# Introduction to Cardiovascular Diseases and Herbal Medicine

CHAPTER 1

**Gnaneswari Kodi[1], Suneetha Achanti[2], Thirumala Devi Siriki[1], and Sree Geetha A[1]**

[1] *Aditya College of Pharmacy, Surampalem, Andhra Pradesh, India*

[2] *KVSR Siddhartha College of Pharmaceutical Sciences, Vijayawada, Andhra Pradesh, India*

## 1.1 INTRODUCTION

### 1.1.1 CARDIOVASCULAR DISEASES

Cardiovascular diseases (CVDs) are a class of disorders that affect the heart and associated blood vessels and encompass a wide range of conditions that involve narrowed or blocked blood vessels, leading to a variety of conditions like peripheral vascular diseases, coronary heart disease, heart failure and heart attacks, dyslipidemias, hypertension, chest pain (Angina pectoris), or stroke, registering universal deaths of more than 17 million and accounting as a considerable burden both economically and health-wise worldwide [1]. The need for more effective preventive and treatment measures for CVDs is essential due to the increased incidence of patients suffering [2]. In the recent era, it is relatively prevalent that the incidence of these CVDs is escalating among young individuals [3, 4]. The main evolution of CVDs is due to the vascular smooth muscle cell (VSMC) impairment, inflammation, and dysfunction of the endothelium, which becomes a paramount offender with absolute cardiovascular risk, leading to atherosclerosis, thrombosis, high blood pressure, coronary vasoconstriction, and myocardial ischemia [5]. Endothelial cell dysfunction is important because this phenomenon could be reversed, and it is stated that a healthy endothelium could reveal vasodilatory and anti-inflammatory properties [5].

### 1.1.2 EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES

Despite drawing attention to healthy lifestyle encouragement, studies in 2019 estimated that 17.9 million deaths were observed due to the risk of CVDs, representing all-inclusive deaths of 32% globally [6, 7]. According to WHO 2024, diseases of the cardiac system remain the prime source of death, increasing to 18.5 million collapses each year, portraying comprehensive deaths of 35%, among which 85% are owing to myocardial infarction, heart attack, or stroke. Low- and middle-income populations are mainly affected, and lifestyle changes, inadequate healthcare infrastructure, and late diagnosis are the main trends. The demographic data [8] reveals that men are more prone to early onset of CVDs, and women in the post-menopause period are also at risk. Mortality from CVDs is highest in developed countries due to an increased workload on the nervous system that leads to hypertension, as well as a sedentary lifestyle, like lack of exercise and poor diet, which ultimately leads to atherosclerotic plaque deposition in blood vessels, heart attacks, or possibility of stroke [3].

#### 1.1.2.1 Epidemiological Models and Assessment Tools

The important epidemiological models for risk assessment include:

- Framingham risk score for evaluating the probability of cardiac attacks based on blood pressure, cholesterol, diabetes, smoking, etc.
- WHO/ISH (International Society of Hypertension) risk prediction charts that guide the interventions based on regional CVD risks [9].
- QRISK (QRESEARCH Cardiovascular Risk Algorithm) and ASCVD (atherosclerotic cardiovascular diseases) are risk estimators that include socioeconomic status and family history, along with more accurate predictors.

### 1.1.3 RISK FACTORS OF CARDIOVASCULAR DISEASES

The leading determinants of CVDs are categorized into environmental, metabolic, and behavioral risk factors like systolic blood pressure, low-density lipoprotein (LDL) cholesterol, body mass index, fasting plasma glucose, kidney dysfunction, diet, smoking, consumption of alcohol, physical activity, pollution, and temperature. [10] Rare and emerging risk factors like vitamin D, homocysteine, plasma concentration of uric acid, gut microbiota, sleep duration, and apnea are also being linked to the development of cardiovascular threat [11].

