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Exploring the Potential Advantages of Chocolate and Cocoa for Cardio and Cerebrovascular Health

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Abstract

Numerous studies have identified cocoa phenolics, procyanidins, and flavan-3-ols as bioactive antioxidant compounds that enhance vascular function, reduce inflammation, and improve lipid metabolism, insulin sensitivity, and platelet aggregation. Research indicates that consuming flavanol-rich cocoa supports cardiovascular health. Given the rising global occurrence of cardiovascular disease and its related risk factors, this review article aimed to investigate the impact of chocolate/cocoa intake on cardio and cerebrovascular conditions and their related risks. Across various clinical trials, moderate flavonol-rich cocoa/chocolate consumption proved to be correlated with better heart health. Advantages include a diminished risk of heart failure, hypertension, platelet aggregation, coronary artery disease, stroke, atrial fibrillation, high cholesterol, and peripheral artery disease. Consuming 50 grams of dark chocolate daily or every other day has been linked to these positive outcomes. While flavanol-rich chocolate shows potential as a complementary therapy for various cardio and cerebrovascular conditions, extensive clinical trials are necessary to confirm its effectiveness.

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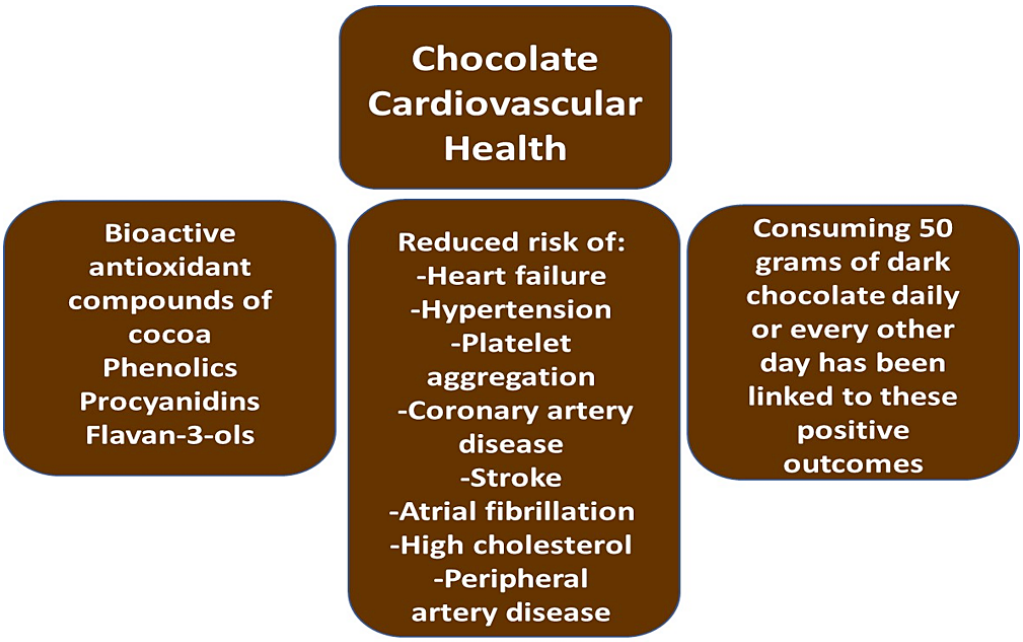
Graphic Abstract



Introduction

Since ancient times, people have enjoyed chocolate's exquisite taste as a food that universally sparks joy and satisfaction. Chocolate's history dates back to the year 400 AD. Theobroma cacao L., the cocoa tree, is a member of the Malvaceae family. It is the only plant commercially used to produce chocolate. While its pulp is flavorful, the cocoa seed is primarily utilized in the food industry, especially for chocolate production.[1] Theobroma cacao L. has four primary varieties [2]: Nacional, Criollo, Forastero, and Trinitario. Forastero dominates global production, accounting for around 80%, due to its greater disease resistance and higher yield.[3] Nacional is the rarest of the four, known for its more refined flavor, being more aromatic and less bitter, which gives it a higher economic value.[4]

The preparation of chocolate from Theobromine cacao seeds involves intricate steps: fermentation to awaken the chocolate flavor, roasting to expel water content, and grinding to produce a velvety cacao liquor. The resulting cacao liquor embarks on its final transformation, combining various ingredients to create diverse chocolate varieties, including white, dark, and milk chocolate.[5] Fermentation of cocoa beans is an essential and transformative process in chocolate production, greatly impacting the flavor and quality of the finished product. Throughout fermentation, cocoa beans undergo a complex interaction of microbial activity and biochemical reactions, creating essential compounds that contribute to the distinctive sensory qualities of chocolate.[6] Another research suggests that some polyphenols and peptides with valuable bioactive properties generated in the process of cocoa fermentation have the potential for bioprospecting beyond chocolate production. However, a substantial portion of these molecules is lost during post-fermentation processes.[7] The quality of cocoa can be enhanced by optimizing the duration of spontaneous fermentation, which influences the formation of volatile aromatic compounds. This adjustment can standardize the process to achieve consistent attributes and quality, ultimately affecting the final chocolate product.[8]

