# Exogenous Ketones, Ketone Esters and Ketone Salts

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# Exogenous Ketones, Ketone Esters and Ketone Salts

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## 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 play a crucial role in the body's metabolic processes, especially during periods of low glucose availability. Endogenous ketone bodies are naturally produced by the liver through the breakdown of fatty acids, a process known as ketogenesis. Acetoacetate, beta-hydroxybutyrate, and acetone are the primary endogenous ketones that serve as fuel for organs such as the brain, heart, and muscles when glucose levels are insufficient.

On the other hand, exogenous ketones are external sources of ketone bodies that can be consumed through supplements or specific diets. This includes ketone salts and ketone esters, which can elevate blood ketone levels and induce a state of ketosis even in the presence of normal glucose levels. The popularity of ketogenic diets, characterized by low carbohydrate intake to promote the production of ketones, has led to an increased interest in exogenous ketones as a way to enhance physical and mental performance.

In addition to their role as an energy source, ketone bodies have been studied for their potential therapeutic effects. Research suggests that ketosis may have neuroprotective properties, potentially benefiting individuals with neurological disorders. Furthermore, the utilization of ketones in weight management strategies has gained attention, as they offer a metabolic alternative for burning fat.

Understanding the dynamic interplay between endogenous and exogenous ketones provides valuable insights into the body's adaptive mechanisms during different nutritional states. As the scientific exploration of ketosis continues, researchers aim to uncover the full spectrum of physiological and therapeutic implications associated with these water-soluble molecules.

## 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

Exogenous ketones, available in the market as either ketone esters or ketone salts, offer a convenient and accessible means to elevate blood ketone levels without the need for strict carbohydrate or calorie restrictions. Ketone salts, commonly found in powder form, contain an additional sodium (Na+) molecule attached to the ketone structure, distinguishing them from ketone esters. Conversely, ketone esters, often available in liquid form, feature a double bond connecting to the oxygen molecule, giving them their distinctive chemical composition.

The prevalence of ketone salts in the market doesn't diminish the fact that both forms effectively serve the purpose of increasing blood ketone concentrations. This rise in ketone levels provides several advantages, making exogenous ketones a subject of interest in various fields. Firstly, they can serve as a quick and efficient energy source, particularly beneficial during physical activities or for individuals adhering to low-carbohydrate diets. The availability of this alternative energy substrate can contribute to enhanced endurance and performance.

Moreover, exogenous ketones have gained attention for their potential cognitive benefits. Some studies suggest that increased ketone levels may positively impact cognitive function, memory, and focus. This has implications not only for athletes seeking improved performance but also for individuals in professions requiring heightened mental acuity.

Another notable advantage is the ability of exogenous ketones to facilitate the induction of ketosis without the necessity of following a strict ketogenic diet. This flexibility allows individuals to experience the benefits of ketosis while still enjoying a varied and less restrictive dietary intake. This aspect is particularly appealing for those who find it challenging to adhere to the stringent dietary requirements of traditional ketogenic regimens.

The availability of exogenous ketones, whether in the form of ketone esters or ketone salts, provides a versatile tool for individuals seeking to harness the benefits of ketosis. As research in this field continues, a deeper understanding of the nuanced effects and potential applications of exogenous ketones is likely to emerge, further shaping their role in nutrition, performance, and overall well-being.

### BIOAVAILABILITY

The ingestion of exogenous ketones, whether in the form of ketone esters or ketone salts, typically triggers a swift elevation in blood ketone levels within a relatively short time frame, ranging from 30 minutes to an hour. This surge in ketones persists for a

duration of approximately 2-3 hours, marking a window of heightened ketosis after consumption. Notably, scientific investigations have revealed that ketone esters, in particular, exhibit a dose-dependent relationship with blood ketone elevation. In other words, higher doses of ketone esters lead to proportionally greater increases in blood ketone levels compared to ketone salts.

