

The mysterious light of dark chocolate

Siyah çikolatanın gizemli ışığı

Tunay Şentürk, M.D., Şeyda Günay, M.D.

Department of Cardiology, Uludag University Faculty of Medicine, Bursa

Summary– A healthy diet plays a key role in the prevention and management of cardiovascular diseases. Dark chocolate in particular has been shown to improve endothelial functions and lipid profile and to have cardiovascular protective effects via an inhibitory action on platelet functions. Recently, several studies have demonstrated the beneficial effects of chocolate, primarily on hypertension and other conditions such as coronary artery disease and hyperlipidemia. The present review provides a summary of the ingredients, bioavailability and cardiovascular protective effects of chocolate / cocoa and the published effects of chocolate on a number of cardiovascular diseases.

Özet– Kardiyovasküler hastalıkların önlenmesinde ve tedavi yaklaşımlarında diyet önemli yer tutmaktadır. Özellikle siyah çikolatanın endotel fonksiyonlarını, lipit profilini iyileştirdiği ve trombosit fonksiyonları üzerindeki inhibitör etkileri aracılığıyla kardiyovasküler koruyucu etkileri olduğu gösterilmiştir. Son zamanlarda giderek artan sayıdaki çalışma çikolatanın başta hipertansiyon, koroner arter hastalığı, hiperlipidemi gibi durumlarda yararlı etkilerini ortaya koymaktadır. Bu derleme çikolata/kakaonun içeriği, biyoyararlılığı, kardiyovasküler sistem üzerindeki koruyucu etkileri ve çeşitli kardiyovasküler hastalıklardaki bulguları özetlemektedir.

In developed countries, cardiovascular disease (CVD) is a major causes of morbidity and mortality, including from stroke. Although endothelial dysfunction, inflammation, platelets and atherosclerosis are responsible for the development of CVD, diet is a key factor in its development and progression. While high caloric intake and fat consumption are known to increase the risk of CVD, several dietary products have been shown to confer protective effects against it.^[1]

Cocoa is nutrient-rich in flavanols. Flavanols belong to the polyphenol class, which contains epicatechin, catechin and procyanidin, found in plants as unconjugated molecules.^[2] Many studies in humans and animals have suggested that cocoa and other nutrients rich in flavanols might have cardiovascular protective effects.^[3-5] A pioneering study on this issue demonstrated an inverse relationship between consumption of foods rich in flavonoids and risk of CVD.^[2]

For hundreds of years, chocolate rich in cocoa, in addition to its savory taste, has been recognized as

having beneficial effects on health. The ancient Incas called it “the drink of the Gods.” The cocoa tree was given the name “*Theobroma*

cocoa” by combining the Greek terms “theo” (meaning God) and “broma” (meaning drink).^[6] Important information on the consumption of cocoa among the Aztecs and Mayans has been collected. In the sixteenth century, the Aztec Emperor Montezuma drank *Theobroma cocoa* in large quantities and described it as “The divine drink, which builds up resistance and fights fatigue”.^[6] Interesting information on cocoa consumption has been obtained from the Kuna, an indigenous people of Panama in Central America. These people consume large amounts of cocoa with a high salt content.^[7] In clinical trials, the Kuna have low blood pressure and do not experience the age-related decrease in renal function that causes changes in blood pressure. Additionally, death rates from cardiovascular disease are lower among the Kuna compared to other

Abbreviations:

ACE	Angiotensin-converting enzyme
CHD	Coronary heart disease
CVD	Cardiovascular disease
MI	Myocardial infarction
NO	Nitric oxide

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Correspondence: Dr. Tunay Şentürk, Uludağ Üniversitesi Tıp Fakültesi, Kardiyoloji Anabilim Dalı, Bursa, Turkey.

Tel: +90 224 - 442 81 91 e-mail: tunaysenturk@hotmail.com

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populations living on the American continent.^[8] However, this protective effect has decreased as a result of Kuna migration to cities, suggesting that the lower death rates were related to environmental and dietary rather than genetic factors.^[7]

After discovery of the American continent, cocoa was brought to Europe, where by the seventeenth century it was thought of as having some beneficial health effects. In the U.S., cocoa was considered a non-healthy food due to its high calorie and fat content.^[9] However, current data suggests that moderate consumption of dark chocolate or foods rich in flavanols could have beneficial cardiovascular effects.

