Short Term Effects of Cocoa Consumption on Blood Pressure

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ABSTRACT

Hypertension, defined as diastolic pressure ≥ 90 mmHg and systolic pressure ≥ 140 mmHg, is a major cause of morbidity and mortality among black populations globally. Several studies have shown that prolonged consumption of cocoa or cocoa containing products leads to decreased blood pressure (BP) in hypertensives. In this study, we investigated the flavonoid content of the top selling cocoa/cocoa based products in Trinidad and Tobago and attempted to determine if consumption of cocoa had any immediate impact on blood pressure levels. The flavonoid content of three 100% cocoa powder products and four cocoa-based formulas was measured using a modified Folin-Ciocalteu procedure. The brand with the highest flavonoid content, 372 gallic acid equivalents, was selected to evaluate the short-term impact of cocoa consumption on blood pressure. Thirty-six participants comprising nineteen hypertensives and seventeen persons with normal blood pressure had their blood pressure recorded on three separate days using ambulatory blood pressure monitors; the blood pressure was recorded every half hour for eight hours. On the first day, the participants received no intervention but on the second and third days, they received either the intervention (5 g cocoa in 125 ml water) or a placebo, in any order. Statistical analysis conducted using t-test statistic and a 95% confidence interval revealed that whether participants regularly took antihypertensive medication or not, a single intervention of cocoa induced decreases in both the diastolic and systolic BPs that were significant ($p = 0.0001$*). Mean decreases of between 8 mmHg and 18 mmHg were observed.*

Keywords: Cocoa consumption, diastolic blood pressure, flavonoid content, high blood pressure, hypertension, systolic blood pressure

Efectos a Corto Plazo del Consumo de Cacao en la Presión Arterial

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RESUMEN

La hipertensión arterial, definida como presión diastólica ≥ 90 mmHg y presión sistólica ≥ 140 mmHg, es una causa importante de morbilidad y mortalidad entre las poblaciones negras en todo el mundo. Varios estudios han demostrado que el consumo prolongado de cacao o productos que contienen cacao, conduce a la disminución de la presión arterial (PA) en los hipertensos. En este estudio, investigamos el contenido de flavonoides en los productos a base de cacao/chocolate más vendidos en Trinidad y Tobago, y tratamos de determinar si el consumo de cacao tenía algún impacto inmediato en los niveles de presión arterial. Mediante un procedimiento modificado de Folin-Ciocalteu, se midió el contenido de flavonoides de tres productos de cacao en polvo al 100%, y cuatro fórmulas con base de cacao. La marca con el mayor contenido de flavonoides, 372 equivalentes de ácido gálico, fue seleccionada para evaluar el impacto a corto plazo del consumo del cacao sobre la presión arterial. A treinta y seis participantes compuestos por diecinueve personas hipertensas y diecisiete personas con presión arterial normal, se les tomó la presión arterial en tres diferentes días con monitores de presión arterial ambulatorios; la presión arterial se registró cada media hora durante ocho horas. En el primer día, los participantes no recibieron ninguna intervención, pero en el segundo y tercer día recibieron una

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*intervención (cacao 5 g en 125 ml de agua) o un plac ebo, en cualquier orden. El análisis estadístico realizado mediante estadística de prueba t y un intervalo de confianza del 95%, independientemente de que los participantes tomaran regularmente medicación antihipertensiva o no, una sola intervención de cacao producía disminuciones significativas (*p = *0.0001) de la PA, tanto diastólica como sistólica. Se observaron disminuciones promedio de entre 8 mmHg y 18 mmHg.*

Palabras claves: Consumo de cacao, presión arterial diastólica, contenido de flavonoides, hipertensión, presión arterial sistólica

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INTRODUCTION

Hypertension or high blood pressure is diagnosed when the average of two or more diastolic blood pressure (BP) measurements, on at least two separate occasions, is ≥ 90 mmHg or when the average of multiple systolic BP readings on two or more separate occasions is consistently ≥ 140 mmHg (1). High BP increases the risk of stroke, end-stage renal disease and cardiovascular disease [CVD] (2). Unfortunately, World Health Organization data indicate that the incidence of stroke and heart disease is increasing and predict that the combined deaths due to these two conditions will be in the region of 16 million persons worldwide by the year 2030 (3). A major contributor to these trends is inadequate control of BP in the hypertensive population, (4, 5).

