Assessment of the Effects of Cocoa Powder on Blood Pressure in Humans – A Preliminary Study in Osogbo

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ABSTRACT

Background: Cocoa powder contains polyphenols (phytonutrients) which are increasingly being used either as dietary supplements or in fortification of foods. Polyphenols exhibit antioxidant activity known to play a vital role in reducing the risk of some diseases (including cardiovascular diseases) in humans by protecting cells in the body from damage during aerobic production of energy. The aim of this study was to investigate the effect of flavonoid-rich Cocoa powder on the blood pressure of clinically stable hypertensive patients.

Materials and Methods: In this intervention study, sixty-eight patients attending cardiology clinics (for treatment of hypertension) in two selected hospitals were serially recruited into the study after ethical approval had been obtained. Physical examination was conducted and selected parameters (including blood pressure, weight and height) were recorded. Each participant was instructed to consume 25g of cocoa powder diluted in 250 ml of water twice daily. Physical examinations were repeated on a 2-weekly basis, BMI was calculated on each visit. They were followed up for 9 weeks and the relevant clinical parameters were repeated at each clinic visit.

Results: Of the 67 subjects examined on the first day, 18 (26.8%) were hypertensive (BP > 140/90 mmHg). During subsequent visits, the proportion of hypertensive BP status gradually declined over the weeks as follows: 19 out of 67 (28.4%), 16 out of 63 (25.4%), 8 out of 60 (13.3%) and 7 out of 60 (11.6) in weeks 3, 5, 7 and 9 respectively. The BMI of the subjects did not show any significant variation over the weeks during the course of the study.

Conclusion: The study showed that daily cocoa consumption may be beneficial in the control of the BP and complimentary to pharmacotherapy in Nigerian hypertensive patients. However, we recommend the conduct of further studies (randomized study on a larger scale) in the Nigerian population in order to further validate the findings of this study.

Keywords: Cocoa powder, blood pressure, hypertensives.

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Évaluation des effets de la poudre de cacao sur la pression artérielle chez l'homme-une étude préliminaire à Osogbo

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Résumé

Contexte général de l'étude : La poudre de cacao contient des poly phénols (phytonutriments) qui sont de plus en plus utilisés comme compléments alimentaires ou pour enrichir les aliments. Les poly phénols présentent une activité antioxydant connue pour jouer un rôle essentiel dans la réduction du risque de certaines maladies (y compris les maladies cardiovasculaires) chez l'homme en protégeant les cellules du corps contre les dommages lors de la production aérobie d'énergie.

Matériaux et méthodes de l'étude : Soixante-huit patients fréquentant des cliniques de cardiologie (pour le traitement de l'hypertension) dans 2 hôpitaux sélectionnés à Osogbo ont été recrutés en série dans l'étude. Un examen physique a été effectué sur eux et certains paramètres (y compris la pression artérielle, le poids et la taille) ont été enregistrés. Chaque participant a été invité à consommer 25 g de poudre de cacao diluée dans 250 ml d'eau deux fois par jour. Les examens physiques ont été répétés toutes les deux semaines, l'IMC a également été calculé à chaque visite. Ils ont été suivis pendant 9 semaines et les paramètres cliniques pertinents ont été répétés à chaque visite

Résultats de l'étude : Sur les 67 sujets examinés le premier jour, 18 (28,5%) étaient hypertendus (TA> 140/90 mmHg). Lors des visites ultérieures, la proportion d'hypertension artérielle a progressivement diminué au fil des semaines comme suit: 19 (28,4%), 16 (25,4%), 8 (13,3%) et 7 (11,6) au cours des semaines 3, 5, 7 et 9 respectivement . L'IMC des sujets n'a pas montré de variation significative au cours des semaines au cours de l'étude

Conclusion: L'étude a montré que la consommation quotidienne de cacao peut être bénéfique pour le contrôle de la TA et complémentaire à la pharmacothérapie chez les patients hypertendus nigérians. Cependant, nous recommandons la conduite d'études complémentaires (étude randomisée à plus grande échelle) dans la population nigériane afin de valider davantage les résultats de cette étude.

