Effect of powdered beverages containing Pu-erh tea extract on postprandial blood glucose levels

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Submission Date: August 1st, 2019. Acceptance Date: August 28th, 2019. Publication Date: August 31st, 2019.

Citation: Takeda R., Furuno Y., Imai S., Ide Y., Wu D., Yan K. Effect of powdered beverages containing Pu-erh tea extract on postprandial blood glucose levels. Functional Foods in Health and Disease 2019; 9(8): 532-542. https://doi.org/10.31989/ffhd.v9i5.578

ABSTRACT

Objective: The current study aimed to examine the effect of a single ingestion of a beverage containing Pu-erh tea extract (Pu-erh tea polyphenol 18.00mg, eq. gallic acid) on postprandial blood glucose levels through a comparison using a crossover test.

Method: A total of 20 participants, of which 10 were men and 10 were women, aged between 29 and 64 years were instructed to ingest beverages containing Pu-erh tea extract or placebo beverages at the same time as load food (in addition to cooked rice). Their blood glucose levels were measured before and 30, 60, 90, and 120 min after ingestion.

Results: In phases I and II of the trial, three participants who had large differences in the quantity of the ingested food on the day before the trial were removed from the study. Finally, the analysis
was conducted on 17 participants. Result showed that the group who ingested the beverage containing Pu-erh tea extract had significantly lower blood glucose levels than the group who consumed the placebo beverage 60, 90, and 120 min after ingestion. In terms of the amount of variation before ingestion, the group who ingested beverages with Pu-erh tea extracts had significantly lower blood glucose levels than the group who consumed the placebo beverage 60, 90, and 120 min after ingestion. In terms of area under the curve (AUC) and increase in the area under the curve (IAUC) for blood glucose levels with some variations, the time it took for the participants to consume the trial beverage compared with the placebo beverage was significantly lower.

**Conclusion:** Beverages containing Pu-erh tea extract were found to be effective in suppressing the increase in postprandial blood glucose levels after being loaded with cooked rice.

**Keywords:** Pu-erh tea, postprandial blood glucose, cooked rice, type 2 diabetes

**INTRODUCTION**

The number of patients with diabetes, obesity, and arteriosclerosis, which are known lifestyle-related diseases, is increasing annually [1]. In Japan, several patients present with type 2 diabetes, and the main cause of this disorder is the over-ingestion of products with high-sugar content. Examples of sugars that are highly ingested from food are sucrose and starch, the latter of which is broken down to maltose using α-amylase in the saliva. Sucrase and maltase, which are present as α-glucosidase in the small intestinal epithelial cells, break down sucrose and maltose into monosaccharides in the form of glucose and fructose, respectively; finally, they are absorbed from the intestinal tract and transported to the blood. People worldwide consume tea, and its polyphenol components, such as catechins and theaflavins, are known to inhibit the activity of α-glucosidase and α-amylase.

Moreover, such components suppress the increase in blood glucose values [2, 3]. Pu-erh tea is a type of Chinese post-fermentation tea that is produced by fermenting microbes, such as *Aspergirus niger* [4], and it activates lipid metabolic enzymes [5]. However, to date, few reports have shown the effect of Pu-erh tea on sugar absorption, and these studies have been limited to glucose load tests in mice [6, 7]. In addition, theaflavins included in black tea, which is a totally fermented tea, suppresses glucose absorption. However, reports about the similar effects of theaflavins with high levels of purity are limited. Therefore, in this study, we performed a double-blind, randomized crossover trial in which healthy participants consumed a beverage containing
Pu-erh tea extract or a placebo beverage in addition to cooked rice, to investigate Pu-erh tea polyphenol effects on postprandial blood glucose levels.

Participants and Methods
This study was approved by the NPO Japan Council on Clinical Research, and it was conducted with strict adherence to ethical principles based on the Declaration of Helsinki (revised 2013) and the ethical principles concerning medical research on humans (partially revised 2017). The trial was carried out in August 2018 after obtaining informed consent from the participants. The inclusion and exclusion criteria were as follows:

【Selection criteria】
1. Healthy men and women aged between 20 and 64 years
2. Fasting blood glucose level ≤125 mg/dL at the time of SCR and blood glucose level ≤199 mg/dL 120 min after food loading
3. Individuals who received sufficient explanation of the study objectives and content, those with the ability to provide consent, those who volunteered to participate, and those who provided written consent to participate in the study

