An extract of black, green, and mulberry teas causes malabsorption of carbohydrate but not of triacylglycerol in healthy volunteers1–3

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ABSTRACT

Background: In vitro studies suggest that extracts of black, green, and mulberry teas could interfere with carbohydrate and triacylglycerol absorption via their ability to inhibit α-amylase, α-glucosidase, sodium-glucose transporters, and pancreatic lipase.

Objective: We measured breath hydrogen and 13CO2 to investigate the ability of an extract of black, green, and mulberry tea leaves to induce malabsorption of carbohydrate and triacylglycerol in healthy volunteers.

Design: In a crossover design, healthy adult volunteers randomly ingested test meals with a placebo beverage or a preparation containing an extract of black (0.1 g), green (0.1 g), and mulberry (1.0 g) teas. One test meal contained 50 g carbohydrate as white rice, 10 g butter, and 0.2 g [13C]triolein, and the beverages contained 10 g sucrose. The calorie content of the second test meal consisted entirely of lipid (30 g olive oil and 0.2 g [13C]triolein). Breath-hydrogen and 13CO2 concentrations were assessed hourly for 8 h, and symptoms were rated on a linear scale.

Results: With the carbohydrate-containing meal, the tea extract resulted in a highly significant increase in breath-hydrogen concentrations, which indicated appreciable carbohydrate malabsorption. A comparison of hydrogen excretion after the carbohydrate-containing meal with that after the nonabsorbable disaccharide lactulose suggested that the tea extract induced malabsorption of 25% of the carbohydrate. The tea extract did not cause triacylglycerol malabsorption or any significant increase in symptoms.

Conclusion: This study provides the basis for additional experiments to determine whether the tea extract has clinical utility for the treatment of obesity or diabetes. Am J Clin Nutr 2006;84:551–5.

KEY WORDS Malabsorption, carbohydrate, triacylglycerol, tea extract, breath-hydrogen test, 13CO2-breath test

INTRODUCTION

It is widely believed that teas contain substances that are beneficial to health. (A search of the key words “tea health benefits” brings up >5 million entries on Google.) Although most of the alleged benefits of tea are not supported by solid scientific evidence, teas contain a variety of biologically active compounds that might influence metabolic reactions. Most of the commonly ingested teas are derived from the leaf of the Camellia sinensis plant, and various types of tea are created via manipulations (eg, drying, fermentation) of this leaf. As green tea is fermented to oolong and then to black tea, polyphenol compounds (catechins) in green tea are dimerized to form a variety of theaflavins (1); thus, these teas may have different biological activities.

A putative beneficial effect of tea is its ability to induce weight loss. Support for this contention includes a controlled human trial that showed weight loss when tea was added to a dietary regimen (2) and a mouse study that showed that administration of a tea extract with a high-fat diet eliminated the weight gain observed in the absence of tea (3). Several mechanisms have been postulated to account for this weight control. Modest increases in energy expenditure have been reported with the ingestion of oolong and green teas (4–6). In addition, tea could inhibit the absorption of carbohydrate or fat. In vitro experiments have shown that constituents of tea inhibit the activities of α-amylase (7–10) and α-glucosidase (11–16) and of intestinal sodium-dependent glucose transporters (17–21). The in vitro inhibition of pancreatic lipase (22–24) by tea extracts suggests that tea might interfere with triacylglycerol absorption. However, no in vivo studies in humans or animals have shown that tea preparations cause malabsorption of carbohydrate or fat. In the present report, we measured breath hydrogen and 13CO2 to investigate the ability of an extract of black, green, and mulberry tea leaves to induce malabsorption of carbohydrate and triacylglycerol in healthy volunteers.

SUBJECTS AND METHODS

The study was approved by the Human Studies Subcommittee of the Minneapolis Veterans Affairs Medical Center, and informed consent was obtained from all subjects.

Study A: carbohydrate- and lipid-containing test meal

Twenty healthy volunteers (10 women and 10 men) aged 23–60 y fasted after their usual dinner until the following morning (~0800), when the experiments were performed at the Minneapolis Veterans Affairs Medical Center. After collection of baseline breath samples for hydrogen and 13CO2 analysis, the subjects ingested a test meal consisting of white rice and butter.

1 From NatureGen Inc, San Diego, CA (LZ), and VAMC (Research Service/151), Minneapolis, MN (JKF and MDL).
2 Supported by NatureGen, Inc, San Diego, CA, and VAMC (Research Service/151), Minneapolis, MN.
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The rice was boiled for 20 min, and then individual portions (176 g containing 50 g carbohydrate) were frozen with 10 g butter. Immediately before being ingested, the meals were warmed in a microwave oven, and 0.2 g \([^{13}\text{C}]\)triolein (Cambridge Isotope Laboratories, Andover, MA) was thoroughly mixed into the meal. Five hundred milliliters warm water and 10 g sucrose were added to the tea extract beverage or placebo preparation, which were well stirred. The subjects were randomly assigned to drink either the tea extract or the placebo beverage concurrently with the meal. Breath samples were then collected at hourly intervals for 8 h. At the end of each test period, the subjects were asked to rate a variety of symptoms—including nausea, bloating, abdominal discomfort, rectal gas, and obfuscating symptoms—on a previously described linear scale that ranged from 0 (none) to 4 (severe) (25). In addition, loose bowel movements were noted. One week later the test was repeated after the subjects ingested the opposite preparation from that ingested in the initial study.