Mots-clés : Poudre de cacao, tension artérielle, hypertendu

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INTRODUCTION

Cocoa powder (CP) is the major ingredient of cocoa based beverages and confectioneries throughout the world. CP contains a good quantity of metabolizable carbohydrate, a high proportion of dietary fiber of up to 30% and minerals among which potassium and sodium are of primary importance (Assa et al., 2019). CP contains polyphenols which are phytonutrients and are sometimes referred to as phytochemicals or nutraceuticals which are increasingly being used as dietary supplements or in fortification of foods (Assa et al., 2019). Polyphenols exhibit antioxidant activity, which has been reported to play a vital role in reducing the risk of some diseases in humans by protecting cells in the body from damage during aerobic production of energy. Polyphenols are also thought to reduce the risk cardiovascular diseases, inhibit the formation of low-density lipoproteins (LDL), cholesterol, and modulate immune functions (Wollgast & Anklam, 2000). Cocoa is a rich source of flavonoids particularly flavanols and procyanidins. CP contains flavonols which are natural compounds in cocoa that may modulate platelet in the process reducing blood clot risks (Katz et al. 2011). This has been increasingly linked to promising circulatory benefits including improved blood flow and a reduced tendency to form damaging clots. However, the preservation of polyphenols during the processing of cocoa is important in order for it to be able to exhibit the health effects associated with cocoa consumption. In Nigeria, where the costs of diabetes and hypertension care are borne almost entirely by the patients, coupled with suboptimal drug compliance with resultant poor control, cost effective and affordable approaches are needed to meet this challenge.

Nigeria bears a double burden of disease because despite the fact that she is still battling with the scourge of communicable diseases, she is now also saddled with life-style related non-communicable diseases (NCDs) that accompany industrialization and urbanization.

The Nigerian National Non-Communicable Disease Survey in 1997 reported an adult national hypertension prevalence of 11.4%; being 14.8% and 9.8% in urban and rural areas, respectively. This would have been higher if the new cutoff value of 140/90 mmHg was used instead of 160/95mmHg. The prevalence of hypertension in both rural and urban communities in Nigeria is increasing. Various community surveys in Nigeria have shown an adult prevalence of 15%–36.6%. (Oladapo et al, 2010)

recently reported a prevalence of 20.8% in the rural community of Egbeda, South-west Nigeria. The prevalence in semi-urban Ile-Ife was 36.6%, while that in Ipetumodu, Osun State, was 26.4% for mild hypertension (BP $\geq$ 140/90 mmHg) and 11.8% for moderate hypertension (BP $\geq$ 160/100 mmHg). The overall prevalence of hypertension ranges from 14.5% in Nigeria, 16.9% in Cameroon, 28.7% in Accra, to 32.6% for blacks in the United States. Cross-migration from rural to urban areas and vice versa, the asymptomatic nature of the disease, changing lifestyles, and the environment are contributing to the rising problem of hypertension. Hypertension has been associated with various factors, including age, gender, family history, alcohol consumption, smoking, obesity, level of education, and occupation (Kapoor et al. 2010). Observational studies have shown that lifestyle changes including physical activity, weight loss, and diet can prevent hypertension and the complications (Knowler et al., 2002). Prevention (primary and secondary) of this disease and its complications through life style modifications is highly desirable.

This study therefore set out to investigate the effect of flavonoid-rich Cocoa powder on the blood pressure of clinically stable hypertensive patients.

METHODOLOGY

This quasi-experimental (intervention) study was carried out at the cardiology clinics of the Ladoke Akintola University of Technology Teaching Hospital (LAUTH) and the State Hospital, Asubiaro; both in Osogbo, Osun State.

The study population comprised of individuals already diagnosed with hypertension and attending the cardiology clinics of the selected hospitals (for treatment of hypertension). Eligible participants were serially recruited into the study and a total of 68 subjects were enrolled for the study. Institutional ethical approval was obtained from both the ethical committee of LAUTECH Teaching Hospital, Osogbo and the State Specialist Hospital, Asubiaro, Osogbo, Nigeria. The study was conducted between September and November 2019. Written informed consent was also obtained from each individual participant. Participation was completely voluntary and confidentiality of all information obtained from the subjects was assured.

The inclusion criteria for recruiting subjects into the study are as stated:

a) individuals previously diagnosed with

hypertension and were already on treatment for at least six months

b) individuals who met the above criterion and were not engaged in regular daily intake of any cocoa-based beverage.

The following are the criteria for excluding individuals from participating in the study:

c) newly diagnosed hypertensive patients (first timers at the clinics)

d) previously diagnosed hypertensive patients who regularly consumed cocoa-based beverages.

