BIOENERGETICS & CARBOHYDRATE METABOLISM
LECTURE 1

Third year-biochemistry subject –
laboratory science departments
Alzahraa university – college of pharmacy

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LEARNING OBJECTIVES

1. Understand Bioenergetics and their role in medicine
2. Knowing the main form of energy source
3. Summarize the Stages or Phases of Metabolism
4. Understand the different pathways of carbohydrate metabolism and the benefits of each

BIOENERGETICS

Bioenergetics is the study of the transformation of energy in living organisms. It focuses on how cells convert food into usable energy.

-Importance: Understanding bioenergetics is crucial for fields like medicine, sports science, nutrition, and physiology, as it underpins how energy is produced and utilized in the body.

- **Adenosine Triphosphate (ATP) Molecule containing high-energy Phosphate bonds**

ENERGY SOURCES

Macronutrients:

1. **- Carbohydrates: Primary source of energy, broken down into glucose.**
2. **- Fats: Provide more energy per gram than carbohydrates and are utilized during prolonged low-intensity exercise.**
3. **- Proteins: Generally used for building and repairing tissues, but can be converted to energy during prolonged fasting or intense exercise.**

OVERVIEW ABOUT METABOLISM

Metabolism: The sum of all chemical reactions occurring in a living organism to maintain life.

Types of Metabolic Pathways

A. Catabolic (degradation) pathways, where energy rich complex macromolecules are degraded into smaller molecules. Energy released during this process is trapped as chemical energy, usually as ATP.

B. Anabolic (biosynthesis) pathways. The cells synthesize complex molecules from simple precursors. This needs energy.

Hormone Regulation of Metabolism

1. **Insulin (anabolic hormone)**

2. **Glucagon , cortisol , epinephrine (catabolic hormone)**

A Tale of 2 worlds

Insulin World

Builder

Feeding State

Glucagon World

Destroyer

Fasting State

VS

* Protein Anabolic

a.a. —(Ptn Synthesis / Proteogenesis)→ Protein

* Protein Catabolic

Protein —(Proteolysis)→ a.a. —(Gluconeogenesis; PC, PEPCK, F-1,6 BPase, G6Pase)→ Glucose

* Glycogen Anabolic

Glucose —(Glycogen Synthesis / Glycogenesis; Glycogen Synthase)→ Glycogen

Glucose —(Glycolysis)→ ATP

* Glycogen Catabolic

Glycogen —(Glycogenolysis; Glycogen phosphorylase)→ Glucose

* Fat Anabolic

FFA —(Lipid Synthesis / Lipogenesis; Acetyl CoA Carboxylase)→ TGLs

* Fat Catabolic

TGLs —(Lipolysis; HSL)→ FFA

FFA —(β-oxidation)→ Ketones

STAGES OR PHASES OF METABOLISM

The degradation of foodstuffs occurs in three stages.

1. In the first stage,digestion in the gastrointestinal tract converts the macromolecules into small units. For example, proteins are digested to amino acids. This is called primary metabolism.

2. Then these products are absorbed,catabolized to smaller components, and ultimately oxidized to CO_2

3. The reducing equivalents are mainly generated in the mitochondria by the final common oxidative pathway, citric acid cycle.

In this process, NADH or $FADH_2$ are generated. This is called secondary or intermediary metabolism.

4 .Then these reduced equivalents enter into the electron transport chain (ETC, or Respiratory chain), where energy is released. This is the tertiary metabolism or Internal respiration or cellular respiration

1- CARBOHYDRATE METABOLISM

Various biochemical processes responsible for the formation (Anabolism, synthesis of big molecules like glycogen from glucose)

Breakdown (Catabolism breakdown of carbohydrates into smaller units like glycogen to glucose) and interconversion of carbohydrates in living organisms.

Almost all reactions are catalyzed by enzymes

METABOLISM STARTS WITH

DIGESTION OF CARBOHYDRATES

In the diet carbohydrates are present as complex polysaccharides (starch, glycogen), and to a minor extent, as disaccharides (sucrose and lactose). They are hydrolysed to monosaccharide units in the gastrointestinal tract.

Cooking makes the digestion process easier.

