Tea Consumption May Improve Biomarkers of Insulin Sensitivity and Risk Factors for Diabetes¹⁻³

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Abstract

Diabetes mellitus and its sequelae are a major and growing public health problem. The prevalence of diabetes worldwide is 194 million persons, or 5.1% of the population, and is projected to increase to 333 million, or 6.3% of the population, by 2025. Type 2 diabetes accounts for ~90-95% of those with diabetes in the United States and other developed countries. Tea is the most widely consumed beverage in the world, second only to water. Tea contains polyphenols and other components that may reduce the risk of developing chronic diseases such as cardiovascular disease and cancer. Some evidence also shows that tea may affect glucose metabolism and insulin signaling, which, as a result, has spurred interest in the health effects of tea consumption on diabetes. Epidemiologic studies suggest some relation between tea consumption and a reduced risk of type 2 diabetes, although the mechanisms for these observations are uncertain. Findings from in vitro and animal models suggest that tea and its components may influence glucose metabolism and diabetes through several mechanisms, such as enhancing insulin sensitivity. Some human clinical studies evaluating tea and its components show improvement in glucoregulatory control and endothelial function. However, further controlled clinical trials are required to gain a better understanding of the long-term effects of tea consumption in persons with diabetes. J. Nutr. 138: 1584S-1588S, 2008.

Introduction

Diabetes mellitus and its sequelae are a major and growing public health problem. The prevalence of diabetes worldwide is 194 million persons, or 5.1% of the population, and is projected to increase to 333 million, or 6.3% of the population, by 2025 (1,2). The number of persons with impaired glucose tolerance is estimated to increase as well. Diabetes is related to obesity, inactivity, population growth, and aging (1,3). In addition, diabetes is recognized as a group of metabolic disorders characterized by hyperglycemia and glucose intolerance as a result of insulin deficiency, impaired effectiveness of insulin action, or both (4). Type 2 diabetes accounts for ~90-95% of those with diabetes in the United States and other developed countries. Additionally, it may account for a higher percentage in developing countries (1,5). Type 2 diabetes is frequently associated with obesity because obesity may cause insulin resistance and lead to hyperglycemia (6,7). Lifestyle strategies that include physical activity and dietary modification, such as consumption of a plant-based diet, may reduce type 2 diabetes (8). Several components of a plant-based diet may contribute to its beneficial health effects, but there has been speculation that plant polyphenols may play a role (9).

Tea is the most widely consumed beverage in the world, second only to water (10). Tea contains polyphenols and other components that may reduce the risk of developing chronic diseases such as cardiovascular disease and cancer. Some evidence also shows that tea may affect glucose metabolism and insulin signaling, which as a result has spurred interest in the health effects of tea consumption on diabetes (11). Of the tea produced worldwide, 78% is black tea, which is typically consumed in North America and Europe; 20% is green, which is favored by Asian countries; and 2% is oolong, commonly consumed in China and Taiwan (12). Black, green, and oolong
Epidemiologic studies: tea consumption and risk of type 2 diabetes mellitus

Several studies have examined the relation between tea consumption and risk of type 2 diabetes. For example, Salazar-Martinez et al. (19) examined the association between tea and coffee consumption and diabetes risk in 41,934 U.S. men from the Health Professionals' Follow-up Study, aged 40-75 y, and 84,276 U.S. women from the Nurses' Health Study, aged 30-55 y, who were followed for 12 y and 18 y, respectively. Diagnosis of diabetes was from self-report on biennial follow-up questionnaires; supplementary questionnaires were subsequently sent to confirm the self-report and to distinguish among type 1, type 2, and gestational diabetes. FFQ assessing beverage and caffeine intake, were obtained at multiple time points. Participants were asked how often on average during the previous year they had consumed tea (1 cup or glass (240 mL)), caffeinated coffee, and decaffeinated coffee (1 cup), different types of caffeinated sodas (1 glass, can, or bottle), and chocolate products (bar or packet). Results showed that tea consumption was not significantly associated with diabetes risk in either cohort. There was an inverse association between coffee intake and risk of type 2 diabetes and a slight inverse association between higher consumption of decaffeinated coffee (>2 cups/d or 960 mL/d) and diabetes risk. Total caffeine intake from coffee and other sources (cola, tea, and chocolate) was associated with a lower risk of diabetes in both men and women.

