Original Article

Black tea consumption improves postprandial glycemic control in normal and pre-diabetic subjects: a randomized, double-blind, placebo-controlled crossover study

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Background and Objectives: Postprandial glycemic control is important for prevention of diabetes. Black tea consumption may improve postprandial glycemic control. The major bioactive compounds are polyphenols, black tea polymerized polyphenol (BTPP).This study examined the effect of black tea consumption on postprandial blood glucose and insulin response following sucrose loading in normal and pre-diabetes subjects. **Methods and Study Design:** This study was a randomized, double-blind, placebo-controlled crossover study. Twenty-four subjects, male and female aged 20-60 years, normal and pre-diabetic, randomly ingested a sucrose solution with a low dose (110 mg BTPP), a high dose (220 mg BTPP) of black tea drink or a placebo drink (0 mg BTPP). Blood samples were collected at 0, 30, 60, 90, and 120 min from commencement of drink ingestion to measure blood glucose and insulin levels. **Results:** The drink containing low dose and high dose BTPP significantly decreased incremental blood glucose area under the curve (AUC) after sucrose intake compared with placebo in the normal (T0-60 min 3,232±356 vs 3,295±312 vs 3,652±454 mg.min/dL; p=0.016) and pre-diabetic subjects (T0-60 min 2,554±395 vs 2,472±280 vs 2,888±502 mg.min/dL; p=0.048). There was no statistically significant difference of changes in insulin levels between the placebo and black tea groups (p>0.05). No significant differences in adverse effects were observed with the placebo, low dose and high dose of BTPP groups. **Conclusion:** Black tea consumption can decrease postprandial blood glucose after sucrose intake.

Key Words: glycemic control, diabetes, black tea, black tea polymerized polyphenols, catechins

INTRODUCTION

Current epidemiology has estimated that the prevalence of diabetes is increasing rapidly with significant medical and economic consequences.[1] The global prevalence of diabetes was 171 million people in the year 2000, and it is projected to increase to 366 million by 2030. The disease is accompanied by high costs mainly due to chronic complications. Diabetes and its complications have many negative effects for health. Cardiovascular disease (CVD) is the most common.

Postprandial glycemic control is important for prevention of diabetes and/or delay of its complications. Moreover, the postprandial hyperglycemia in diabetic patients is a more powerful marker of cardiovascular disease risk than fasting hyperglycemia.[2] Several experimental studies provide a plausible pathophysiological explanation for epidemiological data and give strength to the idea that postprandial hyperglycemia is harmful.

The easiest way to prevent hyperglycemia is to control blood glucose level in the normal range. Management concentrates on keeping blood sugar levels as close to normal as possible, without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications. Nevertheless prevention and treatment of diabetes are not only available with conventional medicine but also with alternative medicine. Functional foods and nutritional supplements are promising alternative medicines which have been used for regulation of plasma glucose to prevent diabetes in order to save costs for treatment of diabetes and complications.

Black tea is produced from the fresh leaves of *Camellia sinensis*. It is one of the most widely consumed beverages in the world. During the oxidation process, polyphenols present in the tea leaf, the catechins, are enzymatically converted to numerous polymerized polyphenols including theaflavins and thearubigens.[3] The major bioactive compounds of black tea areblack tea polymerized polyphenol (BTPP).[4] The health benefits of black tea polyphenols include anti-oxidant,[4-6] anti-inflammatory,[6-8] anti-cancer,[9,10] and anti-hypertensive effects.[11,12] Moreover, *invitro* studies suggest that extracts of black tea could

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interfere with carbohydrate absorption via their ability to inhibit α-amylase, α-glucosidase, and sodium-glucose transporters.[13-16] Also, an animal study has shown the suppressive effect of black tea polymerized polyphenol on postprandial blood glucose in mice (unpublished). Zhong et al found that the black tea extract induced malabsorption of 25% of the carbohydrate in healthy adult human volunteers.[17] Furthermore, Bryans et al established that black tea decreases plasma glucose response in healthy humans with a corresponding increase in insulin level.[18] However, there has been little clinical research on the effects of black tea on postprandial glycemic control and the results are not clear, especially in humans. Therefore, our primary objective was to study the effect of black tea consumption on postprandial blood glucose after sucrose loading in normal and pre-diabetic subjects.

