Nutraceuticals for Cardiovascular Health:

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Abstract

Cardiovascular diseases (CVDs) remain the leading cause of morbidity and mortality worldwide. Increasing scientific interest has focused on nutraceuticals—bioactive compounds derived from foods—as potential preventive and therapeutic agents in cardiovascular health. This review summarizes evidence on key nutraceuticals including omega-3 fatty acids, polyphenols, plant sterols, dietary fibers, coenzyme Q10, and vitamins with demonstrated cardioprotective effects. Their mechanisms of action involve modulation of lipid metabolism, reduction of oxidative stress, anti-inflammatory pathways, endothelial protection, and improvement of blood pressure control. While nutraceuticals show promising benefits, their use should complement, and not replace, conventional therapies. More clinical trials are needed to support efficacy, safety, and dosing guidelines.

Introduction

Cardiovascular diseases (CVDs) such as coronary artery disease, hypertension, and stroke account for nearly one-third of global deaths. Poor diet, oxidative stress, inflammation, dyslipidemia, diabetes, and sedentary lifestyle are major contributors. Nutraceuticals—defined as foods or food-derived products offering medical or health benefits—have emerged as important adjuncts in CVD prevention and management. Nutraceuticals are defined as food-derived products with health benefits, including disease prevention and therapy. Due to their natural origin, lower side-effect profile, and physiological relevance, nutraceuticals are increasingly incorporated in cardiovascular care

Nutraceuticals

The term "nutraceuticals" was introduced by Stephen De Felice, founder and chairman of the Foundation for Innovation in Medicine, in 1989. A nutraceutical is defined as a "food, or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease" (7). The definition encompasses medicinal products made from natural ingredients. Several classes of nutraceuticals have been proposed to have potential benefits in the treatment of CVD and the ones with the strongest evidence

Growing evidence suggests that certain nutraceuticals can:

- Improve lipid profiles
- Reduce blood pressure
- Enhance endothelial function
- Lower oxidative stress and inflammation
- Provide anti-atherosclerotic effects

Key Nutraceuticals for Cardiovascular Health

The recently coined term "nutriceutical" is enjoying increasing popularity for describing a variety of nonprescription products that are used to enhance health. There are several interpretations (and variant spellings) of the term, but it is best reserved to describe products that are (1) naturally occurring substances (e.g., vitamins, amino acids, herbals) or formulations of these substances; (2) based on a strong scientific foundation; and (3) supported by clinical trials of their utility. Nutriceutical is a useful term for a physician to know because it is appearing more frequently in the lay press. However, this term has no legal standing. The US Food and Drug Administration (FDA) recognizes drugs, medical foods, dietary supplements, and food additives as distinct regulatory categories. Most "nutriceuticals" are dietary supplements, although a smaller percentage are medical foods and food additives. Cardiovascular nutriceuticals are agents in this category that have been shown to enhance cardiovascular health. For example, cardiovascular nutriceuticals may stimulate increased release of nitric oxide, block the production or enhance the degradation of superoxide anion, or have beneficial effects in preventing the oxidation of lipoproteins. The nutriceuticals to be discussed in this brief review include vitamin E, vitamin C, coenzyme Q10, carotenoids (beta carotene, lycopene), flavonoids, and l-arginine (Table I).

Vitamin E

A lipid-phase antioxidant, vitamin E (α-tocopherol) protects tissue lipids from attack by oxygen free radicals.1 This extensively investigated antioxidant vitamin increases resistance to lipid peroxidation and reverses endothelial vasodilator dysfunction. Several major studies have demonstrated the cardioprotective benefits of supplemental intake of vitamin E: (1) Cholesterol Lowering Atherosclerosis Study (CLAS)2—men who took ≥100 IU per day of supplementary vitamin E had less progression of coronary artery lesions than did men whose supplementary intake of vitamin E was <100 IU per day; (2) Atherosclerosis Risk in Communities Study (ARIC)3—use of vitamin E slowed the progression of atherosclerosis, measured by intima–media thickness of the carotid artery wall, in both men (nonsignificant difference, $p = 0.13$) and women (significant difference, $p = 0.033$) >55 years old; and (3) Cambridge Heart Antioxidant Study (CHAOS)4—doses of 400–800 IU of vitamin E decreased the relative risks of nonfatal myocardial infarction by 77% in patients with coronary atherosclerosis.