[Exclusion criteria]
1. Individuals with critical illness in the liver, kidneys, heart, lungs, digestive organ, blood, endocrine system, or metabolic system
2. Individuals with conditions that require regular medication, or those with a history of critical illness that required medical treatment
3. Individuals currently receiving treatment at a medical institution for disorders in the digestive organ that may affect the trial, or those with a history of surgery in the digestive organ (excluding appendectomy)
4. Individuals with a past history of hypersensitivity to trial food components
5. Women who are pregnant or breastfeeding, or those who wanted to become pregnant during the trial period
6. Individuals who have participated in other pharmaceutical or food trials within the previous month
7. Individuals who were not qualified for the trial as judged by the principal investigator or sub-investigator of the study
In terms of achieving the number of participants, the following were considered: study design (double-blind, randomized, crossover trial), outcome of this study (postprandial blood glucose levels or area under the curve (AUC) for blood glucose levels), and drop-off number. Based on the track record of similar clinical trials, the required number of cases was set to 20. The test design was that of a double-blind, randomized, crossover trial. In addition, as a restriction during the trial period, the participants were instructed not to significantly change their lifestyle practices before participating in the trial, which include food intake, alcohol consumption, exercise, sleep, or smoking habit. In principle, ingestion of medications (including external medicines), newly designated quasi-drugs, herbal medicines, and health foods and supplements was prohibited, except when medically necessary due to changes in health condition. No food and drinks were ingested after 22:00 on the day before the trial, and the participants fasted during the period of the tests. However, they were allowed to drink cold or lukewarm water.

**Trial foods**

Foods used in the trial (beverages containing Pu-erh tea extract [Pu-erh tea polyphenol 18.00mg/2sticks (2.0g Powder), eq. gallic acid, Tasly Pharmaceuticals Inc.] or placebo beverage) were provided in powdered form. An overview of each food is shown in Table 1. Beverages containing Pu-erh tea extract or the placebo beverages were stirred and dissolved in approximately 250 mL of hot water immediately before the trial and made into a beverage after confirming that they were dissolved.

**Table 1 Composition of the test food**

<table>
<thead>
<tr>
<th>Items</th>
<th>Powdered beverages containing Pu-erh tea extract</th>
<th>Placebo beverages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pu-erh tea Polyphenol (eq. gallic acid)</td>
<td>18.00 mg</td>
<td>0.0 mg</td>
</tr>
<tr>
<td>Energy (kcal)</td>
<td>6.68 kcal</td>
<td>7.44 kcal</td>
</tr>
<tr>
<td>Water contents (g)</td>
<td>0.18 g</td>
<td>0.07 g</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>0.64 g</td>
<td>ND</td>
</tr>
<tr>
<td>Lipid (g)</td>
<td>ND</td>
<td>ND</td>
</tr>
<tr>
<td>Carbohydrate (g)</td>
<td>1.00 g</td>
<td>1.86 g</td>
</tr>
<tr>
<td>Sodium (mg)</td>
<td>1.04 mg</td>
<td>ND</td>
</tr>
</tbody>
</table>

*two sticks/day (2.0g powder)

*ND, Not detected
**Trial method**

This trial involved a double-blind, randomized, crossover trial. For the trial, screening of participants based on the inclusion and exclusion criteria was performed using an SCR test, after which, the trial participants were selected. The trial schedule is shown in Figure 1. The participants visited the hospital for the SCR test, phase 1 test, and phase II test, and for physical measurements (height, weight, and body mass index [BMI]) and assessment of blood pressure and pulse rate. Moreover, they were interviewed for the presence of adverse events. The respective assessment methods are as shown below.

![Fig. 1 Test Schedule](image)

1) **Physical measurements**

Height was measured using pre-test, whereas body weight and BMI were measured three times (at the time of the SCR test, phase I test, and phase II test). In addition, the consumption of alcohol and excessive exercise were prohibited from the day before the measurement until the end of the tests.

