A brief Idea about Carbohydrate Metabolism

(Student references)

Carbohydrate Metabolism

Metabolism is defined as the chemical processes by which cells produce the substances and energy needed to sustain life. It is subdivided into: Catabolism and Anabolism.

Catabolism: The metabolic breakdown of complex (larger) molecules into simpler (smaller) ones, often resulting in a release of energy.

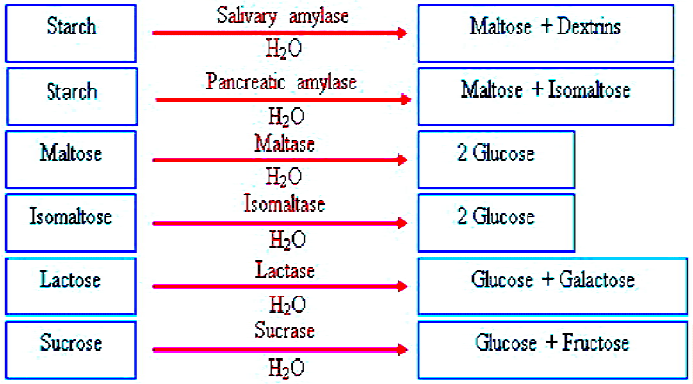
Anabolism: The phase of metabolism in which complex (large) molecules, such as the proteins and fats are formed from simpler (smaller) ones.

The Digestion of Carbohydrates

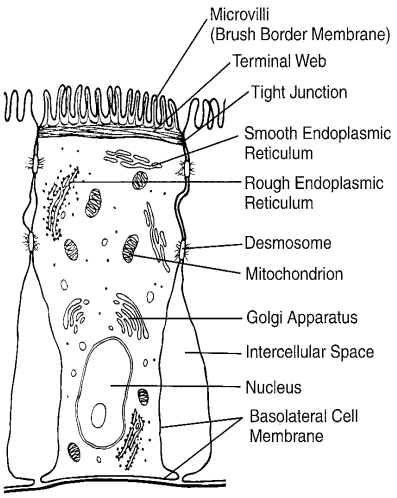
- Carbohydrates impart crucial roles in the metabolic processes of living organisms. They act as energy sources (storage). The digestible carbohydrates provide 4 kcal/g. They also serve as structural elements (cellulose of plant, exoskeleton of insects, glycoproteins & glycolipids of cell membrane and receptor) in living cells. Excess carbohydrate is converted to fat.
- During carbohydrate digestion, disaccharides, oligosaccharides and polysaccharides are hydrolyzed to form monosaccharides (primarily glucose, fructose, and galactose) which are absorbed into the bloodstream through the lining of the small intestine and transported to the liver.
- The liver acts as a regulator of blood glucose level where fructose and galactose are rapidly converted to glucose or to compounds that are metabolized by the same pathway as glucose.

$$\text{polysaccharides} + H_2O \xrightarrow{\text{digestion}} \text{glucose}$$
$$\text{sucrose} + H_2O \xrightarrow{\text{digestion}} \text{glucose} + \text{fructose}$$
$$\text{lactose} + H_2O \xrightarrow{\text{digestion}} \text{glucose} + \text{galactose}$$
$$\text{maltose} + H_2O \xrightarrow{\text{digestion}} \text{glucose}$$

The principle of most dietary carbohydrate digestion is a rapid and catalytic enzymatic hydrolysis of glycosidic linkage by glycoside hydrolase (glycosidase) that occurs at mouth and intestinal lumen.



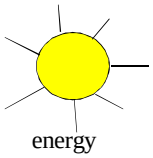
Portal for transport of virtually all nutrients in small intestine



There is water and electrolyte balance. Enzymes associated with intestinal surface membranes

1. Sucrase
2. a dextrinase
3. Glucoamylase (maltase)
4. Lactase
5. Peptidases

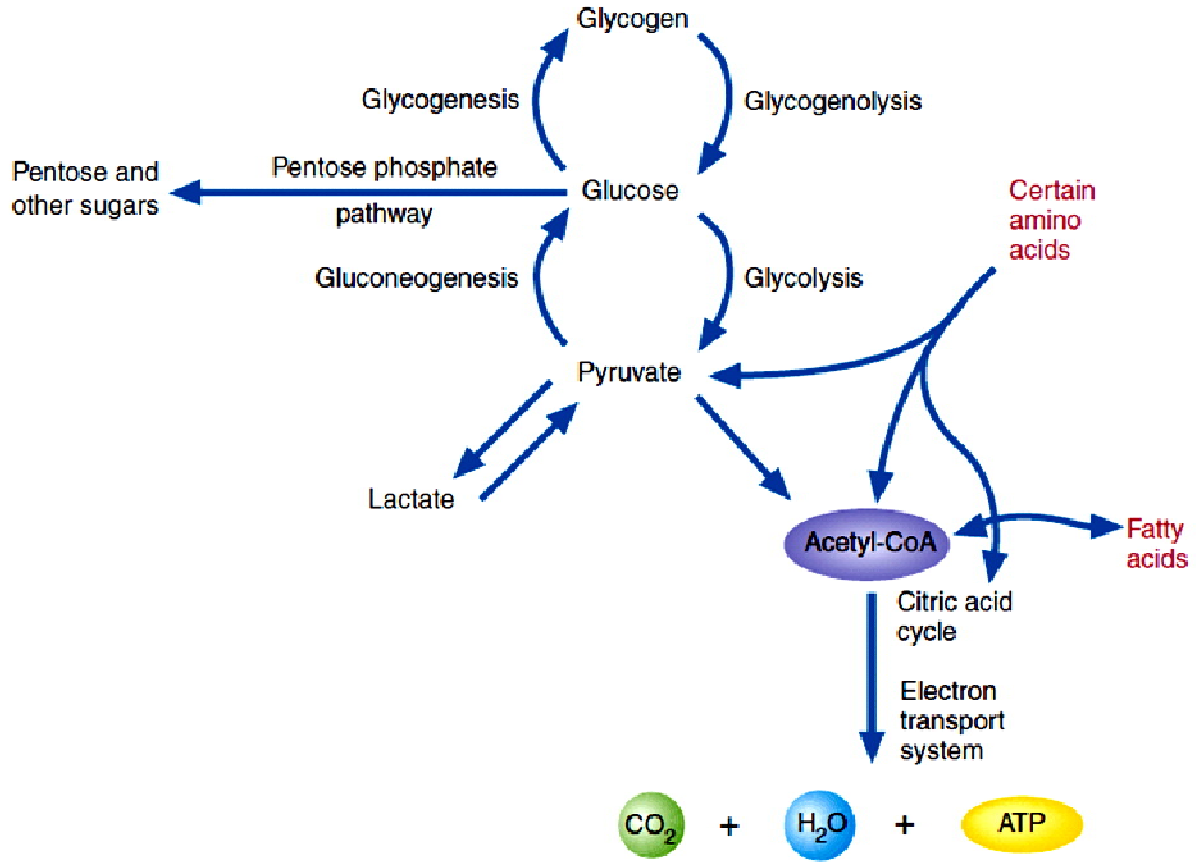
Photosynthesis: Sun's energy becomes part of glucose molecule



energy
Carbon dioxide
Water
Chlorophyll
→ GLUCOSE

$6\,CO_2 + 6\,H_20 + \text{Energy (sun)} \longrightarrow C_6H_{12}O_6 + 6\,O_2$

Major Pathways in Carbohydrate Metabolism



Glycolysis: It is an oxidation of glucose to generate pyruvate under aerobic condition or the oxidation of glucose to lactate under anaerobic state.

Krebs cycle: After oxidation of pyruvate to acetyl CoA, acetyl CoA enters the Krebs cycle for the aim of production of ATP.

Hexose monophosphate shunt: Enables cells to produce ribose-5-phosphate and NADPH.

Glycogen: It is the storage form of glucose in the vertebrates.

Glycogenesis: Synthesis of glycogen from glucose, when glucose levels are high.

Glycogenolysis: Degradation of glycogen to glucose when glucose in short supply.

Gluconeogenesis: Formation of glucose from noncarbohydrate sources.

Glycolysis

Glycolysis occurs in almost every living cell. It is considered as oldest biochemical process. The process is mediated either by both in presence or in absence of oxygen. The small amount of energy captured during glycolytic reactions (≈ 5% of the total) is stored temporarily in two molecules each of ATP and NADH. Glycolysis is also referred to ***Embden-Meyerhof-Parnas pathway***.

Through glycolysis, glucose (6-carbon) is converted to 2 or 3 carbon unit i.e pyruvate. Each glucose molecule is converted to two molecules of pyruvate, ATP and NADH. The metabolic fate of pyruvate depends on the type of organism and its metabolic circumstances. In anaerobic organisms, pyruvate may be converted to waste products such as ethanol, lactic acid, acetic acid. However, aerobic organisms such as animals and plants completely oxidize pyruvate to form CO_2 and H_2O (aerobic respiration).

Glycolysis comprises of 10 reactions. It occurs in two stages.

