

Lipid Metabolism: Fatty Acid Metabolism

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Lipids are organic molecules that are composed of the elements carbon, hydrogen, and oxygen, with the hydrogen to oxygen ratio greater than 2:1. They are highly hydrophobic because of having a long hydrocarbon chain. This family of the compound includes fats, waxes, steroids, and phospholipids. This article focuses more on the metabolic processes involved in processing fats and fatty acids.



Fats and Oils

Fats and oils are the **most common forms of lipids**. Their main roles are to provide energy, insulate the body and facilitate the transport of fat-soluble vitamins. Fat is a natural lipid material that is normally solid at room temperature. Oils are similar to fats except that they are generally liquid at room temperature.

These two materials are integral parts of the **human diet**. They are normally used as a **shortening agent in food processing**. It normally provides **lubrication** in some food products, and may also **give structure** to baked materials such as cakes and doughnuts. Oils are also used for **frying** different food products. Because of the **high heat transfer properties** of the oil, it is normally used to produce foods that are crisp and firm.

Aside from its function as a shortening agent, oil also contributes a great amount in terms of the **taste** of the food. When food products are fried, certain **oxidation reactions** occur producing a complex set of possible flavors. Olive oil, for example, is a good oil to use for gourmet food products and in pasta and salad dressing. Coconut and palm oil, on

the other hand, are very good for frying.

The last main important purpose of fats and oil is that because of their dense nature, they have easily stored **sources of calories**. Also, because of their **non-polar** nature, they can be used to transport various **fat-soluble vitamins** such as vitamins A, D, and E. In the human body, lipids also play a big role in the **synthesis of lipid hormones**. Different **polyunsaturated fatty acids** are needed by the body to produce **prostaglandins**.

Structure of fats and oils

Fats and oils are generally called **triglycerides or triacylglycerols**. The general structure of a triglyceride is composed of three fatty acids units joined to glycerol and trihydroxy alcohol.

Lipid Metabolism

Lipid metabolism can be divided into **two major types**. One of these is **lipogenesis**, which involves the **synthesis of lipids and fatty acid oxidation** in which energy is produced when fatty acids are metabolized. The metabolism of lipids is closely related to the metabolic processes for carbohydrates. This is because there are times when carbohydrates are metabolized, sometimes forming fats.

Triacylglycerols are transported in body fluids by molecules called **lipoproteins**. The general configuration of a lipoprotein involves having the **hydrophobic region** inside the core of the sphere, while the superficial layer is composed of the **hydrophilic regions**.

At different parts of the **digestive tract**, metabolism of triacylglycerols may occur. The mechanism of metabolism is facilitated by a group of enzymes called lipases. **Lipases catalyze the hydrolysis of the ester bond of the triacylglycerol**.

Lipases are generally classified as **intracellular or extracellular**. Intracellular lipases include **hormone-sensitive lipase** in adipocytes and lysosomal lipases. Extracellular lipases, on the other hand, include **pancreatic lipase** and **lipoprotein lipase**.

Hormones control the activity of hormone-sensitive lipase. An example of this is the increase in lipase activity when an individual suffers from stress. The stress triggers a release of the hormones **adrenaline/noradrenaline**.

The hormone attaches itself to a receptor which eventually leads to the processing of inactive lipases to convert them to active ones. **Active lipases** separate the **triacylglycerol into glycerol and free fatty acids**. The fatty acids produced are taken up from the blood plasma by tissues that require nutrients.

On the other hand, **glycerol**, since it cannot be utilized in adipocytes, serves as a substrate for gluconeogenesis in the liver.

Glycerol is acted upon by **glycerol kinase**, consuming one ATP in the process, to produce **L-glycerol-3-phosphate (L-G3P)**. L-G3P will be converted to a **dihydroxyacetone phosphate** using **glycerol phosphate dehydrogenase**. An **NAD⁺** is also converted to **NADH** in the process.

Finally, the dihydroxyacetone phosphate readily isomerizes to form the **D-glyceraldehyde-3-phosphate**.

