METABOLISM
OF
LIPID

METABOLISM OF LIPIDS

- Lipid, any of a diverse group of organic compounds including fats, oils, hormones, and certain components of membranes are grouped together because they do not interact appreciably with water. One simple type of lipid, the triglycerides, is stored as fat in adipose cells, which serve as the energy-storage depot for organisms and also provide thermal insulation. Some lipids such as steroid hormones serve as chemical messengers between cells, tissues, and organs, and others communicate signals between biochemical systems within a single cell. The membranes of cells and organelles (structures within cells) are microscopically thin structures formed from two layers of phospholipid molecules. Lipids are not large macromolecular polymers (e.g., proteins, nucleic acids, and polysaccharides); many are formed by the chemical linking of several small constituent molecules. Many of these molecular building blocks are similar, or homologous, in structure. The homologies allow lipids to be classified into a few major groups: fatty acids, fatty acid derivatives, cholesterol and its derivatives, and lipoproteins.

- Fatty acid
- Fatty acid rarely occur as free molecules in nature but are usually found as components of many complex lipid molecules such as fats (energy-storage compounds) and phospholipids (the primary lipid components of cellular membranes). Biological fatty acids, members of the class of compounds known as carboxylic acids, are composed of a hydrocarbon chain with one terminal carboxyl group (COOH). The fragment of a carboxylic acid not including the hydroxyl (OH) group is called an acyl group.

- Saturated fatty acid--
- The simplest fatty acids are unbranched, linear chains of CH_2 groups linked by carbon-carbon single bonds with one terminal carboxylic acid group. The term saturated indicates that the maximum possible numbers of hydrogen atoms are bonded to each carbon in the molecule. Examples are: lauric acid (12), myristic acid (14).
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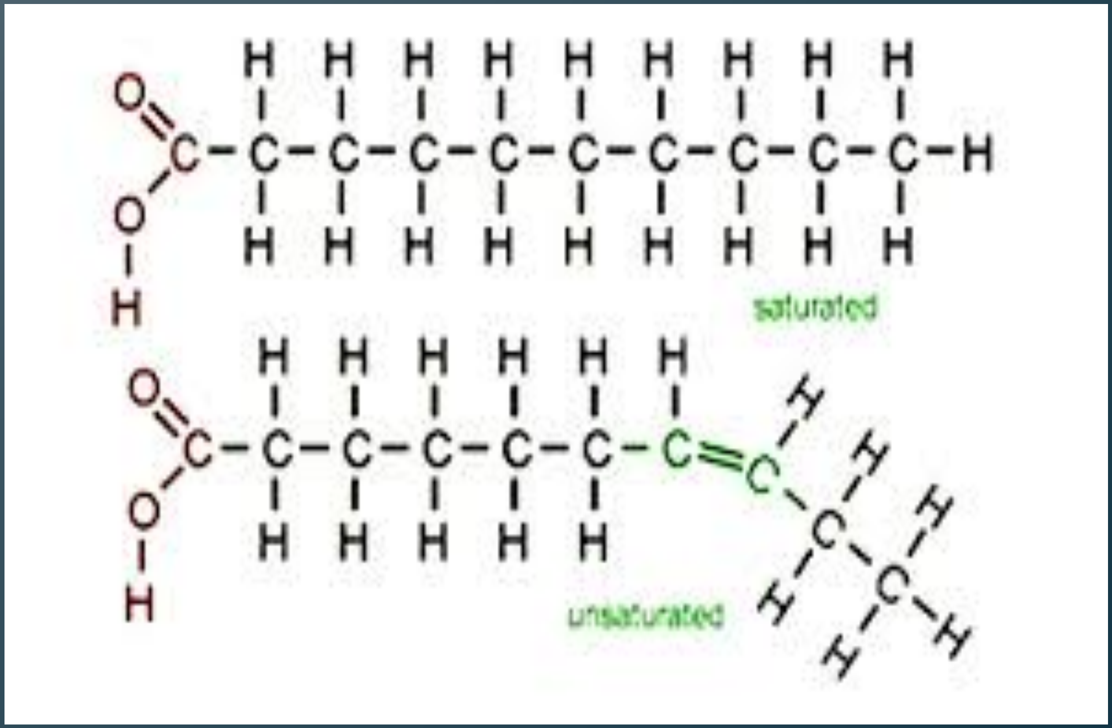


- Unsaturated fatty acid--
- Unsaturated fatty acids have one or more carbon-carbon double bonds. The term unsaturated indicates that fewer than the maximum possible numbers of hydrogen atoms are bonded to each carbon in the molecule. The number of double bonds is indicated by the generic name—monounsaturated for molecules with one double bond or polyunsaturated for molecules with two or more double bonds. Oleic acid is an example of a monounsaturated fatty acid.