Although the evidence from several large-scale randomized, controlled studies indicate that treatment of hypertension reduces morbidity and mortality (6), other studies have shown that more than 50% of patients for whom antihypertensive medications have been prescribed discontinue their therapy within 12 months (7). To overcome the psychological and financial barriers associated with the prospects of a lifetime of prescribed medication, many hypertensives have opted for the use of non-prescription natural products (8, 9). Except in those instances where there is sufficient supporting research data, current guidelines strongly recommend the continued integration of lifestyle modification and complementary treatment with conventional blood pressure medications as the ideal management strategy for hypertension (6). Flavonoids sit at the fault line of these two management strategies.

Flavonoids, found in many vegetables and fruits, belong to a large group of natural substances (> 4000) with variable phenolic structures. An increasing body of evidence supports the view that flavonoids promote good health by attenuating or delaying the onset of various diseases, including cancer, certain neurodegenerative disorders and cardiovascular disease (10–12).

In 1993, Hertog *et al* (13), on the basis of a five-year study, reported an inverse relationship between flavonoid consumption and mortality due to coronary disease (13). Since then, other studies have reported inverse relationships between the consumption of flavonoids and the incidence of stroke, and also between the consumption of flavonoids and mortality due to ischaemic heart disease, (14, 15). Within the last decade, flavonol-rich chocolate and cocoa products have attracted interest as nonpharmacological treatment options for high BP (16, 17).

A number of recent studies have shown that small reductions in BP substantially reduce cardiovascular risk (18, 19). As cocoa is known to contain a range of flavonoids, mainly epicatechin, procyanidrin B2 and catechin (10, 20), a number of studies have looked specifically at the link between cocoa consumption and hypertension (7, 11, 21). Several studies have demonstrated that if cocoa-containing products are consumed regularly over several days, a decrease in BP results (13, 22, 23). For example, it was observed by some researchers that the regular consumption of 100 mL of a cocoa drink with high catechin content increased the plasmatic levels of nitric oxide and decreased BP (13, 22). Similarly, another study demonstrated that eating cocoa-rich chocolate bars for two weeks led to a decrease in BP in hypertensive individuals (24). What is not clear is whether the consumption of cocoa has any immediate effect on BP. Unfortunately, it has been shown that many of the commercially available brands of cocoa contain only small amounts of flavonoids; this has been attributed to roasting and alkalization of the cocoa beans during the manufacturing process (13, 20). Here, we set out to evaluate the short term impact of cocoa on high BP, but before doing so, we first needed to ensure that the cocoa used in the study contained a substantial level of flavonoids.

Trinidad and Tobago has a population of about 1.2 million persons; about 40% are of African descent and hypertension is endemic in this fraction of the population. The country is also an exporter of cocoa. In this study, seven of the most popular brands of cocoa products sold in Trinidad and Tobago were assessed for their flavonoid content. The brand with the highest flavonoid concentration was then used to determine if the consumption of a single drink of cocoa led to an immediate (within hours) decrease in the blood pressure of hypertensive individuals. Because of the powdery nature and characteristic taste of cocoa, careful attention had to be given to the experimental design.

SUBJECTS AND METHODS

A survey conducted at 27 supermarkets spread throughout the island was used to obtain data on the best selling cocoa

products (used for the preparation of beverages). On the basis of the survey, seven brands: three 100% cocoa powder products (*Chiefs, Richmond Valley* and *Roma*) and four cocoa-based formulas (*Cadbury, Milo, Nesquik* and *Ovaltine*) were selected for analysis of their flavonoid content.

Measurement of extractable flavonoids

For each cocoa product, 0.5 g was first shaken at room temperature for 60 minutes with 25 mL of a 50:50 v/v, methanol: water mixture. This mixture was then centrifuged for 15 minutes at 25 ºC and 3000 x g and the supernatant kept. Next, 25 mL of an acetone:water mixture (70:30 v/v) was added to the pellet, the mixture shaken for 60 minutes and the centrifugation step repeated. The supernatants from steps one and two were combined and the flavonoid content measured using a modified Folin-Ciocalteu procedure described by Singleton (25). The concentration of flavonoids in the supernatant was calculated from absorbance readings (at 750 nm) against a gallic acid standard curve. The gallic acid standard curve was prepared by serial dilutions from a stock of 1.005 g/L. For each brand of cocoa product used, a minimum of six extractions were performed.

