

Effects of Acute Ingestion of a Ketone Monoester Beverage on Glycaemic Control, Appetite, and Food Intake

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Abstract

Ketosis is a state in which ketone bodies are hepatically produced, which can lead to weight loss, appetite suppression, and improved glycaemic control. Reaching a state of ketosis can be difficult to attain and can be induced by fasting or restricting dietary carbohydrates. Exogenous ketones in the form of ketone monoesters have been shown to efficiently induce a state of ketosis. Ketone monoesters are synthetic molecules. The aim of the study was to determine the impact of the acute ingestion of a ketone ester beverage upon appetite, food intake, and glycaemic control. Participants ingested the ketone ester beverage and measurements were taken to gauge perceived appetite, food intake, related peripheral hormones, glycaemic control, and blood ketone levels. The results of the study showed that the ketone monoester beverage caused an increase in blood ketone levels and resulted in appetite suppression and improved glycaemic control. The ingestion of a ketone ester beverage may offer therapeutic use for the prevention and treatment of chronic, nutritionally mediated diseases, such as obesity and Type 2 diabetes.

Background

A state of ketosis has been documented to cause benefits ranging from weight loss, appetite suppression and improved glycaemic control (Veech, 2004). Ketosis can be induced through prolonged intensive exercise, fasting, or through the restriction of dietary carbohydrates. These methods of reaching a ketosis state are relatively difficult to attain in the short-term and to sustain long-term.

Consequently, a variety of ketone supplements have been brought to market which allow the exogenous administration of ketone bodies as an assistant to an individual's regular lifestyle practices. Despite the recent popularity of these products, feeding ketones in an acid or salt form is not advisable due to the supraphysiological acid/salt loads which will result (Cox, 2014). In the light of this novel synthetic molecules have been produced by transesterifying ethyl (R)-3-hydroxybutyrate with (R)-1,3-butanediol using lipase (Cox, 2016). The consumption of these isomers, known as ketone esters, has been shown to offer several benefits beyond those associated with the ketogenic diet and other ketogenic supplements. These benefits include improvements in physical performance in athletes, and improved glycaemic control in healthy individuals without a corresponding increase in insulin secretion (Cox, 2016, Myette-Côté, 2018). Furthermore, recent animal studies have shown that the ingestion of ketone esters can also lead to a reduction in adiposity and body weight (Murray, 2016). These findings offer an intriguing proposition for the therapeutic use of these novel molecules for the prevention and

treatment of a range of chronic, nutritionally mediated diseases, such as obesity and Type 2 diabetes.

This study will focus on the impact of the acute ingestion of a commercially sold ketone ester beverage (HVMN) upon appetite, food intake, and glycaemic control.

- 1) To evaluate the effect of a ketone ester beverage on self-reported appetite and associated biochemical markers (i.e. leptin and ghrelin).
- 2) To investigate the initial impact of a ketone ester beverage upon glycaemic control (i.e. blood sugar and insulin) and blood ketone levels (i.e. beta hydroxybutyrate).

Methods

The experiment was a cross-over design, whereby each participant acted as their own control. After participants gave their informed consent, they were screened for their body mass index (BMI). To take part potential participants must fall within the “healthy” range (between 18.5 – 24.9 kg/m²). The participants were asked to fast for a minimum of 8 hours for their visit.

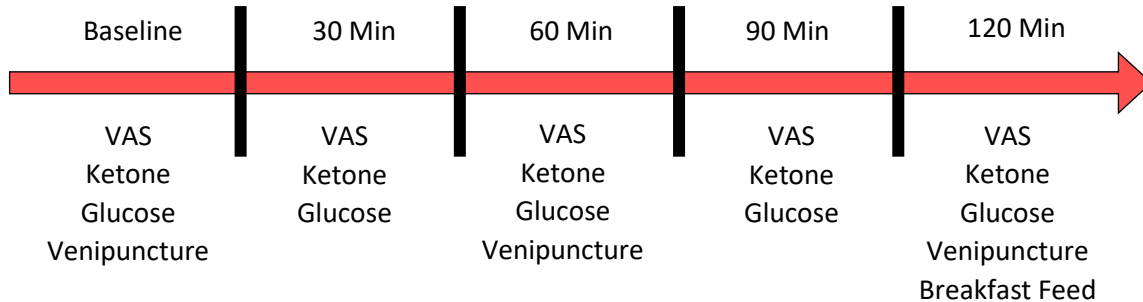
Upon arriving at Liverpool Hope University, baseline measurements were taken consisting of:

- Height
- Weight
- Waist circumference
- Blood pressure
- Blood glucose
- Blood ketones
- Appetite
- Venepuncture blood sample

Immediately after this the participant was randomly allocated to consume either a ketone ester beverage (HVMN) (made up to 1.9 kcal/kg body weight (the equivalent of 0.385 g beta hydroxybutyrate per kg body weight) or a dextrose placebo drink (also made up to 1.9 kcal/kg body weight) which were taste matched. Every 30 minutes several measurements were taken to gauge perceived appetite, glycaemic control and blood ketone levels. Appetite was self-reported by a visual analogue scale (VAS). Blood glucose and ketone levels were measured using a handheld glucose/ketone monitor. Each hour a blood sample was taken for future hormone analysis.

