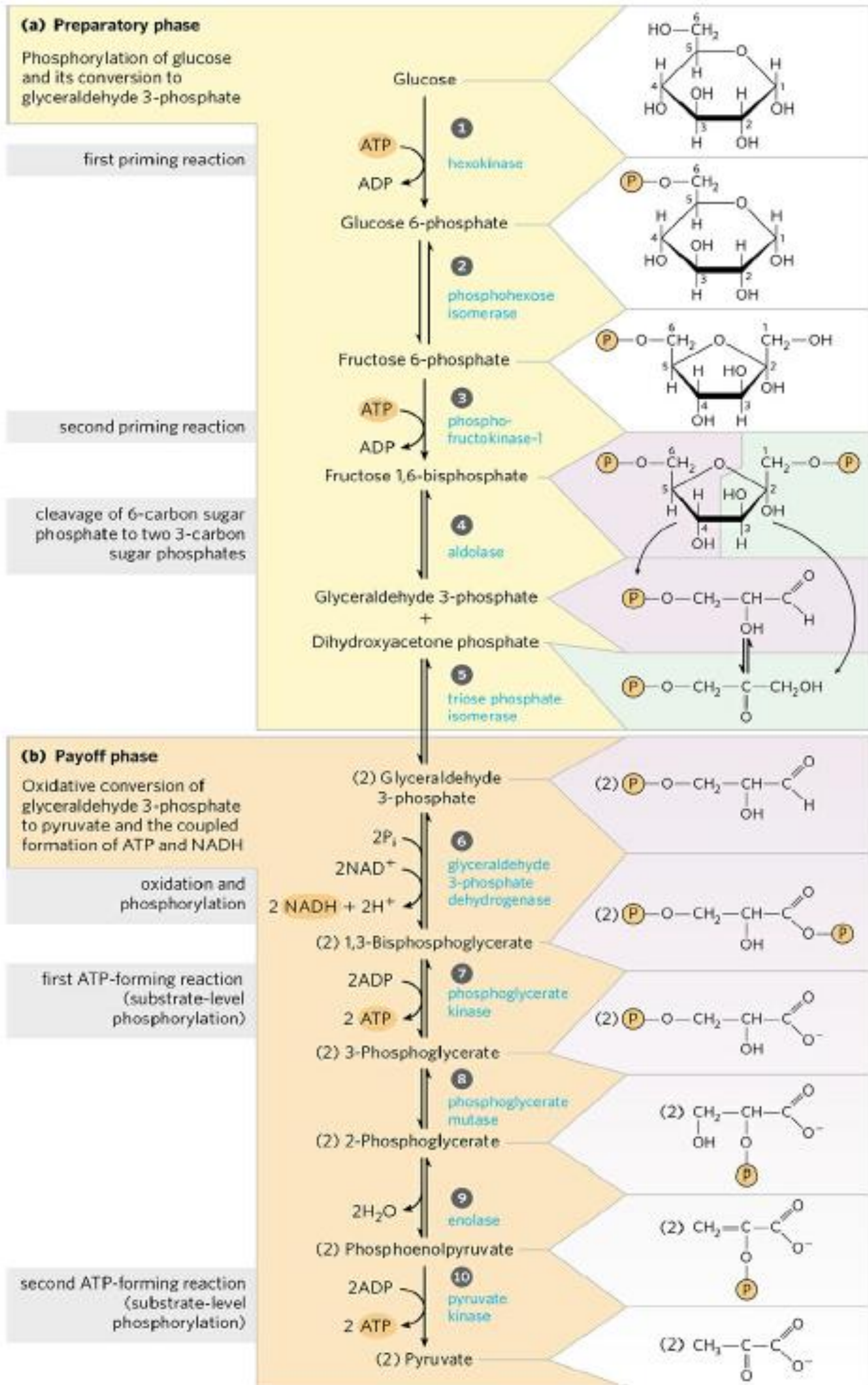
GLYCOLYSIS (from the Greek glykys, ″sweet″ or ″sugar,″ and lysis, ″splitting″)

Glycolysis was the first metabolic pathway to be elucidated and is probably the best understood. The most common type of glycolysis is the *Embden – Meyerhof – Parnas (EMP Pathway)*, which was discovered by **Gustav Embden**, **Otto Meyerhof** and **Jakub Karol Parnas**.