In a similar prospective cohort study, van Dam et al. (20) examined the relation among tea, coffee, and caffeine and risk of type 2 diabetes, as assessed by a FFQ at multiple time points in 88,259 U.S. women aged 26-46 y from the Nurses' Health Study II, followed for 10 y. Diagnosis of type 2 diabetes was based on self-report with follow-up questionnaires for confirmation of the disease. This study showed that tea consumption was not associated with the risk of type 2 diabetes. However, consumption of >2 cups/d (480 mL/d) of coffee was associated with a lower risk of type 2 diabetes; this association was similar for caffeinated and decaffeinated coffee. Higher caffeine intake was associated with a lower risk of type 2 diabetes. The authors also evaluated potential independent effects of coffee and caffeine by investigating cross-categories of coffee and caffeine intake in relation to type 2 diabetes. Higher total coffee consumption was associated with lower risk of type 2 diabetes in each category of caffeine intake; however, higher caffeine intake was not associated with risk of type 2 diabetes within categories of total coffee consumption. Therefore, the risk of type 2 diabetes and coffee consumption was shown to be independent of caffeine intake.

Although these 2 prospective cohort studies showed no association of tea consumption with risk of type 2 diabetes, several studies have suggested a beneficial effect of tea consumption on diabetes risk. A recent study examined the relation between green tea and total caffeine intake and risk of type 2 diabetes among Japanese adults (21). In this retrospective cohort study, 17,413 adults aged 40-65 y completed a 5-y follow-up questionnaire on self-reported physician-diagnosed diabetes and consumption of coffee and green, black, and oolong teas. Tea intake was assessed once, at the baseline of the study, by a FFQ. The self-reported diagnosis of diabetes was compared with fasting serum glucose concentration in a subsample of participants. Adults who consumed >8 cups/d (1440 mL/d) of green tea lowered their risk of diabetes by 33%. No association with diabetes risk was found for oolong or black teas. Consumption of >3 cups/d (720 mL/d) of coffee lowered the risk of diabetes by 42%. High caffeine intake (416 mg/d) was also associated with a 33% reduction in risk of diabetes. For green tea and caffeine consumption, a lowered diabetes risk was observed primarily in women; however, for coffee consumption, a lowered diabetes risk was observed in both men and women. The authors suggested that the inverse associations seen were mostly caused by the relation between caffeine intake and diabetes risk, because green tea and coffee (<45% for both) are major contributors to caffeine intake in Japan. However, potential independent effects of coffee, green tea, and caffeine in relation to type 2 diabetes were not evaluated. The consumption of oolong and black teas is also low in Japan, which possibly contributes to the lack of association with diabetes.

Song et al. (22) examined the association between flavonoid intake and risk of type 2 diabetes for a large cohort of U.S. middle-aged and older women (≥45 y) from the Women's Health Study. Neither the total intake of flavonoids nor the intake of most flavonoid-rich foods was associated with risk of type 2 diabetes. Interestingly, women who consumed ≥4 cups/d (960 mL/d) of tea had a 30% lower risk of developing type 2 diabetes than those who consumed no tea.

