Effect of Green Coffee Bean Extract Consumption on Blood Pressure and Anthropometric Measures in Healthy Volunteers: A Pilot Crossover Placebo Controlled Study

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ABSTRACT

Background: Stress is known to contribute to obesity and hypertension and both are considered to be primary risk factors for cardiovascular disease. Green coffee bean extract (GCBE) contains chlorogenic acid (CGA) which is attributed with several health benefits including anti-obesity and anti-hypertensive effects.

Objectives: To investigate the short term effects of GCBE intake on blood pressure (BP), body mass index (BMI) and anthropometric parameters in healthy volunteers.

Methodology: A single blinded cross-over placebo controlled study was performed on 16 healthy volunteers who consumed either GCBE or caffeine as placebo. The volunteers took the interventions for a week with a one-week wash-out period in between before switching intervention groups.

Results: After administration of GCBE (equivalent to 500mg of CGA/day) for seven days, participant's diastolic and systolic blood pressures were significantly reduced from 76.9± 9.1 at baseline to 72.6±5.9mmHg ($p<0.001$), and from 119.1±11.9 to 114.5±9.6 mmHg ($p=0.001$), respectively. Body mass index (BMI) and body weight were also significantly reduced following GCBE intake. NO significant changes in these parameters were observed after the placebo.

Conclusion: This study showed that 500mg CGA/day can significantly reduce blood pressure (BP), BMI and weight of healthy individuals.

Keywords: Green coffee bean extract, Chlorogenic acid, BP, BMI, Obesity.

1. INTRODUCTION

The prefrontal cortex regulates human behaviour, cognition and emotion. Exposure to acute or chronic stress has been shown to impair these through the activation of calcium and potassium channels, weakening synaptic input and reducing neuronal firing[1]. Many people experience some level on a daily basis of acute or chronic stress, and it can impact on their well-being, sometimes through weight gain and/or hypertension. Coffee is one of the most frequently consumed non-alcoholic beverages and those wanting to adopt a healthier lifestyle may choose better options such as green tea or coffee. Green tea and green coffee bean extract have been shown to have several beneficial effects in reducing BP and body weight[2-6] and there is also the potential for green coffee to produce similar favourable properties. The two commonly known types of coffee, black and green coffee, differ in their roasting process; green coffee beans are usually unroasted whilst black coffee beans are roasted, and the latter results in a

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decrease in their antioxidant and chlorogenic acid (CGA, a polyphenol found in coffee and other botanicals) levels[7-8]. Several fruits and vegetables rich in polyphenols have been reported to reduce blood pressure and possess many health benefits [9-12].

Green coffee bean extract (GCBE) contains CGA which has anti-obesity, anti-hypertensive properties and may also reduce glucocorticoids and vascular stiffness[7-9]. Moreover, CGA is the main ingredient in green coffee and GCBE which produces the desired effects. Other beneficial effects of CGA include possible neuro-protective properties such as in the prevention of Alzheimer's disease although there is limited evidence to support this and further research is needed for this end [13-16]. Hypertension is a primary risk factor for coronary heart disease and cardiovascular disease (CVD) and the risks of these diseases can be reduced with simple lifestyle modifications such as a change in diet, an exercise regime or through drug therapies[17]. Alternatively, GCBE offers a natural diet based approach for reducing BP rather than the use of a drug based approach and may be considered to be more desirable. Suzuki et al. (2002)[17] first reported the antihypertensive properties of GCBE on spontaneously hypertensive rats that were given either single or long-term doses of GCBE. A single dose of GCBE (180, 360 and 720mg/kg) significantly decreased BP compared with the placebo, and there was a statistically significant decrease in BP that followed a dose dependant effect between each of the doses compared to the control. The effects of CGA observed in rats were later confirmed by Kozuma et al. (2005)[18] in humans with mild hypertension. They used 117 healthy volunteers who were given either a placebo or GCBE (46, 93 or 185mg/day) for 28 days. Intake of GCBE significantly decreased volunteer's BP ($p<0.05$ with 93mg and $p<0.01$ with 185mg) compared to the placebo group. Usually, high BP is associated with reduced arterial compliance but CGA may reduce both[14,15]. Few studies choose to use a high dose of CGA which is an important area that should be considered.

