Metabolism of Carbohydrate

Digestion of dietary carbohydrate

The principal sites of dietary carbohydrate digestion are the **mouth** and **intestinal lumen**. This digestion is rapid and is catalyzed by enzymes known as **glycosidases** that hydrolyze glycosidic bonds. Because there is little monosaccharide present in diets of mixed animal and plant origin, the enzymes are primarily endoglycosidases that hydrolyze polysaccharides and oligo and disaccharidases that hydrolyse tri- and disaccharides into their reducing sugar components (Figure 1). The final products of carbohydrate digestion are the **monosaccharides**, **glucose**, **galactose** and **fructose**, which are absorbed by cells of the small intestine.

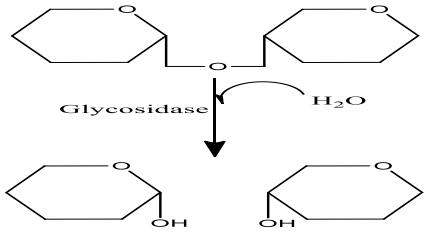


Figure 1: Hydrolysis of glycosidic bond

A. Digestion of carbohydrates begins in the mouth

The major dietary polysaccharides are of plant (starch, composed of amylose and amylopectin) and animal (glycogen) origin. During mastication, salivary α-amylase acts briefly on dietary starch and glycogen, hydrolyzing random α(1→4) bonds. Because branched amylopectin and glycogen also contain α(1→6) bonds, which α-amylase cannot hydrolyze, the digest resulting from its action contains a mixture of short, branched and unbranched oligosaccharides called dextrins (Figure 2).

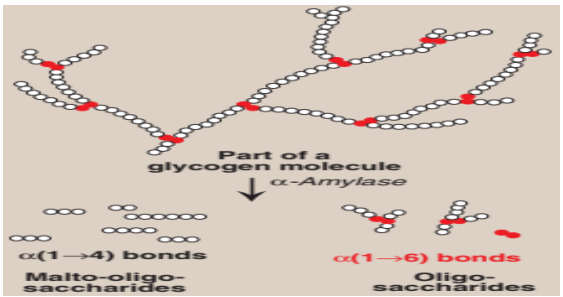


Figure 2: Degradation of dietary glycogen by salivary or pancreatic *α-amylase*

B. Further digestion of carbohydrates by pancreatic enzymes occurs in the small intestine

When the acidic stomach contents reach the small intestine, they are neutralized by bicarbonate secreted by the pancreas, and pancreatic α-amylase continues the process of starch digestion.

C. Final carbohydrate digestion by enzymes synthesized by the intestinal mucosal cells

The final digestive processes occur primarily at the mucosal lining of the upper jejunum, and include the action of several disaccharidases (Figure 3). For example, isomaltase cleaves the α(1→6) bond in isomaltose and maltase cleaves maltose and maltotriose, each producing glucose, sucrase cleaves sucrose producing glucose and fructose, and lactase (β-galactosidase) cleaves lactose producing galactose and glucose.

