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Resveratrol: A Promising Agent for Cardiovascular Disease Prevention and Treatment: A Report

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ABSTRACT

Nutraceuticals are biologically active compounds derived from natural food sources that provide health benefits beyond basic nutrition, including the prevention and management of chronic diseases. Among them, resveratrol, a non-flavonoid polyphenolic phytoalexin found mainly in grapes, red wine, peanuts, and berries, has gained significant attention for its potential role in cardiovascular disease (CVD) prevention. Cardiovascular diseases remain the leading cause of morbidity and mortality worldwide, largely driven by oxidative stress, chronic inflammation, endothelial dysfunction, dyslipidemia, hypertension, and abnormal platelet aggregation. Resveratrol exerts its effects by modulating key signaling pathways, including SIRT1, AMPK, Nrf2, NF-κB, and eNOS, thereby enhancing nitric oxide bioavailability, reducing oxidative stress and inflammation, improving endothelial function, inhibiting platelet aggregation, and regulating lipid metabolism. Preclinical and clinical studies suggest beneficial roles of resveratrol in atherosclerosis, hypertension, myocardial infarction or stroke, endothelial dysfunction, and heart failure. Overall, resveratrol shows strong potential as a safe, natural, and multifunctional nutraceutical for cardiovascular disease prevention and as an adjunct to conventional therapies, although further large-scale clinical trials are required to establish optimal dosage, long-term safety, and clinical effectiveness. However, translation of these promising findings into clinical practice remains constrained by limited human clinical evidence, heterogeneity in study design, short intervention durations, small sample sizes, and substantial variability in clinical outcomes. Furthermore, the clinical utility of resveratrol is hindered by poor oral bioavailability, rapid metabolism, uncertain dose–response relationships, and lack of standardized formulations. Emerging strategies, including micronized, encapsulated, and nano-based delivery systems, may enhance systemic availability and therapeutic efficacy. In conclusion, resveratrol represents a compelling nutraceutical candidate for cardiovascular protection, yet definitive validation through large-scale, well-designed human clinical trials with standardized formulations, optimized dosing, and clinically relevant cardiovascular endpoints is essential before its routine incorporation into CVD prevention and treatment strategies.

Keywords: Cardiovascular disease, nutraceuticals, resveratrol, antioxidant, inflammation, oxidative stress.

INTRODUCTION

The term “nutraceutical” first used by Stephen De Felice (Founder and chairman of the Foundation for innovation in Medicine) is portmanteau of two words, “nutrition” and “pharmaceutical”, a food (or part of food) that provides medical or health benefits, including the prevention and or treatment of a disease. Nutraceuticals are specifically designed formulations developed to meet particular dietary requirements and to provide preventive or therapeutic health benefits [1]. Nutraceuticals are biologically active compound found from the plant and animal origin that posses beneficial role in health. It involves in the prevention of some metabolic disorder e.g., cardiovascular disease, diabetes, cancer etc also it consists as a complement of pharmacological therapy [2]. Nutraceuticals can reduce the risk of many diseases and heFlp in improving the

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quality of life. However, proper administration and prescription of nutraceuticals are necessary to ensure their safe and effective use [3]. Certain nutraceuticals, calcium,omega-3 polyunsaturated fatty acids, vitamin D, folic acid, resveratrol, alpha-lipoic acid, zinc, inositol, and probiotics, have therapeutic potential in the prevention and management of cardiovascular diseases, metabolic disorders, hypertensive conditions, osteoarthritis, and pregnancy related complications. Furthermore, nutraceutical–drug combinations have shown promise in enhancing treatment outcomes while reducing adverse effects, suggesting a significant role for nutraceuticals in integrative and preventive healthcare.These formulations contain nutrients or bioactive compounds that contribute not only to nutritional supplementation but also to the prevention and management of diseases. Nutraceuticals may consist of whole foods or isolated components of foods that exert beneficial physiological effects, including disease prevention and health promotion [4]. Different nutraceuticals found in foods rich in minerals, healthy fats, whole proteins, peptides, amino acids, probiotics, and vitamins. Nutrients like potassium, L-arginine, vitamin C and D, flavanols, beetroot juice, certain probiotics, coenzyme Q10, aged garlic extract, and even coffee have been reported to support health and help manage blood pressure. Other nutraceuticals such as green tea, flaxseed, and resveratrol are commonly used by people for health benefits. However, more clinical research is needed to clearly identify which nutraceuticals are most effective, safe, and cost-efficient with the best balance between benefits and risks [5].

