The Effects of Raspberry Ketone Supplementation on Body Composition

A project completed in partial fulfillment of the requirements for the Honors Program

by

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Introduction

Raspberry ketones are aromatic and phenolic compounds found in red raspberries. They have been used in the fragrance and food industry for their smell and flavor properties and more recently in medical applications (Chia-Hsiang Lin, et. al., 2011). The medical uses for raspberry ketones are currently unknown but show biologic action as a cosmetic agent (anti-melanin action) and as a regulator of fat metabolism. Although the exact mechanism of action for fat oxidation is not completely understood or validated in human studies, raspberry ketones have been introduced to the health supplement market as a weight loss aid and promoted by celebrity endorsements, which have quickly become a common household supplement. Prior to the market explosion of raspberry ketone production, the supplement industry was dominated by weight loss products claiming to increase fat oxidation through large doses of caffeine and other central nervous system activators. The goal of these products was to increase total Caloric expenditure by increasing the metabolic output of the body, however there are adverse side effects to these stimulant-based products cite. Stimulants such as caffeine can increase heart rate, blood pressure, plasma levels of catecholamines, and inhibits digestion and other parasympathetic processes (Roberston, Frolich, Carr, and et al., 1978). Raspberry ketones may provide a safe alternative to stimulant-based drugs and could have potential benefits in the treatment of obesity.

Currently, there are no known metabolic side effects to oral raspberry ketone ingestion, although one study for cosmetic application of raspberry ketones revealed that it may have
action in tissues other than adipose cite. It was shown that topical application of raspberry ketones in mice and zebra fish embryos and in vitro treatment of melanoma cells suppressed melanogenesis through post-transcriptional inhibition of tyrosinase (Chia-Hsiang Lin, et. al., 2011).

Raspberry ketones have been linked to anti-obese actions and weight loss in rodent models, even in the presence of a high fat diet (Morimoto, et al., 2005). These studies have warranted the investigation of raspberry ketones as a potential dietary supplement to combat obesity. Park et. al. (2010) investigated the cellular effects of raspberry ketones at a 10µm concentration on 3T3-L1 white adipocytes. The results of this study showed that 3T3-L1 cells (white adipocytes) significantly increased lipolysis, fatty acid oxidation, and circulating adiponectin, which resulted in the ability to suppress lipid accumulation due to increased lipid metabolism in the presence of raspberry ketones in vitro. Another study investigated the effects of raspberry ketones on the fat metabolism of mice. The authors investigated the effects of raspberry ketones on normal weight mice that were fed a high fat diet and also on obese rats that were fed a high fat diet. The authors concluded that raspberry ketones have the ability to inhibit fat deposition in the presence of a high fat diet and can even reverse an obese condition in the presence of a high fat diet (Morimoto, et al., 2005). The proposed mechanism of action was translocation of hormone sensitive lipase from the cytosol into the fat droplets within the adipocytes (Morimoto, et al., 2005). This study demonstrated that raspberry ketones may be especially useful as a supplement for overweight and obese Americans due to the high fat nature of the typical western diet.
Although the cellular mechanism of action is not completely understood, it is clear that raspberry ketones can inhibit fat deposition and increase levels of fatty acid oxidation \textit{in vitro} and \textit{in vivo} in rodent species (Morimoto, et al., 2005, Park et. al. 2010).

Therefore, the purpose of this study was to determine if the anti-obese actions of raspberry ketones shown in rodent species carry over into human applications for potential use in the treatment of obesity and other metabolic syndromes. Studies have investigated the relationship between disease and mortality rates and body composition and have shown a strong correlation between increased body fat and increased risk of disease and mortality (Berrington de Gonzalez, et. al., 2010). Furthermore, there is a strong correlation between the percent body fat of both male and female children and chronic disease risk factors (Going, et. al., 2011). I hypothesized that raspberry ketone supplementation will lead to a decrease in body fat percentage.

\textbf{Methods}

\textit{Participants:}

The participants for the study were male college students at Ohio Dominican University and The Ohio State University. Twelve healthy athletic men were debriefed on the purpose of the study and the compound being ingested. Their ages varied from 20 to 22 years old. These participants ranged from moderately active (participated in physical activity equivalent to walking 1.5 to 3 miles per day along with typical day-to-day physical activity) to vigorously active (participated in jogging, running, circuit training, competitive sports and heavy labor or housework). The participants were asked to sign a waiver agreeing to standardize their lives as
much as possible including maintaining a uniform, diet and workout routine and restrict other weight loss supplement use during the 3 week testing period. The importance that the participants did not adopt a new diet, workout regiment, supplement plan, etc. during the 3 week testing period was made known, as these lifestyle additions and changes would significantly confound the results of the experiment.

Experimental Protocol:

The participants were randomly divided into 3 groups: 1) placebo 2) low treatment group 3) high treatment group. The placebo group was given capsules containing powdered sugar. The treatment groups were given 125 mg or 250 mg capsules of raspberry ketones depending on their treatment group designation as low or high treatment group. The participants were instructed to take their pill (placebo or treatment) each morning upon waking with an 8 oz glass of water. The participants were informed to take any other supplement (multivitamin) or medication at least 1 hour post ingestion of the experimental supplement. Body composition was measured using BIA (bioelectrical impedance analysis) at the start of the experiment and every 7 days after, for a total of 4 body composition measurements. The participants were instructed to not consume any food or water during the 2-hour time window before the BIA reading was taken. This fasting window was taken as a precaution to decrease the confounding effects of hydration on the BIA readings. At the completion of the study the participants were debriefed on their involvement in the treatment or placebo groups. Within each treatment group, one t-test analysis was run to compare changes in body composition
Conclusions were drawn to determine the effectiveness of raspberry ketone supplementation on non-exercise and non-diet induced weight loss in humans.

