

CHAPTER-IV

LIPID METABOLISM

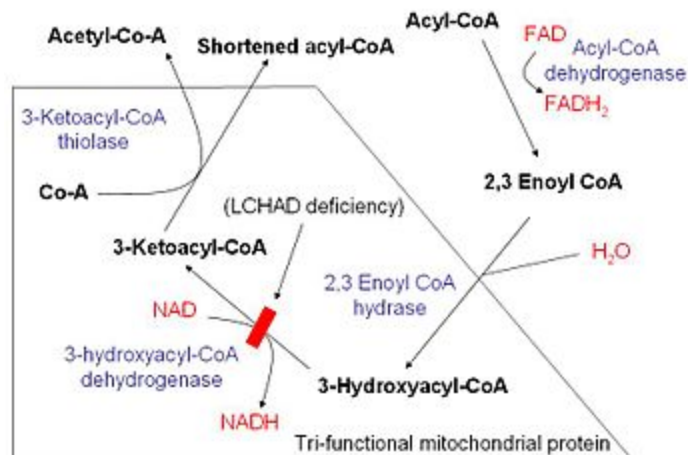
BETA-OXIDATION

Beta-oxidation is the process by which fatty acids, in the form of acyl-CoA molecules, are broken down in mitochondria and/or peroxisomes to generate acetyl-CoA, the entry molecule for the citric acid cycle.

The beta oxidation of fatty acids involve three stages:

1. Activation of fatty acids in the cytosol
2. Transport of activated fatty acids into mitochondria (carnitine shuttle)
3. Beta oxidation proper in the mitochondrial matrix

Fatty acids are oxidized by most of the tissues in the body. However, some tissues such as the adrenal medulla do not use fatty acids for their energy requirements and instead use carbohydrates.



Energy yield

The ATP yield for every oxidation cycle is 14 ATP (according to the P/O ratio), broken down as follows:

Source	ATP	Total
1 FADH ₂	x 1.5 ATP = 1.5 ATP (some sources say 2 ATP) ^[citation needed]	
1 NADH	x 2.5 ATP = 2.5 ATP (some sources say 3 ATP)	
1 acetyl CoA	x 10 ATP = 10 ATP (some sources say 12 ATP)	
TOTAL		= 14 ATP

For an even-numbered saturated fat (C_{2n}), $n - 1$ oxidations are necessary, and the final process yields an additional acetyl CoA. In addition, two equivalents of ATP are lost during the activation of the fatty acid. Therefore, the total ATP yield can be stated as:

$$(n - 1) * 14 + 10 - 2 = \text{total ATP}$$

For instance, the ATP yield of palmitate (C_{16} , $n = 8$) is:

$$(8 - 1) * 14 + 10 - 2 = 106 \text{ ATP}$$

Represented in table form:

Source	ATP	Total
7 $FADH_2$	x 1.5 ATP = 10.5 ATP	
7 NADH	x 2.5 ATP = 17.5 ATP	
8 acetyl CoA	x 10 ATP = 80 ATP	
Activation		= -2 ATP
NET		= 106 ATP

For sources that use the larger ATP production numbers described above, the total would be 129 ATP = $\{(8-1)*17+12-2\}$ equivalents per palmitate.

Beta-oxidation of unsaturated fatty acids changes the ATP yield due to the requirement of two possible additional enzymes.