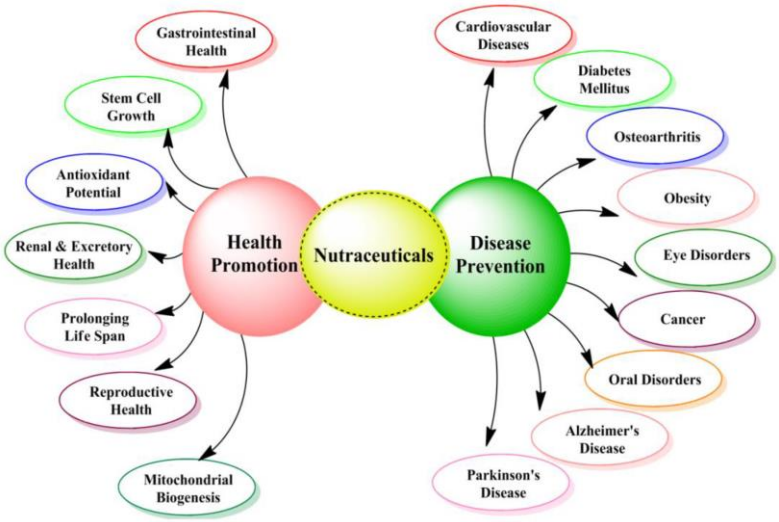

Figure1: Role of nutraceuticals in disease prevention and health promotion

Nutraceuticals play an important supportive role in the prevention and management of cardiovascular diseases (CVD). They help in reducing cardiovascular risk factors and improving overall heart health through multiple mechanisms. Nutraceuticals such as omega-3 fatty acids, plant sterols, soluble fibers, and red yeast rice help lower total cholesterol, LDL-cholesterol, and triglycerides while improving HDL-cholesterol levels. Some compounds like potassium, magnesium, bioactive peptides, garlic, and polyphenols aid in regulating blood pressure by improving vascular relaxation and reducing arterial stiffness. Nutraceuticals rich in antioxidants (e.g., flavonoids, carotenoids, vitamins C and E) reduce oxidative stress and chronic inflammation, which are key contributors to atherosclerosis. Certain nutraceuticals enhance nitric oxide production and improve endothelial health, leading to better blood flow and reduced risk of plaque formation. Nutraceuticals such as dietary fibers, polyphenols, and chromium help to lowering cardiovascular risk associated with diabetes. Some nutraceuticals inhibit platelet aggregation, reduce blood viscosity, and slow plaque development, thereby decreasing the risk of thrombosis and coronary events. Through combined lipid-lowering, blood pressure-

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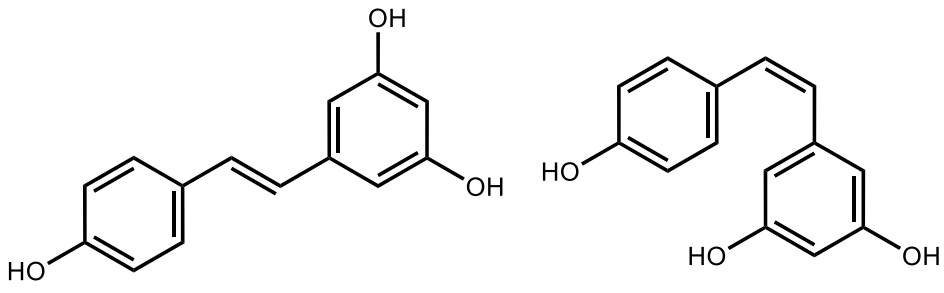
regulating, antioxidant, and metabolic benefits, nutraceuticals contribute to comprehensive cardiovascular protection [5,6]. Furthermore, Certain combined nutraceutical products**,** such as Armolipid Plus, contain multiple natural ingredients and have shown significant reductions in cholesterol levels and mild blood pressure lowering effects. These supplements may be useful for people with mild cardiovascular risk who cannot tolerate conventional drugs [7].



trans-Resveratrol cis-Resveratrol

Figure2: The chemical structure of trans and cis-Resveratrol

Cardiovascular diseases (CVDs), include conditions such as coronary artery disease, stroke, hypertension, peripheral artery disease, cerebrovascular disease, and heart failure. CVDs are one of the leading causes of death worldwide, accounting for about 17.9 million deaths in 2019, with the number expected to exceed 23.6 million annually by 2030.Major risk factors for CVDs include high blood pressure, abnormal lipid levels, diabetes, obesity, smoking, alcohol consumption, physical inactivity, and unhealthy diets. These factors cause oxidative stress, inflammation, endothelial dysfunction, and plaque formation in blood vessels, leading to atherosclerosis and heart failure [8].