- **This process of digestion starts in mouth by the salivary alpha-amylase. However, the time available for digestion in the mouth is limited, because the gastric hydrochloric acid will inhibit the action of salivary amylase.**
- **In the pancreatic juice another alpha-amylase is available which will hydrolyse the alpha-1,4 glycosidic linkages randomly**
- **The cells of brush border of intestine contain the enzymes, sucrase, maltase, isomaltase and lactase. They hydrolyse the corresponding disaccharides into component monosaccharides which are then absorbed**

ABSORPTION OF CARBOHYDRATES

Only monosaccharides are absorbed by the intestine.

Glucose has specific transporters, which are transmembrane proteins ,they are all insulin independent except GLUT 4'

- **Glucose transporter-4 (GluT4) transports glucose from the extracellular fluid to muscle cells and adipose tissue .its under the influence of insulin.**

- **In diabetes mellitus, insulin deficiency hinders the entry of glucose into the peripheral cells. But GluT2 is the transporter in liver cells; it is not under the control of insulin.**

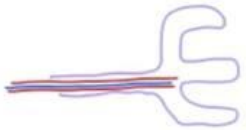
GLUCOSE TRANSPORTERS (GLUTs)

facilitated diffusion

MNEMONICS

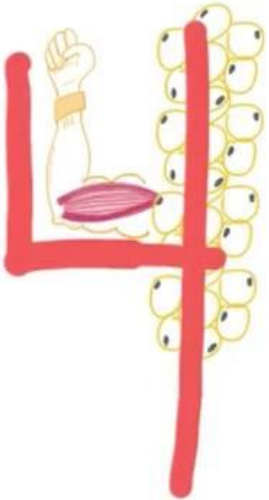
GLUT_1 "Brain, Cornea, RBCs"

GLUT_2 2 kidney "2"ubules, gu2, GI2 tract, Hepa2ocytes, 2 β



GLUT_3 , Brain

GLUT_4 Adipose, Skeletal muscles



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GLUT_5 "Five" Fructose < GI tract

OVERVIEW OF PATHWAYS OF CARBOHYDRATES METABOLISM:

1. **Glycolysis** :- A catabolic pathway that converts glucose into pyruvate, producing ATP and NADH in the process.
2. **Gluconeogenesis**:- An anabolic pathway that synthesizes glucose from non-carbohydrate precursors such as lactate, glycerol, and amino acids.
3. **glycogenesis**:- The synthesis of glycogen from glucose for storage.
4. **glycogenolysis** :- The breakdown of glycogen into glucose-1-phosphate and glucose.
5. **pentose phosphate pathway:-** A parallel pathway to glycolysis that generates NADPH and ribose-5-phosphate from glucose-6-phosphate.

Each metabolic pathway is composed of multi enzyme sequences, and each enzyme,may exhibit important catalytic or regulatory features

The most important carbohydrate is glucose, which can be broken down via glycolysis,

Then enter into the Kreb's cycle and oxidative phosphorylation to generate ATP The chemical energy in the form of adenosine triphosphate

NOTE

- **Pancreas is the main organ involved in carbohydrate digestion**
- **liver is the center of carbohydrate metabolism it is the major regulator of storage and distribution of glucose to the peripheral tissues and, in particular, to glucose-dependent tissues such as the brain and erythrocytes.**

GLYCOLYSIS

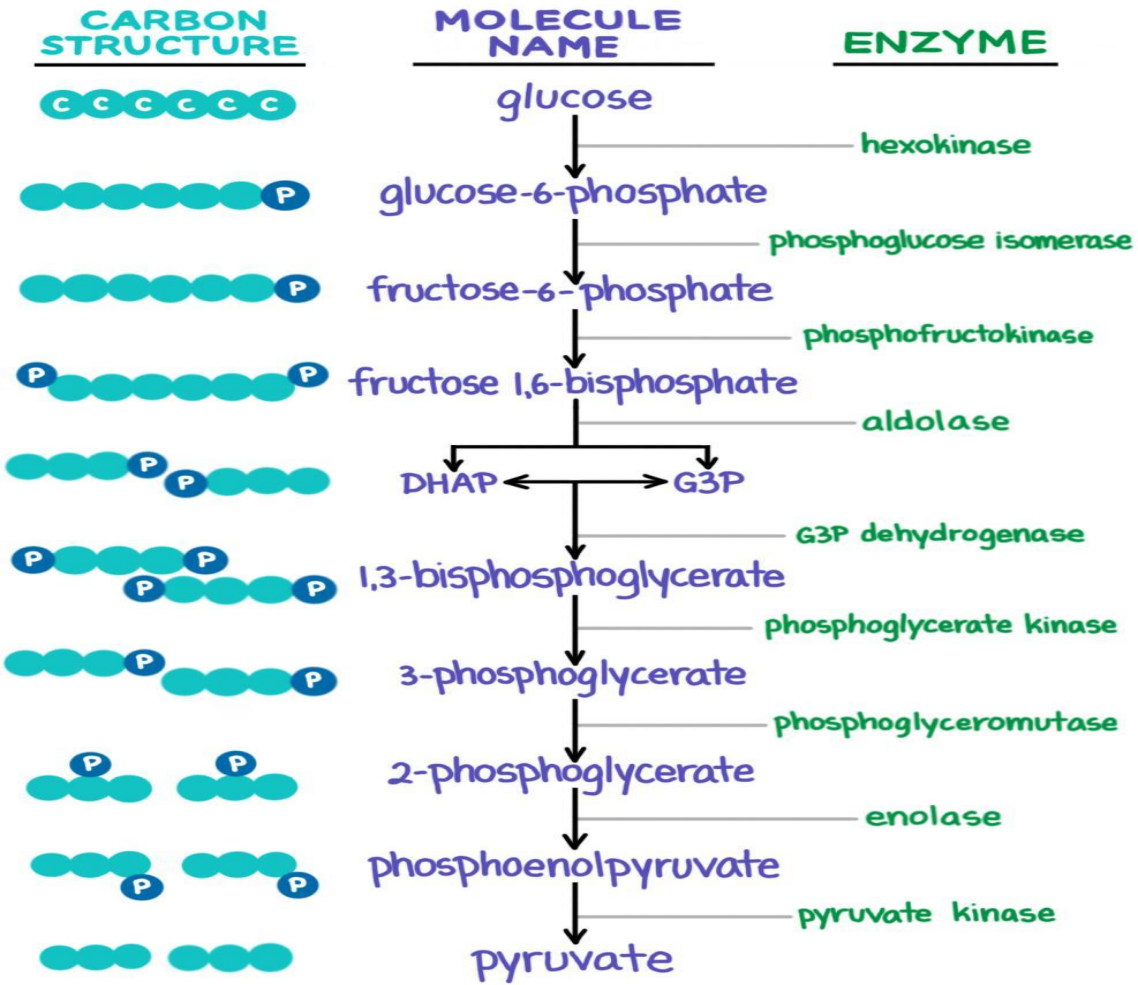
Definition: In the pathway of glycolysis, glucose is split into two 3-carbon pyruvate molecules under aerobic conditions; or lactate under anaerobic conditions, along with production of a small quantity of energy. Glycolysis is derived from the Greek words, glykys = sweet; and lysis = splitting.

steps that are irreversible

1. **Conversion of glucose to glucose 6 phosphate by hexokinase or glucokinase**
2. **Conversion of fructose to fructose 1.6 bisphosphate by phosphofructokinase-1**
3. **Conversion of phosphoenol pyruvate to pyruvate by pyruvate kinase**

Site of reactions: All the reaction steps take place in the cytoplasm.

