

The Significance of Bioactive Compounds in The Complex Realm of Cardiovascular Complications

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ABSTRACT

Leading cause of morbidity and death globally, Cardiovascular Diseases (CVDs) call for sensible preventive and treatment plans. Recent studies have concentrated on bioactive chemicals originating from natural dietary sources like fruits, vegetables, herbs, and marine resources for their cardioprotective action. Key bioactive substances like flavonoids, polyphenols, omega-3 fatty acids, and phytosterols show notable health advantages by enhancing endothelial function, lowering oxidative stress, controlling inflammation, and so changing lipid metabolism. Notwithstanding encouraging results about their capacity to reduce the risks of hypertension and atherosclerosis, practical application of them still faces difficulties including varied bioavailability, individual response variations, and the necessity of regular dosages. This review emphasizes the need for thorough clinical studies to prove their safety and efficacy as well as the possibilities of bioactive substances as supplementary treatments for improving cardiovascular health.

Keywords: Bioactive compounds, Cardiovascular diseases, Oxidative stress, Health Benefits, Challenges and Opportunities.

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INTRODUCTION

The leading causes of illness and mortality worldwide are Cardiovascular Diseases (CVDs), such as heart failure, hypertension, and coronary artery disease. Lifestyle, environmental, and hereditary factors influence cardiovascular disease pathogenesis. Recently, bioactive compounds from nature-especially plants-have been touted for cardiovascular disease prevention and treatment. Polyphenols, flavonoids, alkaloids, carotenoids, and essential fatty acids are among the bioactive chemicals that improve cardiovascular health. Bioactive substances alter inflammation, oxidative stress, lipid metabolism, endothelial function, and vascular tone, which are linked to cardiovascular disease. One cannot overstate their value. Fruit, vegetable, and tea polyphenols have been shown to improve endothelial function, lower blood pressure, and reduce atherosclerosis risk.^[1] Flavonoids, found in many fruits, vegetables, and beverages like wine and tea, have potent anti-inflammatory and antioxidant properties that may prevent cardiovascular disease. Bioactive peptides in milk and soy may lower blood pressure and cholesterol, according to recent studies. Many people die from Cardiovascular Diseases (CVDs), a global health crisis. Given the prevalence of obesity, diabetes, hypertension,

and poor diets, CVDS should be avoided. Healthy living is one of the best CVD prevention methods. Lifestyle changes include regular exercise, a balanced diet, weight control, quitting smoking, and stress management to improve cardiovascular health and minimize heart disease risk. This overview uses clinical studies and guidelines to examine the fundamentals of a healthy lifestyle in preventing cardiovascular disease.^[2,3] Consistent exercise is a proven cardiovascular health method. Exercise improves endothelial function, blood circulation, blood pressure, and lipid profiles.^[4]

Polyphenols

Through a variety of biological processes, polyphenols, a broad class of plant-based chemicals, significantly contribute to the promotion of cardiovascular health. Their strong antioxidant qualities are one of their main advantages. Atherosclerosis is largely caused by oxidative stress, which these substances might lessen by scavenging free radicals. Flavonoids, a significant subclass of polyphenols, have been shown in studies to reduce lipid peroxidation and increase antioxidant enzyme activity, protecting against cardiovascular disease.^[28] Through, their modulation of pathways implicated in chronic inflammation, a major contributor to cardiovascular disease, polyphenols also demonstrate anti-inflammatory properties. For example, resveratrol, which is frequently included in red wine and grapes, effectively lowers vascular inflammation and its effects on heart health by blocking pro-inflammatory cytokines and signaling pathways like NF- κ B.^[29] Furthermore, by raising the bioavailability



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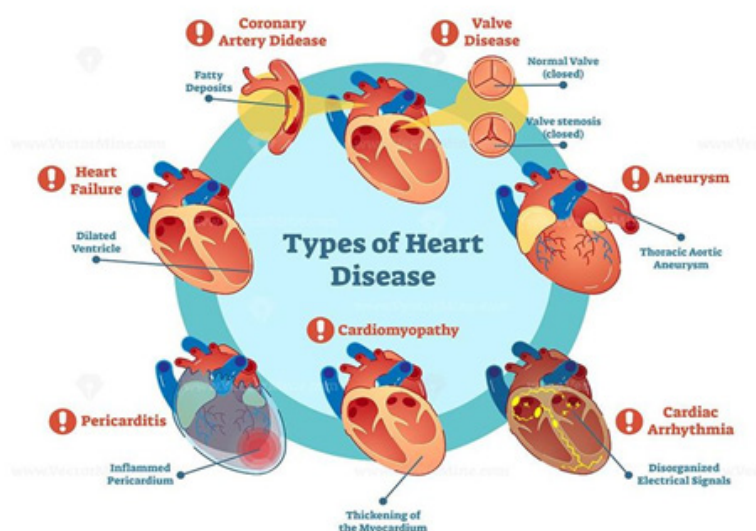


