

The cardiovascular effects of chocolate

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The antioxidants as polyphenols, especially flavanols present in cocoa, exert a favorable effect on endothelium vasodilation, modulate inflammatory markers, and decrease platelet aggregation, lipid oxidation and insulin resistance. Recent nutritional intervention trials and molecular studies demonstrate that consumption of cocoa, particularly rich in flavanols, is beneficial to promote cardiovascular health. This review describes the cardiovascular effects of chocolate.

Keywords

Chocolate; flavanols; cardiovascular; nitric oxide

1. Introduction

Chocolate, specifically dark chocolate, contains flavanols which have shown to increase endothelial nitric oxide formation promoting vascular health via vasodilation and blood pressure reduction (Persson et al., 2011). There are many studies showing that moderate chocolate consumption improves cardiovascular health and reduces risk of various cardiovascular disease. This is a review of the most recent literature regarding the impact of chocolate on cardiovascular diseases and cardiovascular risk factors as: hypertension, cholesterol, arrhythmia, coronary heart disease, heart failure, cerebrovascular disease, and peripheral vascular disease.

1.1 Hypertension

The flavanols in chocolate increase endothelial nitric oxide production, which induces vasodilation and subsequent blood pressure reduction (Persson et al., 2011). A meta-analysis studied the effects of chocolate on blood pressure by analyzing thirty-five trials containing 1804 participants total and 40 different treatments ranging from an average of 1.4 to 105 grams of chocolate (30 to 1218 mg of flavanols per day (Ried et al., 2017). The mean systolic blood pressure difference in 1804 participants after treatment was -1.76 mmHg (95% CI -3.09 to -0.43); mean diastolic blood pressure difference in 1772 available participants was -1.76 (CI 95% -2.57 to -0.94). Baseline blood pressures appear to impact the degree of blood pressure reduction. When dividing the patients by systolic blood pressure, participants initially at > 140 mmHg, > 130 mmHg, and < 130 mmHg saw changes of -4.00 (95% CI -6.71 to -1.30) mmHg, -2.43 (95% CI -5.02 to 0.17) mmHg, and -0.65 (95%

CI -2.13 to 0.84) mmHg, respectively. Similarly, when dividing the patients by diastolic blood pressure, participants initially > 80 mmHg and < 80 mmHg saw changes of -1.98 (95% CI -3.38 to -0.57) mmHg and -1.57 (95% CI -2.54 to -0.61) mmHg respectively. Also duration of treatment seemed to impact the change in blood pressure. Treatment duration of 2 to 4 weeks compared to 6 to 18 weeks duration saw systolic blood pressure changes of -1.37 (95% CI -3.23 to 0.49) mmHg and -2.37 (95% CI -4.30 to -0.44) mmHg respectively and diastolic blood pressure changes of -1.55 (95% CI -2.71 to -0.39) mmHg and -2.04 (95% CI -3.18 to -0.91) mmHg respectively. The most notable effects of chocolate on blood pressure reduction were seen in those patients with initially higher blood pressures and consumed the prescribed amount of chocolate for longer periods of time. Additionally, one randomized control trial of 60 diabetic patients studied the effects of consuming 25g dark chocolate daily for 8 weeks and found, from the beginning to the end of the trial, a mean difference in systolic and diastolic blood pressures of -6.40 mmHg and -5.93 mmHg, respectively, whereas the control group of white chocolate consumption saw no significant difference (Rostami et al., 2015). The studies analyzed were too heterogeneous to provide consolidated results on dosing and blood pressure reduction. Further investigation is therefore needed to provide a clearer relationship between quantity of chocolate consumption and blood pressure reduction.