Cocoa, the building block of chocolate, boasts a substantial amount of fat, with cocoa butter accounting for 40-50% of its composition. This fat comprises palmitic, oleic, and stearic acids with approximately 33, 25, and 33%, respectively. Cocoa beans, which contain more phenolic antioxidants than most foods, are among the most

well-known sources of dietary polyphenols. A trio of polyphenols – (58%) proanthocyanidins, (37%) catechins, and anthocyanidins (4%)– stands out as the highest rich phytonutrients in cocoa beans, contributing significantly to their nutritional profile.[9] Cocoa's nitrogenous components encompass a diverse range of compounds, including proteins and methylxanthines, such as caffeine and theobromine. Beyond its antioxidant content, cocoa boasts an impressive array of minerals, including iron, potassium, zinc, phosphorus, magnesium, and copper, making it a nutritional powerhouse.[10]

Chocolate intake has seen a worldwide surge, incredibly dark chocolate gaining particular popularity due to its high cocoa content and purported health advantages relative to milk or regular chocolate.[10,11] Conversely, milk chocolate's high sugar content has raised concerns about potential adverse health effects.[5] Due to its high levels of cocoa, flavonoids, theobromine, and low sugar content, dark chocolate stands out as the only type of chocolate that holds the potential to confer health benefits.[12] Clinical trials have provided evidence suggesting chocolate consumption enhances cognitive function,[13] further supported by preclinical studies.[13,14] A recent systematic review has also strengthened the proof of chocolate's positive impact on cognitive function, revealing improvements in task performance and cognitive scores among young adults (younger than 25 years) and children who regularly consume chocolate.[15] Chocolate also holds promise as a potential source of anticancer and antimicrobial properties.[16]

Regular cocoa consumption can enhance overall mood and alleviate depression symptoms, contributing to a better quality of life. Research also suggests that cocoa contains components that may help prevent cardiovascular diseases, lower cancer risk, aid in weight management, and provide antioxidants through cocoa fibers. Additionally, cocoa flavanols may diminish the risk of developing type 2 diabetes. Beyond its well-established benefits, chocolate may be preventive against inflammation, oxidative damage, impaired endothelial function, and atherosclerosis, according to several laboratory and clinical investigations.[17] Multiple meta-analyses have consistently highlighted the positive impact of the consumption of chocolate on lowering the cardiometabolic events risk, such as stroke, diabetes, coronary heart disease, and myocardial infarction.[18] Just like chocolate's impact on cardiometabolic events, cocoa similarly exerts beneficial impacts on vascular function, insulin resistance, and blood pressure (BP).[19] Cocoa and dark chocolate possess antioxidant properties such as preventing oxidation the low-density lipoprotein cholesterol (LDL-c) and suppressing ultraviolet-caused DNA damage; also it enhances nitric oxide (NO) production and inhibits angiotensin-converting enzyme.[20] In addition, dark chocolate could help prevent thromboembolic and cardiovascular illnesses by inhibiting platelet aggregation.[21] The health advantages of consuming dark chocolate are well-documented; it is a valuable source of flavonoids and is related to a decrease risk of lower BP, cardiovascular disease, inhibition of platelet aggregation, and antioxidant activity.[22] Besides flavonoids, dark chocolate contains phytochemicals like methylxanthines, which have mood-enhancing effects on the brain .[23] Additionally, there is evidence suggesting that dark chocolate has anti-inflammatory properties.[24]

Cocoa has been investigated for its possible effects on obesity. Research suggests that cocoa consumption may help reduce obesity-related factors by decreasing body weight, reducing fat accumulation, and lowering serum triglyceride levels. It also appears to influence the gene expression related to fat metabolism and thermogenesis, potentially contributing to weight management and a lower risk of obesity-related health issues.[25]

Chocolate contains various bioactive compounds that enhance alertness.[26] A Swiss study also found that chocolate can reduce stress. After fourteen days of consuming dark chocolate, stress markers in adults with high anxiety levels aligned with those of individuals with low stress.[27] Chocolate influences stress by stimulating the production of serotonin, a neurotransmitter known for its calming effects.[28]

Another study using magnetic resonance imaging on young, healthy individuals found that cocoa consumption increases cerebral blood flow, suggesting a potential role for cocoa in treating conditions like dementia and stroke.[29] Also improved cognitive performance with chocolate intake.[30] Another study found that consuming chocolate daily decreases the risk of stroke in men.[31]

Some *in vitro* researches show that cocoa may inhibit the cancerous cells growth, although the precise anticancer pathways remain unclear.[32, 33] However, excessive chocolate consumption has been linked to increased cancer risk.[34,35]

Studies have shown that chocolate consumption prior to exercise aids in quicker recovery from post-exercise metabolic and physiological changes. Blood glucose levels in participants significantly increased 15 minutes post chocolate consumption and remained moderately high for 30 minutes following one hour of running.[36]

The goal of the current investigation is to review the literature about the research concerning the efficacy of cocoa and chocolate consumption against cardiovascular diseases and cardiometabolic indicators.