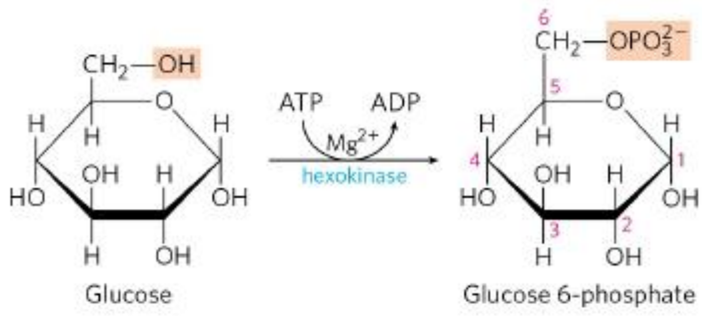
- Glycolysis is a near-universal pathway by which a glucose molecule is oxidized in a series of enzyme catalyzed reactions to two molecules of pyruvate , with energy conserved as ATP and NADH.
- The breakdown of the six-carbon glucose into two molecules of the three carbon pyruvate occurs in 10 steps, the first 5 constitutes the preparatory phase (Wherein ATP is consumed) and next five is payoff phase (wherein ATP is produced).
- All 10 glycolytic enzymes are in the cytosol, and all 10 intermediates are phosphorylated compounds of three or six carbons.
- In the preparatory phase of glycolysis, ATP is invested to convert glucose to fructose 1,6-bisphosphate. The bond between C-3 and C-4 is then broken to yield two molecules of triose phosphate.
- In the payoff phase, each of the two molecules of glyceraldehyde 3- phosphate derived from glucose undergoes oxidation at C-1; the energy of this oxidation reaction is conserved in the form of one NADH and two ATP per triose phosphate oxidized
- Glycolysis is tightly regulated in coordination with other energy-yielding pathways to ensure a steady supply of ATP.



- **FIGURE :** **The two phases of glycolysis. For each molecule of glucose that passes through the preparatory phase (a), two molecules of glyceraldehydes 3-phosphate are formed; both pass through the payoff phase (b). Pyruvate is the end product of the second phase of glycolysis. For each glucose molecule, two ATP are consumed in the preparatory phase and**

four ATP are produced in the payoff phase, giving a net yield of two ATP per molecule of glucose converted to pyruvate. The numbered reaction steps correspond to the numbered headings in the text discussion. Keep in mind that each phosphoryl group, represented here as P , has two negative charges ($-PO_3^{2-}$)

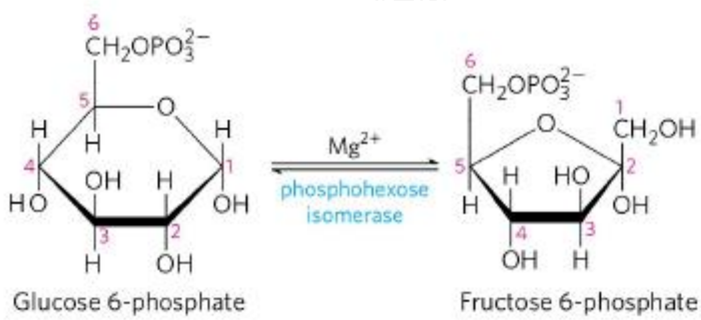
1. **Phosphorylation of Glucose** In the first step of glycolysis, glucose is activated for subsequent reactions by its phosphorylation at C-6 to yield glucose 6-phosphate, with ATP as the phosphoryl donor:



$\Delta G'^{\circ} = -16.7$ kJ/mol

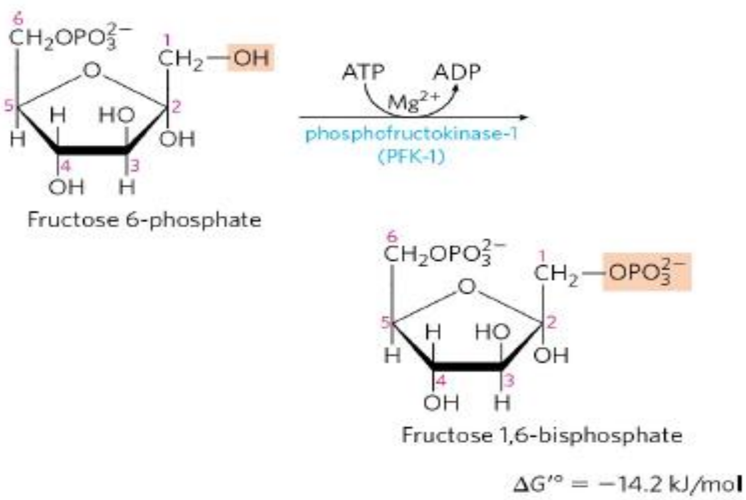
This reaction, which is irreversible under intracellular conditions, is catalyzed by hexokinase.

2. **Conversion of Glucose 6-Phosphate to Fructose 6- Phosphate** The enzyme phosphohexose isomerase (phosphoglucose isomerase) catalyzes the reversible isomerization of glucose 6-phosphate, an aldose, to fructose 6-phosphate, a ketose:

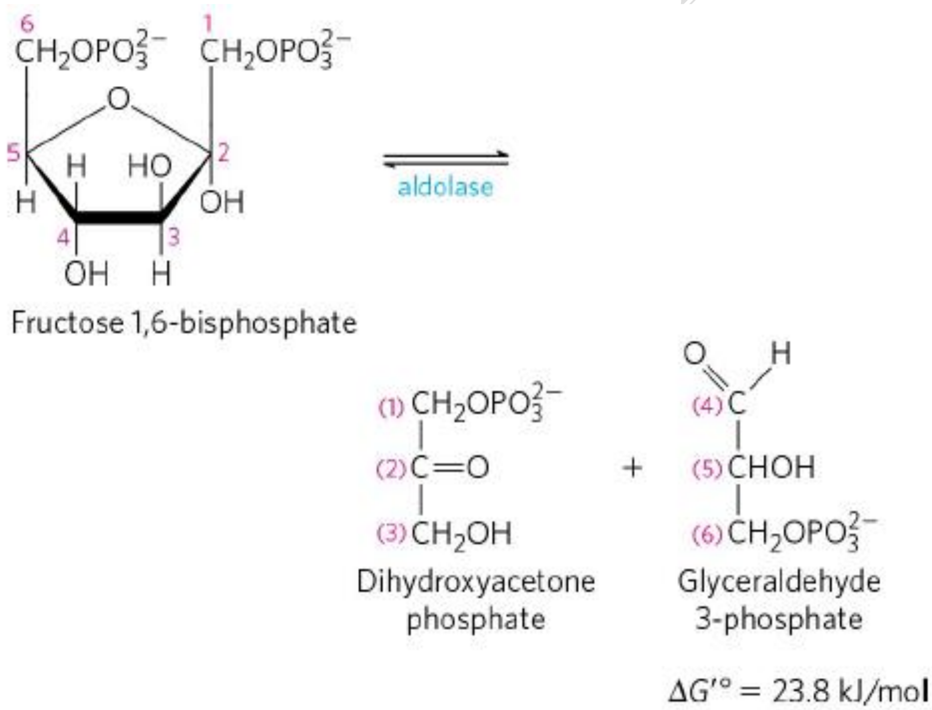


$\Delta G'^{\circ} = 1.7$ kJ/mol

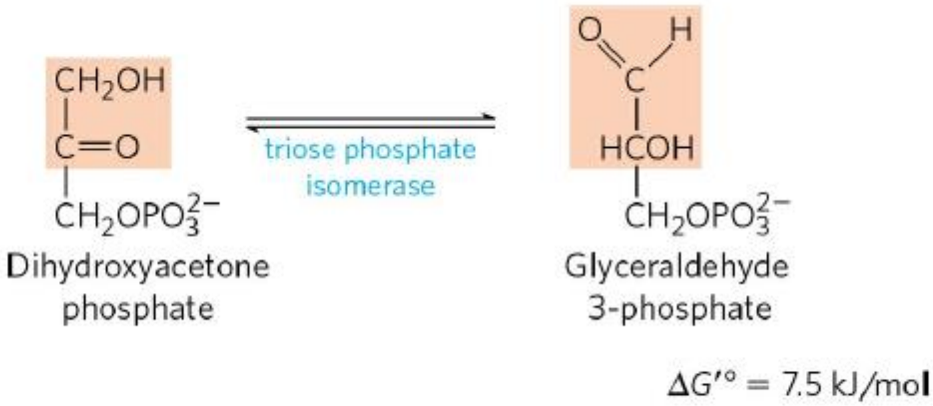
3. **Phosphorylation of Fructose 6-Phosphate to Fructose 1,6-Bisphosphate** In the second of the two priming reactions of glycolysis, phosphofructokinase-1 (PFK-1) catalyzes the transfer of a phosphoryl group from ATP to fructose 6-phosphate to yield fructose 1,6-bisphosphate:



4. **Cleavage of Fructose 1,6-Bisphosphate:** The enzyme fructose 1,6-bisphosphate aldolase, often called simply aldolase, catalyzes a reversible aldol condensation . Fructose 1,6-bisphosphate is cleaved to yield two different triose phosphates, glyceraldehyde 3- phosphate, an aldose, and dihydroxyacetone phosphate, a ketose:

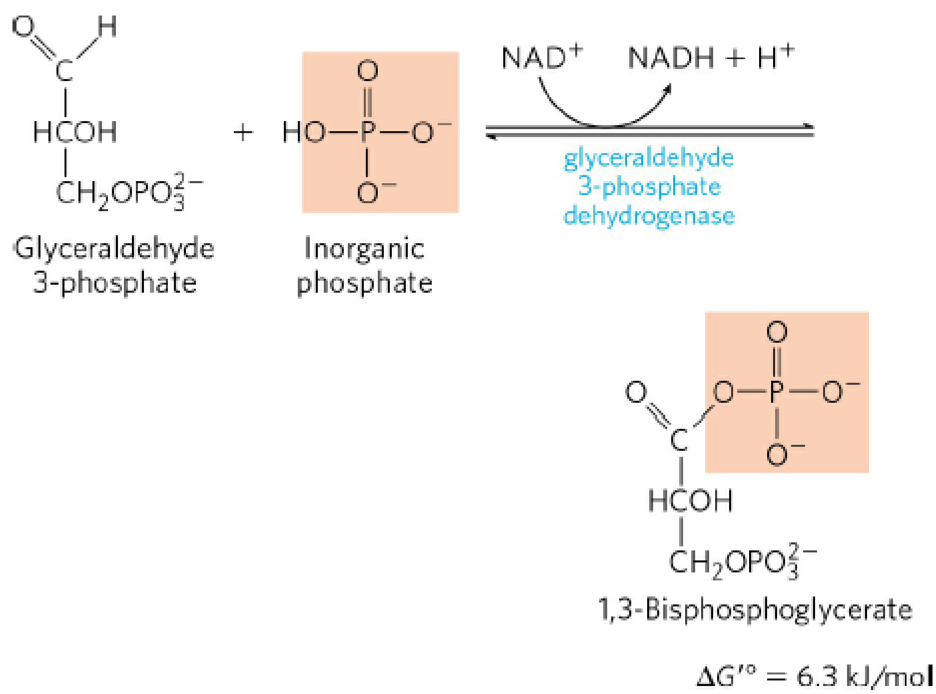


5. **Interconversion of the Triose Phosphates** Only one of the two triose phosphates formed by aldolase, glyceraldehyde 3-phosphate, can be directly degraded in the subsequent steps of glycolysis. The other product, dihydroxyacetone phosphate, is rapidly and reversibly converted to glyceraldehyde 3-phosphate by the fifth enzyme of the glycolytic sequence, triose phosphate isomerase:

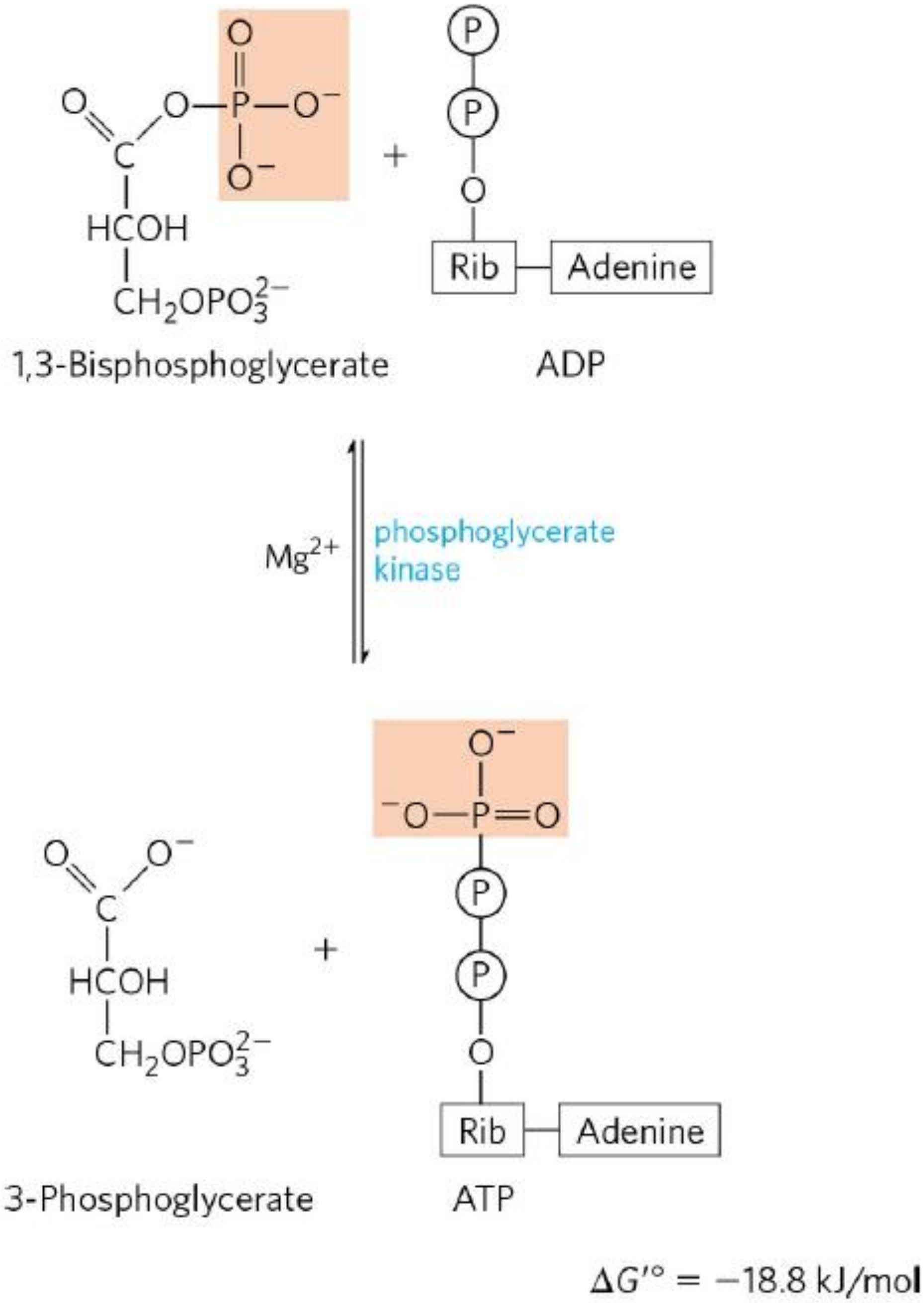


This reaction completes the preparatory phase of glycolysis. The hexose molecule has been phosphorylated at C-1 and C-6 and then cleaved to form two molecules of glyceraldehyde 3-phosphate.

