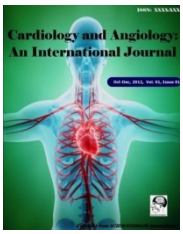

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Cardio Protective Effect of Dark Chocolate Components: Mechanisms of Actions

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Authors' contributions

Author SS wrote the first draft of the manuscript. Author KE managed the literature searches and responded to the queries of the reviewers. Author KE redrafted the manuscript. Both the authors read and approved the final manuscript.

Review Article

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ABSTRACT

Chocolate is made from the seeds of a tropical rainforest tree called "*Theobroma cacao".* When compared with other food sources based on oxygen radical absorbance capacity (ORAC) measurement, dark chocolate is a major source of flavonols with highest antioxidant levels. Some of the health benefits of cocoa consumption include antioxidant properties such as polyphenolic compounds, among others are monomeric flavanols, epicatechin, catechin and oligomeric procyanidins. Both experimental and observational studies have suggested that chocolate consumption has a positive influence on human health, with antioxidant, antihypertensive, anti-inflammatory, anti-atherogenic, and anti-thrombotic effects as well as influence on insulin sensitivity, vascular endothelial function, and bioavailability of nitric oxide. In addition, dark chocolate consumption may alter lipid effects, by lowering total and low density lipoproteins and increasing high density lipoprotein cholesterol levels. The antioxidants found in chocolate have been shown to inhibit plasma lipid oxidation probably by scavenging free radical species. There are some experimental studies to prove that flavonoids could prevent LDL oxidation in vitro by scavenging radical species or sequestering metal ions. Dark chocolate (DC) has beneficial effects in the prevention of cardiovascular diseases (CVD) due to its anti-inflammatory and antioxidant properties. Polyphenols rich dark chocolate showed progress in insulin sensitivity and decreased blood pressure in healthy subjects. Dark Chocolate has a dual effect on platelets by decreasing platelet aggregation and also it reduces platelet adhesion. Chocolate extends its great beneficial effect from being by and

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large a palatable pleasant and hence sustainable therapeutic option. Thus, dark chocolate may be suggested as a potential delicacy and one of the agents for the prevention and control of cardiometabolic syndrome.

Keywords: Dark chocolate; cocoa; polyphenols; flavonols; nitric oxide; cardio metabolic syndrome; antioxidants.

1. INTRODUCTION

Chocolate is made from the seeds of a tropical rainforest tree called "*Theobroma cacao".* Swedish naturalist, Linnaeus named it after the Greek term 'theobroma' literally meaning "food of the Gods" [1]. When compared with other food sources based on oxygen radical absorbance capacity (ORAC) measurement, dark chocolate is a major source of flavonols with highest antioxidant levels [2]. It was merely in the 17th century that the consumption of chocolate spreaded through Europe. Joseph Fry, in 1847 produced the first plain eating chocolate bar in the United Kingdom where cocoa butter was introduced as an ingredient [3]. Food scientists from all over the world report that dark chocolate contains most of the necessary compounds and minerals to prevent major chronic heart condition, cancer and other age related diseases [4-6].

Chocolate is manufactured from cocoa mass (the base product produced by the processing of the cocoa bean), cocoa butter (the natural fat from the cocoa bean) and added sugar [1]. The most common craved food is chocolate and, for most chocolate cravers, non-chocolate substitutes are inadequate [7]. Chocolate contains minerals such as potassium, magnesium, copper and iron and in addition to these, chocolate also contains cocoa butter [8] predominantly as the fat. Which in turn contains approximately 33% oleic acid (monounsaturated), 25% palmitic acid (saturated) and 33% stearic acid (saturated) [9]. In a study conducted by Lee et al.,(2003), cocoa was found to possess much higher levels of total phenolics (611 mg of gallic acid equivalents, GAE) and flavonoids (564 mg of epicatechin equivalents, ECE) per serving than black tea (124 mg of GAE and 34 mg of ECE, respectively), green tea (165 mg of GAE and 47 mg of ECE), and red wine (340 mg of GAE and 163 mg of ECE)[10].They also demonstrated that total antioxidants capacities from ABTS and DPPH assays were higher in cocoa and in turn significantly correlated with the phenol and flavanoid content of cocoa. The picture of the cocoa plant and cocoa pods are shown in the Fig. 1.

