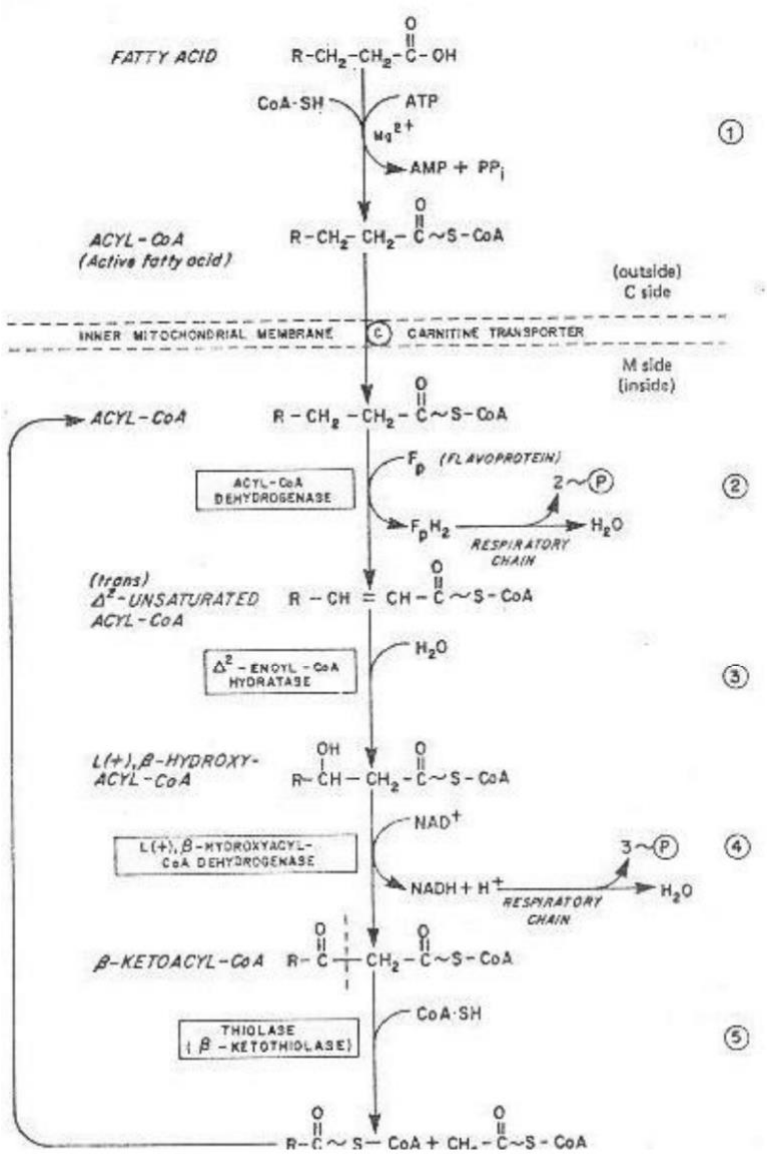
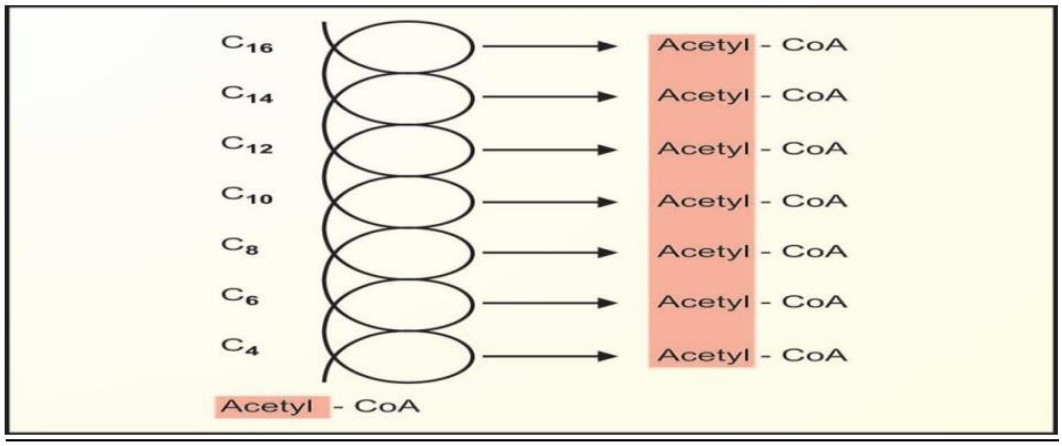
β oxidation

The major pathway for the catabolism of the saturated fatty acid is a mitochonderial pathway called β-oxidation, which was proposed by Knoop. In this process, oxidation of fatty acids occurs at β-carbon atom and two carbon fragments are successively removed from the carboxyl end of fatty acel-CO A. this in result in the elimination of two terminal carbon atoms as acetyl CoA, thereby leaving fattyacyl CoA that has two carbons less than the original fatty acid.