Figure showing the various anomalies associated with the cardiovascular system.^[5-6]

PATHOPHYSIOLOGY OF CVD'S

The segregation of Pathophysiology linked to cardiovascular complications.^[7-11]

| Risk Factor | Physiological Effects |
|---------------------|--|
| Secondary Lifestyle | ↑ Insulin resistance, ↑ blood glucose levels, ↑ pro-thrombotic factors |
| Hypertension | ↑ Endothelial growth factor polymorphism, ↑ vascular damage |
| Smoking | ↑ Oxidative stress, ↑ coronary spasm, ↑ platelet aggregation, ↓ HDL |
| Stress | Imbalance of hypothalamo-pituitary axis, ↑ serum cortisol, ↑ atherosclerosis |
| Obesity | ↑ Dyslipidemia, platelet dysfunction, ↑ insulin resistance |
| Diabetes | ↑ Inflammation, deposition of VLDL and LDL, plaque deposit |
| Dyslipidemia | ↑ Deposit of atheroma plaques on internal walls, thickening of the arterial wall |

BIOACTIVE COMPOUNDS AND THEIR EFFECT ON CVD RISK FACTORS

The various Bioactive compounds and their effect on cardiovascular complications.^[12-14]

| | |
|---|---|
| Lifestyle Modification | ↑ Physical activity, ↓ alcohol consumption & smoking, ↓ obesity → ↓ risk of heart failure |
| Green Tea, Lycopene, Garlic, Grape, Beetroot, Olive Oil | ↓ Blood pressure |
| Apricot | ↓ ACE, ↑ nitric oxide, ↑ vasodilatation |
| Celery, Oats, Soy, Flaxseed, Basil | ↓ Atherosclerosis |
| Proanthocyanidins (Bilberries) | ↓ Cytokines, ↓ Chemokines |
| Green Tea ↓ Cortisol | ↓ Cortisol |
| Hyperforin ↑ Serotonin | ↑ Serotonin |
| Ginseng | ↓ Mental fatigue, ↑ Memory & work performance |
| Carotenoids, EPA & DHA | ↓ Platelet aggregation, ↓ Oxidation |
| Resveratrol | ↓ Fat deposits, ↓ Insulin levels, ↓ Body weight |
| Polyphenols, Flavonoids, Saponins | Anti-hyperglycemic effect |
| Peptides (Soybean) | Prevent Type 2 Diabetes onset |
| Phenolic Compounds, Phytosterols | ↓ LDL-C |

Key Bioactive Compounds and Their Cardiovascular Benefits

Key Bioactive Compounds and Their Cardiovascular Benefits

| Compounds | Sources | Benefits |
|--|--|--|
| Polyphenols ^[15] | Red wine, dark chocolate, coffee, tea (black and green), fruits (grapes, apples, and berries), and vegetables. | Antioxidant qualities aid in lowering inflammation and oxidative stress. Enhance blood pressure regulation and endothelial function. Reduce the oxidation of LDL cholesterol to lower the risk of atherosclerosis. |
| Omega-3 Fatty Acids ^[16] | Walnuts, flaxseeds, chia seeds, fatty fish (salmon, mackerel, and sardines), and supplements made from algae. | Lower triglycerides and raise cholesterol. Lower arterial stiffness and blood pressure. Heart disease prevention by anti-inflammatory properties. |
| Phytosterols ^[17] | Whole grains, nuts, seeds, vegetable oils, and fortified foods (like margarine). | Lower total and LDL cholesterol levels by competing with the gut's ability to absorb dietary cholesterol. |
| Flavonoids ^[18] | Wine, dark chocolate, tea, broccoli, onions, and citrus fruits. | Lower blood pressure and enhance blood vessel function. Have anti-inflammatory and antioxidant properties. |
| Carotenoids ^[19] | Kale, spinach, sweet potatoes, tomatoes, and carrots. | oxidative stress-reducing antioxidants. Guard against inflammation and lipid peroxidation. |
| Fiber ^[20] | Beans, seeds, fruits, vegetables, and whole grains. | Binds to LDL cholesterol in the digestive tract, lowering it. Lowers the risk of hypertension and raises blood sugar levels. |
| Nitric Oxide Precursors (e.g., Nitrates) ^[21] | Leafy greens such as arugula, spinach, beetroot, and others. | Increase nitric oxide synthesis to improve blood flow and vasodilation. Reduce blood pressure and enhance the health of your arteries. |
| Allicin ^[22] | Garlic and other vegetables that contain allium (leeks, onions). | Aids in lowering cholesterol and blood pressure. Has anti-platelet and anti-inflammatory properties. |
| Anthocyanins ^[23] | Purple cabbage, blueberries, blackberries, and cherries. | Reduce oxidative stress and safeguard blood vessels. Improve lipid profiles and lower blood pressure. |
| Coenzyme Q10 (CoQ10) ^[24] | Nuts, vitamins, organ meats, and fatty seafood. | Helps the cardiac cells' mitochondria produce energy. Oxidative damage is lessened by antioxidant qualities. |
| Curcumin ^[25] | Roots and Powder | Lowers the long-term inflammation linked to heart disease. Enhances the function of endothelium. Reduces oxidative damage to prevent atherosclerosis. |
| Lycopene ^[26] | Watermelon, pink grapefruit, red peppers, and tomatoes. | Strong antioxidant lycopene aids in lowering inflammation and oxidative stress. According to studies, it lowers LDL cholesterol and blood pressure, which lowers the risk of heart disease. It also aids in stopping atherosclerosis from getting worse. |
| Resveratrol ^[27] | Peanuts, berries, grapes, and red wine | Resveratrol's antioxidant and anti-inflammatory properties serve to lessen the risk of atherosclerosis, decrease blood clot formation, and enhance endothelial function. |