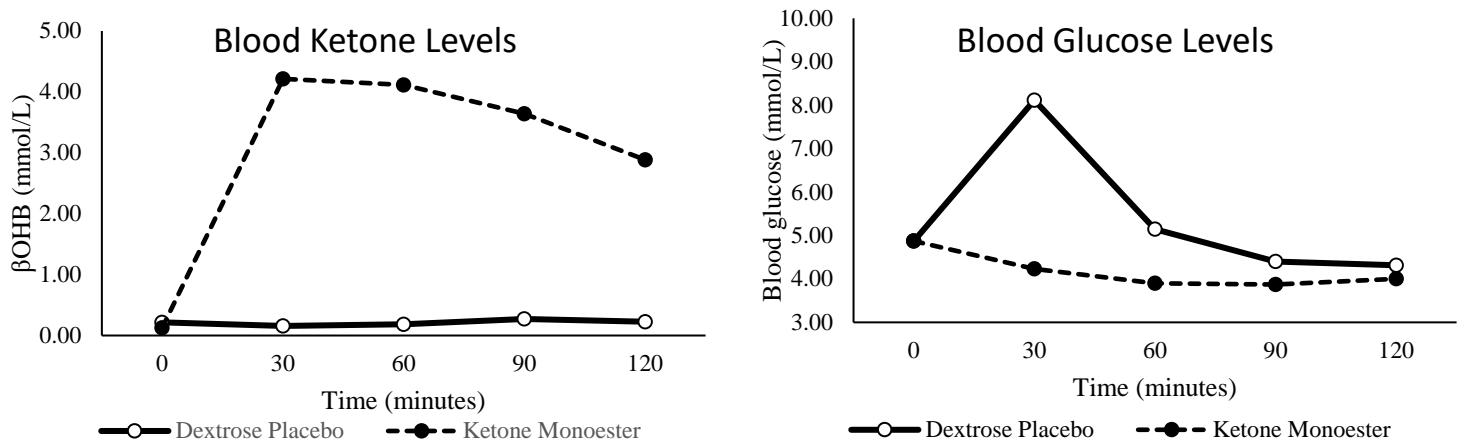
After 120 minutes had passed the participant was then taken to the Food Laboratory and invited to eat a bowl of breakfast cereal (cornflakes) with milk *ad libitum*. The amount consumed was determined when the participant left by measuring the cereal and milk before and after each participant’s visit. Before the participant leaves a second appointment will be arranged. During

the participant's second appointment they will be asked to consume the other drink (either ketone ester or dextrose placebo) and the same set of procedures will occur that the participant encountered during their first visit.