Blood pressure study design

A crossover experimental study was employed to determine if short-term cocoa consumption lowers the BP of otherwise healthy persons with mild hypertension. The sample population was selected from a finite population, based on their suitability as candidates for the experiment. This was determined by the interview and completion of a questionnaire pertaining to their general medical history and current health status. Participants were counselled to refrain from consumption of other cocoa products, alcohol and caffeine-containing products throughout the duration of the study. They were also asked not to make any changes to their lifestyle for the duration of the study. The study was approved by the Ethics Committee, Faculty of Medical Sciences, The University of the West Indies, Trinidad and Tobago.

A total of 45 participants with ages ranging from 35–60 years were included in the study. Of these, 25 were classified as being mildly hypertensive, *ie* either their systolic BP was between 140 and 150 mmHg or their diastolic BP was between 90 and 100 mmHg, or both. The other 20 participants had BP measurements in the normal range and were used as controls. Of the 25 hypertensives in the study, about 50% did not normally take prescribed antihypertensive medication.

On study days, one or two participants were each fitted with a Welch Allyn ambulatory BP monitor, and BP readings taken (automatically) every half an hour for a minimum of eight hours; monitoring normally commenced between 7:00 am and 8:00 am. In phase one, each participant had three separate days of BP readings. Ten of the participants, six hypertensives and four controls chosen randomly, were subsequently asked to return for a second phase comprising two additional days of recordings.

To avoid the complication of controlling for added materials, the cocoa powder was simply added to water but no milk, sugar or other additives were used to make the drink more palatable. This approach presented its own problem. As a result of the powdery nature and distinctive taste of the cocoa drink, the design of an equivalent placebo proved impossible. Instead a double placebo approach was employed. In the first instance, participants were led to believe that the study was comparing the possible effects of cocoa and a green liquid on BP. In the second phase, the BP effects of the first two were compared to those of a colourless solution. The primary intervention was cocoa, 5 g in 125 mL of previously boiled water; the placebo consisted of five drops of green commercial food dye dissolved in 125 mL of previously boiled water. The colourless solution administered in phase two was 125 mL of previously boiled drinking water.

On day one of phase one, 'baseline' BP readings, *ie* in the absence of either intervention, were recorded. On days two and three, participants were given the cocoa-based drink or the placebo (in any order) three hours after BP monitoring commenced. Participants who normally took antihypertensive medication daily delayed doing so until five hours after the interventions (cocoa/placebo) were received. In the first phase of the study, each participant had three sets of BP measurements recorded over the period of a week but not on three consecutive days. In phase two of the study, 10 of the participants, six hypertensives and four controls, received 125 mL of the clear solution.

Statistical analysis of flavonoid content

Analysis of variance (ANOVA) was performed on the mean flavonoid concentrations from the seven brands of cocoa. A Tukey test was used to separate the means. The analyses were performed using the general linear model procedure of SAS [Statistical Analysis System, SAS Institute Inc., Cary, NC, USA; 1989]. The type 1 error was set at $\alpha = 0.05$.

Statistical analysis of blood pressure data

The BP data recorded for the two cohorts, the hypertensives and the controls, were analysed as follows: for each group, the mean systolic and mean diastolic BP were calculated for each half hour interval of the recording. The mean values obtained following the cocoa intervention were then compared to means obtained after use of the placebo. Data were analysed as a crossover design, as described by Rosner (26); calculations were performed manually as described by this worker. The type 1 error was set at $\alpha = 0.05$.

RESULTS

Flavonoid extraction

All seven brands of the cocoa products analysed contained flavonoids, with the mean concentration ranging from 372 ppm gallic acid equivalents at the highest concentration, to 67 ppm gallic acid equivalents at the lowest concentration.

Three of the brands tested had concentrations above 290 ppm while the other four brands had less than 200 ppm (Table). Analysis of variance showed that the difference between the three top brands and the other four was significant (p = 0.0001).

Table: Concentration of flavonoids in cocoa and cocoa-based products

Brand	Mean flavonoid content (ppm)
1	$372.4^{a} \pm 0.4$
2	$334.6^{a} \pm 0.3$
3	$294.3^{ab} \pm 0.5$
4	$186.0^{bc} \pm 0.2$
5	$98.5^{cd} \pm 0.2$
6	$84.3^{cd} \pm 0.1$
7	$67.4^{d} \pm 0.1$

The flavonoid content of three 100% cocoa powders and four cocoa based formulas was measured. Means followed by the same letter are not significantly different when α = 0.05 (17).

