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The Association between Concentrations of Green Tea and Blood Glucose Levels

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Summary **Our objective was to examine whether habitual green tea consumption is associated with blood glucose levels and other biomarkers of glucose metabolism. We conducted a cross-sectional study of 35 male volunteers, 23–63 years old and residing in Shizuoka Prefecture in Japan. Biochemical data were measured and we conducted a questionnaire survey on health, lifestyle, and nutrition, as well as frequency of consumption and concentrations (1%, 2%, and 3%) of green tea. Men who consumed a 3% concentration of green tea showed lower mean values of fasting blood glucose and fructosamine than those who consumed a 1% concentration. Fasting blood glucose levels were found to be significantly associated with green tea concentration ($\beta = -0.14$, $p = 0.03$). However, green tea consumption frequency showed no significant differences in mean levels of blood glucose, fructosamine and hemoglobin A_{1c}. In conclusion, our findings suggest that the consumption of green tea at a high concentration has the potential to reduce blood glucose levels.**

Key Words**: green tea, concentration of green tea, blood glucose, cross sectional study, Japanese**

Introduction

Green tea contains caffeine and catechins which have potential health benefits. Consumption of green tea is common in Japan, with 80% of Japanese adults drinking it for an average per capita consumption of 2 cups per day [*1*]. Since green tea consumption is thus a major dietary source of caffeine and catechins, and could be beneficial for the health benefit of the Japanese population.

A high frequency of green tea consumption is associated with lower levels of body mass index and serum LDL-cholesterol and triglycerides levels [*2–4*], and fasting glucose [*5*]. In addition, a recent prospective study demonstrated that the frequency of green tea consumption was inversely associated with the risk of type 2 diabetes among middle-aged Japanese men and women [*6*], and we indicated that daily supplementary intake of green-tea-extract powder lowered the hemoglobin A1c level in individuals with borderline diabetes by a cross-over randomized controlled trial [*7*].

Findings of a previous cross-sectional study of 638 men and women aged 65–75 years indicate that the concentration of green tea is inversely associated with fasting blood glucose levels. That study, however, did not make adjustments for important confounding variables such as age, sex,

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body weight, smoking status and energy intake [*8*]. Thus, the potential effect of green tea concentration on serum glucose levels and on the risk of diabetes remains to be examined.

The purpose of this study was to examine whether the concentration of green tea as well as the frequency of green tea consumption are associated with blood glucose levels and other biomarkers of glucose metabolism.

Materials and Methods

The study presented here consisted of a baseline survey for a randomized controlled trial to examine whether dietary supplementation with powdered green tea extract improves glucose abnormalities. The subjects were volunteers who were residents of Shizuoka Prefecture, Japan. Their fasting blood glucose level of >6.1 mmol/l and non-fasting blood glucose level of >7.8 mmol/l as determined during a recent health check-up were higher than those for the general Japanese population [*9*].

Form the individuals asked to participate in this study, obtained informed consent from 23–63-year-old males. Subjects on medication for diabetes or who had had breakfast in the morning of the day of the check-up were excluded from this study. The final number of participants was 35 males. This study was approved by the Research Ethics Committee of University of Shizuoka and conducted in early December 2004. Height and body weight were measured for the calculation of body mass index (BMI, kg/m^2). We also measured biochemical data for fasting blood glucose, fructosamine, hemoglobin A_{1c}, and insulin and conducted a questionnaire survey on health, lifestyles, and nutrition by using a self-administered dietary history questionnaire [*10–12*] as well as the concentration of green tea and the frequency of green tea consumption.

For measurement of the serum glucose levels, venous blood was drawn from the seated participant into a plain, siliconized glass tube, and the serum was separated within 30 min. The serum sample was transported on dry ice to the Osaka Medical Central for Health Science and Promotion an international member of the US National Cholesterol Reference Method Laboratory Network (CRMLN) and SRL Co., Ltd., and stored at −70°C until measurement. The serum glucose level was measured by the hexokinase method using an automatic analyzer (Hitachi 7250, Hitachi Medical Corp., Hitachi, Japan). The hemoglobin A1c level was measured by a latex agglutination immunoassay using the Determiner HbA1c kit (Kyowa Medex Co., Ltd., Tokyo, Japan) and an automatic analyzer (Chemistry Analyzer AU2700; Olympus Medical Engineering Company, Tokyo, Japan). The serum fructosamine level was measured by the colorimeter method.

The questionnaire included questions about the frequency and portion size of brewed green tea as well as commercial green tea beverages, since the latter have been popular since the early part of this century. The concentration of brewed green tea usually consumed by the subjects was determined by administering a taste test of three concentrations of green tea, i.e., 1%, 2%, and 3%, prepared by steeping a given amount of tea in hot water at 85°C for 1 min [*7*, *13*]. The concentration of commercial green tea beverages was assumed to be 1.5%, based on the results of an analysis of the concentrations of several commercial green tea beverages. The frequency of green tea consumption (cups/day or week; open-ended question) and the portion size (ml; subjects selected from cups with different capacities, *i.e.*, 80 ml, 100 ml, 130 ml and 200 ml, the one that was closest in size to the one they customarily used) were determined during the interview. We then calculated total green tea intake with the following equation.

Total green tea intake = (frequency of brewed green tea consumption (cups/day) × (portion size (ml)) × (concentration of green tea (%)/100) + (frequency of commercial green tea consumption (cups/day) × (portion size (ml)) × (1.5 (%)/100)

We confirmed the validity of total green tea intake determined by comparing interview data with the 7-d green tea consumption record for 20 men and women. Pearson's correlation coefficient for the two estimates was 0.81 ($p<0.001$) while the mean total green tea intake calculated from interview data was higher than the 7-d record (18.8 vs. 10.6). Two months later, we confirmed the reproducibility of the values for total green tea intake and concentration of brewed green tea, And found that Pearson's correlation coefficient for the two estimates of total green tea intake was 0.60 ($p = 0.005$). The concordance rate for the two estimates of brewed green tea concentrations obtained during the interview was 60%. Validity and reproducibility of total green tea intake and concentration of brewed green tea determined by this procedure were therefore considered acceptable.

The subjects were divided into three categories based on frequency of green tea consumption (tertile), concentration of brewed green tea (%) and total green tea intake (tertile). We evaluated the differences in the mean values for fasting blood glucose and other characteristics according to the frequency of green tea consumption, the concentration of brewed green tea and total green tea intake by means of the Kruskal-Wallis test. We also examined associations of the frequency or the concentration of green tea consumption and total green tea intake with blood glucose levels by using multiple liner regression analysis, adjusted for age, BMI, smoking status and energy intake. Blood glucose level, fructosamine, hemoglobin A_{1c}, and total green tea intake were log-transformed for this analysis. Statistical significance was defined as $p<0.05$ for two-tailed analysis. All statistical analyses were performed with SAS 9.1 for Windows (SAS Institute Inc., Cary, NC).

Table 1. Characteristics of the subjects

Age (year)	49.8 ± 9.2
Fasting blood glucose (mmol/L)	6.7 ± 2.2
Hemoglobin A_{1c} (%)	5.6 ± 1.5
Fructosamine (μmol/L)	278 ± 72
Fasting blood insulin (pmol/L)	75 ± 65
BMI (kg/m^2)	25.8 ± 5.3
Energy intake (kcal)	2120 ± 488
Alcohol intake (g/1000 kcal)	11.9 ± 13.0
Current smoker	16 (45.7)
Frequency of green tea consumption (cups/day)	
3<	11 (31.4)
3–4	12 (34.3)
>=5	12 (34.3)
Concentration of brewed green tea (%)	
1%	6 (17.1)
2%	14 (40.0)
3%	15 (42.9)
Total green tea intake	21 ± 16

Values are means ± standard deviation or the numbers.
The proportions are shown in the parenthesis.

Results

Of the 35 subjects, six (17.1%) reported consuming brewed green tea at a concentration of 1%, 14 (40.0%) of 2% and 15 (42.9%) of 3%, while 11 (31.4%) reported less than 3 cups/day for the frequency of green tea consumption, 12 (34.3%) consumed 3–4 cups/day, and 12 (34.3%) 5 five cups/day or more (Table 1).

Table 2 shows fasting glucose levels and other characteristics in tertiles of frequency of green tea consumption, concentration of brewed green tea and total green tea intake. Mean values of fasting glucose, fructosamine, hemoglobin A_{1c} and other characteristics did not differ according to the frequency of green tea consumption or total intake. Mean values of fasting glucose and fructosamine decreased in parallel with a higher concentration of brewed green tea, and a similar trend was observed for hemoglobin A_{1c}.

The results of multiple regression analyses are shown in Table 3. A significant inverse association was found between the concentration of drew-green tea and fasting blood glucose levels. A similar but weaker inverse association was observed for hemoglobin A_{1c} and fructosamine. There was no association between frequency of green tea consumption or total green tea intake and fasting glucose, fructosamine or hemoglobin A_{1c} levels.

Discussion

The subjects of this study who consumed a 3% concentration of green tea had lower means of fasting blood glucose and fructosamine than those who consumed a 1% concentration of green tea, and the association of the concentration of green tea with fasting blood glucose levels was significant. However, no significant differences were found in mean levels of blood glucose, fructosamine or hemoglobin A_{1c} in terms of frequency of green tea consumption or total green tea intake. The absence of the latter associations may be due in part to the small number of subjects. Moreover, the small variations in the frequency of green tea consumption by subjects of Shizuoka Prefecture, one of Japan's major green tea producing areas, may such associations indistinct and difficult to detect.

The present findings are in line with our previous trial demonstrated that the supplement of green-tea-extract powder, corresponding to the intake of high concentration of brewed green tea, lowered hemoglobin A_{1c} levels [*7*]. However, other trials have failed to detect a hypoglycemic effect of green tea supplement [*2*, *3*, *5*, *14–16*].

The mechanisms for the inverse association between green tea concentration and fasting blood glucose and fructosamine levels warrant discussion. An *in vitro* study found that epicatechin gallate inhibited intestinal Na^+-dependent glucose transporter activity, leading to reduced intestinal glucose uptake [*17*], and induced the down-regulation of hepatic glucose production [*18–20*]. An experimental animal study showed that green tea polyphenol increased insulin activity [*21*], a double-blind, placebo-controlled study that caffeine increased basal energy expenditure and lipolysis from peripheral tissues [*22*], and a cross-over randomized controlled trial that daily supplementary intake of green-tea-extract powder lowered the hemoglobin A1c level [*7*].

In this study, sample size was small, distributions of numeric variables were not normal, and numbers of subjects among concentrations of green tea were different. However, we used nonparametric method which is the Kruskal-Wallis test for evaluate the differences in the mean values and used regression analysis after numeric variables were log-transformed. Apparently, the findings of this study may difficult to be considered generalizability because of small numbers of the subject, but the results of analysis may be excluded influence of the distribution and different of the number of the concentrations.

Our findings suggest that green tea at a high concentration has the potential to reduce blood glucose levels. Since it remains uncertain whether similar benefits can be derived for the control of glucose abnormalities in terms of the concentration of green tea or the amount of green tea consumed, further epidemiological and experimental studies will be necessary to clarify this issue.

