Research Highlights

- Ketosis is a normal physiological response during which the body utilizes fat to produce ketone bodies as its main fuel. 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. Ketogenic diets are very low in dietary carbohydrate (<50 g per day) and high in fat, and provide an adequate amount of protein. Adapting to a ketogenic diet has been shown to have benefits for weight management.

- Ketone bodies may have effects on appetite-controlling hormones (e.g., ghrelin and leptin) or may have direct appetite-suppressing properties, and meta-analysis shows that individuals following a ketogenic diet are significantly less hungry.

- Clinical intervention studies have demonstrated the effectiveness of ketogenic diets for weight loss and weight management.

Mechanisms of action

The following metabolic adaptations (keto-adaptation) occur when consuming a ketogenic diet:

- 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. 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 management.

- In 59 adults with BMI >30 kg/m² 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. 1
- 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. 2
- 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. 3
- A meta-analysis of weight loss trials 21 year found that a ketogenic diet achieved greater reductions in body weight compared to a low-fat diet. 4

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. 5 Although a reduction in satiety-promoting gut peptides has been reported following weight loss, 6 this change in gut peptides was not seen following a ketogenic diet-induced weight loss. 7 Additionally, exogenous ketone supplements were shown to suppress appetite in a clinical study. 8
- 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. 9
- The reduction in fat accumulation and increase in fat oxidation during ketosis helps promote fat loss. 10
- Individuals on a ketogenic diet are less hungry and have a reduced desire to eat. 11

Safety and monitoring on the ketogenic diet

- Ketogenic diets are contraindicated for individuals with inborn metabolic errors in fatty acid metabolism and mitochondrial enzymes. 12 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. 13
- Some individuals on ketogenic diets may experience increases in low-density lipoprotein cholesterol (LDL-C) levels, creatinine clearance, and urinary sodium and calcium excretion. 14
- 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.

References: