Plant Foods Hum Nutr (2011) 66:209–211
DOI 10.1007/s11130-011-0234-4

Acute Effects of *Ginkgo Biloba* Extract on Vascular Function and Blood Pressure

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Published online: 7 June 2011

Abstract We investigated whether a single dose of standardized *Ginkgo biloba* extract (GBE) can improve vascular function. A randomised controlled crossover trial was conducted on 14 young healthy men, who received GBE or placebo. The digital volume pulse was monitored to measure reflection index (DVP-RI) and stiffness index (DVP-SI) and peripheral augmentation index (pAIx) was assessed using radial pulse wave analysis at baseline and 2, 4 and 6 h after treatment. DVP-SI was slightly higher 2 h following GBE compared to placebo ($P<0.05$); other outcome variables were unaffected by treatment.

Keywords Arterial tone · Blood pressure · Flavonoids · *Ginkgo biloba* · Vascular function

Abbreviations

ANOVA	Analysis of variance
BMI	Body mass index
DVP	Digital volume pulse
DVP-RI	Reflection index
DVP-SI	Stiffness index
GBE	*Ginkgo biloba* extract
pAIx	Peripheral augmentation index
PWA	Pulse wave analysis

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Introduction

A standardized extract of *Ginkgo biloba* (GBE), EGb761, is commonly used as a dietary supplement. It contains two fractions: the terpenes, ginkgolides and bilobalide (6%), and the flavonoid glycosides (24%). Vaso-protective effects of GBE have been observed in animals [5, 7, 8], but few studies have investigated this in human beings [3, 6]. GBE constituents peak in the blood around 2 h after ingestion [1]. We report the acute effects of GBE consumption on arterial tone and ambulatory blood pressure in young healthy men.

Materials and Methods

Subjects and Study Design

Male subjects were recruited from King's College London, UK. Men aged <18 or >41 years, smokers, individuals with a reported history of diabetes, thrombosis or cardiovascular disease, those with systolic blood pressure ≥140 and/or diastolic blood pressure ≥90 mmHg, with BMI <18 or >35 kg/m^2 and those taking medication were excluded. Fourteen men aged 18–37 years (mean ± SD: 22±5) consented to take part in the study. They were within the normal range for BMI (mean ± SD: 22.0± 3.2 kg/m^2) and were not hypertensive (mean ± SD: systolic blood pressure 125±8 mmHg; diastolic blood pressure 73±8 mmHg). The study protocol was approved by King's College London Research Ethics Committee and all subjects gave written informed consent. The study

was a single-blind, randomized, placebo-controlled cross-over; subjects were blinded to treatment allocation. Subjects attended the metabolic research unit in the morning on two separate occasions, at least one week apart. On the day before each clinical visit, subjects were provided with a standard low-fat meal to be consumed before 22.00 h. Subjects were requested to refrain from caffeine, alcohol and strenuous exercise for 24 h before the study, and to consume only water from 22.00 h on the previous day.

Following a 10 min supine rest on arrival, baseline vascular and blood pressure measurements were taken. Subjects consumed six capsules containing 360 mg GBE (Vega Nutritionals Ltd., Surrey, UK) or placebo (cornflour) with 200 ml water, and a low-fat breakfast immediately afterwards (2795 kJ, 5.3 g fat, 145 g carbohydrate, 17 g protein). One capsule contained 60 mg GBE (EGb761: minimum 24% ginkgo flavonglycosides and 6% terpene lactones). Vascular measurements were taken at 2, 4 and 6 h after the meal. Ambulatory blood pressure readings were recorded at the following time points following the meal: 30, 60, 90, 120, 150, 180, 210, 240, 270, 300, 330 and 360 min.