All the subjects had baseline physical examination done on them and medication(s) being taken were documented. Blood samples were taken for laboratory investigations at first contact to serve as baseline parameters of the respondents. Hypertension was defined as systolic blood pressure of $\geq$140 mmHg and/or diastolic blood pressure of $\geq$90 mmHg. Parameters, including age, sex, drug therapy, weight, height, and blood pressure, were obtained and BMI for each respondent was calculated as the ratio of weight (kilograms) to height (metres) squared (kg/m^2).

The respondents each received packets of flavonol-rich cocoa powder (Oluji pure cocoa powder) and were trained to prepare and consume 50g of the cocoa powder daily (consumed as 25 mg diluted in 250mls of water twice daily) while the study lasted.

The main study instrument was a semi-structured, interviewer-administered questionnaire which collected information on respondents' socio-demographics, medical history, social history and physical activity as well a section for recording the results of their physical examination (blood pressure, weight, height, BMI). Accoson mercury sphygmomanometer was used to measure the BP in mmHg, a clinic-stationed stadiometer was used for measuring height while a standardized bathroom weighing scale was used to take the weight of the study respondents. Data were analyzed using Statistical Package for Service Solutions (SPSS) version 23. Data were summarized as frequencies and percentages for qualitative variables and mean (standard deviation) for some quantitative variables. Univariate and bivariate analyses were done and results were presented using tables.

RESULTS

Sixty-eight respondents participated in the study and they were aged between 35 and 79 years of which nearly two-thirds (63.2%) were females. Majority of the respondents were Christians (72.1%) and most (95.6%) of them of the Yoruba ethnic group. Fifty-nine (86.8%) of the respondents were married and nearly three-fifths (57.4%) had tertiary education. About two-fifths (41.2%) of the respondents were civil servants while 18 of them (26.5%) were self-employed; 6 (8.8%) were retirees while 9 (13.2%) professionals and only 1 of them (1.5%) was unemployed.

Majority (83.8%) of the study respondents owned their residence while 57.4% of them had at least one vehicle (car, truck or van). Sixty-eight respondents (45.6%) earned between 18,000 and 50,000 naira while 23 (33.8%) of them earned more than ₦50,000.00. (Table 1)

Majority (73.5%) of the respondents were diagnosed of hypertension within 10 years preceding the study while only four of them (5.9%) had their diagnosis made 30 or more years ago. Most of the respondents had already been placed on antihypertensive medications (for a variable length of duration) as at the time of this study; only one (1.5%) of them had ever had a stroke; 10 of them had arthritis while 1 of them had diabetes mellitus. (Table 2A). Thirty-nine (57.4%) of the study participants were on calcium channel blockers, 26 (38.2%) were on Angiotensin converting enzyme inhibitors (ACE-I) inhibitors and 16 (23.5%) were on diuretics. (Table 2B).

Most of the respondents (88.2%) had never smoked tobacco; 20.6% agreed that they were currently taking alcoholic beverages. All but one of the respondents engaged in one form or another of physical exercise (of varying frequencies); brisk-walking was the most common (86.7%) form of exercise that the respondents engaged in, although only 55.8% of them spent at least 15 minutes on daily physical exercise. (Table 3).

Of the 67 respondents who submitted themselves to physical examination on the first day of the study, 18 (26.5%) had their BP in the hypertensive range while the remaining 49 (73.5%) were normotensive. When the BMIs of the study participants were calculated on the same day, 13 (19.4%) of them had their BMI in the healthy range of values, 25 (37.3%) were overweight, 25 (37.3%)

were obese and 4 (6.0%) were morbidly obese. (Table 4).

During subsequent visits, the proportion of hypertensive BP status gradually declined over the weeks as follows: 19 (28.4%), 16 (25.4%), 8 (13.3%) and 7 (11.6) in weeks 3, 5, 7 and 9 respectively. The BMI of the subjects did not show any significant variation over the weeks during the course of the study. Table 5.

Table 6 shows that at recruitment, most of the respondents had their serum lipid and glucose profiles within normal limits but only 21 (31.3%) of them had their high-density lipoprotein being with normal values.

