GLYCOLYSIS

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Glycolysis , which translates to "splitting sugars", is the process of releasing energy within sugars. In glycolysis, a six-carbon sugar known as glucose is split into two molecules of a three-carbon sugar called pyruvate. This multistep process yields two ATP molecules containing free energy, two pyruvate molecules, two high energy, electron-carrying molecules of NADH, and two molecules of water.

Glycolysis is the process of breaking down glucose.

Glycolysis can take place with or without oxygen.

Glycolysis produces two molecules of pyruvate, two molecules of ATP, two molecules of NADH, and two molecules of water.

Glycolysis takes place in the cytoplasm.

There are 10 enzymes involved in breaking down sugar. The 10 steps of glycolysis are organized by the order in which specific enzymes act upon the system.

Glycolysis can occur with or without oxygen. In the presence of oxygen, glycolysis is the first stage of cellular respiration. In the absence of oxygen, glycolysis allows cells to make small amounts of ATP through a process of fermentation.

Glycolysis takes place in the cytosol of the cell's cytoplasm. A net of two ATP molecules are produced through glycolysis (two are used during the process and four are produced.) Learn more about the 10 steps of glycolysis below.

Step 1

The enzyme hexokinase phosphorylates or adds a phosphate group to glucose in a cell's cytoplasm. In the process, a phosphate group from ATP is transferred to glucose producing glucose 6-phosphate or G6P. One molecule of ATP is consumed during this phase.

Step 2

The enzyme phosphoglucomutase isomerizes G6P into its isomer fructose 6-phosphate or F6P. Isomers have the same molecular formula as each other but different atomic arrangements.

Step 3

The kinase phosphofructokinase uses another ATP molecule to transfer a phosphate group to F6P in order to form fructose 1,6-bisphosphate or FBP. Two ATP molecules have been used so far.

Step 4

The enzyme aldolase splits fructose 1,6-bisphosphate into a ketone and an aldehyde molecule. These sugars, dihydroxyacetone phosphate (DHAP) and glyceraldehyde 3-phosphate (GAP), are isomers of each other.

Step 5

The enzyme triose-phosphate isomerase rapidly converts DHAP into GAP (these isomers can inter-convert). GAP is the substrate needed for the next step of glycolysis.

Step 6

The enzyme glyceraldehyde 3-phosphate dehydrogenase (GAPDH) serves two functions in this reaction. First, it dehydrogenates GAP by transferring one of its hydrogen (H^+) molecules to the oxidizing agent nicotinamide adenine dinucleotide (NAD^+) to form NADH + H^+.

Next, GAPDH adds a phosphate from the cytosol to the oxidized GAP to form 1,3-bisphosphoglycerate (BPG). Both molecules of GAP produced in the previous step undergo this process of dehydrogenation and phosphorylation.

Step 7

The enzyme phosphoglycerokinase transfers a phosphate from BPG to a molecule of ADP to form ATP. This happens to each molecule of BPG. This reaction yields two 3-phosphoglycerate (3 PGA) molecules and two ATP molecules.

Step 8

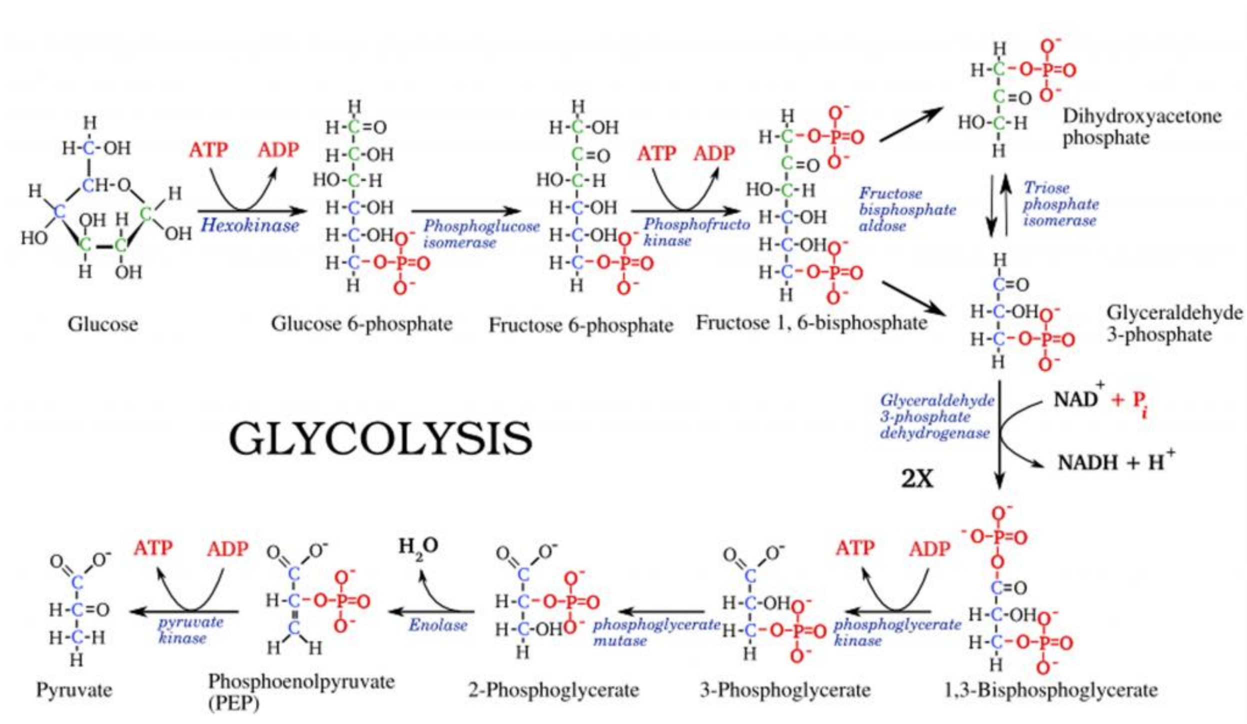
The enzyme phosphoglyceromutase relocates the P of the two 3 PGA molecules from the third to the second carbon to form two 2-phosphoglycerate (2 PGA) molecules.