Materials and Methods

A thorough literature search was performed using the PubMed, Medscape, and Google Scholar electronic databases to find relevant studies published from the beginning up to May 2024. The search terms used were "cocoa," "chocolate," "cardiovascular," "cerebrovascular," "hypertension," "arrhythmia," "heart failure," "platelet aggregation," "coronary artery disease," "atrial fibrillation," "hyperlipidemia," and "peripheral artery disease." For studies to be included, they were necessary to meet the following criteria: (1) to be written in English, and (2) clinical and experimental studies.

Results and Discussion

Heart Failure

Heart failure is a life-threatening disease that influences millions of people globally with a 25% rise in prevalence anticipated by 2030. It is caused by a weakening of the heart muscle, which makes it challenging for the heart to pump blood effectively. The clinical manifestation of heart failure include shortness of breath, fluid retention, and fatigue.[37] Heart failure is one of the greatest common causes of mortality, so improving heart failure primary prevention is crucial for public health.[38] Consuming chocolate may potentially reduce the risk of cardiac failure by reducing the hazard variables associated with heart failure, such as infarction of the heart, coronary artery disease, and elevated BP.[20] On the other hand, eating too much chocolate can lead to increase weight,[39] which is a known hazard factor for heart failure.[40] It is also possible that eating more chocolate makes people eat less of other foods that are good for preventing heart failure. This means that the benefits of the flavonoids in chocolate may be outweighed by the negative outcomes of eating too much energy.[41]

One meta-analysis that included outcomes from 106,109 people who were tracked for nine to fourteen years discovered a strong correlation between the chocolate ingested amount and the likelihood of heart failure. A 50g chocolate square counts as one serving. For one, three, seven, and ten servings/week, the hazard ratios (HR) (95% CI) were 0.92 (0.88-0.97), 0.86 (0.78-0.94), 0.93 (0.85-1.03), and 1.07 (0.92-1.23), in that order. This suggests that whereas consuming ten or more servings of chocolate a week was linked to an elevated likelihood of heart failure, moderate chocolate eating was correlated to a reduce likelihood of heart failure .[41] To assess the correlation between eating chocolate and the possibility of occurrence cardiac failure in the United Kingdom general population, another meta-analysis and systematic review was conducted. Out of the 20,922 individuals (mean 12.5 ± 2.7 years), 53% of whom were females, 1101 of them had cardiac failure within the study duration. After adjustment the dietary and lifestyle variables, researchers observed that a 19% decrease in cardiac failure risk in the highest cohort chocolate intake (up to 100 g/d) of versus the lowest cohort. Additionally, the findings imply that consuming more chocolate is not harmful for heart failure patients.[42]

A cohort prospective research with a follow up period of 14 years involving 30,000 Swedish males who had no prior history of heart illness, diabetes, or cardiac failure found that consuming chocolate one to three serving per month was accompanying with a 12% reduction in the hazard of cardiac failure, while eating one to two servings per week was accompanying with a 17% decrease, and eating three to six servings per week was associated accompanying with a 18% decrease. Eating more than one serving per day was not accompanying with any further decrease in risk. Another large research revealed that eating chocolate in moderation was linked with a decline risk of cardiac failure or mortality, however, those who had more than one serving per day did not see further protective impact.[43] A cohort study assessed

the impact of consumption chocolate in patients established fist acute myocardial infarction. 1169 Sweden patients were self-reported chocolate they ate over the preceding 12 months. Chocolate ingestion, which is a rich source of valuable bioactive constituents, in a dose dependent manner revealed an inverse correlation with cardiac mortality relative to never chocolate consumption.[44]

In accordance with the preceding study, another cohort prospective research of over 31,000 Swedish females - follow up for nine years- revealed that eating one to three servings of chocolate monthly was related with a 24% drop in the cardiac failure risk, while eating one to two servings per week was related with a 32% reduction. However, the beneficial correlation did not materialize when +1 serving was consumed daily.[45]

A study of over 20,000 males, who following for over 9 years, after adjusting energy intake, exercise, age, body mass index (BMI), atrial fibrillation history. The data revealed that those who consumed moderate amounts of chocolate had a decrease risk of cardiac failure. Related to men who eaten less than once per month, men who ate 1-3 times a week had a 14% decreased risk of cardiac failure, men who ate 2-4 times a week had a 20% decreased risk, and men who ate 5 or more times a week had a 18% decreased risk. This association was strongest in men with a BMI < 25 kg/m2.[46]

Hypertension

Chocolate which is a rich source of flavanols boost the synthesis of endothelial NO, causing vasodilation and thus decreasing BP 20. A meta-analysis systematic review conducted on 31 articles revealed that eating dark chocolate for at least 2 weeks lowered (−3.94 mmHg) BP more than drinking cocoa beverages (-1.54 mmHg). This effect was greatest in people who ate chocolate with high levels of flavanols (≥900 mg daily) and epicatechin (≥100 mg daily).[47] Furthermore a meta-analysis in middle-aged and older adults showed a substantial negative correlation between chocolate intake and the level of diastolic and systolic BP.[48]