of Nitric Oxide (NO), which encourages vasodilation and improves blood flow, polyphenols boost endothelial function. Epicatechins generated from cocoa are especially useful in this context because they have a direct impact on endothelial function.^[30] The capacity of polyphenols to stop LDL oxidation, a crucial stage in the development of atherosclerosis, is another important cardiovascular advantage. Olive hydroxytyrosol and green tea catechins have been demonstrated to prevent LDL oxidation and support vascular health.^[31] Additionally, consistent intake of foods high in polyphenols has been linked to blood pressure control, which is an important component in lowering the risk of cardiovascular disease. Research shows

that substances in green tea and berries help lower systolic and diastolic blood pressure in a small but meaningful way.^[32] Additionally, polyphenols modulate platelet function, which lowers the risk of thrombosis. Quercetin, for instance, has been demonstrated to enhance overall hemostatic balance and prevent platelet aggregation.^[33] Additionally, these substances improve High-Density Lipoprotein (HDL) levels while lowering total cholesterol and triglycerides, which has a favorable effect on lipid profiles. Preclinical and clinical research have shown that pomegranate polyphenols have these effects, which lower cardiovascular risk.^[34] Long-term consumption of polyphenol-rich diets has been associated with a reduced risk of

Coronary Heart Disease (CHD), supported by epidemiological evidence. The cumulative effects of their antioxidant, anti-inflammatory, and lipid-modulating properties contribute to this protective outcome.^[35] Additionally, polyphenols interact with gut microbiota, producing metabolites that have systemic anti-inflammatory effects and improve lipid metabolism, further enhancing cardiovascular health.^[36]

Omega-3 Fatty Acids

For several reasons, omega-3 fatty acids are absolutely essential for cardiovascular health. Specifically, Eicosapentaenoic Acid (EPA) and Docosahexaenoic Acid (DHA), present in fatty fish and fish oil, have been demonstrated to reduce triglyceride levels, a main risk factor for cardiovascular disease.^[37] Calder claims that these fatty acids lower the synthesis of inflammatory cytokines and eicosanoids, therefore helping to minimize chronic inflammation linked with atherosclerosis. Regular omega-3 fatty acid intake has been linked to enhanced endothelial function, which lowers the risk of vascular dysfunction and hypertension^[38] and increases blood vessel flexibility and blood flow. Particularly atrial fibrillation and ventricular arrhythmias^[39], omega-3 fatty acids have been proven to stabilize cardiac cell membranes and electrical activity, hence lowering arrhythmias. Particularly helpful in those with hypertension, they also help to somewhat reduce blood pressure by altering systemic inflammation and vascular tone.^[40] Studies have indicated that EPA and DHA can lower platelet aggregation as thrombosis and arterial blockages are the main causes of heart attacks and strokes.^[41] By improving lipid profiles, reducing LDL cholesterol, and raising HDL cholesterol, omega-3 fatty acids help to prevent atherosclerotic plaque development.^[42] Long-term supplements or intake has been associated with a reduced incidence of sudden cardiac mortality^[43] since omega-3 fatty acids have anti-arrhythmic and cardioprotective effects. Omega-3 supplements lower overall cardiovascular mortality, according to clinical studies, therefore verifying their function in the prevention of cardiovascular diseases.^[44] Moreover, omega-3 fatty acids help reduce oxidative stress and systemic inflammation, two major causes of the development of heart disease.^[45]