Step 9

The enzyme enolase removes a molecule of water from 2-phosphoglycerate to form phosphoenolpyruvate (PEP). This happens for each molecule of 2 PGA from Step 8.

Step 10

The enzyme pyruvate kinase transfers a P from PEP to ADP to form pyruvate and ATP. This happens for each molecule of PEP. This reaction yields two molecules of pyruvate and two ATP molecules.

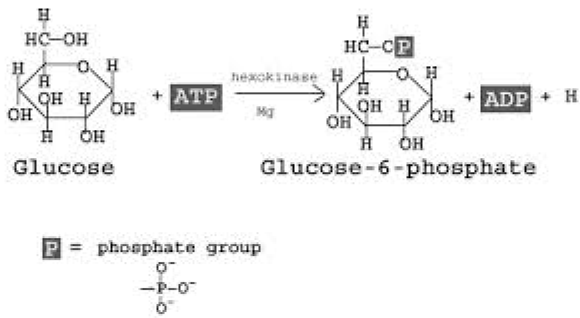


STEPS:

1. Preparatory phase:

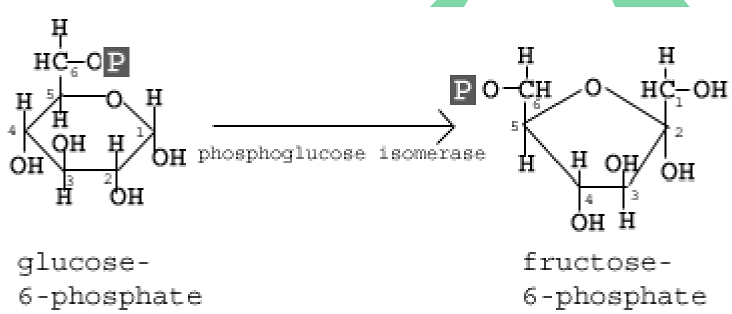
In preparatory phase glucose molecule is activated for breakdown and energy is invested in the process of phosphorylation of glucose. The first five reactions constitutes the preparatory phase.

Step I: Phosphorylation of glucose:



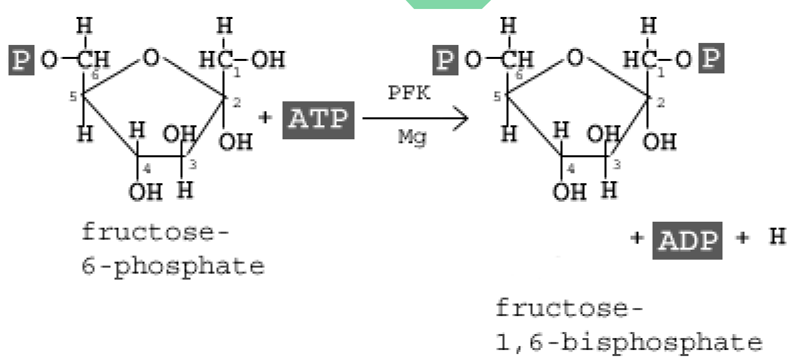
Glucose is phosphorylated at –OH group of C6 in which one molecule ATP is consumed. The reaction is catalyzed by the enzyme Hexokinase in the presence of Mg++ ion.

