

Ketone bodies

Ketone bodies are three water-soluble compounds that are produced as by-products when fatty acids are broken down for energy in the liver and kidney. Two of the three are used as a source of energy in the heart and brain while the third is a waste product excreted from the body. In the brain, they are a vital source of energy during fasting.^[1] Although termed "bodies", they are dissolved substances, not particles.

The three endogenous ketone bodies are acetone, acetoacetic acid, and beta-hydroxybutyric acid,^[2] although beta-hydroxybutyric acid is not technically a ketone but a carboxylic acid. Other ketone bodies such as beta-ketopentanoate and beta-hydroxypentanoate may be created as a result of the metabolism of synthetic triglycerides such as triheptanoin.

Uses in the heart and brain

Ketone bodies can be used for energy. Ketone bodies are transported from the liver to other tissues, where acetoacetate and beta-hydroxybutyrate can be reconverted to acetyl-CoA to produce energy, via the citric acid cycle.

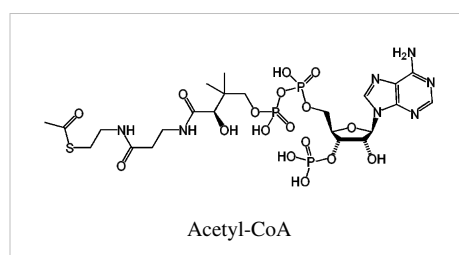
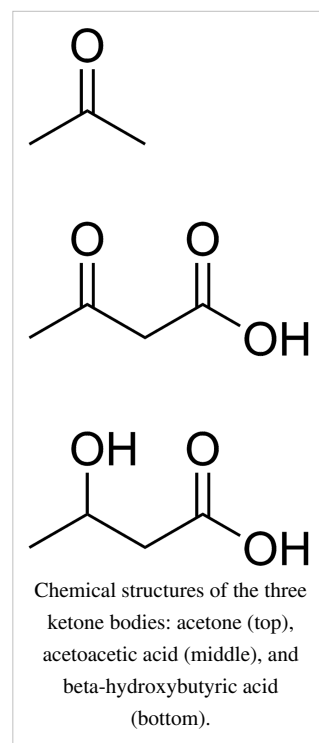
The heart gets little energy from ketone bodies except under special circumstances; it uses mainly fatty acids.^[3]

The brain gets a portion of its energy from ketone bodies when glucose is less available (e.g., during fasting, strenuous exercise, low carbohydrate, ketogenic diet and in neonates). In the event of low blood glucose, most other tissues have additional energy sources besides ketone bodies (such as fatty acids), but the brain does not. After the diet has been changed to lower blood glucose for 3 days, the brain gets 25% of its energy from ketone bodies.^[4] After about 4 days, this goes up to 70% (during the initial stages the brain does not burn ketones, since they are an important substrate for lipid synthesis in the brain).

Production

Ketone bodies are produced from acetyl-CoA (see ketogenesis) mainly in the mitochondrial matrix of hepatocytes when carbohydrates are so scarce that energy must be obtained from breaking down fatty acids. Because of the high level of acetyl CoA present in the cell, the pyruvate dehydrogenase complex is inhibited, whereas pyruvate carboxylase becomes activated. The oxaloacetate produced will enter gluconeogenesis rather than the citric acid cycle, and the latter is also inhibited by the elevated level of NADH resulting from β -oxidation of fatty acids. Unable to be used in the citric acid cycle, the excess acetyl-CoA is therefore rerouted to ketogenesis. Such a state in humans is referred to as the fasted state.

Acetone is produced by spontaneous decarboxylation of acetoacetate (meaning this ketone body will break down in five hours if it is not needed for energy and be removed as waste. This "use it or lose it" factor contributes to much of the weight loss found in ketogenic diets.). Acetone cannot be converted back to acetyl-CoA, so it is excreted in the urine, or (as a consequence of its high vapor pressure) exhaled. Acetone is responsible for the characteristic "fruity" odor of the breath of persons in ketoacidosis.^[5]



Ketosis and ketoacidosis

Any production of these compounds is called ketogenesis, and this is necessary in small amounts.

However, when excess ketone bodies accumulate, this abnormal state is called ketosis. Ketosis can be quantified by sampling the patient's exhaled air, and testing for acetone by gas chromatography.^[6] Many diabetics self test for the presence of ketones using blood or urine testing kits.

When even larger amounts of ketone bodies accumulate such that the blood's pH is lowered to dangerously acidic levels, this state is called ketoacidosis.

Impact upon pH

Both acetoacetic acid and beta-hydroxybutyric acid are acidic, and, if levels of these ketone bodies are too high, the pH of the blood drops, resulting in ketoacidosis.

This happens most often in untreated Type I diabetes, and somewhat less often in Type II (see diabetic ketoacidosis).

References

- [1] Mary K. Campbell, Shawn O. Farrell (2006). *Biochemistry* (5th ed.). Cengage Learning. p. 579. ISBN 0534405215.
- [2] Lori Laffel (1999). "Ketone bodies: a review of physiology, pathophysiology and application of monitoring to diabetes". *Diabetes/Metabolism Research and Reviews* **15** (6): 412–426. doi:10.1002/(SICI)1520-7560(199911/12)15:6<412::AID-DMRR72>3.0.CO;2-8. PMID 10634967.
- [3] Kodde IF, van der Stok J, Smolenski RT, de Jong JW (January 2007). "Metabolic and genetic regulation of cardiac energy substrate preference". *Comp. Biochem. Physiol., Part a Mol. Integr. Physiol.* **146** (1): 26–39. doi:10.1016/j.cbpa.2006.09.014. PMID 17081788.
- [4] Hasselbalch, SG; Knudsen, GM; Jakobsen, J; Hageman, LP; Holm, S; Paulson, OB (1994). "Brain metabolism during short-term starvation in humans.". *Journal of cerebral blood flow and metabolism* **14** (1): 125–31. doi:10.1038/jcbfm.1994.17. PMID 8263048.
- [5] American Diabetes Association-Ketoacidosis (<http://www.diabetes.org/living-with-diabetes/complications/ketoacidosis-dka.html>)
- [6] K. Musa-Veloso, S. S. Likhodii and S. C. Cunnane (2002). "Breath acetone is a reliable indicator of ketosis in adults consuming ketogenic meals" (<http://www.ajcn.org/cgi/content/abstract/76/1/65>). *Am J Clin Nutr* **76** (1): 65–70. PMID 12081817. .

External links

- *emerg/135* (<http://www.emedicine.com/emerg/topic135.htm#>) at eMedicine - Diabetic Ketoacidosis
- Fat metabolism at unisanet.unisa.edu.au (<http://www.unisanet.unisa.edu.au/08366/h&p2fat.htm>)
- NHS Direct Online Health Encyclopaedia, Ketosis (<http://www.nhsdirect.nhs.uk/en.asp?TopicID=274>)
- BioCarta Pathways Formation of Ketone Bodies (<http://www.biocarta.com/pathfiles/ketonebodiesPathway.asp>)
- MeSH *Ketone+Bodies* (http://www.nlm.nih.gov/cgi/mesh/2011/MB_cgi?mode=&term=Ketone+Bodies)

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