1.2 Cholesterol

Many studies have been published regarding chocolate and its benefits on lipid profiles, the probable mechanism being a reduction of LDL oxidative effect and atherogenesis (Baba et al., 2007). A meta-analysis studied the impact of chocolate on lipid profiles by assessing ten clinical trials, containing a total of 320 participants (Tokede et al., 2011). To accommodate for heterogeneity, this study evaluated the difference in post-intervention values of serum total cholesterol, HDL, LDL, and triglycerides, the interventions being chocolate consumption and the control treatments which varied by study. The differences (95% CI) for total cholesterol, HDL, LDL, and triglycerides were -6.23 mg/dl (-11.60, -0.85 mg/dl), -0.76 mg/dl (-3.03, 1.51 mg/dl), -5.90 mg/dl (-10.47, -1.32 mg/dl), and -5.06 mg/dl (-13.45, 3.32 mg/dl), respectively, highlighting a significant reduction in total cholesterol and LDL

after chocolate consumption. This study also evaluated the effect of treatment duration on LDL and found significant reduction of -8.44 mg/dl (-14.23, -2.64 mg/dl) after 2 weeks of treatment, but a non-significant reduction after 4 to 12 weeks of treatment. In accordance with this meta-analysis, a clinical trial studied the effects of a high polyphenol diet consisting of 50g of dark chocolate and six portions of fruits and vegetables daily for eight weeks on serum cholesterol levels compared with a low polyphenol diet, no chocolate, and two portions of fruits and vegetables daily and found a decrease in total cholesterol ($p = 0.042$) and LDL ($p = 0.063$) (Noad et al., 2016). Regarding HDL cholesterol, another randomized, controlled, cross-over trial of 24 participants did find a statistically significant increase in HDL after consuming 30g of chocolate daily for 4 weeks ($p < 0.001$), contrary to the meta-analysis (Sarri  t al., 2014). The benefits of moderate chocolate consumption on cholesterol levels are promising and further study is needed to define clearly the benefits of chocolate on cholesterol levels.

1.3 Arrhythmias

Chocolate consumption has been inconsistently associated with risk of atrial fibrillation. A study of a Danish population-based cohort of 55,502 participants that followed patients for an average of 13.5 years have found a significant association between chocolate consumption and reduced risk of atrial fibrillation. The study found that consuming one to three servings of chocolate per month, one serving per week, and two to six servings per week had hazard ratios (95% CI) of 0.90 (0.82 to 0.98), 0.83 (0.74 to 0.91), and 0.80 (0.71 to 0.91), respectively (Mostofsky et al., 2017). However, two previous studies: the Women's Health Study and a cohort study of US male physicians, found no statistically significant associations between consuming any quantities of chocolate and the atrial fibrillation risk (Conen et al., 2010; Khawaja et al., 2015). The former followed 33,638 female participants for an average of 14.4 years to study risk of atrial fibrillation and caffeine consumption in various forms which included: chocolate, soda, and coffee. The levels of consumption were divided into quintiles, and non-significant hazard ratios were found for each of the quin-

tiles except the third (0.78, 95% CI 0.64-0.95), which indicates that no conclusive associations could be drawn from this study regarding chocolate consumption and risk of atrial fibrillation. The physicians' health study followed 18,819 US male physicians for an average duration of 9 years, hazard ratios (95% CI) for consuming 1-3 servings per month, 1 serving per week, 2-4 servings per week, and > 5 servings per week, were all non-significant. The most recent data from two cohort studies and a meta-analysis, which was comprised of 40,009 men from the Cohort of Swedish Men and 32,486 women from the Swedish Mammography Cohort and a meta-analysis of 5 cohort studies including 180,454 participants, provided no evidence of an association of chocolate consumption with risk of AF (Larsson et al., 2018).