The link between weight reduction and CGA has been well documented and the mechanism for the weight loss effects attributed to CGA[19]. It has been shown to reduce and slow glucose absorption by inhibiting the action of glucose transporters in the small intestine which will lead to an improvement in glucose control and weight loss [20-21]. There is no definitive conclusion as to how CGA reduces weight, but evidence exists to suggest that it plays a role in weight reduction. It is likely that CGA reduces weight by a number of mechanisms: Cho et al. (2010)[22] showed that CGA reduced activity of fatty acid synthase (FAS), HMG-CoA reductase, ACAT and increased fatty acid β-oxidation. They looked at mice on a normal diet, a high fat diet or a diet containing 0.02g/kg CGA over an eight week period. Those on the CGA diet showed lower amounts of each of the components that are used in fat production (FAS, HMG-CoA reductase and ACAT) and also had an increased rate of fatty acid β-oxidation compared with mice on the normal or high fat diet. The aims of this study were to assess whether heart rate, systolic and diastolic BP, and anthropometric measurements including weight and BMI are affected by GCBE short term use.

Materials and Method

Study Design

This was a single-blind, cross-over, placebo-controlled small trial. All measurements were taken in triplicate to improve reliability and the mean was calculated. Volunteers were asked to follow their usual diet and physical activity habits. Questionnaires and 2-day diet diaries, for one weekday and one weekend day, were done at baseline and after taking the GCBE, to determine volunteer's physical activity levels, salt and caloric intake. An increase or decrease of salt or calories may account for a change in weight, BP and anthropometric measures. Questionnaires were used to determine eligibility of the volunteers (see Table 1). An ethical approval was granted by Edinburgh University ethics committee, Edinburgh, UK and subjects were largely students and staff members. Measurements of heart rate, BP, height and weight were taken at baseline and again on days 7 and 21 to detect if the placebo

(containing caffeine) or GCBE had caused any effects. There was a 7-day wash-out period, between days 8-14, to avoid a carry-over effect and to make sure that only either the caffeine or the GCBE was having an effect [23]. On day 14, the groups switched the intervention protocol they were taking to the other arm of the study. The same equipment was used each time to avoid inaccuracies. Figure 1 shows the outline of the cross-over study design.

Table 1. Health status Questionnaire used to determine eligibility of the volunteers

Name:_____ Surname:_____
Gender: □ Male □ Female Age (year):_____
Weight (kg) = _____ Height (metre) = _____
Could you please answer the following questions? (*Tick as appropriate)*

1. Have you ever had or do you currently have any of the following conditions?

Diabetes
Liver problems
Digestive/gastrointestinal diseases
Kidney disease
□ Stroke or heart problems

2. Do you have high blood pressure/hypertension? □ Yes □ No

3. Do you smoke? □ Yes □ No

If yes, could you specify how many cigarettes per day?

4. Do you take any vitamin, mineral or oil supplements? □ Yes □ No

If yes, could you specify type of supplement and amount taken?

5. Do you take any cholesterol-lowering drugs or blood pressure lowering drugs?

□ Yes □ No

6. Are you currently taken contraceptive medication? □ Yes □ No

7. Do you exercise regularly? □ Yes □ No

If yes, what exercise do you do and how often?

8. Do you drink coffee? □ Yes □ No

If yes, how often do you drink it?

□ Never or 1-3 times a week
□1-2 cups a day
□ 2-4 cups a day
□ > than 4 cups a day

9. Do you drink alcohol? □ Yes □ No

If yes, how much and how often?