In this review paper we discuss about the role of resveratrol(RES) as a nutraceuticals how to prevent and to treat the cardiovascular disease. The chemical structure of resveratrol was first identified in 1940 by the Japanese scientist Michio Takaoka, who isolated it from the roots of the plant *Veratrum grandifloru* (commomly known as White Hellebore Hellobore). Resveratrol has a non-flavonoids polyphenolic phytolexin stilbene-based structure. It is made up of two phenolic rings joined by a styrene double bond, forming a compound called 3,4′,5-trihydroxystilbene. The structure of trans-resveratrol consists of two aromatic (benzene) rings joined together by an ethylene (–C=C–) bridge. One benzene ring contains two hydroxyl (–OH) groups at the 3rd and 5th positions, while the other ring has one hydroxyl group at the 4′ position. It has a molecular weight of 228.25 g/mol and exists as two isomeric forms that is trans-resveratrol and cis-resveratrol, only trans-resveratrol is responsible for extending life expectancy and producing cardioprotective benefit but when exposed to light, especially UV light, trans-resveratrol can change into the cis form. Trans-resveratrol found in natural plant components such as grapes and red wine noteably and also in pink skin of peanuts, mulberry, raspberry etc that has a positive effects on heart health [9-12].

Resveratrol is a natural polyphenolic compound that has attracted significant attention for its potential role in the prevention of cardiovascular diseases. Evidence from preclinical and clinical studies suggests several mechanisms through which resveratrol may exert cardioprotective effects. Resveratrol may help reduce vascular inflammation, which is a key contributor to the development of atherosclerosis and other CVDs. Several clinical studies have reported reductions in pro-inflammatory biomarkers such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) following resveratrol supplementation. By suppressing inflammatory signaling pathways and promoting anti-inflammatory mediators, resveratrol may slow the progression of vascular damage. Although its effects on conventional lipid profile parameters such as total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides are inconsistent, resveratrol may still

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improve cardiovascular risk through alternative lipid-related mechanisms [12]. Some studies suggest that resveratrol reduces oxidized LDL and apolipoprotein B levels, which are considered more reliable predictors of cardiovascular risk than LDL-cholesterol alone.Resveratrol may activate cardioprotective molecular pathways, including those involving sirtuin-1 (SIRT1). Activation of SIRT1, AMPK, Nrf2 are associated with improved endothelial function, reduced inflammation, enhanced mitochondrial function, oxidative stress, an platelet oxidation, thrombus formation cell protection and overall vascular protection, all of which are relevant to the prevention of CVDs [13] It has also been found to reduce inflammatory markers like C-reactive protein (CRP), especially in smokers and people at risk of heart disease [14].

Resveratrol may exert beneficial effects on oxidative stress plays a key role in the development of many cardiovascular diseases, including atherosclerosis, ischemia–reperfusion injury, cardiac hypertrophy, fibrosis, and heart failure. By act as an exogenous antioxidant, resveratrol can reduce oxidative damage to low-density lipoproteins (LDL), thereby decreasing the formation of oxidized LDL, a key driver of atherosclerotic plaque formation. Resveratrol can directly scavenge harmful reactive oxygen species (ROS) such as superoxide, hydroxyl radicals, hydrogen peroxide, and peroxynitrite, thereby reducing lipid peroxidation, DNA damage, and cell death in cardiomyocytes, endothelial cells, macrophages, and muscle cells [10,13].

Current evidence on resveratrol (RES) in the prevention of cardiovascular disease (CVD) is limited by short trial durations, small sample sizes, and the frequent use of poorly defined or surrogate endpoints rather than validated cardiovascular outcomes. Inadequate reporting of study design details, including randomization methods and RES formulations, further hampers reproducibility and comparison across trials. Regulatory and financial constraints associated with nutraceuticals restrict large-scale, long-term clinical studies, while the investigation of RES across multiple disease areas may dilute focused CVD research. Resveratrol low systemic bioavailability, unclear dose requirements for cardiovascular benefit, and formulation challenges limit its clinical applicability, highlighting the need for well-designed trials using standardized formulations and clinically meaningful CVD endpoints [15].

Resveratrol has strong future potential as a nutraceutical for the prevention and treatment of cardiovascular diseases due to it is a natural antioxidant that contains anti-inflammatory, and cardioprotective properties. In the future, it may be widely used to prevent heart diseases by protecting blood vessels, reducing oxidative stress, controlling inflammation, improving endothelial function, and lowering bad cholesterol while increasing good cholesterol. Resveratrol may also help manage blood sugar levels and obesity-related risks, which are major contributors to cardiovascular diseases. With progress in nutraceutical research, new formulations like nano-based systems and encapsulated supplements are being developed to help resveratrol get absorbed better in the body and work more effectively. Additionally, resveratrol could be used alongside conventional heart medications to support treatment and reduce disease progression. Overall, with further clinical studies and technological advancements, resveratrol is likely to emerge as a safe, effective, and natural nutraceutical for long-term cardiovascular health management.

