



PHARMACOLEARN

It's Important to Know!

BP203T — Biochemistry

B.Pharm Semester 2 · Unit 3 — Carbohydrate Metabolism

Unit III: Carbohydrate Metabolism

This unit follows the main pathways by which glucose is used, stored and formed. For every pathway, learn the site, purpose, key steps, major regulation points and products.

Glycolysis

Glycolysis is the pathway that converts glucose to pyruvate through a sequence of reactions in the cytosol. It can operate without oxygen, although the fate of pyruvate and the regeneration of NAD⁺ depend on cellular conditions.

The pathway has an energy-investment phase and an energy-generation phase. It produces ATP by substrate-level phosphorylation and produces NADH when glyceraldehyde-3-phosphate is oxidized.

In aerobic conditions, pyruvate can enter mitochondria and be converted to acetyl-CoA by the pyruvate dehydrogenase complex. In anaerobic conditions, pyruvate can be reduced to lactate, which regenerates NAD⁺ for continued glycolysis.

Glycolysis: 10 steps and enzymes

1. Glucose to glucose-6-phosphate: hexokinase or glucokinase; ATP is used.
2. Glucose-6-phosphate to fructose-6-phosphate: phosphoglucose isomerase.
3. Fructose-6-phosphate to fructose-1,6-bisphosphate: phosphofructokinase-1; ATP is used and this is a major control step.
4. Fructose-1,6-bisphosphate to glyceraldehyde-3-phosphate and dihydroxyacetone phosphate: aldolase.
5. Dihydroxyacetone phosphate to glyceraldehyde-3-phosphate: triose phosphate isomerase.
6. Glyceraldehyde-3-phosphate to 1,3-bisphosphoglycerate: glyceraldehyde-3-phosphate dehydrogenase; NADH is formed.
7. 1,3-Bisphosphoglycerate to 3-phosphoglycerate: phosphoglycerate kinase; ATP is formed.
8. 3-Phosphoglycerate to 2-phosphoglycerate: phosphoglycerate mutase.
9. 2-Phosphoglycerate to phosphoenolpyruvate: enolase.
10. Phosphoenolpyruvate to pyruvate: pyruvate kinase; ATP is formed.

The net yield per glucose is two ATP, two NADH and two pyruvate under the usual accounting conditions.

Citric acid cycle

The citric acid cycle occurs mainly in the mitochondrial matrix in eukaryotic cells. Acetyl-CoA is oxidized to carbon dioxide, and the cycle produces NADH, FADH₂ and GTP or ATP, depending on the tissue and nomenclature used.

The reduced coenzymes transfer electrons to the respiratory chain. The cycle also supplies intermediates for biosynthetic pathways.

Citric acid cycle: 8 steps and enzymes

1. Oxaloacetate plus acetyl-CoA to citrate: citrate synthase.
2. Citrate to isocitrate: aconitase.
3. Isocitrate to alpha-ketoglutarate: isocitrate dehydrogenase; NADH and carbon dioxide are formed.
4. Alpha-ketoglutarate to succinyl-CoA: alpha-ketoglutarate dehydrogenase complex; NADH and carbon dioxide are formed.
5. Succinyl-CoA to succinate: succinyl-CoA synthetase; GTP or ATP is formed.
6. Succinate to fumarate: succinate dehydrogenase; FADH₂ is formed.
7. Fumarate to malate: fumarase.
8. Malate to oxaloacetate: malate dehydrogenase; NADH is formed.

Gluconeogenesis

Gluconeogenesis is the formation of glucose from non-carbohydrate precursors such as lactate, glycerol and glucogenic amino acids. It occurs mainly in the liver, with contributions from the kidney during prolonged fasting. It is not simply the reverse of glycolysis because several glycolytic reactions are strongly irreversible and require bypass reactions.

Glycogen metabolism

Glycogenesis is the synthesis of glycogen from glucose. Glycogenolysis is the breakdown of glycogen. Liver glycogen helps maintain blood glucose, while muscle glycogen is used mainly for energy within muscle.

Glycogenesis uses glycogenin to start a primer, glycogen synthase to extend alpha-1,4 chains and a branching enzyme to create alpha-1,6 branches. Insulin promotes activation of glycogen synthase after a carbohydrate-rich meal. Glycogenolysis uses glycogen phosphorylase to release glucose-1-phosphate, a debranching enzyme at branch points and phosphoglucomutase to form glucose-6-phosphate. Liver glucose-6-phosphatase permits free glucose release. Glucagon promotes liver glycogenolysis, while adrenaline can stimulate glycogenolysis in liver and muscle.

Pentose phosphate pathway

The pentose phosphate pathway occurs in the cytosol. It produces NADPH and ribose-5-phosphate. NADPH supports reductive biosynthesis and antioxidant defence. Ribose-5-phosphate is needed for nucleotide synthesis. The pathway does not directly produce

ATP. Its oxidative phase is controlled by glucose-6-phosphate dehydrogenase, and its products support fatty acid synthesis, glutathione reduction and nucleotide synthesis.

Unit III: Frequently asked questions

Q: What is the net purpose of glycolysis?

A: Glycolysis converts glucose to pyruvate and captures part of the released energy as ATP and NADH. It occurs in the cytosol.

Q: Why is gluconeogenesis not the exact reverse of glycolysis?

A: Several glycolytic reactions have a large negative free-energy change in cells. Gluconeogenesis bypasses these steps with different enzymes.

Q: What are the main products of the pentose phosphate pathway?

A: The pathway produces NADPH and ribose-5-phosphate. It also produces sugar intermediates that can enter other carbohydrate pathways.

Q: Which enzyme is a major control point in glycolysis?

A: Phosphofructokinase-1 is a major control enzyme and converts fructose-6-phosphate to fructose-1,6-bisphosphate.

Unit III: Key takeaways

- Glycolysis occurs in the cytosol and forms pyruvate, ATP and NADH.
- Pyruvate dehydrogenase links glycolysis with the citric acid cycle.
- The citric acid cycle produces reduced coenzymes and biosynthetic intermediates.
- Glycogenesis stores glucose as glycogen, while glycogenolysis releases usable glucose units.
- The pentose phosphate pathway supplies NADPH and ribose-5-phosphate.
- Glycolysis has 10 enzyme-catalysed steps, and the citric acid cycle has 8.

Unit III: Clinical correlation

Clinical correlation: diabetes mellitus. In diabetes mellitus, inadequate insulin action changes glucose uptake, glycogen metabolism and gluconeogenesis. Persistent hyperglycaemia can be accompanied by increased lipolysis and ketone-body production.