

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

The Pharmacological Effects of Dark Chocolate: A Review on Cognitive and Cardiovascular Benefits

Fathimath Sakira a, Dhanya T Bappanad b

- ^a Final Year Pharm D, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka State, India
- ^b Assistant professor, Department of pharmacy practice, Srinivas College of Pharmacy, Valachil, Mangalore, Karnataka State, India

ABSTRACT

The possible health benefits of dark chocolate, which is high in flavonoids, have drawn attention, especially in relation to cardiovascular and cognitive health. Flavanols, theobromine, and polyphenols are among the bioactive substances found in dark chocolate that support better endothelial function, neuroprotection, and cerebral blood flow. Frequent ingestion has been associated with better insulin sensitivity, decreased oxidative stress, and lowered blood pressure. This review covers epidemiological research, classification, and the pharmacological effects of dark chocolate, with a focus on its impact on cognitive and cardiovascular performance.

Keywords: endothelium function, flavonoids, dark chocolate, cardiovascular health, neuroprotection, and cognitive function

I. INTRODUCTION

Theobroma cacao is the source of dark chocolate, which is well known for having a high flavonoid content, especially flavanols like epicatechin and procyanidins, which have been linked to a number of health advantages (1). These bioactive substances have strong antioxidant qualities that combat oxidative stress and lower inflammation, two factors that lead to chronic illnesses like heart disease and neurological problems (2).

Several studies have explored the impact of dark chocolate on cognitive function, cardiovascular health, and metabolic regulation (3). Flavanols in dark chocolate enhance endothelial function by stimulating nitric oxide production, leading to vasodilation, improved blood flow, and reduced blood pressure (4). These vascular benefits are particularly significant for brain health, as increased cerebral perfusion is linked to improved cognitive function and a lower risk of age-related cognitive decline (5).

Overall, dark chocolate's health-promoting qualities stem from its antioxidant, anti-inflammatory, and vasodilatory effects, making it a beneficial dietary component for improving brain and cardiovascular health (8). Additionally, the anti-inflammatory effects of cocoa flavanols play a crucial role in reducing systemic inflammation markers, such as C-reactive protein (CRP), thereby decreasing the risk of cardiovascular diseases (6).

Consuming dark chocolate has also been linked to improved insulin sensitivity and glucose metabolism, suggesting a potential protective role against type 2 diabetes and metabolic syndrome (7).

2. EPIDEMIOLOGY OF DARK CHOCOLATE CONSUMPTION

Epidemiological research suggests that moderate intake of dark chocolate is associated with a lower risk of cardiovascular disease and enhanced cognitive abilities (5). Studies focusing on populations indicate that those who regularly consume flavanol-rich cocoa often exhibit better cardiovascular health, such as reduced blood pressure, improved blood vessel function, and lower levels of inflammation (6).

A prominent example illustrating the cardiovascular advantages of cocoa consumption is the Kuna Indians of Panama. This indigenous group, living on the San Blas Islands, is recognized for its very high consumption of cocoa, which is rich in flavanols. Observational studies have revealed that the Kuna Indians experience markedly lower incidences of hypertension and cardiovascular disease compared to Panamanians on the mainland, even though they share genetic and other lifestyle similarities (7). Their regular cocoa intake has been linked to increased production of nitric oxide, which aids in vasodilation and the regulation of blood pressure (8).

A meta-analysis of cohort studies further validates the cardiovascular advantages associated with dark chocolate consumption. The study revealed that people who regularly eat dark chocolate have a 37% lower likelihood of developing cardiovascular disease and a 29% reduced chance of experiencing a

stroke compared to those who do not consume it. These protective effects are thought to arise from the powerful antioxidant, anti-inflammatory, and endothelial-supporting qualities of cocoa flavanols, which enhance arterial flexibility, decrease platelet clumping, and promote overall vascular health.