Aims and Objectives

- To critically evaluate the role of resveratrol in cardiovascular disease based on experimental and clinical evidence.
- To analyze the nutraceutical profile of resveratrol, including its natural sources, chemical characteristics, and bioavailability, in relation to cardiovascular relevance.
- To identify the clinical evidence of resveratrol to prevent cardiovascular disease.
- To examine and compare the molecular and cellular mechanisms underlying the cardioprotective effects of resveratrol, including antioxidant, anti-inflammatory, anti-atherosclerotic, and endothelial actions.

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- To identify current limitations, knowledge gaps, and future research directions regarding the use of resveratrol in cardiovascular disease management.

REVIEW OF LITERATURE

According to Gal, R. et al. Resveratrol also lowers oxidative stress by reducing Reactive Oxygen Species (ROS) production through inhibition of NADPH oxidases (NOX), mainly via SIRT1-mediated suppression of NF-κB, and by preventing eNOS uncoupling through increasing tetrahydrobiopterin (BH4) availability via up-regulation of GTP cyclohydrolase-1. In addition, RES strengthens the endogenous antioxidant defense system by increasing the expression and activity of antioxidant enzymes such as superoxide dismutase (SOD1 and SOD2), catalase, glutathione peroxidase, and glutathione, mainly through activation of SIRT1, FOXO transcription factors, and the AMPK/SIRT1/Nrf-2 pathway. Along with antioxidant effects, RES has potent anti-inflammatory actions by suppressing pro-inflammatory cytokines (TNF-α, IL-1β, IL-6) and inhibiting key inflammatory signaling pathways such as NF-κB, JAK/STAT, TLR4, and AP-1. It also reduces leukocyte adhesion by downregulating adhesion molecules (VCAM-1, ICAM-1, E-selectin), increases anti-inflammatory cytokines like IL-10, activates PGC-1α via SIRT1, and induces the anti-inflammatory enzyme heme oxygenase-1 (HO-1). Furthermore, RES inhibits COX-1 and COX-2 enzymes, reducing prostaglandin and thromboxane production, which contributes to its anti-inflammatory and antiplatelet effects [13]. Its antiplatelet effect resulting in decreased thromboxane A_2 synthesis and reduced platelet aggregation, lowering the risk of thrombotic events such as heart attack and stroke. Moreover, resveratrol improves vascular reactivity by inhibiting phosphodiesterases, blocking calcium entry into vascular smooth muscle cells, reducing oxidative stress, and limiting smooth muscle cell proliferation, all of which contribute to lower blood pressure and reduced progression of atherosclerosis. Overall, resveratrol shows strong potential as a cardioprotective compound by targeting multiple pathways involved in cardiovascular disease [16]. Its antiplatelet effect resulting in decreased thromboxane A_2 synthesis and reduced platelet aggregation, lowering the risk of thrombotic events such as heart attack and stroke. Moreover, resveratrol improves vascular reactivity by inhibiting phosphodiesterases, blocking calcium entry into vascular smooth muscle cells, reducing oxidative stress, and limiting smooth muscle cell proliferation, all of which contribute to lower blood pressure and reduced progression of atherosclerosis. Overall, resveratrol shows strong potential as a cardioprotective compound by targeting multiple pathways involved in cardiovascular disease [17].

Mechanism of action of Resveratrol to Prevent Cardiovascular disease in Animal:

Resveratrol reduces cardiovascular disease in rats by improving metabolic control, decreasing inflammation, and limiting oxidative stress. In diabetic rats with myocardial infarction, resveratrol lowers blood glucose, body weight, plasma triglycerides, heart rate, and the AST/ALT ratio, while increasing total plasma insulin levels.It significantly reduces inflammatory markers and malondialdehyde, indicating decreased oxidative stress. Resveratrol also improves endothelial function by increasing endothelial nitric oxide synthase (eNOS) expression and suppressing vascular endothelial growth factor (VEGF) expression and p38 MAPK phosphorylation. Through these combined effects, resveratrol protects the heart and improves cardiovascular function in rats with diabetes-related myocardial infarction [18].