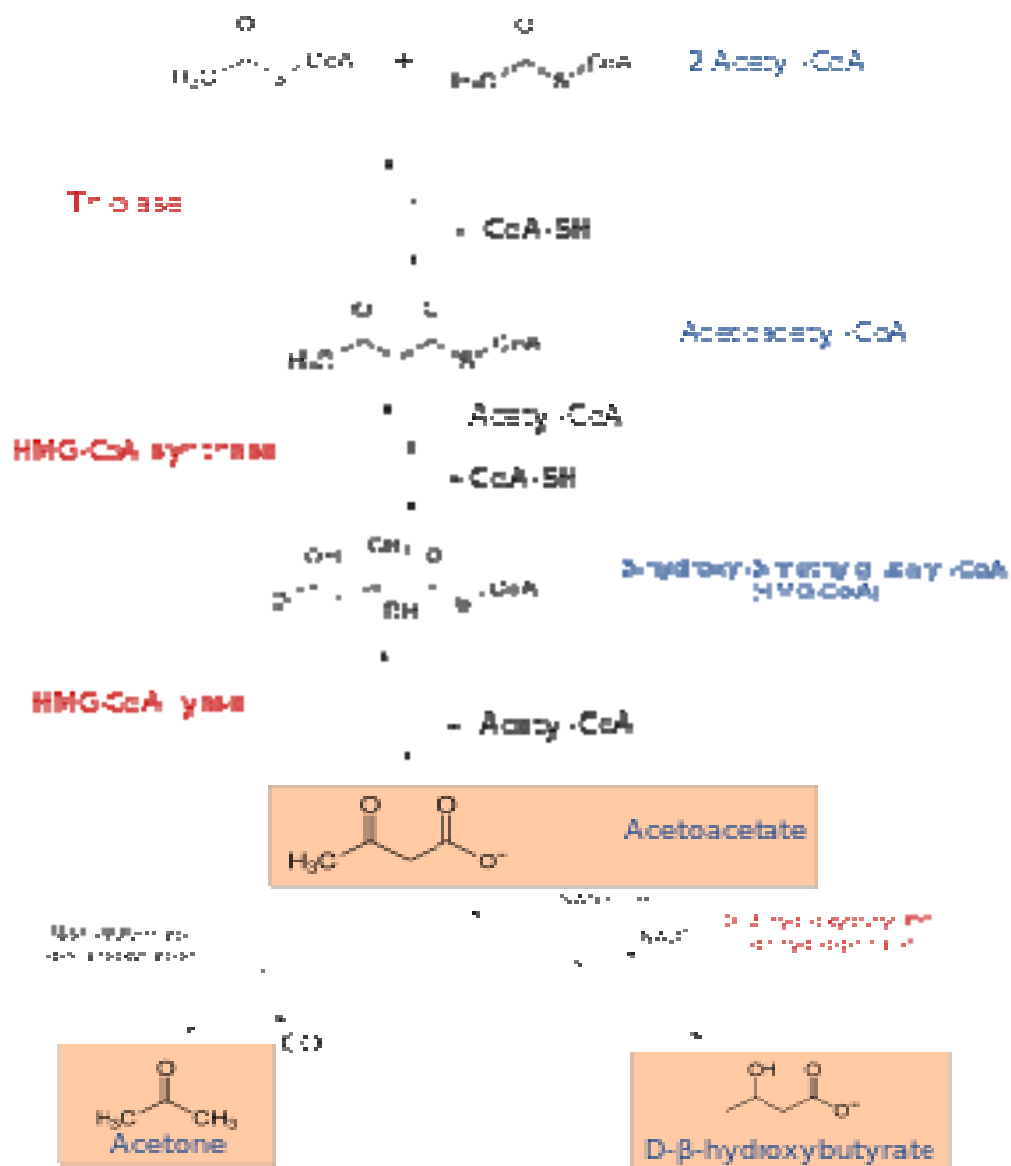
Ketogenesis

Ketogenesis is the process by which ketone bodies are produced as a result of fatty acid breakdown.

Types of ketone bodies

The three ketone bodies are:

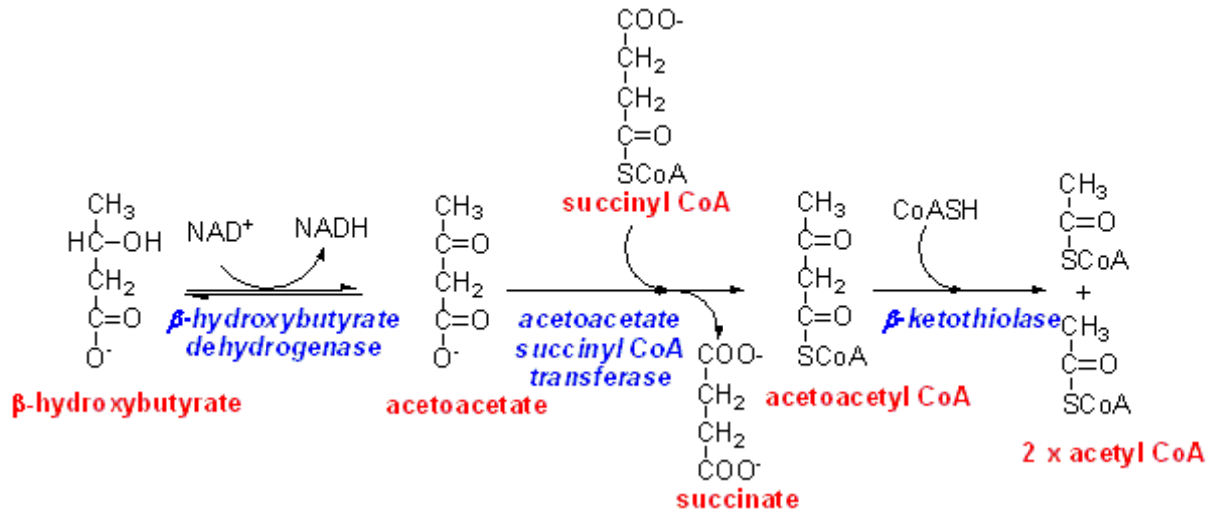
- Acetoacetate, which, if not oxidized to form usable energy, is the source of the two other ketone bodies below
- Acetone, which, unlike free fatty acids, can be used by the brain for energy. Acetone is generated through the decarboxylation of acetoacetate which may occur spontaneously or through the enzyme acetoacetate decarboxylase.
- β -hydroxybutyrate, which is not, in the technical sense, a ketone according to IUPAC nomenclature. It is generated through the action of the enzyme D- β -hydroxybutyrate dehydrogenase on acetoacetate.



Ketogenesis pathway.