2) **Blood pressure/pulse rate measurements**

Blood pressure and pulse rate (sedentary position) were measured a total of three times (at the time of the SCR test, phase I test, and phase II test; test interval at least one week.). Blood pressure measurements were carried out using an automated sphygmomanometer (Omron Healthcare) after resting for at least 10 min after arriving at the hospital. Blood pressure was measured twice, and the final value was adopted. In addition, the consumption of alcohol and excessive exercise were prohibited from the day before the measurement until the end of the tests.
3) Cooked rice load trial

The load food was set to 200 g of cooked rice (product name: Sato-no-gohan, Koshihikari rice from Niigata Prefecture; Sato Foods Industries Co., Ltd.). Table 2 shows an overview of the load food. The trial involved dissolving and stirring the test beverage (Placebo and Pu-erh tea extract) in approximately 180 mL of hot water and making a beverage after confirming dissolution. The beverage was then ingested once along with the load foods. The trial and load foods were ingested within 10 min based on the timing directed by the trial collaborators. Measurements of blood glucose levels were obtained before ingestion and 30, 60, 90, and 120 min after the start of ingestion. The SRL group conducted all the tests.

<table>
<thead>
<tr>
<th>Table 2. Composition of cooked rice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item</td>
</tr>
<tr>
<td>Energy (kcal)</td>
</tr>
<tr>
<td>Protein (g)</td>
</tr>
<tr>
<td>Lipid (g)</td>
</tr>
<tr>
<td>carbohydrate (g)</td>
</tr>
<tr>
<td>Sodium (mg)</td>
</tr>
</tbody>
</table>

4) Food surveys

Food surveys were conducted three times: at the time of the SCR test, phase I test, and phase II test. The test participants recorded the content and quantity of food (including alcohol) a day prior to coming to the hospital, and the data were evaluated.

5) Assessment of adverse events

Based on the assessment of adverse events, all undesirable medical events experienced by the participant from the start of ingestion to the end of the post-observation period (unintended signs, symptoms, and conditions) were considered adverse events. Such events were investigated via an interview conducted by the principal investigator or based on the report of the trial participant.

Method of evaluation

The evaluation items for this test were changes in postprandial blood glucose levels and AUC/IAUC.
Method of statistical analysis

1) Efficacy of the evaluation

The evaluation of the efficacy in this trial was conducted as a related t-test for AUC and IAUC. Changes in postprandial blood glucose levels were compared using a related t-test for the measured values and amount of variation.

2) Level of significance

The level of significance was set at 5% on both sides.

3) Software used in the analysis

The SAS software version 9.4 (SAS Co. Ltd.) was used in all the statistical analysis.

Publication of information related to the study

Information about this trial plan was published through registration on the clinical trial registration system managed by the University Hospital Medical Information Network Research Center before starting the recruitment of trial participants. The registration ID is UMIN000033442, and this was published on July 30, 2018.

RESULTS

This trial was conducted in line with the initial plan, rather than the trial plan that was changed after the start of the study.

During the trial, 20 participants, of which 10 were men and 10 were women, were registered. After completing the trial, results showed that three individuals had significant differences in the quantity of food intake the day before the trial and during phase I and II trials; thus, they were excluded from the analysis. Finally, 17 participants were included in the study. The characteristics of the participants are shown in Table 3.

<table>
<thead>
<tr>
<th>Characteristics of the participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Sex (male/female)</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>BMI</td>
</tr>
<tr>
<td>Fasting blood glucose level</td>
</tr>
</tbody>
</table>

Table3. Characteristics of the participants
1) Changes in blood glucose values

Figure 2 and Table 4 show changes in blood glucose values before and after the ingestion of the trial beverages. Changes in blood glucose values were significantly lower 60, 90, and 120 days after ingesting the trial beverage compared to the placebo beverage.

![Figure 2 Time course of blood glucose level](image)

The left image shows the measured values, whereas the right image shows the changes in the amount. Values were presented as mean ± SD. * p<0.05, vs Placebo

<table>
<thead>
<tr>
<th>Time</th>
<th>Placebo</th>
<th>Test</th>
<th>pValue*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before (0 min)</td>
<td>4.94 ± 0.41</td>
<td>4.93 ± 0.34</td>
<td>0.9314</td>
</tr>
<tr>
<td>30 min</td>
<td>7.64 ± 1.14</td>
<td>7.65 ± 1.01</td>
<td>0.9624</td>
</tr>
<tr>
<td>60 min</td>
<td>9.04 ± 1.63</td>
<td>7.89 ± 1.64</td>
<td>0.0012</td>
</tr>
<tr>
<td>90 min</td>
<td>7.97 ± 1.74</td>
<td>6.79 ± 1.54</td>
<td>0.0067</td>
</tr>
<tr>
<td>120 min</td>
<td>6.82 ± 1.18</td>
<td>5.66 ± 1.18</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

Mean±SD
*Paired t test

2) AUC and IAUC results

Figure 3 shows the AUC and IAUC. For each of these values, the time it took the participants who ingested the trial beverage compared with the placebo beverage was significantly lower.
4) Adverse reactions and events

During the trial period, no adverse events or reactions were observed.