Resveratrol (RES) may help prevent cardiovascular disease in dogs mainly through its anti-inflammatory and antioxidant actions. It reduces oxidative stress by scavenging reactive oxygen species and enhancing antioxidant enzymes such as superoxide dismutase. RES also modulates key signaling pathways involved in cardiac aging and inflammation, particularly by activating SIRT1 and AMPK, which suppress pro-inflammatory mediators like NF-κB and inflammatory cytokines (e.g., TNF-α, IL-1β, and IL-6). By limiting chronic inflammation and oxidative damage, resveratrol may slow age-related cardiac remodeling, reduce fibrosis, and improve endothelial and myocardial function. These effects suggest that resveratrol could serve as a supportive, cardioprotective supplement in dogs predisposed to or suffering from cardiovascular diseases [19].

Resveratrol (RES) exerts multifaceted cardioprotective effects in animal models of cardiovascular disease by targeting endothelial dysfunction, oxidative stress, extracellular matrix (ECM) degradation, and vascular

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smooth muscle cell (SMC) survival. A key mechanism involves restoration of endothelial homeostasis through enhancement of endothelial nitric oxide synthase (eNOS) activity and suppression of inducible nitric oxide synthase (iNOS), thereby improving nitric oxide bioavailability and reducing nitrosative stress. In parallel, RES reduces oxidative stress by inhibiting NADPH oxidase—particularly NOX4—leading to decreased reactive oxygen species (ROS) production and improved vascular function.

RES also preserves aortic structure by limiting ECM degradation. It downregulates matrix metalloproteinases, especially MMP2 and MMP9, which are responsible for elastin and collagen breakdown, thereby maintaining vessel wall integrity and elasticity. In addition, RES modulates microRNA expression by decreasing pro-aneurysmal miR-29b and increasing protective miR-21, actions that enhance ECM stability, promote SMC survival, and reduce apoptosis.

At the cellular level, RES improves SMC function by counteracting senescence and supporting phenotypic flexibility, partly through activation of SIRT1-, AMPK-, and PGC-1α–related pathways. These pathways enhance mitochondrial function, stimulate autophagy, and improve cellular energy metabolism. In cardiac tissue, RES protects cardiomyocytes from apoptosis and oxidative injury, reduces pathological signaling such as p38 MAPK activation, and improves antioxidant defenses, thereby preserving cardiac structure and function.

Collectively, these mechanisms allow resveratrol to slow or prevent the progression of cardiovascular disease in animal models by promoting vascular repair, maintaining ECM integrity, reducing oxidative damage, and enhancing endothelial and myocardial health [20]

Mechanism of action of Resveratrol to Prevent Cardiovascular disease in Human:

Increasing the activity of eNOS :

According to Bonnefont-Rousselot D resveratrol works by an important way is by increasing the activity of eNOS (Endothelial nitric oxide synthase), an enzyme that produces nitric oxide (NO)that plays an important role on vascular health. Nitric oxide aids to relax and extend the blood vessels which improves blood flow and lowers the risk of heart diseases.

Overall, Resveratrol helps protect the heart by:

- Increasing nitric oxide production
- Reducing oxidative stress and inflammation
- Preventing endothelial dysfunction
- Inhibiting atherosclerosis (plaque formation in arteries)

It helps in these conditions by acting as a powerful antioxidant, reducing harmful free radicals and restoring nitric oxide availability [21].

Resveratrol-Mediated Activation of AMPK and SIRT1 in Cardiovascular Disease Prevention

According to Su M. et al. AMP-activated protein kinase (AMPK) and sirtuin-1 (SIRT1) are key metabolic regulators that play an important protective role in cardiovascular health. In cardiovascular disease (CVD), reduced AMPK and SIRT1 activity leads to impaired energy metabolism, endothelial dysfunction, oxidative stress, inflammation, and cardiomyocyte apoptosis.

Resveratrol exerts its cardioprotective effects mainly by activating both SIRT1 and AMPK. Through SIRT1 activation, resveratrol suppresses oxidative stress, inflammation, and apoptosis, while improving endothelial NO production and mitochondrial function. By activating AMPK, resveratrol further enhances energy

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metabolism, antioxidant responses, autophagy, and glucose handling in cardiac tissue. The coordinated activation of AMPK–SIRT1 signaling pathways (such as AMPK–SIRT1–PGC-1α, AMPK–SIRT1–FOXOs, and AMPK–SIRT1–PPARα) ultimately helps prevent and attenuate cardiovascular complications, particularly in diabetes-associated cardiovascular disease [22].

Molecular Mechanisms Underlying the Cardioprotective Effects of Resveratrol

According to Cheng CK. et al. Resveratrol provides cardioprotection through a multi-target mechanism involving endothelial cells, vascular smooth muscle cells, cardiomyocytes, and immune cells.