Results

The overall influence of raspberry ketone supplementation for each treatment group is presented in Figure 1. Analysis showed there was significant difference (decrease) in overall body fat percentage in the high treatment group (p = 0.007) as presented in Figure 1. Additionally, no significant difference was found in the low treatment group (p = 0.359), nor the control, or placebo, group (p = 0.405). The results of the study determined an overall 0.575% decrease in body fat for high treatment groups, whereas the low treatment group experienced a 0.375% decrease and the control group a 0.150% increase in body fat.

Discussion:

As previously stated, the purpose of this study was to investigate the effect of raspberry ketone supplementation on body composition over a 3-week period. It was hypothesized that raspberry ketone supplementation will lead to a decrease in body fat percentage. As a continuation to the minimal previous research about raspberry ketones, this study indicates that raspberry ketone supplementation over three weeks can lead to overall decreases in body fat percentage. The principle finding is that a larger dosage of raspberry ketones (250mg) induces a significant decrease in body fat percentage over a three-week regimen compared to a lower dose group and placebo group.
As previously mentioned, few studies have been conducted to understand the relationship between raspberry ketones and weight/fat loss in humans. However, a few studies were conducted to understand this relationship in mice and rodents. The study by Park et al. (2010) suggests that raspberry ketones play a role in increasing lipolysis and fatty acid oxidation. Another study by Morimoto, et al. (2005), implicates raspberry ketones’ role in interrupting the mechanism of fat deposition and in some cases can facilitate fat loss. These results are consistent with the current study, and thus raspberry ketone dosage appears to have a significant effect on overall fat metabolism.

Figure 1 displays a significant difference in body fat percentage after completion of a large dose raspberry ketone supplementation regimen, as opposed to reduced dosage and placebo group counterparts. Diet, exercise and lifestyle habits were considered and participants were asked to standardize these factors throughout the duration of the three week study. A previous study by Lopez, et. al (2013), was conducted to study the effect of a multi-ingredient weight-loss product (including raspberry ketones), diet restriction, and exercise regimen on a number of health determinants in overweight men and women. Their results determined significant differences in body weight, fat and lean mass, waist and hip girth, and energy levels. The results of our study are in agreement with those of Lopez et. al. (2013) and strongly supports further investigation to understand the exact mechanisms of raspberry ketones in human subjects.

Although our results are based in humans, the results of previous studies findings of raspberry ketones’ anti-obesity actions concerning fat loss and inhibition in rodent species
could carry over into human subjects. An increase in adiponectin levels could be a possible mechanism of action for a reduction in fat mass. Adiponectin is an insulin-sensitizing agent that regulates glucose levels and aids in fat metabolism. Adiponectin markers were not measured in the current study but it is possible raspberry ketones are able to increase adiponectin levels resulting in increased fat oxidation. The high treatment group potentially had the minimal raspberry ketone concentration necessary to increase adiponectin levels. Thus, increased adiponectin levels would lead to increased insulin modulation resulting in potential Malonyl-CoA inhibition and subsequently an increase in CPT-1 activity (Yamauchi, et al., 2001).

**Conclusion:**

The results of this study showed a significant decrease in body fat percentage of high treatment individuals upon completion of a three-week raspberry ketone supplementation regiment. Despite the realized significant difference, considerations to the limitations of the study must be made before broad generalization. The methods of data collection introduce potential sampling bias, meanwhile, there were limitations in duration of supplementation, as well as inability to adequately monitor confounding variables such as diet, exercise and lifestyle. Furthermore, raspberry ketone supplementation cannot be isolated as the sole determinant of the results of the study, nor can a causal relationship be determined. There has been evidence supporting raspberry ketone’s role in inhibiting fat deposition and increasing lipolysis in animal studies. Additionally, increased benefits of fat loss can potentially be experienced if raspberry ketone supplementation is paired with calorie-restricted diet and a consistent exercise plan.
These potential benefits should be investigated further and the elucidation of raspberry ketone’s exact mechanism of action is a critical future area of research.


Park, Kyoung. "Raspberry Ketone Increases Both Lipolysis and Fatty Acid Oxidation in 3T3-L1


<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
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<tbody>
<tr>
<td>Age (years)</td>
<td>21.3 ± 0.98</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>179 ± 7.40</td>
</tr>
<tr>
<td>Body mass (kg)</td>
<td>82.4 ± 12.5</td>
</tr>
</tbody>
</table>

Table 1- Participants’ average physical characteristics. All values reported as mean ± SD.
<table>
<thead>
<tr>
<th>Groups</th>
<th>Pre-supplementation</th>
<th>Post-supplementation</th>
<th>Overall change</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>12.6 ± 3.39</td>
<td>12.0 ± 3.32</td>
<td>-0.575 ± 0.171</td>
</tr>
<tr>
<td>Low</td>
<td>11.5 ± 2.40</td>
<td>11.1 ± 2.40</td>
<td>-0.375 ± 0.695</td>
</tr>
<tr>
<td>Control</td>
<td>9.63 ± 0.68</td>
<td>9.78 ± 0.881</td>
<td>0.150 ± 0.311</td>
</tr>
</tbody>
</table>

Table 2-Body fat percentage measurements, pre- and post supplementation regimen. Values reported as mean ± SD.
Figure 1 – Overall change in body fat percentage post-supplementation for each treatment group. Values represent overall mean. *Significant difference was found (p = 0.007).