Greenberg et al. (23) examined the effect of caffeine and body weight change on the relation between tea and coffee intake and diabetes risk in U.S. adults from the National Health and Nutrition Examination Survey Epidemiologic Follow-up Study. Diagnosis of diabetes was from physician-diagnosed self-report. Beverage (regular tea, herbal tea, ground coffee, ground decaffeinated coffee, instant coffee, instant decaffeinated coffee, and cola) and caffeine intake were assessed once, at baseline of the study, by a FFQ. Increased intake of regular tea and ground coffee was inversely associated with diabetes risk for adults ≥60 y of age who lost weight during the study. No association of diabetes risk was observed for herbal tea or instant coffee. When adults ≥60 y were included in the analysis, the inverse association between tea and diabetes risk was lost. The authors noted that this association did not appear to be caused by caffeine because regular tea consumption remained significant after the effects of caffeine were taken into account. This suggests that another tea component(s) may have contributed to diabetes risk reduction.

Data from these epidemiologic studies are limited, and the results are inconsistent. There is some evidence that tea consumption is associated with reduced risk of type 2 diabetes; however, 2 large U.S. cohort studies (the Health Professionals' Follow-up Study and the Nurses' Health Study) did not detect an association. The lack of an association may have been because of
an inadequate number of persons drinking enough tea to detect a beneficial effect within the population. Several limitations exist for cohort studies examining the relation between tea consumption and type 2 diabetes. First, the majority of the cohort studies, with the exception of the study conducted in Japan, failed to provide detailed information about tea consumption, such as tea type, cup size, and preparation. Second, the diagnosis of diabetes was determined from self-report; few studies utilized serum biomarkers to verify the diagnosis. Diabetes may have been underestimated, potentially affecting the relative risk and the relation between tea consumption and diabetes. Finally, retrospective self-report of dietary intake is susceptible to reporting bias. It may be doubtful that intake measured in the past accurately reflects long-term intake. As tea and its components, such as epigallocatechin gallate, become more pervasive in the food supply, it will be much more difficult to assess dietary intake.

**Potential mechanisms of action**

Findings from both in vitro and animal models suggest several mechanisms by which tea and its components may influence glucose metabolism and diabetes (24). Tea catechins inhibit the carbohydrate digestive enzymes α-amylase, intestinal sucrase, and α-glucosidase in the intestines of rats, which suggests that glucose production may be decreased in the gut, thus lowering glucose and insulin concentrations (25,26). Tea may also increase insulin sensitivity and insulinotrophic activity (27,28). Black, green, and oolong teas were shown to enhance insulin sensitivity by increasing insulin-stimulated glucose uptake in adipocytes. Tea components, including epigallocatechin gallate, epicatechin gallate, tannins, and theaflavins, may be involved in enhancing insulin action (29). Green tea has also been shown to enhance the insulin sensitivity of normal and fructose-fed rats, improving glucose uptake by the myocytes, enhancing insulin binding to the adipocytes, and increasing the expression of intracellular glucose transporters in the myocytes (30,31). Finally, green tea and epigallocatechin gallate may prevent damage to the liver, kidney, and pancreatic β-cells (24,32).

**Human studies: clinical interventions**

Several human clinical interventions have examined the effects of tea consumption on biomarkers of glucoregulatory control (Table 1). Men and women from Taiwan with physician-diagnosed type 2 diabetes, taking oral glucose-lowering medications, consumed 1.5 L oolong tea or water daily along with their typical diet in a randomized crossover design for 4 wk. Subjects were instructed to consume the oolong tea 5 times/d. Food intake and physical activity were assessed by 24-h dietary recalls and pedometers. Components of oolong tea and caffeine were reported. Oolong tea lowered fasting plasma glucose and fructosamine concentrations from 229 ± 54 mg/dL (13 ± 3 mmol/L) to 162 ± 30 mg/dL (9 ± 2 mmol/L) and from 409 ± 96 μmol/L to 323 ± 56 μmol/L, respectively, whereas no changes in biomarkers were seen in the group that consumed water. The authors noted that the mechanism of the hypoglycemic effect of oolong tea is not fully understood (33). Limitations of this study included failure to control for caffeine and dietary intake.