Table 1A: Socio-demographic information of the study respondents (n=68)

Variables	Frequency	Percentage (%)
Age		
Young adults (≤ 39 years)	9	13.2
Middle aged adults (40 – 59 years)	30	44.1
Old adults (≥ 60 years)	29	42.6
Sex		
Male	25	36.8
Female	43	63.2
Religion		
Christianity	49	72.1
Islam	19	27.9
Ethnicity		
Yoruba	65	95.6
Igbo	3	4.4
Marital status		
Single	1	1.5
Married	59	86.8
Separated	1	1.5
Widowed	7	10.3
Level of education		
No formal education	5	7.4
Completed primary education/Standard six	13	19.1
Completed secondary education	11	16.2
Tertiary education	39	57.4
Spouse's level of education		
No formal education	2	2.9
Completed primary education/Standard six	11	16.2
Completed secondary education	12	17.6
Tertiary education	42	61.8
Not applicable	1	1.5
Occupation		
Artisan	6	8.8
Civil servant	28	41.2
Self-employed	18	26.5
Unemployed	1	1.5
Professionals	9	13.2
Retiree	6	8.8
Others	3	4.4

Table 1B: Other socio-demographic information of the study respondents (n=68)

Variables	Frequency	Percentage (%)
Type of housing (A)		
Rented	11	16.2
Owner (landlord/landlady)	57	83.8
Type of housing (B)		
Duplex	2	2.9
3-bedroom flat	50	73.5
2-bedroom flat	12	17.6
Room and parlour	2	2.9
One room	2	2.9
Does your family have car (or truck or van)?		
No	29	42.6
Yes, one	34	50.0
Yes, two or more	5	7.4
Does your family have a motorcycle?		
No	63	92.6
Yes, one	4	5.9
Yes, two or more	1	1.5
Average monthly income (naira)		
< 18000	14	20.6
18000-50000	31	45.6
> 50000	23	33.8
Spouse's average monthly income (n=49)		
< 18000	1	1.5
18000-50000	11	16.2
> 50000	12	17.6
Don't know	25	36.8

DISCUSSION

This study found a general reduction in the BP of the study participants during the study period, a finding similar to that of Jumar and Schmieder (2015) who reported a significant lowering effect in hypertensive subjects (systolic BP > 140/90mmHg at baseline) according to their epidemiologic data from different patient cohorts which revealed a significant drop in the office BP and ambulatory BP in hypertensive patients on cocoa flavanol when compared with normotensive individuals as their study reported that "Cocoa flavanol has been shown to lower systolic and diastolic office and ambulatory BP. Even though there is just a modest BP reduction of 3 mm Hg in an average mixed population, patients with hypertension and people younger than 50 years experienced larger effects". The number of normotensive patients consistently increased over the weeks of the study as shown in table 5. The role of age on the BP-lowering effect of cocoa was not be evaluated in this study although, it has been reported that BP-lowering effect of cocoa is attenuated with increasing age (Ried et al., 2012). Ried et al went on to say that Cocoa flavanols had been shown to reduce vascular resistance and arterial stiffness, and are potent scavengers of free radicals (Schroeter, 2006), which may lead to improved vascular function.

Concerning the BMI of the study subjects, there was no significant variation in any direction. This finding is important because it has been recommended that precaution in all products containing chocolate is mandatory because of high caloric load of commercially available chocolate (about 500 kcal/100 g) and associated weight gain, a risk factor for hypertension, diabetes, and dyslipidemia (Corti et al. 2009). Furthermore, this study is in agreement with previous epidemiological investigations which reported that normotensive and mildly hypertensive patients with daily intake of 50mg epicatechin revealed a significant reduction in mean arterial systolic and diastolic BP compared with placebo (Hooper et al. 2012, Taubert et al. 2007)

Table 2A: Medical history of the study respondents (n = 68)

Variables	Frequency	Percentage (%)
When were you diagnosed of hypertension (years ago)?		
≤ 10 years	50	73.5
11 -29 years	14	20.6
≥ 30 years	4	5.9
For how long have you been taking antihypertensive medications? (n=65)		
1 – 3 years	28	41.2
4 – 6 years	8	11.8
7 – 9 years	5	7.5
≥ 10 years	21	30.9
Not on medications	3	4.4
Have you ever had a stroke? (n=68)		
Yes	1	1.5
No	67	98.5
Have you ever been diagnosed with diabetes mellitus? (n=68)		
Yes	1	1.5
No	67	98.5
If yes to above, how long ago were you diagnosed? (n=1)		
1 – 3 years	1	1.5
Have you been diagnosed of any other chronic non-communicable diseases (diabetes, arthritis, cancer)? (n=68)		
Yes	11	16.2
No	57	83.8
If yes to above, state the names of the diseases (n=11)		
Arthritis	10	90.9
Diabetes mellitus	1	10.1

Table 2B: Medications currently being taken by the respondents (n = 68)

