



PHARMACOLEARN

It's Important to Know!

BP203T — Biochemistry

B.Pharm Semester 2 · Unit 4 — Lipid Metabolism

Unit IV: Lipid Metabolism

This unit covers digestion, transport, storage and oxidation of lipids, together with fatty acid synthesis and ketone-body formation. Keep the direction of each pathway clear: synthesis stores energy, while oxidation releases energy.

Digestion and absorption of lipids

Dietary triacylglycerols are emulsified in the intestine and hydrolysed by lipases. Products of digestion form mixed micelles with bile salts and are absorbed by intestinal cells. Long-chain fatty acids are reassembled into triacylglycerols and packaged into lipoprotein particles for transport.

Lipoproteins

Lipoproteins transport lipids through blood. They contain a hydrophobic core and a surface containing phospholipids, cholesterol and apoproteins. Their density and composition differ according to the amount of lipid and protein they contain.

Beta-oxidation of fatty acids

Each beta-oxidation cycle has four reactions: oxidation by acyl-CoA dehydrogenase forms a double bond and FADH₂; hydration by enoyl-CoA hydratase adds water; oxidation by beta-hydroxyacyl-CoA dehydrogenase forms NADH; and thiolysis by beta-ketothiolase releases acetyl-CoA. The shortened acyl-CoA repeats the cycle.

Beta-oxidation is the stepwise oxidation of fatty acyl-CoA. In each cycle, the chain is shortened by two carbon atoms and acetyl-CoA is produced. NADH and FADH₂ are also formed. Long-chain fatty acids require transport into mitochondria, and the carnitine shuttle is involved in this transport.

Ketone bodies

Ketone-body synthesis occurs in liver mitochondria. Two acetyl-CoA molecules form acetoacetyl-CoA through thiolase. HMG-CoA synthase forms HMG-CoA, HMG-CoA lyase forms acetoacetate, and acetoacetate can be reduced to beta-hydroxybutyrate or spontaneously decarboxylated to acetone. Extrahepatic tissues convert beta-hydroxybutyrate to acetoacetate

and then to acetoacetyl-CoA, which thiolase converts to acetyl-CoA. The liver cannot use ketone bodies because it lacks thiophorase.

The liver forms ketone bodies from acetyl-CoA when carbohydrate availability or carbohydrate use is insufficient for the current energy demand. The main ketone bodies are acetoacetate, beta-hydroxybutyrate and acetone. Extrahepatic tissues can use some ketone bodies, but the liver cannot use them as a major fuel because it lacks the required utilization enzyme.

Fatty acid synthesis

Cholesterol synthesis outline

Cholesterol synthesis begins with acetyl-CoA. Acetyl-CoA is converted to HMG-CoA, HMG-CoA is reduced to mevalonate by HMG-CoA reductase, and mevalonate is converted through activated isoprenes to squalene. Squalene is cyclized to lanosterol and then modified to cholesterol. HMG-CoA reductase is a major regulatory step. The pathway uses ATP and NADPH.

Lipoprotein classes

- Chylomicrons transport dietary triacylglycerol from intestine to tissues. Their remnants are taken up by the liver.
- VLDL transports triacylglycerol made by the liver to peripheral tissues. Its metabolism produces remnant particles and then LDL.
- LDL delivers cholesterol to peripheral cells through LDL receptors. Excess LDL is associated with atherogenic risk.
- HDL participates in reverse cholesterol transport from tissues toward the liver and exchanges apoproteins with other lipoproteins.

Fatty acid synthesis occurs mainly in the cytosol and uses acetyl-CoA, ATP and NADPH. Acetyl-CoA is converted to malonyl-CoA, and the fatty acid synthase system adds two-carbon units during chain elongation. Synthesis and beta-oxidation are separated by cellular location and regulated in opposite directions.

Unit IV: Frequently asked questions

Q: What is beta-oxidation?

A: Beta-oxidation is the mitochondrial pathway that removes two-carbon units from fatty acyl-CoA as acetyl-CoA while producing NADH and FADH₂.

Q: What are ketone bodies?

A: Ketone bodies are water-soluble products made from acetyl-CoA in the liver. They can provide fuel to extrahepatic tissues during selected metabolic states.

Q: Why are bile salts important in lipid digestion?

A: Bile salts emulsify dietary lipids and help form micelles, increasing the surface available for lipase action and supporting intestinal absorption.

Q: What are the main roles of LDL and HDL?

A: LDL delivers cholesterol to peripheral cells. HDL participates in reverse cholesterol transport toward the liver.

Unit IV: Key takeaways

- Lipids are emulsified, digested and transported in organised particles.
- Beta-oxidation releases acetyl-CoA, NADH and FADH₂.
- Ketone bodies are formed mainly in the liver from acetyl-CoA.
- Fatty acid synthesis uses acetyl-CoA and NADPH in the cytosol.
- Lipid synthesis and oxidation are separated and oppositely regulated.
- Chylomicrons carry dietary lipid, VLDL carries liver triacylglycerol, LDL delivers cholesterol and HDL supports reverse transport.

Unit IV: Clinical correlation

Clinical correlation: jaundice. Bilirubin is produced from heme breakdown and is transported to the liver for conjugation and excretion in bile. Accumulation of bilirubin causes jaundice.