A study in elderly patients has shown that cocoa intake was associated with reduced blood pressure and total cardiovascular mortality.^[10] A case-control study from Italy reported an inverse relationship between chocolate consumption and myocardial infarction, and a cardiovascular risk reduction of 77% was shown in individuals who consumed more than 3 chocolate bars a day compared to those who consumed less than one.^[11] In light of data from in vitro studies, the beneficial effects of flavanols were attributed to their antioxidant effects, regulation of gene expression and signaling pathways, and changes they bring about in the cell membrane and receptor functions.^[12,13]

Chocolate

The cocoa bean (*Theobroma cocoa*) has long been the main component of cocoa and chocolate.^[14] Cocoa is a food source rich in polyphenols, which represent 6-8% of the dry weight of cocoa beans.^[15] The term cocoa refers to the natural product, whereas chocolate is a processed food containing sugar, fat, other additives and sometimes milk in addition to cocoa. Dietary flavonoids have thousands of derivatives and belong to the polyphenol family. Subgroups of flavonoids include flavonols, flavone, flavanone, flavan-3-ols (sometimes known as flavanols), isoflavones and anthocyanins (Figure 1). They are found in many commonly consumed vegetables, fruits, grains, plants and beverages. In addition to cocoa, flavanol compounds are naturally found in strawberries, apricots, grapes, apples, pomegranates, black tea and green tea (Table 1).^[16]

The macronutrients of chocolate are carbohydrates (approximately 50-60% of the weight), followed by

Table 1. Flavanol content of various nutrients^[16]

Nutrient	Content (mg/L)
Chocolate	460-610
Green tea	100-800
Black tea	60-500
Apple	20-120
Apricot	100-250
Strawberry	130

fats (32-35%) and proteins (3-7%). Fats are mostly found in the form of triglycerides composed of saturated fatty acids. Additionally, chocolate contains theobromine, minerals (magnesium, phosphorus), trace elements and vitamins in low quantities.^[9]

Flavanols reach their peak plasma concentration within 2-3 hours following intake in a dose-dependent manner and are detectable in the plasma even after 8 hours.^[17] However, their bioavailability is low and can be detected only at nanomolar levels.^[18] The presence of hydrophobic and hydrophilic residues of flavanol molecules allow interaction with phospholipid groups and adsorption to membrane surfaces. Such interactions alter the functions of membrane-related enzymes, receptors and other functional protein receptors.^[19]

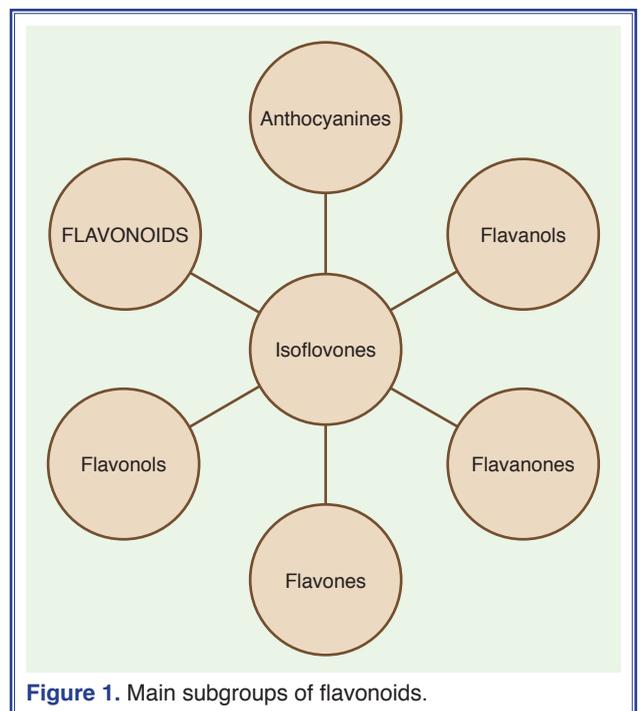


Figure 1. Main subgroups of flavonoids.