Class of Medication*	Frequency	Percentage (%)
Diuretics (bumetanide, furosemide, torsemide, hydrochlorothiazide (HCT), indapamide, amiloride)	16	23.5
Calcium channel blockers (amlodipine, clevidipine, felodipine, nicardipine, nifedipine, nisoldipine, verapamil)	39	57.4
ACE inhibitors (lisinopril, perindopril, benazepril, captopril)	26	38.2
Angiotensin II receptor antagonists (azilsartan, candesartan, valsartan, losartan)	10	14.7
Adrenergic receptor antagonists (acebutolol, atenolol, carvedilol, nadolol, timolol, doxazosin, prazosin, carvedilol)	4	5.9
Aldosterone receptor antagonists (eplerenon, spironolactone)	1	1.5
Alpha 2 adrenergic receptor agonists (clonidine, guanabenz, guanfacine, moxonidine)	0	0.0

*Multiple responses allowed

Table 3: Social history and physical activity of the respondents (n=68)

Variable	Frequency	Percentage (%)
Do you smoke tobacco?		
Yes	4	5.9
Previously	4	5.9
Never	60	88.2
If yes, or previously to above, for how long? (n=8)		
1 – 3 years	5	62.5
> 9 years	3	37.5
How many sticks per day?		
1 – 3	6	75.0
4 – 6	2	25.0
Do you take alcoholic beverages drinks?		
Yes	14	20.6
Previously	3	4.4
Never	51	75.0
If yes or previously to above, for how long? (n=17)		
1 – 3 years	7	41.2
4 – 6 years	2	11.8
> 9 years	8	47.0
Quantify bottles per day (n=17)		
1 – 3	17	100.0
Type of alcoholic beverage (n=17)		
Alcohol	13	76.5
Palm wine/other local beer	4	23.5
What is the physical exercise you engage in?		
None	1	1.5
Brisk walking	59	86.7
Jogging	6	8.8
Cycling	1	1.5
Swimming	1	1.5
How frequently do you engage in the physical exercise specified in above?		
Less than 15 minutes daily	14	20.5
At least 15 – 30 minutes daily	38	55.8
2 to 3 days weekly	8	11.6
4 – 5 days weekly	1	1.5
Everyday	5	7.7
Occasionally	2	2.9

Table 4: Findings on physical examination of the respondents on the day of recruitment into the study (n = 67), Week 1

Variable	Frequency	Percentage
Blood pressure		
Hypertensive	18	26.8
Normotensive	49	73.2
Weight		
30 – 50 kg	2	3.0
51 – 70 kg	26	38.8
71 – 90 kg	30	44.8
> 90 kg	9	13.4
Height		
1.41 – 1.6 m	39	58.2
1.61 – 1.80 m	27	40.3
> 1.80 m	1	1.5
Body Mass Index (BMI)		
18.5 – 24.9 (healthy range)	13	19.4
25 – 29.9 (overweight)	25	37.3
30 – 39.9 (obese)	25	37.3
≥ 40 (morbidly obese)	4	6.0

Table 5: Findings on physical examination of the respondents in weeks following recruitment into the study (n = 67)

Variable	Frequency	Percentage
Week 3		
Blood pressure status (n=67)		
Hypertensive	19	28.4
Normotensive	48	71.6
Body Mass Index (BMI)		
18.5 – 24.9 (healthy weight range)	13	19.4
25 – 29.9 overweight	26	38.8
> 30 – 39.9 obese	25	36.8
≥ 40 (Morbid obesity)	3	4.4
Week 5		
Blood pressure status (n=63)		
Hypertensive	16	25.4
Normotensive	47	74.6
BMI		
18.5 – 24.9 (healthy weight range)	11	17.5
25 – 29.9 overweight	26	41.3
> 30 – 39.9 obese	23	36.5
≥ 40 (Morbid obesity)	3	4.7
Week 7		
Blood pressure status (n=60)		
Hypertensive	8	13.3
Normotensive	52	86.7
BMI		
18.5 – 24.9 (healthy weight range)	11	17.5
25 – 29.9 overweight	26	41.3
> 30 – 39.9 obese	23	36.5
≥ 40 (Morbid obesity)	0	0.0
Week 9		
Blood pressure status (n=60)		
Hypertensive	7	11.6
Normotensive	53	88.4
BMI		
18.5 – 24.9 (healthy weight range)	12	20.0
25 – 29.9 overweight	26	43.4
> 30 – 39.9 obese	22	36.6
≥ 40 (Morbid obesity)	0	0.0

Table 6: Cholesterol, triglicerides, hdl, ldl and glucose profile of respondents on the day of recruitment (n = 67)