Phytosterols

Particularly regarding heart health and cholesterol control, natural plant-based compounds known as phytosterols have shown significant cardiovascular benefits. Because they have a structural resemblance to cholesterol, phytosterols can compete in the intestine for absorption. This rivalry lowers intestinal cholesterol absorption, therefore lowering LDL cholesterol levels and preserving HDL cholesterol levels free from side effects. Clinical studies show that daily phytosterol intake between two and three grams can reduce LDL cholesterol by 8-10%. This is a key component in reducing the atherosclerosis and coronary heart disease risk. Phytosterols' ability to decrease cholesterol is

particularly strong when combined with a heart-healthy diet, therefore enhancing cardiovascular results and general lipid profiles. Apart from their impact on cholesterol, phytosterols may have antioxidant properties that reduce oxidative stress and inflammation, two elements that are very essential for the development of cardiovascular disease. Phytosterol addition has been linked to improved endothelial function, hence improving blood flow and vascular health. Moreover, studies have indicated that phytosterols help to lower the absorption of dietary cholesterol, which is particularly beneficial for those with hypercholesterolemia and other risk factors for cardiovascular disease. Considered as part of dietary therapy to reduce the risk of cardiovascular disease, foods high in phytosterols-such as dairy products, spreads, and fortified margarine-have been advised for frequent consumption. Meta-analyses show that phytosterols are a main preventative tool against cardiovascular disease by reducing LDL cholesterol and having other lipid-modulating actions.^[46,47]

Flavonoids

The cardiovascular health advantages of flavonoids, a broad class of polyphenolic chemicals present in fruits, vegetables, tea, wine, and chocolate, have been extensively researched. These substances have strong antioxidant qualities, scavenging Reactive Oxygen Species (ROS) and lowering oxidative stress, which is a primary cause of endothelial dysfunction and atherosclerosis. Flavonoids like quercetin and catechins help shield vascular tissues from oxidative damage by increasing the activity of endogenous antioxidant enzymes. Apart from their antioxidant properties, flavonoids also have anti-inflammatory effects through the modulation of important signaling pathways and the reduction of pro-inflammatory cytokines including Interleukin-6 (IL-6) and Tumor Necrosis Factor-alpha (TNF- α).^[48]

To reduce chronic inflammation, which is a major cause of Cardiovascular Diseases (CVDs), several steps are essential. Flavonoids also increase the bioavailability of Nitric Oxide (NO), which enhances endothelial function. Studies have demonstrated that epicatechin, a flavonoid present in cocoa, increases endothelial NO generation, enhancing arterial elasticity and lowering blood pressure. NO is necessary for vasodilation and preserving vascular tone. Flavonoids also prevent Low-Density Lipoprotein (LDL) from oxidizing, which is a critical stage in the development of atherosclerotic plaques. In human trials, for example, green tea catechins have been shown to improve lipid profiles and lower LDL oxidation.

Modulating platelet aggregation is another significant way that flavonoids promote cardiovascular health. Flavonoids such as hesperidin and naringenin have been discovered to suppress platelet aggregation, lowering the likelihood of clot formation. Excessive platelet activity is a risk factor for thrombosis. Frequent intake of foods high in flavonoids has also been associated with

reduced blood pressure and improved arterial stiffness, both of which promote cardiovascular health in general.

New research demonstrates how flavonoids affect gut microbiota, which may have an indirect effect on cardiovascular health by lowering systemic inflammation and enhancing lipid metabolism. These positive effects are believed to be mediated by metabolites that are produced by flavonoid interactions with the gut microbiota. Higher dietary intake of flavonoids may be linked to a lower risk of Coronary Heart Disease (CHD) and stroke, according to long-term observational studies, highlighting their potential in cardiovascular preventative strategies.^[49]

Carotenoids

Carotenoids are potent antioxidants that reduce oxidative stress, which is a key cause of atherosclerosis and other cardiovascular disorders, and neutralize Reactive Oxygen Species (ROS).^[64] Beta-carotene, for example, has been demonstrated to reduce lipid peroxidation, shielding lipoproteins and cell membranes from oxidative damage. Tomatoes contain a lot of lycopene, a carotenoid that has been studied extensively because it can stop Low-Density Lipoprotein (LDL) oxidation, which is essential for stopping atherosclerosis from getting worse.^[50]

By modifying inflammatory cytokines and signaling cascades, carotenoids not only exhibit antioxidant activity but also have anti-inflammatory properties. According to studies, zeaxanthin and lutein help to promote vascular health by lowering levels of pro-inflammatory

indicators including C-Reactive Protein (CRP). Additionally, these carotenoids are linked to improved endothelial function, in part because they increase the bioavailability of Nitric Oxide (NO), which encourages vasodilation and lessens arterial stiffness.

