Science Review:
The Ketogenic Diet for Weight Management

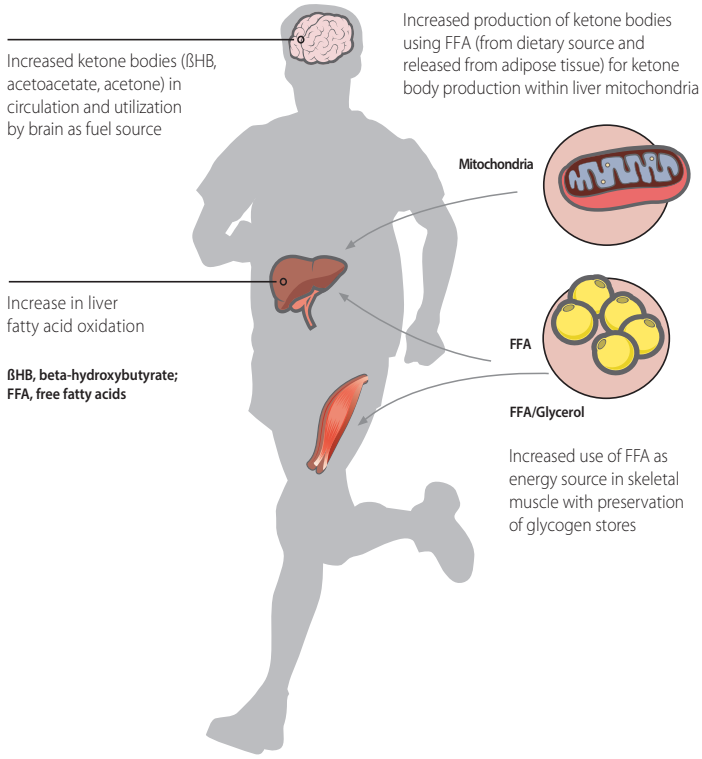
Introduction
Ketosis is a normal physiological process during which the body utilizes fat to produce ketone bodies as its main fuel.[1] Ketosis occurs when there is an absence or shortage of carbohydrates in the diet or glycogen storage in the body, such as during overnight fasting or prolonged fasting, during extended exercise, or when following a ketogenic diet.[1] Ketogenic diets are very low in dietary carbohydrate (<50 g per day) and high in fat, and provide an adequate amount of protein.[2] Adapting to a ketogenic diet has been shown to have benefits for weight management.[1,2]

Research Highlights
- ✓ Ketosis is a normal physiological response during which the body utilizes fat to produce ketone bodies as its main fuel.[1]
- ✓ Ketone bodies may have effects on appetite-controlling hormones (e.g., ghrelin and leptin) or may have direct appetite-suppressing properties,[3-5] and meta-analysis shows that individuals following a ketogenic diet are significantly less hungry.[6]
- ✓ Clinical intervention studies have demonstrated the effectiveness of ketogenic diets for weight loss and weight management.[7-9]

Mechanisms of action
The following metabolic adaptations (keto-adaptation) occur when consuming a ketogenic diet:[10,11]

- Glucose levels decrease as a result of reduced carbohydrate intake.
- Due to reduced glucose, circulating insulin is reduced.
- A reduction in circulating insulin levels helps reduce lipogenesis (fat accumulation) and increases lipolysis (release of fatty acids from adipose tissue), resulting in increased levels of free fatty acids (FFA).
- FFA are used by some tissues (e.g., skeletal muscle) directly as the source of energy in a keto-adapted state.
- FFA are also used by the body to generate ketone bodies (i.e., acetoacetate, β-hydroxybutyrate [βHB], and acetone), which act as the main source of energy in the keto-adapted state.
- Ketone bodies in circulation provide a stable source of fuel for the body and the brain, thereby sparing the need to convert protein into glucose for energy supply.

Composition and structure of the ketogenic diet
Studies of ketogenic diets that have demonstrated weight loss have included some energy restriction with a composition of ~10% of energy coming from carbohydrate, 20-30% of energy coming from protein, and 60-70% of energy coming from dietary fat.[7-9] This macronutrient distribution is a general rule-of-thumb to help guide diet planning, and may vary depending on body size, physical activity, and caloric intake. The consumption of very low amounts of carbohydrate (<50 g per day) and adequate but not high protein intakes with remaining calories from fat, is key to achieving nutritional ketosis. Coaching on ketogenic meal planning and meeting dietary goals on a ketogenic diet weight-loss program is important to maintain ketosis.



Clinical evidence of the ketogenic diet for weight management

Ketogenic diets have been shown to be efficacious for weight and fat mass loss:

- In 59 adults with BMI >30 kg/m^2 who participated in a ketogenic dietary intervention study, the mean reduction in body weight was 12.0 kg over 24 weeks, or a 12.9% change in body weight. Reductions in body fat mass of 9.4 kg were reported, with 69% of participants losing >10% of initial body weight at 24 weeks.[7]
- In 33 adults with abdominal obesity who completed a ketogenic dietary intervention study, the mean reduction in body weight and body fat mass after 12 months was 14.5 kg and 11.3 kg, respectively. Thirty out of 33 (91%) of the participants lost ≥5% of body weight, and 25 out of 33 (76%) lost >10% of body weight at 12 months.[8]
- In 153 adults with obesity participating in a ketogenic intervention, the mean weight loss at 6, 12, and 24 months was 12.2 kg, 10.9 kg, and 6.3 kg, respectively.[12]
- A meta-analysis of weight loss trials ≥1 year found that a ketogenic diet achieved greater reductions in body weight compared to a low-fat diet.[9]

