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Review

Physiological Effects of Red-Colored Food-Derived Bioactive Compounds on Cardiovascular and Metabolic Diseases

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Abstract: Cardiovascular diseases (CVDs) are a major global cause of disease and mortality. CVDs are a group of disorders of the heart and blood vessels and include coronary artery disease, cerebrovascular disease, heart failure, and other conditions. The most important behavioral risk factors for heart disease and stroke are diet, physical activity, smoking, and drinking. Increased intake of fruits and vegetables is associated with reducing the risk of metabolic syndrome and CVDs. Red-colored foods align with cardiovascular health by protecting the heart and blood vessels. Red fruits and vegetables include tomatoes, strawberries, raspberries, cranberries, cherries, red apples, beets, and pomegranate. In vitro and in vivo studies, as well as clinical trials, show that the components of red foods demonstrate various potential health benefits against disease. In conclusion, there are many advantages to eating vegetable foods, especially red fruits and vegetables.

Keywords: red-colored food; cardiovascular disease; metabolic disease; phenolic compounds; flavonoids; carotenoids

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1. Introduction

Cardiovascular diseases (CVDs) are the leading global cause of illness and mortality [1]. CVDs are a group of disabilities in the heart and blood vessels and include coronary artery disease, cerebrovascular disease, heart failure, and other conditions [2]. The most important behavioral risk factors for heart disease and stroke are diet, physical activity, smoking, and drinking [3]. In addition, risk factors are clustered together. Metabolic syndrome is a combination of risk factors of metabolic origins, such as inflammation and oxidative stress, and is associated with cardiovascular disease and type 2 diabetes [4]. Chronic inflammation is closely related to an imbalanced immune response and ultimately results in a variety of conditions, such as cardiovascular diseases, diabetes, obesity, pulmonary diseases, immunological diseases, and other life-threatening diseases [5]. The effects of behavioral risk factors can appear in individuals as elevated blood pressure, raised blood glucose levels, increased lipid markers, and obesity. These intermediate-risk factors can be estimated and indicate an increased risk of heart attack, stroke, heart failure, and other complications [6]. Cessation of tobacco use, reduced dietary salt intake, consumption of more fruit and vegetables, regular physical activity, and avoidance of alcohol consumption have been shown to reduce the risk of cardiometabolic disease [7].

Recently, awareness of the importance of dietary factors as a major determinant of metabolic syndrome has increased. Increased intake of fruits and vegetables is associated with a reduced risk of metabolic syndrome and CVDs [8–11]. Plant parts such as fruits, bark, roots, peels, leaves, and flowers contain several important nutritional and functional compounds that play various roles in the treatment, management, and prevention of chronic diseases [12–15]. In particular, the 2015–2020 Dietary Guidelines emphasize a healthy dietary habit throughout life that encourages diversity and nutrient density across several color categories, such as dark-green, red, and orange vegetables [16].

Red-colored foods align with the cardiovascular system by protecting the heart and blood vessels [17]. Popular red fruits and vegetables are tomatoes, strawberries, raspberries, cranberries, cherries, red apples, beets, and pomegranates. These foods also tend to be high in certain phytonutrients that may have health benefits, such as antioxidant, anti-inflammatory, and immune-modulating activities, and may improve lipid levels and reduce blood pressure. The main phytonutrients include anthocyanins, astaxanthin, and lycopene, and the wider class of flavonoids represents the various colors and has physiological effects [18,19]. In vitro and in vivo studies, along with clinical trials, have indicated that the components of red foods have various potential health benefits against diseases. These studies report the health effects of red fruits and vegetables and different mechanisms that are involved in these protective effects. Therefore, this review focuses on the physiological effects of red-colored food on metabolic and cardiovascular risk factors.

However, many studies have focused on each red-colored vegetable or fruit and the efficacy of phytochemicals contained in them, and comprehensive studies are lacking. Therefore, this review focuses on the physiological effects of red-colored food on metabolic and cardiovascular risk factors, comprehensively deals with most red color groups of vegetables and fruits, and classified by the bioactive compounds.

2. Red-Colored Foods and Bioactive Compounds

Red-colored foods have been shown to contain much higher levels of bioactive compounds such as phenolic compounds, flavonoids, and carotenoids than other foods. The high amount of bioactive compounds in red-colored food can be utilized as a functional food source against many diseases, such as diabetes, cardiovascular disease, and various other oxidative stress-induced metabolic diseases.

Table 1 and Supplementary File S1, are from FooDB (https://foodb.ca/ (accessed 15 January 2022)). Web-based searches of the PubMed database were performed using the following terms: (“Beet” OR “Tomato” OR “Italian sweet red pepper” OR “Red radish” OR “Cranberry” OR “Pomegranate” OR “Cherry” OR “Red sweet potato” OR “Strawberry” OR “Red raspberry” OR “Watermelon” OR “Red grapefruit” OR “Hibiscus” OR “Red apples” OR “Prickly pear” OR “Plum” OR “Red onion” OR “Radicchio” OR “Acerola” OR “Redcurrant” OR “Red huckleberry” OR “Fig” OR “Adzuki bean”) and (“flavonoid” OR “carotenoids” OR “phenolic acid” OR “bioactive compounds”) and (“cardiovascular disease”) and (“metabolic disease) and (“clinical trial”). The summaries of these published articles in Tables 2–5 include intervention studies.

Table 1. Bioactive compounds of red-colored food and their dietary sources.