While the substantial rise in blood ketones might be viewed as advantageous, it's essential to scrutinize the potential drawbacks associated with such elevation. Despite the dose-response pattern observed with ketone esters, the magnitude of this increase may not necessarily confer additional benefits. Studies suggest that there is a threshold beyond which further escalation in blood ketone levels might not yield significant advantages and could even be counterproductive.

Additionally, the rapid and substantial elevation of blood ketones, particularly with ketone esters, may be accompanied by side effects or tolerability issues. Some individuals may experience gastrointestinal discomfort or other mild adverse effects when consuming higher doses of ketone esters. These considerations underscore the importance of balancing the desired effects of exogenous ketones with potential drawbacks, ensuring that their consumption aligns with individual goals, tolerances, and overall well-being.

As the scientific community delves deeper into understanding the nuanced effects of exogenous ketones, it becomes crucial to establish optimal dosing strategies that maximize benefits while minimizing potential downsides. This ongoing exploration is integral to refining the use of exogenous ketones as a tool for metabolic modulation, performance enhancement, and cognitive support.

## 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

Claims surrounding the cognitive benefits and appetite suppression attributed to exogenous ketones have generated considerable interest, with some researchers proposing detailed mechanisms based on studies of ketones' effects on appetite in the context of ketogenic diets. While these theoretical frameworks exist, it's essential to note that, as of now, there is a lack of concrete evidence in humans supporting these claims. The purported cognitive enhancements and appetite-suppressing effects of exogenous ketones remain unresolved due to the absence of robust scientific validation.

Similarly, another assertion regarding the potential alleviation of flu-like symptoms during the initial stages of nutritional ketosis through exogenous ketone supplementation lacks substantial backing in current literature.

Despite the intuitive appeal of the theory, a thorough examination of existing studies fails to unveil any conclusive evidence supporting this claim. The absence of well-designed investigations into the specific relationship between exogenous ketones and the mitigation of typical ketosis-related symptoms underscores the need for more targeted research to either substantiate or disprove these assertions.

As the scientific community strives to unravel the multifaceted effects of exogenous ketones, it becomes imperative to approach such claims with a cautious and discerning perspective. Rigorous, controlled studies are necessary to elucidate the true extent of the cognitive, appetite-related, and symptom-alleviating effects attributed to exogenous ketones. Until a more comprehensive body of evidence emerges, the current status of these claims remains in a realm of uncertainty, emphasizing the importance of continued research to establish the true potential and limitations of exogenous ketone supplementation.

**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.

**4 | CONCLUSION**

Concluding, this paper has delved into the intricate world of ketone bodies, exploring their pivotal role in metabolic processes, both endogenously and through exogenous supplementation. Endogenous ketones, produced naturally by the liver during periods of low glucose availability, serve as crucial fuel sources for organs when glucose levels are insufficient. On the other hand, exogenous ketones, available in the market as esters or salts, offer a practical means to elevate blood ketone levels, presenting advantages for energy, performance, and cognitive function.

The exploration of exogenous ketones has uncovered potential benefits, such as glycogen conservation and aid in exercise recovery. However, nuanced discussions around fat loss, cognitive enhancements, appetite suppression, and symptom alleviation reveal areas where claims may outpace current scientific validation. While exogenous ketones have shown promise in certain contexts, their indiscriminate use without

without careful consideration of individual needs and goals may lead to undesired consequences.

Cautionary notes emphasize the importance of responsible consumption, as excessive intake can interfere with endogenous ketone production and potentially lead to ketoacidosis. The paper underscores the need for further research to substantiate or refute claims surrounding cognitive benefits, appetite suppression, and symptom alleviation attributed to exogenous ketones.

In navigating the complexities of exogenous ketones, this paper encourages a balanced perspective, recognizing both their potential benefits and the importance of cautious use. As the scientific community continues to unravel the multifaceted effects of exogenous ketones, ongoing research will play a crucial role in refining our understanding and optimizing their application in nutrition, performance, and overall well-being.

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