STEPS OF GLYCOLYSIS

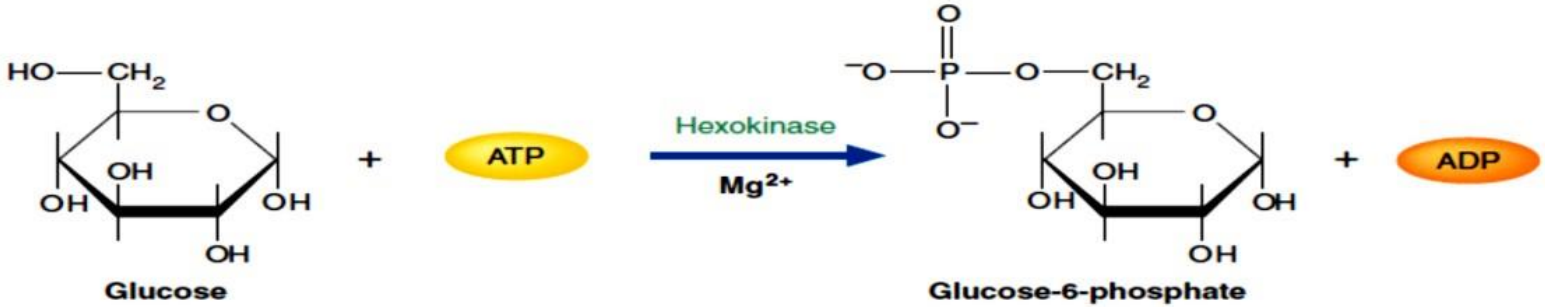


STEPS OF GLYCOLYSIS

Stage 1

A phosphate group is added to glucose in the cell cytoplasm, by the action of enzyme hexokinase.In this, a phosphate group is transferred fromATP to glucose forming glucose,6-phosphate.

Hexokinase is a key glycolytic enzyme. Hexokinase catalyses a regulatory step in glycolysis that is irreversible.



Under physiological conditions, this reaction is irreversible. Hexokinase has a high affinity (low Km) for glucose, and it is saturated under normal conditions

Liver cells contain glucokinase, which has a Km very much higher than the normal intracellular concentration of glucose. The function of glucokinase in the liver is to remove glucose from the hepatic portal blood following a meal, so regulating the concentration of glucose available to peripheral tissues

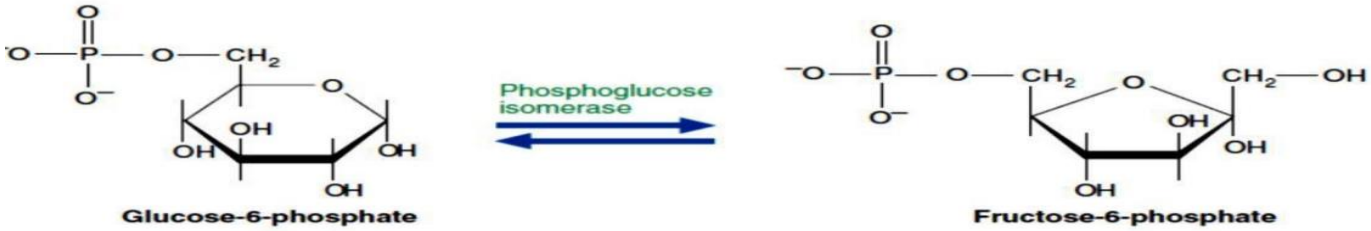
KEY DIFFERENCES BETWEEN HEXOKINASE & GLUCOKINASE

- **Affinity for Glucose (Km):**
  - **Hexokinase** has a low Km meaning it efficiently phosphorylates glucose even at very low concentrations.
  - **Glucokinase** has a high Km allowing it to act as a sensor of glucose concentration, becoming active only when glucose levels are high (e.g., after a meal).

- **Tissue-Specific Roles:**
  - **Hexokinase** ensures essential tissues like the brain and muscles have a constant supply of phosphorylated glucose, even under fasting conditions.
  - **Glucokinase** helps regulate blood glucose levels by promoting glucose uptake and storage in the liver and insulin secretion in the pancreas.

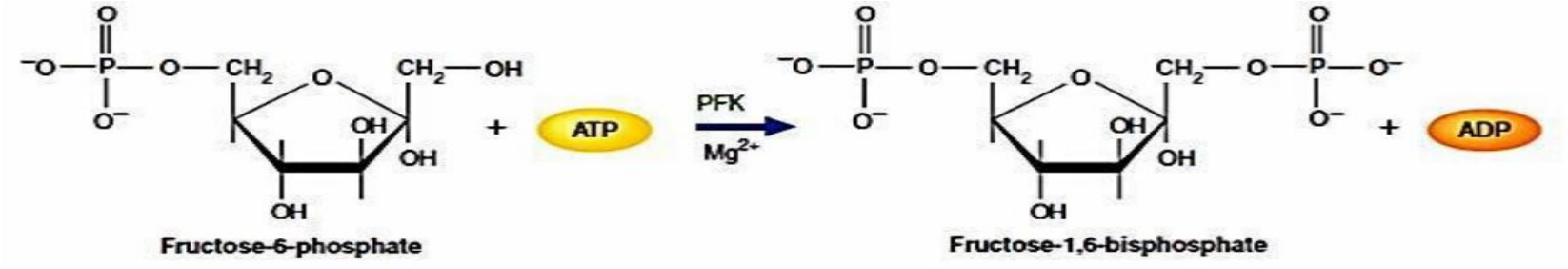
STAGE 2

Glucose-6-phosphate is isomerized into fructose,6-phosphate by the enzyme phosphoglucomutase.