After absorption, it enters cells via passive diffusion and SGLT1 transport and mainly activates SIRT1, a key regulator of aging, metabolism, oxidative stress, and inflammation. SIRT1 activation enhances eNOS activity directly and via AMPK, increasing nitric oxide production and improving vascular function. Through the SIRT1–LKB1–AMPK axis, resveratrol supports energy homeostasis, reduces cardiac hypertrophy, limits vascular smooth muscle cell proliferation, and suppresses inflammatory macrophage responses.

It also regulates gene expression by activating FOXO and inhibiting NF-κB, thereby enhancing antioxidant defenses and reducing inflammation, while modulating KLF2 and PPAR signaling for vascular protection.

Additionally, resveratrol improves mitochondrial function, activates Nrf2 and autophagy pathways, mimics exercise-related benefits, regulates circadian rhythm, and beneficially alters gut microbiota, collectively contributing to its cardiovascular protective effects [23].

Health Benefits of Resveratrol in Cardiovascular Diseases

Atherosclerosis:

- According to Raj P.et al. Resveratrol is a promising compound for reducing the risk and progression of atherosclerosis due to its multiple beneficial actions. It improves lipid profiles by lowering total cholesterol, LDL, VLDL, triglycerides, free fatty acids, and apolipoprotein B, while increasing HDL (good cholesterol) [24].

- Its antioxidant properties also reduce oxidized LDL. Animal studies show that resveratrol decreases fatty streak formation, limits atherosclerotic lesion development, and improves plaque stability, with effects comparable to statins in some models.

- These benefits are partly mediated by modulation of hepatic enzymes such as HMG-CoA reductase and cholesterol 7α-hydroxylase, leading to reduced cholesterol synthesis and enhanced bile acid production. Overall, resveratrol shows strong anti-atherogenic potential [24,25].

Hypertension (High Blood Pressure):

- According to Wahab A. et al., Hypertension is another important cause of CVD. Research has shown that resveratrol supplementation at doses of 150 mg/day or higher can lower systolic blood pressure (the top pressure reading), but it does not significantly affect diastolic blood pressure [25].

- Ramírez-Garza SL. et al., shown that resveratrol improves endothelial function by activating calcium-dependent potassium channels and increasing nitric oxide production, which helps blood vessels relax [26].

Stroke:

- According to Koushik, M. et al., Resveratrol protects brain blood vessels during ischemic conditions by improving endothelial function and reducing inflammation and oxidative stress. Although human trials are limited, RES has been shown to increase cerebral blood flow in healthy individuals [27].

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Myocardial Infarction (Heart Attack):

- According to Kazemirad, H. et al., RES reduces infarct size, improves heart function, promotes new blood vessel formation, and protects heart cells from oxidative damage. It also helps by activating and regulating microRNAs involved in heart repair and remodeling [27].

- In myocardial infarction, RES protects cardiomyocytes by reducing oxidative damage, inhibiting platelet aggregation, promoting autophagy via SIRT1/AMPK activation, and enhancing tissue repair and regeneration in infarcted myocardium [28].

Endothelial dysfunction:

- According to Marques,B. et al., it is an early warning sign of cardiovascular disease, and although resveratrol has been shown to improve endothelial function in animal studies, evidence from human studies is limited. In this study, researchers examined whether a single dose of trans-resveratrol could improve endothelial function [29].

Heart Failure:

- According to Gal R. et al., Resveratrol improves cardiac function by reducing oxidative stress, inflammation, fibrosis, and abnormal heart remodeling. It activates protective pathways such as AMPK and SIRT-1 and improves calcium handling in heart muscle cells [30].

Treatment of Cardiovascular disease by using Resveratrol

A new micronized form of resveratrol called SRT501 has been developed and shows better potential. Treatment with resveratrol significantly restored antioxidant levels, reduced harmful oxidative markers, and lowered indicators of heart injury resveratrol can protect the heart from damage caused by isoprotereno. Heart function was checked using echocardiography, and blood and tissue samples were analyzed for markers of oxidative stress, inflammation, and organ damage [31].

Additionally, resveratrol may provide end-organ protection and can be used alongside standard antihypertensive drugs, such as ACE inhibitors, without the need for additional medications. Overall, while current clinical evidence remains inconclusive, dose-dependent reductions in SBP suggest that resveratrol, particularly at higher doses, may play a supportive role in preventing or managing hypertension, warranting further well-designed clinical trials. Although clinical trial results are inconsistent, several randomized controlled trials and meta-analyses indicate that resveratrol can reduce systolic blood pressure (SBP), especially at higher doses (≥300 mg/day) [32].