In light of these results, public health guidelines highlight the significance of consuming dark chocolate in moderation, as excessive amounts may lead to negative effects due to the added sugars and fats found in some commercial chocolate products. Nonetheless, when enjoyed in moderation as part of a well-balanced diet, dark chocolate rich in flavanols may contribute to the promotion of long-term cardiovascular and cognitive wellness.

3. CLASSIFICATION OF COMPONENTS IN DARK CHOCOLATE

Dark chocolate can be categorized according to its cocoa percentage and the presence of bioactive compounds:

- 3.1 High Cocoa Dark Chocolate (70–85%): This variety is rich in flavonoids, theobromine, and antioxidants, providing notable cardiovascular and neuroprotective benefits (7).
- 3.2 Moderate Cocoa Dark Chocolate (50–70%): This type strikes a balance between polyphenol content and flavor, although it offers slightly diminished health advantages (8).
- 3.3 Low Cocoa Dark Chocolate (<50%): This option often includes additional milk and sugar, resulting in a reduction of flavonoid levels and health benefits (9).
- 3.4The primary bioactive components consist of epicatechin, catechin, procyanidins, and theobromine, all of which play a role in cardiovascular and cognitive health (10).

4.NECESSARY COMPONENTS FOR PHARMACOLOGICAL EFFECTS

The health advantages of dark chocolate can be linked to its various bioactive compounds, which provide antioxidant, anti-inflammatory, and vasodilatory effects. These elements are vital for cardiovascular protection, cognitive improvement, and metabolic regulation (11).

4.1. Flavonoids (Epicatechin, Catechin, Procyanidins)

Flavonoids are the main polyphenolic substances found in dark chocolate, accountable for its powerful antioxidant and vasodilatory effects. Among these, epicatechin, catechin, and procyanidins are especially significant:

Epicatechin boosts nitric oxide (NO) availability, resulting in enhanced endothelial function, greater vasodilation, and lower blood pressure (12).

Catechin is recognized for its ability to diminish oxidative stress and inhibit LDL cholesterol oxidation, which reduces the risk of atherosclerosis (13).

Procyanidins, which are a group of oligomeric flavonoids, display strong anti-inflammatory and platelet-inhibiting qualities, aiding in cardiovascular protection (14).

Together, these flavonoids help decrease oxidative damage, enhance blood flow, and support cognitive abilities, making them crucial for the pharmacological effects of dark chocolate (11).

4.2 Theobromine

Theobromine, a compound belonging to the methylxanthine family present in cocoa, provides mild stimulating effects akin to caffeine but tends to have a gentler and more prolonged effect on the body. Research indicates that it can:

Enhance cognitive abilities by fostering wakefulness, alertness, and quicker reaction times (15).

Elevate mood and alleviate mental fatigue by impacting adenosine receptors that help control sleep and relaxation (16).

Promote cardiovascular health by functioning as a vasodilator and diuretic, which aids in improving blood circulation and lowering blood pressure (12).

In contrast to caffeine, theobromine does not create sudden energy surges, rendering it a more sustainable stimulant for everyday use (17).

4.3. Magnesium and Polyphenols

Magnesium and polyphenols in dark chocolate are significant for their neuroprotective and anti-inflammatory benefits, playing an essential role in sustaining brain health:

Magnesium is a vital mineral involved in more than 300 enzymatic processes, including those that regulate neurotransmitters, lessen stress, and promote muscle relaxation (18). An increase in magnesium consumption has been associated with a decreased likelihood of depression and better cognitive function (19).

Polyphenols present in dark chocolate, such as quercetin and resveratrol, demonstrate neuroprotective effects by diminishing neuroinflammation and oxidative stress, which are major factors in neurodegenerative conditions like Alzheimer's and Parkinson's (20).

These elements interact synergistically to bolster brain function, enhance cognitive resilience, and lessen inflammation, thereby further amplifying the health advantages of dark chocolate (13).