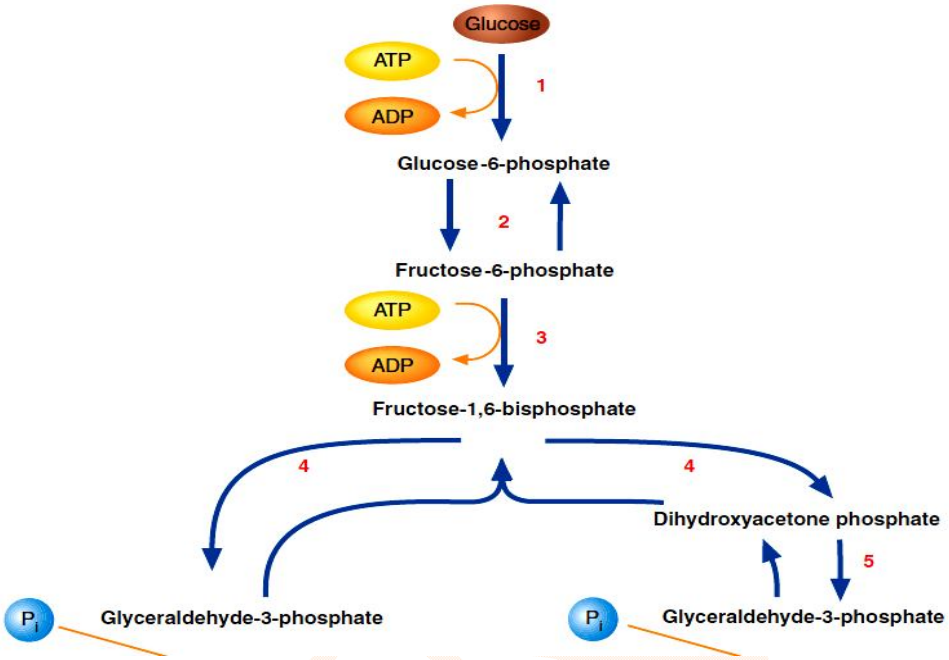
Stage 1: Glucose is phosphorylated twice and cleaved to form two molecules of glyceraldehyde-3-phosphate (G-3-P). The two ATP molecules consumed during this stage are like an investment, because this stage creates the actual substrates for oxidation in a form that is trapped inside the cell.

Stage 2: Glyceraldehyde-3-phosphate is converted to pyruvate. Four ATP and two NADH molecules are produced. Because two ATP were consumed in stage 1, the net production of ATP per glucose molecule is 2.

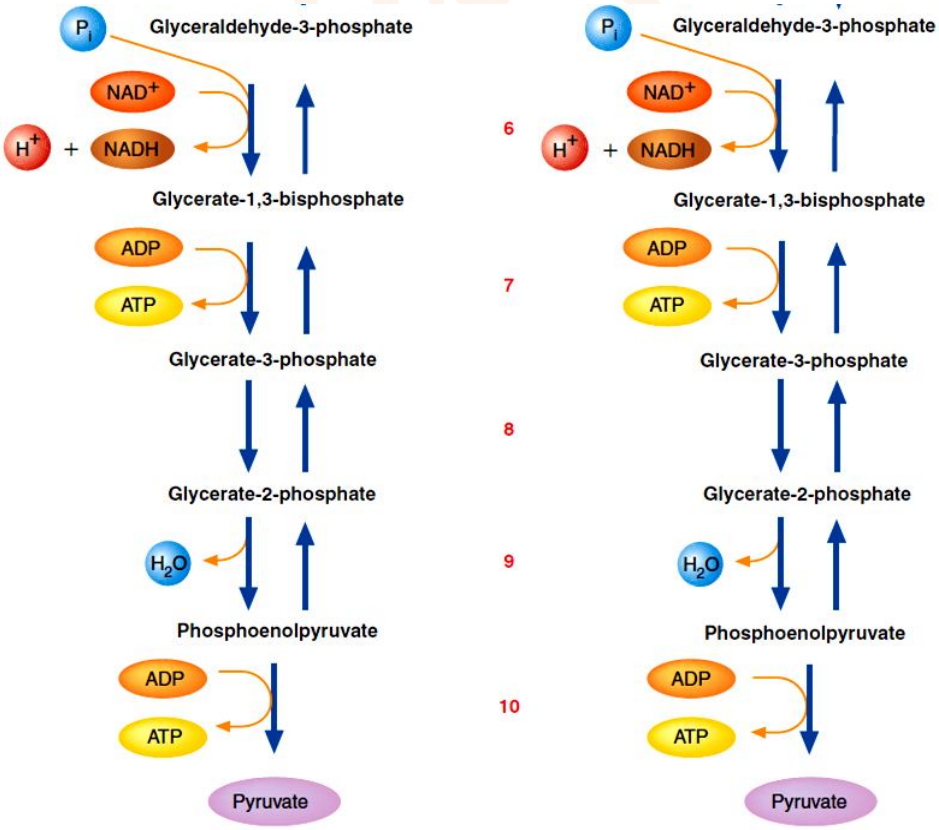
The glycolytic pathway can be summed up in the following equation:

$$\text{D-Glucose} + 2\,\text{ADP} + 2\,P_i + 2\,\text{NAD}^+ \rightarrow 2\,\text{pyruvate} + 2\,\text{ATP} + 2\,\text{NADH} + 2\text{H}^+ + 2\text{H}_2\text{O}$$

Stage 1 of The Glycolytic Pathway



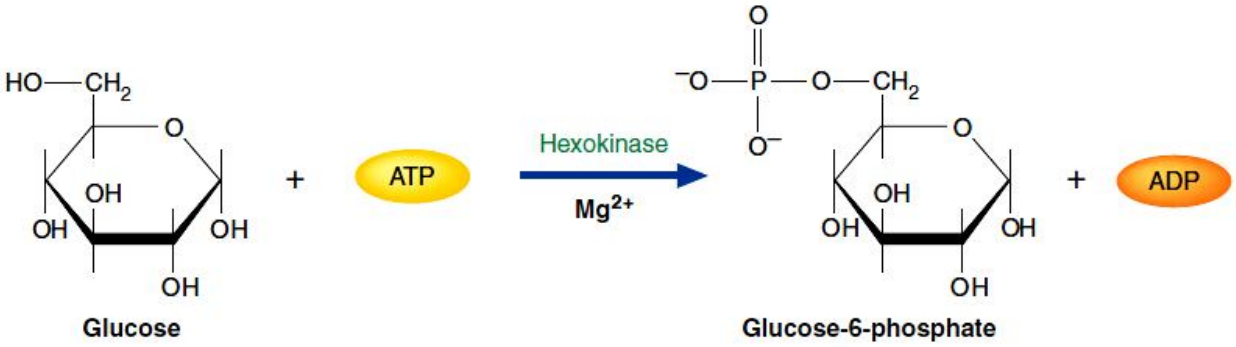
Stage 2 of The Glycolytic Pathway



The Reactions of Glycolytic Pathway

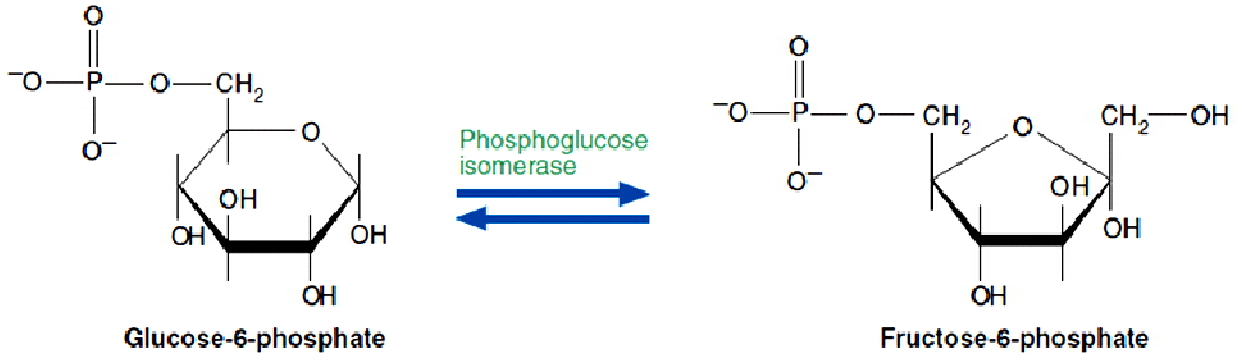
Step 1: Synthesis of glucose-6-phosphate

The first step is the phosphorylation of glucose and other sugar molecules right after entering a cell which is catalyzed by hexokinases with the help of ATP in complex with Mg^{2+} following a irreversible pathway under intracellular conditions.



Step 2: Conversion of glucose-6-phosphate to fructose-6-phosphate

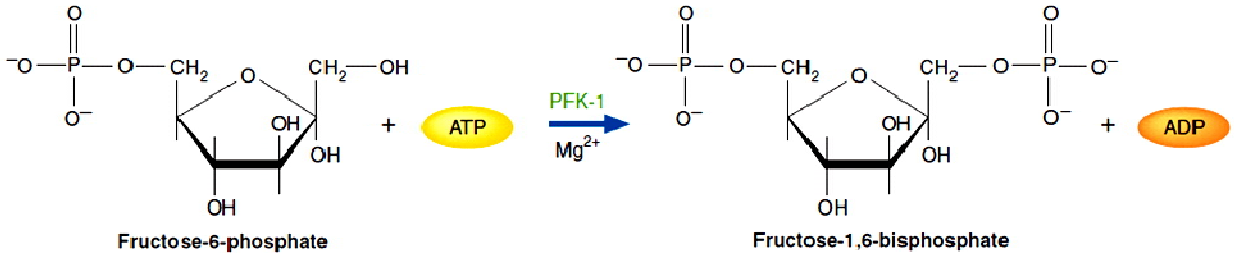
A readily reversible isomerization reaction in which the open chain form of the aldose glucose-6-phosphate is converted to ketose fructose-6-phosphate via the open chain form by phosphoglucose isomerase (PGI).



Step 3: The phosphorylation of fructose-6-phosphate

Phosphofructokinase-1 (PFK-1) irreversibly catalyzes the phosphorylation of fructose-6-phosphate to form fructose-1,6-bisphosphate under cellular conditions. Since ATP is used as the

phosphorylating agent, the reaction proceeds with a large decrease in free energy (ΔG^{*} = -ve). After fructose-1,6-bisphosphate has been synthesized, the cell is committed to glycolysis.



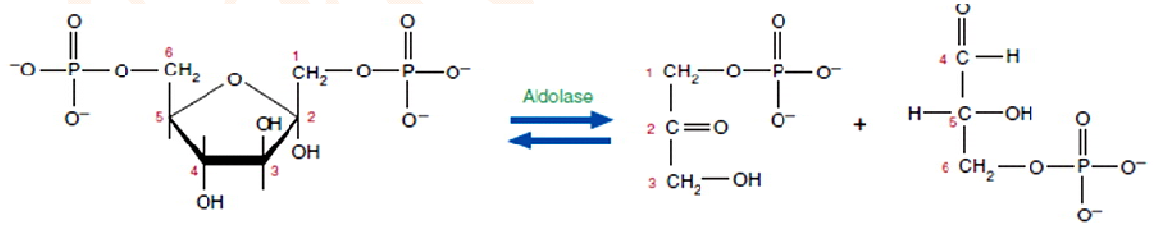
Fructose-6-phosphate Fructose-1,6-bisphosphate

Since in next step, fructose-1,6-bisphosphate splits into two trioses, the phosphorylation prevents them from diffusing out of the cell because charged molecules cannot cross membranes easily.

Step 4: Cleavage of fructose-1,6-bisphosphate

Aldoses reversibly cleaves fructose-1,6-bisphosphate into two three-carbon molecules: glyceraldehyde-3-phosphate (G-3-P) and dihydroxyacetone phosphate (DHAP).

Although the cleavage of fructose-1,6-bisphosphate is thermodynamically unfavorable (ΔG^{o*} = +5.6 kcal/mol), the reaction proceeds because the products are rapidly removed.

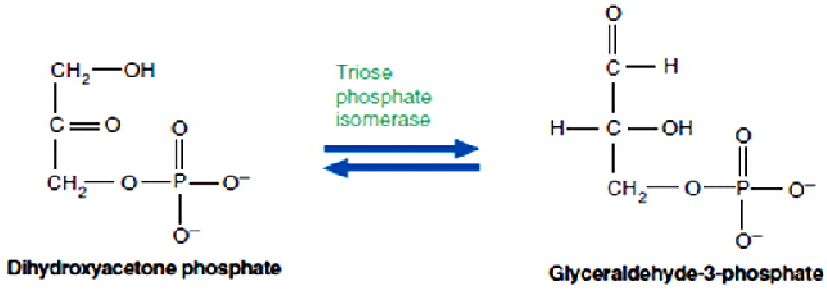


Fructose-1,6-bisphosphate Dihydroxyacetone phosphate Glyceraldehyde-3-phosphate

Step 5: Interconversion of Glyceraldehyde-3-phosphate (G-3-P) and dihydroxyacetone phosphate (DHAP)

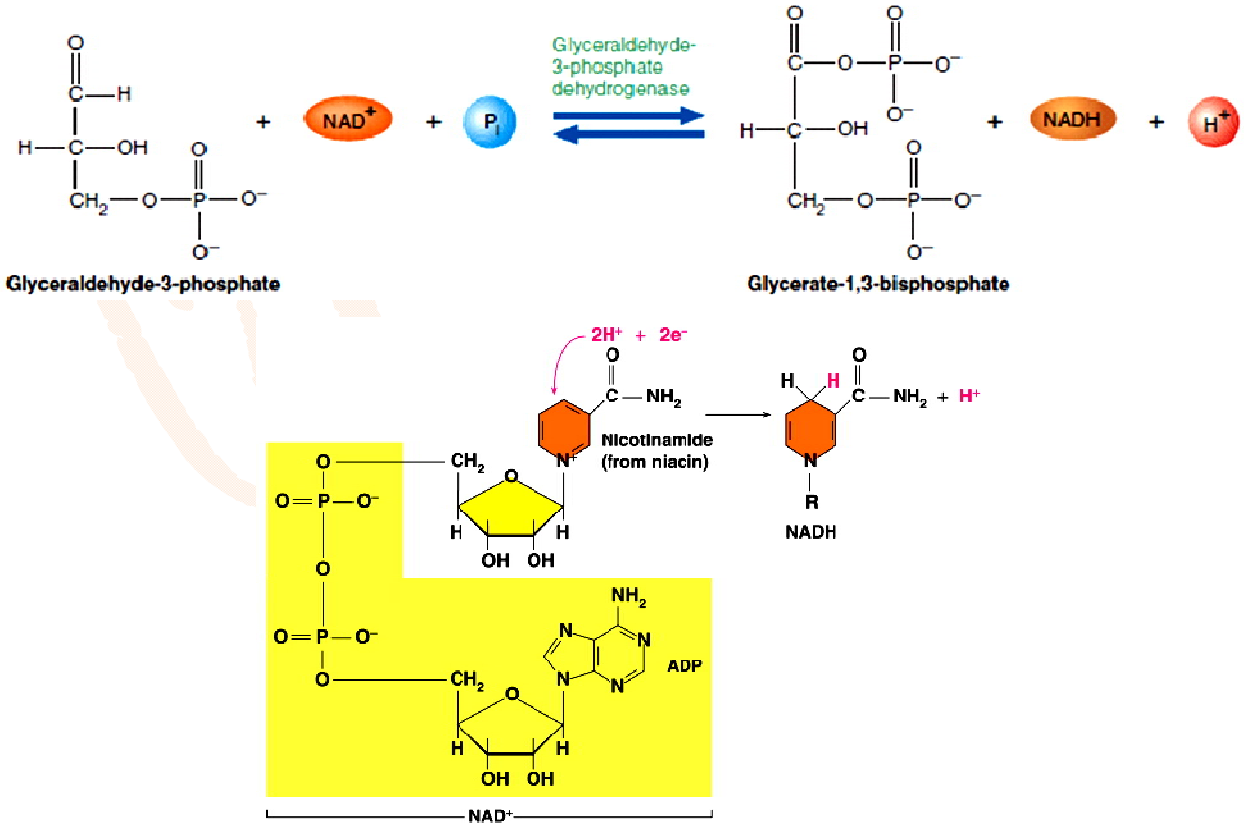
The enzyme called Triose phosphate isomerase catalyzes the reversible conversion of DHAP to G-3-P. The ketose sugar is isomerized to aldosee

sugar and vice-versa. After this reaction, the original molecule of glucose has been converted to two molecules of G-3-P.

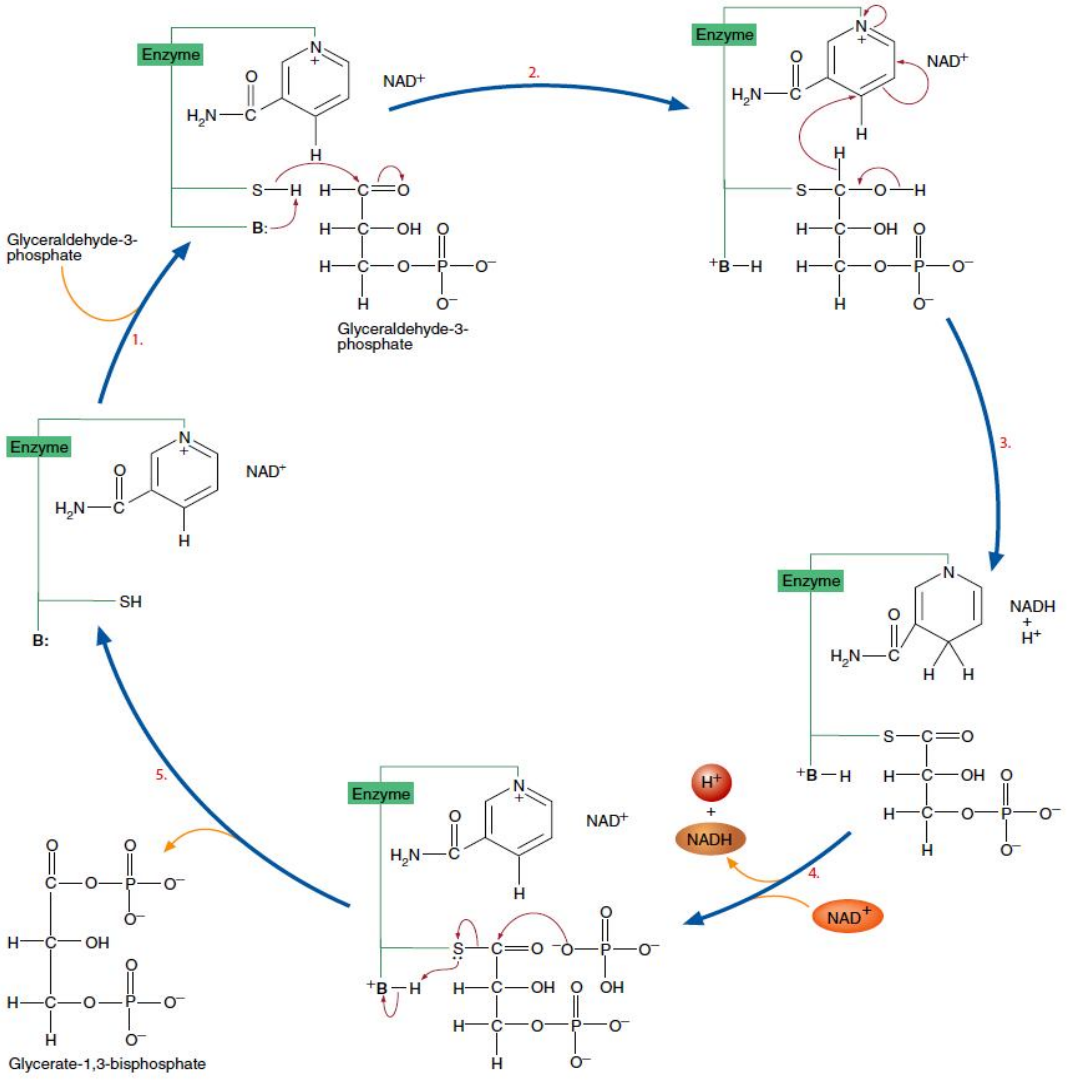


Step 6: Oxidation of Glyceraldehyde-3-phosphate (G-3-P)