Although, resveratrol shows promising benefits for cardiovascular diseases, several research gaps still exist. Most of the positive results are based on animal and laboratory studies, while large and long-term human clinical trials are limited. Resveratrol also has low bioavailability, meaning only a small amount is absorbed and used by the body. The ideal dose, duration, and formulation are not clearly established, and clinical studies have shown mixed results. In addition, there is limited information on its long-term safety, drug interactions, and exact mechanisms in humans. Therefore, future studies should focus on well-designed human trials, improved formulations to increase absorption, standardized dosing, long-term safety evaluation, and understanding how resveratrol works in different patient groups before it can be widely recommended for cardiovascular disease prevention or treatment.

Application

The major applications of resveratrol are given below:

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Control of Hypertension

Resveratrol has attracted considerable attention as a potential preventive or supportive therapy for hypertension because of its beneficial cardiovascular actions. Preclinical studies consistently show that resveratrol can lower blood pressure through several mechanisms, including increased endothelial nitric oxide (NO) production, reduced vascular inflammation and oxidative stress via SIRT1 activation, and decreased calcium (Ca^{2+}) influx in vascular smooth muscle cells.

These effects suggest improved endothelial function and vasodilation, both of which are important in preventing hypertension and its complications. Although clinical trial results are inconsistent, several randomized controlled trials and meta-analyses indicate that resveratrol can reduce systolic blood pressure (SBP), especially at higher doses (≥300 mg/day). Since SBP is considered a stronger predictor of cardiovascular risk than diastolic blood pressure, this effect may still be clinically meaningful. Additionally, resveratrol may provide end-organ protection and can be used alongside standard antihypertensive drugs, such as ACE inhibitors, without the need for additional medications [33].

Management of Atherosclerosis

Resveratrol is applied in the prevention and slowing of atherosclerotic plaque development. It improves lipid profiles by reducing total cholesterol, LDL, VLDL, triglycerides, and oxidized LDL, while increasing HDL levels. It also stabilizes plaques and prevents endothelial damage, thereby lowering the risk of heart attack and stroke.

It helps prevent atherosclerosis by improving lipid metabolism**,** reducing oxidative stress**,** lowering inflammation**,** and regulating important signaling pathways involved in vascular health. These protective effects make resveratrol a promising natural compound for the prevention and treatment of atherosclerosis [34].

Improvement of Endothelial Function

Endothelial dysfunction is an early marker of cardiovascular disease. Resveratrol improves endothelial health by activating eNOS and increasing nitric oxide availability, which enhances blood flow and reduces vascular stiffness. This application is especially important in individuals with diabetes, obesity, and metabolic syndrome [35].

Support in Heart Failure Management

Resveratrol helps prevent heart failure by protecting the heart through several interconnected mechanisms. It improves left ventricular function, allowing the heart to pump blood more effectively even after injury, while also reducing cardiac hypertrophy, which is the abnormal enlargement of heart muscle cells. Resveratrol decreases interstitial fibrosis and collagen deposition, thereby preventing stiffness of the heart muscle and preserving normal cardiac structure. It also lowers plasma levels of BNP(B-type Natriuretic peptide), a marker of cardiac stress, indicating an overall improvement in heart condition,significantly reduces oxidative stress and inflammation by decreasing the production of reactive oxygen species (ROS) .

Resveratrol also restores MKP-1 activity, which helps regulate excessive stress signaling. Through these combined effects—reducing oxidative damage, inflammation, fibrosis, maladaptive signaling, and structural remodeling and also it effectively slows the progression of heart failure [36].

Cardioprotection in Ischemic Heart Disease

Resveratrol may prevent ischemic heart disease primarily through its ability to preserve mitochondrial function and reduce oxidative stress in the myocardium. In ischemic conditions, excessive generation of reactive oxygen species (ROS) disrupts mitochondrial integrity, impairs ATP production, and promotes cardiomyocyte injury and death, ultimately leading to left ventricular dysfunction.

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Resveratrol exerts cardioprotective effects by restoring the balance between ROS production and antioxidant defenses within cardiac mitochondria. It enhances endogenous antioxidative capacity through upregulation of antioxidant enzymes such as heme oxygenase-1, superoxide dismutase, catalase, and glutathione, thereby limiting oxidative damage during ischemia and reperfusion.

By reducing mitochondrial oxidative stress, resveratrol helps maintain mitochondrial bioenergetics, prevents energy depletion, and attenuates apoptosis and necrosis of cardiomyocytes. Collectively, these actions protect myocardial tissue from ischemic injury, support left ventricular function, and highlight the potential of resveratrol as a preventive and therapeutic agent in ischemic heart disease [37].