The product with the highest flavonoid content (372 ppm gallic acid equivalents) was selected as the intervention in the study. Only 36 (19 hypertensives and 17 normotensives) of the 45 participants completed the study. Figure 1 shows the BP readings from a typical mildly hypertensive patient. The figure shows that a single drink of the intervention (5 g of cocoa in 125 mL water) caused fairly large decreases (up to 20 mmHg) in both systolic and diastolic BP. Overall, for the mildly hypertensive participants, the maximum decreases in both systolic and diastolic BP was 20 mmHg and decreases in BP of between 10 and 20 mmHg were observed in 56% of all mildly hypertensive participants. A decrease of some magnitude was observed in 71% of the hypertensives.

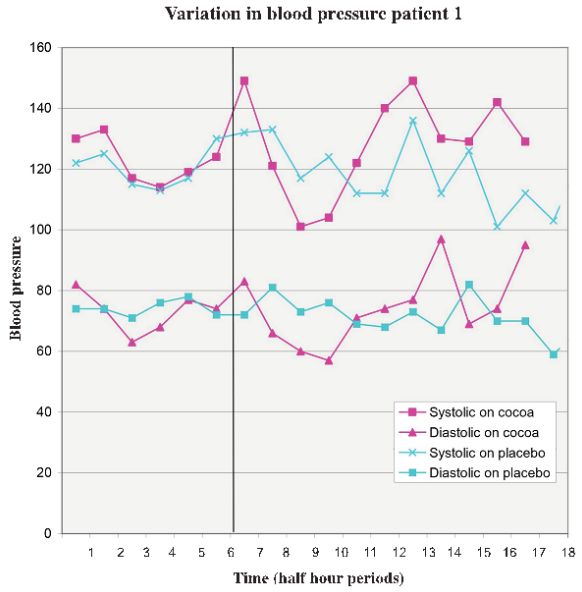

Fig. 1: Typical blood pressure recording for a mildly hypertensive patient in the presence of cocoa or a placebo. The solid vertical line denotes the time at which the intervention, *ie* either the cocoa or the placebo, was taken.

The mean changes in BP are shown in Figs. 2 and 3. Statistical analysis using the t-test (95% confidence interval)

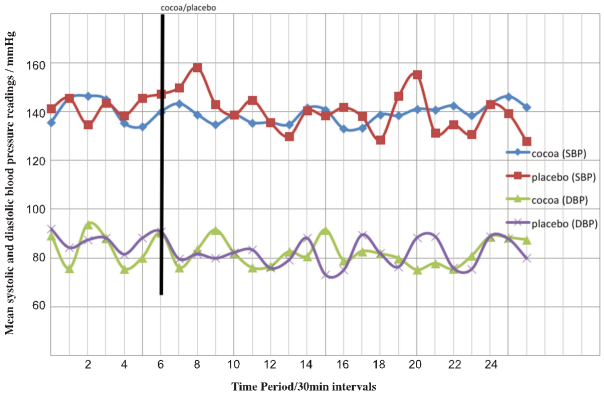

Fig. 2: Graph showing the variation of mean systolic and diastolic blood pressure as a function of time for ten hypertensive patients who did not normally take antihypertensive medication. The solid vertical line denotes the time at which the intervention, *ie* either the cocoa or the placebo, was taken.

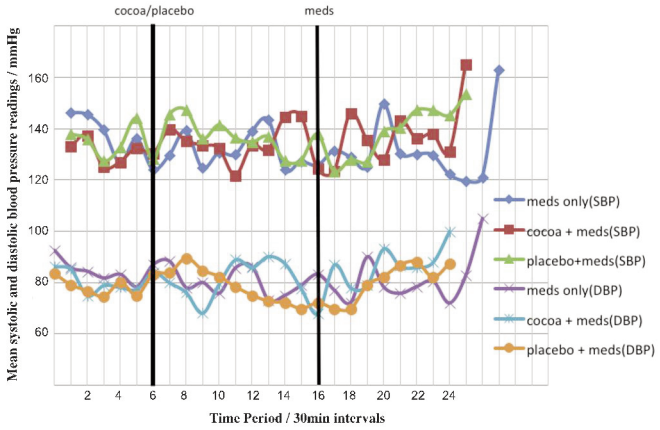

Fig. 3: Graph showing the variation of mean systolic and diastolic blood pressure as a function of time for nine hypertensive patients who normally took antihypertensive medication. The first solid vertical line denotes the time at which the intervention, *ie* either the cocoa or the placebo, was taken. The second solid vertical line denotes the time at which the subject took his/her prescribed antihypertensive medication.