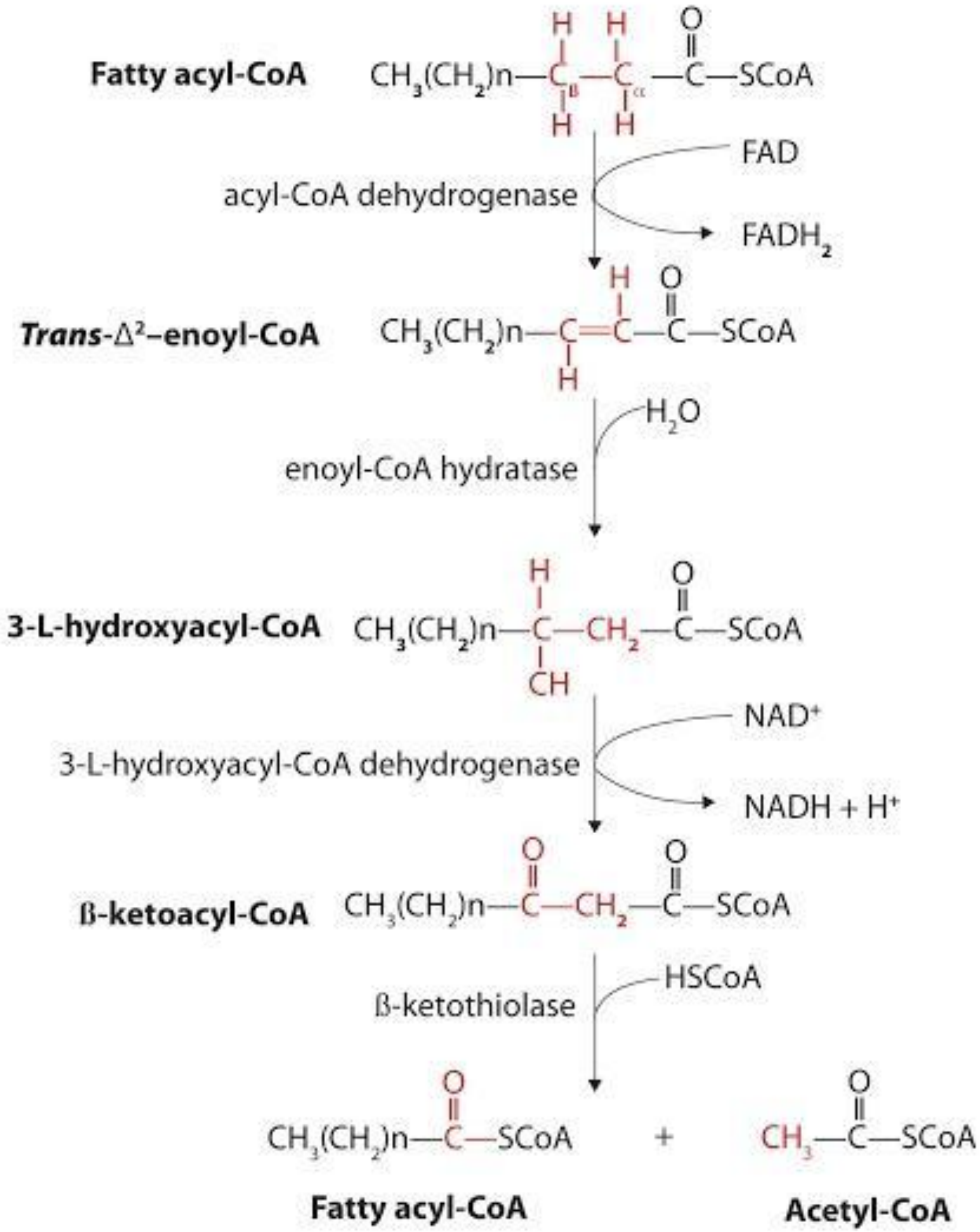
- Catabolism of lipids—
- At first Dietary triglycerides solubilization into finely dispersed microscopic micelles by bile acid. These micelles are accessible for intestinal lipases and converts triglycerides into monoacylglycerols, diacylglycerols, free fatty acid, glycerol.
- TYPES OF FATTY ACID OXIDATION
- 1) Beta oxidation- Major mechanism occurs in the mitochondria matrix. 2-C units are released as acetyl CoA per cycle.
- 2) Alpha oxidation- Predominantly takes place in brain and liver, one carbon is lost in the form of CO2 per cycle.
- 3) Omega oxidation- Minor mechanism, but becomes important in conditions of impaired beta oxidation
- 4) Peroxisomal oxidation- Mainly for the trimming of very long chain fatty acids.

