Botanical interventions in cardiovascular health

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1. Introduction

Cardiovascular disease (CVD) remains the most prominent cause of morbidity and mortality across the world. In fact, the World Health Organization (WHO) estimated nearly 18 million global deaths due to CVD in 2019 [1]. In the North American continent alone, CVD accounted for 36.4 million years of life lost and 4.5 million years lived with disability between 2000 and 2019 [2]. In view of its high prevalence and cost, there is still an urgent need to discover the pathophysiology of CVD, as much remains to be understood about its therapeutics and management.

Although there exists a diverse array of heart disease aetiologies, aberrant inflammatory processes appear to be a common link between different types of CVDs [3]. The management of lifestyle diseases, including CVD, involves reduction or elimination of risk factors, early non-pharmacological and pharmacological treatment to prevent adverse outcomes, and preservation of workability and quality of life.

Herbal medicines have attracted great interest from scientists due to their remarkable efficacy and safety profiles. Increasing scientific evidence has shown that various herbal medicines achieve adequate efficacy in the treatment of CVD through their antioxidant, antiapoptotic, and anti-inflammatory properties [5]. According to WHO, 85% of people worldwide use medicinal plants for treatment, and 80% of people in developing countries rely on traditional and complementary medicine for their primary health care needs in prevention, diagnosis, or treatment of physical and mental illnesses, even if not approved by regulatory agencies [4].

Numerous herbal interventions have demonstrated promising cardiovascular benefits. Medicinal herbs well identified for treating CVD include *Moringa oleifera*, Ginseng, *Ginkgo biloba*, *Celosia argentea*, *Gongronema latifolium*, *Gynostemma pentaphyllum*, *Bombax ceiba*, *Gentiana lutea*, *Allium sativum*, *Crataegus* spp, *Curcuma longa*, *Camellia sinensis*, and *Zingiber officinale*. Mechanistic insights reveal that herbal interventions often target multiple pathways involved in CVD pathogenesis, encompassing anti-inflammatory, antioxidant, anti-thrombotic, anti-hypertensive, and lipid-lowering effects [6].

Some herbs enhance endothelial function, promote nitric oxide production, and exert vasodilatory effects, thereby contributing to improved cardiovascular health. Clinical studies have provided evidence of the efficacy of certain herbal interventions in reducing CVD risk factors and improving patient outcomes. However, more rigorous, large-scale clinical trials are needed to establish their long-term safety and effectiveness. It is crucial to consider potential herb-drug interactions and to standardise dosages for reliable therapeutic outcomes [6]. This review explores the pathogenesis of CVDs, current treatments, and evidence-based herbal interventions elaborating phytoconstituents, mechanisms of action, and clinical relevance. While promising, integration into modern medicine requires rigorous standardisation and clinical validation.

2. Pathogenesis and Signs

The development of cardiovascular diseases (CVDs) involves several interlinked pathological mechanisms: [1,12]

Endothelial Dysfunction:
This is an early marker in CVD pathogenesis, characterised by reduced nitric oxide availability leading to impaired vasodilation. The endothelium loses its antithrombotic properties, resulting in increased vascular tone, platelet adhesion, and promotion of clot formation.

Oxidative Stress:

An imbalance between reactive oxygen species (ROS) production and antioxidant defences leads to oxidative stress. Excess ROS damage vascular cells, oxidise LDL cholesterol, and accelerate atherosclerotic plaque development and instability.

Chronic Inflammation:

Persistent low-grade inflammation plays a central role in CVD. Elevated pro-inflammatory cytokines like TNF-α and IL-6 induce endothelial dysfunction, enhance vascular smooth muscle proliferation, and promote plaque formation and rupture.

Thrombogenesis:

Thrombogenesis involves enhanced platelet aggregation and activation of the coagulation cascade. This creates a pro-thrombotic environment, increasing the risk of events such as myocardial infarction and stroke.