Table 2. Mechanisms implicated in the cardiovascular effects of flavanol-rich dark chocolate

Decreased LDL-C and TG levels, increased HDL-C level
Inhibition/reduction of LDL oxidation
Reduced endothelial NO activity and flow-mediated dilation
Reduced platelet aggregation
Reduced expression of several inflammatory genes (IL1 β , IL2, IL4, IL6 and TNF- α)
Reduced expression of cellular adhesion molecules (VCAM-1, ICAM-1)
ACE inhibition

Various interactions with foods may also alter the bioavailability and potential biological activities of cocoa flavanols and procyanidins. A recent study showed that milk proteins reduced the antioxidant capacity of milk chocolate compared with dark chocolate.^[17] Differences in antioxidant activity and bioavailability between dark and milk chocolate were the result of food matrix interactions altering the kinetics of absorption.^[17] Serafini et al. showed that 100 grams of dark chocolate reduced antioxidant activity when taken with 200 ml of milk, or consumed in the form of 200 grams of milky chocolate.^[17]

Effects of dark chocolate on a range of cardiovascular diseases

An increasing body of evidence demonstrates the favorable effects of flavonoid-rich dark chocolate, primarily on coronary artery disease, hypertension, heart failure, hyperlipidemia, inflammation, oxidative stress, insulin resistance and platelet functions via several mechanisms (Table 2, Figure 2).

Coronary artery disease

Many epidemiological studies have reported the beneficial cardiovascular effects of flavonoids. Flavonoids have antioxidant properties and can reduce LDL oxidation, which is critical in the onset of atherosclerotic diseases.^[20] Flavonoids improve endothelial functions, and have been shown to reduce blood pressure in human studies and inhibit the development of atherosclerotic plaques in animal studies.^[3] Additionally, flavonoids have anti-inflammatory features and inhibit platelet functions.^[21,22]

“The Seven Countries” study, with a follow-up period of 25 years, showed an inverse relationship between flavonoid intake and coronary artery disease

mortality.^[23] The Stockholm Heart Epidemiology Program (SHEEP)^[24] investigated the long-term effects of chocolate. In this study, when compared with those who never ate chocolate, the hazard ratios were 0.73 (95% confidence interval, 0.41-1.31), 0.56 (0.32-0.99) and 0.34 (0.17-0.70) for those consuming chocolate less than once per month, up to once per week and twice or more per week respectively. Chocolate consumption was associated with lower cardiac mortality in a dose-dependent manner in patients who were free of diabetes and had survived their first acute myocardial infarction.^[24]

In a cross-sectional study, Djoussé et al.^[25] evaluated the relationship of chocolate consumption with coronary artery calcification as confirmed by computed tomography. Consuming chocolate 2 or more times per week had an inverse association with coronary artery calcification.

This was the first observational study to demonstrate an association between the frequency of chocolate consumption and coronary artery calcification. In a multivariate analysis, a U.S. study reported an inverse correlation between consuming chocolate with 6% catechin and cardiovascular deaths, when comparing the third and first quartile of chocolate consumption.^[24]

Various mechanisms have been suggested for the reduction of cardiovascular risk associated with chocolate consumption. The consumption of dark chocolate reduces both systolic and diastolic blood pressures,^[15] enhances nitric acid bioactivity and improves endothelial functions.^[4]

Metalloproteinases are enzymes with a demonstrated effect on the rupture of atheromatous plaques. Cocoa procyanidins inhibit the expression and activity of metalloproteinase-2 in smooth muscle cells and may mediate the anti-atherosclerotic actions of cocoa.

[26] A prospective cohort reported a 40% lower risk of cardiovascular disease comparing the fourth and first quartile of chocolate consumption, and approximately 12% of that reduction was attributable to the beneficial effects of chocolate on blood pressure.^[27] In addition, dark chocolate improves insulin sensitivity and beta cell function in healthy or hypertensive subjects after 15 days of intervention.^[15] There is evidence that chocolate might suppress epinephrine-stimulated platelet activation.^[21]

In a separate study, Djouessé et al.^[25] examined the association between frequent chocolate consumption and reduced prevalence of coronary heart disease (CHD) in females and males without any risk factors. In this cross-sectional study with 4.970 participants aged 25 to 93 years, relative risks for CHD were 1.01, 0.74 and 0.43 for subjects consuming 1-3 times/month, 1-4 times/week, and >5 times/week respectively, when compared to subjects who did not report any chocolate intake. This association also applied to individuals aged less or greater than 60 years, and smokers or non-smokers. In contrast, the consumption of non-chocolate candy was associated with a 49% higher prevalence of coronary heart disease, comparing ≥ 5 times/week vs. 0/week.^[25]