Another meta-analysis research of 35 study with 1804 individuals examined the impact of chocolate on BP. The studies used 40 different interventions with chocolate doses ranging from 1.4 -105 g/ day (30-1218 mg/day flavanols). The results of 40 different interventions with mostly healthy subjects found that flavanol-rich cocoa products slightly and significantly lowered BP (- 1.76 mmHg both systolic (1804 subjects) and diastolic (1772 subjects)). The results also showed that, cocoa may be more effective in lowering BP in people with high or borderline high BP than in people with normal BP. Among participants with systolic BP above 140 mmHg, above 130 mmHg, and below 130 mmHg, the average changes in systolic BP were -4.00 mmHg, -2.43 mmHg, and -0.65 mmHg, respectively. Moreover, among participants with diastolic BP above 80 mmHg and below 80 mmHg, the average changes in diastolic BP were -1.98 mmHg and -1.57 mmHg, respectively. Blood pressure reduction was greater after 6 to 18 weeks of treatment than after 2 to 4 weeks of treatment. For systolic BP, the changes were -2.37 mmHg and 1.37 mmHg, respectively. For diastolic BP, the changes were -2.04 mmHg and -1.55 mmHg, respectively. The findings concluded that, chocolate may lower BP most in people who started with high BP and took chocolate for a longer period of time.[49]

Another research revealed that overweight middle-aged, or obese adults who ate a daily meal for 4 weeks supplemented with 1.4 g of cocoa extract (415 mg of flavanols) showed a greater decrease in their postprandial systolic BP relative to participants who only followed a calorie-restricted diet, even if they did not lose weight.[50]

A randomized, double-blind, placebo-controlled research of patients had type II diabetes (n=60) showed that eating dark chocolate (25 g/ day) for eight weeks lowered their systolic and diastolic BP by an average of 6.40 and 5.93 mmHg, respectively. The control group, who ate white chocolate, revealed not substantial change in their BP.[51] The studies were too different from each other to give us clear answers about how much chocolate you need to eat to lower your BP. Further research is required to figure out this relationship.[52]

3- Platelet Aggregation

Platelet activation and aggregation are essential for blood clotting. Diets and nutrition can affect how cardiovascular disease develops, especially by affecting how platelets work. Dark chocolate reduces platelet aggregation and platelet activation markers

(P-selectin (CD62P) and activated glycoprotein (GP) IIb/IIIa complex), and platelet microparticle formation.[53] Some studies suggest that chocolate can work together with antiplatelet drugs to make them more effective, but this can also increase the risk of bleeding because chocolate inhibits cyclooxygenase-1 (COX-1) enzyme in platelets.[54]

A study of 32 people found that eating dark chocolate, whether it was high in flavanols (a type of antioxidant) or low in flavanols, did not change platelet aggregation in response to collagen or a thromboxane analogue. However, both types of dark chocolate reduced platelet aggregation in response to adenosine diphosphate (ADP) and a thrombin receptor activator peptide. Pre-treating platelets with theobromine (a compound in chocolate) also reduced platelet aggregation in response to ADP and a thrombin receptor activator peptide. This suggests that theobromine, rather than flavanols, is responsible for the dark chocolate impact on platelet aggregation.[55]

A study of 42 healthy people was conducted to investigate the influences of dark chocolate enriched with white chocolate, standard dark chocolate, and flavan-3-ol on platelet functions. The participants were classified at random to receive a single chocolate bar of one of the three types of chocolate. Prior to, two, and six hours after consuming chocolate the urine and blood samples were collected from each participant. Dark chocolate enriched with flavan-3-ol significantly reduced platelet aggregation and expression of P-selectin in males. Also, diminished thrombin receptor-activating peptide-induced platelet aggregation and rose thrombin receptor-activating peptide-induced fibrinogen binding in females. There was elevated collagen/epinephrine-induced ex vivo bleeding time in both males and females. White chocolate significantly elevated collagen/epinephrine-induced ex vivo bleeding time in men only and declined ADP-induced platelet P-selectin expression. The researchers concluded that flavan-3-ols found in dark chocolate, as well as other compounds in white chocolate, could enhance platelet functions in a gender-dependent manner.[56]

The influences of eating dark chocolate for one week in 28 healthy people was assessed. The dark chocolate provided 700 mg of flavonoids per day. After a week, the participants had better cholesterol levels and decreased platelet reactivity (arachidonic acid-induced activated GPIIb/IIIa expression was lowered).[57] A study of 1535 healthy adults found that those who ate chocolate within 48 hours of platelet testing had lower urinary 11-dehydro thromboxane B2 levels and longer platelet function closure times, suggesting that chocolate has antiplatelet effects.[58]

Dark chocolate decreased platelet adhesion in 22 heart transplant recipients 2 hours after consumption.[59] A examine of 30 healthy participants found that eating dark chocolate diminished collagen-induced platelet aggregation, while milk and white chocolate had no substantial influence on platelets.[21]