Results

Glucose and Ketone Levels

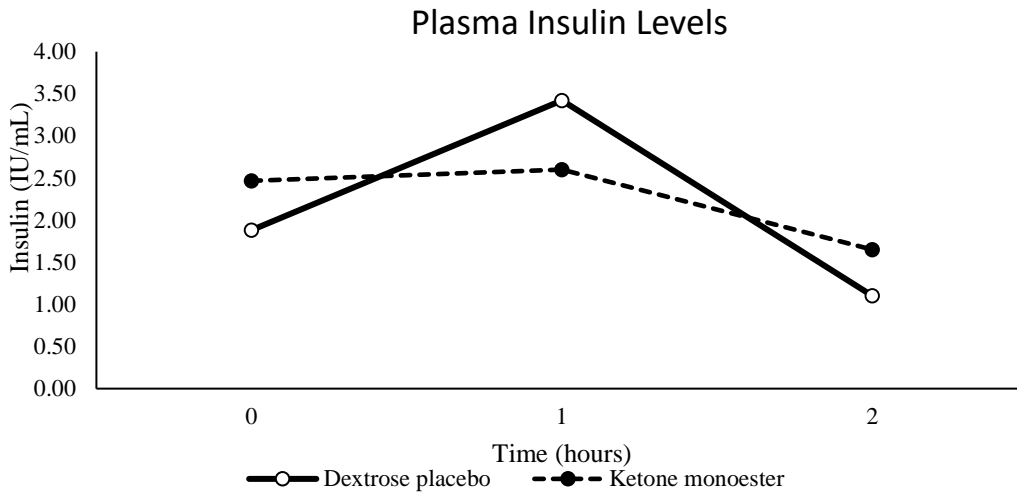
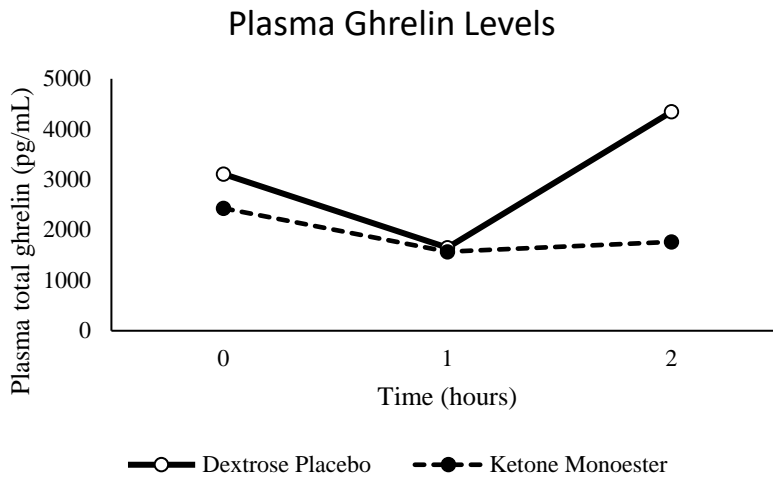
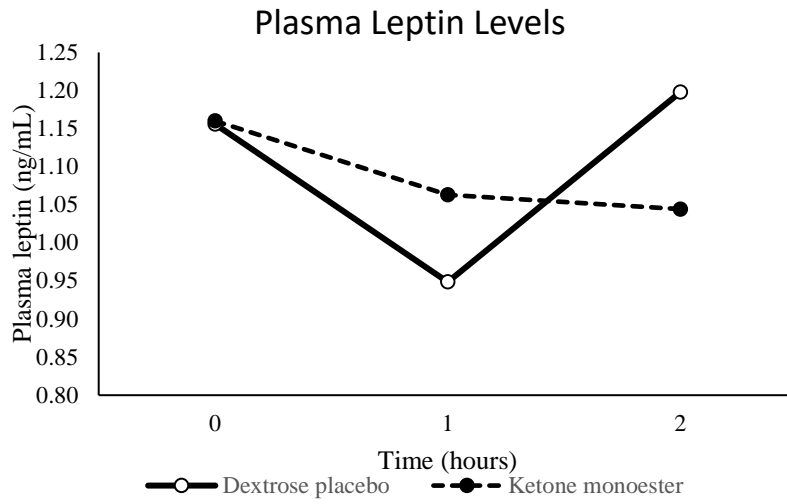


After consumption of either the ketone or placebo beverage, blood glucose and ketone levels were measured each thirty minutes for two hours. The measurements were taken on a handheld blood glucose/ketone monitor using blood from a finger prick. The ketone beverage was shown to increase blood ketone levels over 3mmol/L for a period of almost two hours. The ketone beverage also did not increase blood glucose levels as much compared to the dextrose placebo.