Grassi et al.^[28] reported no changes in HDL, LDL and triglyceride levels following ingestion of 100 grams of dark chocolate for 2 weeks. Cocoa butter contains a high level of saturated fats, including 35% stearic acid and 25% palmitic acid; results from separate studies show that stearic acid does not have an unfavorable effect on cholesterol levels.^[28] Possible explanations include inadequate absorption, chain length of stearic acid and hepatic conversion of stearic acid to oleic acid.

Hypertension

Hypertension is a major risk factor in the development of cardiovascular diseases, stroke and heart failure. Regulating blood pressure is critical for prevention of end-organ damage. Initial management of hypertension includes lifestyle modifications and dietary recommendations, followed by pharmacological agents. Dietary approaches include salt restriction and ingestion of fruits, vegetables and low-fat foods. The health benefits of fruits and vegetables are mainly associated with their flavonoid content.^[29] Apart from fruits and vegetables, cocoa, chocolate, black tea and green tea are valuable sources of flavonoids. Observational and epidemiological studies have shown that diets rich in polyphenols result in lower blood pressures, and that prevention of diverse pathologies is related to blood pressure. Cocoa ingestion has also been associated with reduction in blood pressure. An association of cocoa intake with a low hypertension incidence was observed in the Kuna people.^[7] In that population, dietary changes involving less consumption of cocoa, and cultural changes were implicated in the elevated blood pressure.^[7,8] These findings were supported by the positive effects of cocoa ingestion on endothelial functions, measured as flow-mediated dilation of blood vessels.^[29]

Observations on the relationship between cocoa ingestion and blood pressure among the Kuna people were supported by major studies. In a Dutch study, blood pressure measurements were obtained from 470 elderly males without any chronic illnesses at baseline, and then obtained again after a five-year interval, with a follow-up for causes of mortality at 15 years.^[10] Compared to subjects with a daily cocoa ingestion

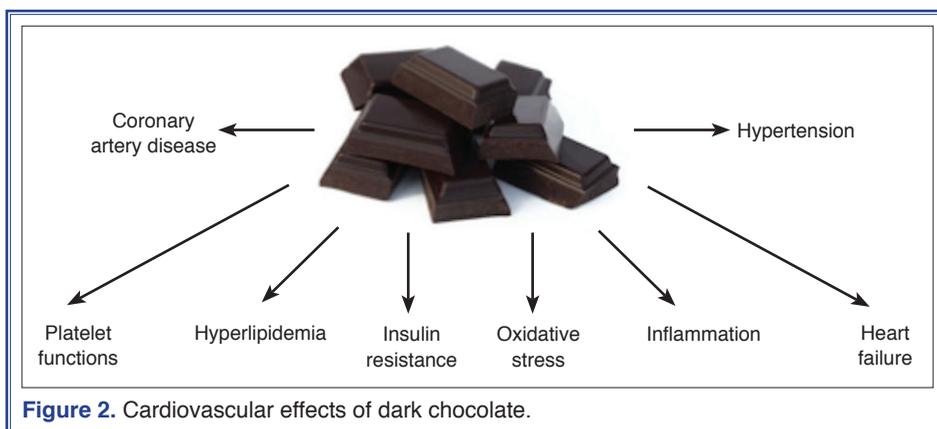


Figure 2. Cardiovascular effects of dark chocolate.

of <0.36 grams, those who ingested >2.36 grams of cocoa per day had an average 3.7 mm Hg reduction in systolic blood pressure and 2.1 mm Hg reduction in diastolic blood pressure. Additionally, the group with greater cocoa ingestion had significantly lower rates of cardiovascular mortality and total mortality.^[10]

Buijsse et al.^[30] followed approximately 19,000 subjects who were free of myocardial infarction (MI), stroke and not using antihypertensive medication for a mean 8 years. Participants were divided into four groups based on their chocolate consumption. Mean systolic and diastolic blood pressures were lower by 1.0 and 0.9 mm Hg respectively in subjects in the fourth quartile (7.5 g/day chocolate) compared with the first quartile (1.7 g/day chocolate). A significant reduction in the risk of MI and stroke ($p=0.014$) was observed in the group with greater chocolate ingestion and this was attributed to the 12% decrease in blood pressures. The lower reduction in blood pressure in that study compared to other studies was associated with the lower baseline blood pressure.