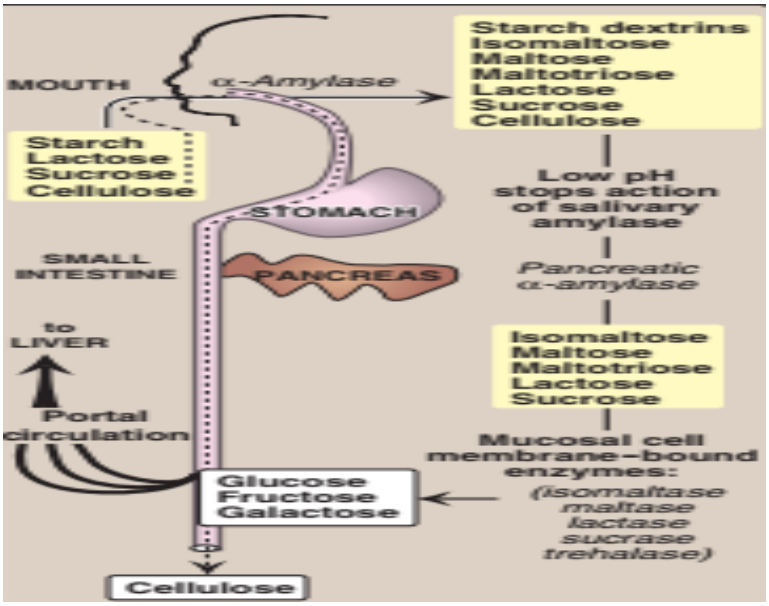


Figure 3: Digestion of carbohydrates

D. Absorption of monosaccharides by intestinal mucosal cells

The duodenum and upper jejunum absorb the bulk of the dietary sugars. However, different sugars have different mechanisms of absorption.

Glycolysis

In this part, individual enzymic reactions were analyzed in an effort to explain the mechanisms of catalysis. However, in cells, these reactions rarely occur in isolation, but rather are organized into multistep sequences called pathways, such as that of glycolysis. In a pathway, the product of one reaction serves as the substrate of the subsequent reaction. Different pathways can also intersect, forming an integrated and purposeful network of chemical reactions. These are collectively called metabolism, which is the sum of all the chemical changes occurring in a cell, a tissue, or the body. Most pathways can be classified as either catabolic (degradative) or anabolic (synthetic). Catabolic reactions break down complex molecules, such as proteins, polysaccharides, and lipids, to a few simple molecules, for example, CO_2, NH_3 (ammonia), and water. Anabolic pathways form complex end products from simple precursors, for example, the synthesis of the polysaccharide, glycogen, from glucose.

In glycolysis (from the Greek glykys, meaning "sweet," and lysis, meaning "splitting"), a molecule of glucose is degraded in a series of enzymecatalyzed reactions to yield two molecules of the three-carbon compound pyruvate. During the sequential reactions of glycolysis, some of the free energy released from glucose is conserved in the form of ATP and NADH. Glycolysis was the first metabolic pathway to be elucidated and is probably the best understood. From Eduard Buchner's discovery in 1897 of fermentation in broken extracts of yeast cells until the elucidation of the whole pathway in yeast.

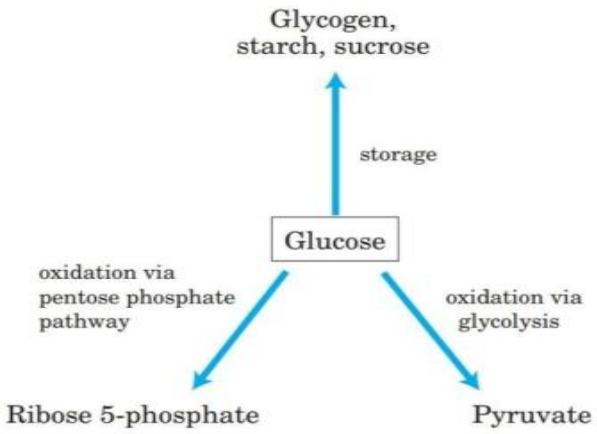


Fig. 4: Major pathways of glucose utilization

Glycolysis Has Two Phases

The breakdown of the six-carbon glucose into two molecules of the three- carbon pyruvate occurs in ten steps, the first five of which constitute the **preparatory phase** (Figure 5).