4- Coronary Artery Disease

Coronary artery disease, as well known as myocardial ischemia, ischemic heart disease, coronary heart disease,[60] develops when plaque, a hard substance made up of cholesterol, fat, and other materials, accumulates within the walls of the coronary arteries, narrowing the passageway for blood flow and restricting the amount of oxygen and nutrients reaching the heart muscle.[61] Coronary artery disease presents in three main categories: stable angina, unstable angina, and myocardial infarction. Stroke and coronary artery disease, continue to be the primary cause of sickness and mortality globally.[18] The correlation of chocolate eating and the likelihood of developing coronary artery disease was assessed by analyzing data from multiple prospective researches. A total of 14 prospective studies focused on primary prevention were selected for the analysis, involving 508,705 participants and follow-up periods ranging from five to sixteen years. People who ate the largest amount of chocolate had a 10% reduce risk of developing coronary artery disease relative to people who consumed the least amount of chocolate. This trend continued in a dose-dependent manner, with people who ate three, seven, and ten servings/week of chocolate having a 9%, 11%, and 12% lower risk of coronary artery illness, respectively.[18]

Another study investigate whether regular chocolate consumption among Million Veteran Programme (MVP) participants is correlated with a reduced risk of developing coronary artery illness. A separate analysis was also conducted to determine if this

association also holds true for participants with diabetes type II. The research involving 188,447 individuals from the MVP revealed that repeated ingestion of chocolate was corelated with a reduce hazard of coronary artery disease consequences. The individuals were predominantly male with mean age of 64 years. Participants who ingested chocolate more frequently had reduce incidence rates of coronary artery disease events relative to participants who ingested chocolate less often. This association remained significant even after adjusting factors such as lifestyle habits, age, gender, and race. However, this protective effect was not observed among participants with diabetes.[62] Furthermore, ingested chocolate intake (10 g daily) was found to have a slight negative relationship with the incidence of coronary artery illness events according to a dose-response meta-analysis (risk ratio (RR): 0.96; 95% CI: 0.93, 0.99).[63]

Another research involving 67,640 Swedish women and men investigated the link between chocolate ingesting and myocardial infarction and ischemic cardiac disease. The contributors fulfilled a food-frequency survey to assess their chocolate intake. Over a 12-year period, researchers discovered that people who consumed three to four servings/ week of chocolate had a 13% decreased risk of myocardial infarction relative to people who did not eat chocolate. When the researchers combined data from six studies involving over 6,800 people with coronary artery disease, they found that people eating the largest amount of chocolate had a 10% reduce risk of developing this condition relative to people who eating the lowest amount.[64]

A previous comprehensive analysis involving 20,951 males and females and an average follow-up time of 11.3 years investigating the link between chocolate ingesting and coronary artery illness showed that, after adjusting for various factors, people who consumed the most chocolate had a reduce risk of coronary cardiac illness (12%) relative to those who consumed the least chocolate (HR: 0.88; 95% CI: 0.77, 1.01).[65]

Another study investigated the association between chocolate intake and the presence of coronary artery illness in a study involving 4,970 contributors (25 to 93 years). They found that people who intake chocolate 1-4 times a week and 5 or more times a week had a 26% and 57% decreased risk of coronary artery illness, respectively, relative to people who did not eat chocolate. This association was even after considering other factors that could affect coronary artery disease risk, such as sex, age, lifestyle habits, diet, and family history of coronary artery illness. However, eating non-chocolate sweets was also correlated with a 49% greater risk of coronary artery illness.[66]

5- Cerebrovascular Diseases

Concerning the correlation between chocolate intake and brain stroke, some studies suggests that chocolate may have preventive effect against stroke, however two were conducted during the first ten years of 2000 44,67 and two more were carried out between 2011 and 2015.[65, 68] In two situations,[67,68] the papers suggests that chocolate may have preventive effect against stroke, however, in other investigations, the connection was not statistically significant.[44,65]

In another research, a sizable population-based cohort of males and females was used to discover the potential relationships between chocolate consumption and stroke risk. Researchers followed a large group of males (38,182) and females (46,415) aged 44 to 76 who were not suffer from diabetes, cardiovascular disease, and cancer at the start of the study in 1998. The participants were tracked until the end of 2010. Over a 12 years follow-up period on average, researchers identified 3,558 cases of stroke, including 2,146 cases of ischemic stroke and 1,396 cases of hemorrhagic stroke. They found that women who ate chocolate had a 16% reduce risk of stroke relative to females who did not eat chocolate. However, there was no substantial correlation between chocolate intake and stroke risk in men.[62]

In a comparable manner, a meta-analysis compared excessive chocolate intake to reduced chocolate intake and strock, discovered a pooled RR of 0.84 (95% CI: 0.78-0.90, n = 7). Similar RR were found in dose-related analyses for individuals that ingested three, seven, and ten servings weekly, as follows: 0.87 (95% CI: 0.81-0.94), 0.85 (95% CI: 0.76-0.93), and 0.83 (95% CI: 0.72-0.94).[18]

A large-scale study involving five prospective cohorts showed that people who consumed chocolate had a reduce risk of having a stroke (pooled RR 0.79,