Additionally, carotenoids help to enhance lipid profiles. Frequent intake of foods high in carotenoids has been linked to higher levels of HDL cholesterol and decreased levels of LDL cholesterol in the blood. For instance, lycopene intake has been proven to have a preventive impact against Coronary Heart Disease (CHD) and is negatively connected with total cholesterol levels.

Another significant component of carotenoids' cardiovascular advantages is their anti-hypertensive properties. According to research, lower blood pressure levels are associated with higher plasma concentrations of carotenoids, specifically lutein and beta-carotene. Improved vascular relaxation and decreased oxidative stress inside artery walls mediate these effects.

Additionally, carotenoids help lower the incidence of stroke and myocardial infarction. Long-term research has shown that the incidence of these cardiovascular events is much reduced in people who consume more carotenoid-rich foods. Carotenoids' combined anti-inflammatory, antioxidant, and lipid-regulating qualities are responsible for this protective effect.^[51,52]

Fiber

Fiber influences a number of important aspects that are vital to cardiovascular health. Foods including oats, legumes, and some fruits include soluble fiber, which lowers LDL cholesterol by binding to bile acids in the stomach and encouraging their excretion, so reducing the risk of atherosclerosis. Diets high in fiber have been linked to lower blood pressure, most likely because they reduce inflammation and preserve arterial flexibility. According to Weickert and Pfeiffer (2008), consuming fiber can improve glycemic control by lowering insulin resistance, decreasing the absorption of carbohydrates, and reducing a significant risk factor for heart disease. Additionally, fiber promotes the formation of short-chain fatty acids, which have systemic anti-inflammatory effects and are beneficial to cardiovascular health, by maintaining a healthy gut flora. Fiber lowers the cardiovascular risks associated with obesity, such as hypertension and metabolic syndrome, by improving satiety and encouraging weight management. High fiber intake, especially from whole grains, is consistently associated with lower risks of cardiovascular mortality and coronary artery disease, according to epidemiological research. Higher dietary fiber consumption has also been linked to improved lipid profiles, which are defined by decreased LDL cholesterol and stabilized triglyceride levels. Additionally, it has been demonstrated that consuming fiber improves endothelial function, which improves circulation and blood vessel health. Lastly, meta-analyses highlight the importance of dietary fiber for long-term heart health by showing a substantial correlation between increased intake and a decrease in cardiovascular mortality.^[53]

Nitric Oxide Precursors

Precursors of Nitric Oxide (NO), like L-arginine and L-citrulline, affect endothelial function and vascular homeostasis, which are important for cardiovascular health. Vasodilation and blood pressure maintenance depend on the synthesis of NO, which is facilitated by L-arginine, a substrate for endothelial Nitric Oxide Synthase (eNOS). L-citrulline, which the body converts to L-arginine, has been demonstrated to increase NO bioavailability by supplementation, improving endothelial function and decreasing arterial stiffness. By lowering oxidative stress and preventing inflammatory cells from adhering to the endothelium, elevated NO levels help prevent atherosclerosis. Additionally, NO precursors contribute to better blood flow and oxygen delivery, which is advantageous for ailments including exercise-induced ischemia and peripheral artery disease.^[53] L-arginine's significance in blood pressure management is supported by research showing that it may reduce systolic and diastolic blood pressure in people with hypertension. Supplementing with L-citrulline has been linked to improved NO-dependent vasodilation, which enhances vascular function overall and reduces cardiovascular risk factors. Furthermore, NO precursors may lower the risk of thrombosis and platelet aggregation, protecting the cardiovascular system

as a whole. A natural way to increase NO synthesis and support cardiovascular health may be through dietary sources of NO precursors, such as watermelon, which is high in L-citrulline. Increased NO bioavailability via precursor supplementation aids in lipid profile control and may lower the risk of plaque development and LDL oxidation. By improving hemodynamic parameters, increased NO production has also been connected to improved myocardial function and a lower risk of heart failure. Clinical and experimental evidence clearly supports the significance of NO precursors in maintaining vascular health and lowering the risk of cardiovascular disease, highlighting their therapeutic potential.^[54]