In the 6th step of glycolytic reaction, G-3-P undergoes oxidation and phosphorylation to glycerate-1,3-bisphosphate which is catalyzed by glyceraldehyde-3-phosphate dehydrogenase, a tetramer composed of four identical subunits. Each subunit contains one binding site for G-3-P and another for NAD, an oxidizing agent.



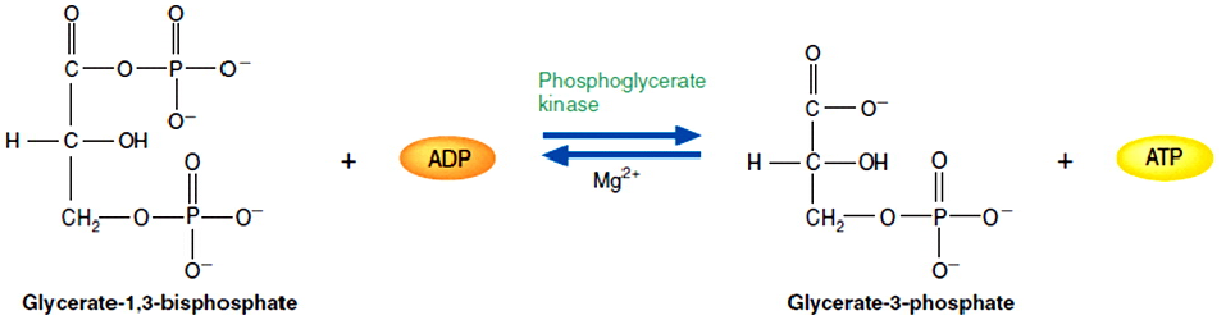
Glyceraldehyde-3-Phosphate Dehydrogenase Reaction



Step 7: Phophorylation of ADP to ATP

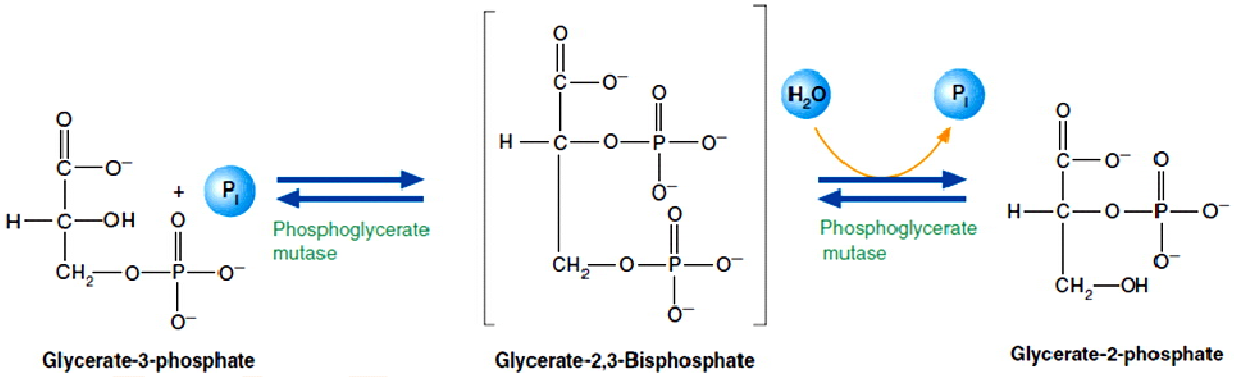
Phosphoglycerate kinase catalyzes the synthesis of ATP (with a phosphoryl lower transfer potential) by the transfer of the high-energy phosphoryl group of glycerate-1,3-bisphosphate (with a high phosphoryl transfer potential) to ADP. The free energy change $\Delta G < 0$. Because two molecules of glycerate-1,3-bisphosphate are formed for every glucose molecule, this reaction produces two ATP molecules, and the investment of phosphate bond energy is recovered.

The synthesis of ATP is endergonic, it requires an energy source. The reaction is an example of a substrate-level phosphorylation.



Step 8: Interconversion of 3-phosphoglycerate and 2-phosphoglycerate

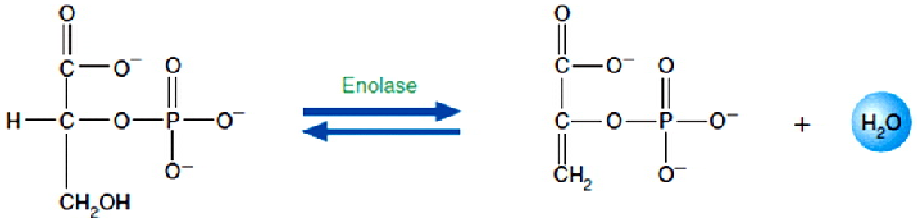
The Glycerate-3-phosphate (at step 7) has a low phosphoryl group transfer potential for further ATP synthesis (ΔG^{o} = –30.5 kJ/mol for ATP synthesis). Thus, phosphoglycerate mutase catalyzes the conversion of a C-3 phosphorylated compound to a C-2 phosphorylated compound through a two-step addition/elimination cycle.



Step 9: Dehydration of 2-phosphoglycerate

Enolase initiates the tautomerization of glycerate-2- phosphate to its enol form, phosphoenolpyruvate (PEP). This tautomerization is restricted by the presence of the phosphate group, as is the resonance stabilization of the free phosphate ion. As a result, phosphoryl transfer to ADP in reaction 10 is highly favored.

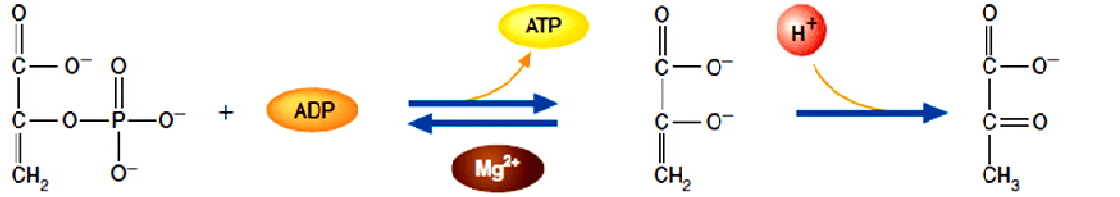
In contrast to glycerate-2- phosphate, PEP has rather a higher phosphoryl group transfer potential since it contains an enol-phosphate group instead of a simple phosphate ester.



Glycerate-2-phosphate Phosphoenolpyruvate (PEP)

Step 10: Synthesis of pyruvate

In the final reaction of glycolysis, pyruvate kinase irreversibly catalyzes the transfer of a phosphoryl group from PEP (with a high transfer potential) to ADP (with a low transfer potential) with an exceptionally large loss of free energy. Two molecules of ATP are formed for each molecule of glucose.



PEP Pyruvate (enol form) Pyruvate (keto form)

Summary of Glycolysis

Step	Reaction	Enzyme	Reaction type	ΔG in kcal mol^{-1} (kJ mol^{-1})
1	Glucose + ATP ⟶ glucose 6-phosphate + ADP + H^+	Hexokinase	Phosphoryl transfer	−8.0 (−33.5)
2	Glucose 6-phosphate ⇌ fructose 6-phosphate	Phosphoglucose isomerase	Isomerization	−0.6 (−2.5)
3	Fructose 6-phosphate + ATP ⟶ fructose 1,6-bisphosphate + ADP + H^+	Phosphofructokinase	Phosphoryl transfer	−5.3 (−22.2)
4	Fructose 1,6-bisphosphate ⇌ dihydroxyacetonephosphate + glyceraldehyde 3-phosphate	Aldolase	Aldol cleavage	−0.3 (−1.3)
5	Dihydroxyacetone phosphate ⇌ glyceraldehyde 3-phosphate	Triose phosphate isomerase	Isomerization	+0.6 (+2.5)
6	Glyceraldehyde 3-phosphate + P_i + NAD^+ ⇌ 1,3-bisphosphoglycerate + NADH + H^+	Glyceraldehyde 3-phosphate dehydrogenase	Phosphorylation coupled to oxidation	+0.6 (+2.5)
7	1,3-Bisphosphoglycerate + ADP ⇌ 3-phosphoglycerate + ATP	Phosphoglycerate kinase	Phosphoryl transfer	+0.3 (+1.3)
8	3-Phosphoglycerate ⇌ 2-phosphoglycerate	Phosphoglycerate mutase	Phosphoryl shift	+0.2 (+0.8)
9	2-Phosphoglycerate ⇌ phosphoenolpyruvate + H_2O	Enolase	Dehydration	−0.8 (−3.3)
10	Phosphoenolpyruvate + ADP + H^+ ⟶ pyruvate + ATP	Pyruvate kinase	Phosphoryl transfer	−4.0 (−16.7)