MATERIALS and METHODS

The study was approved by the Ethical Review Committee for Human Research, Faculty of Public Health, Mahidol University (MUPH 2014-145). Furthermore, this study was conducted in accordance with the Declaration of Helsinki on human subjects.

Subjects

We conducted a study in subjects with different backgrounds by selecting normal subjects and pre-diabetic subjects in order to ascertain the suppressive effect of the black tea on sugar absorption. Twenty-four subjects aged 20-60 years were recruited at the Department of Nutrition, Faculty of Public Health, Mahidol University. The inclusion criterion for the normal group was fasting blood glucose level of 70 to 100 mg/dL, pre-diabetic group was fasting blood glucose level of 100-125 mg/dL. Subjects had no diabetes, kidney or liver disease. Subjects who were smokers, pregnant or nursing, regular users of a pharmaceutical or food supplement that impacts glucose metabolism were excluded. Also subjects were excluded if they drank more than three cups daily of tea. Subjects voluntarily participated in the study and provided written informed consent.

Study materials

Menu set

The dinner for the day before the test day was prepared by research assistants. The dinner consisted of rice, minced fish dip with vegetables and rib soup, with energy distribution carbohydrate 57%, protein 13%, and fat 30%.

Beverages

The test drink and placebo drink were manufactured by Suntory Beverage & Food Limited (Japan). The composition of the test drinks and placebo drink are shown in Table 1. Black tea drink was produced by extraction of black tea leaves by hot water, and removing caffeine and catechins. There were 2 doses of black tea drinks, low dose (110 g BTPP) and high dose (220 g BTPP). Placebo drink contained water and caramel coloring. The test drink and placebo drink were packaged in cans.

Study design

This study design was a randomized, double-blind, placebo-controlled, crossover trial. The study consisted of one baseline visit on the screening day and three visits on the test day. Twenty-four subjects were selected from 72 candidates by a screening test and physical examination. Blood pressure was measured by nurse after at least 5 min of seated rest in a chair. Subjects were allocated to different groups by the allocation manager based on their sex and fasting glucose values. A total of 24 subjects were randomly assigned into 2 major groups, normal and pre-diabetic. There were 13 normal subjects (7 men and 6 women) and 11 pre-diabetic subjects (5 men and 6 women). Then subjects were randomly divided again to 3 minor groups for each test drink: a drink containing low dose (110 g BTPP), a drink containing high dose (220 g BTPP) and a placebo drink (0 g BTPP). Subjects consumed the test drink with a 50 g sucrose solution (200 mL) prepared separately on each study day.

On the day before the study day, subjects abstained from excessive eating and consumed the dinner specified by the researcher. The specified dinner was picked up by the subjects themselves from the Department of Nutrition, Faculty of Public Health, Mahidol University. Alcohol consumption was prohibited on the day before the study, and the consumption of all foods and drinks except water was also prohibited after 9 pm. Physical exercise was also prohibited. Subjects reported to the study institution in a fasting state. Then, a blood sample was collected from the subjects at 0 min before sucrose loading. After that, the beverage given to the treatment group was black tea drink (500 mL) containing 110 mg of BTPP or 220 mg of BTPP while the control group was given a placebo drink. Then, each subject from the 3 groups was asked to ingest 50 grams of sucrose solution (200 mL) within 5 min. Subsequently, subjects rested in the examination room and blood was collected at 30, 60, 90, and 120 minutes after sucrose loading (blood sample volume, 3 mL each).

