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B.Sc. Part III, Paper V, Gr-I

Topic: Metabolism of Carbohydrates:

Glycolysis

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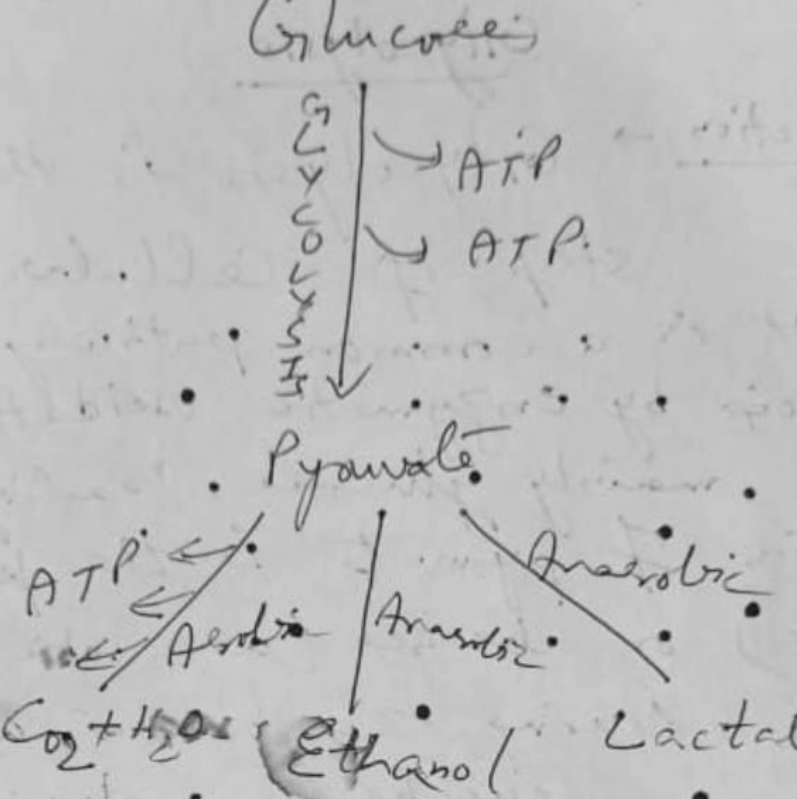
Glycolysis is the first step of Cellular Respiration and is a common pathway of ATP Synthesis by enzymatic oxidation of hexose, mainly glucose, leading to the formation of pyruvate in the presence (aerobic) or absence (anaerobic) of oxygen. During this process, a six Carbon monosaccharide molecule is degraded to two molecules of three Carbon pyruvate. In Aerobic glycolysis, pyruvate is further oxidized to CO_2 and water through Kreb's Cycle and respiratory chains for the Synthesis of a large amount of ATP, whereas in anaerobic glycolysis, pyruvate gets reduced to lactate or is decarboxylated to acetaldehyde and finally to ethanol. Anaerobic glycolysis occurs in cytosol after lactate accumulates during intense muscular activity, exercise or running by athletes when ATP requirement of

muscles exceeds their oxygen supply.



Steps of Glycolysis

Glycolysis involves reactions catalyzed by 10 enzymes acting in sequence and found in the cytosolic component of the cell.

The steps are —

1. **Phosphorylation of glucose** — Glucose is first activated by phosphorylation of its sixth carbon forming glucose-6-phosphate. ATP complexed with Mg^{+2} ions donate phosphate and energy for

phosphorylation and is left out as ADP. The enzyme Hexokinase bringing out this reaction is found in all tissues except liver and Pancreas.

Glucose $\xrightarrow[\text{Hexokinase}]{ATP \rightarrow ADP+P}$ Glucose 6-Poy

2. Isomerization of glucose-6-Poy to Fructose-6-Poy

In this step, glucose-6-Poy become converted into Fructose-6-Poy by the enzyme phosphohexose isomerase bringing about transfer of oxygen from Carbon 1 to Carbon-2.

