Antihyperglycemic Effect of Oolong Tea in Type 2 Diabetes

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OBJECTIVE — To determine the efficacy of oolong tea for lowering plasma glucose in type 2 diabetic patients in Miaoli, Taiwan.

RESEARCH DESIGN AND METHODS — A total of 20 free-living subjects who had type 2 diabetes and took hyperglycemic drugs as prescribed were enrolled in the present study. Subjects consumed oolong tea (1,500 ml) or water for 30 days each in a randomized crossover design. Tea was not consumed for 14 days prior to treatments.

RESULTS — Relative to initial concentrations, oolong tea markedly lowered concentrations of plasma glucose (from 229 ± 53.9 to 162.2 ± 29.7 mg/dl, $P < 0.001$) and fructosamine (from 409.9 ± 96.1 to 323.3 ± 56.4 μmol/l, $P < 0.01$), whereas the water control group had not changed (208.7 ± 61.0 vs. 232.3 ± 63.1 mg/dl for glucose and from 368.4 ± 85.0 to 340.0 ± 76.1 μmol/l for fructosamine).

CONCLUSIONS — Oolong tea may be an effective adjunct to oral hypoglycemic agents in the treatment of type 2 diabetes.

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Recently, consumption of tea has become even more popular in Taiwan, Japan, and China. Consumption of tea leaves in Taiwan increased 2.2 times during last 20 years (1). Tea consumption may have an impact on plasma glucose concentrations. The concept was supported by in vivo studies of tea fed to diabetic rodents (2–4) and by in vitro studies where tea components were incubated with brush border membrane vesicles of rabbit small intestine (5).

Caffeine is one of the most important components in tea. There are some studies examining caffeine, for example, in healthy volunteers (6,7), in type 1 diabetes (8–10), and in type 2 diabetes (11). However, the efficacy of tea in lowering plasma glucose concentrations in humans was limited.

There are three types of tea: green, oolong, and black. They are produced from a single plant species, but they are distinguished by the processing technique. Oolong tea is partially fermented during processing, whereas green tea is not fermented, and black tea is fully fermented (12).

In general, the amount of the polymerized polyphenols is determined by the level of the fermentation. The degree of fermentation of oolong tea leaves from Taiwan is very low because of the preparation method. In contrast, oolong tea leaves from China contained an especially large amount of polymerized polyphenols, and fermentation was strong (13). For these reasons, oolong tea from China was used in this study.

The purpose of this study was to assess the ability of oolong tea to lower plasma glucose concentrations in subjects with type 2 diabetes.

RESEARCH DESIGN AND METHODS

— The ethical committee of Providence University, an institutional review board, approved the study, and subjects gave informed consent. A total of 10 men and 10 women (average age 61.2 years, duration of diabetes 4.8 years) were recruited through their physicians at Chorng Kuang Hospital, Miaoli, Taiwan.

The study used a crossover design; sex-matched subjects were randomly assigned to treatment order. Subjects were divided into two groups at random. The washout period was set for 2 weeks from the start of the examination (first washout period), and only water was permitted for drinking throughout this period. The next 4 weeks was the treatment period (first treatment period). During this period, water or oolong tea was drunk in each group. After that, the second washout period of 2 weeks was begun (second washout period), and drinking water was permitted during this period. It was continuously made to replace the beverage with each group and to take the next four compliance weeks in that water or oolong tea was drunk in each group (second treatment period). All subjects regularly received doctor examinations, dietary intervention by a national registered dietitian, and patient instructions additionally every week throughout the examination period.

During the tea treatment, subjects consumed 1,500 ml of oolong tea per day. Oolong tea was provided to subjects as tea bags. Subjects prepared the tea each morning by adding 1,500 ml of boiling water to five tea bags (15 g of tea leaf) and steeping for 10 min. Tea was taken five times per day independent of water body

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Abbreviations: HPLC, high-performance liquid chromatography.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Components of caffeine and oolong tea polyphenols*

Components	Oolong tea of China (mg/1,500 ml)
Gallic acid	32.9
Caffeine	352.7
Gallocatechine	100.2
Epigallocatechine	242.1
Catechine	24.8
Epicatechine	76.2
Epigallocatechine gallate	386.0
Allocatechine gallate	27.8
Epicatechine gallate	86.0
Catechine gallate	9.0
Polymerized polyphenols	504.8
Total polyphenols	1,489.8

Data are mean amount of daily consumption of oolong tea components.

requirements. In addition, participants were not allowed to use any type of tea (except oolong tea) during the study. For the water treatment, subjects drank 1,500 ml of water but no tea.