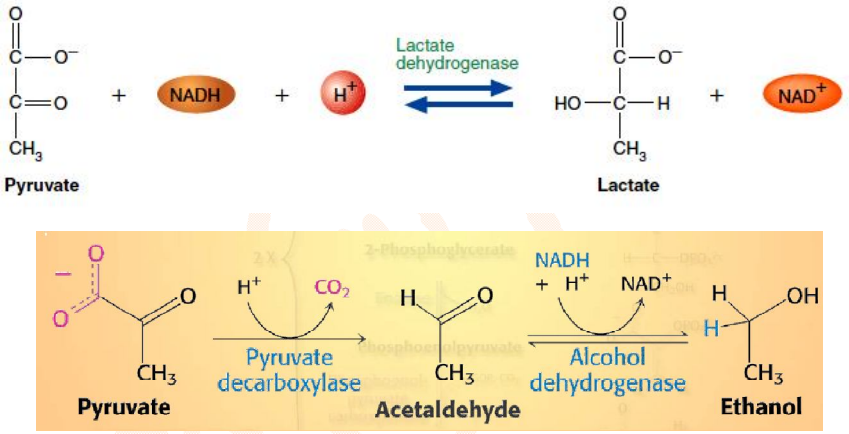
The glycolysis is characterized by negative free energy change (ΔG^0). The overall free energy for glycolysis is ΔG^0 = -17.3 kcal/mole

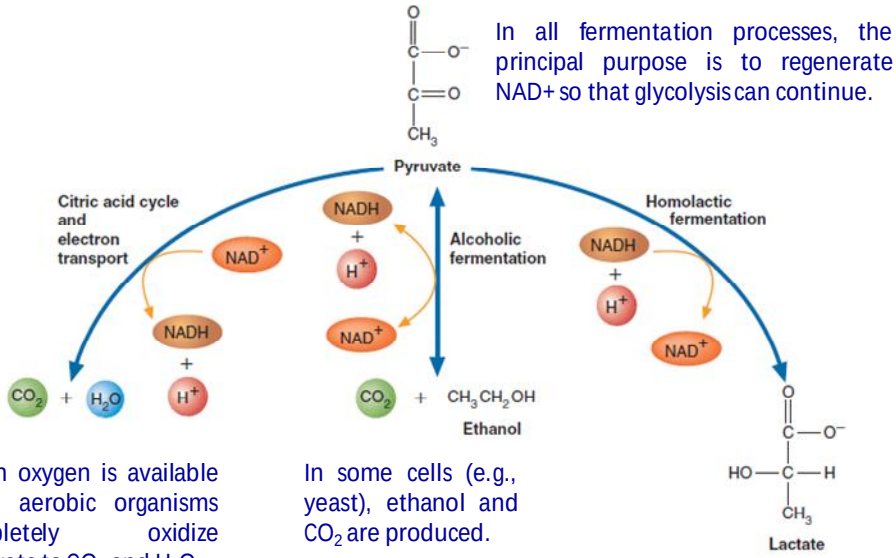
A concern about glycolysis

- Catalytic amount of NAD+ are present in the cell. To carry on glycolysis to generate ATP, reoxidation of NADH + H^+ that is formed in glycolysis, are essential.

Way out?

Both the formation of lactate and the fermentation process to generate ethanol from of pyruvate are associated with production of NAD^+. So, its catalytic concentration in cell is mitigated by these two process.





In all fermentation processes, the principal purpose is to regenerate NAD+ so that glycolysis can continue.

When oxygen is available (left), aerobic organisms completely oxidize pyruvate to CO_2 and H_2O.

In some cells (e.g., yeast), ethanol and CO_2 are produced.

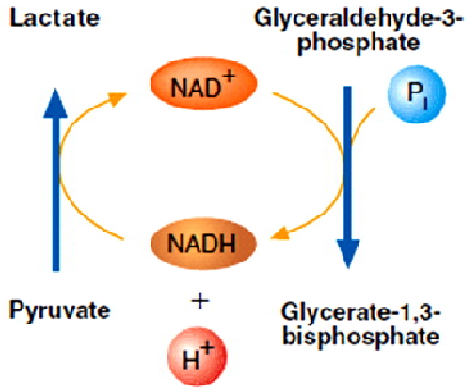
In others (e.g., muscle cells), homolactic fermentation occurs in which lactate is the only organic product.

The Fates of Pyruvate

- Glycolysis results in the production of an energy-rich molecule pyruvate, two ATPs and two NADHs from per molecule of glucose.
- Under aerobic conditions, most cells in the body convert pyruvate into acetyl-CoA, the entry-level substrate for the citric acid cycle, an amphibolic pathway that completely oxidizes the two acetyl carbons to form CO_2 and the transfer electrons from NADH and FADH2 to O_2 to form water. The energy that is released during electron transport is coupled to a mechanism that synthesizes ATP.
- Under anaerobic conditions, further oxidation of pyruvate is impeded.

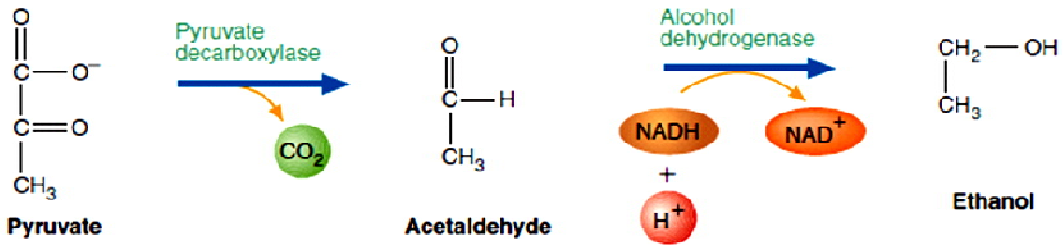
Recycling of NADH during Anaerobic Glycolysis

The NADH produced during the conversion of glyceraldehyde-3-phosphate to glycerate-1,3-bisphosphate is oxidized when pyruvate is converted to lactate. This process allows the cell to continue producing ATP under anaerobic conditions as long as glucose is available.

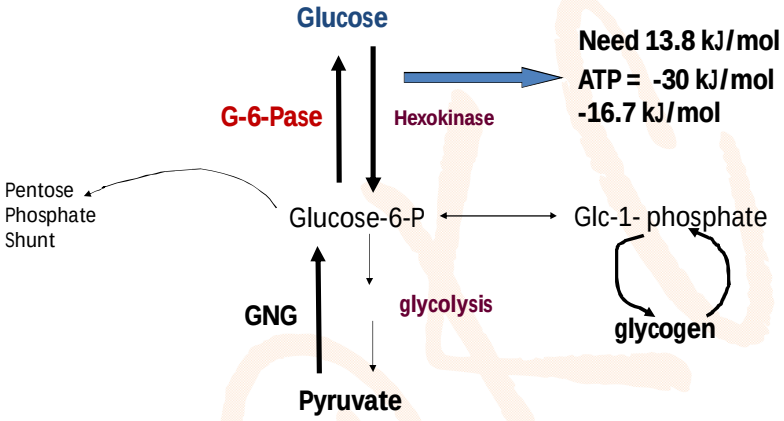


Decarboxylation of pyruvate to ethanol

In yeast and certain bacterial species, pyruvate is decarboxylated to form acetaldehyde, which is then reduced by NADH to form ethanol.



Fasted State



Some common facts of glycolysis

- Glycolysis is the only pathway that produces ATP in absence of O_2.
- The best known inhibitors of the glycolytic pathway include:

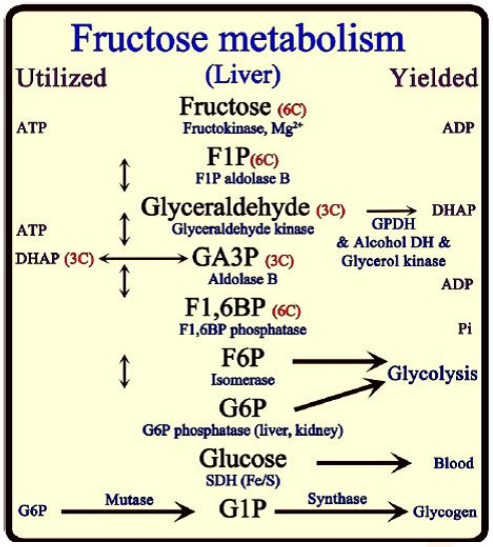
  i) 2-Deoxyglucose: causes inhibition of hexokinase.

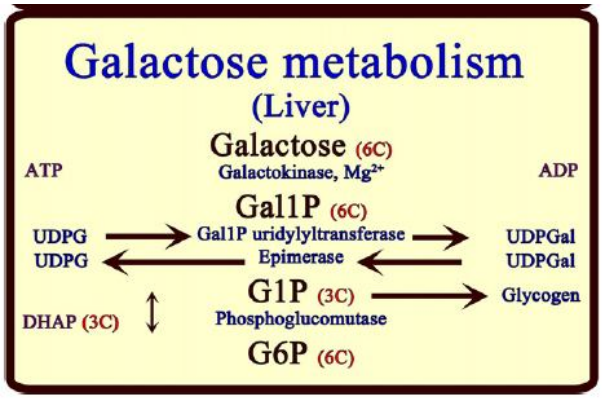
  ii) Sulfhydryl reagents (e.g. Hg-compounds and alkylating agents as iodoacetate); inhibit glyceraldehydes-3-phosphate dehydrogenase which has cysteine residue in the active site.