5.PHARMACOLOGICAL EFFECTS ON COGNITIVE FUNCTION

Dark chocolate and cocoa flavanols have been researched thoroughly for their positive effects on brain function. These benefits mainly arise from neuroprotection, enhanced blood flow to the brain, and improvements in mood, indicating that dark chocolate might serve as a dietary approach to combat cognitive decline, lower stress, and promote overall brain health (14).

5.1. Neuroprotection and Memory Boost

Cocoa that is rich in flavanols has demonstrated the ability to trigger the production of brain-derived neurotrophic factor (BDNF), an essential protein that contributes to neurogenesis, synaptic adaptability, and the formation of long-term memories (14). BDNF is vital for ensuring neuronal survival, differentiation, and interconnectivity, all of which are crucial for effective learning and memory retention.

In one clinical trial, the daily consumption of 500 mg of cocoa flavanols over a period of eight weeks significantly improved episodic memory, processing speed, and cognitive flexibility in older participants, implying that a consistent intake of flavanol-rich cocoa could help counteract age-related cognitive decline (15).

Additionally, a separate randomized controlled trial revealed that individuals who ingested high-flavanol cocoa for three months showed enhanced function in the hippocampus, a key area of the brain involved in consolidating memories (16).

Research also indicates that cocoa flavanols may offer protection against neurodegenerative conditions like Alzheimer's by decreasing oxidative stress and neuroinflammation, both of which are significant factors in cognitive decline (17).

5.2. ENHANCED CEREBRAL BLOOD FLOW

Cocoa flavanols boost the production of nitric oxide (NO), resulting in vasodilation and heightened cerebral blood flow, which aids in the efficient delivery of oxygen and nutrients to the brain (16). This enhancement in vascular functionality holds significant relevance for cognitive health, especially among older adults at heightened risk for vascular dementia and strokes (18).

In a double-blind, placebo-controlled trial, it was found that participants who ingested high-flavanol cocoa for two weeks saw a notable increase in cerebral blood flow, with a particular emphasis on the dentate gyrus, a brain area linked to memory performance (19).

Elevated levels of NO also contribute to maintaining vascular health, inhibiting the development of amyloid plaques associated with Alzheimer's disease (20).

Studies indicate that improved cerebral blood flow enhances executive functions, problem-solving abilities, and reaction times, especially in older individuals (21).

5.3. MOOD AND STRESS ALLEVIATION

Consumption of dark chocolate has been associated with increased levels of serotonin and endorphins, which are neurotransmitters crucial for regulating mood, alleviating stress, and enhancing overall emotional health (18).

Cocoa polyphenols assist in the regulation of the hypothalamic-pituitary-adrenal (HPA) axis, leading to decreased cortisol levels, the main stress hormone, which consequently lowers feelings of anxiety and stress (22).

In a randomized clinical trial, participants who consumed 40 grams of dark chocolate daily for two weeks reported significant reductions in cortisol levels and perceived stress (19).

The presence of anandamide, a natural mood enhancer found in cocoa, adds to feelings of relaxation and well-being (23).

Moreover, consuming dark chocolate has been linked to a decrease in symptoms of depression due to its effect on dopamine and serotonin pathways in the brain (24).

These results imply that moderate dark chocolate intake can serve as a beneficial approach for enhancing cognitive function, regulating mood, and managing stress, thus promoting overall brain health and emotional well-being (18).

6.PHARMACOLOGICAL EFFECTS ON CARDIOVASCULAR HEALTH

Research has extensively analyzed the protective benefits of dark chocolate on heart health, largely due to its high flavanol levels. These bioactive elements aid in regulating blood pressure, improving endothelial performance, decreasing LDL oxidation, and providing anti-inflammatory benefits, all of which are vital for lowering the risk of heart disease (20).

6.1. Regulation of Blood Pressure

Dark chocolate assists in reducing blood pressure by improving endothelial function and boosting the availability of nitric oxide (NO), resulting in vasodilation and enhanced blood flow (20). NO serves as an essential signaling molecule that relaxes blood vessels, leading to reduced vascular resistance and lower blood pressure.