1.4 Coronary artery disease

Chocolate consumption has also been associated with reduced coronary artery disease (CAD) incidence and mortality (Baba et al., 2007; Persson et al., 2011). A systematic review by Kwok et al, pooled data from nine studies with 157,809 participants and follow-up durations of 8-16 years studied chocolate consumption and CAD. They performed a met-analysis on data from five of the studies which demonstrated, after propensity score matching, a significant association between chocolate consumption and reduced risk of CAD (pooled RR 0.72, 95% CI 0.55 to 0.93) (Kwok et al., 2015). A significantly lower risk of cardiovascular mortality was noted in three of the available prospective cohort studies (pooled RR 0.55, 95% CI 0.36 to 0.83). This corroborates a systematic review that highlighted significant association between frequent chocolate consumption and reduction in CAD risk across the five selected studies (Khawaja et al., 2015). These findings were further supported by a meta-analysis by Larsson et al, of six prospective studies containing 144,823 patients with follow-up of 8-16 years which studied chocolate consumption and risk of myocardial infarction and ischemic heart disease (Larsson et al., 2016). A decreased risk of myocardial infarction and ischemic heart disease was noted in those who consumed the highest quantities of chocolate when compared with those who consumed the lowest quantities of chocolate (pooled RR 0.90, 95% CI 0.82 to

Table 1. Summary of benefits and potential harms associated with regular chocolate intake

Condition/ Marker	Variable	Value	95% CI
Hypertension	Systolic Blood Pressure Difference (mmHg)	-1.76	-3.09 to -0.43
	Diastolic Blood Pressure Difference (mmHg)	-1.76	-2.57 to -0.94
Hypertension with Diabetes	Systolic Blood Pressure Difference (mmHg)	-6.40	-
	Diastolic Blood Pressure Difference (mmHg)	-5.93	-
Cholesterol	Total Cholesterol Difference (mg/dl)	-6.23	-11.60 to -0.85
	LDL Difference (mg/dl)	-5.90	-10.47 to -1.32
	Triglyceride Difference (mg/dl)	-5.06	-13.45 to 3.32
Atrial Fibrillation	Hazard Ratio	0.80	0.71 to 0.91
Coronary Heart Disease	Pooled Relative Risk	0.90	0.82 to 0.97
Heart Failure*	Hazard Ratio	0.86	0.78-0.94
Cerebrovascular Accident	Pooled Relative Risk	0.84	0.78-0.90
Peripheral Vascular Disease	Mean Walking Distance Improvement (meters)	+11.5	-
	Mean Walking Time Improvement (s)	+17.4	-

*Heart Failure benefits ceased to be realized after consuming 500 grams or more of chocolate per week.

Table 2. Summary of major studies evaluating chocolate intake and cardiovascular outcomes

Author	Publication year	Study type	No. of pts. or papers	Central message
(Ried et al., 2017)	2017	Meta-analysis	35 papers	Flavanol-rich chocolate and cocoa products cause a small decrease in blood pressure over the course of weeks with greater blood-pressure reduction in hypertensive patients compared to normotensive patients.
(Tokede et al., 2011)	2011	Meta-analysis	10 papers	Dark chocolate consumption reduces serum LDL and Total Cholesterol, especially in patients with higher risk for cardiovascular disease.
(Kwok et al., 2015)	2015	Meta-analysis	5 papers	Higher chocolate consumption is associated with significantly lower CHD risk, composite adverse cardiovascular outcomes, and cardiovascular mortality.
(Larsson et al., 2016)	2016	Meta-analysis	6 studies	Consuming higher quantities of chocolate is associated with lower risk of MI and ischemic heart disease.
(Mostofsky et al., 2010)	2010	Population- based prospective cohort	31,823 women	Consuming up to 7g of dark chocolate per week is associated with reduced risk of Heart Failure.
(Steinhaus et al., 2017)	2017	Population- based prospective cohort	31,917 men	Consuming up to 6g of dark chocolate per week is associated with reduced risk of Heart Failure.
(Kwok et al., 2015)	2015	Meta-analysis	5 papers	Higher chocolate consumption is associated with significantly lower stroke risk.
(Loffredo et al., 2014)	2014	Randomized Control Trial	20 participants	Dark chocolate consumption acutely improves mean walking distance and overall walking autonomy in patients with Peripheral Artery Disease.