95% CI 0.70 to 0.87) or dying from a stroke (RR 0.85, 95% CI 0.74 to 0.98) relative to those who did not consume chocolate. The research adjusted for other factors that could influence stroke risk, such as age, smoking, and diet.[42]

6- Atrial Fibrillation

Studies have produced mixed data regarding the relation between chocolate eating and atrial fibrillation risk. The anti-platelet and anti-inflammatory properties of chocolate may be linked to a decreased incidence of flutter or atrial fibrillation. Within the population-based Danish Diet, Cancer, and Health Investigation, which included over 55,000 participants, 3346 instances (6%) of atrial fibrillation were identified over a 13.5 years median follow-up period of. With an HR 0.84 for ≥1 serving/day, HR 0.80 for 2-6 servings/week, HR 0.83 for 1 serving/week, and HR of 0.90 for 1-3 servings/month. The findings indicated that the risk of atrial fibrillation was decreased in those who ate chocolate more frequently than once per month. The results were identical between males and females.[70]

In another investigation, the American male physicians, however, did not discover any definite evidence relating chocolate eating in any form to an raised risk of atrial fibrillation.[71] There was no evidence of a relation between eating chocolate and the development of atrial fibrillation according to the most recent data from a meta-analysis and two cohort studies, which included 32,486 women and 40,009 men from the Swedish Mammography Cohort and five cohort studies totalling 180,454 participants.[72]

7- Hyperlipidemia

A major hazard cause for cardiovascular disease is dyslipidemia, particularly in those with diabetes type II. Dyslipidemia refers to an imbalance in blood lipid levels, characterized by elevated levels of LDL-c, total cholesterol, and triglycerides, or by low levels of high-density lipoprotein cholesterol (HDL-c), or a combination of these abnormalities .[73] Cocoa-based drinks and dark chocolate are rich in polyphenols, which are plant-based compounds that may help enhance lipid profiles. Those with normal to increased LDL cholesterol was advised to include cocoa in their diets as part of a healthy lifestyle.[74] Cocoa is a valuable source of antioxidants, particularly epicatechin, which is thought to lower cholesterol production, raise HDL-c levels, and help prevent atherosclerosis. A systematic review demonstrated that chocolate eating and cocoa beverage did not substantially influence on triglycerides, total cholesterol, or LDL cholesterol, however cocoa beverages significantly improved HDL-c by 0.05 mmol/L.[75]

A study compared a low polyphenol diet, with no chocolate and two daily servings of vegetables and fruits, to a high polyphenol diet, which included 50 grams of dark chocolate and six daily servings of vegetables and fruits. After 8 weeks, the high polyphenol diet group resulted in a substantial decrease in total cholesterol ($p = 0.042$).[76] Ingesting 166–2110 mg of flavanols daily significantly impacts triglycerides and HDL cholesterol, but not LDL or total cholesterol.[43]

A randomised, crossover experiment with 42 high-risk (to coronary heart disease) volunteers was conducted. For four weeks, each person got of chocolate powder (40 g) along with skimmed milk (MIL) (500 mL) each day (cocoa plus MIL) or just 500 mL of MIL each day. The Cocoa + MIL intervention lowers oxLDL levels and raises HDL cholesterol in comparison to MIL. Additionally, there were markedly raises in HDL cholesterol and significant declines in oxLDL levels in the participants with greater rises in urine cocoa flavonoid metabolites.[76]

In diabetic (type II) people, ingestion of high-polyphenol chocolate increased HDLC and the TC:HDL ratio, whereas low-polyphenol chocolate had no discernible benefits. A randomised , double-blind, placebo-controlled crossover research studied how chocolate affected the lipid profiles of twelve diabetic (type II). Eight weeks of eating 45 g of chocolate with or without a high polyphenol content were randomly allocated to the participants, who then had a four-week washout period. Chocolate with high polyphenol content markedly raised HDL cholesterol while lowering the ratio of total cholesterol to HDLC. Low-polyphenol chocolate did not cause any changes in any of the metrics.[77] Consuming 100 g of dark chocolate-rich flavanol daily for fifteen days significantly reduced TC (-6.5%) and LDLC (-7.5%) in 19 hypertensive individuals with impaired glucose tolerance.[78]

8- Peripheral Artery Disease

Patients with lower extremity peripheral artery disease (PAD) exhibit a diminished ability to walk for 6 minutes compared to those without PAD. In the absence of effective treatment, individuals with PAD generally experience a progressive deterioration in their walking ability. For those with lower extremities PAD, cocoa and its primary flavanol, epicatechin, may offer therapeutic benefits that enhance blood flow to the legs and raise mitochondrial activity in the calf muscles.[79]

A randomised clinical experiment examined the effect of cocoa beverage on PAD patients' capacity to walk. A chocolate beverage with 75 mg epicatechin and 15 g cocoa each day, or a placebo beverage, was given to the testers at random. When compared to a placebo, the 6-minute walk distance improved significantly when participants had cocoa 2.5 hours after the last research beverage. In addition, related to placebo, cocoa consumption improved calf muscle perfusion, raised capillary density, decreased central nuclei, and boosted mitochondrial performance in calf muscle biopsies.[80]