6. **Oxidation of Glyceraldehyde 3-Phosphate to 1,3-Bisphosphoglycerate** The first step in the payoff phase is the oxidation of glyceraldehyde 3-phosphate to 1,3-bisphosphoglycerate, catalyzed by glyceraldehyde 3-phosphate dehydrogenase:



7. **Phosphoryl Transfer from 1,3-Bisphosphoglycerate to ADP** 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:

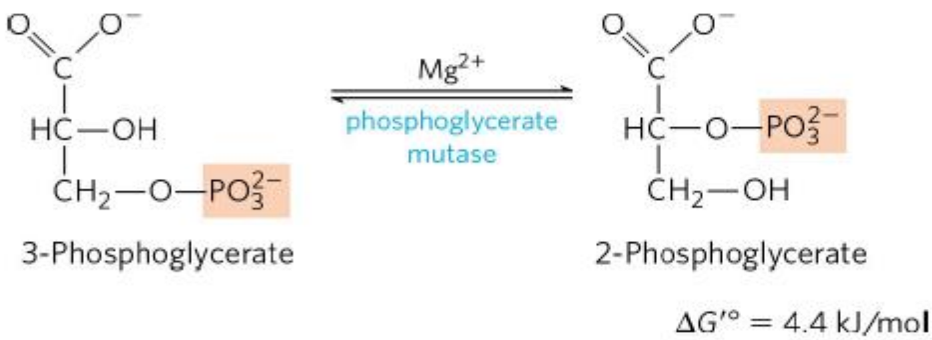


Steps 6 and 7 of glycolysis together constitute an energy-coupling process in which 1,3-bisphosphoglycerate is the common intermediate; it is formed in the first reaction (which wou ld be endergonic in isolation), and its acyl phosphate group is transferred to ADP in the second reaction (which is strongly exergonic). The sum of these two reactions is

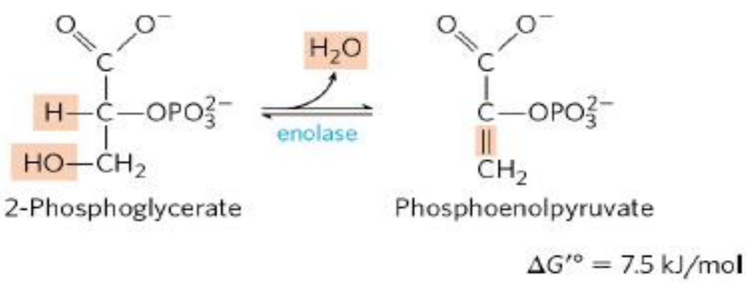
$$\text{Glyceraldehyde 3-phosphate} + \text{ADP} + P_i + \text{NAD}^+ \rightleftharpoons \text{3-phosphoglycerate} + \text{ATP} + \text{NADH} + \text{H}^+$$
$$\Delta G'^\circ = -12.2\ \text{kJ/mol}$$

Thus the overall reaction is exergonic.