Study B: lipid-containing, carbohydrate-free test meal

Ten of the subjects took part in a second study that followed the same format as study A; however, the caloric content of the meal consisted entirely of lipid (30 g olive oil plus 0.2 g \([^{13}\text{C}]\)triolein). The tea leaf extract or placebo was similar to that described in the previous study; however, sucrose was replaced with 1 g of the noncaloric sweetener sucralose (Splenda McNeil Nutritionals, Fort Washington, PA). Breath samples were obtained for \([^{13}\text{C}]\)CO₂ measurements as described in study A.

Test products

The active preparation, a proprietary product, consisted of a mixture of extracts of green (0.1 g), black (0.1 g), and mulberry (1.0 g) tea leaves. The approximate quantities of the potential antiabsorptive components per dose of our tea extract beverage (measured by HPLC) were as follows: 5 mg deoxynojirimycin-type compounds, 100 mg epicatechin gallate, 300 mg epigallocatechin gallate, and 100 mg theaflavin. The control beverage consisted entirely of lipid (30 g olive oil plus 0.2 g \([^{13}\text{C}]\)triolein). The tea leaf extract or placebo was similar to that described in the previous study; both products were supplied by NatureGen Inc, San Diego, CA.) The taste of the 2 test materials differed, and subjects were aware of the preparation they received.

Breath collections

Expired air was sampled for hydrogen concentration as described previously (26). Breath samples for \([^{13}\text{C}]\)CO₂ analysis were collected by having the subject expire through a straw into a glass tube (Labco Exetainer; Labco International Inc, Houston, TX), which was sealed immediately after withdrawal of the straw.

Analyses

Each breath collection for hydrogen measurement was analyzed for carbon dioxide (Capstar 100; CWE Inc, Ardmore, PA) to ensure that an adequate alveolar sample had been collected. The hydrogen concentration of the rare sample that contained <4.5% CO₂ (5 of 360 samples) was normalized to 5% CO₂ (observed hydrogen concentration \(\times 5\% /\text{observed carbon dioxide concentration}\)). The hydrogen concentration was measured by gas chromatography with a molecular sieve column, nitrogen as the carrier gas, and a reduction detector (Trace Analytic, Menlo Park, CA). The atom percent (atom%) excess of \([^{13}\text{C}]\)CO₂ in each breath sample relative to that of the baseline sample was determined by mass spectroscopy, which was performed by a commercial laboratory (Metabolic Solutions Inc, Nashua, NH).

Statistics and calculations

The significance of differences between means observed with the 2 treatments was determined by 2-tailed paired \(t\) test. Values obtained with the 2 treatments were not significantly different between the 0- and 1-h measurements. Each hourly measurement from 2 to 8 h, however, was significantly greater when the tea extract was ingested (\(P = 0.026\) at 2 h, \(P = 0.013\) at 3 h, and \(P < 0.003\) from 4 to 8 h).

RESULTS

Breath-hydrogen concentration

The mean (±SEM) hourly breath-hydrogen concentrations observed after ingestion of the rice and butter meal with each of the 2 treatments are shown in Figure 1. The hydrogen concentration at baseline was not significantly different from that at 1 h. However, the curves significantly diverged by 2 h, with the breath-hydrogen concentration being significantly greater in the group receiving the tea extract beverage at each hourly time point from 2 to 8 h. The sum of the breath-hydrogen concentrations for hours 1–8 (a value that closely approximated the area under the
carbohydrate as rice, 10 g butter, and 0.2 g \([13C]\)triolein with the tea extract

Study A: results for 20 healthy subjects who ingested a meal consisting of 50 g
Breath-\(13\)CO\(_2\) measurements

The mean (±SEM) hourly \(13\)C atom% excesses (hourly values minus baseline value) for the 2 treatments when subjects ingested the rice and butter meal (study A) are shown in Figure 2. Although the measurements at hours 1–4 were not significantly different between the 2 treatments, the values were significantly higher for tea extract than for placebo at hours 5–8. The sum of the values for hours 1–8 averaged 0.0256 ± 0.0017 and 0.0213 ± 0.0019 atom% excess for the tea extract and the placebo, respectively (\(P = 0.014\)). The \(13\)C atom% excess values after ingestion of the lipid-containing (30 g olive oil plus \(13\)Ctriolein), carbohydrate-free meal (study B) are shown in Figure 2. In contrast with the results in study A, the sum of the values for hours 1–8 for the tea extract (0.012 ± 0.0025 atom% excess) was virtually identical to that with the placebo (0.012 ± 0.0023 atom% excess) (\(P = 0.95\)), and none of the hourly measurements showed significant differences (\(P > 0.2\)) between the 2 treatments.