Only a limited number of studies have been conducted to evaluate the effects of black tea on glucoregulatory biomarkers. Recently, in a short-term randomized crossover trial, healthy British men and women consumed 75 g glucose in either 250 mL water (control), 250 mL of water with caffeine (matched for the 1 g of instant black tea), or 250 mL water plus 1 g or 3 g of instant black tea. Blood samples were collected at fasting and then at 30-min intervals for 150 min after treatment ingestion. Results from only 3 treatments were reported because the 3 g of instant black tea caused emesis and tachycardia in the subjects. After consumption of the 1 g of black tea, plasma glucose was lowered at 120 min compared with the control and caffeinated treatments. Insulin concentrations were higher compared with the caffeine and the control treatments at 90 min and compared with the caffeine treatment alone at 150 min. The authors suggested that black tea can influence postprandial glycaemia by inhibiting intestinal glucose transport and enhancing insulin secretion by the pancreatic β-cells. The study was well designed; it accounted for caffeine as a confounding variable. This study included young healthy adults; further research is required to gain a better understanding of both the acute and long-term effects of black tea on glucose metabolism in those with diabetes (34).

Human studies evaluating the effects of green tea consumption on glucoregulatory biomarkers are inconsistent. Fukino et al. (35) conducted a randomized controlled trial examining the effects of green tea extract supplementation on glucose metabolism and diabetes (Table 1). Men and women from Taiwan with physician-diagnosed type 2 diabetes, taking oral glucose-lowering medications, consumed 1.5 L oolong tea or water daily along with their typical diet in a randomized crossover design for 4 wk. Subjects were instructed to consume the oolong tea 5 times/d. Food intake and physical activity were assessed by 24-h dietary recalls and pedometers. Components of oolong tea and caffeine were reported. Oolong tea lowered fasting plasma glucose and fructosamine concentrations from 229 ± 54 mg/dL (13 ± 3 mmol/L) to 162 ± 30 mg/dL (9 ± 2 mmol/L) and from 409 ± 96 μmol/L to 323 ± 56 μmol/L, respectively, whereas no changes in biomarkers were seen in the group that consumed water. The authors noted that the mechanism of the hypoglycemic effect of oolong tea is not fully understood (33). Limitations of this study included failure to control for caffeine and dietary intake.