Step II: Isomerization of glucose-6 phosphate to fructose-6- Phosphate



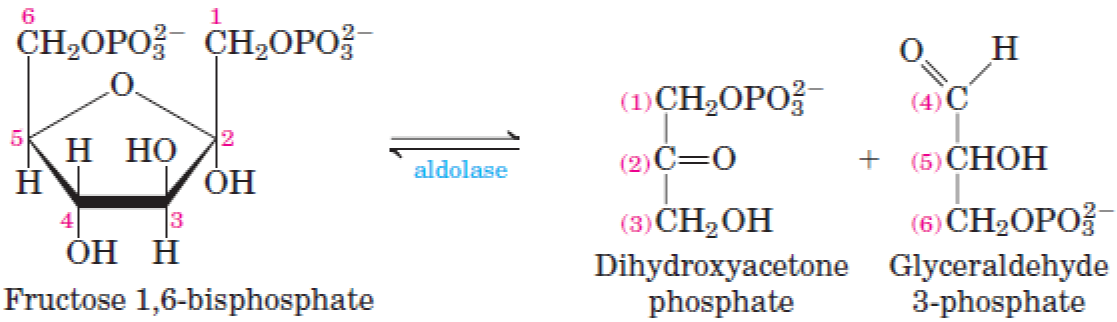
This reaction is catalyzed by the enzyme phosphoglucose isomerase.

Step III: Phosphorylation of fructose-6-phosphate:



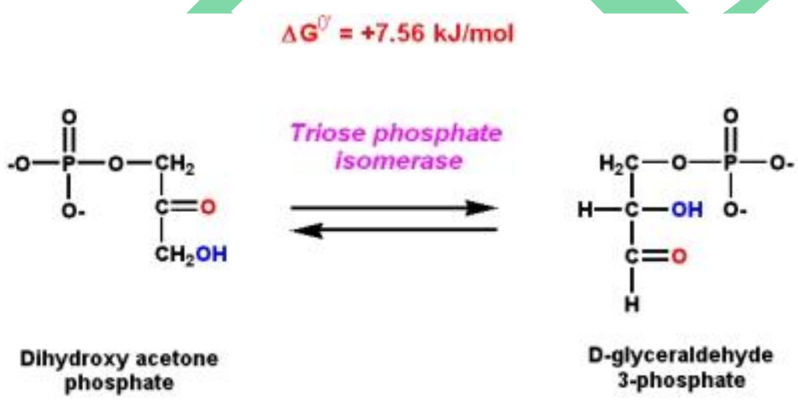
This reaction is catalyzed by Phospho-fructo-kinase (PFK) in the presence of Magnesium ion, in which fructose-6-phosphate is converted into fructose-1,6-bisphosphate. One molecule of ATP is consumed.

Step IV: Cleavage of Fructose-1,6-bisphosphate



The enzyme Aldolase (fructose-1,6-diphosphate aldolase) cleave fructose-1,6-bisphosphate to yield two molecule glyceraldehyde-3-phosphate and dihydroxy-acetone phosphate.

Step V: Conversion of dihydroxy-acetone phosphate to glyceraldehyde-3-phosphate.

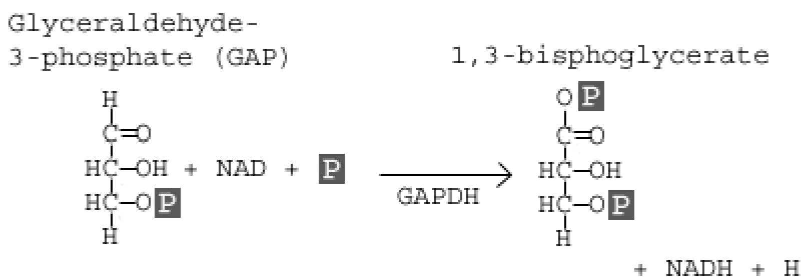


Dihydroxy-acetone phosphate and glyceraldehyde-3-phosphate are isomers. The reaction is catalyzed by the enzyme triose phosphate isomerase.

2. Payoff phase:

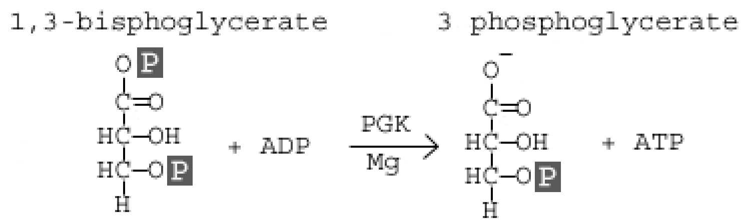
In payoff phase oxidation of glucose releases energy in the form of ATP and NADH. The remaining five reactions constitutes payoff phase

Step VI: Oxidation of glyceraldehyde-3-phosphate:



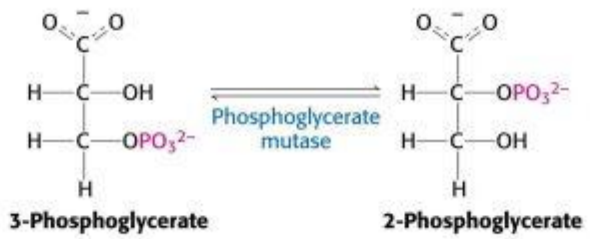
The glyceraldehyde-3-phosphate is oxidized into 1,3-bisphospho-glycerate in the presence of enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDH). In this reaction one molecule of NADH is released.