Typical symptoms include [2]:

CVDs manifest with varied symptoms depending on the underlying pathology. Common clinical presentations include:

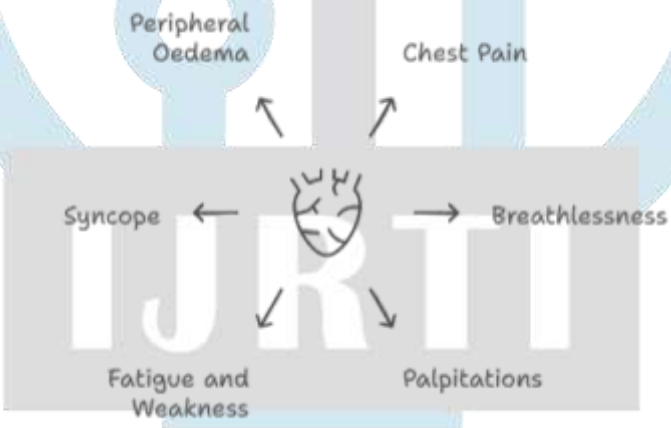

Figure 1. Typical symptoms

- Chest pain (Angina pectoris): Often radiating to the left arm or jaw, indicating myocardial ischemia.
- Breathlessness: Due to reduced cardiac output or pulmonary congestion.
- Palpitations: Perception of abnormal heartbeats, often in arrhythmias.
- Fatigue and weakness: Resulting from impaired perfusion to tissues.
- Syncope: Temporary loss of consciousness due to reduced cerebral blood flow.
- Peripheral oedema: Especially in congestive heart failure [2].

3. Current Therapeutic Approaches [4]

While botanical interventions hold promise for cardiovascular protection, it is essential to understand the current pharmacological strategies employed in cardiovascular disease management. Conventional therapies primarily target risk reduction through antiplatelet, anticoagulant, antihypertensive, and lipid-lowering mechanisms, effectively reducing morbidity and mortality associated with cardiovascular events. The following therapeutic classes and their mechanisms illustrate the established pharmacological approaches that serve as the standard of care against which novel botanical interventions are evaluated.

Table 1. Current therapeutic approaches

Drug Class	Examples	Mechanism
Antiplatelets	Aspirin, Clopidogrel	Inhibit platelet aggregation
Anticoagulants	Warfarin, Rivaroxaban	Inhibit coagulation cascade
Beta-blockers	Metoprolol, Propranolol	Reduce HR and myocardial oxygen demand
ACE inhibitors	Enalapril, Lisinopril	Prevent angiotensin II formation
Calcium channel blockers	Amlodipine, Diltiazem	Vasodilation via calcium channel inhibition
Diuretics	Hydrochlorothiazide, Furosemide	Reduce plasma volume and BP
Statins	Atorvastatin, Rosuvastatin	Lower LDL cholesterol synthesis

However, the long-term use of conventional pharmacological treatments for cardiovascular diseases is often limited due to their associated adverse effects. For instance, diuretics and certain antihypertensive drugs can cause electrolyte imbalances, leading to complications such as hypokalaemia or hyperkalaemia, which may further exacerbate cardiac dysfunction. Additionally, some medications, including statins and other lipid-lowering agents, carry the risk of hepatotoxicity, necessitating regular monitoring of liver function to prevent serious hepatic damage. Antithrombotic and anticoagulant drugs, while effective in preventing clot formation, significantly increase the risk of bleeding, including gastrointestinal haemorrhage and intracranial bleeding, especially with prolonged use. [9] These safety concerns have fuelled growing interest in exploring complementary and alternative therapies, particularly botanical interventions, which are perceived to offer cardioprotective benefits with potentially fewer adverse effects.[10]

4. Mechanisms of Cardiovascular Protection by Botanicals

Antioxidant Properties:

Oxidative stress arises when excessive production of reactive oxygen species (ROS) overwhelms the cellular antioxidant defense system, leading to damage of DNA, proteins, and lipids. Elevated ROS levels not only cause direct cellular injury but also trigger inflammatory processes by promoting the synthesis and release of pro-inflammatory cytokines. In cardiovascular disease, oxidative stress plays a central role in the development of atherosclerosis by disrupting the balance between pro-oxidants and antioxidants, resulting in endothelial dysfunction. ROS contribute to both the initiation and progression of atherosclerosis through multiple mechanisms[18]. One key process is the oxidation of low-density lipoprotein (LDL) to form oxidized LDL (Ox-LDL), which is highly atherogenic and stimulates inflammatory responses within the arterial wall. This oxidative modification of LDL is considered an early and critical event in atherosclerosis, initiating a cascade of inflammatory processes that drive plaque formation[11,12].

ROS activate several inflammatory pathways that exacerbate vascular injury. They stimulate nuclear factor-kappaB (NF-κB) by oxidizing the IκB kinase (IKK) complex, leading to phosphorylation and degradation of IκB, which allows NF-κB to translocate into the nucleus and upregulate pro-inflammatory cytokines (IL-1β, IL-6, IL-8, IL-18, TNF-α), adhesion molecules (VCAM-1, ICAM-1), and chemokines (MCP-1), thereby creating a pro-inflammatory environment that causes endothelial injury and intimal thickening[13,16]. ROS also stabilize hypoxia-inducible factor-1 alpha (HIF-1α), enhancing the expression of HIF-1α-associated pro-inflammatory genes. Additionally, ROS activate the NLRP3 inflammasome complex, composed of NLRP3, ASC, and caspase-1, which cleaves pro-IL-1β and pro-IL-18 into their

mature forms, promoting adhesion molecule and chemokine expression to recruit leukocytes and monocytes during early atherogenesis. Furthermore, TNF-α exacerbates oxidative stress by increasing mitochondrial ROS (mtROS) production, activating NADPH oxidase, and upregulating inducible nitric oxide synthase (iNOS) in endothelial cells. Thus, oxidative stress, inflammation, and endothelial dysfunction are tightly interconnected processes in the pathogenesis of atherosclerosis[12,13].

Botanicals with antioxidant properties, such as curcumin, resveratrol, and polyphenol-rich plant extracts, may protect against cardiovascular disease by reducing ROS levels, preventing LDL oxidation, and modulating these inflammatory pathways.

Anti-Inflammatory Effects:

Inflammation plays a central role in the pathogenesis of atherosclerosis, involving a complex interplay between immune cells, cytokines, and lipid metabolism. The process is primarily initiated by the accumulation of oxidized low-density lipoprotein (Ox-LDL) within the arterial wall, which triggers a robust inflammatory response[18]. Ox-LDL promotes the recruitment of inflammatory cells, particularly monocytes, which adhere to the endothelium, migrate into the intima, and differentiate into macrophages. These macrophages engulf Ox-LDL, transforming into foam cells, which are characteristic of atherosclerotic plaques. Additionally, Ox-LDL stimulates the release of pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) from macrophages and endothelial cells, further amplifying the inflammatory response[17].

The inflammatory pathway is also mediated by Toll-like receptor 4 (TLR4), which recognizes Ox-LDL and activates downstream signaling cascades that enhance cytokine production and inflammation within the vascular wall. This chronic inflammatory environment leads to endothelial dysfunction, an early hallmark of atherosclerosis, and promotes the migration of smooth muscle cells, deposition of extracellular matrix, and formation of the fibrous cap. Over time, the continued accumulation of foam cells and inflammatory mediators contributes to plaque growth and instability. Plaque rupture can result in thrombosis, leading to serious cardiovascular events such as myocardial infarction or stroke[17,18].

Botanicals with anti-inflammatory properties, including polyphenol-rich plant extracts, curcumin, and resveratrol, exert protective cardiovascular effects by modulating these inflammatory pathways. They inhibit the activation of pro-inflammatory cytokines, suppress TLR4 signaling, and reduce macrophage-mediated foam cell formation, thereby attenuating vascular inflammation and slowing the progression of atherosclerosis.