Healthy volunteers (n = 47) were given test drinks containing varying concentrations of methylxanthines (0–220 mg) and cocoa flavanols (0–820 mg), either separately or in combination, in four different clinical studies, three using a randomised, double-masked crossover design and one with 4 parallel crossover studies. Consuming cocoa flavanols with methylxanthines enhanced flow-mediated vasodilation more than just consuming cocoa flavanols alone, even though both raised flow-mediated vasodilation two hours after ingestion. Consuming methylxanthine by itself did not cause statistically significant alterations in flow-mediated vasodilation. It is significant to notice that when methylxanthines and cocoa flavanols were consumed together, the area under the curve representing the plasma concentration of (2)-epicatechin metabolites over time was larger than when cocoa flavanols were consumed alone.[81]

In a single blind design cross-over, the maximum walking distance and duration were examined in 20 PAD patients who were randomised to ingested dark chocolate (40g) or milk chocolate (40 g). The ingestion of dark chocolate was the only factor that considerably raised the maximum walking duration and distance. Only after eating dark chocolate did serum epicatechin and its methylated metabolite substantially rise.[82]

Contribution of Post-Harvest Processes in Obtaining Potentially Beneficial Chocolates

Postharvest processes like fermentation, drying, roasting, and conching play a central role in developing the aroma and flavor of cocoa beans while also contributing to the creation of bioactive compounds helpful to human health. Cocoa beans are rich in various bioactive components, which have gained attention for their potential health benefits. Key efficient metabolites in cocoa include catechins, polyphenols, epicatechins, cocoa alkaloids, and flavonoids.[83] Cocoa is abundant in polyphenols, stored in the pigmented cells of the cotyledons (the cocoa beans used to make chocolate). These polyphenolic compounds possess potent antioxidant properties, acting as metal chelators, free radical scavengers, and reducing agents.[84] They are closely linked to the sensory qualities of processed cocoa products, contributing to the bitterness and astringency, as well as the green and fruity aromas of the beans.[85]

Xanthines, such as theobromine and caffeine, are present in the cotyledon both before and after postharvest processing. During fermentation, the levels of polyphenols and xanthines in the cotyledon decrease. Meanwhile, volatile components originate from the pulp, which is high in fermentable sugars. The polyphenols biosynthesis follows the shikimate pathway via phenylalanine,[86] while alkaloids like caffeine and theobromine are synthesized from the precursor Xanthosine.[87] Fine aroma cocoa paste contains volatile metabolites like myrcene, derived from the biosynthetic precursor Geranyl diphosphate 88, and aromatic compounds such as benzaldehyde, which imparts a fruity aroma, along with ketones, esters, and aldehydes that contribute notes of caramel, fruit, floral, and green. These aromas may develop through pulp fermentation or secondary reactions during postharvest processing.[83]

Fermentation is a critical stage in producing flavor cocoas and fine aroma, as improper fermentation can lead to a loss of value and quality.[2] The drying and roasting processes also significantly impact the flavor, aroma, and health-related compounds in cocoa.[89] Fermentation helps remove the viscous pulp,

enhances color and flavor, and reduces bitterness and astringency by facilitating compound diffusion between the cocoa beans and their environment.[90] Proper fermentation, indicated by a final pH of 4.75 to 5.19, ensures optimal flavor development, while deviations from this pH range can lead to poor quality and undesirable taste.[91] During fermentation, the concentrations of volatile metabolites raise as the fruit pulp ferments, enriching the cocoa bean and unlocking the full flavor potential within the cotyledon. This process generates heat and acidity, activating enzymes that produce flavor and aroma precursors, enhancing the cocoa's distinctive taste. The cocoa shell becomes permeable, allowing metabolites to move between the pulp and cotyledon. Volatile metabolites are purely a result of post-harvest processing, while non-volatile compounds like theobromine, polyphenols, and caffeine exist before fermentation but may partially decrease due to diffusion or chemical transformations during the process. Some metabolites, such as caffeine and theobromine, move from the cotyledon to the shell, reducing bitterness in the cocoa paste. Additionally, the antioxidant activity of cocoa paste is linked to three classes of metabolites: fatty acids (like oleic acid), polyphenols, and flavonoids, with cocoa butter's unsaturated fatty acids contributing to this activity.[83] Cocoa beans contain (-)-epicatechin and (+)-catechin, with (-)-epicatechin being more abundant. Fermentation leads to a decrease in (-)-epicatechin and (+)-catechin, with the formation of (-)-catechin, likely influenced by the heat of fermentation. During roasting, there's a further reduction in (-)-epicatechin and (+)-catechin and rise in (-)-catechin, possibly due to the epimerization of (-)-epicatechin caused by the heat.[92]