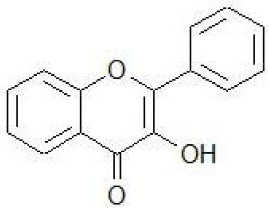
Major Flavonoid Classes	Structure	Family Members	Dietary Sources
Flavonols		- Quercetin [1) 5) 6) 7) 8) 9) 11) 12) 14) 16) 17) 18) 19)] - Quercetin 3,4′-diglucoside [15)] - Quercetin 4′,7-diglucoside [15)] - Quercetin 7-glucuronoside 3-sophoroside [15)] - Quercetin 3-rutinoside [9) 10) 14) 17) 19)] - Quercetin 3-alpha-D-galactoside [9)] - Quercetin 3-O-xylosyl-glucuronide [9)] - Quercetin 3-xyloside [12)] - Quercitrin [3) 5)] - Isoquercetin [7) 9) 12) 14) 17) 19)] - Kaempferol [2) 4) 5) 6) 8) 9) 11) 12) 14) 16)] - Kaempferol 3-glucuronide [8) 9)] - Kaempferol 3-rutinoside [19)] - Kaempferol 3-neohesperidoside 7-(2″-feruloylglucoside) [15)] - Kaempferol 3-neohesperidoside 7-(2″-p-coumaroylglucoside) [15)] - Kaempferol 3-neohesperidoside 7-(2″-p-coumaroyllaminaribioside) [15)] - Kaempferol 3-sophoroside 7-(2-feruloylglucoside) [15)] - Kaempferol 3-sophoroside 7-glucuronide [15)] - Kaempferol 3,4′-diglucoside 7-(2-feruloylglucoside) [15)] - Kaempferide [14)] - Dihydrokaempferol [14)] - Isorhamnetin [6) 13) 15)] - Isorhamnetin 3-O-(beta-D-glucopyranosyl-(1-> 6)-beta-D-glucopyranoside) [1)] - Isorhamnetin 4′-glucoside [15)] - Myricetin [5) 6) 8) 12) 14) 17)]	Beet[1)], Tomato[2)], Italian sweet red pepper[3)], Red radish[4)], Cranberry[5)], Cherry[6)], Red sweet potato[7)], Strawberry[8)], Red raspberry[9)], Watermelon[10)], Red grapefruit[11)], Red apples[12)], Prickly pear[13)], Plum[14)], Red onion[15)], Acerola[16)], Redcurrant[17)], Red huckleberry[18)], Fig[19)]

Table 1. *Cont.*

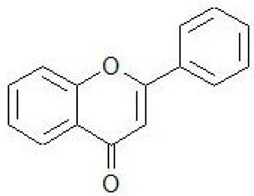
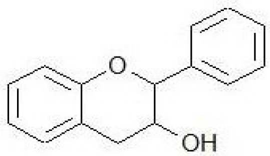
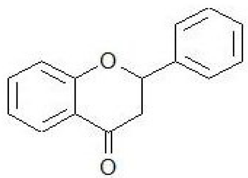
Major Flavonoid Classes	Structure	Family Members	Dietary Sources
		- Myricetin 3-arabinofuranoside [5)] - Myricetin 3-glucoside [17)] - Hyperin [5) 12) 14)] - Avicularin [5) 12)] - Astragalin [5) 8) 9) 19)] - Astragalin 4′-glucoside [15)] - Morin [8)]	
Flavones		- Luteolin[1) 2) 4) 5)] - Luteolin 7-O-(2-apiosyl-6-malonyl)-glucoside [2)] - Apigenin [3)] - Apigenin 7-glucoside [5)] - Apigenin 6-C-arabinosyl-8-C-glucoside [6)] - Apigenin 6-C-glucosyl-8-C-arabinoside [6)]	Beet[1)], Italian sweet red pepper[2)], Red sweet potato[3)], Watermelon[4)], Red apples[5)], Fig[6)]
Flavanols		- Catechin [3) 4) 5) 7) 8) 9)] - alpha-Catechin [1) 2) 3) 6) 9)] - Catechin 3-gallate [3) 6)] - Epicatechin 3-gallate [3) 4)] - Epigallocatechin [1) 3) 4) 6) 8)] - Gallocatechin [4) 8)] - ent-Epicatechin [6)]	Cranberry[1)], Pomegranate[2)], Cherry[3)], Strawberry[4)], Red raspberry[5)], Red apples[6)], Plum[7)], Redcurrant[8)], Fig[9)]
Flavanones		- Betagarin [1)] - (S)-Naringenin [2)] - Hesperetin [2)]	Beet[1)], Red grapefruit[2)]

Table 1. *Cont.*

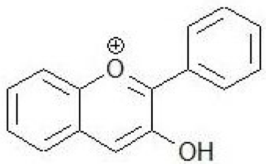
Major Flavonoid Classes	Structure	Family Members	Dietary Sources
Anthocyanins		- Anthocyanins [1) 11)] - Proanthocyanidin A2 [6)] - Cyanidin [1) 2) 4) 5) 6) 7) 9) 11)] - Cyanidin 3-arabinoside [1) 6)] - Cyanidin 3-galactoside [1) 6)] - Cyanidin 3-(caffeoyl-sophoroside) 5-glucoside [3)] - Cyanidin 3-(dicaffeoyl-sophoroside) 5-glucoside [3)] - Cyanidin 3-(6″-succinyl-glucoside) [4)] - Cyanidin 3-(2G-glucosylrutinoside) [5) 10)] - Cyanidin 3-(2G-xylosylrutinoside) [10)] - Cyanidin 3-(3″-malonyl-glucoside) [8)] - Cyanidin 3-(3″,6″-dimalonylglucoside) [4) 8)] - Cyanidin 3-laminaribioside [8)] - Cyanidin 3-O-[4-Hydroxy-E-cinnamoyl-(- > 6)-b-D-glucopyranosyl-(1- > 2)-b-D-glucopyranoside] 5-glucoside [8)] - Cyanidin 3-sambubioside [10)] - Cyanidin 3-glucosyl-rutinoside [10)] - Cyanidin 3-xylosyl-rutinoside [10)] - Procyanidin trimer EEC [4) 7)] - Procyanidin B1 [2) 4) 7)] - Procyanidin B2 [2) 4) 5) 7)] - Procyanidin B3 [2) 4) 7) 10) 11)] - Procyanidin B4 [2) 4) 5) 6) 7)] - Procyanidin B5 [2) 5) 6) 7)] - Procyanidin B7 [2) 7)] - Procyanidin B8 [5)] - Procyanidin C1 [2) 6)] - Delphinidin [1) 6)] - Delphinidin 3-glucoside [5)] - Delphinidin 3-sambubioside [10)] - Prodelphinidin B3 [10)]	Cranberry[1)], Cherry[2)], Red sweet potato[3)], Strawberry[4)], Red raspberry[5)], Red apples[6)], Plum[7)], Red onion[8)], Acerola[9)], Redcurrant[10)], Fig[11)]