Study Population

A total of 16 healthy volunteers (7 males, 9 females) were recruited and were placed into two groups. This number of was chosen because of the Ethics committee requirements for pilot studies. The number was thought to be sufficient for a pilot study. Volunteers were given randomly a participant number and those who had an even number were allocated to begin the GCBE first, whilst those who had an odd number began the placebo first. Volunteers signed a consent form after reading an information sheet about the study. Those who were caffeine sensitive and had a history of cardiovascular disease, kidney disease, diabetes or were smokers and pregnant females were excluded from the study. Also,

only those who had a BMI of 18-35 kg/m^2 were included in the study and were asked to reduce caffeine containing drinks such as coffee, tea and fizzy drinks during the study, but none of these contain CGA. All data collected was stored electronically with a password and kept anonymous.

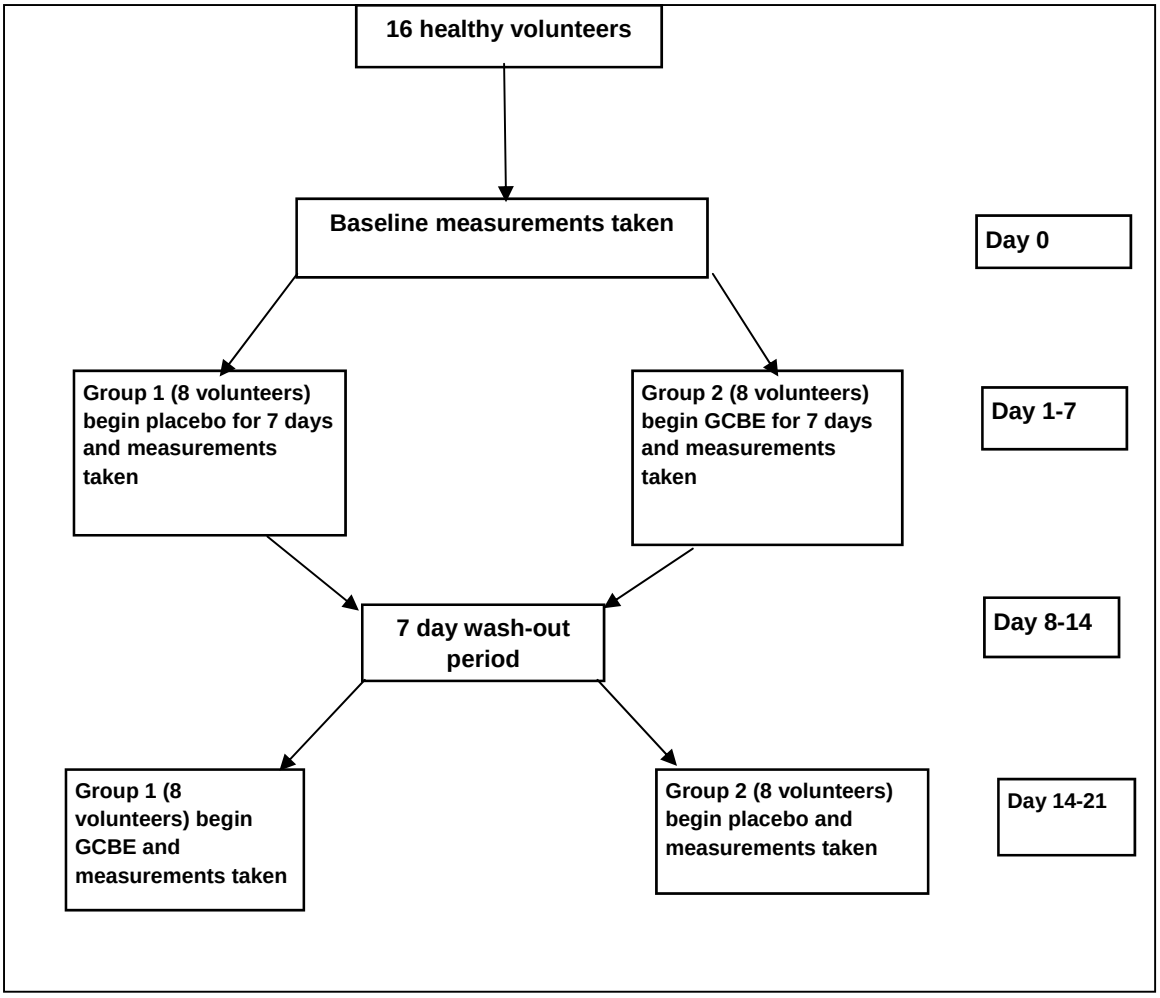

Figure 1: Shows the outline of the cross-over study design

Baseline Measurements

Volunteers had their baseline measurements taken for BP (3 readings of systolic and diastolic BP were taken each time) using an A&D digital sphygmomanometer This is a very reliable device and applied by thousands of studies with errors of <0.1% mmHg), as well as height (m) using a Seca height measure and weight (kg) using a Salter weight measurement scale. The digital assessment of BP is regarded a very reliable and have been used by most research studies. BMI was then calculated as weight/(height)^2. Volunteers were asked to remove their shoes and jackets for measurements. All measurements were taken on day 0, day 7 and day 21 to determine if the placebo or GCBE intake had caused any effect.

Green Coffee Bean Extract Intake

Volunteers were asked to take two 500mg GCBE (Nature's way premium extract, Nature Best, Tunbridge

Wells, England) tablets per day, each containing 250mg of CGA and 12.5 mg of caffeine (total caffeine per day=25mg); one in the morning and one in the evening. The dose of 500mg of CGA was chosen because it was found to reduce BP and weight in previous other studies[19].

Placebo Intake

When taking the placebo, volunteers were asked to take half a 50mg tablet of caffeine (Bayer pro-plus) per day. This was very closely matched the amount of caffeine in the 2 GCBE tablets taken during the intervention (25mg). As caffeine can cause weight loss, so the amount of caffeine in both the placebo and GCBE tablet should be similar as much as possible. Volunteers were further asked to take both interventions at the same time of the day.