revealed that whether subjects regularly took antihypertensive medication or not, a single intervention of the cocoa drink induced mean decreases of up to 18 mmHg in the systolic BP; these decreases were significant (p = 0.0001) when compared to the effects of the placebo. For both cohorts, the decreases in diastolic BP were also significant (p = 0.0001) but in the group that did not regularly take antihypertensive medication, the mean decreases were small (4–8 mmHg). Overall, the largest mean decrease in diastolic BP at any point was 14 mmHg. For both cohorts, the mean BP decreases were evident within an hour of consumption of the cocoa drink and were sustained for about two and a half

to three hours. The study found that BP changes in the non-hypertensive cohort were small and not significant. In phase two of the study, it was found that there was no significant difference between the effects of plain drinking water and the water containing the green food dye added.

DISCUSSION

Several studies have demonstrated that the prolonged consumption of cocoa, whether as a beverage or as confectionary, has significant health benefits (10–15) and leads to a decrease in BP (7, 11, 13, 21–24, 27, 28). For example, the low cardiovascular mortality seen among the Kuna Indians, who live on the San Blas Islands off the coast of Panama, has been attributed to their high ingestion of cocoa-rich beverages (29). Similarly, some studies (22–24, 30) have also reported that the eating of dark chocolate for at least one week produces a decrease of 3 mmHg in BP. The compounds thought to be responsible for the modulation of BP in these instances are flavonoids. These flavonoids, which are known to be present in cocoa beans, are believed to function as nitric oxide stimulants (13, 22, 24). Unfortunately, roasting and other manufacturing processes often decrease the flavonoid concentration of commercially available cocoa products (20).

Our chemical analysis of the seven top selling brands of cocoa/cocoa-containing products in Trinidad and Tobago revealed that all of them contained varying quantities of flavonoids, with the top three containing at least three times as much as the others. This result suggests that for the brands studied, the manufacturing processes did not totally deplete their flavonoid and that these cocoa/cocoa products could, to a varying extent, be used as a source of flavonoids. Given the established health benefits of these compounds, it would be worthwhile for manufacturing companies to review their production procedures in an effort to maintain flavonoid levels as high as possible.

Our finding that consumption of a single cup of cocoa (5 g in 125 mL water) led to immediate (within an hour) significant decreases in the BP of persons with mild HBP was very noteworthy. Of particular interest was the fact that the decreases were observed both in subjects who regularly took antihypertensive medication as well as in those who had never taken such medication. To minimize the dangers of stroke and other health hazards associated with high BP, the wash-out period, in which persons who normally took antihypertensive medication abstained from doing so during the study, was short, lasting only about 20 hours. The fact that the decreases in BP were also observed in the participants who did not normally take BP medication therefore ruled out residual drug carry-over as the cause of the decreases. This finding therefore suggests that in addition to its established long-term control of BP *via* nitric oxide stimulation (13, 22), cocoa also exerts a short-term effect on BP, most probably *via* an alternative mechanism.

The decreases in BP seen in this study tended to be fairly large, measuring as much as 20 mmHg in some instances, but on the other hand, the decreases were only sustained for two and a half to three hours. These decreases were triggered by a cocoa intake of 5 g in 125 mL of water which corresponds to about 300 ppm gallic acid equivalents. This finding suggests that a regiment employing smaller quantities of cocoa taken at regular three to four-hour intervals may lead to smaller but more sustained decreases in BP. Studies have shown that a decrease in BP of 3 mmHg is enough to significantly reduce the risk of morbidity and mortality associated with cardiovascular disease (18, 19). There was one other interesting observation for the high BP cohort that did not normally take antihypertensive medication. For this group, even after the initial cocoa-induced decrease in BP had disappeared, the cocoa still appeared to have a steadying effect on the systolic blood pressure, as the large hourly fluctuations seen with the placebo were absent. Finally, although our finding that cocoa had a negligible effect on the BP of normotensive individuals is consistent with previous reports (24, 31), we are unwilling at this stage to be dogmatic about that position. Given that the BP changes in the normotensive group were small, it will require further studies to say definitely whether these BP changes are significant or not.

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