Some lactic acid bacteria involved in cocoa bean fermentation are considered probiotics—live microorganisms that provide health benefits when consumed in adequate amounts.[93] The potential of incorporating probiotics and postbiotics in fermented cocoa beans and their products is a promising area for development. *Lactobacillus plantarum*, a probiotic found in fermented cocoa beans, produces postbiotic metabolites such as bacteriocins, which have shown cytotoxic effects against various cancer cells.[94] Additionally, other probiotics like *Bifidobacterium lactis, Lactobacillus rhamnosus,* and *Lactobacillus acidophilus* can be introduced during fermentation or chocolate processing to enhance the probiotic content 95,96. In a study, *L. plantarum* was successfully isolated from fermented cocoa beans and applied to dark chocolate, creating a product with significant potential health benefits.[94]

As pods matured, flavonol levels increased while nitrogen content decreased. Mature pods yielded beans with higher flavonol, catechin, and total phenolic content. During fermentation, the beans' fat, total phenolic content, antioxidant activity, and catechin levels rose, regardless of pod maturity at harvest. Beans fermented for 5 days had the highest free fatty acid levels. In contrast, beans fermented for 3 days had significantly higher epicatechin levels and lower free fatty acid content. Chocolate made from mature beans with 3-day fermentation was more enjoyable, scoring highest in flavor intensity and complexity while having the lowest acidity and astringency.[97]

Post-harvest processing of cocoa beans, such as fermentation, plays a crucial role in creating flavor and aroma compounds and also impacts on the formation of bioactive health benefits compounds.[98] While many studies link these health benefits primarily to polyphenols,[99] there is limited knowledge about the possible health impacts of other cocoa components, such as bioactive peptides.[98] Amino acids and peptides produced during artisanal cocoa fermentation are known to be key precursors for developing cocoa's aroma.[100] However, research on their potential bioactivity and health contributions is still limited. Additionally, there is a growing consumer interest in wholesome, natural, and health-promoting fermented foods.[101] Therefore, cocoa bean fermentation should be explored not only for creating enjoyable beverage and food products but also for developing functional and healthy products.

Cocoa beans are a notable source of peptides formed during fermentation,[100, 102, 103] originating primarily from two major storage protein fractions: albumin and vicilin-like proteins.[98] Research has explored oligopeptides not only for their role in developing chocolate flavor but also for their potential biological effects. Several studies have identified peptide sequences in cocoa bean proteins that may offer various health benefits when released.[104-108] These studies have focused on bioactive peptides released through three methods: 1) cocoa bean autolysis,[105]

2) hydrolysis with exogenous commercial enzymes,[106, 107] and 3) fermentation of cocoa beans.[98, 100, 104] Numerous antioxidant peptides from various food proteins have been identified, and their antioxidant properties have been examined. These properties include the peptides' ability to protect cells from oxidative stress, neutralize reactive oxygen species (ROS), scavenge free radicals, chelate oxidative metals, and stimulate the activation of intracellular antioxidant enzymes.[109, 110] Many research has assessed the potential antioxidant activity of hydrolysates and peptides derived from cocoa beans.[104, 107, 111] The hydrolyzed cocoa protein fraction with the highest prolyl endopeptidase inhibition activity was chosen for in vivo testing. The transgenic Caenorhabditis elegans strain CL4176, which is induced to experience oxidative stress, was used as an Alzheimer's disease model. The results indicated that the hydrolyzed samples significantly improved the progression of body paralysis compared to untreated samples. Among these, a 13-residue peptide sequence (DNYDNSAGKWWVT) in the hydrolyzed sample offered the most protection against oxidative stress, notably delaying paralysis in the nematodes. Additionally, a reduction in Aβ deposits was observed.[106]

Sun-drying is the most common and straightforward technique used in cocoa-producing countries. Depending on the weather, beans are sun-dried for 12 to 20 days, yielding high-quality cocoa in sunny climates 112. Fermented beans initially have a moisture content of about 55–60%, which is too high for storage as it can lead to rotting. To ensure safe storage and transport, moisture content should be lowered to 6–7% 112, 113. Roasting is the most crucial step, affecting the level of flavor, bioactive compounds, color, texture, and overall organoleptic properties of the final product.[114] During roasting, the Maillard reaction occurs, contributing to the brown color, pleasant aroma, and texture of the roasted beans.[115]

Conclusion

Moderate chocolate consumption has been shown to have positive effects on numerous medical disorders such as heart failure, hypertension, platelet aggregation, coronary artery disease, cerebrovascular illnesses, atrial fibrillation, hyperlipidemia, and peripheral artery disease. Dark chocolate is generally favored over milk and white chocolate due to its elevated concentration of flavonols. Consuming 50 grams of dark chocolate daily or every other day has been associated with improvements in various heart health conditions. The validity of these studies is limited due to their single-center design and reliance on self-reported chocolate consumption. Future research should focus on well-designed, randomized clinical trials that target specific cohorts, such as individuals with cardiovascular risk factors, and consider particular locations and conditions to offer definitive evidence of the advantages of chocolate consumption. It is also essential to suggest future studies to better understand the technology underlying chocolate's science.

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- **Eman Abbas Abduljawad:** EA conceptualization, literature review, writing editing, and final manuscript review.

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