To be able to synthesize triacylglycerol back, a glycerol-3-phosphate can be processed by

first reacting it with a fatty acid in the presence of an **acyltransferase** and in the expense of a FAD molecule. Addition of one fatty acid leads to the production of a **lysophosphatidic molecule**. The process can be repeated to add another fatty acid to glycerol, forming a **phosphatidic acid**.

The next step is to **remove the phosphate group** using **phosphatase**. The product for this step is a **diacylglycerol**. Another fatty acid may then **esterify** with the last OH group of the diacylglycerol to produce the triacylglycerol.

Fatty Acid Metabolism

Fatty acids metabolism involves a catabolic process that generates energy and an anabolic process that creates biologically important molecules (triglycerides, phospholipids, second messengers and hormones). Fatty acids are one of the major forms of storage of metabolic energy. They are good sources of energy because they are mainly composed of **-CH₂ groups** which can be readily reduced. Because of their **hydrophobic** nature, they need not to be solvated, compared to carbohydrates. The long hydrophobic tail of fatty acids can be packed tightly in storage tissues. This allows for concentrated storage.



Image: "1st step of beta-oxidation." by NEUROtiker - Own work.
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One of the important metabolic processes that occur in fatty acids is **β-oxidation**. Here, short fatty acid chains are transported into the **mitochondrial matrix** as free acids. As they enter the mitochondrial matrix, they are activated by the enzyme **acyl-CoA synthetase** to convert it into **acyl-CoA**. Long chains of fatty acids move to inner parts of the mitochondrial membrane and are converted to **acyl-carnitine**. The acyl group of the molecule is then transferred to CoA to form **acyl-CoA**.

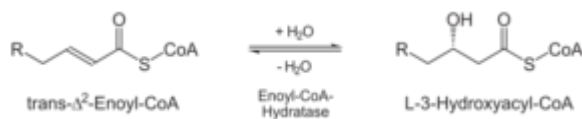


Image: "2nd step of beta-oxidation." by NEUROtiker - Own work.
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The **saturated fatty acyl-CoA** molecule will be degraded in a series of four reactions that are part of the β-oxidation. The first reaction involves **oxidizing the molecule through the α and β-carbon forming a double bond**. **Acyl-CoA dehydrogenase** catalyzes this process at the expense of a **FAD molecule**. The product of this process is **trans-Δ²-enoyl CoA**.

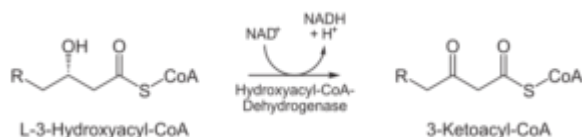


Image: "3rd step of beta-oxidation." by NEUROtiker - Own work.
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In the second step, the trans- Δ^2 -enoyl CoA will be **hydrated** in the presence of an **enoyl-CoA hydratase** forming an **L-3-hydroxy acyl CoA**. It is then oxidized further to **3-ketoacyl CoA** using **L-3-hydroxy acyl CoA dehydrogenase** as a catalyst. This process proceeds using up one NAD⁺ to form NADH and H⁺.

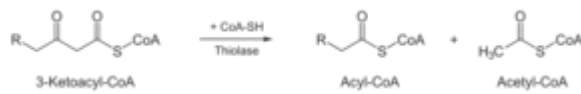


Image: "4th step of beta-oxidation." by NEUROtiker - Own work.
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The final step is **catalyzing by thiolase**. A **cysteine residue** in the enzyme attacks the **β -keto carbon atom**. **Bond cleavage** occurs producing the **enolate of acetyl CoA** and a **thioester intermediate**. The final product of β -oxidation is a **2-carbon shorter acyl-CoA**. These β -oxidation steps are successively repeated until enough acetyl CoA units are produced.

Fatty Acid Biosynthesis

Fatty acid synthesis follows the **same sequence as β -oxidation**, except it is in the **reverse order**. It is the creation of fatty acids from acetyl CoA and NADPH through actions of fatty acid synthetases in the cytoplasm of cells. Here, **NADPH acts as a reductant** to reduce the **ketoacyl** and **enoyl intermediate** of the process.

The whole synthesis process obtains **enough energy** from the **decarboxylation** step for it to occur.

References

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