Table 1. *Cont.*

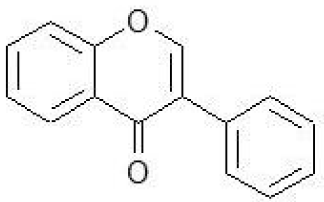
Major Flavonoid Classes	Structure	Family Members	Dietary Sources
		- Malvidin [1)] - Malvidin 3-glucoside [5)] - Peonidin [1) 2) 3) 6)] - Peonidin 3-arabinoside [1)] - Peonidin 3-glucoside [1) 2) 5) 7)] - Peonidin 3-galactoside [1)] - Peonidin 3-rutinoside [2) 7)] - Pelargonidin [2) 4) 6) 9) 11)] - Pelargonidin 3-arabinoside [4)] - Pelargonidin 3-glucoside [4) 5)] - Pelargonidin 3-(6″-succinyl-glucoside) [4)] - Pelargonidin 3-(6″-malonylglucoside) [4)] - Pelargonidin 3-sophoroside [5)] - Pelargonidin 3-(2gluglucosylrutinoside) [5)] - Pelargonidin 3-rutinoside [2) 4) 5)]	
Isoflavone		- Betavulgarin [1)] - Genistein [2)]	Beet[1)], Cherry[2)]

Table 1. *Cont.*

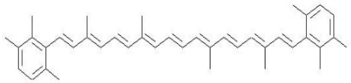
Major Flavonoid Classes	Structure	Family Members	Dietary Sources
Carotenoids		- Carotene [15) 16)] - alpha-Carotene [3) 5) 6) 8)] - beta-Carotene [1) 2) 3) 4) 5) 6) 7) 8) 9) 10) 11) 12) 13) 14) 15)] - beta-Carotene 5,6-epoxide [11)] - gamma-Carotene [15) 15)] - delta-Carotene [2)] - delta-Carotene-1,2-epoxide [2)] - epsilon-Carotene [11)] - epsilon, gamma-Caroten-3-ol [2)] - (S)-1′,2′-Epoxy-1′,2′-dihydro-b,y-carotene [2)] - Lycophyll [2)] - Lycopene [2) 9)] - (9Z)-Lycopene [2)] - (15Z,9′Z)-7,7′,8,8′,11,12-Hexahydrolycopene [2)] - 7,8-Dihydrolycopene [9)] - (9Z,7′Z,9′Z)-7,8-Dihydrolycopene [2)] - (9Z,9′Z)-7,7′,8,8′-Tetrahydrolycopene [2) 5) 6)] - Prolycopene [2)] - Phytoene [6)] - Phytofluene [6) 9) 15)] - Lutein [2) 5) 8) 9) 11) 13) 14) 15)] - Zeaxanthin [2)] - (3R,3′R, all-E)-Zeaxanthin [2) 4) 9) 11) 14) 15)] - alpha-Cryptoxanthin [15)] - beta-Cryptoxanthin [3) 8) 9) 11) 12)] - Luteoxanthin [11)] - Flavoxanthin [13)] - Rubixanthin [15)] - Violaxanthin [15)]	Beet[1)], Tomato[2)], Italian sweet red pepper[3)], Red radish[4)], Cranberry[5)], Red sweet potato[6)], Strawberry[7)], Red raspberry[8)], Watermelon[9)], Red grapefruit[10)], Red apples[11)], Prickly pear[12)], Plum[13)], Redcurrant[14)], Fig[15)], Adzuki bean[16)]