Arts et al. [11] reported that dark chocolate contains catechins (a group of flavan-3-ol flavonoid compounds) at an average concentration of 0.535 mg/g, four times that of tea (0.139 mg/g). Vinson et al. [12] showed that chocolates had a higher flavonoid antioxidant quantity-quality index when compared with fruit, vegetables, red wine, and black tea. Some of the health benefits of cocoa consumption include antioxidant properties such as polyphenolic compounds, among others are monomeric flavanols, epicatechin, catechin and oligomeric procyanidins [13-15].

Fig. 1. Theobroma cacao with ripe pods

According to the World Health Organization and American Heart Association, by 2030 nearly 23.6 million people will die from cardiovascular disorders [16,17]. Ogbera [18] reported that about a fifth of the world's adult population have metabolic syndrome, a cluster of factors associated with an increased risk of type 2 diabetes and cardiovascular disease. Both experimental and observational studies have suggested that chocolate consumption has a positive influence on human health, with antioxidant, antihypertensive, anti-inflammatory,

anti-atherogenic, and anti-thrombotic effects as well as influence on insulin sensitivity, vascular endothelial function, and bioavailability of nitric oxide [19,20].

2. IMPACT OF DARK CHOCOLATE ON LIPID STATUS

The effects of dark chocolate and its various components on lipid levels are not quite conclusive as differential inferences are made by different authors. A meta-analysis of all randomized controlled trials documented that dark chocolate consumption could alter lipid effects by lowering total and low density lipoproteins but not increasing in high density lipoprotein (HDL) cholesterol levels [21]. In contrast, Mursu et al. [22] showed that HDL cholesterol level is greater in healthy humans ingesting chocolate that contained a large amount of cocoa mass. Chocolate consumption is coupled with short term improvement in the delayed oxidation of LDL cholesterol with enhanced endothelial function [23,24], decreased blood pressure [25], increased insulin sensitivity [25] and with improved platelet function [24,26,27]. The consumption of cocoa and dark chocolate has been reported to increase HDL cholesterol level and to amplify plasma antioxidant capacity and to reduce the formation of lipid oxidation products (TBARS) [22,28,29].

3. RICH SOURCE OF ANTIOXIDANTS

Chocolate is the third highest daily source of antioxidants for Americans [30]. Wiswedel et al. [31] documented that the antioxidants in chocolate have been shown to inhibit plasma lipid oxidation probably by scavenging free radical species. The lipoprotein-binding antioxidant property is found in chocolate extracts [32]. Similarly, Wang et al. [29] reported that a dose-dependent increase in plasma epicatechin is related with an increase in plasma antioxidant capacity and a decline in plasma lipid peroxidation 2 and 6 hours after procyanidin-rich chocolate consumption. Contrary to the above reports, Lotito et al. [33] reported that there is a greater increase in plasma total antioxidative capacity after the consumption of flavonol-rich food, which is not likely due to flavonols but is possibly a consequence of the increased uric acid levels resulting from fructose metabolism. There are some experimental studies to prove that flavonoids could prevent LDL oxidation in vitro by scavenging radical species or sequestering metal ions [34,35,36].

4. EFFECT IN LOWERING BLOOD PRESSURE

Grassi et al. [37] studied the effects of consumption of dark chocolate 100 g (88 mg flavanol) daily in hypertensive subjects for fifteen days, showed a significant decrease in systolic and diastolic blood pressure. The authors explained that increased endothelial NOS expression and NO bioavailability due to anthocyanin cyanidin-3-glucoside contained in dark chocolate that would ameliorate endothelial dysfunction, and thereby have the potential to decrease blood pressure, increase insulin sensitivity, and slow down atherogenesis processes. Taubert et al. [38] compared the effects between the consumption of dark chocolate at 6.3 g/day with white chocolate at 5.6 g/day for 18 weeks in hypertensive subjects with prehypertension and stage 1. The results showed a significant decrease in systolic and diastolic blood pressure in people receiving dark chocolate. A Dutch epidemiological study in elderly men revealed that blood pressure was significantly lowered in the group of men consuming cocoa or chocolate. In addition, it was evident that the group with the highest cocoa and chocolate consumption was also reported to have a lower incidence of death due to cardiovascular diseases compared with men who did not consume cocoa or chocolate [39]. Furthermore, many recent researches suggested that dark chocolate consumption

