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Coffee polyphenols improve peripheral endothelial function after glucose loading in healthy male adults

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ABSTRACT

Brewed coffee is a widely consumed beverage, and many studies have examined its effects on human health. We investigated the vascular effects of coffee polyphenols (CPPs), hypothesizing that a single ingestion of CPP during glucose loading would improve endothelial function. To test this hypothesis, we conducted a randomized acute clinical intervention study with crossover design and measured reactive hyperemia index (RHI) to assess the acute effects of a 75-g glucose load with CPP in healthy, nondiabetic adult men. Blood glucose and insulin levels were elevated after glucose loading with and without CPP, with no significant differences between treatments. The RHI did not significantly decrease after glucose loading without CPP. With CPP, however, RHI significantly ($P < .05$) increased over baseline after glucose loading. The difference between treatments was statistically significant ($P < .05$). No significant changes were observed in an oxidative stress marker after glucose loading with or without CPP. These findings suggest that a single ingestion of CPP improves peripheral endothelial function after glucose loading in healthy subjects.

1. Introduction

Coffee is a widely ingested beverage that has been consumed for many centuries worldwide, and there are many studies of the effects of brewed coffee in association with human health. Coffee intake has protective effects against various diseases, such as type 2 diabetes, hypertension, liver dysfunction, and Parkinson disease [1-3]. It has been suggested that these health benefits are due to coffee polyphenols (CPPs), some of the main antioxidants in coffee [4-6]. Coffee polyphenol is composed of many phenolic compounds, most of them chlorogenic acids (CQAs) [7]. Chlorogenic acids in coffee beans are primarily composed of the following 9 compounds: 5-caffeoylquinic acid (5-CQA), 3-caffeoylquinic acid (3-CQA), 4-caffeoylquinic acid (4-CQA), 3,4-dicaffeoylquinic acid (3,4-diCQA), 3,5-dicaffeoylquinic acid (3,5-diCQA), 4,5-dicaffeoylquinic acid (4,5-diCQA), 3-feruloylquinic acid (3-FQA), 4-feruloylquinic acid (4-FQA), and 5-feruloylquinic acid (5-

Abbreviations: 3-CQA, 3-caffeoylquinic acid; 4-CQA, 4-caffeoylquinic acid; 5-CQA, 5-caffeoylquinic acid; 3,4-diCQA, 3,4-dicaffeoylquinic acid; 3,5-diCQA, 3,5-dicaffeoylquinic acid; 4,5-diCQA, 4,5-dicaffeoylquinic acid; 3-FQA, 3-feruloylquinic acid; 4-FQA, 4-feruloylquinic acid; 5-FQA, 5-feruloylquinic acid; BP, blood pressure; CPP, coffee polyphenol; CQAs, Chlorogenic acids; FMD, flow-mediated dilation; Glu, glucose; RHI, reactive hyperemia index; ROS, reactive oxygen species.

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FQA). 5-Caffeoylquinic acid (formerly called 3-CQA or CQA) is the main component of both roasted beans and green beans. Chlorogenic acid levels are reduced by the process of roasting coffee beans, and the reductions of dicaffeoylquinic acid are especially remarkable [8]. A cup of coffee typically contains 20 to 675 mg of CQAs, and the daily intake of CQAs by a coffee drinker is as much as 1 g [7].

Habitual consumption of CPPs, which are abundantly present in coffee beans, improves endothelial function [9], which is impaired in early-stage cardiovascular disease. As to the effects of a single ingestion of CPP on endothelial function, there was no effect in a study of reagents of CQA [10], but improved of endothelial function was observed with decaffeinated coffee [11]. However, these reports cannot be directly compared because their test conditions are different. When evaluating acute endothelial function, the medical significance is important. We have focused on postprandial glucose (Glu) levels because postprandial hyperglycemia was identified as a novel, independent risk factor for coronary heart disease [12,13] and because an important mechanism of coronary heart disease has been attributed to endothelial dysfunction. Kawano et al [14] reported decreased flow-mediated dilation (FMD) and increased levels of oxidative stress markers during a Glu tolerance test in patients with diabetes or impaired Glu tolerance as well as in healthy subjects. In addition, recent reports demonstrated that the ingestion of the antioxidant vitamin C or a Glu absorption inhibitor attenuates the impairment of vascular endothelial function induced by a Glu tolerance test [15,16].