Vascular tone regulation involves interactions of peptides, such as catecholamines, angiotensin II, vasopressin, prostaglandins, and particularly molecules containing nitric oxide (NO). Studies with isolated flavonoids showed that epicatechin and cocoa products had comparable vascular effects, suggesting that flavonoids were responsible for these effects.^[18]

Cocoa products rich in flavanols were found to have an effect on NO-dependent vasodilation in healthy individuals and elderly subjects with isolated systolic hypertension.^[22] However, separate studies reported no beneficial effects of cocoa polyphenols on blood pressure and flow-mediated dilation.^[4]

Grassi et al. hypothesized that flavanols found in dark chocolate might be responsible for favorable effects on regulation of nitric oxide production, insulin sensitivity and blood pressure.^[28]

Following a study examining the effects of isocaloric 100 g dark chocolate and 90 g white chocolate on blood pressure, Grassi et al. concluded that dark, but not white, chocolate decreases blood pressure in healthy persons. As observed in the Grassi et al. study, flavanol-rich dark chocolate significantly increased NO-dependent flow-mediated dilation ($p<0.001$), and there was an inverse relationship between the reduced blood pressure and increased flow-mediated dila-

tion.^[28] Ingestion of flavanol-rich dark chocolate for 15 days was associated with a significant reduction in systolic and diastolic blood pressures among both healthy and hypertensive subjects.^[28]

The blood pressure-lowering effect of flavanol-rich dark chocolate is mostly associated with NO. Inhibition of the angiotensin-converting enzyme (ACE), which is involved in the conversion of angiotensin I to angiotensin II, is the major goal of hypertension treatment. In a study designed to elucidate on the blood pressure-lowering effects of cocoa, cocoa polyphenols were shown to inhibit ACE activity, thereby contributing to reduced blood pressure.^[31] Flavanols and procyanidins present in cocoa were shown to provide ACE inhibition.^[32] In relation to ACE inhibition, NADPH oxidase activity and angiotensin II and superoxide anion production were shown to be decreased.^[33]

A meta-analysis was published in 2012 reviewing the effect of cocoa on blood pressure.^[34] This meta-analysis of 20 studies involving 856 patients found a significant reduction in blood pressure among subjects consuming flavanol-rich cocoa products for 2 to 18 weeks compared to a control group. On average, a 2.77 mm Hg reduction in systolic blood pressure and a 2.2 mm Hg reduction in diastolic blood pressure were observed. In the meta-analysis, the active intervention group consisted of subjects ingesting 30-1,080 mg of flavanol (average 546 mg) with 3.6-105 grams of cocoa per day. The control group subjects included those ingesting food free of flavanols or cocoa powder with a low content of flavanols (6.4-41 mg). Gastrointestinal complaints were reported by 5% of subjects using a flavanol-rich cocoa product and 1% of the control group.

Heart failure

Endothelial dysfunction is present in patients with heart failure, who have been shown to have 4% lower flow-mediated dilation (FMD) compared to healthy individuals.^[35] Increases in reactive oxygen derivatives and oxidized LDL are found in heart failure and are associated with an unfavorable effect on the vasodilating action of NO. Cocoa polyphenols were shown to improve endothelial functions by enhancing NO synthase activity.^[28]