DISCUSSION

Nutraceuticals have emerged as an important link between nutrition and pharmaceuticals, has a preventive and therapeutic benefits for several chronic diseases, particularly cardiovascular diseases (CVDs). Among various nutraceuticals, resveratrol has gained significant attention due to its broad spectrum of biological activities and natural origin. The present review highlights that resveratrol acts on multiple molecular targets involved in cardiovascular pathology, making it a promising candidate for integrative cardiovascular health management. Cardiovascular diseases are strongly associated with oxidative stress, inflammation, endothelial dysfunction, abnormal lipid metabolism, platelet aggregation, and impaired energy homeostasis. The reviewed literature clearly indicates that resveratrol counteracts these pathological mechanisms through activation of key signaling pathways such as SIRT1, AMPK, Nrf2, eNOS, and inhibition of NF-κB. By enhancing nitric oxide bioavailability through eNOS activation, resveratrol improves endothelial function and vascular relaxation, thereby reducing hypertension and atherosclerotic risk. Resveratrol plays a vital role in lipid regulation by lowering total cholesterol, LDL, VLDL, triglycerides, and oxidized LDL, while increasing HDL levels. These effects contribute to plaque stabilization and prevention of atherosclerosis. Its anti-inflammatory action, mainly mediated via SIRT1-dependent inhibition of NF-κB signaling, reduces vascular inflammation, cytokine production, and adhesion molecule expression, limiting immune cell infiltration into the vascular wall. Resveratrol also demonstrates antiplatelet and antithrombotic effects, decreasing the risk of myocardial infarction and stroke. In ischemic heart conditions, resveratrol protects cardiomyocytes by reducing oxidative damage, promoting angiogenesis, enhancing mitochondrial function, and regulating autophagy and microRNA expression. Additionally, its ability to improve calcium handling and reduce myocardial fibrosis makes it beneficial in heart failure management. A major limitation in the clinical development of resveratrol is the inconsistency of trial outcomes. While some randomized controlled trials and meta-analyses report beneficial effects—particularly on systolic blood pressure, inflammatory markers, and endothelial function—others fail to demonstrate significant improvements in lipid profiles, glycemic control, or vascular outcomes. These conflicting results may be partly explained by pronounced dose-dependency, as several studies suggest that cardiometabolic benefits are observed primarily at higher doses (≥300 mg/day), whereas lower doses often yield negligible effects. Higher doses raise concerns regarding long-term safety, tolerability, and interindividual variability in response. Compounding these issues is resveratrol's poor oral bioavailability, resulting from rapid intestinal absorption followed by extensive first-pass metabolism and rapid conversion to glucuronide and sulfate conjugates with uncertain biological activity. Consequently, circulating levels of free, bioactive resveratrol remain low, potentially limiting its clinical efficacy. The lack of standardized formulations and dosing strategies further exacerbates variability across studies. Emerging delivery approaches, including micronized formulations, encapsulation, liposomal systems, and nano-based carriers, show promise in enhancing systemic exposure and tissue targeting, but their clinical relevance requires rigorous validation.

CONCLUSION

This review concludes that resveratrol is a potent nutraceutical with significant cardioprotective potential. Its antioxidant, anti-inflammatory, anti-atherosclerotic, antihypertensive, and endothelial-protective properties make it a valuable candidate for the prevention and management of cardiovascular diseases. By targeting multiple molecular pathways such as SIRT1–AMPK–eNOS–Nrf2 and suppressing pro-inflammatory signaling like NF-κB, resveratrol effectively addresses the underlying mechanisms of cardiovascular

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pathology.Although preclinical and early clinical studies strongly support its benefits, limitations related to bioavailability and inconsistent clinical outcomes necessitate further research. Future studies should focus on improved delivery systems, standardized dosing regimens, and long-term clinical trials to fully establish resveratrol's role as a complementary or adjunct therapy alongside conventional cardiovascular drugs. Overall, with continued scientific and technological advancements, resveratrol holds great promise as a natural, safe, and effective nutraceutical for long-term cardiovascular disease prevention and health promotion. These findings should be interpreted cautiously, as current clinical evidence remains inconsistent and is constrained by short study durations, small sample sizes, heterogeneous dosing strategies, variable formulations, and reliance on surrogate endpoints rather than definitive cardiovascular outcomes. Importantly, resveratrol's low oral bioavailability, rapid metabolism, and uncertain dose–response relationships further limit conclusions regarding its clinical effectiveness. Therefore, while resveratrol holds conditional promise as a safe, natural adjunct to conventional cardiovascular therapies, its routine clinical use cannot yet be recommended. Future validation requires large-scale, well-designed randomized controlled trials employing standardized, bioavailable formulations, optimized dosing regimens, long-term safety assessments, and clinically meaningful cardiovascular endpoints. Until such evidence is available, resveratrol should be regarded as a promising but investigational nutraceutical whose therapeutic potential in cardiovascular disease remains to be conclusively established.

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