Statistical Analysis

Variables were tested for normality on SPSS (version 21.0.0.2). All data were parametric and a student's two-tail paired t-test was done in SPSS between volunteers measurements at baseline and both the GCBE and placebo. The test was done for weight, BMI, systolic and diastolic BP. Descriptive statistics were done in Excel 2010. Diet diaries were analysed using Windiet (2005) and a paired t-test was also calculated for mean caloric and sodium intake between baseline and whilst taking the GCBE. All the data were presented as mean±SD. Any p value ≤ 0.05 was considered to be significant.

Results and Discussion

Volunteer's Characteristics

All healthy volunteers (7 males and 9 females), aged between 19 and 32 year with a mean±SD of 24.6±3.3year were recruited and all completed the study. All were recruited for the study with exclusion criteria given above (Study population). No adverse effects to either the caffeine or GCBE were reported. Mean baseline, post caffeine and post GCBE values are shown in Table 1. The main limitations of this study: the small sample size and thus the results may not reflect the true population and compliance was checked only verbally and there was no true way to know if the volunteers have taken all the tablets they were supposed to. A seven day period was allocated for each intervention with a week wash-out period in between. It would have been more desirable to use a longer intervention period and a longer wash-out period [24].

Table 2. Characteristics of volunteers at baseline, after placebo and after GCBE intake

Parameter	Mean value (± SD) at baseline	Mean value (± SD) after Placebo	Mean value (± SD) after GCBE
Age (Years)	24.6 ± 3.3		
Weight (kg)	72.16 ± 16.53	72.1 ± 16.45	71.64 ± 16.35***
BMI (kg/m^2)	24.41 ± 4.38	24.33 ± 4.39	24.09 ± 4.26*
SBP (mmHg)	119.1 ± 11.9	118.3 ± 10.5	114.5 ± 9.6**
DBP (mmHg)	76.9 ± 9.1	76.5 ± 8.4	72.6 ± 5.9***
Heart rate (BPM)	80.5 ±13.4	79.5 ± 9.2	79.4± 9.4
Energy intake (kcal/day)	1355±429	1367±532	1386±745
Sodium intake (g/day)	2.12±1.2	2.14±0.95	2.08±0.7

Basal versus GCBE (two-tail paired t-tests): *: p=0.025, **: p=0.001, ***: p<0.001. Placebo versus GCBE: For the difference in weight: p=0.005; for DPB: p=0.002 and for SBP: p=0.05. Basal versus placebo p values were all not significant (range from p=0.112 to p=0.578).