The β-oxidation



Summary of beta-oxidation of palmitic acid (16 C). It undergoes 7 cycles, which give rise to 8 molecules of acetyl CoA

Table 10.1. Difference in the two pathways

	Beta-oxidation	Fatty acid synthesis
Site	Mitochondria	Cytoplasm
Intermediates	Present as CoA derivatives	Covalently linked to SH group of ACP
Enzymes	Present as inde-pendent proteins	Multi-enzyme complex
Sequential units	2 carbon units split off as acetyl CoA	2 carbon units added, as 3 carbon malonyl CoA
Co-enzymes	NAD^+ and FAD are reduced	NADPH used as reducing power

Energetics of Beta-oxidation (ATP Yield)

Palmitic acid (16 C) needs 7 cycles of beta-oxidation, which give rise to 8 molecules of acetyl CoA (Fig. 10.7). Every molecule of acetyl CoA when oxidized in the TCA cycle gives 12 molecules of ATP. Each molecule of FADH 2 produces 2 molecules of ATP and each NADH generates 3 molecules of ATP when oxidized in the electron transport chain.

Hence, the energy yield from one molecule of palmitate may be calculated

as:

8 acetyl CoA × 12 = 96 ATP

7 FADH 2 × 2 = 14 ATP

7 NADH × 3 = 21 ATP

Gross total = 131 ATP

Net yield = 131 minus 2 =129 ATP

(In the initial activation reaction, the equivalent of 2 high energy bonds are utilized). The efficiency of beta-oxidation is about 40 percent.

DE NOVO SYNTHESIS OF FATTY ACIDS

The process of fatty acid synthesis was studied by Feodor Lynen, who got Nobel prize in 1964. The pathway is referred to as Lynen's spiral. It is not a reversal of oxidation. Important differences in synthesis and breakdown of fatty acids are given in Fatty acids are synthesized mainly by a de novo synthetic pathway operating in the cytoplasm. So, it is referred to as extramitochondrial or cytoplasmic fatty acid synthase system. The major fatty acid synthesized de novo is palmitic acid, the 16 C saturated fatty acid. The process occurs in liver, adipose tissue, kidney, brain, and mammary glands. Summary of de novo Synthesis The net reaction of de novo synthesis of fatty acid may be summarized as:

1Acetyl CoA +7Malonyl CoA +14NADPH +14H +

→ 1Palmitate + 7CO 2 +14NADP + + 8CoA+ 6H 2 O

Fatty acid synthesis is not an exact reversal of beta-oxidation.

