Impact of cocoa flavanol consumption on blood pressure responsiveness to exercise

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Abstract

Impaired endothelial vasodilatation may contribute to the exaggerated blood pressure (BP) responses to exercise in individuals who are overweight/obese. This study investigated whether consumption of cocoa flavanols, which improve endothelium-dependent flow-mediated dilatation (FMD), can modify BP responsiveness to exercise. 21 volunteers (8 females, 13 males, 54.9 (2.2) years, BMI: 31.6 (0.8) kg/m^2, systolic BP 134 (2) mmHg, diastolic BP 87 (2) mmHg) were randomised to consume single serves of either a high flavanol (HF, 701mg) or a low flavanol (LF, 22mg) cocoa beverage in a double-blind cross-over design with 3-7 day washout between treatments. Two hours after cocoa consumption FMD was measured, followed by continuous beat to beat assessment (Finapres™) of BP prior to and during 10 min of cycling at 75% of age-predicted maximum heart rate. Averaged data from 2 assessments on each type of beverage were compared by analysis of covariance using pre-exercise BP as the covariate. Pre-exercise BP was similar after taking LF and HF (153 (3)/88 (3) vs 153 (4)/87 (2) mmHg respectively, *P* >0.05). However, the BP response to exercise (area under BP curve) was attenuated by HF compared with LF. BP increases were 68% lower for diastolic BP (*P*=0.03) and 14% lower for mean BP (*P*=0.05). FMD measurements were higher after HF than LF (6.1 (0.6)% vs 3.4 (0.5)%, *P*<0.001). By facilitating vasodilation and attenuating exercise induced increases in BP, cocoa flavanols may decrease cardiovascular risk and enhance the cardiovascular benefits of moderate intensity exercise in at-risk individuals.

INTRODUCTION

Impaired endothelial vasodilator function is an important contributor to the development of cardiovascular disease [1], but it is not yet clear how it impacts on other biomarkers of cardiovascular health.

It has been well-established that obesity and hypertension are associated with impaired nitric oxide (NO) dependent vasodilatation [2-3]. Reduced availability of NO significantly impairs the degree of blood vessel dilatation in response to cardiovascular stressors, such as exercise [4].

The typical cardiovascular response to aerobic exercise is an increase in heart rate (HR) and cardiac output which elicits an increase in systolic BP (SBP). Diastolic BP (DBP) either remains unchanged or decreases slightly due to vasodilatation in the exercising muscles, resulting in increased pulse pressure. Impaired endothelial function (as measured by flow mediated dilatation (FMD)) has been associated with exaggerated BP responses to exercise [5] which have been linked to an increased risk of developing future hypertension [6-8]. This therefore suggests that individuals with impaired vasodilatation such as those who are obese or have elevated BP may have exaggerated BP responses to exercise, thus making them predisposed to acute risk during exercise [9].

Previous attempts to evaluate this emerging risk factor have been limited by the techniques available to measure BP responsiveness to exercise. Most studies have used graded exercise tests with single BP measurements taken at the end of each workload. The introduction of non-invasive techniques for continuous beat-to-beat monitoring of BP enables cardiovascular responses to be measured *during* rather than *after* exercise, thus offering a more physiological representation of the effects of impaired dilatation on cardiovascular function, compared with the commonly used but somewhat artificial FMD response to passive hyperaemia.

Recent studies have shown that the short-term intake of cocoa polyphenols can lower blood pressure (BP) and improve endothelium-dependent vasodilatation [10-13]. The mechanism by which cocoa exerts its antihypertensive effect is yet to be determined but the effect may be mediated through enhanced endothelial function [14], with the cocoa polyphenols increasing the activity of nitric oxide synthase in endothelial cells [15-16], which can lead to enhanced endothelium-dependent vasodilatation [17-18] and improved blood pressure. . Thus, there may also be potential for cocoa flavanols to attenuate the BP increases in response to physiological stressors such as exercise.

The aim of this study was to see whether improvements in FMD seen in overweight individuals following consumption of flavanol-rich cocoa [11] can also improve their exaggerated BP responses to aerobic exercise (measured by decreased area under the curve for SBP, DBP and mean arterial pressure (MAP) during submaximal exercise).

METHODS

A randomised, double-blind, cross-over trial to test acute effects of cocoa flavanols on BP responsiveness to exercise was conducted. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the University of South Australia Human Research Ethics Committee and conducted at the Nutritional Physiology Research Centre. Written informed consent was obtained from all subjects.