Vitamin C:

The major aqueous-phase antioxidant, vitamin C (ascorbate) traps peroxyl radicals in the aqueous phase before they can initiate lipid peroxidation.1 Vitamin C enhances the activity of vitamin E,1, 5 and it improves and normalizes endothelial vasodilator function in patients with chronic heart failure by increasing the availability of the potent vasodilator nitric oxide.6, 7 Improved endothelial function with vitamin C has also been observed in patients with hypertension, hypercholesterolemia, and diabetes mellitus.6, 7, 8

As was the case with vitamin E, the ARIC study found that vitamin C slowed the progression of atherosclerosis in men and women >55 years old.3 However, the CLAS study did not show any cardiovascular benefit with high intake of supplementary vitamin C.2

Coenzyme Q10:

The lipid-phase antioxidant coenzyme Q10 is a free radical scavenger that regenerates vitamin E.1 It inhibits the oxidation of low-density lipoprotein. In both animal and human models, coenzyme Q10 protects left ventricular function from ischemia reperfusion injury,9 apparently through its antioxidant properties.9 The synthesis of coenzyme Q10 is inhibited by 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase inhibitors ("statins"). At the present time, although it is a fairly popular (yet expensive) dietary supplement, there are insufficient clinical data to recommend the use of coenzyme Q10 as a cardiovascular agent.

Table I. Potential Cardiovascular Benefits of Nutriceuticalslegend

Nutriceutical	Potential Benefit	Cautions
Vitamin E	↓ progression of CAD in M (CLAS)	
	↓ progression of atherosclerosis, M/W >55 yr (ARIC)	
	↓ risk of nonfatal MI (CHAOS)	
Vitamin C	↓ progression of atherosclerosis, M/W >55 yr (ARIC)	
Coenzyme Q10	Protects LV function from ischemic perfusion injury	Synthesis inhibited by HMG-CoA reductase inhibitors
Beta carotene	↓ risk of CAD (SHHS; NHS; HPFS)	↑ risk of lung cancer among smokers (CARET; ATBC) ↑ ischemic heart disease mortality (ATBC)
Lycopene	↓ risk of MI (EURAMIC)	
Flavonoids	↓ CAD mortality (ZES)	
	↓ CAD mortality in men with previous CAD (HPS)	

Soybean products	Genistein inhibits thrombus formation	
Red wine	Quercetin may contribute to cardioprotective effect	
Blueberries	Potential cardioprotective effect on LDL	
Licorice root	Potent antioxidant	High intake can cause hypokalemia and hypermineralcorticoidism
l-Arginine	↑ Coronary and peripheral blood flow27, 28, 29	No convenient capsule formulation available
	↓ Angina and intermittent claudication24, 25	
	Mild antiplatelet effect	

legend

ARIC = Atherosclerosis Risk in Communities study; ATBC = Alpha-Tocopherol, Beta-Carotene cancer prevention study; CAD = coronary artery disease;CARET = Carotene and Retinol Efficacy Trial; CHAOS = Cambridge Heart Antioxidant Study; CLAS = Cholesterol Lowering Atherosclerosis Study; EURAMIC = European Community Multicenter Study on Antioxidants, Myocardial Infarction and Breast Cancer; HMG-CoA = 3-hydroxy-methylglutaryl coenzyme A; HPFS = Health Professionals Follow-up Study; HPS = Health Professionals Study; LDL = low-density lipoprotein; LV = left ventricular; M = men; MI = myocardial infarction; NHS = Nurses' Health Study; SHHS = Scottish Heart Health Study; W = women; ZES = Zutphen Elderly Study.

Carotenoids

There have been >600 naturally occurring carotenoids that have been identified. These substances are fat-soluble plant pigments that provide the bright color of various fruits and vegetables.10, 11 They are transported in the body via lipoprotein.11 The singlet oxygen-quenching properties of carotenoids contribute to the prevention of lipid peroxidation.10

Beta carotene

The most ubiquitous and thoroughly studied carotenoid is β carotene.1 The major precursor of vitamin A, β carotene is found in many yellow, orange, and dark green leafy vegetables and in some yellow fruits.12 In the Health Professionals Follow-up Study,5 men in the highest quintile of β carotene intake had a significantly lower risk of coronary artery disease than did those in the lowest quintile of intake. In the Nurses' Health Study,13 women in the highest quintile of intake had a 22% reduction in risk of coronary artery disease compared with those in the lowest quintile.