Transport of Acetyl CoA to Cytoplasm

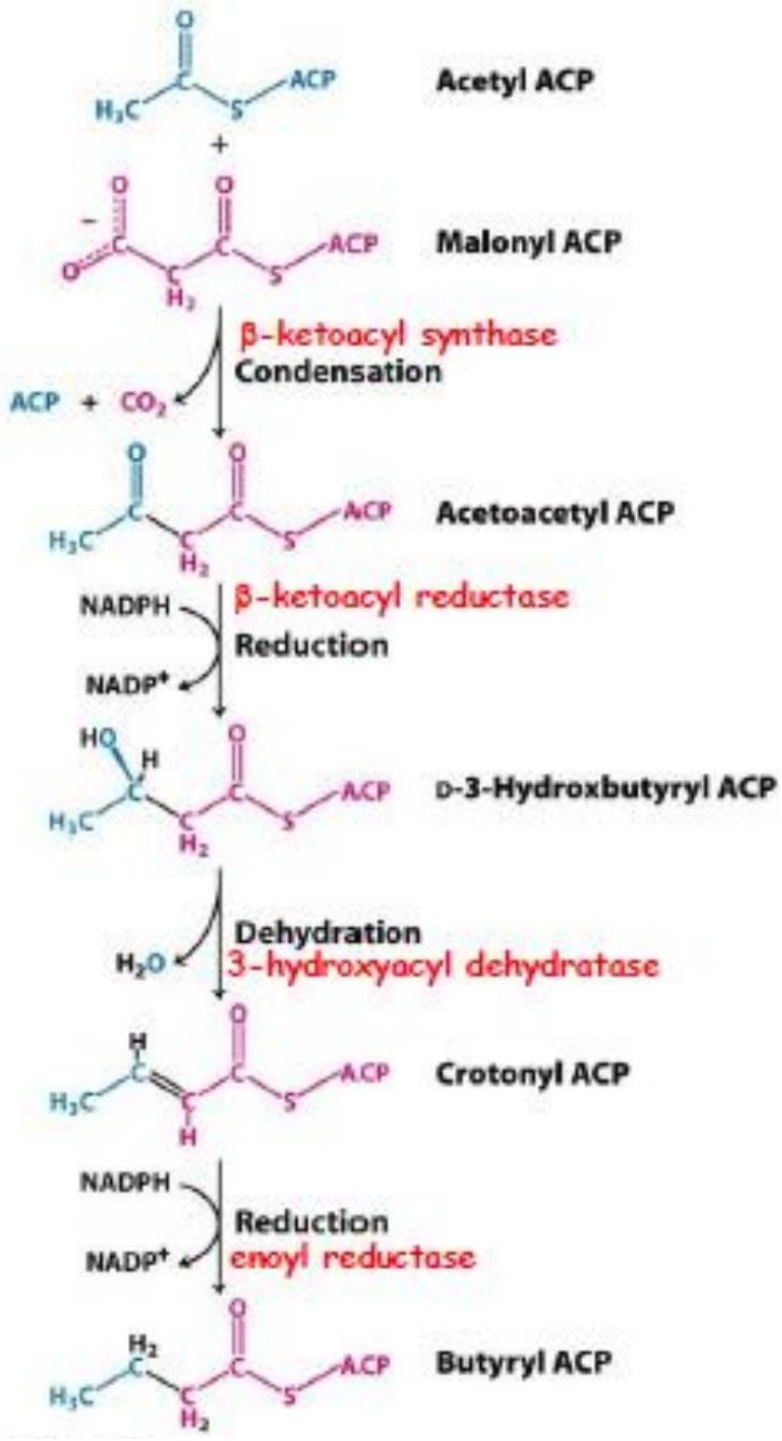
The starting material for de novo synthesis is acetyl CoA. It is formed inside the mitochondria from pyruvate. The inner membrane is not freely permeable to acetyl CoA. Hence the acetyl CoA units are delivered to the cytoplasm as citrate. Citrate is transported from mitochondria by a tricarboxylic acid transporter. In the cytoplasm, citrate is cleaved to oxaloacetate and acetyl CoA in the cytoplasm. The enzyme is ATP citrate lyase. The oxaloacetate can return to the mitochondria by the malate shuttle.

Regulation of Fatty Acid Synthesis

1. Acetyl CoA Carboxylase It is the key enzyme; citrate activates this enzyme. The citrate level is high only when both acetyl CoA and ATP are abundant. Fatty acid synthesis decreases when glucose level is low. The enzyme is inhibited by palmitoyl CoA, the end product.

2. Insulin Favors Lipogenesis Insulin enhances the uptake of glucose byadipocytes and increases the activity of pyruvate dehydrogenase, acetyl CoA carboxylase and glycerol phosphate acyl transferase. Insulin also depresses the hormone sensitive lipase. Insulin also causes inhibition of hormone sensitive lipase, and so lipolysis is decreased.

3. Glucagon Inhibits Lipogenesis Glucagon and epinephrine inactivate the acetyl CoA carboxylase.



Stages of FA Synthesis

1. Transfer of acetyl-CoA from mitochondria to cytosol.

2. Activation of acetyl-CoA; synthesis of malonyl-CoA.

3. Five step elongation cycle of FA synthesis via ACP intermediates.

FA are synthesized by the repetitive condensation of two-carbon units derived from malonyl CoA

Loading of precursors via thioester derivatives, followed by chain elongation

(1) Condensation of the precursors

(2) Reduction

(3) Dehydration

(4) Reduction