Stage 3

One more ATP molecule transfers a phosphate group to fructose 6-phosphate and converts it into fructose 1,6-bisphosphate by the action of the enzyme phosphofructokinase is an important key enzyme of this pathway.



This irreversible step is the rate limiting reaction in glycolysis,.

Stage 4

The enzyme aldolase converts fructose 1,6- bisphosphate into glyceraldehyde 3-phosphate & dihydroxyacetone phosphate, which are isomers of each other.

STEP 5

Triose-phosphate isomerase converts dihydroxyacetone phosphate into glyceraldehyde 3-phosphate which is the substrate in the successive step of glycolysis.

STEP 6

This step undergoes two reactions:

1. The enzyme glyceraldehyde 3-phosphate dehydrogenase transfers 1 hydrogen molecule from glyceraldehyde phosphate to nicotinamide adenine dinucleotide to form NADH + H+

2. Glyceraldehyde 3-phosphate dehydrogenase adds a phosphate to the oxidized glyceraldehyde phosphate to form 1,3-bisphosphoglycerate

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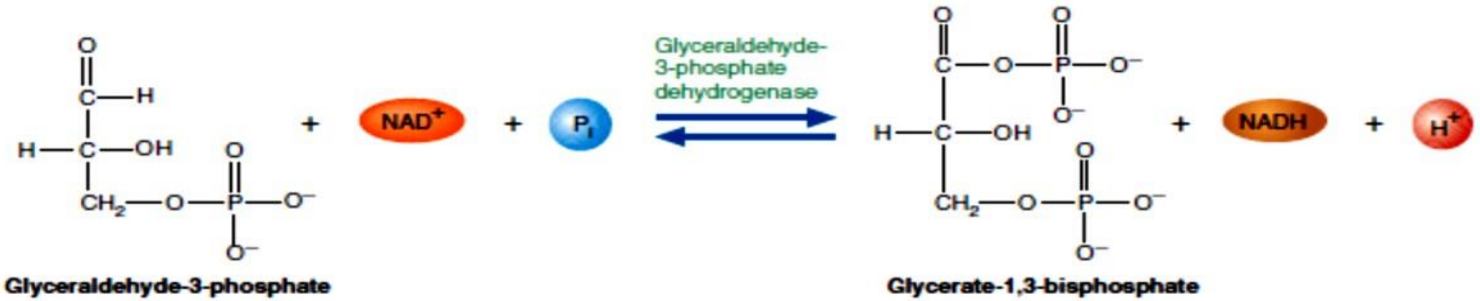
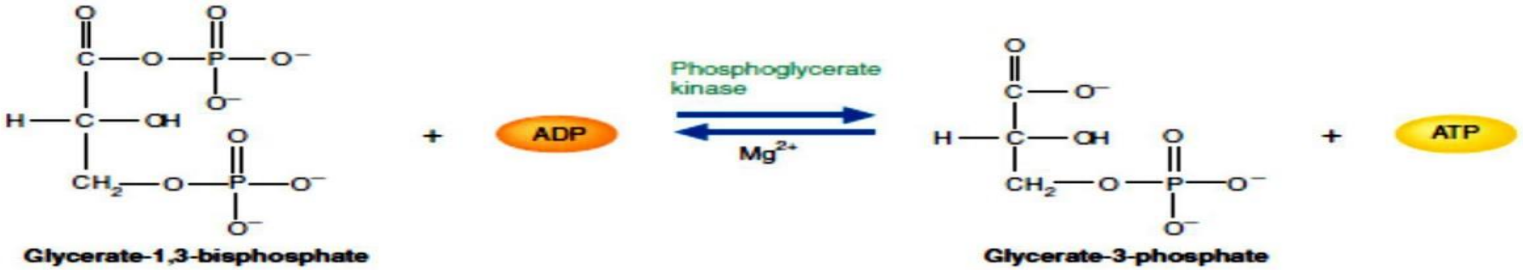