Lipid Metabolism Modulation:

Botanical compounds often improve lipid profiles by reducing cholesterol synthesis, enhancing LDL clearance, and modulating lipid absorption. For instance, a systematic review of herbal interventions revealed that green tea, flavonoid-rich extracts, and berberine significantly lowered total cholesterol, LDL-C, and triglycerides in patients with metabolic syndrome or hyperlipidemia. Berberine specifically has been shown in clinical trials to reduce LDL-C and increase HDL-C in hyperlipidemic and type 2 diabetes patients . These phytochemicals act via mechanisms such as upregulating LDL receptors in the liver and inhibiting HMG-CoA reductase, mimicking statin-like effects without pharmaceutical intervention[33].

Vasodilation and Blood Pressure Regulation:

Several botanicals promote vasodilation and reduce blood pressure by enhancing nitric oxide (NO) bioavailability and relaxing vascular smooth muscle. Garlic supplementation (650–1500 mg/day) has been associated with systolic blood pressure reductions of 9–17 mmHg in hypertensive subjects, likely via enhanced endothelial NO production . Curcumin meta-analyses of 35 RCTs also show modest but statistically significant reductions in systolic and diastolic blood pressure as well as improved flow-mediated dilation. Other herbs such as hibiscus and Nigella sativa demonstrate antihypertensive effects comparable to captopril or lower-dose garlic, supporting their role in non-pharmaceutical blood pressure management[34].

Antithrombotic and Anti-Platelet Effects:

Botanicals exert antithrombotic effects by inhibiting platelet aggregation and supporting fibrinolysis. Garlic-derived organosulfur compounds, such as allicin and ajoene, inhibit platelet aggregation via ADP and thromboxane pathways, paralleling the mechanism of clopidogrel[35]. A randomized controlled trial showed garlic powder (Allicor) decreased ADP-induced aggregation by 25% and increased fibrinolysis by 22%[36]. These properties make garlic a valuable adjunct, particularly for patients at risk of atherosclerotic plaque rupture and thrombosis.

Anti-Obesity and Metabolic Effects:

Botanical extracts can aid weight management and metabolic health by enhancing energy expenditure, suppressing appetite, and improving insulin sensitivity. A meta-analysis of 279 clinical trials found that green tea, Nigella sativa, and other herbals significantly reduced weight, BMI, waist circumference, total cholesterol, and triglycerides [37,38]. Ginger supplementation has been reported to increase calorie burn, reduce hunger, and decrease cholesterol, blood sugar, and blood pressure in overweight adults[39]. Berberine also shows preliminary anti-obesity effects in animals and is under active clinical investigation[40]. These botanicals offer holistic support for metabolic syndrome, though larger RCTs are needed to confirm their long-term efficacy.

5. Botanical Interventions in Cardiovascular Health

Botanical interventions have gained increasing attention for their potential role in the prevention and management of cardiovascular diseases. Various medicinal plants contain bioactive phytochemicals that exhibit antioxidant, anti-inflammatory, vasodilatory, and cardioprotective effects, contributing to improved vascular health and reduced cardiovascular risk. The table below summarizes key botanicals traditionally and clinically used for cardiovascular benefits, highlighting their active constituents, mechanisms of action, and clinical relevance in cardiovascular care.