Table 1. The composition of the test drinks and placebo drink

Nutritional content	Test drinks (500 mL)		Placebo drink (500 mL)
	Low dose BTPP	High dose BTPP	
Energy (kcal)	0	0	0
Carbohydrates (g)	ND	ND	ND
Fat (g)	ND	ND	ND
Protein (g)	ND	ND	ND
Sodium (mg)	ND	ND	ND
Caffeine (mg)	0	0	0
BTPP (mg)	110	220	0

ND: Not detectable (<0.1 g/100 mL).

The plasma was separated from the samples and used to measure blood glucose and insulin levels.

After the experiment, all subjects were asked to keep a diary of severity of abdominal and other symptoms to monitor the effect of the beverages they received. All subjects were tested with the other groups as cross-over study. Each participant received all treatments on the same day of the week and had a 1 week washout period between treatments: low dose BTPP, high dose BTPP and placebo drink. This included result measurements and monitoring of adverse events.

Analyses of blood samples

The following parameters were measured for screening test and general characteristic of subjects: serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), fasting blood glucose (FBG), HbA1C, insulin, hemoglobin (Hb), hematocrit (Hct), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase (ALP), gamma-glutamyl transpeptidase (γ-GTP), uric acid, blood urea nitrogen (BUN), creatinine, bilirubin, lactate dehydrogenase, and creatine kinase. All biomarkers were measured at N-Health Asia Lab, Thailand, a medical laboratory with ISO15189:2007 certification.

Statistical analysis

The data were presented as mean±SD. Statistical differences of the means of incremental blood glucose AUC and incremental blood insulin between the treatment and the placebo groups were tested by one-way ANOVA and post-hoc (Tukey) analysis. The adverse symptoms were compared between ingestion of black tea and placebo using one-way ANOVA. The levels of significance were set to $p<0.05$.

RESULTS

Characteristics of subjects at baseline

Twenty four volunteers (13 normal subjects; 7 men, 6 women and 11 pre-diabetic subjects; 5 men, 6 women) were recruited for the study. The mean ages of normal and pre-diabetic subjects were 33.9 and 44.6 years, the average BMI were 25.0 and 28.7 kg/m^2, and mean glucose levels were 89.9 and 108 mg/dL, respectively. Other biochemical markers are shown in Table 2. All the subjects were able to follow the study protocol and finish the study.

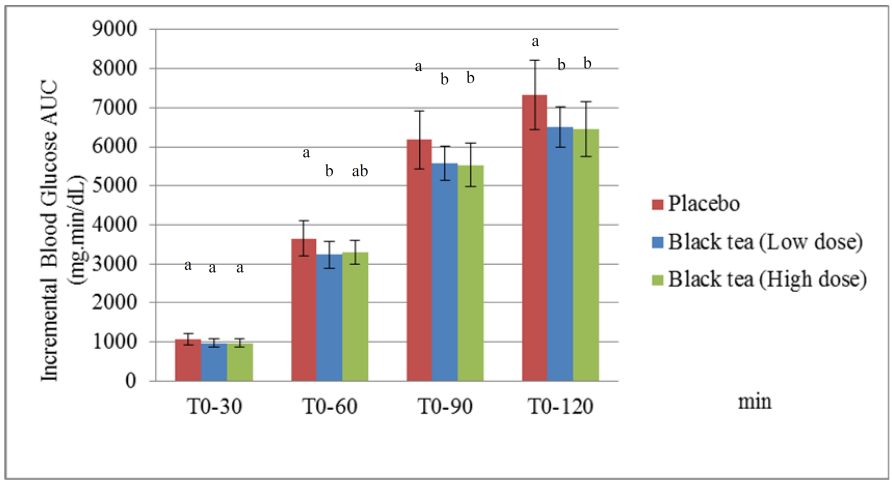
Postprandial glucose and insulin response

The effect of the black tea on blood glucose and insulin levels after sucrose loading in normal subjects