Ketogenic diets may aid weight loss in the following ways:

- Ketone bodies generated while in a state of ketosis may have effects on appetite-controlling hormones (e.g., ghrelin and leptin) or may have direct appetite-suppressing properties.[3-5] Although a reduction in satiety-promoting gut peptides has been reported following weight loss,[13] this change in gut peptides was not seen following a ketogenic diet-induced weight loss.[4,14] Additionally, exogenous ketone supplements were shown to suppress appetite in a clinical study.[15]
- Meta-analysis of ketogenic diets showed that individuals in ketogenic diet groups were significantly less hungry and had significantly reduced desire to eat compared with baseline measures, which may help facilitate adherence to lower calorie intakes.[6]
- The reduction in fat accumulation and increase in fat oxidation during ketosis helps promote fat loss.[16,17]
- Individuals on a ketogenic diet are less hungry and have a reduced desire to eat.[3,6]

Safety and monitoring on the ketogenic diet

- Ketogenic diets are contraindicated for individuals with inborn metabolic errors in fatty acid metabolism and mitochondrial enzymes.[18,19] Some individuals on ketogenic diets may encounter tolerance issues or mild-to-moderate adverse effects such as headache, asthenia, nausea and/or vomiting, and muscle cramps.[20]
- Some individuals on ketogenic diets may experience increases in low-density lipoprotein cholesterol (LDL-C) levels, creatinine clearance, and urinary sodium and calcium excretion.[21,22]
- Ketones can be measured in the breath, blood, and urine. Circulating levels of ketone bodies on a well-planned ketogenic diet range from 0.5-1.5 mmol/L. These levels are markedly lower than those identified in diabetic ketoacidosis (>25 mmol/L) or other pathological states such as alcoholic ketoacidosis, salicylate poisoning, and some inborn errors of metabolism.

For more information, visit **MetagenicsInstitute.com**

References:

1. VanItallie TB et al. Ketones: metabolism's ugly duckling. *Nutr Rev*. 2003;61(10):327-341.
2. Bilsborough SA et al. Low-carbohydrate diets: what are the potential short- and long-term health implications? *Asia Pac J Clin Nutr*. 2003;12(4):396-404.
3. McClernon FJ et al. The effects of a low-carbohydrate ketogenic diet and a low-fat diet on mood, hunger, and other self-reported symptoms. *Obesity* (Silver Spring). 2007;15(1):182-187.
4. Sumithran P et al. Ketosis and appetite-mediating nutrients and hormones after weight loss. *Eur J Clin Nutr*. 2013;67(7):759-764.
5. Johnstone AM et al. Effects of a high-protein ketogenic diet on hunger, appetite, and weight loss in obese men feeding ad libitum. *Am J Clin Nutr*. 2008;87(1):44-55.
6. Gibson AA et al. Do ketogenic diets really suppress appetite? A systematic review and meta-analysis. *Obes Rev*. 2015;16(1):64-76.
7. Yancy WS et al. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: a randomized, controlled trial. *Ann Intern Med*. 2004;140(10):769-777.
8. Brinkworth GD et al. Long-term effects of a very-low-carbohydrate weight loss diet compared with an isocaloric low-fat diet after 12 mo. *Am J Clin Nutr*. 2009;90(1):23-32.
9. Bueno NB et al. Very-low-carbohydrate ketogenic diet v. low-fat diet for long-term weight loss: a meta-analysis of randomised controlled trials. *Br J Nutr*. 2013;110(7):1178-1187.
10. Paoli A et al. Beyond weight loss: a review of the therapeutic uses of very-low-carbohydrate (ketogenic) diets. *Eur J Clin Nutr*. 2013;67(8):789-796.
11. Cox PJ et al. Acute nutritional ketosis: implications for exercise performance and metabolism. *Extrem Physiol Med*. 2014;3:17.
12. Foster GD et al. Weight and metabolic outcomes after 2 years on a low-carbohydrate versus low-fat diet: a randomized trial. *Ann Intern Med*. 2010;153(3):147-157.
13. Sumithran P et al. Long-term persistence of hormonal adaptations to weight loss. *N Engl J Med*. 2011;365(17):1597-1604.
14. Chearskul S et al. Effect of weight loss and ketosis on postprandial cholecystokinin and free fatty acid concentrations. *Am J Clin Nutr*. 2008;87(5):1238-1246.
15. Stubbs BJ et al. A Ketone Ester Drink Lowers Human Ghrelin and Appetite. *Obesity* (Silver Spring). 2018;26(2):269-273.
16. Volek JS et al. Rethinking fat as a fuel for endurance exercise. *Eur J Sport Sci*. 2015;15(1):13-20.
17. Volek JS et al. Body composition and hormonal responses to a carbohydrate-restricted diet. *Metabolism*. 2002;51(7):864-870.
18. Kossoff EH et al. Optimal clinical management of children receiving the ketogenic diet: recommendations of the International Ketogenic Diet Study Group. *Epilepsia*. 2009;50(2):304-317.
19. Wheless JW. The ketogenic diet: an effective medical therapy with side effects. *J Child Neurol*. 2001;16(9):633-635.
20. Goday A et al. Short-term safety, tolerability and efficacy of a very low-calorie-ketogenic diet interventional weight loss program versus hypocaloric diet in patients with type 2 diabetes mellitus. *Nutr Diabetes*. 2016;6(9):e230.
21. McAuley KA et al. Comparison of high-fat and high-protein diets with a high-carbohydrate diet in insulin-resistant obese women. *Diabetologia*. 2005;48(1):8-16.
22. Johnston CS et al. Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. *Am J Clin Nutr*. 2006;83(5):1055-1061.