Glucose-6-Poy $\xleftarrow[\text{isomerase}]{\text{phosphohexose}}$ Fructose-6-Poy

3. phosphorylation of Fructose-6-Poy →

In this step, Fructose-6-Poy is phosphorylated to Fructose 1.6-biPoy by enzyme phosphofructokinase in the presence of ATP complexed with Mg^{+2}

Fructose-6-Poy $\xrightarrow[ATP \rightarrow ADP+P_i]{\text{phosphofructokinase}}$ Fructose 1.6 diphosphate

4. Cleavage of Fructose 1,6. biphosphate →

Fructose 1,6 - biphosphate is cleaved in the middle by the enzyme Aldolase forming glyceraldehyde - 3 - POy and Dihydroxy acetone phosphate.

Fructose 1,6 BiPOy $\xleftarrow{\text{Aldolase}}$ Dihydroxy Acetone POy. (DHAP) + Glyceraldehyde 3 POy.

5. Isomerization of triose phosphates -

The enzyme phosphotriose isomerase brings about interconversion of glyceraldehyde - 3 - POy and Dihydroxy Acetone : POy.

Dihydroxy Acetone POy $\xleftarrow{\text{Phosphotriose isomerase}}$ glyceraldehyde - 3 - POy.

However, in the subsequent steps of glycolysis only glyceraldehyde - 3 - POy undergoes further metabolism.

6. Oxidation of glyceraldehyde - 3 - POy -

In this step, glyceraldehyde - 3 - POy undergoes dehydrogenation by the enzyme glyceraldehyde - 3 - PDy Dehydrogenase.

Glyceraldehyde-3-PO4 ⟷ (Dehydrogenase; NAD → NADH) 1,3 diphosphoglycerate

7. Transfer of energy-rich PO4 from 1.3-biphosphoglycerate to ADP. →

This is a phosphorylation reaction, in which 1,3 diphosphoglycerate phosphorylate to form 3 phospho-glycerate and ATP.

3-Phosphoglycerate ⟷ (Phosphoglycerate kinase) 2 phospho-glycerate.

8. Conversion of 3-phosphoglycerate to 2-phosphoglycerate →

In this step, 3 phosphoglycerate isomerises to form 2 phosphoglycerate under the action of enzyme phosphoglycerate mutase.

3 phosphoglycerate —(Phosphoglycerate mutase)→ 2 Phosphoglycerate

9. Dehydration of 2-phosphoglycerate →

A molecule of water is removed by enzyme Enolase, forming phosphoenol pyruvate in presence of Mg^{+2} ions.

2 – Phosphoenol Pyruvate $\xrightarrow[Mg^{+2}]{Enolase}$ Phosphoenol Pyruvate

Transfer of energy-rich POy from phosphoenolpyruvate to ADP →

This is virtually the last enzymatic step in glycolysis when energy rich POy is shifted from phosphoenol pyruvate to ADP by enzyme Pyruvate kinase in the presence of Mg^{+2}.

Phosphoenol Pyruvate $\xrightarrow[Mg^{+2}]{\text{Pyruvate kinase}}$ Pyruvate.

Regulation of Glycolysis →

Glycolysis is the most primitive pathway of energy synthesizing system and remains linked to other pathways of ATP synthesis. It is influenced mainly by energy requirement of the cell. However, the enzymes of glycolysis as Hexokinase, phosphofructokinase and Pyruvate kinase are the main enzymes, which are allosteric are regulated by reactant

and products of glycolysis and Krebs's Cycle.

Hexokinase, in muscle, brings about the formation of glucose-6-Poy, which induces allosteric inhibition of its activity. This keeps the concentration of glucose and glucose-6-Poy is equilibrium.

PFK (Phosphofructokinase) activity is muscle is regulated by relative concentration of a large no. of substances including its reactants and products.

Pyruvate kinase also an allosteric enzyme; is inhibited by high concentration of ATP, Acetyl Co-A and long chain fatty acids; oxidation of last two provides ATP.