Hormone Levels

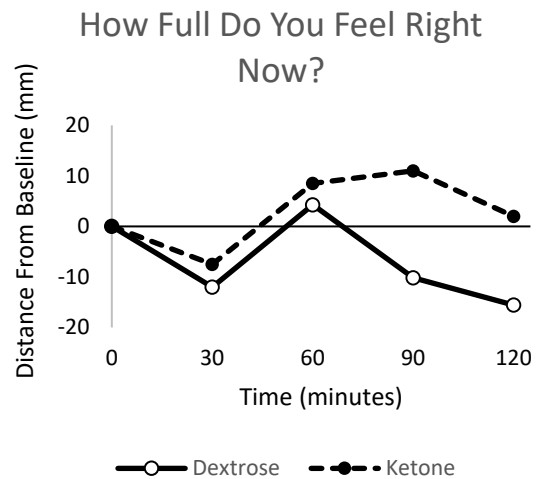
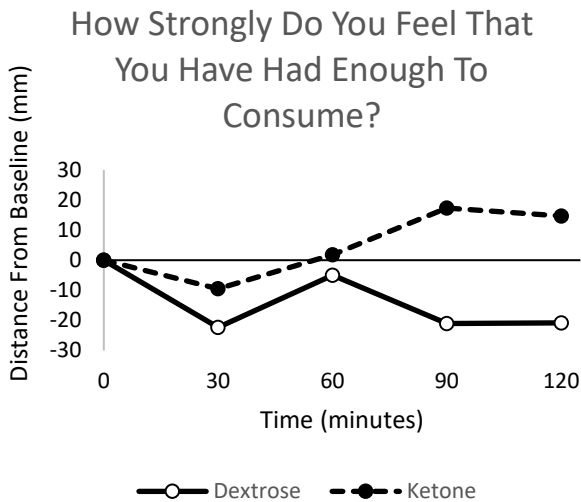
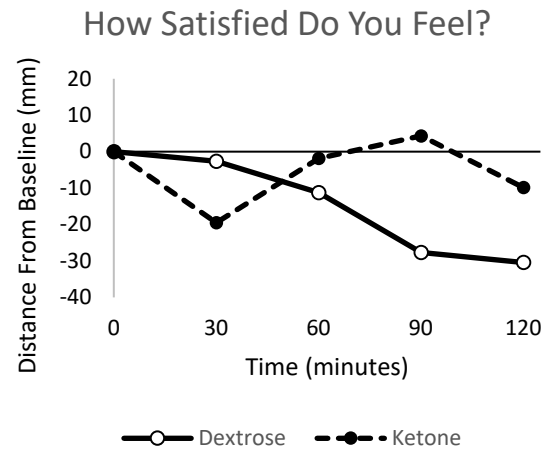
Peripheral hormone levels were measured to quantify appetite based on ghrelin and leptin concentrations along with glycaemic control by measuring insulin concentration. Minimally invasive blood draws were taken at baseline and then each hour for two hours. Blood analyses were done to determine the concentration of the hormones in the blood. Ghrelin concentration was determined by using an ELISA and the concentration of leptin and insulin were measured by using an Evidence Investigator. The results showed that ghrelin and leptin levels decreased after ingestion of a ketone monoester beverage. The insulin levels did not change significantly after

the baseline after ingestion of the ketone monoester beverage meaning that it was not necessary for the metabolization of the drink.



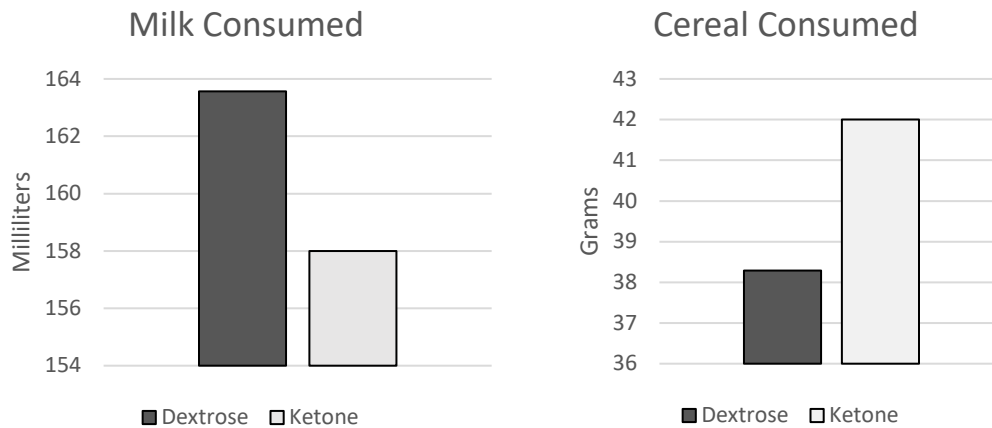
Self-Reported Appetite

Self-reported appetite was measured using visual-analogue scale (VAS). A question related to appetite was asked, and the participants marked on a line to answer to the question. The participants were asked the same questions at baseline and then each thirty minutes for two hours. The difference between baseline and each thirty-minute interval answer was used to quantify a change in appetite over time. The results show that self-reported appetite was slightly suppressed by the ketone monoester beverage.



Food Consumption

The amount of milk and cereal consumed was measured by weighing the milk and cereal before and after the meal at the end of the experiment. The results showed that after ingesting the ketone ester beverage the participants ate more cereal compared to the dextrose placebo ingestion, however it was also shown that the ketone ester beverage resulted in less cereal drank compared to the dextrose placebo.



Conclusions

The HVMN ketone ester beverage could induce a state of ketosis for a period of at least two hours. The ketone ester beverage was also shown to slightly decrease appetite, but it did not consistently affect food consumption. Since the ketone ester beverage was capable of increasing blood ketone levels without increasing blood glucose, then it could possibly be used as a fuel source for people with Type 2 diabetes or obesity.

Future Direction

Future studies can be conducted to determine long-term effects of the ketone monoester beverage on appetite and food consumption. Future research needs to be done in order to determine the effects of a ketone ester beverage on people with Type 2 diabetes or obesity.

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