Concentration of caffeine, gallic acid, flavanols, and other polyphenols (fraction including polymerized flavanols and other flavonoids) in the oolong tea were analyzed by high-performance liquid chromatography (HPLC) with UV detection at 280 nm (13). Analysis was performed with a Cosmosil 5PE-MS column (4.6 mm internal diameter ×150 mm; Nakarai Tesuque, Kyoto, Japan) at 40°C. Compounds were eluted (eluent A: 0.05% trifluoroacetic acid in water; eluent B: 0.05% trifluoroacetic acid in acetonitrile) at a flow rate of 2 ml/min using a gradient program (eluent B content: 10% for 5 min, 21% for 8 min, 90% for 1 min, and 90% for 6 min). The quantification of caffeine, gallic acid, and flavanols was determined using standard calibration curves for marketed compounds. Other polyphenols were quantified using a calibration curve that was derived from other polyphenols that had been isolated from tea by HPLC.

Height was measured only at the first washout period. Body weight was measured and BMI computed in every period. Blood pressure was also measured in every period of the study. Dietary intakes were assessed from 24-h dietary recalls conducted by dietitians four times on 3 consecutive days (middle 3 days of every period). Energy intake; nutrient consumption (protein, lipid, and carbohydrate); the amount of dark green, yellow, and light vegetable intake; and the amount of fruit intake were calculated by nutritive analysis software using the Taiwan food composition table (14).

Blood was collected five times: at the start of the study (−2 weeks), at the end of the first washout period (0 weeks), at the end of the first treatment period (4 weeks), at the end of the second washout period (6 weeks), and at the end of the second treatment period (10 weeks). Collected blood was centrifuged, and separated plasma was stored at −80°C. Plasma glucose was measured by a glucose oxidase method and fructosamine by reduction of nitro-blue tetrazorium (by blood analysis company SRL, Tokyo). To measure physical activity, subjects wore pedometers daily during waking hours. The identity and treatment regimen of subjects were blinded to the technicians who analyzed plasma samples, and values for outcome variables were locked in place before statistical analysis.

Inclusion criteria were fasting plasma glucose concentration ≥126 mg/dl and a glucose level ≥200 mg/dl 2 h after a 75-g glucose load (15). Subjects were taking oral blood glucose–lowering drugs for type 2 diabetes under the supervision of a physician. Subjects took sulfonylurea drugs alone ($n = 11$) or in combination with biguanide drugs ($n = 9$); both the type and amount were constant across the study.

Data were presented as means ± SD. The Wilcoxon's signed-rank test was used to compare the mean and test for significant differences. P values <0.05 were considered as significant. All statistical analyses were performed with the SPSS Advanced Model version 10 (SPSS Japan, Tokyo).

RESULTS — The daily serving of caffeine and tea polyphenols of oolong tea is presented in Table 1. Total caffeine and tea polyphenol consumption for subjects consuming 1,500 ml of the oolong tea were 352.7 and 1,490 mg, respectively (Table 1).

Subjects received a physical examination every week. There were no adverse events in the subjects throughout the study period. Clinical features, exercise,