Allicin

Garlic has a sulfur containing chemical called allicin, which has shown promise for cardiovascular health through a number of pathways. By encouraging vasodilation through the increased synthesis of nitric oxide, which relaxes blood vessels and improves blood flow, allicin lowers blood pressure. According to studies, allicin reduces the risk of atherosclerosis and its associated consequences by lowering total cholesterol and LDL ("bad") cholesterol levels while having little effect on HDL ("good") cholesterol. Strong antioxidant qualities in allicin fight oxidative stress and stop LDL cholesterol from oxidizing, which is a critical stage in the development of heart disease. Furthermore, allicin reduces inflammation by inhibiting inflammatory pathways and cytokines, which are important contributors to endothelial dysfunction and vascular inflammation. Allicin also prevents platelets from aggregating, which lowers the risk of thrombus formation and the ensuing cardiovascular events, including myocardial infarction and stroke. By increasing endothelial cell activity and shielding blood arteries from oxidative stress and hypertension, the chemical also helps to improve vascular function. Allicin, which is found in garlic, has been shown in studies to improve lipid profiles overall, lower triglyceride levels, and promote a better lipid metabolism. Additionally, it has been demonstrated that allicin controls blood glucose levels, reducing the cardiovascular risks linked to insulin resistance and diabetes. By treating several risk factors, such as inflammation, dyslipidemia, and hypertension, garlic-derived allicin has been shown in long-term studies and meta-analyses to be effective in lowering cardiovascular mortality. It has been demonstrated that anthocyanins, a type of flavonoids present in red cabbage, berries, and other vibrantly colored fruits and vegetables, have important cardiovascular advantages. By improving nitric oxide bioavailability, anthocyanins enhance endothelial function, improve blood flow and vasodilation, and lower blood pressure. They have strong antioxidant qualities that lower oxidative stress and stop the oxidation of LDL cholesterol, which is a crucial stage in the development of atherosclerosis. By modifying inflammatory markers like interleukins and C-Reactive Protein (CRP), which are strongly linked to the risk of cardiovascular

disease, anthocyanins help lessen systemic inflammation. Eating foods high in anthocyanins has been associated with decreased arterial stiffness, which improves vascular health and lowers the risk of hypertension. By raising HDL cholesterol and decreasing total and LDL cholesterol, anthocyanins enhance lipid profiles and promote cardiovascular health in general. Because they enhance insulin sensitivity and glucose metabolism, they also play a significant role in glycemic control by lowering the risk of diabetes, a significant cardiovascular risk factor. According to epidemiological research, diets high in anthocyanins are linked to a lower incidence of stroke and coronary artery disease, underscoring their preventive function in cardiovascular health.^[55]

Coenzyme Q10

Coenzyme Q10 (CoQ10) is an essential component of cellular energy production and a strong antioxidant, which contributes to cardiovascular health. In order to ensure adequate energy availability for highly energy-dependent cardiac cells, CoQ10 is necessary for the electron transport chain in mitochondria, where it promotes ATP synthesis. Endothelial dysfunction and the advancement of atherosclerosis are largely caused by free radicals and oxidative stress, which are counteracted by its antioxidant qualities. Enhancing endothelial function through supplementation with CoQ10 has been demonstrated to increase blood flow and vascular health, which is especially advantageous in diseases such as hypertension. Low CoQ10 levels are common in heart failure patients, and supplementation has been linked to better cardiac function overall, exercise capacity, and ejection fraction. In patients with coronary artery disease, taking a CoQ10 supplement dramatically lowers oxidative damage and inflammatory indicators, which helps to halt the illness's progression.^[56]

Curcumin

Curcumin, the primary component of turmeric, has several biological actions displaying significant cardiovascular impact. Strong anti-inflammatory effects of curcumin are obtained by blocking Nuclear Factor-kappa B (NF- κ B) and pro-inflammatory cytokines, which are fundamental in the development of atherosclerosis and other cardiovascular diseases. Its antioxidant properties help Reactively Oxygen Species (ROS) to be neutralised, therefore reducing oxidative stress that damages endothelial cells and accelerates the ageing of the cardiovascular system. Curcumin improves endothelial function by raising Nitric Oxide (NO) bioavailability, thereby encouraging vasodilation, reduction of blood pressure, and good circulation. Studies find that curcumin can change lipid profiles by increasing HDL cholesterol and lowering LDL and triglyceride levels, therefore reducing the risk of coronary artery disease and plaque production. Additionally reducing platelet aggregation by curcumin helps to reduce thrombosis risk and associated

cardiovascular events including myocardial infarction. It has been shown that by reducing oxidative damage and apoptosis in cardiac tissues, myocardial injury and ischemia-reperfusion damage is lowered. Treating the challenges of diabetes helps curcumin indirectly protect cardiovascular health by regulating insulin sensitivity and glucose metabolism. Furthermore, it reduces the production of adhesion molecules such as VCAM-1 and ICAM-1 which help to produce atherosclerosis and endothelial dysfunction. Furthermore, meta-analyses show that by reducing systemic inflammatory markers including C-Reactive Protein (CRP), curcumin supplementation has generally cardioprotective effects. Taken overall, the evidence highlights how curcumin's anti-inflammatory, lipid-modulating, antioxidant properties help treat and prevent cardiovascular disease.^[57]

Opportunities and Challenges related to bioactive compounds

Natural Medicines: Polyphenols, flavonoids, alkaloids, and terpenoids are examples of plant bioactive substances that are known to prevent and treat Cardiovascular Diseases (CVDs) with fewer adverse effects than manufactured medications. These substances offer intriguing substitutes for traditional therapies since they can target important elements like inflammation, oxidative stress, and endothelial dysfunction.