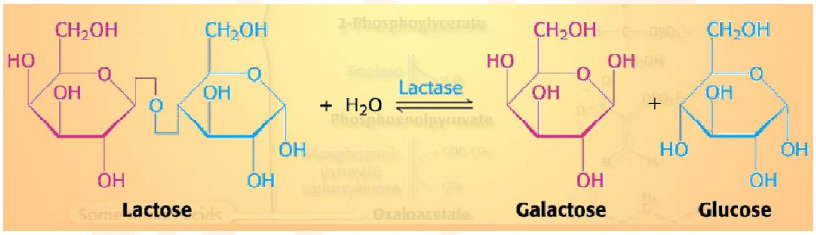
  iii) Fluoride: a potent inhibitor of enolase. Thus, fluoride is usually added to blood samples to inhibit glycolysis before estimation of blood glucose.
- Magnesium: required for kinase reactions by forming Mg-ATP complex.
- Accumulation of lactate is responsible for muscle fatigue and cramps observed under heavy exercise (anaerobic glycolysis).
- In RBCs, glycolysis is the major source of ATP since RBCs lack mitochondrial oxidation.

Metabolism of other carbohydrates

Carbohydrates such as fructose galactose, lactose are metabolized to pyruvate via glucose metabolism pathway.





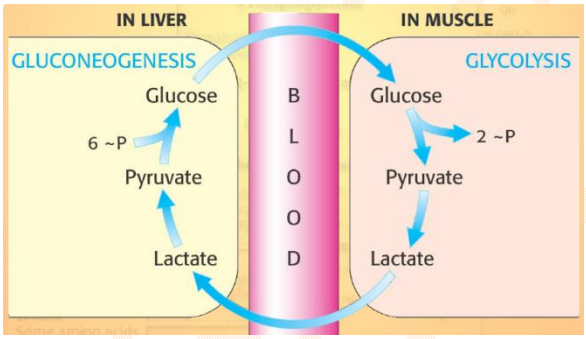


Gluconeogenesis

Gluconeogenesis is the synthesis of new glucose molecules from noncarbohydrate precursors e.g. pyruvate, lactate, glycerol and amino acids etc. in the liver. It occurs when blood sugar levels are low and liver glycogen is depleted (owing to prolonged fasting or vigorous exercise). The brain has a strong preference for glucose and the red blood cells have absolute requirement for glucose as energy source. The brain requires 120 g of glucose/day. The liver stores about 190 g of glucose as glycogen. Gluconeogenesis is not exactly the reverse of glycolysis; but the 7 out of 10 reaction sequences in gluconeogenesis are reverse of glycolysis. The $\Delta G°$ for this reaction is +20 kcal/mol. The use of phosphatase reverses the hexokinase and phosphofructokinase reactions and turns the above reaction $\Delta G°$ negative.

$$2\ \text{Pyruvate} + 2\ \text{ATP} + 2\ \text{NADH} + 2\ H^+ + 2\ H2O \rightarrow \text{Glucose} + 2\ \text{ADP} + 2\ \text{Pi} + 2\ NAD^+$$

The major substrates for gluconeogenesis are lactate (formed in muscle and red blood cells), certain amino acids (derived from muscle) and glycerol (produced from the degradation of triacylglycerols). Glycolysis occurs in cytoplasm but gluconeogenesis occurs within the mitochondria.



Link reaction between Glycolysis and Krebs cycle

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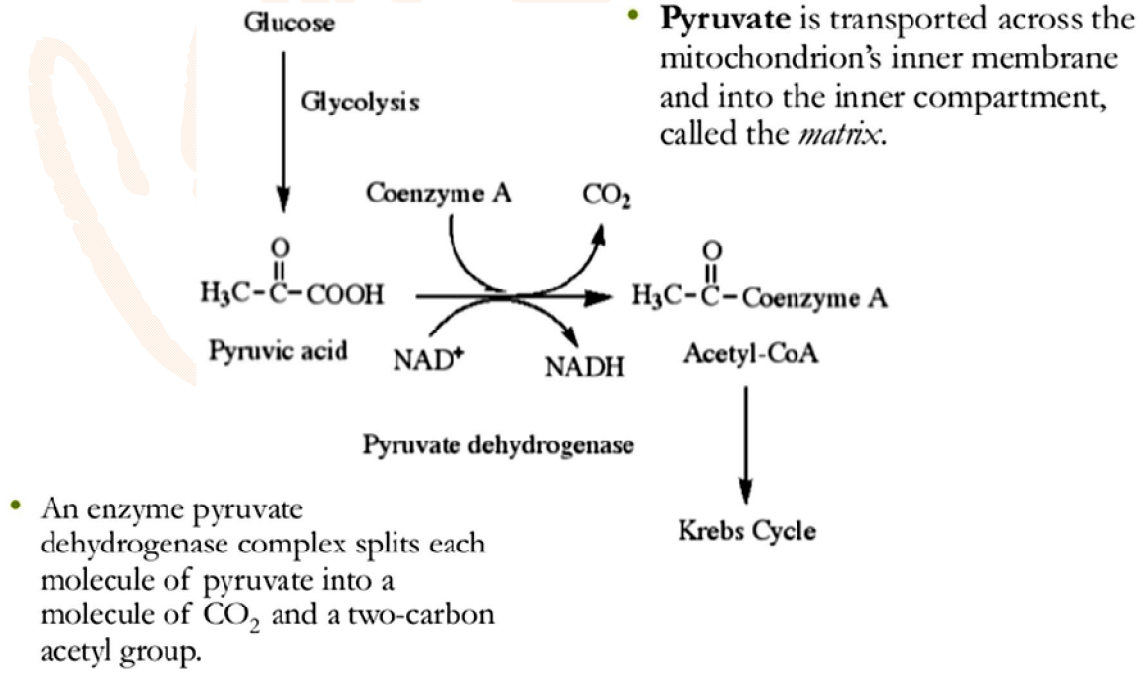
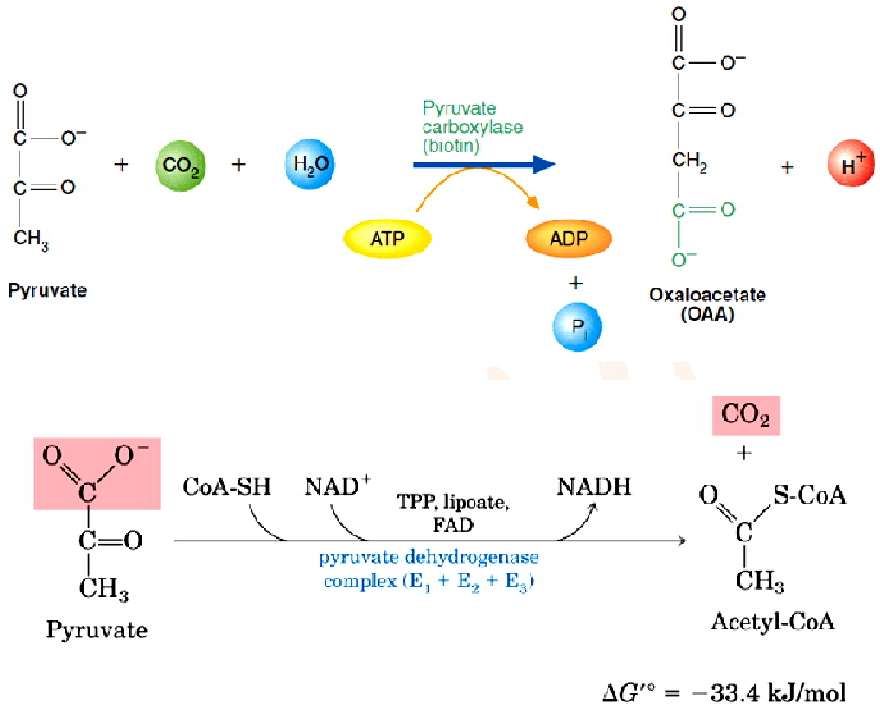
Conversion of Pyruvate to Acetyl CoA



Step 1: Pyruvate to Oxaloacetate and Acetyl-CoA

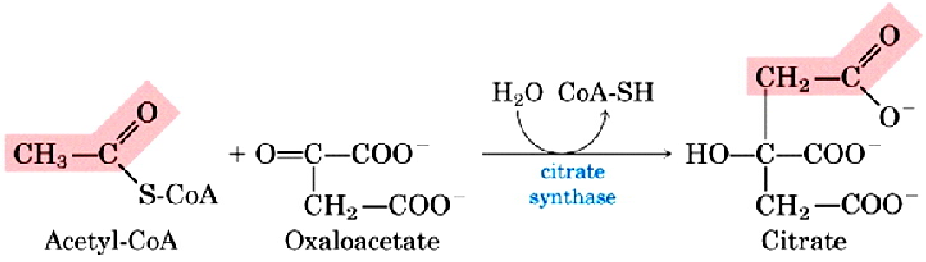


$\Delta G'^{\circ} = -33.4$ kJ/mol

Reactions of Krebs cycle (citric acid or tricarboxylic acid (TCA) cycle)

Reaction 1: Formation of Citroyl CoA intermediate

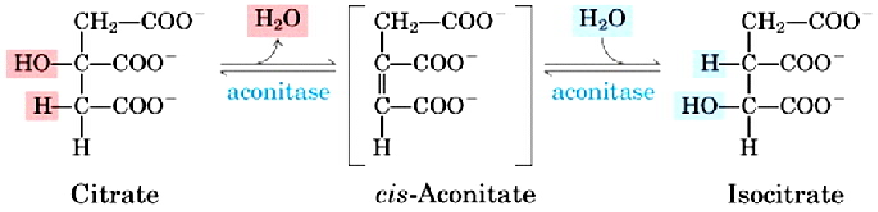
Binding of oxaloacetate to the Citrate synthase enzyme results in conformational change which facilitates the binding of the next substrate, the acetyl Coenzyme A. There is a further conformational change which leads to formation of products. This mechanism of reaction is referred as induced fit model.



$\Delta G'^{\circ} = -32.2$ kJ/mol

Reaction 2: Formation of isocitrate from citrate

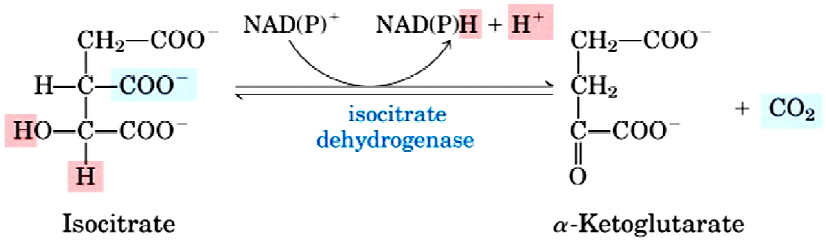
Aconitase enzyme catalyses the isomerization reaction by removing and then adding back the water (H and OH) to cis-aconitate in at different positions. Isocitrate is consumed rapidly by the next step thus deriving the reaction in forward direction.



$\Delta G'^{\circ} = 13.3$ kJ/mol

Reaction 3: Formation of α–ketoglutarate from Isocitrate

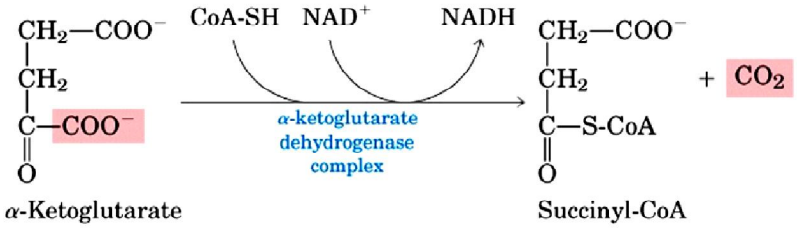
Isocitrate dehydrogenase has two isoforms, one uses NAD+ and other uses NADP+ as electron acceptor. It converts isocitrate to α–ketoglutarate.



$\Delta G'^{\circ} = -20.9$ kJ/mol

Reaction 4: Formation of succinyl-CoA from α–ketoglutarate

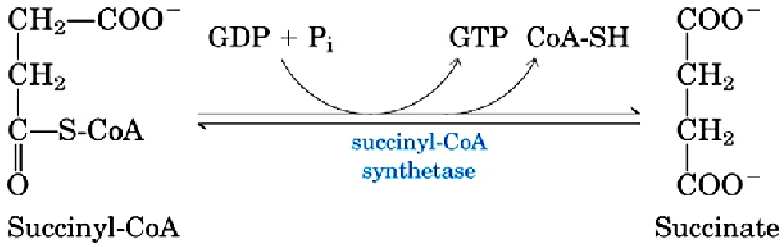
The α-Ketoglutarate dehydrogenase selectively introduces CoA-SH group to a-Ketoglutarate to form succinyl-CoA in which NAD+ is an electron acceptor.



$\Delta G'^{\circ} = -33.5$ kJ/mol

Reaction 5: Formation of succinate from succinyl-CoA

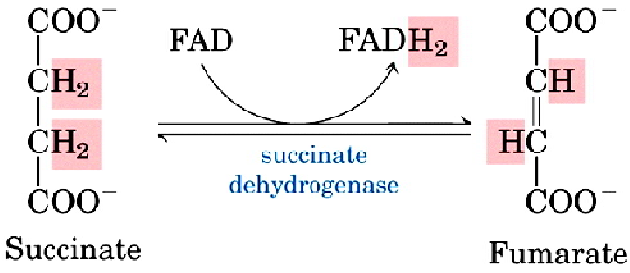
Succinyl CoA synthatse: Sccinyl CoA, like Acetyl CoA has a thioester bond with very negative free energy of hydrolysis. In this reaction, the hydrolysis of the thioester bond leads to the formation of phosphoester bond with inorganic phosphate. This phosphate is transferred to Histidine residue of the enzyme and this high energy, unstable phosphate is finally transferred to GDP resulting in the generation of GTP.



$\Delta G'^{\circ} = -2.9$ kJ/mol

Reaction 6: Formation of fumarate from succinate

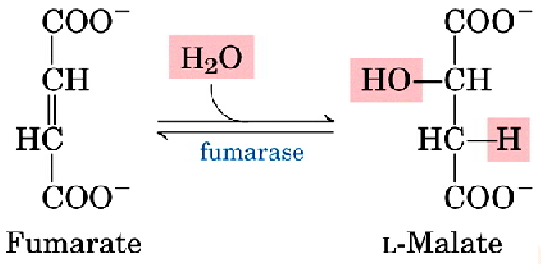
Succinate Dehydrogenasecarries out oxidation of succinate to fumarate. This is the only citric acid cycle enzyme that is tightly bound to the inner mitochondrial membrane. It is an FAD dependent enzyme. Malonate has similar structure to Succinate, and it competitively inhibits SDH.



$\Delta G'^{\circ} = 0$ kJ/mol

Reaction 7: Formation of malate from fumarate

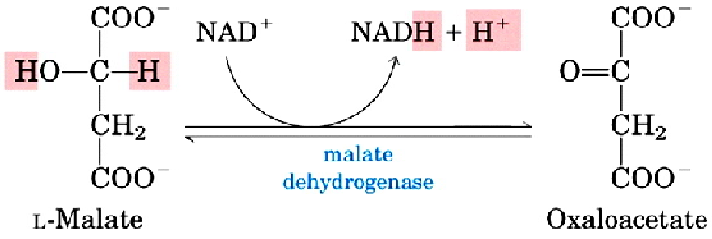
Fumarase initiates hydration of fumarate to malate: It is a highly stereospecific enzyme. Cis-Maleate (the cis form of fumarate is not recognized by this enzyme.



$\Delta G'^{\circ} = -3.8$ kJ/mol

Reaction 8: Formation of oxaloacetate from L-malate

L-Malate dehydrogenase oxidizes alate to oxaloacetate: It is an NAD+dependent enzyme. Reaction is pulled in forward direction by the next reaction (citrate synthase reaction) as the oxaloacetate is depleted at a very fast rate.



$\Delta G'^{\circ} = 29.7$ kJ/mol

Regulation of glycolysis

Allosteric regulation

The rate of glycolytic pathway in cell is controlled by kinetic properties of its hexokinase isoenzymes and the allosteric regulation by the three key enzymes: hexokinase, Phosphofructokinase-1 (PFK-1) and pyruvate kinase.

- **Kinetic regulation of hexokinases isoenzymes**

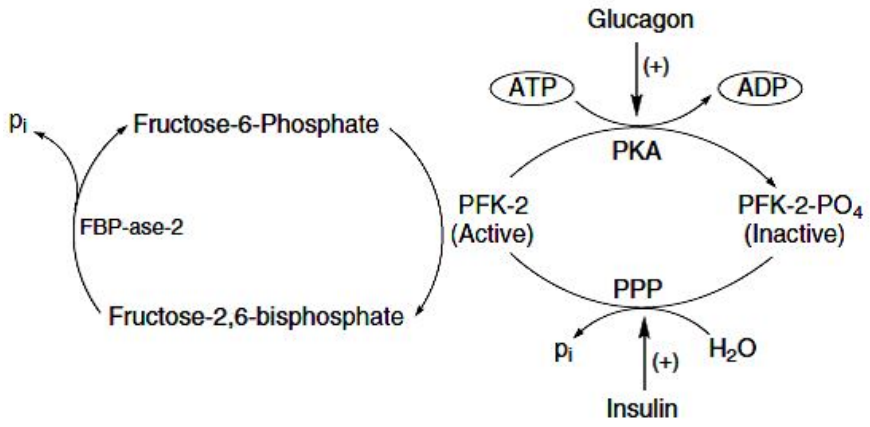
The four hexokinases (I-IV) of liver have high affinity to glucose and can bind reversibly to outer membrane of mitochondria where ATP is readily available for conversion of glucose to glucose-6-phosphate. Incidentally, glucose-6-phosphate inhibits hexokinase (I-III). So, when blood glucose levels are high, cells do not phosphorylate more glucose molecules. As a result, the glycolysis process becomes slowed down for diabetic patients.

The fourth enzyme, called hexokinase IV or glucokinase(GK) is not inhibited by glucose-6-phosphate. GK is glucose sensor.GK converts glucose to glycogen in liver to mitigate the high blood glucose. GK initiates the release of insulin (the hormone that promotes the uptake of glucose into muscle and adipose tissue cells) by pancreatic β-cells in response to rising blood levels of glucose.