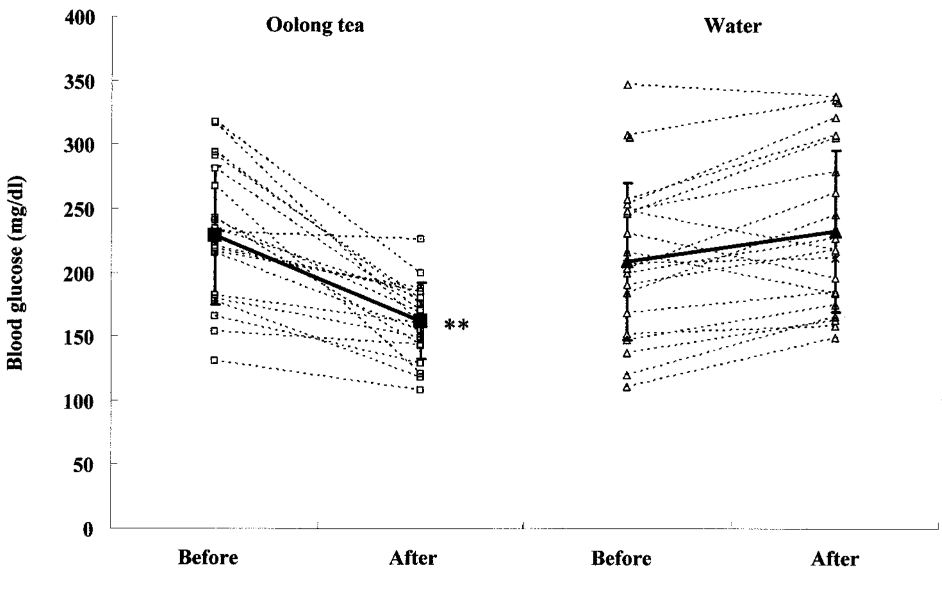

Figure 1—*Changes in fasting blood glucose concentration before and after subjects consumed oolong tea or water for 4 weeks. Bold line, mean ± SD; dotted fine line, individual data. **Significantly different from initial value by Wilcoxon's signed-rank test at* $P < 0.001$.

Table 2—*Changes in clinical features, exercise, and food intake of subjects throughout the study*

	First washout	First treatment	Second washout	Second treatment
Age (years)				
All subjects	61.2 ± 7.65	—	—	—
Group 1	63.2 ± 9.26	—	—	—
Group 2	59.2 ± 5.37	—	—	—
Duration of diabetes (years)				
All subjects	4.78 ± 2.48	—	—	—
Group 1	4.87 ± 2.42	—	—	—
Group 2	4.69 ± 2.67	—	—	—
Body weight (kg)				
All subjects	61.9 ± 7.79	62.0 ± 7.85	62.0 ± 7.85	62.0 ± 7.81
Group 1	61.7 ± 7.41	61.7 ± 7.48	61.7 ± 7.47	61.8 ± 7.39
Group 2	62.2 ± 8.55	62.2 ± 8.60	62.2 ± 8.62	62.2 ± 8.61
BMI (kg/m^2)				
All subjects	22.6 ± 1.06	22.6 ± 1.11	22.7 ± 1.06	22.6 ± 1.04
Group 1	23.4 ± 2.17	23.4 ± 2.24	23.5 ± 2.18	23.6 ± 2.11
Group 2	23.7 ± 2.11	23.8 ± 2.13	23.8 ± 2.13	23.8 ± 2.15
Systolic blood pressure (mmHg)				
All subjects	131.1 ± 13.30	129.0 ± 12.10	129.8 ± 12.62	129.5 ± 12.34
Group 1	130.6 ± 9.14	129.0 ± 7.38	129.0 ± 7.38	130.0 ± 8.16
Group 2	131.5 ± 17.00	129.0 ± 15.95	130.5 ± 16.74	129.0 ± 15.95
Diastolic blood pressure (mmHg)				
All subjects	84.8 ± 6.58	84.0 ± 5.98	83.8 ± 5.82	84.3 ± 5.91
Group 1	86.0 ± 5.68	84.0 ± 5.16	83.5 ± 4.74	84.5 ± 4.97
Group 2	83.5 ± 7.47	84.0 ± 6.99	84.0 ± 6.99	84.0 ± 6.99
Exercise (steps/day)				
All subjects	6,955 ± 1,137	7,086 ± 1,138	7,126 ± 1,185	7,128 ± 1,154
Group 1	7,093 ± 1,249	7,201 ± 1,277	7,214 ± 1,256	7,198 ± 1,233
Group 2	6,817 ± 1,062	6,971 ± 1,036	7,039 ± 1,171	7,057 ± 1,131
Energy intake (kcal/day)				
All subjects	1,868 ± 148	1,856 ± 134	1,858 ± 133	1,860 ± 140
Group 1	1,854 ± 132	1,853 ± 124	1,859 ± 116	1,860 ± 132
Group 2	1,881 ± 168	1,858 ± 151	1,857 ± 155	1,860 ± 154
Protein (g/day)				
All subjects	62.6 ± 7.40	62.7 ± 6.36	61.4 ± 5.71	63.5 ± 7.02
Group 1	65.9 ± 7.26	66.1 ± 4.66	64.1 ± 3.95	67.5 ± 5.85
Group 2	59.4 ± 6.27	59.2 ± 6.12	58.8 ± 6.15	59.5 ± 5.88
Fat (g/day)				
All subjects	56.5 ± 5.35	56.2 ± 4.48	55.4 ± 5.29	55.4 ± 4.54
Group 1	54.3 ± 4.06	54.7 ± 2.86	54.1 ± 4.15	54.3 ± 4.10
Group 2	58.6 ± 5.80	57.7 ± 5.40	56.6 ± 6.22	56.6 ± 4.86
Carbohydrate (g/day)				
All subjects	277.2 ± 23.75	274.7 ± 22.60	278.9 ± 18.42	276.4 ± 22.86
Group 1	275.4 ± 21.02	274.1 ± 23.76	278.9 ± 17.43	275.4 ± 23.20
Group 2	279.0 ± 27.24	275.4 ± 22.63	279.0 ± 20.32	277.4 ± 23.72
Dark green vegetables (g/day)				
All subjects	180.0 ± 36.99	182.5 ± 30.24	173.5 ± 34.07	181.0 ± 33.54
Group 1	194.0 ± 30.26	190.0 ± 25.82	183.0 ± 30.93	189.0 ± 33.81
Group 2	166.0 ± 39.21	175.0 ± 33.75	164.0 ± 35.96	173.0 ± 33.02
Yellow vegetables (g/day)				
All subjects	240.0 ± 32.28	242.5 ± 30.24	241.0 ± 26.34	239.0 ± 31.61
Group 1	242.0 ± 23.48	242.0 ± 19.89	243.0 ± 22.14	243.0 ± 21.63
Group 2	238.0 ± 40.50	243.0 ± 39.17	239.0 ± 31.07	235.0 ± 40.07
Fruit (g/day)				
All subjects	318.3 ± 38.30	317.0 ± 40.01	312.5 ± 41.60	313.9 ± 42.91
Group 1	310.0 ± 29.06	311.5 ± 34.00	305.5 ± 35.47	308.5 ± 30.28
Group 2	326.5 ± 45.83	322.5 ± 46.44	319.5 ± 47.81	319.3 ± 53.90