Table 1. *Cont.*

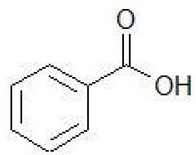
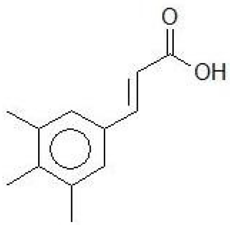
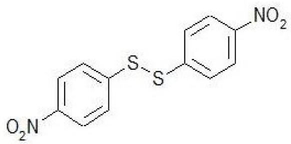
Major Phenolic Acid Classes	Structure	Family Members	Dietary Sources
Hydroxybenzoic acids		- Benzoic acid [3) 7)] - 3-Hydroxybenzoic acid [3)] - 4-Hydroxybenzoic acid [1) 3) 4) 5) 6) 7) 11) 12)] - 2,3-Dihydroxybenzoic acid [3)] - 2,4-Dihydroxybenzoic acid [3)] - 2,4,6-Trihydroxybenzoic acid [9)] - 6-O-Benzoyl-alpha-D-glucose [3)] - Salicylates [1) 7)] - Ethyl salicylate [2)] - Methyl salicylate [11)] - Salicylic acid [1) 3) 5) 6) 7) 8) 11)] - Syringic acid [1)] - Gentisic acid [7)] - Gallic acid [6) 7) 10)] - Phthalic acid [5)] - Vanillic acid [1) 3) 4) 5) 6) 7)]	Beet[1)], Tomato[2)], Cranberry[3)], Strawberry[4)], Red raspberry[5)], Red grapefruit[6)], Red apples[7)], Plum[8)], Red onion[9)], Radicchio (Red chicory)[10)], Redcurrant[11)], Red huckleberry[12)]
Hydroxycinnamic acids		- Caffeic acid [1) 4) 5) 6) 7) 8) 9) 10) 11) 12) 14) 16) 17)] - 1-O-Caffeoylglucose [7) 15)] - p-Coumaric acid [1) 4) 5) 7) 8) 10) 11) 12) 15) 16) 17)] - trans-p-Coumaric acid [11)] - 1-O-p-Coumaroyl-beta-D-glucose [3) 7) 15)] - Cinnamic acid [15)] - Hydroxycinnamic acid [8) 11)] - Ferulic acid [1) 4) 5) 10) 11) 12) 16) 17)] - Diferuloylputrescine [2)] - trans-Sinapic acid [4) 5) 10) 11)] - (3b,5a,6b,22a,25R)-Furostane-22-methoxy-3,6,26-triol 3-[glucosyl-(1- > 2)-[xylosyl-(1- > 3)]-glucosyl-(1- > 4)-galactoside] 26-glucoside [13)]	Beet[1)], Tomato[2)], Italian sweet red pepper[3)], Red radish[4)], Cranberry[5)], Red sweet potato[6)], Strawberry[7)], Red raspberry[8)], Watermelon[9)], Red grapefruit[10)], Red apples[11)], Plum[12)], Red onion[13)], Radicchio (Red chicory)[14)], Redcurrant[15)], Red huckleberry[16)], Fig[17)]

Table 1. *Cont.*

Major Organosulfur Compound Classes	Structure	Family Members	Dietary Sources
Organosulfur compounds		- Indole [4)] - 1H-Indole-3-acetic acid [2)] - 1H-Indole-3-carboxaldehyde [1)] - Cycloalliin [3)]	Tomato[1)], Red radish[2)], Red onion[3)], Fig[4)]

Identical superscript numbers in dietary sources and family members column represents pairs.

Table 2. Biological activities of red-colored food-derived flavonols, flavones, flavanols, and flavanones.

The First Author (Publication Year)	Study Design	Duration	Intervention	Control	Participants	Mean Age	Main Outcome
Koutsos, Athanasios, et al. (2020) [20]	Double-blind, randomized, placebo-controlled, crossover	8 weeks	2 apples/d (340 g without core) (n = 40)	Sugar-and energy-matched apple control beverage (n = 40)	29–69 years old, with BMI 19–33 kg/m^2 and TC > 5.2 mmol/L (mildly hypercholesterolemic)	51.0 ± 11.0	Total cholesterol (TC) ↓ Low-density lipoprotein (LDL) ↓ Triacylglycerol ↓ Intercellular adhesion molecule 1 (ICAM-1) ↓
Chai, Sheau C., et al. (2012) [21]	Randomized, placebo-controlled	12 months	Dried apple (75 g/day) (n = 45)	Placebo (n = 55)	Postmenopausal women (1 to 10 years past menopause)	56.6 ± 4.5	Atherogenic cholesterol levels ↓
Asgary, Sedigheh, et al. (2016) [22]	Assessor-blind, randomized, placebo-controlled, crossover	4 weeks	Beetroot juice 250 mL (n = 12)	Cooked beet 250 g (n = 12)	25–68 years old, SBP 130–139 mm Hg or DBP 85–89 mm Hg	52.8 ± 5.8	High-sensitivity C-reactive protein (hs-CRP) ↓ Tumor necrosis factor-alpha (TNF-α) ↓ Flow-mediated dilation (FMD) ↑ Total antioxidant capacity ↑ High-density lipoprotein (HDL) cholesterol ↑ Low-density lipoprotein (LDL) cholesterol ↓ Total cholesterol (TC) ↓
Moazzen, Hossein, and Mohammad Alizadeh. (2017) [23]	Double-blind, randomized, placebo-controlled, crossover	acute	500 mL of pure pomegranate juice (n = 31)	Placebo (n = 31)	18–70 years old, having at least three out of five components of metabolic syndrome	51.6 ± 10.0	High-sensitivity C-reactive protein (hs-CRP) ↓ Systolic blood pressure ↓ Diastolic blood pressure ↓
Ebrahimi-Mamaghani, Mehranghiz, et al. (2014) [24]	Single-blind, randomized, placebo-controlled, parallel	8 weeks	Red onion 2 × 40–50 g/day for overweight/2 × 50–60 g/day for obese (n = 27)	2 × 10–15 g/day (n = 27)	17–37 years old, BMI between 25 and 40 kg/m^2, low intake (< 93 g) of liliaceous vegetables	26.6 ± 5.8	Low-density lipoprotein (LDL) cholesterol ↓ Total cholesterol (TC) ↓
Dow, Caitlin A., et al. (2012) [25]	Randomized, placebo controlled, parallel	6 weeks	Grapefruit with each meal (3 x daily) (n = 42)	Placebo (n = 32)	Overweight and obese men and premenopausal women	41.2 ± 11.0	Systolic blood pressure ↓ Low-density lipoprotein (LDL) cholesterol ↓ Total cholesterol (TC) ↓

Table 3. Biological activities of red-colored food-derived anthocyanins.

