



KETOGENIC DIET RESEARCH

Exogenous Ketones, Ketone Esters and Ketone Salts

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Department of Standards, Paleo Foundation, Encinitas, CA**Contact**¹Email: karen@paleofoundation.com¹Twitter: @5WordsorlessKP²Email: zad@paleofoundation.com²Twitter: @dailyzad**Abstract**

Ketones, which provide an alternative source of fuel when glucose stores are low can be classified into those produced by the body (endogenous) and those produced synthetically (exogenous). Exogenous ketones are typically used to rapidly increase ketone levels even without the restriction of carbohydrates. In addition to discussing the distinction between exogenous and endogenous ketones, we review some of the evidence for claims that are often made about exogenous ketones.

KEYWORDS

Ketones, Exogenous Ketones, Ketone Salts, Ketone Esters

1 | BACKGROUND

Ketone bodies are water-soluble molecules that provide an alternative source of energy to various tissues within the body when the amount of glucose is low and are responsible for a person entering and staying in a state of ketosis. They can be typically classified into two types: endogenous and exogenous.

2 | ENDOGENOUS KETONES**PRODUCTION**

Endogenous ketones are produced within the liver via ketogenesis when the amount of glucose and glycogen is low within tissues, often from restricting the consumption of carbohydrates or even just calories. As a result, the liver begins to produce glucose from other sources, such as amino acids, and fatty acids through gluconeogenesis, and blood levels of the hormones glucagon and epinephrine also begin to rise, while insulin levels begin to fall. This leads to more fatty acids being released into the blood from

adipose tissue (stored fat) via lipolysis.

These free fatty acids are then oxidized via beta-oxidation, and converted into acetyl coenzyme A (acetyl coA), and the buildup of acetyl coA within the hepatic mitochondria leads to the conversion of it into ketone bodies such as beta-hydroxybutyrate (the main ketone body), which is circulated throughout the blood to various tissues and taken up by those tissues to be converted back to acetyl coA which generates ATP molecules. All in all, the process is quite complex in order to generate endogenous ketone bodies.

3 | EXOGENOUS KETONES**TYPES**

On the other hand, exogenous ketones are synthetic ketone bodies that can be consumed via supplements to increase the amount of blood ketones without restricting carbohydrates or calories. They come in two forms, ketone esters (often liquids) and ketone salts (often powders).

The main difference between these two forms is that the salts have an Na⁺ (sodium) molecule attached to the end of the structure (hence the name 'ketone salts'), while ketone esters have a double bond that connects to the oxygen molecule (hence the name 'ketone ester'). The vast majority of products found in the market are usually ketone salts but consuming either one of them can increase the amount of blood ketones without the restriction of carbohydrates or calories. This can provide some advantages, which we will touch on below.

BIOAVAILABILITY

Consumption of these products often leads to a rapid increase in blood ketone levels (taking from 30 minutes to an hour), which often stay elevated for 2-3 hours. Although both esters and salts increase blood ketone levels, studies have found that esters lead to larger increases in blood ketone levels in a dose-response manner, although this may not be advantageous as we later discuss below.

POSSIBLE BENEFITS

The likely advantages of using exogenous ketones to quickly increase blood ketone levels is that they may help conserve glycogen/glucose stores because the ketones within the blood would be used as an energy source before any other substrates are used, such as glucose, amino acids, and fatty acids. This can be particularly useful from a physical performance perspective where you'd like to use a quick source of energy (ketone bodies) and conserve glycogen stores. While in theory it makes sense, the literature has shown mixed results, with some studies showing that consumption of exogenous ketones led to a small advantage, and others showing that it did not. The literature on recovery from exercise, however, is somewhat more consistent, and suggests that it may be useful due to conservation of glycogen post exercise.

There is also some suggestive/preliminary evidence that they may provide anti-seizure properties, which a classical ketogenic diet has been established to help with in individual with epilepsy.

GRAY AREAS

Exogenous ketones have been claimed to aid cognition and suppress appetite, and detailed mechanisms for these claims have been laid out by some researchers as a result of studying ketones and their affect on appetite on the ketogenic diet, however, there is no evidence in humans to support the claims about appetite suppression and improved focus/cognition for exogenous ketones, therefore, it currently remains unresolved.

Another that is not well substantiated by any current evidence is the claim that taking exogenous ketones may help reduce the typical flu-like symptoms that one experiences during the initial stages of nutritional ketosis. And while the theory behind this claim seems like it may make sense, investigations into the literature fail to produce any studies that have carefully investigated this.

CAUTIONS

Exogenous ketones are also often claimed to help with fat loss, however, this is contrary to what is true due to the fact that exogenous ketones actually contain energy (kilocalories) and would be used by the tissues as energy first, hence, stopping the body from breaking down its own fat stores to produce free fatty acids from adipose tissue and converting them into ketone bodies. Thus, exogenous ketones would halt the production of endogenous ketones and not aid fat loss and may even restrict it if constantly consumed throughout the day.

As mentioned above, consumption of exogenous ketones can interfere with the production of endogenous ketones, however, this is not the only concern, if consuming too much exogenous ketones, the rapid increase in blood ketone levels, which may become too high depending on how much is consumed and the amount of existing ketones within the blood, can be highly undesirable because ketone bodies are acidic in nature, and this can lead to ketoacidosis.

This is problematic because the accompanying tissues would not be able to deal with the sudden large increase of ketone bodies in time (which typically involves converting the ketones back to acetyl coA and buffering the pH within the blood via the bicarbonate buffering system). Therefore, more ketones in the blood is not always better! Furthermore, several studies have found that exogenous ketone supplements are often associated with various side effects (often temporary) such as nausea, bloating, diarrhea, and dizziness.

It is important to be mindful when taking such supplements as they may be useful for certain contexts, but irresponsible use can lead to undesirable scenarios.

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