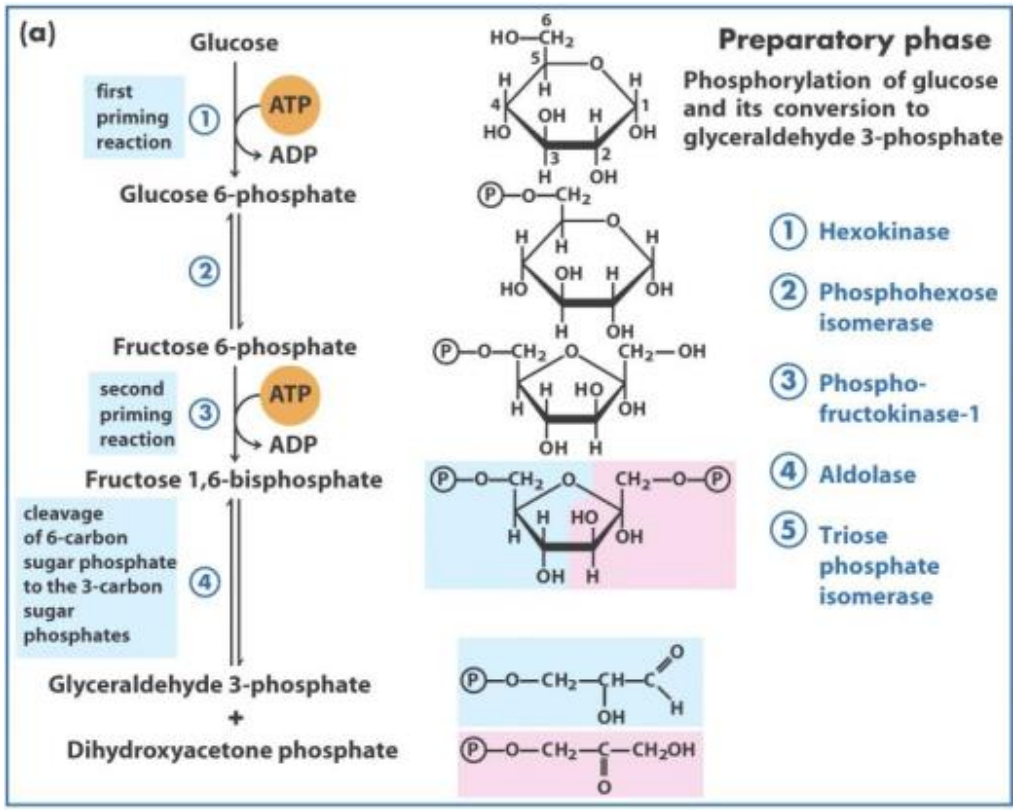


Figure 5: Preparatory phase of glycolysis

In these reactions, glucose is first phosphorylated at the hydroxyl group on C-6 (**step 1**), the D-glucose-6-phosphate thus formed is converted to D-fructose-6- phosphate (**step 2**), which is again phosphorylated, this time at C-1, to yield D-fructose-1,6-bisphosphate **(step 3**), Fructose 1,6-bisphosphate is split to yield two three-carbon molecules, dihydroxyacetone phosphate and glyceraldehyde 3-phosphate (**step 4**); this is the "**lysis**" step that gives the pathway its name.

The dihydroxyacetone phosphate is isomerized to a second molecule of glyceraldehyde 3-phosphate (**step 5**).

The energy gain comes in the **payoff phase** of glycolysis (Figure 6).