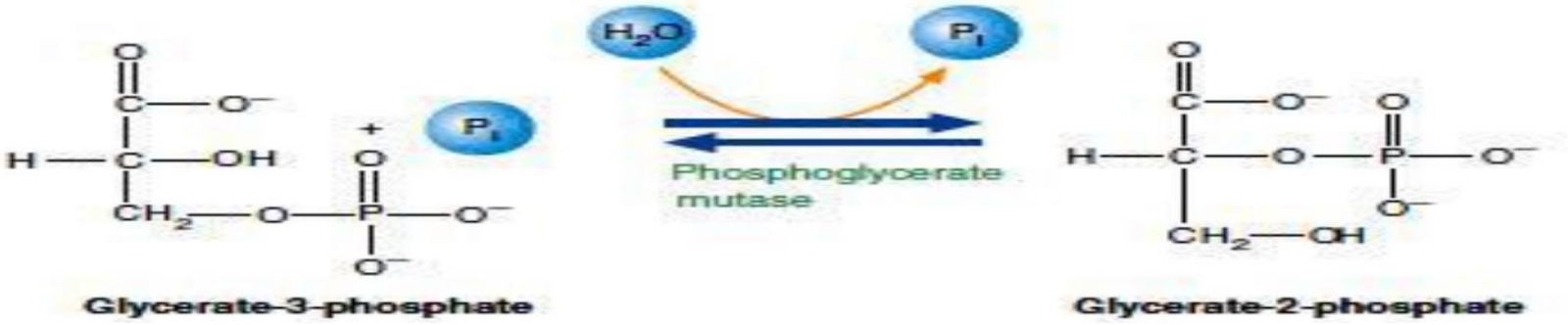
STEP 7

Phosphate is transferred from 1,3- bisphosphoglycerate to ADP to form ATP with the help of phosphoglycerokinase.Thus two molecules of 3 phosphoglycerate and ATP are obtained at the end of this reaction.



STEP 8

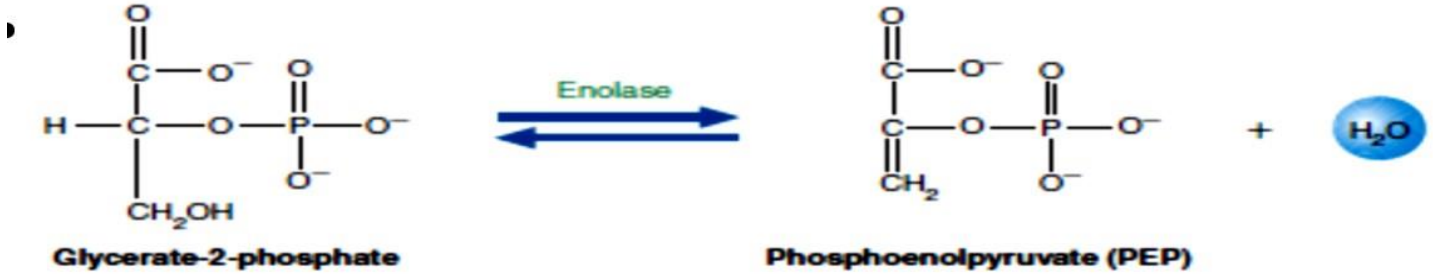
The phosphate of both the phosphoglycerate molecules is relocated from the third to the second carbon to yield two molecules of 2-phosphoglycerate by the enzyme phosphoglyceromutase.



STEP 9

The enzyme enolase removes a water molecule from 2-phosphoglycerate to form phosphoenolpyruvate.