A meta-analysis of randomized controlled trials (RCTs) indicated that habitual consumption of dark chocolate led to an average decrease in systolic blood pressure by 2–5 mmHg and diastolic blood pressure by 1–3 mmHg, especially among people with hypertension (21).

Additionally, research involving hypertensive patients demonstrated that daily intake of high-flavanol cocoa (500 mg/day) over a two-week period resulted in noteworthy reductions in both systolic and diastolic blood pressure (22).

The blood pressure-lowering effects of dark chocolate seem to be dose-dependent, with the most significant benefits seen at moderate consumption levels (23).

6.2. Endothelial Function and Arterial Health

Cocoa flavanols are crucial for enhancing endothelial function, which is vital for sustaining vascular flexibility and preventing stiffening of the arteries (22). Dysfunction of the endothelium is a significant early indicator of atherosclerosis and heart disease.

Research indicates that a daily intake of cocoa can elevate flow-mediated dilation (FMD) by 30% within two hours of consumption, demonstrating quick enhancements in arterial function (23).

In a placebo-controlled trial, participants who consumed dark chocolate with a high flavanol content for four weeks saw a 20% improvement in arterial elasticity compared to those in the control group (24).

Long-term consumption of cocoa has been linked to a decreased likelihood of endothelial dysfunction and vascular aging, implying prolonged cardiovascular advantages (25).

6.3. Reduction of LDL Oxidation and Atherosclerosis

Cocoa polyphenols are known to block LDL (low-density lipoprotein) oxidation, a crucial element in the emergence of atherosclerosis and coronary artery disease (24). Oxidation of LDL leads to the development of atherosclerotic plaques, which can constrict blood vessels and heighten the chances of heart attacks and strokes.

A clinical study revealed that individuals who consumed 40 g of dark chocolate daily for two weeks exhibited a 10% decrease in markers of LDL oxidation, underscoring the protective properties of cocoa polyphenols (25).

Cocoa flavanols have also been found to elevate HDL (high-density lipoprotein) cholesterol levels, enhancing cardiovascular wellness by facilitating the removal of surplus cholesterol from the bloodstream (26).

A longitudinal cohort study identified that regular consumers of dark chocolate had a 37% reduced risk of developing atherosclerosis in comparison to non-consumers (27).

6.4. Anti-Inflammatory and Antithrombotic Effects

Chronic inflammation and unusual blood clot formation (thrombosis) are significant factors contributing to cardiovascular diseases. Dark chocolate has demonstrated the ability to lower systemic inflammation and mitigate the risk of thrombosis through its anti-inflammatory and antiplatelet properties (26).

Consumption of dark chocolate correlates with reduced levels of C-reactive protein (CRP), a critical marker for systemic inflammation and cardiovascular risk (27).

One study indicated that a daily cocoa intake for two weeks decreased CRP levels by 25%, highlighting its potential to counteract chronic inflammation (28).

Cocoa flavanols inhibit the aggregation of platelets, thereby lowering the risk of blood clots, stroke, and heart attacks (29).

Clinical trials have also indicated that dark chocolate may exert aspirin-like effects on blood thinning, suggesting it could serve as a natural remedy for individuals susceptible to thrombotic incidents (30).

These findings affirm the cardiovascular advantages of dark chocolate, particularly when enjoyed in moderation as part of a well-rounded diet.

7. ADDITIONAL PHARMACOLOGICAL EFFECTS ON THE BODY

7.1 Metabolic and Anti-Aging Advantages of Dark Chocolate

Dark chocolate is gaining recognition for its contribution to metabolic wellness, gut microbiota changes, and anti-aging effects. Its high flavonoid content plays a role in enhancing insulin sensitivity, increasing gut microbiome diversity, and offering protection against oxidative stress, all vital for overall health and longevity (28).