However, in studies among patients at high risk for lung cancer—Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC) and Carotene and Retinol Efficacy Trial (CARET)—high doses of β carotene correlated with an increased risk of lung cancer.12, 14 Neither of these studies, nor the Physicians' Health Study, showed a protective effect of β carotene on cardiovascular disease.11 Indeed, in ATBC, participants who received β carotene had higher mortality due to ischemic heart disease than did participants who did not receive β carotene.15

Lycopene

The carotenoid lycopene gives tomatoes their red color. Lycopene appears to be a more potent antioxidant than β carotene and may be responsible for many of the cardiovascular attributes originally claimed for β carotene.11 In the European Community Multicenter Study of Antioxidants, Myocardial Infarction, and Cancer of the Breast (EURAMIC),11 high tissue levels of lycopene were associated with a low risk of myocardial infarction. Lycopene also appears to have protective effects against prostatic and gastrointestinal tract cancer.10, 11 In contrast, low intake of lycopene is associated with macular degeneration.10

Flavonoids

There are >4,000 naturally occurring flavonoids found in fruits, vegetables, red wine, and tea, for which they provide color, texture, and taste.5, 16 As free radical scavengers, flavonoids inhibit lipid peroxidation, promote vascular relaxation, and help prevent atherosclerosis.16, 17 Various flavonoids have antihypertensive, antiarrhythmic, anti-inflammatory, and antiallergenic properties.16

A study in the Netherlands, the Zutphen Elderly Study,18 found a strong inverse association between the intake of various flavonoids and coronary artery disease, with a >50% reduction in mortality risk. Similar results were reported in a Finnish study in which participants were followed for 2 years. In the United States, the Health Professionals Study19 found a modest, but not insignificant, inverse association between flavonoid intake and coronary mortality in men with previous coronary heart disease.17

Following is a brief discussion of 4 flavonoid-rich food products that may provide cardioprotective benefits.

Soy bean products

Soy beans are rich in flavonoids, the most prevalent of which, genistein, inhibits thrombus formation.20 Substitution of soy protein for animal protein in human diets decreases the levels of both total cholesterol and low-density lipoprotein cholesterol. The precise contribution of flavonoids to this effect, however, has not been elucidated.20

Red wine

Quercetin, the most common food flavonoid, is found in abundance in red wine.16 It has been suggested that quercetin is responsible for the cardioprotective effect of moderate intake of red wine, although ethanol itself may have cardioprotective attributes.16 The beneficial effects of quercetin that affect the cardiovascular system include inhibition of platelet aggregation and prevention of oxidative modification of low-density lipoprotein, both of which processes are involved in the development of atherosclerotic lesions.

Blueberries

The aqueous extract of *Vaccinium myrtillus* (blueberry) is rich in antioxidants and exerts a potent protective action in preventing the oxidation of low-density lipoprotein. On a molar basis, *Vaccinium myrtillus* appears to be a more potent antioxidant than vitamin C.21

