Metabolic pathway and bioenergetics –Glycolysis

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Introduction

- Carbohydrates are major sources of energy for living organisms.
- The **chief source of carbohydrate** in human food is **starch**, which is the storage form of glucose in plants.
- Plants may store relatively large amounts of starch within their own cells in time of abundant supply, to be used later by the plant itself when there is a **demand for energy production.**
- **Glycogen** is the glucose storage polysaccharide of animals.
- It accounts for upto 10% of the mass of the liver and one percent of the mass of the muscle.
- Glycogen is larger and highly branched than amylopectin.
- By the action of several enzymes, such as α**-amylase,** β**-amylase, amylo** α**(1→6) glucosidase and** $\propto$**(1→4) glucosidase,** starch and glycogen from dietary intake are degraded finally to glucose.
- Carbohydrate is utilized by cells mainly in the form of glucose.
- The three principal monosaccharides resulting from the digestive processes are **glucose, fructose and galactose**.
- Both fructose and galactose are readily converted to glucose by the liver.
- Pentose sugars such as xylose, arabinose and ribose may be present in the diet, but their fate after absorption is obscure.
- Since glucose is the compound formed from starch and glycogen, the carbohydrate metabolism commences with this monosaccharide.

The major metabolic processes in carbohydrates are:

i. Glycolysis:

Glycolysis is the sequence of reactions that convert **glucose into pyruvate** with the concomitant trapping of the energy as ATP.

ii. The citric acid cycle:

It is the final **common oxidative pathway for carbohydrates, fats and proteins**. It is also a source of precursors for biosynthesis of various biomolecules. The **acetyl CoA** that enters in this pathway is completely oxidised to **carbon dioxide and water** with concomitant production of reducing equivalents, namely **NADH and** $FADH_2$**.**

iii. The hexose monophosphate shunt:

It is an **alternative pathway** to the glycolytic pathway and the citric acid cycle for the oxidation of glucose to carbon dioxide and water with the **generation of reduced nicotinamide adenine dinucleotide phosphate (NADPH) molecules and ribose 5-phosphate.**

iv. Gluconeogenesis:

It is a biosynthetic pathway that generates **glucose from non-carbohydrate precursors.**

v. Glycogenesis:

It is a pathway by which **glycogen is synthesised** from glucose.

vi. Glycogenolysis:

Glycolysis

❖ Glycolysis, also called as **Embden-Meyerhof-Parnas pathway (EMP pathway),** consists of a series of reactions through which glucose is converted to pyruvate with the concomitant production of relatively small amounts of adenosine triphosphate (ATP).

❖ It is derived from the Greek stem '**glykys'** meaning sweet and **'lysis'** meaning splitting.

❖ It is the primary pathway occurring in the cytoplasm of all the tissues of biological systems.

❖ All the enzymes responsible for the catalysis are found in the **extra-mitochondrial soluble fraction of the cells (cytoplasm).**

In plants, glucose and fructose are the main monosaccharides catabolised by glycolysis although others are also converted into these sugars.

❖ Glucose entering the glycolysis is derived from **starch or sucrose**, and fructose is derived from **sucrose.**

❖ The starch is either from seeds or chloroplasts of matured plants.

❖ Glycolysis normally takes place in the **presence of O_2** in higher plant cells.

The enzymes in the cytoplasm catalyse the reactions involved in the conversion of **glucose to pyruvate** .

The series of reactions indicated take place in 3 stages.

Stage 1: Conversion of glucose to fructose 1,6-bisphosphate

❖ The formation of fructose 1,6-bisphosphate takes place in three steps catalysed by enzymes.

- The purpose of these reactions is to form a compound that can be readily cleaved into phosphorylated three carbon units from which, through a series of reactions, ATP is formed.
- After the **first phosphorylation** reaction to form glucose 6-phosphate, isomerisation of glucose 6-phosphate to **fructose-6-phosphate** occurs which is conversion of an aldose into a ketose.
- A second phosphorylation reaction follows the isomerization, catalysed by **phosphofructokinase** resulting in the formation of fructose 1,6-bisphosphate.
- **Phosphofructokinase** is the key enzyme in the control of glycolysis.