Anti-inflammatory and Antioxidant Properties: Numerous substances originating from plants, including those in turmeric, berries, and green tea, have strong anti-inflammatory and antioxidant properties. These characteristics lessen chronic inflammation and oxidative blood vessel damage, two factors that significantly contribute to atherosclerosis and other cardiovascular diseases.

Management of Lipids and Cholesterol: Plant sterols, stanols, and saponins are examples of bioactives that lower intestine absorption and increase lipid metabolism to help control cholesterol levels. They are therefore useful in preventing diseases like coronary artery disease and hyperlipidemia.

Control of Blood Pressure: It has been demonstrated that flavonoids, which are present in foods like grapes and cocoa, increase the availability of nitric oxide, which improves vascular relaxation and lowers blood pressure. The management of hypertension, a major risk factor for CVDs, benefits greatly from this antihypertensive impact.

Nutraceuticals and Functional Foods: Functional foods, drinks, and dietary supplements that support cardiovascular health can contain bioactive substances. Because consumers are becoming more conscious of natural health solutions, products enhanced with plant bioactives are becoming more and more appealing.

Healthcare Prevention: Plant bioactive chemicals help to promote the move to preventive healthcare by reducing risk factors such

as metabolic syndrome, diabetes, and obesity. CVD onset can be postponed or avoided by incorporating them into regular diets.

Abundance and Sustainability: Since many bioactive chemicals are obtained from readily accessible crops or agricultural leftovers, plants represent a renewable resource that may be produced and studied at a reasonable cost.

New Technologies: The medicinal potential of plant-derived chemicals is increased by improvements in their bioavailability and efficacy brought about by advancements in extraction, formulation, and delivery methods such as nanoencapsulation.^[58,59]

Challenges in the Application of Plant Bioactive Substances to Cardiovascular Conditions (CVDs)

Insufficient Bioavailability: The limited water solubility, fast metabolism, and instability in physiological conditions of bioactive substances frequently result in inadequate bioavailability. This restricts how well they can be absorbed and used by the body. Compounds like polyphenols, for instance, have been shown to have therapeutic promise, but they struggle to reach adequate concentrations in target tissues, which lessens their effectiveness. Techniques like lipid-based delivery systems and nanoencapsulation are being investigated to get around this restriction.

Restricted Accessibility

Oral transport of bioactive substances is severely hampered by physiological barriers, including the mucus layer in the gastrointestinal tract, enzymatic destruction by digestive enzymes, and pH fluctuations along the digestive system. These obstacles may limit the compounds' therapeutic effects by lowering the quantity that enters the systemic circulation. For example, gut bacteria may significantly alter the bioactivity of phenolic chemicals by metabolizing them before they are absorbed.

Deterioration

Bioactive compounds are susceptible to deterioration at many phases, such as formulation, processing, and storage. The structural integrity of these compounds can be jeopardized by elements like heat, light, oxygen exposure, and pH variations. It is difficult to maintain consistent therapeutic effects because of this degradation, which also reduces their biological usefulness and antioxidant activity. To solve this problem, stabilization methods including microencapsulation and the use of protective matrices are essential.

Unwanted Flavor and Odor

Some plant bioactive substances, such as terpenoids and flavonoids, have strong or disagreeable smells and aromas that can make it challenging to include them in food products. Particularly in the case of functional foods and nutraceuticals, these sensory characteristics may restrict consumer acceptability.

To increase their palatability, tailored delivery methods, flavor modification, and masking technologies are being explored.

Interaction with Additional Elements

During processing or digestion, bioactive substances may interact with other nutrients or components of the food matrix, reducing their absorption and bioavailability. For instance, polyphenols can form less bioavailable complexes by binding to proteins or dietary fiber. Maximizing the therapeutic potential of these drugs requires an understanding of these interactions and formulation optimization to reduce side effects.^[60-63]

Future Perspectives of Bioactive Compounds as a Holistic Basis for Cardiovascular Health

The future of bioactive compounds in the realm of cardiovascular health is promising, with a holistic approach potentially leading to significant advancements in prevention, management, and treatment. Here are several key aspects of prospects:

Integration into Personalized Nutrition

Advances in genetics and metabolic profiling are paving the way for personalized nutrition plans. Bioactive compounds could be tailored to individual health profiles, taking into account genetic predispositions, lifestyle factors, and existing health conditions. This personalized approach may enhance the efficacy of these compounds, ensuring that individuals receive the right types and amounts for their specific cardiovascular needs.