8. **Conversion of 3-Phosphoglycerate to 2- Phosphoglycerate** The enzyme phosphoglycerate mutase catalyzes a reversible shift of the phosphoryl group between C-2 and C-3 of glycerate; Mg^{2+} is essential for this reaction:

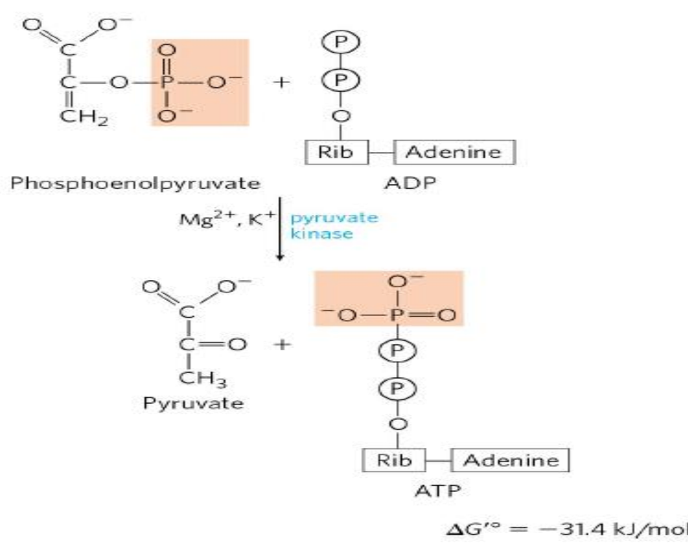


9. **Dehydration of 2-Phosphoglycerate to Phosphoenolpyruvate** Enolase promotes reversible removal of a molecule of water from 2- phosphoglycerate to yield phosphoenolpyruvate (PEP):

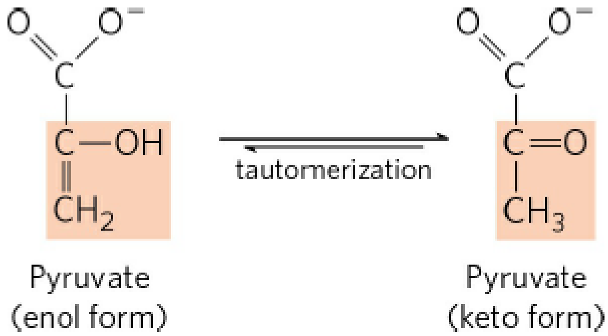


The mechanism of the enolase reaction involves an enolic intermediate stabilized by Mg^{2+}.

10. **Transfer of the Phosphoryl Group from Phosphoenolpyruvate to ADP** The last step in glycolysis is the transfer of the phosphoryl group from phosphoenolpyruvate to ADP, catalyzed by pyruvate kinase, which requires K^+ and either Mg^{2+} or Mn^{2+}:



In this substrate-level phosphorylation, the product **pyruvate** first appears in its enol form, then tautomerizes rapidly and nonenzymatically to its keto form, which predominates at pH 7:



Fates of Pyruvate With the exception of some interesting variations in the bacterial realm, the pyruvate formed by glycolysis is further metabolized via one of three catabolic routes. In aerobic organisms or tissues, under aerobic conditions, glycolysis is only the first stage in the complete degradation of glucose . Pyruvate is oxidized, with loss of its carboxyl group as CO_2, to yield the acetyl group of acetyl-coenzyme A; the acetyl group is then oxidized completely to CO_2 by the citric acid cycle . The electrons from these oxidations are passed to O_2 through a chain of carriers in mitochondria, to form H_2O. The energy from the electron-transfer reactions drives the synthesis of ATP in mitochondria.