0.97). The study also performed a dose-response meta-analysis and found that the risk ratio per 50 g/week increment was 0.95 (95% CI 0.92 to 0.98). These findings were supported by the most recent meta-analysis by Yuan et al, which studied chocolate consumption and CAD, stroke, and diabetes and contained a total of 14 prospective studies, 508,705 participants, with follow-up duration of 5-16 years (Yuan et al., 2017). Pooled RR for developing CAD among the highest chocolate consumption compared with lowest chocolate consumption was 0.90 (95% CI: 0.82-0.97; n = 6). A dose-dependent analysis revealed similar RR for groups that consumed 3, 7, and 10 servings per week: 0.91 (95% CI: 0.85-0.97), 0.89 (95% CI: 0.83-0.95), and 0.88 (95% CI: 0.81-0.95), respectively.

1.5 Heart failure

Chocolate consumption may also lower the risk of heart failure (HF) by mitigating the risk factors of HF which include hypertension, CAD, and myocardial infarction. A prospective cohort study of 31,823 Swedish women aged 48 to 83 years followed over 9 years, found a significant relationship between servings of chocolate consumed and the risk of HF. For consumption of 1 to 3 servings per month, 1 to 2 servings per week, 3 to 6 servings per week, and greater than one serving per day, the corresponding rate ratios (95% CI) were 0.76 (0.58 to 0.98), 0.68 (0.50 to 0.93), 1.09 (0.74 to 1.62), and 1.23 (0.73 to 2.08), respectively, indicating reduced HF incidence with moderate chocolate consumption, but the protective association was not observed with intake of ≥ 1 servings per day (Mostofsky et al., 2010). This study was corroborated by one meta-analysis which analyzed data from 106,109 participants who were followed for 9 to 14 years and found a significant relationship

between servings of chocolate consumed and risk of HF; one serving of chocolate being a 50g chocolate square (Gong et al., 2017). The hazard ratios (95% CI) for 1, 3, 7, and 10 servings per week 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), respectively. This indicates that moderate consumption of chocolate was associated with reduced HF risk, while ten or more servings of chocolate per week were associated with increased risk of HF.

1.6 Cerebrovascular accidents

Chocolate consumption is also associated with lower stroke incidence and mortality according to the meta-analysis by (Kwok et al., 2015). The meta-analysis evaluated five prospective cohort, and found that after adjusting for other possible covariates, chocolate consumption significantly decreased risk of both stroke incidence (pooled RR 0.79, 95% CI 0.70 to 0.87) and stroke mortality (RR 0.85, 95% CI 0.74 to 0.98). Also, a Japanese population-based prospective cohort study consisting of 38,182 men and 46,415 women, ages 44-76 years, who were free of cardiovascular disease, diabetes, and cancer, evaluated the association of chocolate consumption and the risk of stroke (Dong et al., 1979). After a mean follow-up of 12.9 years, it was demonstrated that chocolate consumption was significantly associated with lower incidence of stroke in women (HR = 0.84; 95% CI, 0.71-0.99), but not in men (HR = 0.94; 95% CI, 0.80-1.10). The stroke risk reduction in women was noted only in the highest quartile of chocolate consumption (37.5 grams/week). Similarly, the previously mentioned meta-analysis by Yuan et al, found a pooled RR of 0.84 (95% CI: 0.78-0.90, n = 7) when comparing high chocolate consumption with the low chocolate consumption (Yuan et al., 2017). A dose-

Table 3. Relationship between fat and nonfat contents in cocoa and chocolate product relative to portion sizes (Steihaus et al., 2017)