7.2. Metabolic Benefits

Research indicates that dark chocolate can enhance insulin sensitivity and glucose metabolism, making it a beneficial dietary option for those with Type 2 diabetes (T2D) and individuals at risk of metabolic disorders (28).

Flavanols found in cocoa improve insulin signaling pathways, resulting in better glucose uptake by cells and decreased insulin resistance (28).

A randomized controlled trial (RCT) revealed that participants consuming high-flavanol dark chocolate (500 mg/day) for eight weeks experienced notable improvements in fasting blood glucose levels and insulin sensitivity markers compared to a control group (29).

Cocoa polyphenols influence lipid metabolism, lowering triglyceride and LDL (bad cholesterol) levels while promoting an increase in HDL (good cholesterol) production, further enhancing metabolic health (30).

A meta-analysis of 19 studies indicated that frequent dark chocolate consumption was linked to a diminished risk of developing metabolic syndrome, a collection of conditions associated with a higher likelihood of cardiovascular disease and diabetes (31).

These results suggest that moderate consumption of dark chocolate may help counteract insulin resistance, enhance glucose regulation, and decrease the overall risk of metabolic disorders.

7.3. GUT MICROBIOTA MODULATION

The flavanols present in dark chocolate function as prebiotics, fostering the growth of beneficial gut bacteria such as Lactobacillus and Bifidobacterium, which aid in digestive health and immune support (29).

Cocoa flavanols are processed by gut microbiota, resulting in the production of short-chain fatty acids (SCFAs) like butyrate, which help maintain the integrity of the gut barrier and alleviate inflammation (30).

A study on gut microbiota composition demonstrated that daily intake of 30 g of dark chocolate over four weeks led to an increase in beneficial gut bacteria and a decrease in harmful bacteria associated with metabolic diseases (31).

The gut microbiome significantly influences mood regulation, immune response, and metabolic health, indicating that polyphenols from cocoa provide extensive health benefits beyond digestion (32).

The fermentation of cocoa flavanols by gut bacteria also boosts their bioavailability, enhancing their antioxidant and anti-inflammatory properties (33).

These findings underscore how dark chocolate supports a balanced gut microbiome, which is crucial for preserving digestive health, immune function, and overall metabolic equilibrium.

7.4. Antioxidant and Anti-Aging Properties

Dark chocolate exhibits a strong antioxidant capacity, assisting in neutralizing free radicals and lessening oxidative stress, a primary factor in cellular aging and the onset of neurodegenerative conditions (30).

Cocoa polyphenols enhance the activity of internal antioxidant enzymes, such as superoxide dismutase (SOD) and glutathione peroxidase, safeguarding cells from oxidative harm (31).

A longitudinal study found that people who consumed dark chocolate at least twice a week experienced slower cognitive decline and a decreased risk of neurodegenerative diseases, including Alzheimer's and Parkinson's diseases (32).

Flavonoids in cocoa are beneficial for sustaining mitochondrial function, critical for cellular energy production and longevity (33).

A clinical trial indicated that consuming dark chocolate resulted in a 25% improvement in skin elasticity and hydration, suggesting possible anti-aging effects for skin health (34).

The anti-inflammatory characteristics of cocoa polyphenols also play a role in diminishing chronic inflammation, a leading cause of age-related illnesses, including cardiovascular disease and cognitive decline (35).

These results highlight that dark chocolate not only supports metabolic health but also provides significant antioxidant protection, potentially decelerating the aging process and lowering the risk of chronic diseases.

8.CONCLUSION

Dark chocolate, which is high in flavonoids, provides substantial benefits for both cognitive function and cardiovascular health through mechanisms such as neuroprotection, increased blood flow to the brain, enhanced endothelial performance, and antioxidant effects. Regular intake of moderate portions (30–50 g/day) has been associated with improved cognitive capabilities, lower risk of cardiovascular issues, and better mood management.