Innovative Delivery Systems

Advances in biotechnology and food science are expected to improve the bioavailability of bioactive compounds. Techniques such as nanoencapsulation and lipid-based delivery systems can enhance absorption and efficacy, allowing for lower dosages of active compounds to achieve desired health outcomes. These innovations could make functional foods and nutraceuticals more effective in preventing and managing cardiovascular diseases.

Long-term Clinical Studies

To fully understand the therapeutic potential of bioactive compounds, ongoing long-term clinical studies are essential. Research should focus on establishing well-defined guidelines regarding dosages, combinations, and long-term safety to provide robust evidence for their use in clinical practice.

Research on Synergistic Effects

Future research should explore the synergistic effects of various bioactive compounds when consumed together and their interactions with pharmaceutical therapies. Understanding how different compounds can work in tandem may open up new avenues for combination therapies that enhance cardiovascular health by leveraging multiple mechanisms of action.

Sustainability and Accessibility

As the demand for health-promoting foods increases, sustainable sourcing of bioactive-rich plants and marine resources will be essential. Developing agricultural practices that support the growth of these compounds while ensuring environmental sustainability will allow for greater accessibility to bioactive-rich foods. Public health policies may also need to focus on making these foods affordable and available across all demographics.^[64-70]

DISCUSSION

In the framework of cardiovascular health, the possibilities of bioactive compounds to change many risk factors and support the prevention and treatment of Cardiovascular Diseases (CVDs) have attracted much interest. Found in many different food sources including fruits, vegetables, and herbs, these compounds have properties that can influence vascular health, oxidative stress, inflammation, and lipid metabolism. Many bioactive compounds have been shown to reduce platelet aggregation, change lipid profiles, lower blood pressure, and increase endothelial function. These comprise polyphenols, flavonoids, and omega-3 fatty acids. For instance, flavonoids buffer blood arteries from oxidative damage and have anti-inflammatory and antioxidant effects that reduce atherosclerosis risk. They also aid in controlling nitric oxide generation, therefore enhancing vascular relaxation and lowering blood pressure. Polyphenols—especially those found in red wine and green tea—have been shown to lower another risk factor for cardiovascular events, arterial stiffness. Frequently found in fatty fish, omega-3 fatty acids have been shown to reduce triglyceride levels, stop blood clots, and have anti-inflammatory action supporting heart health. While the results of bioactive compounds are promising, it is crucial to realize that personal medical conditions, the type and quantity of chemicals consumed, and their bioavailability determine the overall impact on cardiovascular health among several factors. Moreover, bioactive compounds should be seen as extra components of a well-balanced diet that reduces cardiovascular risk instead of as magic bullets. Moreover, more clinical trials and long-term studies are needed to ascertain the optimal dosages and the exact ways in which these drugs influence cardiovascular results. In essence, both the prevention and treatment of cardiovascular diseases depend on bioactive compounds. They offer a good path for intervention especially when accompanied by a complete plan for cardiovascular health including dietary changes, exercise, and lifestyle changes. More study is needed to completely understand their efficacy and possibilities in different groups and therapeutic environments.

CONCLUSION

Antioxidant, anti-inflammatory, antihypertensive, antithrombotic, and lipid-lowering activities are just a few of the many pharmacological characteristics that make bioactive

substances extremely promising for the prevention and treatment of cardiovascular-related problems. These compounds, which are derived from natural sources like fruits, vegetables, whole grains, herbs, and functional foods, help alleviate major risk factors for Cardiovascular Diseases (CVDs) by enhancing endothelial function, controlling blood pressure, lowering oxidative stress, and modifying hormone profiles. Their potential to target oxidative damage and inflammation-related molecular pathways further emphasizes their therapeutic value in lowering the occurrence and advancement of CVDs. The bioavailability, dosage adjustment, and long-term safety of these drugs need additional clinical investigation to guarantee their effectiveness in real-world applications, even in the face of encouraging preclinical and epidemiological findings.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHOR CONTRIBUTIONS

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by Adib Hussain, Sreejita Chakraborty, and Arabinda Nayak. Sreejita Chakraborty wrote the first draft of the manuscript and all authors commented on previous versions. All authors read and approved the final manuscript.

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