**TABLE 1** Summary of clinical trials on the effects of tea consumption on biomarkers of glucoregulatory control

<table>
<thead>
<tr>
<th>Reference</th>
<th>Duration</th>
<th>Study design</th>
<th>Subjects</th>
<th>Treatment</th>
<th>Control</th>
<th>Daily dose</th>
<th>Significant results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hosoda et al. (33) (Taiwan)</td>
<td>30 d</td>
<td>Randomized crossover trial</td>
<td>20 adults (10 F, 10 M) with type 2 diabetes</td>
<td>Oolong tea (15 g tea leaf)</td>
<td>Water</td>
<td>1.5 L</td>
<td>Plasma glucose (P &lt; 0.001) and fructosamine (P &lt; 0.01) lowered</td>
</tr>
<tr>
<td>Bryan et al. (34) (Britain)</td>
<td>150 min</td>
<td>4-way randomized crossover trial</td>
<td>16 healthy adults (12 F, 4 M)</td>
<td>75 g glucose, 0.053 g caffeine, 1 g instant black tea</td>
<td>75 g glucose, 250 mL of water mixed with each treatment</td>
<td>for 1 g tea (P &lt; 0.01), insulin increased at 80 min (P &lt; 0.01) for 1 g tea</td>
<td></td>
</tr>
<tr>
<td>Fukino et al. (35) (Japan)</td>
<td>8 wk</td>
<td>Randomized parallel trial</td>
<td>60 adults (11 F, 49 M) with borderline diabetes</td>
<td>Green tea extract containing 544 mg polyphenols (456 mg catechins)</td>
<td>None</td>
<td></td>
<td>Homoglobin A1c lowered (P = 0.03)</td>
</tr>
<tr>
<td>Ryu et al. (36) (South Korea)</td>
<td>4 wk</td>
<td>Randomized crossover trial</td>
<td>55 adults (24 F, 31 M) with type 2 diabetes</td>
<td>Green tea (9 g)</td>
<td>Water</td>
<td>Green tea extract mixed with water</td>
<td>No effects on fasting insulin, fasting glucose, and homeostasis model assessment of insulin resistance</td>
</tr>
</tbody>
</table>
metabolism and insulin sensitivity. Overweight Japanese men and women with borderline diabetes (not taking oral glucose-lowering medications) consumed green tea extract containing 544 mg polyphenols and 102 mg caffeine dissolved in hot water daily for 8 wk along with their usual diet. The subjects were asked to consume the treatment with meals and snacks. Food intake was assessed by 24-h dietary recalls at baseline, 4 wk, and 8 wk. The results showed that daily supplementation with the green tea extract lowered hemoglobin A1C, although very small changes were observed. No significant changes were reported in fasting glucose concentrations, insulin concentrations, or homeostasis model assessment of insulin resistance values. The study limitations included not controlling for caffeine or dietary intake and exclusion of a washout period. Ryu et al. (36) examined the effects of green tea consumption on insulin resistance in a randomized crossover design. South Korean men and women with physician-diagnosed type 2 diabetes consumed either 900 mL water with 9 g of green tea or water without tea for 4 wk along with their typical diet. No significant changes were observed in fasting glucose concentrations, insulin concentrations, or homeostasis model assessment of insulin resistance values. The previous studies failed to detect effects on glucose and insulin concentrations in fasting samples. This observation raises the question of whether biomarkers should be evaluated after tea consumption because dietary polyphenols are so rapidly metabolized. For example, after consumption of green tea, catechin concentrations in human plasma have been shown to reach their peak within 1.5 to 2 h and to decline to undetectable levels after 24 h (37). Measuring the effects of tea after a 12-h fast may produce inconsistent results.

Diabetes causes both microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (myocardial infarction and stroke) complications (7). Black tea may help to reverse some vascular complications, such as endothelial dysfunction. In 1 study, U.S. adults with coronary artery disease were randomly assigned to consume black tea or water in a crossover design. Short-term and long-term effects of tea consumption on brachial artery flow-mediated dilation were measured after 2 h and 4 wk, respectively. Both short-term and long-term tea consumption improved endothelium-dependent flow-mediated dilation of the brachial artery. Adults with diabetes were included as participants in the study; thus, black tea consumption may improve endothelial function in persons with diabetes (38).

Few clinical trials have examined the effects of tea consumption on biomarkers of glcoregulatory control in persons with diabetes. The majority of the clinical trials, with the exception of the study from Britain, failed to control for caffeine consumption. Additionally, the studies did not control for dietary intake; other dietary components may have influenced study outcomes. Tea components were reported in only 1 clinical study; future clinical trials should further describe tea and its components. Clinical trials should be appropriately designed to control for caffeine intake and other confounding variables such as diet and lifestyle. Additional controlled clinical trials are also required to confirm the health effects of tea and its components, including the dose of polyphenols and the duration of consumption, on glucose metabolism in persons with diabetes.

Because of the increased consumption of tea and rising global rates of diabetes, it is important to clearly establish tea's association with diabetes risk. Epidemiologic evidence suggests some relation between caffeine and tea consumption and reduced risk of type 2 diabetes. Further well-designed epidemiologic studies should provide more detailed information about tea consumption, such as type, cup size, and preparation. Findings from in vitro and animal models suggest that tea and its components may influence glucose metabolism and diabetes through several mechanisms, such as enhancing insulin sensitivity. Some human clinical studies evaluating tea and its components show improvement in glucose regulatory control and endothelial function. However, further controlled clinical trials are required to gain a better understanding of the long-term effects of tea consumption in persons with diabetes.

Other articles in this supplement include references (39–48).

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