The First Author (Publication Year)	Study Design	Duration	Intervention	Control	Participants	Mean Age	Main Outcome
Basu, Arpita, et al. (2011) [26]	Double-blind, randomized, placebo-controlled	8 weeks	Cranberry juice (480 mL/day) (n = 36)	Placebo (480 mL/day)	Metabolic syndrome	52.0 ± 8.0	Plasma antioxidant capacity ↑ Oxidized-low-density lipoprotein (Ox-LDL) ↓ Malondialdehyde (MDA) ↓

Table 3. *Cont.*

The First Author (Publication Year)	Study Design	Duration	Intervention	Control	Participants	Mean Age	Main Outcome
Novotny, Janet A., et al. (2015) [27]	Double-blind, randomized, placebo-controlled, parallel	8 weeks	Cranberry juice (240 mL) (n = 30)	Placebo (n = 30)	25–65 years of age with a BMI between 20 and 38 kg/m^2	50.6 ± 1.2	Diastolic blood pressure ↓ Fasting plasma glucose ↓
Richter, Chesney K., et al. (2021) [28]	Double-blind, randomized, placebo-controlled, parallel	12 weeks	Cranberry juice (500 mL/d) (n = 30)	Placebo juice (n = 30)	Middle-aged adults with overweight/obesity	49.8 ± 1.3	24-h diastolic ambulatory blood pressure ↓
Aboo Bakkar, Zainie, et al. (2019) [29]	Double-blind, randomized, placebo-controlled, crossover	4 weeks	1.7 g freeze-dried cherry (235 mg/day anthocyanins) (n = 12)	Placebo (n = 12)	Nonsmokers, with no known history of disease	52.8 ± 5.8	Flow-mediated dilation (FMD) response ↑ Plasma nitrate and nitrite ↑ Plasma peroxiredoxin concentration ↑
Johnson, Sarah A., et al. (2020) [30]	Single-blind, randomized, placebo-controlled, parallel	12 weeks	Cherry juice 240 mL (n = 9)	Isocaloric placebo-control drink (n = 10)	20–60 years of age with MetS	29.3 ± 1.1 (cherry) 44.2 ± 4.1 (control)	Total cholesterol ↓ Oxidized-low-density lipoprotein (Ox-LDL) ↓ Vascular cell adhesion protein 1 (VCAM-1) ↓
Kent, Katherine, et al. (2016) [31]	A pilot crossover study	acute	Cherry juice 100 mL × 3 (0, 1, 2 h) (n = 13)	Cherry juice 300 mL (0 h) (n = 13)	Young (18–35 years of age) and older adults (55 + years of age)	21.8 ± 0.9 (young) 77.5 ± 6.2 (older)	Systolic blood pressure ↓ (cherry juice 300 mL) Diastolic blood pressure ↓ (cherry juice 300 mL) Heart rate ↓ (cherry juice 300 mL)
Keane, Karen M., et al. (2016) [32]	Double-blind, randomized, placebo-controlled, crossover	acute	60 mL dose of Cherry juice (n = 15)	Placebo (n = 15)	Early hypertension (systolic blood pressure (SBP) ≥ 130 mm Hg, diastolic blood pressure ≥80 mm Hg, or both)	31.0 ± 9.0	Systolic blood pressure ↓
Desai, Terun, Michael Roberts, and Lindsay Bottoms (2021) [33]	Single-blind, randomized, placebo-controlled, crossover	7 days	Cherry juice (n = 12)	Placebo (n = 12)	Metabolic syndrome	50.0 ± 10.0	Systolic blood pressure ↓ Diastolic blood pressure ↓ Glucose ↓ Total cholesterol ↓Low-density lipoprotein (LDL)-cholesterol ↓
Basu, Arpita, et al. (2010) [34]	Randomized, placebo-controlled	8 weeks	2 cups strawberry beverage + 2 cups of water a day (50 g freeze-dried strawberries) (n = 12)	4 cups of water a day (n = 15)	Metabolic syndrome	47.0 ± 3.0	Total cholesterol ↓ Low-density lipoprotein (LDL)-cholesterol ↓ Vascular cell adhesion protein 1 (VCAM-1) ↓
Basu, Arpita, et al. (2021) [35]	Double-blind, randomized, placebo-controlled, crossover	14 weeks	32 g strawberry powder/day (n = 33)	Placebo (n = 33)	Metabolic syndrome	53.0 ± 10.0	Insulin ↓ Lipid article profiles ↓ Serum PAI-1 ↓

Table 4. Biological activities of red-colored food-derived carotenoids.

The First Author (Publication Year)	Study Design	Duration	Intervention	Control	Participants	Mean Age	Main Outcome
Colmán-Martínez, Mariel, et al. (2017) [36]	An open, prospective, randomized, placebo-controlled, crossover	4 weeks	Tomato juice (n = 28)	Water (n = 28)	High cardio-vascular risk	69.7 ± 3.1	Intercellular adhesion molecule 1 (ICAM-1) ↓ Vascular cell adhesion protein 1 (VCAM-1) ↓
Ferro, Yvelise, et al. (2021) [37]	Crossover study	6 weeks	Tomato sauce 150 mL/day (Carotenoids 3.5 mg/g) (n = 61)	Sterol-enriched yogurt (n = 91)	Between 30 and 45 years of age and BMIs between 19 and 22 kg/m^2	54.0 ± 11.0	Low-density lipoprotein (LDL)-cholesterol ↓
Wolak, Talia, et al. (2019) [38]	Double-blind, randomized, placebo-controlled	8 weeks	Tomato nutrient complex (30 mg lycopene) (n = 12)	Placebo (n = 12)	Hypertensive subjects	52.4 ± 8.2	Systolic blood pressure ↓
Xaplanteris, Panagiotis, et al. (2012) [39]	Single-blind, randomized, placebo-controlled, crossover	14 days	70 g tomato paste (n = 19)	Placebo (n = 19)	Young, healthy volunteers	39.0 ± 13.0	Flow-mediated dilation (FMD) response ↑
Ghavipour, Mahsa, et al. (2013) [40]	Double-blind, randomized, placebo-controlled	20 days	330 mL/d of tomato juice (n = 53)	Water (n = 53)	Overweight and obese females	23.3 ± 0.5	TNF-α ↓ IL-8 ↓
Ellis, Amy C., et al. (2021) [41]	Double-blind, randomized, placebo-controlled, crossover	4 weeks	Watermelon juice (n = 9)	Placebo (n = 8)	Postmenopausal women 55–70 years of age with BMI < 30 kg/m^2 (non-obese)	60.0 ± 4.3	Serum glucose ↓
Lum, Tiffany, et al. (2019) [42]	Crossover	4 weeks	Watermelon (2 cups) (n = 33)	Isocaloric low-fat cookies (n = 33)	55–70 years of age with overweight or obese subjects	-	Systolic blood pressure ↓
Shanely, R. Andrew, et al. (2020) [43]	Randomized, placebo-controlled	6 weeks	710 mL of Water-melon/day (n = 26)	Placebo (n = 19)	50–75 years of age with Overweight and obese post-menopausal women	59.8 ± 0.87	Soluble vascular cell adhesion molecule-1 ↓