Men and post-menopausal women who were overweight or obese (BMI> 25 kg/m^2) but otherwise healthy were recruited. Volunteers had no history of cardiovascular disease, diabetes or renal disease, were not taking diabetic or BP lowering medication and had seated clinic SBP ≤160 mmHg and DBP ≤100 mmHg. Participants were not intolerant to alkaloids (caffeine, theobromine) or dairy, currently smoking or using nicotine replacement therapy.

Volunteers visited the Centre at the same time of day on 5 occasions. At the first (screening) visit, they undertook an exercise test on a cycle ergometer (Monark, Model 828, Vansbro, Sweden) to determine the required workload for subsequent exercise tests. They were required to ride the cycle ergometer for 10 minutes at a workload eliciting a HR equivalent to 75% of their age-predicted maximum (208–(0.7 x age [yr]))*0.75) [19] and their ECG was monitored by a medical practitioner to confirm their suitability to continue exercising.

Volunteers were then provided with a dairy-based cocoa beverage powder which was either high (HF) or low (LF) in cocoa flavanols (refers herein to epicatechin and catechin as well as their procyanidin oligomers up to and including decamers). Reconstituted in 200 ml water, the cocoa beverages provided a total of either 701 mg of cocoa flavanols (HF: 139 mg epicatechin, 39 mg catechin and 523 mg procyanidins) or 22 mg of cocoa flavanols (LF: 0 mg epicatechin, 9 mg catechin and 13 mg procyanidins). The LF and HF cocoa drinks were matched in appearance, macronutrient, micronutrient, and alkaloid (caffeine and theobromine) content, with the only exception being the cocoa flavanol content, see Table 1 for nutrient composition of products. The sachets were labelled with a three-digit numerical code, blinding both volunteers and investigators to their identity throughout the study. Empty sachets were collected to monitor compliance.

The sequence of events on each of the four visits was as follows:

1. Volunteers fasted from food and drink (except water) for ≥ 4 hours

2. Supplement was consumed.

3. FMD was conducted 2 hours after supplementation. Previous research has demonstrated a peak effect of cocoa flavanols on FMD at 2 hours after consumption [16] which returns to baseline 6 hours after consumption [20-21]. The assessment of FMD in the brachial artery was performed using 2-dimensional B-mode ultrasound (LOGIQ 5; GE Medical Systems, Waukesha, WI). Optimal imaging of the artery was achieved using the method of Raitakari and Celermajer [22]. A sphygmomanometer cuff was placed around upper forearm in line with the cubital fossa (ie, distal to the scanned part of the artery) and inflated to supra-systolic pressure (200 mmHg) for 5 min. Images of the artery were taken before cuff inflation, 10 s before cuff release, 10 s after cuff release, and then every 30 s for an additional 3 min to assess the EVF response to reactive hyperaemia.

4. Clinic BP was measured by oscillometry (SpaceLabs Model 90217, SpaceLabs Medical, Florida, USA) while subjects were seated on the cycle ergometer prior to the commencement of exercise.

During the subsequent exercise test BP and HR were measured continuously using a Finapres™ BP monitor (Ohmeda Inc., Englewood, Colorado) with the hand steadied in a support which was maintained at a constant height for all occasions. The test commenced with a 5 minute pre-exercise period of sitting on the cycle ergometer before a 10 min bout of exercise at a workload eliciting 75% of the subject's age predicted maximum HR [19].

This protocol was repeated twice with each cocoa drink (LF or HF) in random order at with a 3-7 day washout between visits and the repeat measures for each supplement were averaged.

Diet and lifestyle requirements during the study

Volunteers were asked to consume a low-flavanol diet during the study period, specifically participants were asked to limit their intake of fruit or fruit containing juices, apples, tea (green, black, herbal, chai, brewed or bottled), coffee or caffeinated beverages, cocoa/chocolate or cocoa/chocolate containing products, honey, soybeans, and soy containing products, nuts/nut products containing nut skins, red wine. Participants were provided with written and verbal reminders to ensure compliance with this request.

Data analysis

Using the Finapres™ BP monitor, data was obtained for every heart beat during the 15 minute protocol, then averaged in 30 second blocks. The final 30 seconds of the seated BP and HR assessment was taken to be the pre-exercise HR and BP.

The changes in BP and HR during exercise were calculated by subtracting the average of each 30 second block during exercise from this pre-exercise average. These 30 second averages were used to calculate the area under the curve (AUC) for the change in BP from pre-exercise values to give an integrated BP response to exercise.

Brachial artery diameter was assessed manually at each time point using the integrated digital callipers by a single observer who was blinded to the treatment group. FMD was reported as the maximum % change from baseline in blood vessel diameter following the cuff occlusion, as described previously [11].