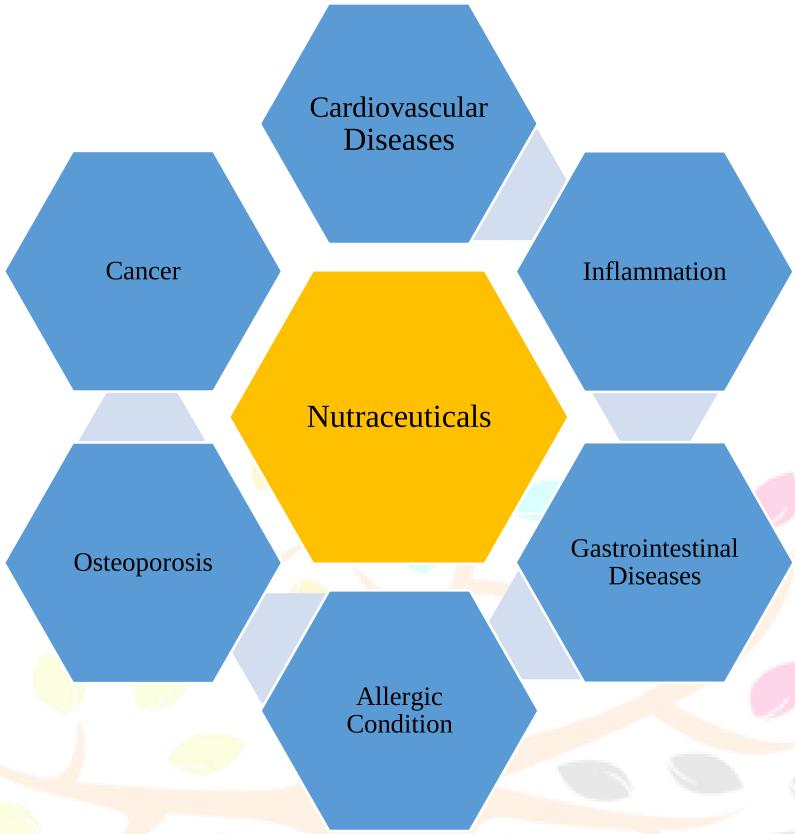
Licorice root

Chinese licorice (*Glycyrrhiza glabra*) has been used for medicinal purposes for 6,000 years. It has antioxidant, antiplatelet, anti-inflammatory, and antiviral properties. However, high intake of glycyrrhizic acid, the predominant flavonoid-containing component of licorice, can cause hypokalemia and hypermineralocorticoidism, which leads to sodium retention and potassium loss, edema, and increased blood pressure.22, 23

l-arginine

Accumulating clinical evidence indicates that this semi-essential amino acid may be useful in patients with cardiovascular disease. l-Arginine appears to exert its beneficial effect via its metabolism to nitric oxide (NO) and citrulline by the enzyme NO synthase.24 NO is the most potent endogenous vasodilator. NO also inhibits key processes involved in atherogenesis, including platelet aggregation, monocyte adherence and infiltration, vascular smooth muscle cell proliferation, and oxidative enzyme activity.25 The NO synthase pathway is impaired in persons with atherosclerotic arterial disease. This appears to be due in part to increased circulating levels of the endogenous NO synthase inhibitor, asymmetric dimethylarginine (ADMA).26 ADMA is a competitive antagonist of NO synthase, and its adverse impact can be overcome by the administration of supplemental l-arginine. Administration of l-arginine can improve coronary and peripheral blood flow in humans.27, 28 A recent Mayo Clinic trial29 revealed that oral supplementation with l-arginine (9 g/day) improved coronary blood flow response to acetylcholine by 150% and significantly decreased angina in patients with coronary artery disease. Because the dosage of l-arginine required to have a beneficial effect is not convenient to take in the form of capsules (e.g., eighteen 500-mg capsules per day were used in the Mayo Clinic study), we have recently developed an l-arginine–enriched nutrient bar (the HeartBar) that may be a palatable way for patients to incorporate this supplement into their diets.

Role of Nutraceuticals in Cardiovascular Prevention:



Primary Prevention

- Nutraceuticals contribute to reducing initial risk of cardiovascular disease by:
- Lowering LDL and total cholesterol (e.g., plant sterols, soluble fiber)
- Reducing blood pressure (e.g., garlic, omega-3 fatty acids)
- Enhancing endothelial function (e.g., polyphenols, vitamins C & E)
- Reducing obesity and insulin resistance (e.g., fiber, green tea extracts)
- Reducing oxidative stress and inflammation

Secondary Prevention

In patients with existing cardiovascular disorders, nutraceuticals help in:

- Improving lipid control when combined with statins (e.g., omega-3, CoQ10)
- Enhancing energy metabolism in heart failure (e.g., CoQ10, L-carnitine)
- Reducing recurrence of cardiac events
- Managing hypertension, diabetes, and metabolic syndrome

Mechanisms of Cardiovascular Protection

Nutraceuticals show benefits through multiple mechanisms:

- **Antioxidant activity**: Reduction of ROS and prevention of LDL oxidation
- **Anti-inflammatory effect**: Downregulation of cytokines
- **Lipid-lowering**: Reduced cholesterol synthesis or absorption
- **Improved endothelial function**: Increased NO availability
- **Antithrombotic action**: Reduced platelet aggregation

Limitations and Future Prospects

- Variability in product quality and composition
- Limited large-scale randomized trials
- Potential interactions with medications
- Need for standardized dosing

Evidence From Research on Phytochemicals and Cardiovascular Health:

Extensive evidence from epidemiological, clinical, and preclinical studies has substantiated the cardiovascular action of phytochemicals (Haines et al. 2024). According to Dwyer et al. (2018), a complete understanding of their therapeutic activity and mechanisms is provided by this multilevel evidence base.

Epidemiological Studies

There is an inverse relationship between phytochemical-rich food intake and cardiovascular disease risk, large cohort studies reveal. The myocardial infarction hazard was 32% lower among the highest percentile anthocyanin food consumers, as revealed by the Nurses' Health Study (Hu et al. 2025; Zhang et al. [2021]) Martínez-González et al. (2019) reported that higher polyphenol consumption was associated with a 46% reduction in cardiovascular mortality in the PREDIMED group. Geographical research has revealed incredible patterns in this regard. Daily intake of red wine polyphenols has been proposed as an explanation for the "French Paradox"– low levels of cardiovascular disease (CVD) in a high population with saturated fat consumption (Haseeb et al. 2017).