Anthropometrical Measurements

At baseline, the participants mean weight and BMI were respectively 72.16±16.53 kg and 24.41±4.38 kg/m^2. Mean weight and BMI decreased to 71.64±16.35 kg ($p<0.001$) and 24.09±4.26 ($p=0.025$) respectively after taking the GCBE. A very slight mean decrease was observed for weight and BMI following the caffeine placebo but were not significant; $p=0.373$ for weight and $p=0.095$ for BMI. Our findings were similar to other studies. In a six month randomized placebo controlled trial, Boozer et al. (2002)[25] showed that GCBE intake had significantly reduced body weight after taking an herbal ephedra and caffeine/day ($n=167$, $P<0.001$). Our study used more females than males and consequently the menstrual cycle may impact on weight changes. Other studies have included a greater percentage of males to obtain a more accurate representation of the effects of CGA on weight loss [26].

GCBE have the potential to reduce weight which could benefit health. One mechanism stands out more in the literature for the effect of CGA plus caffeine on body weight was that due to the increase in resting energy expenditure and thermogenesis [21,23, 25]. Most authors agree that CGA in GCBE slows absorption of glucose in the small intestine. If glucose absorption is reduced, the glucose blood level will be reduced improving glucose control and reducing weight. Interestingly, Gavrieli et al (2013)[27] have reported that a moderate coffee intake can effectively reduce energy intake in the following meal and during the whole day.

Effect of GCBE on Physiological Markers

Supplementing volunteers with GCBE had significantly reduced mean DBP. It decreased from baseline of 76.9± 9.1 to post GCBE of 72.6±5.9mmHg ($p<0.001$), and also SBP significantly decreased from a mean of 119.1±11.9 at baseline to 114.5±9.6 mmHg after taking GCBE ($p=0.001$). See Table 2 and figure 2. No significant decrease or changes were found in other physiological markers after the intake of GCBE (heart rate, energy intake or sodium intake). There were no significant differences between any baseline measurements and post placebo (caffeine) values (p values were all not significant and ranged from $p=0.112$ to $p=0.578$). The antihypertensive effects of GCBE seen in this study were similar to those found by Yamaguchi et al. (2008)[28]. In their randomized, double-blind study, they showed that BP significantly decreased after 4 weeks of CGA intake in 203 volunteers ($p<0.001$). The present study has substantiated the work of Yamaguchi and collegues (2008)[28], showing that GCBE, a natural nutraceutical reduces both systolic and diastolic BP. In addition, Mubarak et al. (2012)[29] has also concluded that GCBE reduced BP. However, Ochiai et al. (2004)[30] have reported inconsistent results as far as the antihypertensive actions of GCBE. After a four month study they found no significant differences in the BP when volunteers took 140mg/day CGA. The drawback of their study was the small sample group ($n=10$), that might have produced a statistical error. Doses of 0.25%, 0.5% and 1% of CGA in the diet, were used for the long-term intervention and there was a statistically significant decrease in BP between each of the doses compared to the control diet, $p<0.01$ for 0.25% and $p<0.001$ for doses of 0.5% and 1%. Therefore, CGA may play some role in down-regulating FAS, HMG-CoA reductase and ACAT whilst up-regulating fatty acid β-oxidation on short term basis and could be on long term use[17].

Hypertension can cause several serious consequences; kidney disease, diabetes, stroke, heart disease and many others. Each 2 mmHg rise in systolic BP corresponds to a 7% increased risk of mortality from heart disease and a 10% increased risk of stroke[31]. Taking GCBE has been shown to reduce BP and possibly its associated risks. It is recommended that more extensive human trials on the benefits of GCBE for hypertensive people should be conducted. Consumption of Green Coffee and GCBE rich in CGA has been reported to reduce BP and BMI by Influencing 11β-HSD1 Enzyme Activity through the reduction of the stress hormone level, cortisol [7, 32]. However, some studies have shown that increased intake of coffee and caffeine increased blood pressure within the healthy physiological levels, in a gender specific manner [33-35]. Other researchers found no significant effects of

coffee consumption on BP[36-37].