Two-way analysis of covariance (ANCOVA) was used to compare the effects of cocoa supplementation on both FMD and the BP response to exercise, with baseline arterial diameter and pre-exercise BP used as covariates using STATISTICA v5.1 (StatSoft Inc, Tulsa, OK, USA). Relationships between FMD and the BP responses to exercise were determined by linear regression analysis. $P < 0.05$ was taken to indicate statistical significance. All data are presented as mean ± standard error unless otherwise stated.

RESULTS

A total of 21 volunteers (thirteen men and eightwomen, age 55 ± 2.2 years, height 1.7 ± 0.02 m, weight 94.1 ± 3.5 kg, BMI 31.6 ± 0.8 kg/m2, SBP 134 ± 2 mmHg, DBP 87 ± 2 mmHg) completed the trial. Using an existing database of potential volunteers, individuals identified as having a BMI> 25 kg/m^2 were invited to return to perform this trial. Of the 25 people who were contacted, 21 volunteers agreed to participate. There were no withdrawals from this study.

Flow Mediated Dilatation

Fig 1 demonstrates the FMD response to HF and LF cocoa. Two hours after consumption, the HF cocoa beverage resulted in a significantly greater FMD response than the LF cocoa beverage, p<0.001.

Pre-exercise BP

Pre-exercise BP and HR were measured by Finapres finger plethysmography whilst on cycle ergometer. Data were averaged from the final 30 seconds of the pre-exercise period prior to the commencement of exercise. These readings are likely to differ from the clinic BP readings due to hydrostatic differences between the relative heights of the finger cuff and the brachial artery. There were no significant differences between HF and LF cocoa beverage consumption on the pre-exercise BP (HF: SBP/DBP 153 ± 3/88 ± 3 mmHg, HR 79 ± 2 bpm; LF: SBP/DBP 153 ± 4/88 ± 2 mmHg, HR 79 ± 2 bpm).

Responses to exercise.

Both HR and BP increased in response to the cycling exercise. However, there were no significant differences in the HR response following consumption of the HF or LF cocoa beverages. On the other hand, the increases in BP were attenuated by HF cocoa consumption compared with LF cocoa consumption. Fig 2 demonstrates the changes from pre-exercise values for the BP responses to exercise for each 30 second block over the entire 10 minute exercise bout. Table 2 shows the integrated responses for BP increases during exercise. After adjusting for pre-exercise BP, the AUC was reduced 68% for DBP (P=0.03) and 14% for MAP (P=0.05) following HF cocoa consumption compared to LF cocoa consumption

Relationship between changes in FMD and changes in BP response to exercise.

Comparison of differences between HF and LF in the FMD and BP responses to exercise revealed no significant relationships between the differences in FMD and the differences in SBP (r=0.06, P=0.78), DBP (r= 0.42, P=0.06) or MAP (r=0.28, P=0.22), although the relationship between FMD and DBP approached statistical significance.

DISCUSSION

Results of the present study confirm that consuming a single dose of HF cocoa results in a significant improvement in FMD after two hours. Moreover, they demonstrate that acute ingestion of HF cocoa can also attenuate the BP response to exercise.

Conditions such as obesity, diabetes and hypertension are known to impair vasodilatation [2-3] and may potentially cause an increase in DBP during exercise. In the present study, there was indeed an exercise-induced increase in DBP (Fig 2), but the increase was attenuated by supplementation with HF cocoa.

This reduction in DBP response tended to correlate with the increase in FMD following HF consumption (P = 0.06), suggesting that this benefit may be due to improved endothelium dependant dilatation. While some published studies have also found a relationship between exercise BP and FMD [5, 23], others have not [24]. Green et al [25] found no relationship between improvements in conduit vessel function (as measured by FMD) or resistance vessel function (strain gauge plethysmography of total forearm blood flow) and improvements in exercise-induced vasodilatation following exercise training. The role of NO as a mediator of exercise-induced vasodilatation is controversial. A recent review by Tzemos et al. [4] concluded that there may be a role for NO in mediating exercise-induced vasodilatation but, of the studies that have examined the role of NO in exercise-induced vasodilatation [5, 23-24], most have reported that, while NO does contribute [5, 23], there are also many other factors which mediate the vasodilatory response to exercise. Although the relationship between improvement in FMD and attenuation of the blood pressure response to exercise was not significant, it is likely that this study was not sufficiently powered to confirm this relationship.