Table 5. Biological activities of other red-colored food-derived compounds.

The First Author (Publication Year)	Study Design	Duration	Intervention	Control	Participants	Mean Age	Main Outcome
Abubakar, Salisu M., et al. (2019) [44]	Single-blind, randomized, placebo-controlled, crossover	acute	250 mL of the aqueous extract of hibiscus with a high-fat meal (*n* = 25)	Placebo (*n* = 25)	1% to 10% cardiovascular disease risk in 10 years	49.0 ± 2.0	% FMD ↑ Serum glucose ↓ Plasma insulin ↓ Serum triacylglycerol ↓ C-reactive protein (CRP) ↓
Takemura, Shigeki, et al. (2014) [45]	Double-blind, randomized, placebo-controlled	12 weeks	800 mg plum capsule (4 capsule/day) (*n* = 15)	Placebo (*n* = 15)	Normal-high BP or hypertension level 1	43.3 ± 12.9	Diastolic blood pressure ↓

2.1. Biological Activities of Flavonoids

A great variety of flavonoids are widely distributed in vegetables [46]. In general, flavonoids are classified as flavonols, flavones, flavanols, flavanones, anthocyanins, isoflavones, and chalcones, according to their structure, based on the C6-C3-C6 carbon skeleton that combines two 6-carbon benzene rings with 3-carbons of the heterocyclic ring [47]. One of the major subgroups that commonly occurs in vegetables is flavonoids of the flavonol type, including kaempferol, quercetin, and myricetin. Quercetin and other flavonoids exist as glycosides in vegetables [48]. Flavonoids are highly abundant as vegetable natural products and vary in their therapeutic benefits and biological activity [49]. In recent decades, many studies have been conducted to explain the mechanisms associated with flavonoid biosynthesis in plants. Several intervention studies about the biological activities of flavonoids are summarized in Tables 2 and 3.

2.1.1. Flavonols, Flavones, Flavanols, and Flavanones

A flavonol is a flavonoid metabolite that is hydroxylated at the C-3 position of the heterocyclic ring [50]. Flavonols are widely present in vegetables, fruits, and grains. They are generally present as an aglycon-based glycoside such as kaempferol, quercetin, myricetin, isorhamnetin, and rhamnetin [51]. Common flavonols and aglycones have a minimum of 279 and 347 different glycosidic combinations, respectively [52]. Among them, quercetin 3-*O*-glycosides such as isoquercitrin, quercitrin, and rutin are categorized as representatives of the flavonol family, one of the subclasses of flavonoid compounds, and are the most abundant flavonols [53]. In particular, they are frequently found in cranberry, strawberry, apple, kale, and red pepper [51].

Compared with flavonols, flavone-containing plants are limited. The main flavones in edible plants are glycosides of apigenin, luteolin, and diosmetin [51]. Flavones are structurally very similar to flavonols, and there are few hydroxyl groups at the C-3 position. Flavones have three functional groups: hydroxy, carbonyl, and conjugated double bonds. Thus, flavones show a characteristic reaction of the three functional groups [54].

Flavanols have no double bond between C-2 and C-3 and no carbonyl at C-4 in the heterocyclic ring. Therefore, there are two chiral centers (C-2 and C-3) that result in four isomeric structures for each flavan-3-ol molecule. Common examples of flavanols are catechin (*trans*) and epicatechin (*cis*), which exist in two isomeric forms. (+)-catechin and (−)-epicatechin are often found in food plants [55]. Skins of grapes, apples, and blueberries are also rich in flavanols [56,57]. Unlike other flavonoids, flavanols are not glycosylated in food [58]. Catechin and epicatechin can easily condense into oligomeric procyanidins, which produce anthocyanidins under aqueous acidic conditions with heating [59,60].

Flavanones are widely distributed in approximately 42 larger plants. In particular, they are found in the Compositae, Leguminosae, and Rutaceae. Heterocyclic flavanones also contain a ketone group, but there is no unsaturated carbon-carbon bond [61]. Flavanones, called dihydroflavones, lack the double bond between C-2 and C-3 in the heterocyclic ring of the flavonoid skeleton, which is present in flavones and flavonols, and flavanone is found in high concentrations in citrus fruits. They are also found in tomatoes and aromatic plants, but their main sources are citrus fruits, especially grapefruit. Flavanones naturally exist in the form of aglycon and glycoside, while the major aglycones are naringenin in grapefruit and hesperetin in oranges [62].