The volunteers diet diaries showed that there was no significant difference in the salt intake of participants between baseline and whilst taking the GCBE. Any significant reduction in salt intake may have accounted for a reduction in BP and thus the reduction in the volunteers BP was most likely a consequence of the GCBE intake. Throughout the day BP will vary, however, participants were unable to have their measurements taken at the same time of the day due to inconvenience. Therefore, circadian changes in BP may mean the results might be questionable, and to improve the study, the volunteers BP should be taken at the same time of day or a 24 hour BP monitor could be employed.

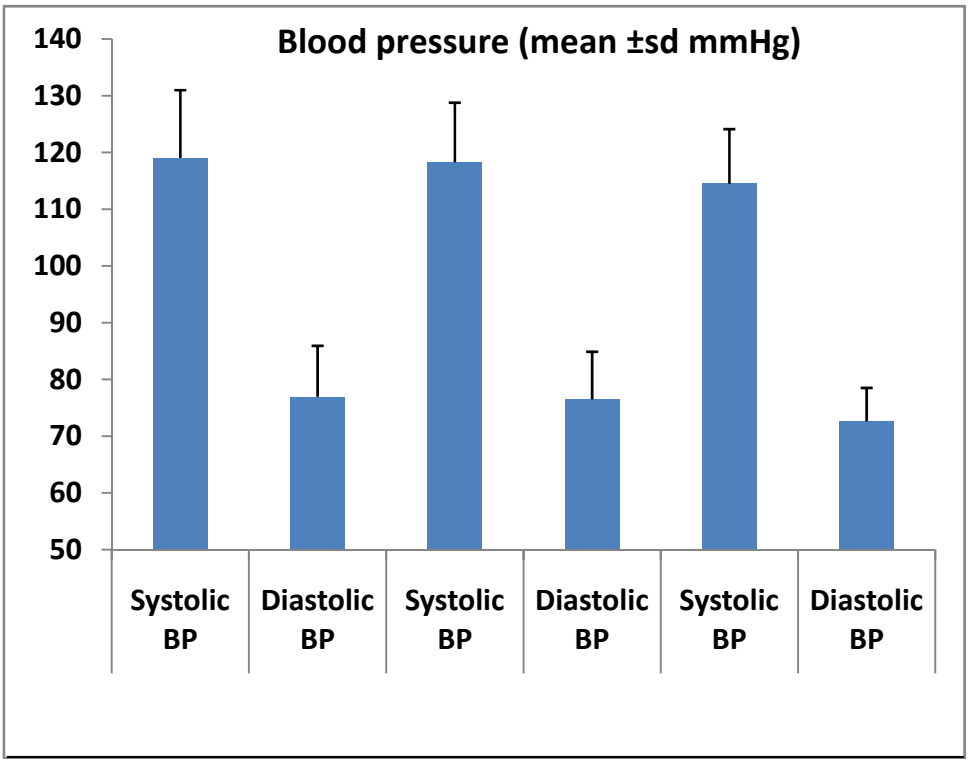

Figure 2: A graph shows the mean systolic BPand diastolic BP at baseline and after taking the placebo or GCBE. Both systolic and diastolic BP were significantly reduced following GCBE intake (p=0.001: compared to basal values)

Physical Activity and Diet

Diet diaries were used to determine if average baseline sodium and caloric intake was significantly different from the average values whilst taking the GCBE. A physical activity questionnaire was used to determine if there was a change in physical activity at baseline and whilst taking the GCBE. Analysis of diet diaries showed that there was no significant difference in the sodium and caloric intake between baseline and GCBE values. There was also no significant difference in physical activity between baseline and whilst taking the GCBE. It follows that the decrease in weight was not due to a change in diet or physical activity but due to the intake of GCBE rich in CGA. Questionnaires and diet diaries were used to determine volunteer's physical activity levels and caloric intake, and this technique is considered to be the norm in such studies. No significant changes in these measures were found between baseline and post GCBE, therefore the decrease in body weight may be attributed to the GCBE intake.