Ketolysis

Each of these compounds is synthesized from acetyl-CoA molecules



BioSynthesis of Fatty Acids

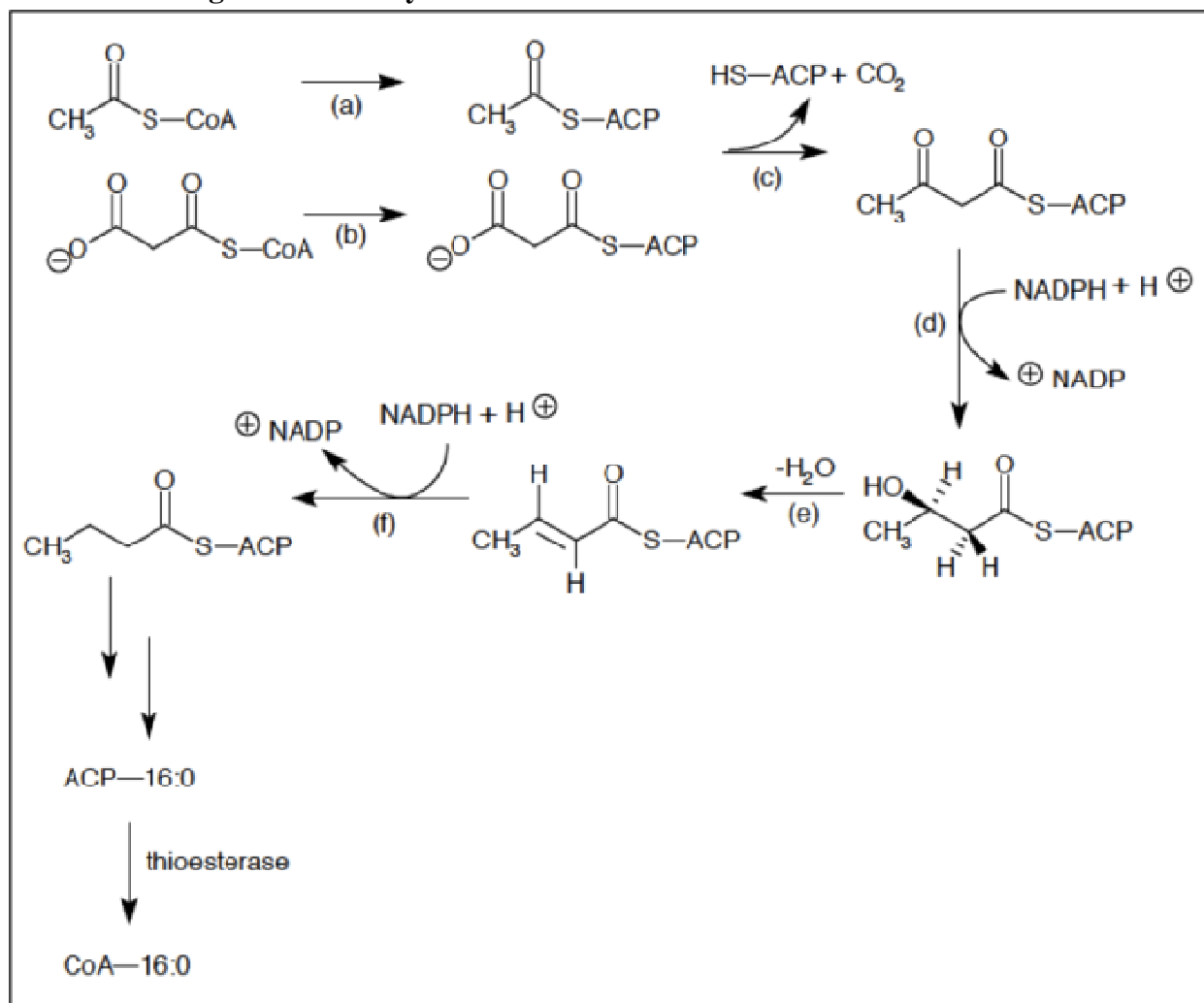
Fatty acid synthesis is the creation of fatty acids from acetyl-CoA and malonyl-CoA precursors through action of enzymes called fatty acid synthases. It is an important part of the lipogenesis process, which - together with glycolysis - stands behind creating fats from blood sugar in living organisms.

Much like β -oxidation, straight-chain fatty acid synthesis occurs via the six recurring reactions shown below, until the 16-carbon palmitic acid is produced.

The diagrams presented show how fatty acids are synthesized in microorganisms and list the enzymes found in *Escherichia coli*. These reactions are performed by fatty acid synthase II (FASII), which in general contain multiple enzymes that act as one complex. FASII is present in prokaryotes, plants, fungi, and parasites, as well as in mitochondria.

In animals, as well as yeast and some fungi, these same reactions occur on fatty acid synthase I (FASI), a large dimeric protein that has all of the enzymatic activities required to create a fatty acid. FASI is less efficient than FASII; however, it allows for the formation of more molecules, including “medium-chain” fatty acids via early chain termination.

Saturated Straight-Chain Fatty Acids



Once a 16:0 carbon fatty acid has been formed, it can undergo a number of modifications, in particular by fatty acid synthase III (FASIII), which uses 2 carbon molecules to elongate preformed fatty acids.

Regulation

Acetyl-CoA is formed into malonyl-CoA by acetyl-CoA carboxylase, at which point malonyl-CoA is destined to feed into the fatty acid synthesis pathway. Acetyl-CoA carboxylase is the point of regulation in saturated straight-chain fatty acid synthesis, and is subject to both phosphorylation and allosteric regulation. Regulation by phosphorylation occurs mostly in mammals, while allosteric regulation occurs in most organisms. Allosteric control occurs as feedback inhibition by palmitoyl-CoA and activation by citrate. When there are high levels of palmitoyl-CoA, the final product of saturated fatty acid synthesis, it allosterically inactivates acetyl-CoA carboxylase to prevent a build-up of fatty acids in cells. Citrate acts to activate

acetyl-CoA carboxylase under high levels, because high levels indicate that there is enough acetyl-CoA to feed into the Krebs cycle and produce energy.

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