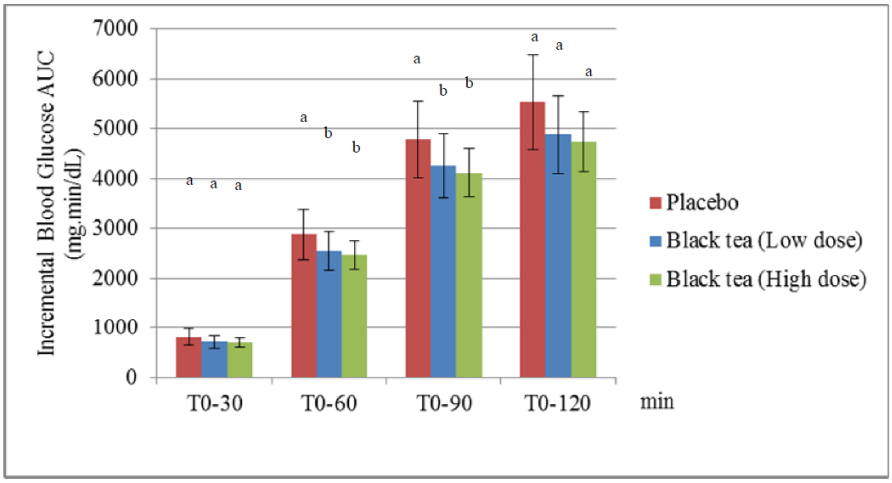
The postprandial responses in the blood glucose levels following the ingestion of sucrose with the black tea drink containing BTPP (low dose) significantly decreased incremental blood glucose area under the curve (AUC) after sucrose intake at 60, 90 and 120 mins compared with placebo (Figure 1A). Likewise, the BTPP (high dose) significantly suppressed the postprandial elevation in incremental blood glucose area under the curve (AUC) at 90 and 120 mins compared with placebo (Figure 1A). Moreover, the incremental blood glucose after the intake of sucrose with the black tea drink containing BTPP (low dose) was significantly decreased at 60 min (91.4±8.19 vs 101±13.3 mg/dL) and 120 min (3.15±4.30 vs 9.46±3.93 mg/dL) compared with placebo. Also, the incremental blood glu-

Table 2. General characteristic and blood chemistry of subjects

General characteristic and biochemical parameters	Normal	Pre-diabetic
Total number, men/women (n)	13 (7/6)	11 (5/6)
Age (years)	33.9±9.24	44.6±10.3
BMI (kg/m^2)	25.0±3.72	28.7±5.56
Body fat (%)	27.8±7.59	33.9±7.85
Waist circumference (cm)	83.8±8.65	94.1±10.2
Systolic blood pressure (mm Hg)	125±8.77	1230±10.3
Diastolic blood pressure (mm Hg)	78.5±7.24	80.6±3.75
Pulse rate (beat/min)	76.7±8.23	75.9±6.95
Total cholesterol (mg/dL)	216±39.9	244±52.9
LDL-C (mg/dL)	154±32.7	151±30.9
HDL-C (mg/dL)	52.9±9.94	60.6±16.4
Triglyceride (mg/dL)	114±43.0	153±68.4
FBG (mg/dL)	89.9±3.36	108±6.48
HbA1C (%)	5.36±0.18	5.88±0.38
Insulin (μIU/mL)	5.36±3.92	10.2±4.30
Hb (g/dL)	14.3±1.54	13.7±1.73
Hct (%)	43.1±4.22	42.2±3.74
SGOT (U/L)	19.9±7.16	18.8±6.63
SGPT (U/L)	24.2±12.9	22.1±13.0
ALP (U/L)	61.4±14.3	64.8±9.34
γ-GTP (U/L)	32.4±31.4	48.9±33.1
Uric acid (mg/dL)	4.88±1.15	6.07±1.69
BUN (mg/dL)	10.3±2.23	11.3±2.81
Creatinine (mg/dL)	0.75±0.14	0.79±0.13
Bilirubin (mg/dL)	0.44±0.10	0.48±0.12
Lactate dehydrogenase (U/L)	162±17.5	172±32.53
Creatine kinase (U/L)	112±35.4	110±55.1