**TABLE 1**
Comparison of symptoms reported by healthy subjects in the 8-h period after ingestion of a standard carbohydrate- and lipid-containing meal plus a tea extract or placebo

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Tea extract group</th>
<th>Placebo group</th>
<th>(P^2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>1.16 ± 0.27*</td>
<td>0.71 ± 0.27</td>
<td>0.11</td>
</tr>
<tr>
<td>Fullness</td>
<td>0.77 ± 0.17</td>
<td>0.59 ± 0.19</td>
<td>0.44</td>
</tr>
<tr>
<td>Itching</td>
<td>0.07 ± 0.05</td>
<td>0.02 ± 0.02</td>
<td>0.33</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>0.23 ± 0.14</td>
<td>0.13 ± 0.10</td>
<td>0.33</td>
</tr>
<tr>
<td>Nausea</td>
<td>0.70 ± 0.23</td>
<td>0.23 ± 0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>Excessive rectal gas</td>
<td>0.61 ± 0.21</td>
<td>0.21 ± 0.12</td>
<td>0.12</td>
</tr>
<tr>
<td>Fatigue</td>
<td>1.13 ± 0.25</td>
<td>0.97 ± 0.26</td>
<td>0.56</td>
</tr>
<tr>
<td>Bloating</td>
<td>0.45 ± 0.19</td>
<td>0.26 ± 0.13</td>
<td>0.31</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>0.41 ± 0.20</td>
<td>0.13 ± 0.17</td>
<td>0.67</td>
</tr>
</tbody>
</table>

*Symptoms were rated on a linear scale of 0 (none) to 4 (severe).

**Symptoms**

The severity of symptoms reported by the subject for the 8 h of study A are shown in Table 1. No significant differences (\(P < 0.05\)) in symptoms were observed for any symptom between the 2 treatment groups. Similarly, no significant differences in symptoms were observed between the 2 treatment groups in study B (data not shown).

**DISCUSSION**

We used measurements of breath-hydrogen and of breath-\(13\)CO\(_2\) to determine whether ingestion of a tea extract preparation induced malabsorption of carbohydrate or fat. Carbohydrate malabsorption provides substrate for most of the hydrogen produced in humans, which can be assessed by measuring breath-hydrogen concentrations (28, 29). In contrast, fat is not fermented to carbon dioxide by the colonic bacteria, and carbon dioxide production from lipid reflects the host’s metabolism of absorbed lipid. Studies using triolein labeled with \(13\)C (30, 31) or \(14\)C (32, 33) showed that fat malabsorption documented by fecal fat measurements was associated with a reduction in labeled carbon dioxide excretion.

In the present study, the subjects ingested standard meals with a beverage containing tea extract or placebo. The initial test meal contained 60 g carbohydrate (50 g starch as white rice and 10 g sucrose in the tea extract or the placebo) and 10.2 g fat. White rice was used as the complex carbohydrate because, in contrast with most complex carbohydrates, rice starch is nearly completely absorbed by healthy subjects (34). Thus, a rice meal allows breath testing to more sensitively determine whether a manipulation significantly increases hydrogen excretion, ie, causes starch malabsorption. As shown in Figure 1, the breath-hydrogen concentration declined with the placebo, which indicated that residual fermentable colonic substrate was not replenished via malabsorption of carbohydrate in the test meal. In contrast, the ingestion of tea extract resulted in increased breath-hydrogen concentrations, which were significantly greater than the values observed with placebo for each hourly measurement between 2 and 8 h. Thus, the tea extract clearly induced malabsorption of the carbohydrate.
Lipid-containing (30 g olive oil containing [13C]triolein), differentiae between these 2 possibilities, 10 subjects ingested a hypoglycemic effect generally has been attributed to alterations in glucose for energy utilization. It is also possible that the tea extract—induced carbohydrate malabsorption is associated with fewer symptoms than has been observed with α-glucosidase–inhibiting drugs. Indeed, it would be surprising if the degree of malabsorption observed with the tea extract (25% of total ingested carbohydrate) were not associated with some degree of gaseousness and loose stools.

Extracts of black, green, and mulberry teas have been consumed for many years by enormous numbers of Asians, and these products are considered safe. Green and black tea extracts also are widely used in the Western world. Although tea extracts have been shown to interact with the metabolism of other drugs (46, 47), serious complications possibly attributable to ingestion of these extracts are rare (48). Thus, although the potential for unintended serious side effects is seemingly low, rare unexpected side effects of the extract can be confidently excluded only after the product has been consumed in an environment where medical surveillance is adequate to detect the problem.

JFK helped design the protocol, recruited the subjects, and analyzed the data. MDL contributed to the design of the protocol, analyzed the data, and wrote the manuscript. LZ was involved in the design of the protocol but had no involvement in the collection or analysis of the data. LZ is president of NatureGen, the company that provided the tea extract and placebo used in this study. JFK and MDL had no financial interest in NatureGen or any other type of conflict of interest with the material presented in this article.

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