Vascular Measurements

Ambulatory blood pressure was recorded half-hourly (just before treatment or placebo administration and for 6 h afterwards) with a SpaceLabs 90207 monitor (SpaceLabs, Issaqua, WA). Supine measurements of arterial tone were performed following at least 10 min of rest. Pulse wave analysis (PWA) was carried out as previously described to determine the peripheral augmentation index (pAIx), a measure of both arterial stiffness and vasodilation of small muscular arteries/arterioles [2, 4]. DVP was obtained by photoplethysmography (PulseTrace, Micro Medical Ltd., Kent, UK) and used to calculate stiffness index (DVP-SI, m/s) and reflection index (DVP-RI, %), which is related to vascular tone of small/medium arteries.

Statistical Analysis

All variables were tested for normal distribution, before any statistical analysis was applied. Repeated measures ANOVA was performed (treatment and time as within-subject factors) on change from baseline data. A P value$<$ 0.05 was considered statistically significant. *Post hoc* analysis using Bonferroni t tests was conducted when main effects were identified. Data analysis was performed using the SPSS statistical package for Windows (version 15.0, SPSS Inc., Chicago, IL).

Results and Discussion

We hypothesized that a reduction in arterial stiffness (DVP-SI), in pressure wave reflection (DVP-RI and pAIx) and blood pressure would follow a single dose of

Table 1 Acute changes in vascular function following GBE in young healthy men[1]

	Baseline	2 h	4 h	6 h
pAIx (%)				
Placebo	42.4±9.1	38.6±11.4	40.6±12.5	41.7±11.9
GBE	43.9±8.9[a]	36.9±10.5[b]	40.7±9.9	39.9±9.4
Placebo – GBE	−1.5 (−6.8 to 3.8)	1.7 (−3.6 to 7.0)	−0.1 (−5.4 to 5.2)	1.9 (−3.4 to 7.2)
DVP-RI (%)				
Placebo	69.6±9.7	69.8±12.9	72.0±15.6	68.7±14.8
GBE	68.4±11.4	67.4±11.5	72.0±12.1	69.4±11.6
Placebo – GBE	1.2 (−10.9 to 13.3)	2.4 (−9.7 to 14.5)	0.0 (−12.1 to 12.1)	−0.7 (−12.8 to 11.4)
DVP-SI (m/s)[2]				
Placebo	5.96±0.65	5.71±0.46	5.75±0.53	5.64±0.34
GBE	5.96±0.57	5.99±0.46	5.91±0.50	5.85±0.62
Placebo – GBE	0.00 (−0.51 to 0.50)	−0.28 (−0.78 to 0.23)*	−0.16 (−0.66 to 0.35)	−0.21 (−0.71 to 0.30)

[a, b] Means in a row without a common letter differ, $P<0.05$

[1] Values are means ± SD and mean difference between treatments with 95% CI, $n=14$

[2] Treatment effect, $P<0.05$

*Difference between treatments at that time point with Bonferroni correction, $P<0.05$

GBE. Peripheral AIx decreased at 2 h following both GBE and placebo ($P<0.05$) but there was no difference in response between treatments (Table 1). This observation replicates the decrease in pAIx following high-carbohydrate meals reported previously [2]. There was no effect of either GBE or placebo on DVP-RI. DVP-SI was significantly higher following GBE compared to placebo ($P<0.05$); *post hoc* comparisons revealed a significant treatment difference at 2 h ($P<0.05$). Ambulatory blood pressure and heart rate were unaffected by GBE (data not shown). Only one study has investigated the acute vascular effects of GBE in human subjects [3], reporting no change in blood pressure or heart rate over 4 h, although a marked increase in blood flow in the nail fold capillaries was observed after 1 h, indicating potent effects on the microcirculation. Although stiffness index was significantly higher at 2 h following GBE compared to control, the difference was small and further investigation is required to confirm this observation. The results of the present study suggest that GBE has no acute beneficial effect on arterial tone or blood pressure.

Acknowledgements This study was funded by King's College London. We thank Phil Chowienczyk, Karen McNeill and Sally Brett for providing training in the use of PWA and DVP techniques, and for the loan of the ambulatory blood pressure monitors.

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