Data are means ± SD. Group 1, treatment from oolong tea to water; group 2, treatment from water to oolong tea.

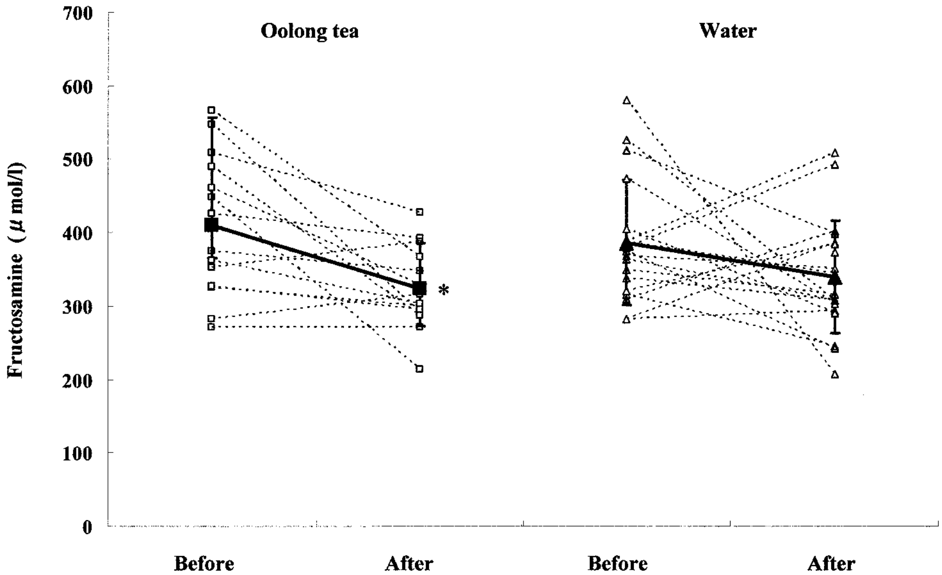

Figure 2—*Changes in fructosamine concentration before and after subjects consuming oolong tea or water for 4 weeks. Bold line, mean ± SD; dotted fine line, individual data. *Significant difference from initial value by Wilcoxon's signed-rank test at* P < *0.01.*