Considering the potential beneficial effects of

flavanol-rich chocolate, Flammer et al. assessed the short-term (2 hours after ingestion of 1 chocolate bar) and long-term effects (ingestion of 2 chocolate bars/day for 4 weeks) of consuming flavanol-rich dark chocolate on endothelial and platelet functions compared with control chocolate in 20 patients with heart failure in a placebo-controlled, randomized study.^[36] The beneficial vascular effects observed in heart failure patients consuming flavanol-rich dark chocolate were maintained through 4 weeks. An interesting finding of that study was a significant reduction in platelet adhesion 2 hours after ingestion of flavanol-rich dark chocolate. This was the first study to show the beneficial effects of a commercially available flavanol-rich dark chocolate on vascular and platelet functions. Parallel examination of the metabolic effects of chocolate ingestion revealed that calorie-neutral supplementation did not have an effect on body weight and fasting blood glucose values. There was no change in insulin sensitivity compared to the control group. Flammer et al. used a dark chocolate containing 70% cocoa and its level was confirmed by measurement of serum polyphenol level. Polyphenols exert antioxidant, anti-inflammatory and anti-aggregating actions, enhance NO bioavailability and reduce blood pressure and insulin resistance.^[16]

Effects on lipid levels

Elevated LDL-cholesterol and low HDL-cholesterol levels are associated with the development of atherosclerosis and cardiovascular disease. Oxidized LDL plays a key role in the development of atherosclerosis. LDL cholesterol levels were reduced by polyphenol treatment provided by dietary products.^[37]

Several studies in humans and animals have demonstrated that LDL becomes more resistant to oxidation following the ingestion of cocoa products.^[38,39] In one study, 23 healthy individuals were randomized into 2 groups. The first group was given an average American diet and the second group received the same diet, supplemented with 16 g dark chocolate containing 22 g cocoa powder and 466 mg procyanidin per day. Cocoa powder and dark chocolate moderately reduced LDL oxidation and enhanced serum total antioxidant capacity and HDL-cholesterol levels.^[39] Nanetti et al.^[40] showed that consuming 50 g flavanol-rich dark chocolate daily for 3 weeks was associated with a significant increase in HDL concentration and

a significant decrease in triglyceride levels. Significant reductions in LDL levels were observed only in female subjects. Chocolate ingestion led to the inhibition of LDL and HDL oxidation, which was more prominent among females. These beneficial effects were not accompanied by significant changes in the metabolic parameters or body weight.

Mursu et al.^[41] found that ingesting dark chocolate for 15 days increased HDL cholesterol levels without any changes in total and LDL cholesterol levels. In a separate study, Fraga et al. found that the consumption of flavanol-containing milk chocolate (168 mg flavanol) for 2 weeks led to 15% reduction of LDL cholesterol levels in young individuals with normal cholesterol levels.^[42] LDL cholesterol levels were reduced by 11% following ingestion of 100 g dark chocolate (88 mg flavanol) daily for 15 days in patients with essential hypertension.^[3]

A meta-analysis of 8 studies which examined the effects of cocoa consumption on lipid levels showed that, compared to the control group, short-term ingestion of cocoa products provided reductions in LDL cholesterol levels, but did not significantly change triglyceride and HDL cholesterol levels.^[43]

Several studies have examined the mechanism of the cholesterol-lowering action of flavanols. LDL cholesterol-lowering actions of flavanols are related to the ability of flavanols to reduce absorption of cholesterol from the gastrointestinal tract, inhibit hepatic LDL cholesterol synthesis, suppress hepatic apoB100 secretion and enhance LDL receptor expression in the liver.^[37,38]

Chocolate has diverse effects on different lipid components and further large-scale, standardized trials are needed to shed light on such effects.

Inflammation

Inflammation plays a key role in the onset and progression of atherosclerosis and plaque rupture. A study comparing individuals who did not consume chocolate for one year with individuals who regularly consumed dark chocolate showed a significant association between moderate levels of cocoa ingestion and inflammation. Serum CRP levels were significantly lower in subjects consuming 20 g cocoa every 3 days compared to subjects with either no or greater cocoa consumption.^[44] Experimental studies showed

that cocoa procyanidins and cocoa extracts inhibited Mitogen-activated protein-kinase activity.^[42-44]

Wang-Polagruto et al.^[45] showed that ingesting flavanol-rich cocoa (446 mg flavanol/day) for 6 weeks was associated with an 11% reduction in VCAM-1 levels in postmenopausal hypercholesterolemic females. In another study, a significant reduction in ICAM-1 levels was found following consumption of dark chocolate (41 g/day) in healthy women.^[46]

