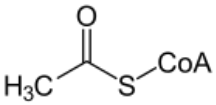
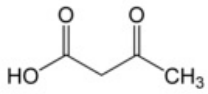
Ketones

Ketone bodies are the product of the **oxidation of fatty acids**. Acetyl-CoA molecules are either passed directly to the citrate cycle , where they are oxidized to carbon dioxide and water to release energy , or they are the building blocks for the synthesis of fatty acids and cholesterol in the physiological state. During starvation or dietary regimens with strict carbohydrate restrictions or in pathological conditions such as diabetes , excess acetyl-CoA is converted to ketone bodies - acetoacetate, acetone and β-hydroxybutyrate . When there is a lack of glucose in the bloodstream, the body uses fat stores as a source of energy. In order for this energy to be released, the fats must first be converted to ketone bodies.



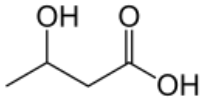
Acetyl-CoA

Ketones



Acetoacetic acid

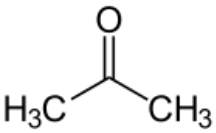
- **Acetoacetic acid**
- **β-hydroxybutyric acid**
- **Acetone**



Beta-hydroxybutyric acid

Ketone bodies are produced by the liver and from there it passes into the blood. They are further processed by extrahepatic tissues. Their levels increase during starvation and diabetes . The essence of ketone bodies is increased mobilization of fatty acids from adipose tissue → transport to the liver. This is reflected in the increased production of acetyl-CoA by the β-oxidation mechanism of fatty acids. Subsequently, the capacity of the citrate cycle will be exceeded (oxaloacetate is missing) → synthesis of ketone bodies.

Synthesis of ketone bodies



Acetone

- **1.** Acetoacetyl-CoA is an intermediate in fat breakdown. Acetoacetyl-CoA can be formed by the condensation of two acetyl-CoA.
- **2.** Condensation of acetoacetyl-CoA with the acetyl-CoA molecule gives β-hydroxy-β-methylglutaryl-CoA = HMG-CoA. It is used in the physiological state to produce steroid substances such as cholesterol. In plants, it is used to synthesize terpenes and carotenes.
- **3.** HMG-CoA can be further cleaved by lyase to acetoacetate and acetyl-CoA.
  1. Acetoacetate is formed by non-enzymatic (spontaneous) decarboxylation to form acetone.
  2. Another possibility is the reduction of acetoacetate by liver dehydrogenase to β-hydroxybutyric acid (β-hydroxybutyrate).

Conversion of ketone bodies to acetyl-CoA

Under normal circumstances, ketone bodies serve as *metabolic fuel* for some peripheral tissues - heart, skeletal muscle, kidneys, and for longer tissue during brain starvation (60-70%). They are water-soluble equivalents of fatty acids, so their utilization always takes place on the periphery. They do not bind to proteins.

The human body uses only acetoacetate and β-hydroxybutyrate as its energy source. Acetone is exhaled with exhaled air or excreted in the urine. β-hydroxybutyrate is oxidized to acetoacetate. Acetoacetate must first be activated to the active form acetoacetyl-CoA. Coenzyme A donor is succinyl-CoA, from which coenzyme A is enzymatically transferred to acetoacetate. The enzyme responsible for this reaction is found in all tissues except the liver, and for this reason, ketone bodies are used by extrahepatic tissues, but not by the liver. Acetoacetyl-CoA can be broken down into 2 molecules of acetyl-CoA, which are oxidized in the citrate cycle.

Ketosis

- Normal ketone blood levels: < 0.2 mmol/L
- **Ketosis** – a physiological condition during starvation and low-carbohydrate diets, when glycogen is depleted and body fat has become a source of energy, ketonemia 1–3 mmol/L
- Ketoacidosis – a pathological condition in diabetes mellitus, characterized by acidosis, high ketosis > 3 mmol/L , ketonuria, manifested by nausea and vomiting

Links

Related articles

- Slimming diet
- β-oxidation
- Diabetes mellitus
- Acetyl-CoA

Bibliography

- DOLEČEK, Rajko, Prof. MUDr., DrSc .. *Metabolic syndrome* [lecture on the subject Monitoring and therapy of obesity, field of study Medicine, 1st Faculty of Medicine Charles University]. Prague. 9/10/2012
- KOOLMAN, Jan and Klaus-Heinrich RÖHM. *Color atlas of biochemistry.* 1st edition. Prague: Grada, 2012. 512 pp. ISBN 978-80-247-2977-0 .
- MATOUS, Bohuslav, et al. *Basics of medical chemistry and biochemistry.* 1st edition. Prague: Galén, 2010. 540 pp. ISBN 978-80-7262-702-8 .
- ŠKARYDOVÁ, Lucie, Mgr .. *Metabolism of fats and fatty acids II.* [lecture on the subject General Biochemistry, field of study Pharmacy, Faculty of Pharmacy Charles University]. Hradec Králové. 3/29/2011
- WEDNESDAY, Leos, Doc. MUDr., Ph.D .. *Therapy of overweight and obesity, active diets* [lecture on the subject Monitoring and therapy of obesity, field of study Medicine, 1st Faculty of Medicine Charles University]. Prague. 9/10/2012

References

1. MATOUŠ, Bohuslav and ET AL .. *Basics of medical chemistry and biochemistry.* 1st edition. Prague: Galén, 2010. 540 pp. 156. ISBN 978-80-7262-702-8 .