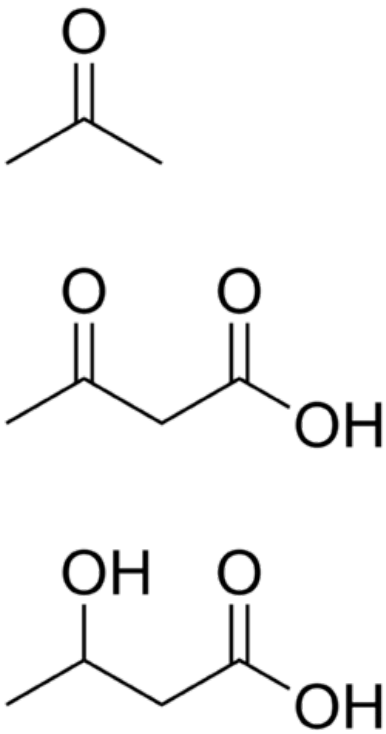
Formation of ketone bodies

Ketone (*bodies*) include **acetoacetate**, **β-hydroxybutyrate** and **acetone**. The main site of their formation is the **mitochondria of hepatocytes**. Ketones represent a water-soluble transport form of acetyls. It is formed when there is an **excess of acetyl~CoA** produced by liver beta-oxidation – the liver „pre-chews“ fatty acids and provides the body with ketone bodies as **an alternative source of energy**.



Chemical structures of various ketone bodies – acetone, acetoacetate, β-hydroxybutyrate

The entry of AcCoA into the Krebs cycle depends on the availability of oxaloacetate. It is produced by the carboxylation of pyruvate. During starvation or diabetes mellitus OAA is consumed in the process of gluconeogenesis. The lack carbohydrates leads to a decrease in the amount of OAA and thus to a slowing down of the Krebs cycle. It could be said that "fats burn in the fire of carbohydrates"..

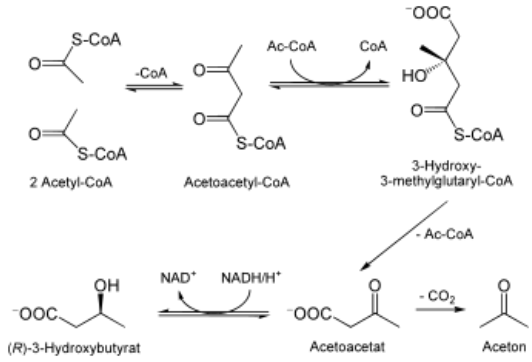
The environment of the organism

Before we get to the specific reactions of the formation of ketone bodies – **ketogenesis**, we will describe the situation in the organism under which it takes place. At the beginning is the **activation of lipolysis** through **hormone-sensitive lipase** (HSL). After the activation of lipolysis, plasma concentrations of fatty acids increase, which enter the liver cells to an increased extent. In them, they undergo **β-oxidation**, which produces **an excess of AcCoA**. It cannot be used sufficiently in other pathways and therefore enters ketogenesis. Therefore, the source of carbon atoms in ketogenesis is only **acetyl~CoA**.

The course of the formation of ketone bodies

The course of the formation of ketone bodies can be described by the following reactions:

1. **Condensation of two molecules of AcCoA → acetoacetyl~CoA** .
2. **Reaction with another AcCoA → 3-hydroxy-3-methylglutaryl~CoA** (HMG~CoA).
3. **Cleavage of HMG~CoA → AcCoA and acetoacetate**.
4. **Reversible conversion of acetoacetate and β-hydroxybutyrate**.
5. **Decarboxylation of acetoacetate**.



Ketogenesis

β-Ketothiolase

β-Ketothiolase catalyzes the last step of β-oxidation of fatty acids – **thiolytic cleavage**. During the formation of ketone bodies, the **reaction is reversed** and one molecule of acetoacetyl~CoA is formed from two molecules of AcCoA. The reaction takes place in the **matrix of mitochondria**.

3-hydroxy-3-methylglutaryl-CoA synthase

This enzyme catalyzes **the condensation of acetyl-CoA with acetoacetyl-CoA**. Condensation takes place on the third carbon of acetoacetyl~CoA to form **3-hydroxy-3-methylglutaryl-CoA**. This important intermediate occurs not only in the metabolism of ketone bodies, but also occurs during the **synthesis of cholesterol**.

3-hydroxy-3-methylglutaryl-CoA lyase

This enzyme catalyzes the **cleavage of HMG-CoA** into acetoacetate and AcCoA. This **creates the first ketone body**.

β-hydroxybutyrate dehydrogenase

This enzyme catalyzes the mutua **reversible conversion of** two ketone bodies – acetoacetate and β-hydroxybutyrate. The cofactor is NAD^+. During the massive formation of ketone bodies **β-hydroxybutyrate** is quantitatively the most important ketone body in the blood, i.e. most of the acetoacetate is converted to it.

Decarboxylation of acetoacetate

Part of the acetoacetate molecules **spontaneously** i.e. **non-enzymatically decarboxylates into acetone**, which has no use in the human body and is **excreted by** breathing or urine.

Links

related articles

- Keto bodies
- Ketone bodies in the urine
- Ketoacidosis

External links

- Ketomolecules (Czech wikipedia) (https://cs.wikipedia.org/wiki/Ketol%C3%A1tky%7C)

Template:Navbox - Transformation of substances and energy in the cell