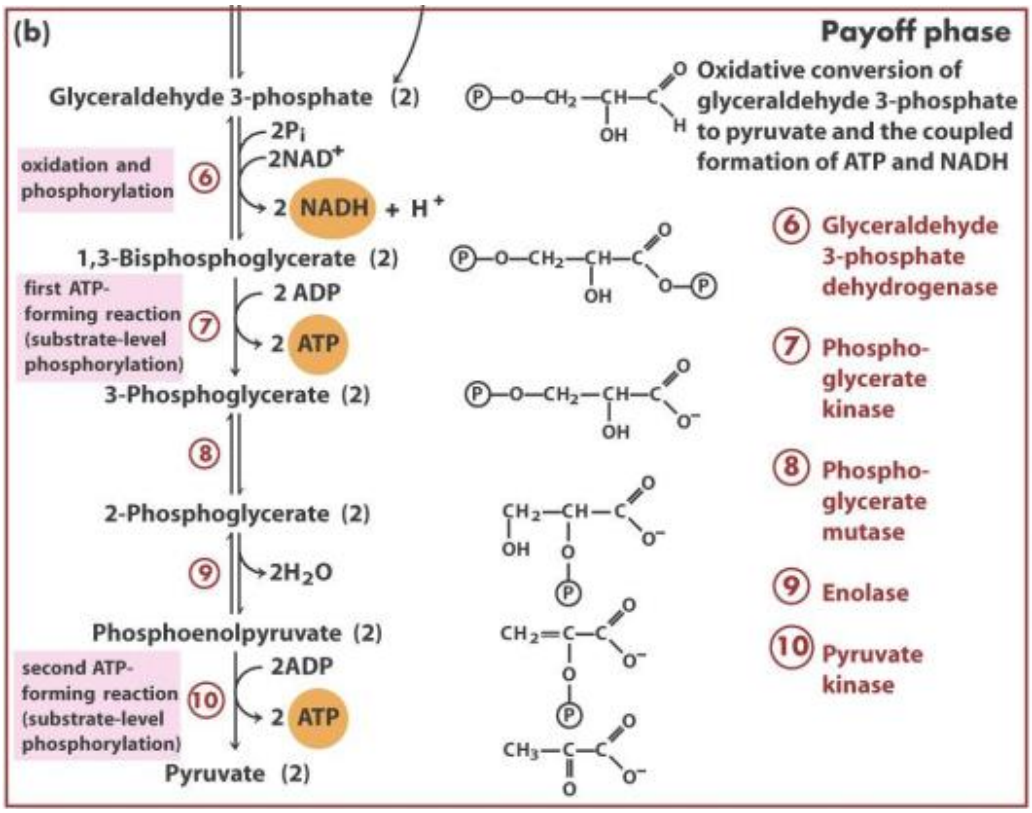


Figure 6: Payoff phase of glycolysis

Each molecule of glyceraldehyde 3-phosphate is oxidized and phosphorylated by inorganic phosphate (not by ATP) to form 1,3-bisphosphoglycerate (**step 6**), then energy is released as the two molecules of 1,3-bisphosphoglycerate are converted to two molecules of pyruvate (**steps 7 to 10**).

In the sequential reactions of glycolysis, three types of chemical transformations are particularly noteworthy:

(1) Degradation of the carbon skeleton of glucose to yield pyruvate.

(2) Phosphorylation of ADP to ATP by high-energy phosphate compounds formed during glycolysis.

(3) Transfer of a hydride ion to NAD, forming NADH.

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 (figure 7).

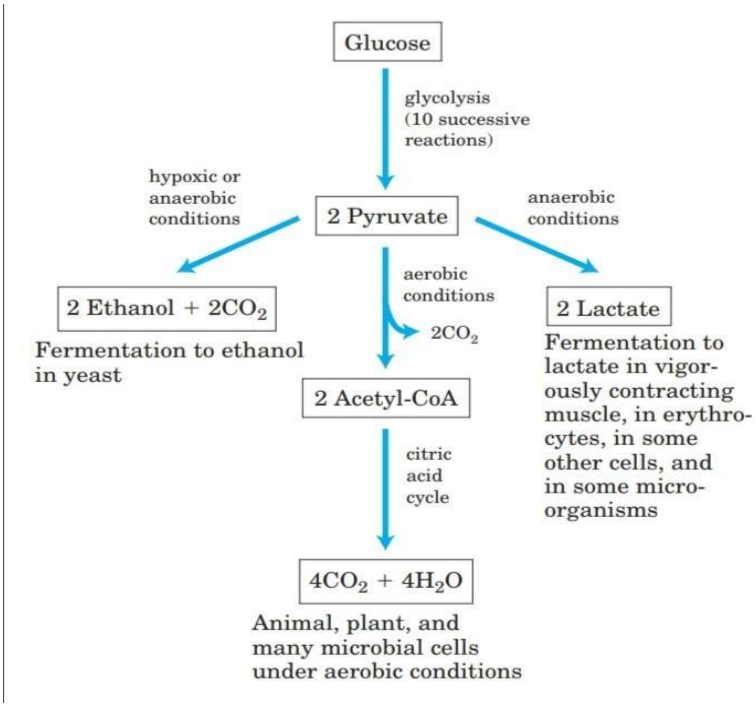
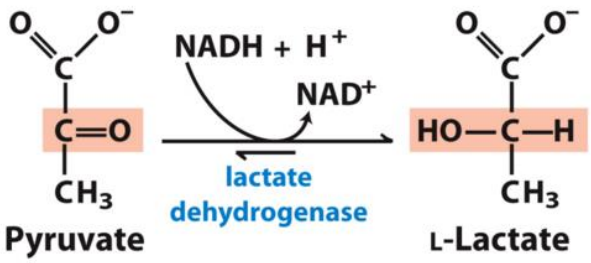
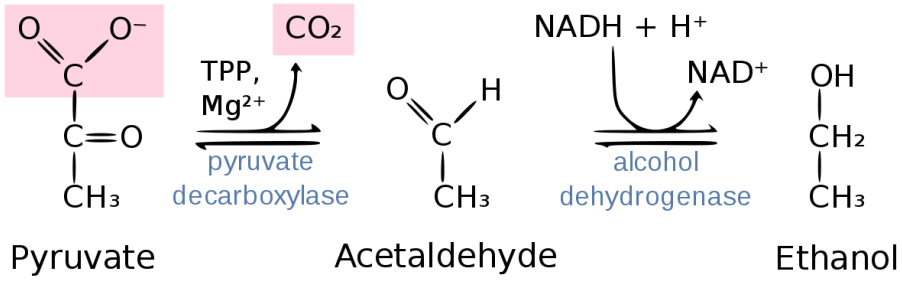