Table 2.Botanical Interventions in Cardiovascular Health

Plant	**Active Constituents**	**Mechanisms of Action**	**Clinical Relevance**
Green Tea (*Camellia sinensis*)	Catechins (EGCG)	Antioxidant; improves endothelial function; reduces LDL oxidation [6]	Lowers BP, enhances vascular health
Garlic (*Allium sativum*)	Allicin, sulfur compounds	Lowers cholesterol; antiplatelet; enhances NO production [7]	Reduces cholesterol and BP in meta-analyses
Hawthorn (*Crataegus spp.*)	Flavonoids, procyanidins	Positive inotropic; vasodilatory; antioxidant [8]	Used for mild CHF; improves exercise tolerance
Arjuna (*Terminalia arjuna*)	Triterpenoids, flavonoids	Improves coronary perfusion; cardioprotective; antioxidant [9]	Beneficial in ischemic heart disease
Danshen (*Salvia miltiorrhiza*)	Tanshinones	Antioxidant; antiplatelet; vasodilatory [10]	Used in TCM for angina and ischemia

Ginkgo (*Ginkgo biloba*)	Flavonoids, ginkgolides	Vasodilatory; antioxidant; PAF inhibition [11]	Enhances peripheral and cerebral blood flow
Ginseng (*Panax ginseng*)	Ginsenosides	Positive inotropic; calcium modulation; anti-inflammatory [10]	Used in TCM for heart failure and fatigue
Moringa (*Moringa oleifera*)	Flavonoids (quercetin, kaempferol), phenolic acids	Antioxidant; anti-inflammatory; hypolipidemic; improves endothelial function [12]	Lowers cholesterol, improves lipid profile, reduces BP
Turmeric (*Curcuma longa*)	Curcumin	Anti-inflammatory via NF-κB inhibition; antioxidant; reduces lipid peroxidation [13]	Improves endothelial function, lowers LDL, potential anti-atherosclerotic agent
Resveratrol (from grapes, berries)	Stilbenes (resveratrol)	Antioxidant; activates SIRT1; improves mitochondrial function; vasodilatory [14]	Reduces BP, improves endothelial function, cardioprotective
Berberine (from *Berberis spp.*)	Isoquinoline alkaloids (berberine)	AMPK activation; lipid lowering; improves insulin sensitivity; anti-inflammatory [15]	Reduces cholesterol, triglycerides, improves cardiovascular risk in diabetics
Brassica (e.g., broccoli, cabbage)	Glucosinolates, sulforaphane	Antioxidant via Nrf2 activation; anti-inflammatory; improves endothelial function [16]	Associated with reduced CVD risk, improves vascular health

6. Preclinical and Clinical Evidence

Botanical and plant-based interventions have emerged as promising strategies in the prevention and management of cardiovascular diseases. Numerous clinical trials and systematic reviews have investigated the effects of phytochemicals such as those found in plant-based diets, garlic, resveratrol, and curcumin, demonstrating their potential to improve lipid profiles, lower blood pressure, and reduce inflammatory markers. Despite these encouraging findings, many studies are constrained by small sample sizes and a lack of large-scale Phase III trials, limiting definitive conclusions. Nonetheless, this growing body of evidence underscores the importance of integrating phytochemical-rich diets and herbal formulations as complementary approaches in cardiovascular health, while highlighting the need for further rigorous research to establish their clinical efficacy and safety.

Table 3.Preclinical and Clinical Evidence

No.	Study / Source	NCT Number / Reference	Intervention	Phase	Population	Status	Key Outcomes & Findings
1	Do Cardiac Health Ecosystem	NCT03178305 [27]	Do Change behavioral intervention incl. plant-based diet	Phase 2 (RCT)	Cardiac patients with ≥2 risk factors	Completed	Improved behavioral flexibility linked to better health behaviors; cost-effectiveness shown; CV outcomes monitored (details not in excerpt).