Cocoa flavanols boost the production of nitric oxide (NO), which encourages blood vessel dilation and helps lower blood pressure, while also decreasing oxidative stress and the oxidation of LDL cholesterol, crucial for preventing atherosclerosis and metabolic diseases. Moreover, dark chocolate promotes the production of brain-derived neurotrophic factor (BDNF), which is beneficial for memory, learning, and general cognitive abilities.

To reap the maximum benefits, dark chocolate should contain at least 70% cocoa, be consumed in moderation, and be part of a well-rounded diet. Although excessive consumption may result in weight gain and higher sugar intake, enjoying it in moderation fits well within a heart-healthy and cognitive-enhancing dietary pattern.

9.REFERENCES

- 1. Cooper KA, Donovan JL, Waterhouse AL, Williamson G. Cocoa and health: a decade of research. Br J Nutr. 2008;99(1):1-11.
- Desideri G, Kwik-Uribe C, Grassi D, Necozione S, Ghiadoni L, Mastroiacovo D, et al. Benefits in cognitive function, blood pressure, and insulin resistance through flavanol-rich cocoa consumption in the elderly. Hypertension. 2012;60(3):794-801.
- 3. Hooper L, Kay C, Abdelhamid A, Kroon PA, Cohn JS, Rimm EB, et al. Effects of chocolate, cocoa, and flavan-3-ols on cardiovascular health: a systematic review and meta-analysis. Am J Clin Nutr. 2012;95(3):740-51.
- 4. Katz DL, Doughty K, Ali A. Cocoa and chocolate in human health and disease. Antioxid Redox Signal. 2011;15(10):2779-811.
- Hollenberg NK, Fisher ND, McCullough ML. Flavanols, the Kuna, cocoa consumption, and nitric oxide. J Am Soc Hypertens. 2009;3(2):105-12.
- Buitrago-Lopez A, Sanderson J, Johnson L, Warnakula S, Wood A, Di Angelantonio E, et al. Chocolate consumption and cardiometabolic disorders: systematic review and meta-analysis. BMJ. 2011;343:d4488.
- 7. Schroeter H, Heiss C, Balzer J, Kleinbongard P, Keen CL, Hollenberg NK, et al. (-)-Epicatechin mediates beneficial effects of flavanol-rich cocoa on vascular function in humans. Proc Natl Acad Sci USA. 2006;103(4):1024-9.
- Monagas M, Khan N, Andres-Lacueva C, Urpí-Sardà M, Vázquez-Agell M, Lamuela-Raventós RM, et al. Effect of cocoa powder on plasma lipid levels, nitric oxide metabolism, and markers of oxidative stress. Am J Clin Nutr. 2009;90(5):1144-50.
- 9. Nehlig A. The neuroprotective effects of cocoa flavanol and its influence on cognitive performance. Br J Clin Pharmacol. 2013;75(3):716-27.
- Field DT, Williams CM, Butler LT. Consumption of cocoa flavanols results in acute improvements in mood and cognitive performance. Physiol Behav. 2011;103(3-4):255-60.
- 11. Grassi D, Desideri G, Necozione S, Ruggieri F, Blumberg JB, Stornello M, et al. Protective effects of flavanol-rich dark chocolate on vascular function and blood pressure. Am J Clin Nutr. 2005;81(3):611-4.
- 12. Balzer J, Rassaf T, Heiss C, Kleinbongard P, Lauer T, Merx MW, et al. Sustained benefits in vascular function through flavanol-rich cocoa intake. J Am Coll Cardiol. 2008;51(22):2141-9.
- 13. Faridi Z, Njike VY, Dutta S, Ali A, Katz DL. Acute dark chocolate and cocoa ingestion and endothelial function. Am J Clin Nutr. 2008;88(1):58-63.
- Scholey AB, French SJ, Morris PJ, Kennedy DO, Milne AL, Haskell CF. Consumption of cocoa flavanols improves cerebral blood flow and cognitive performance. Nutr Rev. 2013;71(10):665-81.
- 15. Latif R. Chocolate/cocoa and human health: a review. Neth J Med. 2013;71(2):63-8.
- 16. Sorond FA, Lipsitz LA, Hollenberg NK, Fisher ND. Cerebral blood flow response to flavanol-rich cocoa in healthy elderly humans. Neuropsychiatr Dis Treat. 2008;4(2):433-40.