- Fatty acid beta –oxidation--
- Fatty acid β-oxidation is a multistep process by which fatty acids are broken down by various tissues to produce energy. Fatty acids primarily enter a cell via fatty acid protein transporters on the cell surface. Beta-oxidation takes place in mitochondrial compartment and their transport from cytosol to this compartment happens through a system known as carnitine –shuttle system. Once the fatty acid is inside the mitochondrial matrix, beta-oxidation occurs by cleaving two carbons every cycle to form acetyl-CoA. The process consists of 4 steps:

1. First step, a long-chain fatty acid is dehydrogenated to create a Trans double bond between C2 and C3. This is catalyzed by acyl CoA dehydrogenase to produce trans-delta 2-enoyl CoA. It uses FAD as an electron acceptor and it is reduced to FADH2.
2. Second step, Trans-delta2-enoyl CoA is hydrated at the double bond to produce L-3-hydroxyacyl CoA by enoyl-CoA hydratase.
3. Third step, L-3-hydroxyacyl CoA is dehydrogenated again to create 3-ketoacyl CoA by 3-hydroxyacyl CoA dehydrogenase. This enzyme uses NAD as an electron acceptor.
4. Fourth step, Thiolysis occurs between C2 and C3 (alpha and beta carbons) of 3-ketoacyl CoA. Thiolase enzyme catalyzes the reaction when a new molecule of coenzyme A breaks the bond by nucleophilic attack on C3,beta carbon that’s why it is known as beta oxidation. This releases the first two carbon units, as acetyl CoA, and a fatty acyl CoA minus two carbons. The process continues until all of the carbons in the fatty acid are turned into acetyl CoA.

- Fatty acids are oxidized by most of the tissues in the body. However, some tissues such as the red blood cells of mammals (which do not contain mitochondria), and cells of the central nervous system do not use fatty acids for their energy requirements, instead use carbohydrates.

- Beta-oxidation is a significant source of metabolic energy during starvation periods and high energy demand states, such as exercise. These metabolic conditions induce the release of fatty acids from adipose tissue due to the secretion of circulating mediators, such as epinephrine and glucagon, which increase the rate of lipolysis. This metabolic pathway provides a large portion of the energy requirement of skeletal muscle, heart muscle, and kidneys when glycogen and gluconeogenic precursors concentration becomes small.



Fatty acyl-CoA
CH3(CH2)n—Cβ—Cα—C—SCoA
FAD
acyl-CoA dehydrogenase
FADH2
Trans-Δ2–enoyl-CoA
CH3(CH2)n—C=C—C—SCoA
H2O
enoyl-CoA hydratase
3-L-hydroxyacyl-CoA
CH3(CH2)n—C—CH2—C—SCoA
NAD+
3-L-hydroxyacyl-CoA dehydrogenase
NADH + H+
ß-ketoacyl-CoA
CH3(CH2)n—C—CH2—C—SCoA
HSCoA
ß-ketothiolase
CH3(CH2)n—C—SCoA
+
CH3—C—SCoA
Fatty acyl-CoA
Acetyl-CoA

- Anabolism of fatty acid
- Fatty acids are synthesized using fatty acid synthases(FAS) that polymerize and then reduce acetyl-CoA units.
- In animals and fungi, all these fatty acid synthase reactions are carried out by a single multifunctional type I protein. In plants, plasmids and bacteria separate type II enzymes perform each step in the pathway.
- Acetyl-CoA is transported to the cytoplasm from the mitochondrion in the form of citrate and other most required is a reducing equivalent is NADPH so both acetyl-COA and NADPH are base of fatty acid formation. the process takes place in three major steps: the citrate shuttle, acetyl-CoA carboxylase (the rate-limiting step), and fatty acid synthase complex.

- ACETYL CO-A CARBOXYLASE –this enzyme catalyzes conversion of a 2 carbon compound acetyl co-A into malonyl co-A which undergoes 4 steps of sequential reactions catalyzed by fatty acid synthase complex:
- Condensation
- Reduction
- Dehydrogenation
- Reduction
- An acetyl co-A act as primer for this reaction and malonyl co-A act as chain extender in this process. FAS extend this chain by two carbon after each CRDR reaction and ultimately a 16 C Palmittic acid is formed, which can be further elonagate to make more than 16C carbon fatty acid.
- Fatty acid are converted into their tryglyceride form for further storage and during high demand of energy of body can be used.