(A)



(B)

Figure 1. Effect of the black tea consumption on blood glucose levels after sucrose loading in normal and pre-diabetic subjects. (A) Incremental blood glucose AUC after sucrose loading in normal subjects. (B) Incremental blood glucose AUC after sucrose loading in pre-diabetic subjects. [a-b] Values with different superscripts are significantly different from each other (p<0.05).

cose after the intake of sucrose with the black tea drink containing BTPP (high dose) was significantly decreased at 60 min (90.3±9.94 vs 101±13.3 mg/dL) and 120 min (2.46±3.07 vs 9.46±3.93 mg/dL) compared with placebo. These results indicated that the black tea drink containing BTPP could decrease postprandial blood glucose after sucrose intake in normal subjects. There were no significant differences between low dose and high dose of BTPP.

The postprandial responses in the blood insulin levels following the ingestion of sucrose with or without black tea drink containing the BTPP (low dose and high dose) in normal subjects was not statistically significant different between placebo, low dose and high dose of BTPP groups (Figure 2A).

The effect of the black tea on blood glucose and insulin levels after sucrose loading in pre-diabetic subjects

The postprandial responses in the blood glucose levels following the ingestion of sucrose with the black tea drink containing BTPP (low dose and high dose) significantly decreased incremental blood glucose area under the curve (AUC) after sucrose intake at 60 and 90 min compared with placebo (Figure 1B). These results indicated that the black tea drink containing BTPP could decrease postprandial blood glucose after sucrose intake in pre-diabetic subjects. There was no significant difference in effect between low dose and high dose of BTPP.

The postprandial responses in the blood insulin levels following the ingestion of sucrose with or without black tea drink containing the BTPP (low dose and high dose) in pre-diabetic subjects were not statistically significantly different between placebo, low dose and high dose of BTPP groups (Figure 2B).

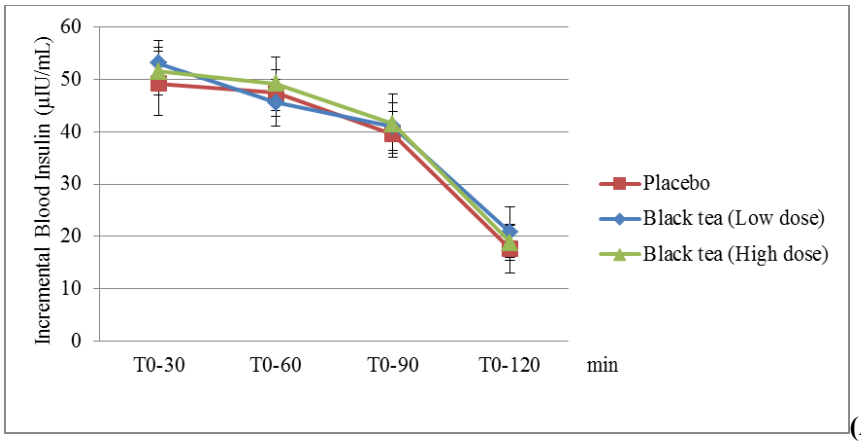
Adverse effects

Adverse events were assessed for any symptom in the placebo, low dose and high dose of BTPP groups. They were rare and no significant differences between the groups.