Product type	Fat and Nonfat Cocoa Solid (NFCS) Contents in Cocoa and Chocolate Products		
	% Fat- average	Grams of Fat in a typical 50g serving	% NFCS supplied by manufacturers- average
Milk chocolate	32	16.0	7.1
Dark chocolate	36	18.0	22.9
Baking chips	29	14.5	18.6
Unsweetened chocolate	50	25.0	49.5
Natural powders	13.6	6.8	87.4
Dutched powders	15.5	7.8	80.2
Condition/ Marker	Doses of chocolate at which improvements were seen		
Hypertension	Not available		
Cholesterol	Not available		
Coronary Heart Disease	50 g at 3-10 servings/week		
Heart Failure	50 g at 1-7 servings/week		
Cerebrovascular Accident	50 g at 3-10 servings/week		
Peripheral Vascular Disease	40 g, 1 serving 2 hours before walking		

dependent analysis revealed similar RR for groups that consumed 3, 7, and 10 servings per week: 0.87 (95% CI: 0.81-0.94), 0.85 (95% CI: 0.76-0.93), 0.83 (95% CI: 0.72-0.94), respectively.

1.7 Peripheral vascular disease

Dark chocolate is also thought to improve outcomes in patients with peripheral arterial disease, but there is some discord. A randomized, controlled, cross-over trial of 20 participants with peripheral arterial disease, evaluated the effects of flavonoid-rich dark chocolate compared with milk chocolate (Loffredo et al., 2014). The participants were assessed at baseline and 2 hours after consuming a 40 g piece of dark chocolate or a 40 g piece of milk chocolate. This study found increased mean walking distance from 110.7 ± 64.5 to 122.2 ± 61.5 meters ($p < 0.001$) and mean walking time from 124.8 ± 60.8 to 142.2 ± 62.0 seconds ($p < 0.001$), but no such difference was after found after consuming milk chocolate. Similarly, serum nitrate/nitrites and flow-mediated dilation, which measures endothelial function, both increased from $2.3 \pm 2.2\%$ to $6.3 \pm 2.7\%$ ($p < 0.001$) and from 11.0 ± 5.8 to $17.3 \pm 5.8 \mu\text{mol/L}$, ($p = 0.001$) after consuming dark chocolate. No such difference was seen after milk chocolate consumption. These measures indicated significant improvements in walking autonomy and in endothelial function. In Switzerland, a randomized, controlled cross-over trial evaluated the acute impact of dark chocolate consumption on peripheral vascular health of 21 patients with symptomatic peripheral arterial disease (Hammer et al., 2015). Flow-mediated dilation of the brachial artery and Laser Doppler fluximetry were used to assess endothelial and microvascular function, respectively, before and two hours after consuming a 50 g piece of dark chocolate. Before and after chocolate consumption, no significant difference was found in endothelial function by flow-mediated dilation ($p = 0.57$). This study also found no difference in perfusion values upon Laser Doppler studies. The studies evaluating the effects of chocolate on peripheral arterial disease were small and more data are needed to better define the impact of chocolate on these patients.

2. Discussion

The studies reviewed show that moderate consumption of chocolate is beneficial for a variety of conditions including hypertension, cholesterol, coronary heart disease, heart failure, cerebrovascular accidents and peripheral vascular disease. Summary is demonstrated in Table 1. Dark chocolate is preferred over white or milk chocolate because of the higher flavonol content. Serving size of 50 g once a day or once every other day have been shown to help with all these conditions. Upon consuming more than ten servings per week, adverse outcomes begin to be observed such as increased risk of HF. A summary of the major studies evaluating chocolate intake and cardiovascular outcomes is summarized in Table 2. Also, the relationship between fat and nonfat contents in cocoa and chocolate product relative to portion sizes is highlighted in Table 3. However, there are limitations in the available data that make it difficult to draw firm conclusions. Firstly, many of these studies evaluated patient populations that tended to be fairly homogenous comprised of middle-aged and older Caucasian men and women, and may not be generalizable to younger individuals and other ethnic groups. Secondly, many of these studies were single center, cohort studies which relied on self-reporting the amount of chocolate consumed. Therefore, randomized, adequately powered, clinical trials are needed to provide more precise information on the benefits of chocolate consumption.

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Conflict of Interest

The authors declare no competing interests.

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