and dietary intakes of the study population are shown in Table 2. Body weight, BMI, blood pressure, and physical activities of the subjects were constant during all study periods. As shown in Table 2, energy intake, yellow or dark green vegetable intake, and fruit intake were unchanged during the study.

We measured two parameters of plasma fructosamine and glucose concentration in an effort to assess short-term as well as long-term glucose metabolic status. Glucose reflects plasma glucose concentrations at the time of measurement, and fructosamine reflects plasma glucose concentrations over the last 1–2 weeks. Oolong tea significantly decreased plasma glucose (from an initial concentration of 229 ± 53.9 to 162.2 ± 29.7 mg/dl, $P < 0.001$), whereas water did not (from 208.7 ± 61.0 to 232.3 ± 63.1 mg/dl) (Fig. 1). Fructosamine concentration decreased significantly (from 409.9 ± 96.1 to 323.3 ± 56.4 μmol/l with the tea treatment, $P < 0.01$) but did not change significantly with the water treatment (from 368.4 ± 85.0 to 340.0 ± 76.1 μmol/l) ($P \geq 0.05$) (Fig. 2).

CONCLUSIONS

— The plasma glucose and fructosamine concentrations of diabetes patients decreased significantly ($P < 0.001$ and 0.001, respectively) after drinking oolong tea but did not change after drinking water. This brew was stronger than that typically consumed in Taiwan (Table 1), yet no adverse effects from the tea were reported. In this study, we tried to eliminate the confounding factors that affect the blood glucose concentration. Antihyperglycemic medicines were the strongest confounding factors. Medications used in this study were sulfonylurea and biguanide drugs. Subjects took sulfonylurea drugs alone ($n = 11$) or in combination with biguanide drugs ($n = 9$); both the types and amount were constant across the study. Thus, we believe that the confounding factors of the medicines might be eliminated. Physical activity is also an important confounding factor. We measured the daily activity using a pedometer. The counts of the step were similar in all four periods, indicating that physical activity was constant throughout the study and that physical activity was not a significant confounding factor (Table 2). Intakes of energy and other nutrients are also important confounding factors. They were assessed from 24-h dietary recalls conducted by dietitians four times on 3 consecutive days (middle 3 days of the washout, water, and oolong tea periods). Energy intake was similar in all four measurements (Table 2). These results indicated that energy and nutrient intakes were not confounding factors in this study.

Caffeine is one of the most important components in tea. The influence of caffeine on normal adults and diabetes was observed in recent studies; however, the results are still being debated. According to Keijzers et al. (6), caffeine can decrease insulin sensitivity by increasing the concentration of serum epinephrine. However, on the other hand, caffeine was found to substantially lower risk of clinical type 2 diabetes in previous studies (8–11).

In this study, the study period of each beverage was 1 month. With a longer study, we might have clearer data and we could also add HbA_{1c} measurement, which is the indicator of blood glucose concentration for ~3 months. Another limit of our study was the sample size. To assess the whole efficacy of oolong tea on diabetes, large-scale surveys should be conducted in the future.

The mechanism of the antihyperglycemic effect of oolong tea is not yet clear. There are some studies that have shown the insulin-like activity of tea polyphenols in rats (16,17) and the delay of glucose absorption by tea in rats (3) and rabbits (5). We need further studies to clarify the mechanisms.

In conclusion, this study supports the concept that oolong tea is effective in lowering the plasma glucose levels of subjects who have type 2 diabetes and who take oral antihyperglycemic agents. Furthermore, oolong tea, in conjunction with antihyperglycemic agents, was more effective in lowering plasma glucose than were the drugs alone.

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