Huang et al. (2017) found that Asian populations with high soy isoflavone consumption had a 30%–40% lower age-adjusted CVD mortality rate than Western societies. These findings are supported by recent meta-analyses. Zhang et al. (2021), found that cardiovascular disease-related death was reduced by 10% for each 100 mg/day increment in flavonoid intake. Based on estimates by modeling using dietary consumption data and Asia CVD trends, Chong et al. (2024) estimated that up to 3.2 million Asia preventable annual deaths by 2050 could be averted by the universalization of phytochemical-abundant diets.

Clinical Trials and Human Studies

Evidence from randomized controlled trials can be used to support the benefits of phytochemicals. Cocoa flavonoid supplementation for six months improved endothelial function (FMD by 2.1%) in hypertensive patients, as per the FLAVIUS HEALTH study (Khan et al. 2012). Pagliaro et al. (2015) reported that patients who received purified omega-3 phytochemicals had a 25% reduced risk of cardiovascular mortality following myocardial infarction (MI). Nutraceuticals are the most promising formulations. Within a period of 18 months, a trial by Mohamed et al. (2022) showed that administering 180 mg/day of nanoformulated curcumin reduced the coronary plaque volume by 15%. Furthermore, Guasch-Ferré et al. (2018) discovered that consuming 30–60 g of walnuts per day lowers LDL-C by 0.19 mmol/L. However, several trials have uncovered these limitations. Dwyer et al. (2018) reported that whole-food matrices are significant since the VITAL study found no effect of isolated vitamin E or sea omega-3s on cardiovascular disease. A balanced strategy is essential, since the SELECT study showed the potential harm of supplementing smokers with high levels of β-carotene (Miller and Snyder 2012).

Mechanistic and Preclinical Studies

The fundamental mechanisms have been explained through in vitro and animal studies. Resveratrol increases NO production by endothelial cells threefold as per cell culture experiments, demonstrating that resveratrol stimulates SIRT1 (Haseeb et al. 2017). Quercetin has been reported to reduce inflammation in blood vessels by inhibiting the migration of NF-κB, as per studies done on rats (Boissier et al. 2012). New information was obtained from genomic technologies (Lodi et al. 2025). Metabolomic research has indicated that more than 40% of food polyphenols are converted into bioactive byproducts by the stomach bacteria (Pagliaro et al. 2015). Proteomic investigations have shown that soy isoflavones enhance the heart-protecting expression of 32 proteins, while reducing the expression of 18 atherosclerosis-promoting proteins (Mangano et al. 2013).

New nanotechnology enhances transport. To address atherosclerotic plaques, Pala et al. (2020) designed nanoparticles loaded with phytochemicals, which enhanced bioavailability15 to 200 times. These advances bridge the gap between what is found in the laboratory and what is applied clinically (Mohamed et al. 2022). When used in conjunction with other food components and lifestyle variables, phytochemicals have a multiplicative effect on cardiovascular health (Liu 2013). Epidemiological research, clinical trials, and mechanistic research are ongoing (Haines et al. 2024). Chong et al. (2024) stated that, to optimize the efficacy of phytochemicals in cardiovascular health, future research should focus on personalized approaches that consider genetic, microbiological, and lifestyle heterogeneity. Overall, the best evidence from randomized controlled trials (RCTs) is the cardiovascular effects of polyphenol-rich interventions, especially cocoa and tea-derived flavonoids, to improve endothelial function, lower LDL cholesterol, and lower cardiovascular event risk (Loffredo et al. 2017). Conversely, the activities of purified phytochemicals (e.g., vitamin E and β-carotene) and purified supplements remain inconclusive or even toxic in some populations, such as smokers (Haider et al. 2017). Emerging areas such as nanoformulated phytochemicals, microbiome-mediated metabolism, and gene-phytochemical interactions are promising, but remain extremely speculative and require more human trials for affirmation.

Conclusion

Nutraceuticals play an important complementary role in cardiovascular health by improving lipid metabolism, reducing inflammation, enhancing endothelial function, and decreasing oxidative stress. They offer promising benefits when combined with lifestyle modifications and medical therapy. However, evidence varies among compounds, and clinical recommendations should be individualized. Continued research is essential to establish standardized guidelines for effective use

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