In many studies, the therapeutic effects of red beetroot have been shown under a variety of conditions, including complications associated with metabolic syndrome [63]. One of the main mechanisms by which flavonols can reduce cardiovascular risk is their vasodilatory and antihypertensive effects [64]. The data suggest improvements in endothelial function, an effect that would also be expected to reduce the risk of hypertension and the development of atherosclerosis. One study examined the blood pressure-lowering effects of 0, 100, or 200 mg red raspberry extracts/(kg·d) in normal and spontaneously hypertensive rats. After 5 weeks, the red raspberry extracts demonstrated a dose-dependent antihypertensive effect in spontaneously hypertensive rats, effects that coincided with an increase in nitrogen oxide (NO) activation, a decrease in vasoconstrictive endothelin-1, dose-specific antioxidative actions, and improved vascular endothelial dysfunction [65]. It is well-known that in endothelial cells, NO plays an important role in regulating vascular relaxation and blood pressure [66].

In general, apple flavonoids may have beneficial effects on blood pressure, vascular function, and blood lipid levels. Moreover, plum juice consumption modulates a cluster of pathways that are deregulated in obesity and prevents obesity-associated metabolic disorders and the increased risk for cardiovascular disease. Koutsos, Athanasios, et al. [20] showed the beneficial hypocholesterolemic and vascular effects of the daily consumption of apples by mildly hypercholesterolemic individuals. Flavonoid-rich beetroot was effective in improving blood pressure, endothelial function, and systemic inflammation, and raw beetroot juice had greater antihypertensive effects than cooked beet [22]. In a study by Moazzen, Hossein, and Mohammad Alizadeh [23], pomegranate juice supplementation was shown to lower the levels of systolic and diastolic blood pressure in patients with metabolic syndrome as well as blood levels of hs-CRP. Consumption of raw red onion, which is rich in quercetin, significantly decreased total cholesterol levels in women with polycystic ovary syndrome [24]. The many beneficial effects of flavonoids include the ability to interfere with lipid metabolism, reduce platelet adhesion, and enhance endothelial function.

2.1.2. Anthocyanins

Anthocyanins are one of the most commonly used water-soluble phenolic compounds and principally represent natural pigments from red to purple. Anthocyanin is found in various tissues of plants, such as flowers, fruits, stems, and roots, and has proven to be protective against many cardiovascular risk factors [67,68].

Most types of anthocyanins are based on cyanidin, delphinidin, and pelargonidin along with methylation, methoxylation, hydroxylation, and glycosylation. The most important physical parameter of anthocyanins is color, which depends on pH. They turn red under acidic conditions and blue under basic conditions. The degree of hydroxylation, methylation and glycosylation also affects color [69,70].

In particular, berries such as cranberry, strawberry, and red raspberry are good sources of anthocyanins, and red apple, red currant, cherry, and plum are also rich in anthocyanidins [71]. Cranberry flavonoids may have several distinct effects on the development of atherosclerosis. Monomers and oligomer flavonoids, for example, can be absorbed and metabolized and have postabsorptive effects on the development of atherosclerosis and cardiovascular diseases such as LDL protection against oxidation by arterial endothelial cells, arterial smooth muscle cells, and intimal macrophages; inhibition of the inflammatory response of these cells to modified LDL and direct effects on immune cells involved in the inflammatory process; vasodilation and improved blood flow; and inhibition of platelet aggregation and thrombosis [72].

Additionally, Basu, Arpita, et al. [26] revealed that cranberry reduces lipid oxidation and increases plasma antioxidant capacity in women with metabolic syndrome, and Novotny, Janet A., et al. [27] showed that cranberry improved several risk factors for cardiovascular disease in adults, including circulating triglycerides, CRP, glucose, insulin resistance, and diastolic blood pressure.

Numerous in vitro and in vivo studies have suggested that strawberry supplementation reduces the risk of CVDs. In other animal models (obese and lean C57BL/6 mice), strawberry supplementation decreased overall blood glucose concentrations independent of the content of dietary fat and reduced plasma CRP, supporting a potential protective effect against cardiovascular risk.

Intervention studies have reported many cardiometabolic disease outcomes affected by cherry. Aboo Bakkar, Zainie, et al. [29], Johnson, Sarah A., et al. [30], Kent, Katherine, et al. [31], and Keane, Karen M., et al. [32] showed significantly lower levels of blood pressure, lipid-related markers, and adhesion molecules and evidence of cardiovascular-related outcomes (FMD, nitrate and nitrite, PRX1) after consumption of cherry. Short-term strawberry supplements improved the risk factors for selected atherosclerosis, including dyslipidemia and adhesion molecules in subjects with metabolic syndrome [34].

2.1.3. Isoflavones

Isoflavones are mainly distributed in legume plants, with phenol rings attached to the C-3 and C-4 positions of the heterocyclic ring [51,52]. Genistein, daidzein, glycitein, biochanin A, and formononetin are different isoflavones found in soy, red clover, and cherry. They generally exist as glycosides in plants. Chalcones have different structures than other flavonoids. C-3 is an open ring and is mainly found in apples and hops [56].

Betavulgarin in beet and genistein in cherry are classified as isoflavonoids. The cardioprotective effects of beetroot are from the combination of nitrate/nitrite and bioactive compounds that limit the production of free radicals and regulate gene expression. In vitro and in vivo studies and clinical trials have shown that beets and their bioactive phytochemicals are promising in the development of new adjuvant therapies to improve cardiovascular diseases [73,74].

2.2. Biological Activities of Carotenoids

Carotenoids are a natural pigment found in plants and microorganisms, but they are not synthesized in animals [75,76]. These are micro components of fruits and vegetables which contribute to the inverse relationship between fruit and vegetable consumption and the risk of cardiovascular disease, cancer, and other metabolic diseases [77,78]. As substantial dietary sources of vitamin A, they have excellent antioxidant properties [77]. In plants, carotenoids, along with chlorophyll, are essential pigments for photosynthetic organs and are responsible for the yellow, orange, red and purple colors of fruits and vegetables [79].