Respondents' blood parameter (mmol/L)	Frequency (%)	Mean	Std. Deviation
Total Cholesterol			
Normal (< 5.2)	46 (68.7%)		
Borderline (5.2 – 6.2)	18 (26.9%)	4.78	1.00
High (≥ 6.3)	3 (4.5%)		
Triglycerides			
Normal (≤ 1. 7)	54 (80.6%)		
Borderline (1.8 – 2.4)	11 (16.4%)	1.25	0.65
High (≥ 2.5)	2 (3.0%)		
HDL-C			
Low (< 1.0)	38 (56.7%)		
Normal (1.0 – 1.6)	21 (31.3%)	1.05	0.56
High (≥ 1. 7)	8 (11.9%)		
LDL-C			
Normal (optimal/near optimal: < 3.4)	45 (67.2%)		
Borderline (3.4 – 4.1)	10 (14.9%)	3.08	1.14
High (≥ 4. 2)	12 (17.9%)		
Glucose (Random blood sugar)			
Low (< 3.89)	3 (4.5%)		
Normal (acceptable: 3.89 – 11.0)	62 (92.5%)	5.59	1.31
High (≥ 11. 1)	1 (1.5%)		

CONCLUSION

The study demonstrated that daily consumption of cocoa product in hypertensive patient may be associated with a slight reduction in blood pressure while having no significant effect on the BMI of individuals hence suggesting no significant increased risk of the development of weight-related pathologies.

RECOMMENDATION

Further studies need to be done on a larger scale to further substantiate the findings of this study and also evaluate the role of hypertension-related blood parameters (e.g. serum lipids) on the relationship between cocoa consumption and BP control.

DISCLOSURE

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REFERENCES

1. Assa A, Asriati DW, Indriana D, Sampebarra AL. Mineral contents in fermented bean shells of Forastero-cocoa (Theobroma cacao L) clones. ICP Conference Series Earth and Environmental Science 355:012108 DOI: 10.1088/1755-1315/1/012108

2. Corti R, Flammer AJ, Hollenberg NK, Luscher TF. Cocoa and cardiovascular health. *Circulation*. 2009; 119: 1433–1441.

3. Lee Hooper , Colin Kay, Asmaa Abdelhamid, Paul A Kroon, Jeffrey S Cohn, Eric B Rimm et al. Effects of chocolate, cocoa, and flavan-3-ols on cardiovascular health: a systematic review and meta-analysis of randomized trials. *Am J Clin Nutr*. 2012; 95: 740–751.

4. Jumar A, Schmieder R E. Cocoa Flavanol Cardiovascular Effects Beyond Blood Pressure Reduction. The Journal of Clinical Hypertension. 2016; 18 (4):352-8.

5. Kapoor S, Tyagi R, Saluja K, Chaturvedi A, Kapoor AK. Emerging health threats among a primitive tribal group of Central India. Journal of Public Health and Epidemiology. 2010; 2: 13–19.

6. Katz DL, Doughty K, Ali A. Cocoa and Chocolate in Human Health and Disease. Antioxid Redox Signal. 2011; 15(10):2779-2811.

7. William C Knowler , Elizabeth Barrett-Connor, Sarah E Fowler, Richard F Hamman, John M Lachin,

Elizabeth A Walker, et al. Diabetes Prevention Program Research Group. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin, N Engl J Med, 2002;346:393-403.

8. Oladapo O. O. Falase A. O. Adedapo K. A prevalence of cardiometabolic risk factors among a rural Yoruba south-western population: a population-based survey. Cardiovasc J Afr. 2010; 21(1): 26-31.

9. Karin Ried , Thomas R Sullivan, Peter Fakler, Oliver R Frank, Nigel P Stocks. Effect of cocoa on blood pressure. *Cochrane Database Syst Rev*. 2012;(8): CD008893.

10. Taubert D, Roesen R, Lehmann C, et al. Effects of low habitual cocoa intake on blood pressure and bioactive nitric oxide: a randomized controlled trial. *JAMA*. 2007; 298: 49– 60.

11. Wollgast J, Anklam E. Review on polyphenols in Theobroma cacao: changes in composition during the manufacture of chocolate and methodology for identification and quantification. Food Research International. 2000; 33(6):423-447.

12. Schroeter H, Heiss C, Balzer J, Kleinbongard P, Keen CL, Hollenberg NK et al. Epicatechin mediates beneficial effects of flavanol-rich cocoa on vascular function in humans. PNAS. 2006; 103(4):1024-1029.