Figure 7: Three possible catabolic fates of the pyruvate formed in glycolysis

In anaerobic organisms : The first route for pyruvate is its reduction to **lactate via lactic acid** fermentation. When vigorously contracting skeletal muscle must function under lowoxygen conditions (**hypoxia**), NADH cannot be reoxidized to NAD, but NAD is required as an electron acceptor for the further oxidation of pyruvate. Under these conditions pyruvate is reduced to lactate, accepting electrons from NADH and thereby regenerating the NAD necessary for glycolysis to continue.



The second major route of pyruvate catabolism under anaerobic condition is **fermentation** leads to ethanol.



In some plant tissues and in certain invertebrates, protests, and microorganisms such as brewer's yeast, pyruvate is converted under hypoxic or anaerobic conditions into ethanol and CO_2, a process called **ethanol (alcohol) fermentation** (Fig. 7).

In aerobic organisms or tissues, under aerobic conditions, glycolysis is only the first stage in the complete degradation of glucose (Figure 7).

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 the mitochondrion, to form H_2O. The energy from the electron-transfer reactions drives the synthesis of ATP in the mitochondrion**.**

Conversion of pyruvate to acetyl Co-A

In aerobic oxidation, pyruvate molecules are converted to acetyl CoA within the mitochondria to be ready to enter the Krebs cycle (Figure 8).

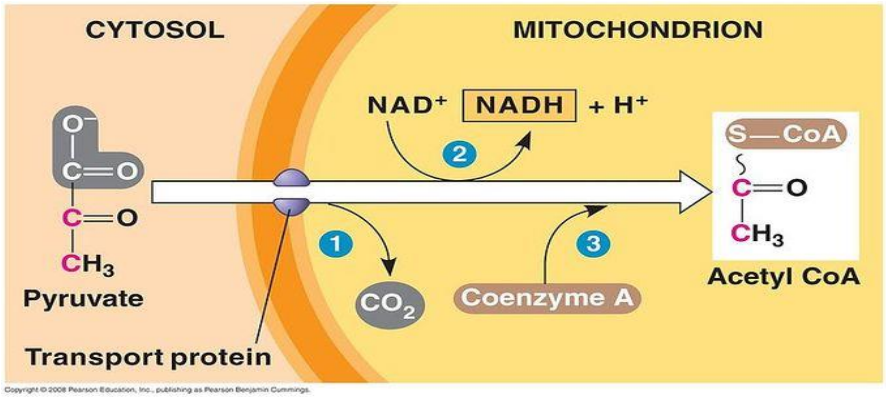


Figure 8: Convert pyruvate molecules to acetyl CoA within the mitochondria

Citric Acid Cycle

The tricarboxylic acid cycle (TCA cycle, also called the Krebs cycle or the citric acid cycle) plays several roles in metabolism. It is the final pathway where the oxidative metabolism of carbohydrates, amino acids, and fatty acids converge, their carbon skeletons being converted to CO2. This oxidation provides energy for the production of the majority of ATP in most animals, including humans (Figure 9). The cycle occurs totally in the mitochondria and is, therefore, in close proximity to the reactions of electron transport, which oxidize the reduced coenzymes produced by the cycle.