would lower blood pressure in healthy individuals and in people with metabolic syndrome by improving endothelial function and increasing insulin sensitivity [40-42]. For instance, D'El-Rei et al. [43] have shown one-week dark chocolate intake significantly improved endothelial function and reduced blood pressure in treated younger participants with impaired endothelial function in spite of lower cardiovascular risk.

5. ANTI-INFLAMATORY EFFECT

Di Renzo et al. [44] reported that dark chocolate has beneficial effects in the prevention of cardiovascular diseases (CVD) due to its anti-inflammatory and antioxidant properties. Mao et al. and Ramiro et al stated that several in vitro studies have emphasized that cocoa polyphenols can modulate the transcription and secretion of pro-inflammatory cytokines in human peripheral blood mononuclear cells and macrophages [45,46]. With reference to cytokines, Schramm et al. [47] found that consumption of chocolate with high procyanidin content significantly lowers the levels of leukotrienes and increased the levels of prostacyclin compared with a group consuming a low-procyanidin chocolate. Monagas et al. [48] further demonstrated a positive influence of cocoa powder on the modulation of inflammatory mediators in human subjects at high risk of CVD. Presumably, as dark chocolate is universally made out with higher concentrations of cocoa, the mechanism in attenuating inflammatory cytokines may also explain to the effective prevention of CVD in many clinical observational studies.

6. ANTIDIABETIC EFFECT

Low prevalence of atheroscelerosis, type 2 diabetes mellitus and hypertension have been reported among Kuna Indians of Islands of Panama due to regular day to day consumption of homemade cocoa drink [24]. Insulin resistance is defined as an inadequate response by insulin target tissues, such as skeletal muscle, liver, and adipose tissue, to the physiologic effects of circulating insulin. Konopatskaya et al. [49] showed a close association between NO bioavailability in endothelial cells and insulin sensitivity, thus such insulin sensitivity may be mitigated by polyphenols of dark chocolate. Nitric Oxide availability enhanced by the flavolnols of dark chocolate significantly improve insulin-mediated glucose uptake in healthy person [50,51]. Grassi et al. [52] conducted a study in hypertensive adults with impaired glucose tolerance following flavonol-rich chocolate ingestion and he showed a positive impact on glucose and insulin responses to an oral glucose tolerance test. Additionally, there has some evidence incidicating a decrease in insulin resistance and a raise in insulin sensitivity after the consumption of flavonol rich chocolate in obese men and women [44,53].

7. IMPACT OF DARK CHOCOLATE ON BLOOD VESSELS AND PLATELETS

Simon et al. [54] reported that the antioxidant property of dark chocolate would lead to diminished inactivation of NO by free radicals through inhibition of NADPH oxidase. The mechanism was reconfirmed by Afoakwa et al. [35] who suggested that inhibition of NADPH oxidase and its manifestation on endothelial lining leads to vasodilation and lowering of blood pressure. Dark chocolate consumption has been reported to protect the vascular endothelium by augmenting nitric oxide availability and thereby improving endothelium dependent vasorelaxation [55,54,56,57,58]. Steinberg et al. [59] suggests that just by reducing hypercholesterolemia, coronary heart disease will not disappear, because a high cholesterol level is by no means the only causative factor yet there are many other factors that contribute to aberrated vascular consequences. Karim et al. [56] stated that flavonals, a

component of dark chocolate, have the ability to increase NO level in the endothelium cells by activating vascular endothelial NO synthase. In addition, Hermann et al. [24] reported that dark chocolate has a dual effect on platelets by decreasing platelet aggregation and also it reduces platelet adhesion. All these vascular protective process to reduce the risk of acute coronary events by consuming cocoa products or dark chocolate has been observed in a number of studies [24,44,60,61-71].