Oxidative stress

Plant-derived polyphenols have long been considered as physiological antioxidants. Flavanols present in the circulation and vascular structures may increase vascular NO concentration by interfering with reactions between NO and superoxides. Inhibition of NADPH-dependent superoxide production, NO production through NOS and scavenging activity against superoxide radicals, H₂O₂ and other oxidants involved in cell damage play critical roles in this process.^[47]

Cocoa flavanols and procyanidins have direct effects on the expression and activity of eNOS and have potent antioxidant properties. Cocoa polyphenols reduce LDL oxidation.^[48] In a study by Serafini et al.,^[17] improvements in plasma total antioxidant capacity and plasma (-)-epicatechin levels were observed following ingestion of 100 g dark chocolate in healthy subjects. A striking finding was that these effects were markedly reduced when dark chocolate was taken with milk.

Insulin resistance

Insulin-mediated NO release influences insulin sensitivity. Flavanols and dietary antioxidants are believed to reduce insulin resistance by improving NO bioavailability. Grassi et al. demonstrated reduced insulin resistance in patients with essential hypertension who consumed 100 grams of flavanol-rich chocolate for 15 days.^[3,28] Blood pressure was reduced, insulin sensitivity increased and endothelial functions improved in glucose-intolerant, hypertensive patients after consuming flavanol-rich dark chocolate.^[15] In another study, consuming flavanol-rich dark chocolate was shown to decrease daytime and nighttime blood pressure levels, reduce insulin resistance and improve NO-dependent vasodilation. Decreased NO bioavailability also leads to diminished insulin-dependent glucose uptake.

Platelet functions

The anti-aggregating effects of cocoa polyphenols have been reported by a number of studies.^[5,21] Rein et al. compared cocoa containing 897 mg total EC and oligomeric procyanidin with placebo to examine the effects of cocoa on platelet functions in healthy individuals. Cocoa reduced ADP/collagen- and adrenaline/collagen-activated, platelet-related hemostasis within hours after consumption of high (897 mg) or moderate (220 mg) amounts of cocoa flavanols. These anti-aggregatory effects observed with cocoa were shown to be attributable, in part, to a reduction in the ADP- and adrenaline-induced expression of the activated conformation of the GPIIb/IIIa surface protein.^[5]

Additionally, NO might reduce platelet reactivation. Flammer et al. showed that dark chocolate (containing 70% cocoa) induces coronary vasodilation and decreased platelet adhesion 2 hours after consumption. These effects were considered to be associated with an increased plasma epicatechin concentration.^[49]

Cocoa polyphenols have a moderate level of anti-aggregating effects. Moderate amounts of cocoa flavanols result in decreases in P-selectin expression, platelet aggregation induced by epinephrine and ADP, and platelet volume.^[5,21] In studies with healthy volunteers, dark chocolate rich in flavonoids was associated with increased leukotriene levels and decreased prostacyclin levels.^[9]

Conclusion

Lifestyle modifications and dietary interventions are critical for prevention and treatment of cardiovascular diseases. The major consideration for studies examining the effects of dietary products is to achieve adequate standardization. In this respect, varied cocoa concentrations found in different types of chocolate may influence study results. Dark chocolate contains 50-85% cocoa and milk chocolate between 20-30%. In Europe, commercially produced dark chocolate has 35-50% cocoa, whereas in the U.S., it has approximately 15%. While cocoa content may be kept at 70%, differences in the chocolate manufacturing processes may result in variable quantities of flavonoids. One factor affecting interpretation of these study results is the interaction potential of flavonoid-rich chocolate with other foods, each and all of which complicates interpretation of study results. However, flavanol-rich

dark chocolate has been shown to confer beneficial effects on hypertension, coronary artery diseases, hyperlipidemia and positive effects on insulin resistance and platelet functions. The aforementioned study by Flammer et al.^[36] in heart failure patients signals the great potential for flavanol-rich chocolate in providing some benefits in heart failure. More and larger randomized studies are needed to provide clear dietary recommendations for patients.

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Key words: Cacao; chocolate; cardiovascular diseases; flavanones; food/adverse effects; heart diseases/epidemiology; hypertension/diet therapy.

Anahtar sözcükler: Kakao; çikolata; kardiyovasküler hastalıklar; flavonoller; gıda/yan etkileri; kalp hastalıkları/epidemioloji; hipertansiyon/diyet tedavisi.