More than 600 carotenoids have been identified in nature, of which approximately 40 are present in a typical human diet, and approximately 20 have been identified in blood and tissues. ß-Carotene, α-carotene, lycopene, β-cryptoxanthin, and lutein account for more than 90% of the carotenoids in humans [80]. All carotenoids have certain common chemical features, such as a polyisoprenoid structure, the long conjugated chain of double bonds at the center of the molecules, and almost bilateral symmetry around the central double bond [81]. Carotenoids are rich in conjugated double bonds and may undergo cis-trans isomerization. The variant is more stable and is the most common form in food [78].

Tomatoes, in particular, contain many carotenoids. Watermelon contains the carotenoids lycopene and lutein. Additionally, beet, Italian sweet red pepper, red radish, cranberry, red raspberry, red sweet potato, strawberry, apple, and fig contain carotenoids. Several studies have elucidated the cardiovascular effect of tomatoes, as shown in Table 4. In studies by Colmán-Martínez, Mariel, et al. [36] and Ferro, Yvelise, et al. [37], participants at cardiovascular risk were treated with tomato, which contains lycopene and carotene, in a crossover design. Systolic blood pressure and adhesion molecules were significantly lower in the treatment group than in the placebo group. Another double-blind, randomized, placebo-controlled study [38] found that the tomato nutrient complex is effective in maintaining normal blood pressure in untreated hypertensive individuals. Daily tomato paste consumption exerts a beneficial effect on endothelial function [39] and reduces the risk of inflammatory diseases such as CVDs and diabetes, which are associated with obesity [40].

Carotenoid is a regulator of free radicals and NOS, so antioxidant and anti-inflammatory activity can help cardiovascular risk factors such as inflammation, high lipid levels, high blood pressure, insulin resistance, and obesity. As a result, the reduction in blood pressure levels and inflammation, as well as the improvement of lipid profiles, can lead to cardiovascular health benefits [82]. Since carotenoids have hydrophobic characteristics, interactions with carotenoids and free radicals occur in cell membranes and lipoprotein components in a lipophilic environment [83].

2.3. Biological Activities of Other Compounds (Organosulfur Compounds, Phenolic Acids)

Phenolic acids are widely distributed in almost all fruits [84]. There are two types of phenolic acids as derivatives of benzoic acid and derivatives of cinnamic acid. Benzoic acid derivatives have a C1-C6 skeleton, while cinnamic acid derivatives have a C3-C6 backbone [85,86]. The most common hydroxybenzoic acids are *p*-hydroxybenzoic acid, vanillic acid, and syringic acid, whereas *p*-coumaric, caffeic, ferulic, and sinapic acids are the common hydroxycinnamic acids in fruit [87]. For example, they exist in complex structures such as hydrolyzable tannin, gallotannins of mango, and ellagitannins of red fruits such as strawberries, raspberries, and blackberries [88].

In fruits, vegetables, and grains, phenolic acids are distributed throughout the plant, including the seeds, roots, and stems. Most of these compounds are linked and hydrolyzed with structural components of plants (cellulose, proteins, and lignin), larger polyphenols (flavonoids), smaller organic molecules (glucose, quinic, maleic, or tartaric acid), or other natural products (terpenes) through acetal bonds and can be hydrolyzed upon acid or alkaline hydrolysis or by enzymes [52].

Folic acid, which is abundant in hibiscus, belongs to the class of organic compounds known as methoxyphenols. Methoxyphenols are compounds containing a methoxy group attached to the benzene ring of a phenol moiety. Additionally, gallic acid, 3-O-methylgallic acid, 4-O-methylgallic acid, and hippuric acid are the main phenolic metabolites detected in hibiscus. Hibiscus extract improves postprandial vascular function and reduces endothelial dysfunction and cardiovascular risk [44].

3. Conclusions and Future Perspectives

Modern nutritional science explains the diversity of ingredients and mechanisms in which foods affect health. Regarding the chemical composition of food, many bioactive compounds present in plants, fruits, and vegetables are currently known. Biologically active compounds from food play a substantial role in preventing diseases. Such compounds are related to the essential aspects of the health benefits of food, and potentially valuable compounds such as isoflavone, and phytochemicals are used as effective preventive strategies for the occurrence of various human cardiovascular diseases, diabetes, and metabolic disorders [89].

Red fruits and vegetables have positive beneficial effects on the human body. Various fruits, such as berries, cherries, apples, watermelons, and tomatoes, are related to heart health improvement. Various ingredients in red foods can help reduce basic irritation and strengthen health status by reducing disease. These factors not only help to fight inflammation but also improve body function [19].

Numerous in vitro, in vivo, and clinical studies support the multifarious beneficial effects of red-colored food on several risk factors and pathways associated with cardiometabolic diseases. In several animal experiments and intervention studies, the administration of bioactive compounds of red food exhibited vasorelaxation effects and reduced blood pressure with the regulation of lipid levels with evidence for both direct and indirect mechanisms. Overall, increasing evidence supports the significant cardiometabolic benefits of red-colored foods rich in flavonoids, carotenoids, and other phenolics. Since nutritional intake is important for cardiovascular and metabolic health, these results support the need for further active research on the relevant ingredients, biological mechanisms, and clinical effects of food [90].

In conclusion, there are numerous benefits to eating plant-based foods, especially red fruits and vegetables. Ensuring the consumption of red foods will enable the individual to reduce the development of cardiovascular diseases and metabolic diseases. Phytochemicals in red foods may help to offset an increased risk of chronic disease.

Supplementary Materials: The following supporting information can be downloaded at: https://www.mdpi.com/article/10.3390/app12041786/s1, Supplementary File S1: Red colored food.

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