Table 2. Fasting blood glucose and other characteristics according to tetiles of the frequency of green tea consumption, the concentration of brewed green tea and total green tea intake

Frequency of green tea consumption	Low (3< cups/day) (n = 11)	Middle (3–4 cups/day) (n = 12)	High (>=5 cups/day) (n = 12)	p value
Median of total green tea intake	5	20	33	—
Age (year)	46.6 ± 11.8	50.8 ± 7.1	51.7 ± 8.4	0.528
Fasting blood glucose (mmol/L)	6.4 ± 1.5	6.7 ± 2.1	7.1 ± 2.9	0.844
Hemoglobin A_{1c} (%)	5.2 ± 0.7	5.7 ± 1.7	5.8 ± 1.9	0.951
Fructosamine (μmol/L)	253 ± 26	287 ± 91	293 ± 78	0.225
Fasting blood insulin (pmol/L)	78 ± 71	86 ± 71	62 ± 57	0.689
BMI (kg/m^2)	25.8 ± 6.4	24.5 ± 3.9	27.2 ± 5.6	0.899
Energy intake (kcal)	1973 ± 445	2116 ± 485	2260 ± 526	0.323
Alcohol intake (g/1000 kcal)	11 ± 14	15 ± 14	10 ± 12	0.602
Concentration of brewed green tea	Low (1%) (n = 6)	Middle (2%) (n = 14)	High (3%) (n = 15)	p value
Median of total green tea intake	6	15	24	—
Age (year)	46.5 ± 12.9	50.5 ± 8.5	50.5 ± 8.6	0.768
Fasting blood glucose (mmol/L)	7.9 ± 1.6	6.6 ± 1.8	6.4 ± 2.7	0.038
Hemoglobin A_{1c} (%)	6.0 ± 1.0	5.6 ± 1.4	5.4 ± 1.8	0.083
Fructosamine (μmol/L)	300 ± 51	285 ± 78	264 ± 74	0.045
Fasting blood insulin (pmol/L)	106 ± 87	53 ± 36	84 ± 74	0.476
BMI (kg/m^2)	27.8 ± 6.9	23.8 ± 3.8	27.0 ± 5.5	0.336
Energy intake (kcal)	2328 ± 554	2122 ± 491	2036 ± 467	0.620
Alcohol intake (g/1000 kcal)	13 ± 16	9 ± 10	14 ± 14	0.710
Total green tea intake	Low (n = 11)	Middle (n = 12)	High (n = 12)	p value
Median of total green tea intake	5	19	33	—
Age (year)	44.5 ± 11.2	52.9 ± 5.0	51.5 ± 9.1	0.227
Fasting blood glucose (mmol/L)	6.2 ± 1.5	7.2 ± 2.0	6.8 ± 2.9	0.789
Hemoglobin A_{1c} (%)	5.1 ± 0.8	6.0 ± 1.5	5.6 ± 1.9	0.998
Fructosamine (μmol/L)	260 ± 29	294 ± 92	280 ± 78	0.797
Fasting blood insulin (pmol/L)	66 ± 74	75 ± 66	84 ± 62	0.493
BMI (kg/m^2)	24.8 ± 6.6	24.6 ± 3.3	28.1 ± 5.3	0.857
Energy intake (kcal)	1972 ± 436	2255 ± 526	2122 ± 494	0.289
Alcohol intake (g/1000kcal)	11 ± 14	15 ± 13	10 ± 12	0.671

Values are means ± standard deviation.

Table 3. Associations of the frequency of green tea consumption, the concentration of brewed green tea and total green tea intake with blood glucose, fructosamine and hemoglobin A_{1c} levels: the multiple liner regression analysis.

	Frequency of green tea			Concentration of green tea			Total green tea intake		
	β	SE	p value	β	SE	p value	β	SE	p value
Fasting blood glucose	0.03	0.06	0.69	–0.14	0.06	0.03	–0.01	0.05	0.83
Fructosamine	0.05	0.05	0.32	–0.09	0.05	0.09	0.01	0.04	0.74
Hemoglobin A_{1c}	0.03	0.05	0.61	–0.08	0.05	0.11	0.01	0.04	0.89

Test by using multiple regression analysis, adjusted for age, BMI, smoking status and energy intake.
Total green tea intake, fasting blood glucsose, fructsamine, hemoglobin A_{1c} and energy intake were log-transformed.

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