Stage 2: Conversion of fructose 1,6-bisphosphate to 3-phosphoglycerate.

- The **splitting of fructose 1,6-bisphosphate** occurs in the second stage of glycolysis resulting in the formation of a molecule of glyceraldehyde 3-phosphate and a molecule of dihydroxyacetone phosphate catalysed by **aldolase.**
- The dihydroxyacetone phosphate is isomerised to glyceraldehyde 3-phosphate by **phosphotriose isomerase.** The isomerisation reaction is rapid and reversible.
- In the next step, glyceraldehyde 3- phosphate is oxidised to 1,3-bisphosphoglycerate catalyzed by **glyceraldehyde 3-phosphate dehydrogenase.**
- The product is further converted into 3-phosphoglycerate and a molecule of ATP is formed. The phosphorylation of ADP to ATP is called **substrate level phosphorylation** since the phosphate group from a substrate molecule is transferred to ADP.

Stage 3: Formation of pyruvate

- An intramolecular rearrangement of the phosphoryl group occurs resulting in the formation of 2-**phosphoglycerate from 3-phosphoglycerate catalyzed by phosphoglycerate mutase.**
- The 2-phosphoglycerate formed undergoes **dehydration** forming phosphoenolpyruvate which gives rise to pyruvate and a molecule of ATP (substrate level phosphorylation).
- The reaction is irreversible and catalyzed by **pyruvate kinase.**

The net reaction in the transformation of glucose to pyruvate is

Glucose + 2 Pi + 2ADP + 2 NAD^+ ---→ 2 pyruvate + 2 ATP + 2 NADH + 2 H^+ + H_2O

Once pyruvate is formed, further degradation is determined by the **presence or absence of oxygen.**

Under anaerobic conditions, in one of the pathways, pyruvate undergoes reduction yielding **lactic acid.**

The formation of lactic acid is very rare in plants with exception of potato tubers maintained under anaerobic condition and some green algae.

In the second pathway, pyruvate is converted to **ethyl alcohol and carbon dioxide**. The **alcoholic fermentation** is the basis of the beer and wine-making industries.

Under **aerobic conditions**, pyruvate is **oxidatively decarboxylated to acetyl CoA** which is then completely oxidised to CO_2 and water through the **citric acid cycle**

Energetics of glycolysis

From glucose, two molecules of glyceraldehyde 3-phosphate are formed in the second stage of glycolysis from which two molecules of pyruvate are obtained as end products of glycolysis. Hence energetic of glycolysis is calculated by taking into account two molecules of glyceraldehyde 3-phosphate.

Energetics of glycolysis

Stages/steps	Enzyme	Method of high energy bond formation	No. of ATP formed
Stage 1			
Formation of1,3-bisphospho glycerate from glyceraldehydes 3-phosphate	Glyceraldehyde3-phosphate dehydrogenase	Respiratory chain oxidation of 2 NADH	5
Stage 2			
Formation of 3 phosphoglycerate from 1,3 bisphospho glycerate	Phosphoglycerate kinase	Phosphorylation at subtrate level	2
Stage 3			
Formation of pyruvate from phosphoenol pyruvate	Pyruvate kinase	Phosphorylation at subrate level	2
Allowance for consumption of ATP by reactions catalysed by hexokinase and phosphofructokinase.			2
Number of ATP molecules generated by the catabolism of one molecule of glucose under aerobic conditions.			**7**
Number of ATP molecules generated by the catabolism of one molecule of glucose under anaerobic conditions.			2

Significance of glycolysis

- Glycolysis is an almost **universal central pathway** of glucose catabolism occurring in the cytoplasm of all the tissues of biological systems leading to generation of energy in the form of ATP for vital activities.
- It is the pathway through which the **largest flux of carbon** occurs in most cells.
- Some plant tissues which are modified for the storage of starch such as potato tubers and some plants adapted to growth in inundated water such as water cress derive most of their energy from glycolysis.

- In plants, glycolysis is the **key metabolic component of the respiratory process,** which generates energy in the form of ATP in cells where photosynthesis is not taking place.
- Many types of **anaerobic microorganisms** are entirely dependent on glycolysis.
- Mammalian tissues such as renal medulla and brain solely dependent on glycolysis for major sources of metabolic energy.