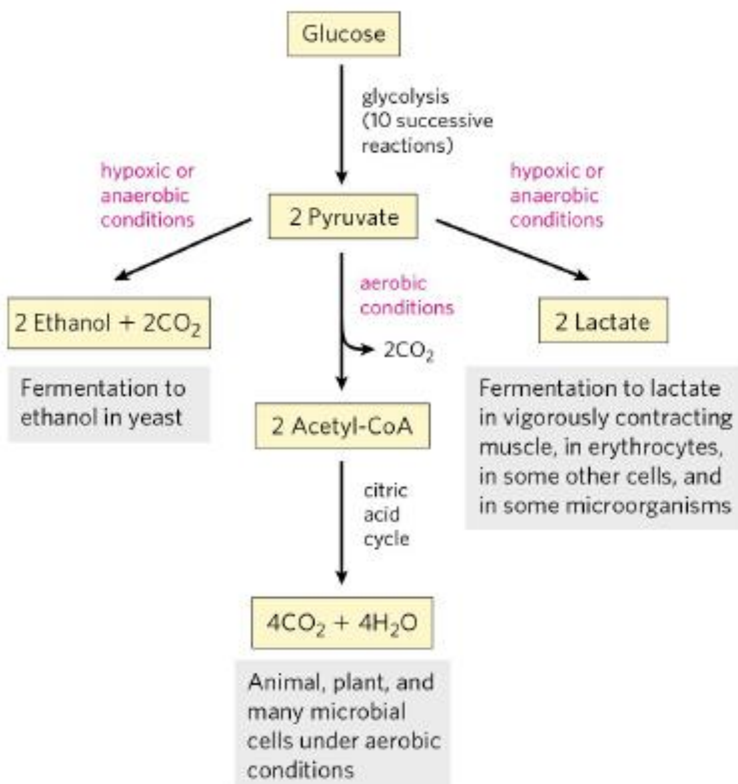


FIGURE Three possible catabolic fates of the pyruvate formed in glycolysis.

The Overall Balance Sheet of glycolysis:

$$\text{Glucose} + 2\text{ATP} + 2\text{NAD}^+ + 4\text{ADP} + 2\text{P}_i \rightarrow 2\,\text{pyruvate}$$
$$+ 2\text{ADP} + 2\text{NADH} + 2\text{H}^+ + 4\text{ATP} + 2\text{H}_2\text{O}$$

Canceling out common terms on both sides of the equation gives the overall equation for glycolysis under aerobic conditions:

$$\text{Glucose} + 2\text{NAD}^+ + 2\text{ADP} + 2\text{P}_i \rightarrow 2\,\text{pyruvate} + 2\text{NADH}$$
$$+ 2\text{H}^+ + 2\text{ATP} + 2\text{H}_2\text{O}$$

The two molecules of NADH formed by glycolysis in the cytosol are, under aerobic conditions, reoxidized to NAD^+ by transfer of their electrons to the electron-transfer chain, which in eukaryotic cells is located in the mitochondria. The electron-transfer chain passes these electrons to their ultimate destination, O_2:

$$2\text{NADH} + 2\text{H}^+ + \text{O}_2 \rightarrow 2\text{NAD}^+ + 2\text{H}_2\text{O}$$

Standard free-energy change of glycolysis:

We can resolve the equation of glycolysis into two processes—

1. The conversion of glucose to pyruvate, is exergonic:

$$\text{Glucose} + 2\text{NAD}^+ \rightarrow 2\,\text{pyruvate} + 2\text{NADH} + 2\text{H}^+ \qquad (14\text{-}2)$$
$$\Delta G'^{\circ}_1 = -146\,\text{kJ/mol}$$

2. Formation of ATP from ADP and Pi, is endergonic:

$$2\text{ADP} + 2\text{P}_i \rightarrow 2\text{ATP} + 2\text{H}_2\text{O} \qquad (14\text{-}3)$$
$$\Delta G'^{\circ}_2 = 2(30.5\text{kJ/mol}) = 61.0\,\text{kJ/mol}$$

The sum of Equations 14-2 and 14-3 gives the overall standard free-energy change of glycolysis,

$$\begin{aligned}\Delta G'^{\circ}_{\text{Sum}} = \Delta G'^{\circ}_1 &= -146\,\text{kJ/mol} + 61.0\,\text{kJ/mol}\\ &= -85\,\text{kJ/mol}\end{aligned}$$

In the overall glycolytic process, one molecule of glucose is converted to two molecules of pyruvate (the pathway of carbon). Two molecules of ADP and two of Pi are converted to two molecules of ATP (the pathway of phosphoryl groups). Four electrons, as two hydride ions, are transferred from two molecules of glyceraldehyde 3-phosphate to two of NAD^+ (the pathway of electrons).