Conclusions and Future Research

This study has shown that for normotensive individuals, short term dietary supplementation with GCBE can significantly decrease systolic and diastolic BP. Also a mean decrease was observed for body weight and BMI. Only a seven day intervention was used and a more significant change may have arisen if the study duration was extended over a longer period. Further research using a larger sample size and longer intervention period, for GCBE intake is warranted to clarify the effects in overweight and obese subjects, and whether salivary stress hormones will be reduced during GCBE intake. We also suggest that future studies should look at the effects of GCBE intake in mildly hypertensive and hypertensive patients. Future trials should also use a longer study than the one adopted in the present study. In addition, it may be beneficial to carry out research on those who have a BMI of >30kg/m^2 as a possible weight loss method, as most studies tend to use patients who have normal BMI.

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Abbreviations:

ACAT= Acyl-CoA:cholesterol acyltransferase
Body mass index =BMI
Blood pressure = BP
BPM = beats per minute
Cardiovascular disease = CVD
Chlorogenic acid = CGA
Diastolic blood pressure = DBP
FAS= Fatty acid synthase
Green coffee bean extract = GCBE
HMG- CoA reductase= Hydroxy-3-methylglutaryl CoA reductase
Nitric oxide = NO
Systolic blood pressure = SBP

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تأثير مستخلص حبوب البن الأخضر على ضغط الدم وقياسات الجسم للمتطوعين الأصحاء

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ملخص

خلفية الدراسة: يساهم القلق والإجهاد في زيادة احتمالية الإصابة بالسمنة المفرطة وارتفاع ضغط الدم ويعتبر كلاهما عامل الخطورة الأساسي لأمراض القلب والشرايين. حيث تحتوي مستخلص حبوب البن الأخضر (GCBE) على حمض الكلوروجينك (CGA) الذي يرتبط مع فوائد صحية عديدة مثل مكافحة السمنة وخفض ضغط الدم.

الأهداف: يهدف البحث إلى دراسة تأثير القصير المدى لتناول حبوب البن الأخضر على ارتفاع ضغط الدم (BP)، مؤشر كتلة الجسم (BMI)، وقياسات الجسم للمتطوعين الأصحاء.

منهجية البحث: عمل دراسة مخفية مطبقة على ستة عشر متطوعا من الأصحاء الذين تناولوا مستخلص البن الأخضر أو حبوب الكافيين للمقارنة. تم إعطاء المتطوعين العينات لمدة أسبوع مع توقف عن اخذ العينات لمدة أسبوع (wash-out) ثم تبادل عينات البحث بين أ لمتطوعين .

النتائج: بعد اخذ العينات من مستخلص البن التي تحتوي على 500 ملغم من حمض الكلوروجينك (CGA) لمدة سبعة أيام، لوحظ انخفاض ضغط الدم الانبساطي والانقباضي للمشاركين من 76.9 ±9.1 في الأساس إلى 72.6 ± 5.9 ملليميتير زئبقي (P<0.001)، ومن 119±11.9 إلى 114±9.6 ملليميتير زئبقي (P<0.001) على التوالي. مؤشر كتلة الجسم (BMI) ووزن الجسم انخفضوا بشكل ملحوظ بعد أخذ مستخلص حبوب البن. وحيث لم يلحظ أي تغيرات ملموسة في هذه القياسات بعد إعطاء عينات الكافيين فقط.

الاستنتاج: أظهرت هذه الدارسة ان تناول 500 ملغم من حمض الكلوروجينك (CGA) يوميا يقلل إلى حد ملحوظ من ارتفاع ضغط الدم، مؤشر كتلة الجسم، ووزن الجسم للمتطوعين الأصحاء.

الكلمات الدالة: حبوب البن الأخضر، مؤشر كتلة الجسم، قياسات الجسم للمتطوعين الأصحاء، البدانة.

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