DISCUSSION

The present study aimed to investigate the effect of a single dose of a beverage containing Pu-erh tea extract on postprandial blood glucose values. With the use of a double-blind, randomized, crossover test, healthy male and female participants aged between 29 and 64 years were loaded with cooked rice, and changes in blood glucose values after loading were evaluated.

The results showed that the group who ingested the beverage containing Pu-erh tea extract significantly lowered their blood glucose values 60, 90, and 120 min after ingestion compared with the placebo beverage. In terms of the amount of variation before ingestion, the group ingesting beverages containing Pu-erh tea extract had significantly lower amounts of blood glucose values 60, 90, and 120 min after ingestion compared with the group who ingested the placebo beverage. The increase in the AUC and IAUC for blood glucose levels was significantly lower after the ingestion of the trial product compared to the placebo beverage, and this result showed the inhibitory effects of the beverage containing Pu-erh tea extract on postprandial blood glucose values.

Carbohydrates, such as starches and sucrose, in food are digested using salivary amylase and pancreatic amylase within the body and metabolized using oligosaccharides containing small quantities of glucose molecules. α-Glucosidase is the enzyme that participates in these mechanisms, which is found in the intestinal wall brush border, and its main roles are stimulating
the breakdown and absorption of starch dextrin, polysaccharides, sucrose, and maltose in the intestines, and in the non-reducing end of oligosaccharides, as described above, thereby breaking the $\alpha$-1, 4 glycosidic bond and releasing the molecular form of glucose. The glucose molecules released in this manner, which are absorbed from the epithelium of the small intestine, enter the bloodstream and become blood glucose, causing an increase in postprandial blood glucose level. In metabolic disorders, such as diabetes, when insulin levels are decreased, the absorbed blood glucose does not decrease, and the hyperglycemic state is maintained. The maintenance of the hyperglycemic state is correlated to various illnesses, and this can cause conditions such as the saccharification action, causing protein to be saccharified in blood vessels. Inhibiting $\alpha$-glucosidase is a method of mitigating this hyperglycemic state. Inhibitors of $\alpha$-glucosidase reversibly inhibit the brush border $\alpha$-glucosidase (including amylase, sucrase, and maltase) and reduce the increase in postprandial blood glucose levels by slowing down the conversion of polysaccharides and disaccharides into absorbable monosaccharides [8]. The effects of $\alpha$-glucosidase inhibitory action are recognized in a variety of natural products.

Polyphenols, such as catechins, which are found in tea, inhibit $\alpha$-glucosidase. The Pu-erh tea used in this trial contains polyphenol, and since it is a semi-fermented tea manufactured in the same way as oolong tea, the substance contributing to the inhibition of the increase in postprandial blood glucose values is polymerized polyphenol.

**CONCLUSION**

Based on the abovementioned results, beverages containing Pu-erh tea extracts are effective in decreasing postprandial blood glucose values. In addition, since no adverse events or reactions were observed after the ingestion of the trial beverages, it is considered safe for consumption.

**List of Abbreviations:** SCR, screening; UMIN; University Hospital Medical Information Network Research Center; BMI, Body Mass Index; SD, Standard deviation; AUC, Area Under Curve; IAUC, Incremental Area Under Curve

**Authors’ Contributions:** Ryuji Takeda, Yumiko Furuno, Shigeru Imai designed the study; Yumiko Ide, performed the practical part of the study, in addition to the statistical analysis of the data with supervision from Ryuji Takeda; Danyong Wu, Kaijing Yan and all authors engaged in the manuscript work. All authors have read and approved the final manuscript.
Competing Interests: Danyong Wu and Kaijing Yan employed by Tasly Japan Co., Ltd

Acknowledgements and Funding: TASLY Japan Co., Ltd provided financial assistance for the costs related to this trial, which include those for manufacturing the trial food and trial execution.

REFERENCES