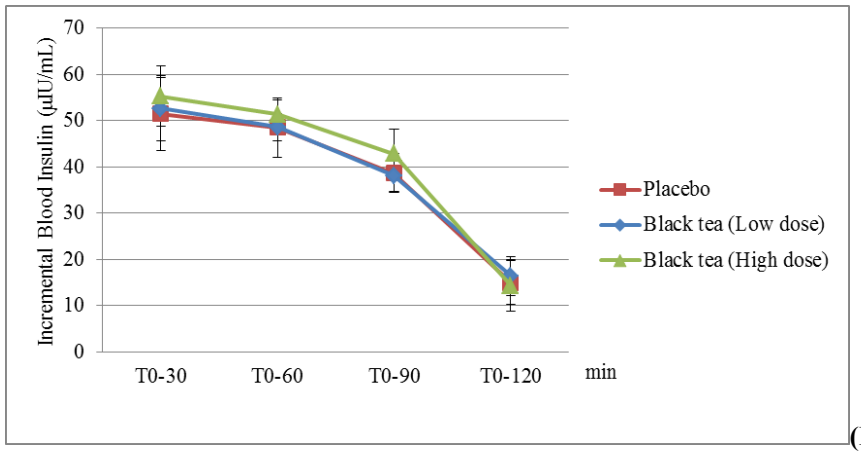
DISCUSSION

In this study, we determined the extent to which BTPP decreased the postprandial elevation in blood glucose after sucrose intake in normal and pre-diabetic subjects. We demonstrated that black tea reduced the incremental blood glucose after sucrose consumption. This is consistent with a previous study which showed that black tea decreased the plasma glucose response in healthy humans.[17]

A possible mechanism of action by which BTPP sup-



(A)



(B)

Figure 2. Effect of the black tea consumption on blood insulin levels after sucrose loading in normal and pre-diabetic subjects. (A) Incremental blood insulin after sucrose loading in normal subjects. (B) Incremental blood insulin after sucrose loading in pre-diabetic subjects. No statistically significant difference between groups.

presses elevation of postprandial blood glucose after sucrose intake is blocking carbohydrate absorption.[16] *In vitro* studies found that extracts of black tea interfere with carbohydrate absorption via their abilities to inhibit α-amylase,[12,13] α-glucosidase[14] and sodium glucose transporter[15] The abilities are similar to those found by Adisakwattana et al[19] who demonstrated that cinnamon bark extracts may be potentially useful for the control of postprandial glucose in patients with diabetes through the ability to inhibit of intestinal α-glucosidase and pancreatic α-amylase. Likewise, Beejmohun et al[20] demonstrated that cinnamon extract significantly reduced the glycemic response also in *in vitro* and *in vivo* studies by inhibiting α-amylase activity. They found that 1 g of cinnamon extract reduced the AUC of glycemia at 0-60 mins ($p<0.05$) compared with placebo, but cinnamon extract has no effect on insulin level. This efficacy of cinnamon for reduction of postprandial hyperglycemia but not change in insulin level showed the same result as the consumption of black tea in this study.

Moreover, the result of black tea consumption in this study is similar to that of Zhong et al.[17] They found the mechanism of black tea extract is its ability to cause carbohydrate malabsorption. The conclusion from their study was that the consumption of black tea extract induced malabsorption of carbohydrate absorption by 25%.

Based on these findings it is suggested that black tea inhibited carbohydrate absorption. On the other hand, the effect of black tea on insulin sensitivity is still inconclusive, since in this study there was no significant difference in the effects of black tea on insulin sensitivity. However, the study of Bryans et al[18] found black tea reduced the late phase plasma glucose response in healthy humans with a corresponding increase in insulin.

Furthermore, the adverse events and the severity of symptoms reported by the subjects for the 8 hrs of study showed no significant differences in symptoms for the placebo, low dose and high dose of BTPP groups. Nevertheless, some normal subjects drinking the high dose of BTPP had nausea that may have been due to their fasting overnight and the taste of black tea.

Based on our result and previously published data, we have shown that BTPP can decrease postprandial glucose after sucrose intake. The drinks containing BTPP might inhibit α-amylase, α-glucosidase, and sodium-glucose transporters activity resulting in block of carbohydrate absorption causing decreased postprandial blood glucose. Our findings suggest that ingestion of black tea with food containing sugar is beneficial in glycemic control and diabetic prevention.

Conclusion

The consumption of black tea containing BTPP can decrease postprandial blood glucose after sucrose intake in both normal subjects and pre-diabetes subjects, suggesting that black tea may be a promising anti-diabetic agent for glycemic control.

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AUTHOR DISCLOSURES
The authors declare no conflict of interest regarding this paper.

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