- **Allosteric regulation of glycolysis**

Allosteric effectors are the molecules that regulates the glycolysis; for instances, a) glucose-6-phosphate that inhibits hexokinase (I-III) b) AMP that activates pyruvate kinase, c) High ATP concentration inhibits pyruvate kinase d) acetyl Co-A inhibits pyruvate kinase.
Among the three key enzymes, PFK-1 is mostly regulated. PFK-1 is inhibited by high concentration of ATP and citrate while AMP and fructose-2,6-bisphosphate are the allosteric activator of PFK-1 in liver.

Fructose-2,6-bisphosphate is synthesized by phosphofructokinase-2 (PFK-2). At high blood glucose level, fructose-2,6-bisphosphate increases the activity of PFK-1 and hence activates glycolysis. PFK-2 is, in turn, activated by a dephosphorylation reaction catalyzed by phosphoprotein phosphatase (PPP), an enzyme activated by insulin. Glycolysis is inhibited when fructose-2-6-bisphosphate levels are low, which is the result of a glucagon-stimulated and protein kinase A (PKA)-catalyzed phosphorylation reaction that inactivates PFK-2. In liver, glucagon also inactivates pyruvate kinase.



Enzyme	Activator	Inhibitor
Hexokinase		Glucose-6-phosphate, ATP
PFK-1	Fructose-2,6-bisphosphate, AMP	Citrate, ATP
Pyruvate kinase	Fructose-1,6-bisphosphate, AMP	Acetyl-CoA, ATP

Hormone regulation

Glycolysis is further regulated by the peptide hormones glucagon and insulin.

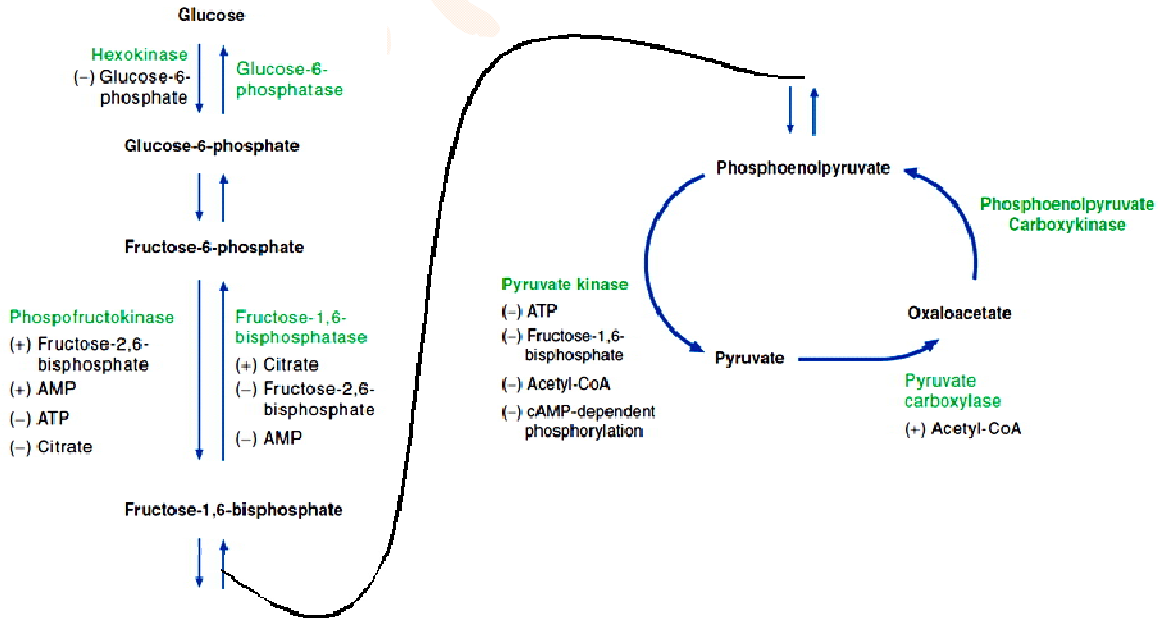
When blood glucose is low, glucagon is released by pancreatic α-cells and it activates the phosphatase function of PFK-2 by reducing the level of fructose-2,6-bisphosphate in the cell. As a result, PFK-1 activity and glycolysis are decreased. Phosphofructokinase-1 (PFK-1)

irreversibly catalyzes the phosphorylation of fructose-6-phosphate to form fructose-1,6-bisphosphate. In liver, glucagon also inactivates pyruvate kinase.

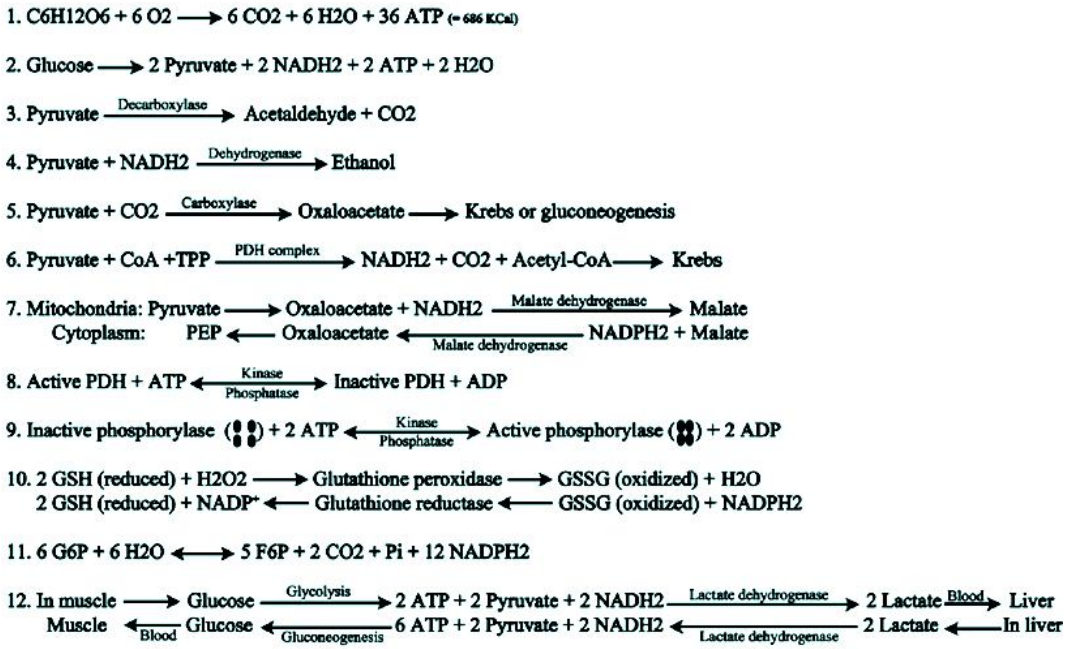
When blood glucose levels are high, insulin, a peptide hormone, is released from pancreatic β-cells. The effects of insulin on glycolysis include activation of the kinase function of PFK-2, which increases fructose-2,6-bisphosphate level in the cell, therby accelerating glycolytic flux.

In cells containing insulin-sensitive glucose transporters (muscle and adipose tissue but not liver or brain) insulin promotes the translocation of glucose transporters to the cell surface. When insulin binds to its cell-surface receptor, the receptor protein undergoes several autophosphorylation reactions, which trigger numerous intracellular signal cascades that involve phosphorylation and dephosphorylation of target enzymes and transcription factors.

Illustration of Allosteric Regulation of Glycolysis and Gluconeogenesis: Allosteric effectors: Activator +; inhibitor-.



Summary of biochemical reactions in carbohydrate metabolism



Pathway	VR	Place	Substrate	Product	Utilized	Yielded
Glycolysis (aerobic)	C	Cyt	1 Glucose	2 Pyruvate	Mg^{2+}	2 ATP, 2 NADH2
Glycolysis (anaerobic)	C	Cyt	1 Glucose	2 Lactic acid	Mg^{2+}	2 ATP
PDH reaction (aerobic)	C	Mit	2 Pyruvate	2 Acetyl-CoA	Lipoic acid, 2 CoA	2 NADH2
Krebs cycle (aerobic)	C	Mit	2 Acetyl-CoA, 2 OAA	2 Citrate	4 H_2O, Fe^{2+}, Mg^{2+}, Mn^{2+}, Fe/S	6 NADH2, 4 CO_2, 2 GTP, 2 FADH2, 2 CoA
Electron transport chain	C	Mit	1 NADH2 & 1 FADH2	3 ATP & 2 ATP	Oxygen	H_2O
Glycogenesis	A	Cyt	Glucose	Glycogen	2 ATP, Mg^{2+}	
Glycogenolysis	C	Cyt	Glycogen	G6P, glucose, F6P		
Gluconeogenesis	A	Both	2 Pyruvate (or 2 lactate)	G6P, glucose, F6P	2 HCO_3^-, 4 NADH2, 4 ATP, 2 GTP, 2 H_2O	2 NADPH2, 2 CO_2, 6 Pi
Fructose metabolism	A	Cyt	Fructose	G6P, glycogen	2ATP	Pi
Galactose metabolism	A	Cyt	Galactose	G6P, lactose	1 ATP, UDPG	
Pentose phosphate	A	Cyt	G6P	F6P, GA3P, 4C-P, 5C-P, 7C-P	1 H_2O, TPP	2 NADPH2, 1 CO_2, 1 H^+

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