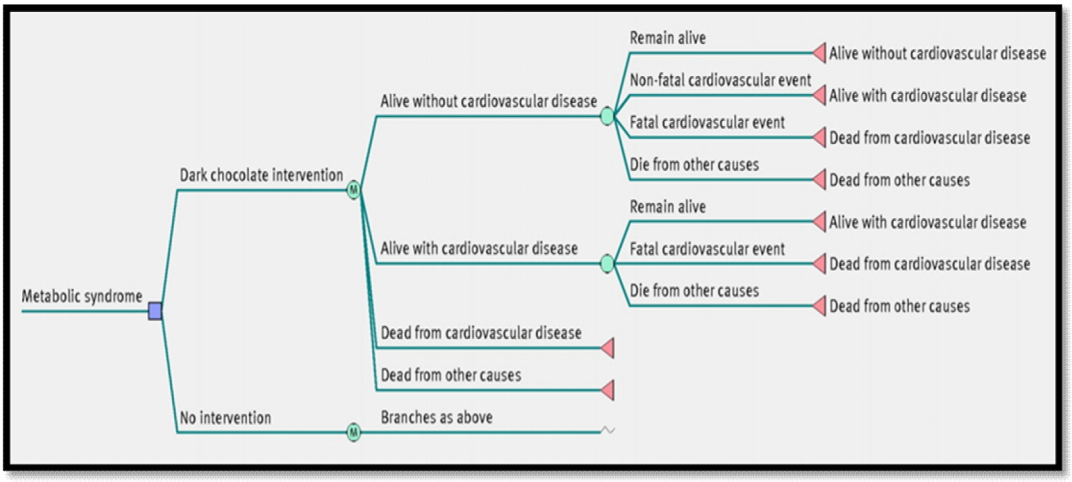

Fig. 2. MARKOV model for case analysis in people with dark chocolate intervention
Source: Ella Zomer , BMJ 2012;344:e3657

The above Fig. 2 represents MARKOV model for case analysis in people with dark chocolate intervention. This model was used in a study conducted by Zomer et al. [61] by which it was revealed that the usage of plain dark chocolate could serve potentially as an economical and effective strategy for the prevention of CVD.

Recently, Shadwell et al. [72] further proved that regular dark chocolate consumption would increase the antioxidant effect and modulate the gene expression involved in lipid metabolism which may improve the status of metabolic syndrome in an animal model.

8. CONCLUSION

Cardio-metabolic disorders are certainly preventable if people are keenly concerned about their lifestyle. A better understanding of the factors that being in the pathogenesis and implementation of strategies to modify these factors would be highly appreciable in managing the current epidemic. Diet is one of the key lifestyle factors associated in the genesis, prevention and management of cardio-metabolic disorders. From various studies it has been evident that cocoa products containing flavanoids have been found to have potential effect in preventing cardio metabolic disorders and lowering blood lipids and pressure. With these documentations, it is quite apparent that plain dark chocolate could represent an effective and cost effective strategy for the prevention of cardiovascular disease in people with metabolic syndrome.

Dark chocolate may be suggested as a potential delicacy and one of the agents for the prevention and control of cardio metabolic syndrome. However, evidence to date

recommends that the chocolate would be really dark and of at least 60-70% cocoa or at least as chocolates enriched with flavonols or polyphenols. Thus, chocolate extends its great beneficial effect from being, by and large a palatable, pleasant and hence sustainable therapeutic option. Of course, if other saturated, trans- fat and refined carbohydrates dietary sources are restricted then prudently dark chocolate may be given as prophylactic regimen for the subjects with risk of metabolic syndrome. However, further studies are required to understand the cardio protective benefits of other bioactive compounds apart from flavanoids present in the dark chocolate.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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