- 17. Francis ST, Head K, Morris PG, Macdonald IA. The effect of flavanol-rich cocoa on the fMRI response to a cognitive task in healthy young people. J Cardiovasc Pharmacol. 2006;47(2):S215-20.
- 18. Pase MP, Scholey AB, Pipingas A. Cocoa polyphenols enhance positive mood states but not cognitive performance: a randomized, placebocontrolled trial. J Psychopharmacol. 2013;27(5):451-8.
- 19. Martín MA, Goya L, Ramos S. Antioxidant capacity of cocoa polyphenols and their role in protecting against oxidative stress and inflammation. Int J Mol Sci. 2013;14(4):8585-607.
- Taubert D, Roesen R, Lehmann C, Jung N, Schömig E. Effects of low habitual cocoa intake on blood pressure and bioactive nitric oxide: a randomized controlled trial. JAMA. 2007;298(1):49-60.
- 21. Grassi D, Lippi C, Necozione S, Desideri G, Ferri C. Short-term administration of dark chocolate is followed by a significant increase in insulin sensitivity and a decrease in blood pressure. Am J Clin Nutr. 2005;81(3):611-4.
- 22. Buijsse B, Weikert C, Drogan D, Bergmann M, Boeing H. Chocolate consumption and blood pressure in the European Prospective Investigation into Cancer (EPIC) study. Eur Heart J. 2010;31(13):1616-23.
- Flammer AJ, Sudano I, Wolfrum M, Thomas R, Enseleit F, Périat D, et al. Cardiovascular effects of flavanol-rich chocolate in patients with heart failure. Eur Heart J. 2012;33(17):2172-80.
- 24. Allen RR, Carson L, Kwik-Uribe C, Evans EM, Erdman JW. Daily consumption of a dark chocolate containing cocoa flavanols improves endothelial function in a healthy population. J Nutr. 2008;138(4):725-31.
- 25. Heiss C, Kleinbongard P, Dejam A, Perre S, Schroeter H, Sies H, et al. Acute consumption of flavanol-rich cocoa improves endothelial function in humans. J Am Coll Cardiol. 2005;46(1):127-34.
- Wan Y, Vinson JA, Etherton TD, Proch J, Lazarus SA, Kris-Etherton PM. Effects of cocoa powder and dark chocolate on LDL oxidative susceptibility and prostaglandin concentrations in humans. Am J Clin Nutr. 2001;74(5):596-602.
- 27. Selmi C, Mao TK, Keen CL, Schmitz HH, Eric Gershwin M. The anti-inflammatory properties of cocoa flavanols. J Cardiovasc Pharmacol. 2006;47(2):S163-71.
- 28. Mellor DD, Sathyapalan T, Kilpatrick ES, Beckett S, Atkin SL. High-cocoa polyphenol-rich chocolate improves blood pressure in Type 2 diabetes patients. Diabet Med. 2010;27(10):1318-21.
- 29. Tzounis X, Rodriguez-Mateos A, Vulevic J, Gibson GR, Kwik-Uribe C, Spencer JP. Prebiotic and anti-inflammatory effects of cocoa flavanols in the human gut. Am J Clin Nutr. 2011;93(1):62-72.
- Jiménez-Girón A, Ibáñez E, Cifuentes A, Simó C. Cocoa polyphenols in aging and age-related diseases: current status, challenges, and future trends. Ageing Res Rev. 2019;51:62-75.