Step VII: Transfer of phosphoryl group from 1,3-bisphosphoglycerate to ADP



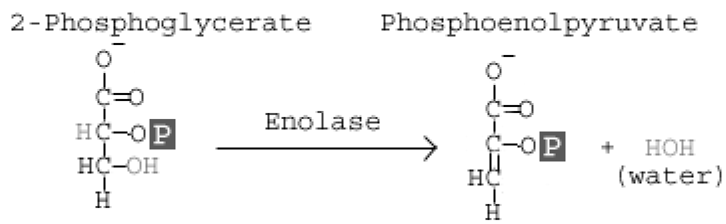
The enzyme phosphoglycerate kinase (PGK) transfer phosphoryl group from 1,3 bisphosphate glycerate to ADP forming ATP and 3-phospholycerate. This reaction is an example of substrate level phosphorylation in which phosphoryl group is transfer from substrate ie 1,3-bisphosphoglycerate to ADP to form ATP.

Step VIII: Conversion of 3-phosphoglycerate to 2-phoshoglycerate



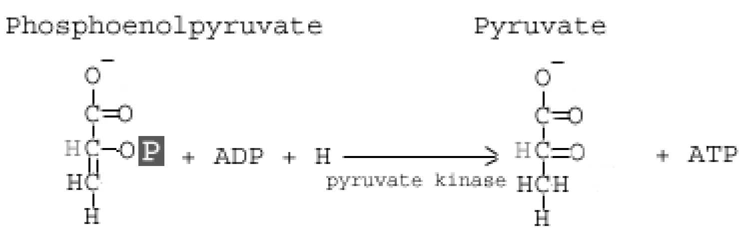
The enzyme phosphoglycerate mutase catalyses reversible shift of phosphoryl group between C2 and C3 of phosphoglycerate. Mg++ is essential for this reaction.

Step IX: Dehydration of 2-phosphoglycerate (Removal of H2O from 2-phosphoglycerate)



Enolase promote reversible removal of a molecule of water from 2-phosphoglycerate forming Phosphoenol-pyruvete (PEP).

Step X: Transfer of phosphoryl group from PEP to ADP



This reaction is catalyzed by the enzyme pyruvate kinase in the presence of K+ and Mg++ or Mn++ions. This is also a substrate level phosphorylation in which phosphoryl group is transferred from PEP to ADP forming ATP and Pyruvate. In this substrate level phosphorylation, the product pyruvate first appears in its enol form which then tautomerize rapidly and non-enzymatically to its keto form.

Thermodynamics of Glycolysis:

In glycolysis, one molecule of glucose is break down into two molecules of pyruvate releasing 2 ATP and 2 NADH. The overall equation of aerobic glycolysis is

Glucose + 2NAD+ 2ATP +2Pi ———————— 2pyruvate + 2ADP +2NDAH +2H2O + 2H+

Conversion of glucose to pyruvate is an exothermic reaction with net free energy of

ΔG= -85KJ/mole

Resolving above equation into two equations.

1. Formation of NADH is exothermic

Glucose + 2NAD+ ———— 2pyruvate + 2NDAH +2H2O + 2H+

$\Delta G1$= -146KJ/mole

2. Formation of ATP is endothermic reaction

2ADP +2Pi———————— 2ATP + 2H2O

$\Delta G1$= +61KJ/mole

Net free energy= -146+61= -85KJ/mole

Regulation of glycolysis:

The reaction catalyzed by Phosphofructose kinase is the rate limiting step or control point of glycolysis. However glycolysis is regulated by two mechanism.

1. Allosteric regulation:

ATP and citrate are allosteric inhibitor of phosphfructo kinase. Therefore glycolysis stops in cell having large amount of ATP and citrate (High energy condition). AMP and ADP are allosteric activator and they get accumulated in cell when energy content is depleted.

2. Reciprocal regulation:

Fructose-2,6 bisphosphate is potent activator of phosphofructose kinase while Fructose-1,6-bisphosphate is inhibitor of phosphofructose kinase. Increased concentration of fructose-1,6-bisphosphate favor formation of glucose from pyruvate (gluconeogenesis).