2	Botanical Drug Trials (2016–2019)	PMC7438343 [28]	Various botanical drugs for CV and other diseases	14% Phase I; mostly Phase II/III	Mixed (81 CV-related)	Varies	Small sample sizes (≤100/arm) limit power; garlic showed no LDL-C reduction over 6 months; Phase I often redundant for botanicals with traditional use.
3	NHLBI Diet Research	NHLBI [29]	Dietary interventions rich in phytochemicals	NA	General US cohorts	Ongoing	Framingham study links flavonoid-rich diets to lower CVD risk; ENRICH includes maternal dietary counseling to reduce long-term heart disease risk.
4	Systematic Review of Herbal Interventions	PubMed 2022 [30]	Moringa, Ginseng, Ginkgo, Garlic, Turmeric, Green Tea	Review	Patients with CV risks (HTN, hypercholesterolemia)	NA	Herbal trials show anti-inflammatory, antioxidant, lipid-lowering effects; e.g., polyphenols lowered LDL-C/HDL-C ratio; most trials small, lacking Phase III.
5	Garlic (Allium sativum)	JACC 2009 [31]	Garlic extract	NA (example: 6m trial)	Moderate hypercholesterolemia	Completed	No significant LDL-C reduction; antiplatelet effects raise bleeding risk when combined with anticoagulants.
6	Resveratrol Trials	PMC4609427 [32]	Resveratrol (≥150 mg/d)	NA	Obese, post-MI patients	Varies	Reduced SBP and improved flow-mediated dilation; diastolic BP effect inconsistent; lacks long-term trials.
7	Curcumin, Berberine, Brassica Trials	PMC4609427 [32]	Extracts of curcumin, berberine, Brassica oleracea	NA	Mixed populations	Varies	Small heterogeneous trials show antioxidant and anti-inflammatory benefits but limited generalizability.
8	Online Plant-Based Dietary Program for T2DM	NCT05777746 [26]	Online plant-based diet education	Not specified (RCT)	Adults with T2DM on stable meds	Unknown (Mar 2023)	Aimed to reduce HbA1c, LDL-C, BP; plant-based diets reduced LDL by ~0.33 mmol/L vs omnivorous low-fat diets; BP reduction likely in SBP>130 mmHg; inflammation data limited.

7. Safety Considerations and Challenges

Despite their benefits, botanical therapies pose challenges:

Standardisation: Variability in bioactive constituent concentrations due to cultivation and processing factors.

Herb-drug interactions: For example, garlic may enhance anticoagulant effects, increasing bleeding risk.

Lack of large-scale RCTs: Many studies are preclinical or involve small sample sizes, limiting conclusive evidence.

8. Conclusion

Cardiovascular diseases continue to pose a formidable challenge to global health, driven by complex interplays of oxidative stress, inflammation, endothelial dysfunction, and metabolic disturbances. While conventional pharmacotherapies remain the cornerstone of CVD management, their long-term use is often limited by adverse effects and incomplete risk mitigation. In this context, botanical interventions emerge

as promising complementary or alternative strategies owing to their multitargeted actions, favourable safety profiles, and centuries of traditional use.

A diverse array of medicinal plants, including *Moringa oleifera, Curcuma longa, Camellia sinensis, Allium sativum, Berberis spp., Brassica vegetables, Panax ginseng*, and *Ginkgo biloba*, has demonstrated significant cardioprotective effects in preclinical and clinical studies. Their bioactive constituents exert antioxidant, anti-inflammatory, lipid-lowering, vasodilatory, antithrombotic, and metabolic regulatory actions, thereby addressing the multifactorial nature of CVD pathogenesis. Moreover, certain botanicals improve endothelial function, modulate nitric oxide bioavailability, and reduce blood pressure, supporting vascular health and reducing cardiovascular risk.

Despite these promising benefits, challenges remain regarding standardisation, dose optimisation, herb–drug interactions, and clinical validation. The variability in phytochemical composition due to cultivation, processing, and extraction methods necessitates stringent quality control for safe and effective use. Furthermore, robust large-scale randomised controlled trials are essential to establish the long-term efficacy and safety of botanical interventions and to integrate them responsibly into evidence-based cardiovascular care.

In conclusion, botanical interventions represent a valuable addition to modern cardiovascular therapeutics. By harnessing their multifaceted pharmacological potential through rigorous scientific validation, they can contribute meaningfully to holistic cardiovascular disease prevention and management, ultimately improving patient outcomes and quality of life.

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