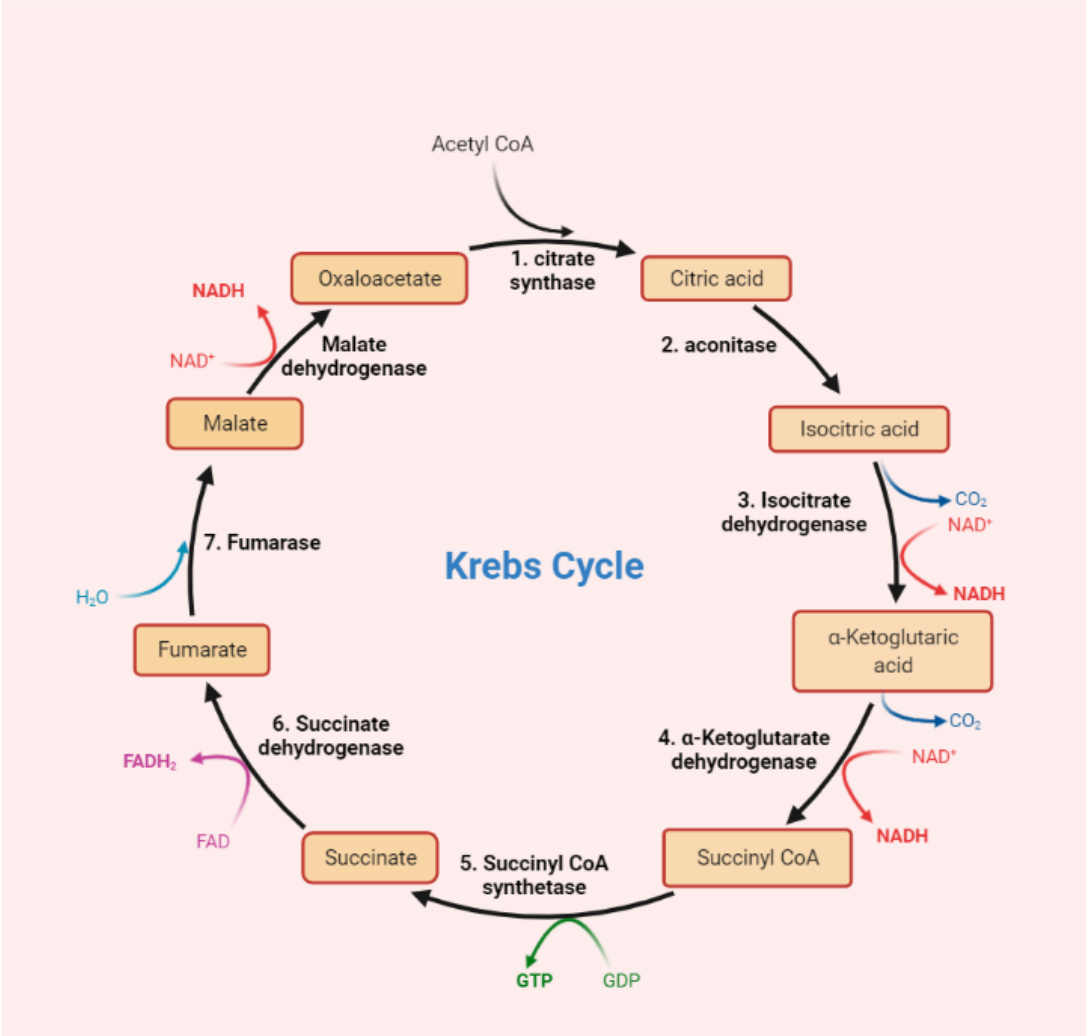


Figure 9: Krebs cycle