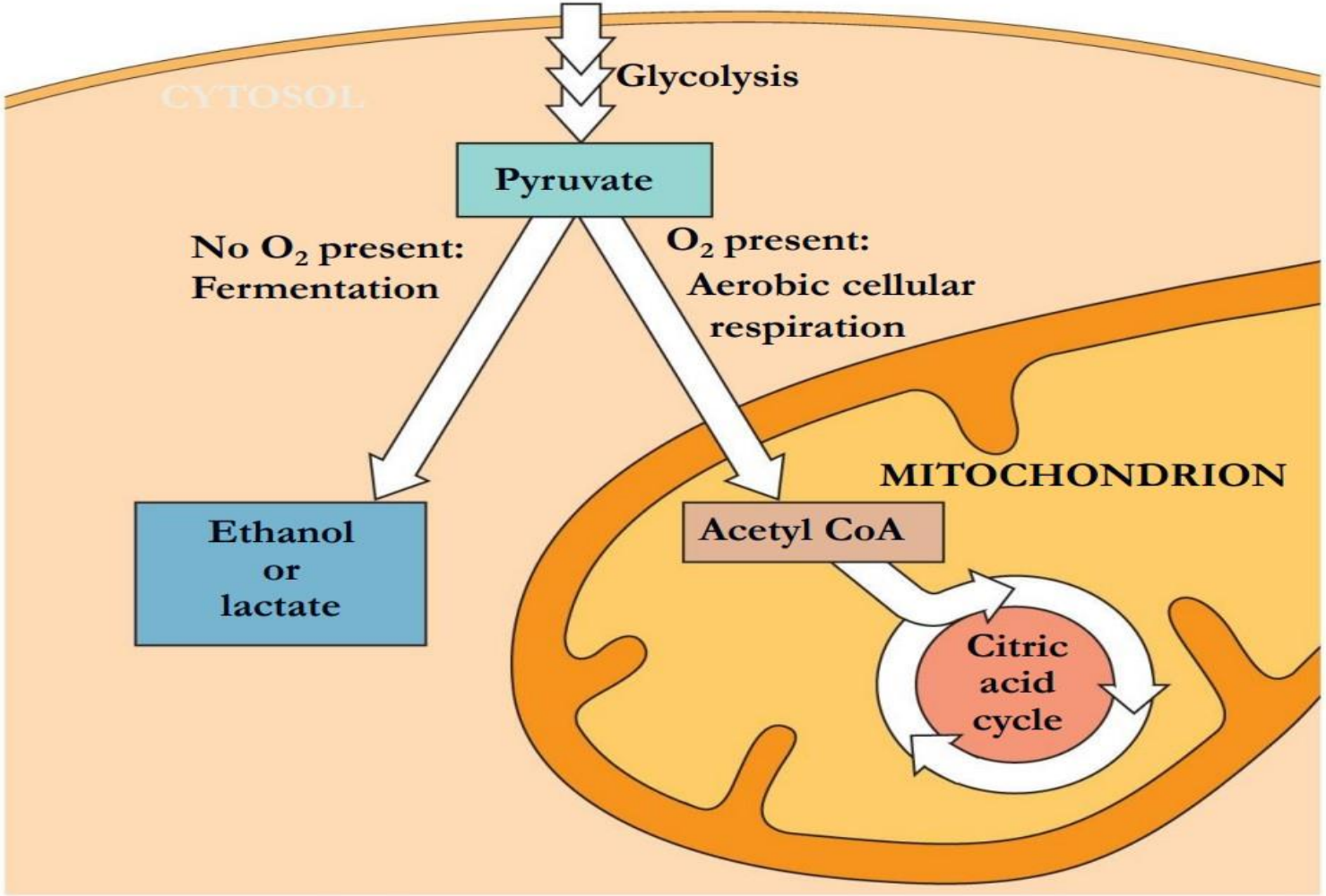
Enolase is inhibited by fluoride, and when blood samples are taken for measurement of glucose, glycolysis is inhibited by taking the sample into tubes containing fluoride



STEP 10

A phosphate from phosphoenolpyruvate is transferred to ADP to form pyruvate and ATP by the action of pyruvate kinase. Two molecules of pyruvate and ATP are obtained as the end products.

- **Fates of Pyruvate:**
  1. **Aerobic Conditions:** Pyruvate → Acetyl-CoA (via pyruvate dehydrogenase complex).
  2. **Anaerobic Conditions:** Pyruvate → Lactate (via lactate dehydrogenase).
  3. **Conversion to Oxaloacetate** by Pyruvate carboxylase
  4. **Conversion to Alanine** by Alanine aminotransferase (ALT).



Thank you

Any questions