We hypothesize that improvements in vascular function are observed after a single ingestion of CPP during Glu loading in healthy male subjects. To test this hypothesis, we conducted a randomized acute clinical intervention study with crossover design and measured reactive hyperemia index (RHI) to assess the acute effects of a 75-g Glu load with CPP in healthy, nondiabetic adult men.

2. Methods and materials

2.1. Subjects

The subjects were 15 healthy Japanese men, aged 20 to 60 years upon initiation of the study. The subjects were recruited through the in-house mail system. All subjects had no medications and lifestyle interventions. Subjects were also excluded if they had allergies or hypersensitivity to caffeine and coffee, heavy alcohol use, or were otherwise ineligible as judged by the physician in charge. The Human Ethics Committee of Kao Corporation approved the study protocol. All subjects provided written informed consent. The present study was conducted under the supervision of the chief investigator in accordance with the Declaration of Helsinki.

2.2. Materials

Coffee polyphenol was prepared from green coffee beans by hot water extraction followed by spray drying and grinding for this study. Caffeine was not detected. Chlorogenic acids mainly include the following 9 compounds: 5-CQA as the most abundant component, 3-CQA, 4-CQA, 3,4-diCQA, 3,5-diCQA, 4,5-diCQA, 3-FQA, 4-FQA, and 5-FQA. The CPP composition was measured by high-performance liquid chromatography. Total CQA content of the CPP was 80.7%. The composition of CQAs was 58.3% CQA (total 3-CQA, 4-CQA, and 5-CQA), 19.9% feruloylquinic acid (3-FQA, 4-FQA, and 5-FQA), and 21.8% dicaffeoylquinic acid (3,4-diCQA, 3,5-diCQA, and 4,5-diCQA).

2.3. Study design

We examined the acute effects of Glu loading, either with a single ingestion of CPP (coadministered with the Glu solution) or Glu alone, on endothelial function in a single-blind, randomized, controlled, crossover trial with a washout period of at least 3 days. The washout period of 3 days was set for the following reasons: CQA metabolites were also detected 24 hours after ingestion [17], diet was restricted the day before the test, and blood sampling was conducted 3 times in a single test. Subjects consumed a lunch box on the market before 9 PM on the night before each study session, followed by fasting and nonsmoking (only water was allowed). On the day of the session, the subjects presented in our testing room at 8:30 AM and were asked to void before the session, followed by measurements of constitutional parameters, such as body temperature and blood pressure (BP), as well as a health status interview. After the collection of baseline blood and urine samples and BP measurement at 9:30 AM, endothelial function was evaluated using an Endo-PAT 2000 (Itamar Medical Ltd, Caesarea, Israel). Then, the subjects ingested 225 mL of a 75-g Glu-equivalent test solution (Trelan-G, Takeda, Japan), either alone (Glu) or with CPP (600 mg CQAs; Glu + CPP), within 3 minutes. Blood and urine samples were collected at 1 and 2 hours after ingestion, and the BP and Endo-PAT scores were measured at 1.5 hours after ingestion. During each of the 2 study sessions, subjects remained in a room maintained at 25°C ± 2°C with 50% humidity until the session was complete.

2.4. Noninvasive evaluation of peripheral endothelial function (Endo-PAT)

As described previously [18], the principle of measuring endothelial function using the Endo-PAT 2000 is based on the detection of changes in the pulse wave amplitude in the fingertip that is observed during reactive hyperemia. After resting in a seated position for at least 20 minutes in a room at 25°C ± 2°C, the subjects underwent Endo-PAT tests in a supine position, with a BP cuff applied to the upper arm and 2 fingertip probes attached to the index fingers of the cuffed (occluded) and contralateral (control) arms. The pulse wave amplitudes in the fingertips were recorded continuously during a 5-minute baseline (in which the probe pressure was maintained at 60 mm Hg), a 5-minute occlusion period (by inflating the upper arm BP cuff to 200 mm Hg), and a 5-minute postocclusion period (after cuff deflation). The Endo-PAT data were analyzed using accessory software for the Endo-PAT 2000. The RHI, a measure of endothelial function [19], was calculated from the ratio of pulse wave amplitudes before and after occlusion in each arm.