The finding of an improvement in FMD following consumption of HF in the current study is consistent with a growing body of evidence indicating beneficial effects of cocoa flavanols for endothelial function [10-11, 13, 17-18, 21]. The mechanism by which cocoa flavanols influence vasodilatation is yet to be clearly identified although it appears to be via an increase in the bioavailability of NO due to increased NO production [13, 26-27]. Previous research has shown that after consumption of a similar cocoa product, plasma levels of flavanols peak at approximately 2 hours post-consumption. In addition pure epicatechin consumption closely mimicked the effect of the cocoa beverage, suggesting that epicatechin may be the flavanol responsible for the improvements in vascular function [28], however this study was a proof of concept study with N=3. Therefore further research is required to fully elucidate which flavanols in cocoa can provide the observed benefits in vascular function.

It is important to note that the flavanol rich cocoa beverages used in this study may not deliver the same benefits as dark chocolate consumption. In a study by Hammerstone et al 2000, it was demonstrated that dark chocolate contains approximately 4.3 mg of flavanols per gram. To achieve the amount of flavanols seen in this study (701mg) would require the consumption of 163g of dark chocolate or approximately double that amount of milk chocolate [29]. Given that 163g of dark chocolate provides approximately 3526 kJ and 28g of saturated fat [30] it would be preferable to deliver cocoa flavanols for health benefits in a beverage form such as that used in this study which delivered 610 kJ and 0.9g of saturated fat.

In conclusion, the results of the present study provide further support for acute consumption of cocoa flavanols to improve FMD, and they provide new evidence that cocoa flavanols can also attenuate the BP responses to exercise.

These findings suggest that the consumption of cocoa flavanols may be able to enhance muscle blood flow to allow for improved nutrient delivery and removal to exercising muscles and attenuate the blood pressure responses to exercise, which could allow for safer and more efficient exercise performance in an at risk population such as that include in this study, thus placing less stress on the cardiovascular system during exercise. Furthermore these improvements in FMD and BP response to exercise add to growing evidence that HF cocoa consumption may benefit individuals with cardiovascular risk factors.

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All authors contributed to study design, interpretation of outcomes and preparation of the manuscript; NB and KD collected and analysed the data.

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Table 1: Nutritional profile for each cocoa dose (2 sachets) of cocoa product.

Flavanols (mg)	22	701
Weight (g)	39	39
Energy (kJ)	603	610
Total fat (g)	1.7	1.7
Sat fat (g)	0.9	0.9
Total CHO (g)	20.6	20.6
Sugars (g)	11.5	11.8
Protein (g)	11.4	11.4
Caffeine (mg)	31.1	27.2
Theobromine (mg)	268.1	307.0

Table 2. Area under the curve for the blood pressure responses to exercise between high flavanol and low flavanol cocoa (mean and standard error). *= significant decrease in the BP response to exercise when analysed with pre-exercise BP as the covariate ($p<0.05$).

	SBP (mmHg x sec)		DBP (mmHg x sec)		MAP (mmHg x sec)		PP (mmHg x sec)	
	mean	SE	mean	SE	mean	SE	mean	SE
LF (22 mg)	30155	2021	2359	822	10570	1090	27796	1913
HF (712 mg)	28850	2234	743	1098	9067	1281	28106	1971
Δ	-1305	1904	-1616	902*	-1503	962*	310	59

SBP, systolic blood pressure, DBP, diastolic blood pressure, MAP, mean arterial pressure, PP, pulse pressure LF, low flavanol, HF, high flavanol, Δ, difference between high flavanol and low flavanol response.

Figure Captions

Figure 1. %FMD following high and low flavanol cocoa consumption. * = significant difference ($p<0.05$) between HF (white bars) and LF (black bars).

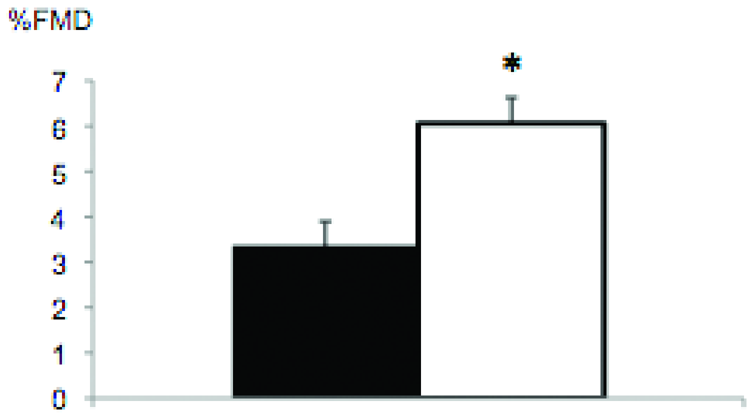

Figure 2. BP responses to exercise represented high (white circles) and low flavanol (black circles) cocoa consumption as change from pre-exercise values.