**Adaptable Determinants**

- Exalted blood pressure
- Hyperlipidemia
- Tobacco consumption

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- Diabetes mellitus
- Adiposity
- Quiescence
- Processed foods
- Intemperate alcohol consumption
- Psychosocial stress

**Unalterable Risk Factors**

- Age and gender [12]
- Ancestry and heredity
- Ethnicity

#### 1.1.3.1 Risk Factor Clustering

This involves a cluster of metabolic conditions like obesity, hypertension, dyslipidemia, and insulin resistance that act synergistically to raise the risk of CVDs and the social determinants of health that influence the risk distribution [12].

#### 1.1.3.2 Strategies to Prevent the Risk Factors

- Salt reduction
- Tobacco cessation
- Public campaigns for physical activity and healthy diets
- Early screening for hypertension, diabetes, and dyslipidemia
- Preventive pharmacotherapy (antihypertensive drugs, statins) [9]
- Counseling regarding lifestyle

### 1.1.4 MAJOR TYPES OF CARDIOVASCULAR DISEASES

Heart diseases are allied to the transgression of blood supply to the heart muscles, violation of ions like potassium, sodium, and calcium, infringement of the heart's nerve fibers. Owing to changes in the permeability of blood vessels, vascular diseases originate.

#### 1.1.4.1 Hypertension

Hypertension is a dominant player in the advent of heart disorders like atherosclerosis, stroke, artery diseases, and heart failure [13]. It is also referred as a silent killer due to the delayed onset of symptoms until advanced stages of the disease. Hypertension is defined as tenacious escalation of arterial blood pressure exceeding systolic pressure of 140 mmHg and a diastolic pressure of 90 mmHg [14]. An unmanaged and elevated blood pressure can influence changes like arterial remodeling, potentially making the walls narrower by thickening and causing them to lose their elasticity. This mechanism is termed arteriosclerosis, which can trigger target organ damage [15, 16], affecting brain, kidney, retina, and so on [17, 18].

**1.1.4.1.1 Pathophysiology** The two principal elements of hypertension involve cardiac output and systemic vascular resistance that elevate the blood pressure. Sodium intake, renal system function, and mineralocorticoids are the key contributors to an amplified cardiac output. The sympathetic nervous system, renin–angiotensin system, local autoregulation, and humoral factors are the main influencers of vascular resistance [19]. Activation of the sympathetic and renin–angiotensin systems cause vasoconstriction and sodium retention, along with humoral mediators like angiotensin, endothelin, and catecholamines [20], thus ultimately altering blood viscosity and flow, increasing stiffness of the vascular wall, and promoting oxidative stress in vascular smooth muscle and endothelial cell proliferation [21].

#### 1.1.4.2 Atherosclerosis

Atherosclerosis is a chronic progressive disease of the arterial wall that leads to conditions like coronary artery disease (CAD), peripheral vascular disease, and stroke. It is not only a risk factor but also a major contributor to the incidence of heart disease.

**1.1.4.2.1 Pathophysiology** It is characterized by inflammation arising from the impairment of endothelial cells, permitting accumulation of LDLs within the intima of the vessel wall, which are converted into oxidized LDL. These oxidized LDL particles initialize and expose cell adhesion molecules of the endothelium and recruit more inflammatory leukocytes into the sub-endothelial space [22]. Interleukins, cytokines, and reactive oxygen species (ROS) are secreted by these inflammatory blood cells, forming an inflamed arterial wall microenvironment. This microenvironment creates buildup of matrix, proliferation of VSMCs, and deposition of lipids, forming an atherosclerotic plaque [23–26]. In the course of time, progressive thickening occurs, persistently expanding and provoking occlusion of blood flow to other organs, and ensuing disorders like myocardial infarction, unstable angina, or stroke [27, 28].

Figure 1.1a,b illustrates the core pathological events underlying the development and progression of CVDs, with various predisposing factors such as hypertension involving alterations in cardiac output and systemic vascular resistance that initiate pathological changes primarily through endothelial injury and VSMC (Vascular Smooth Muscle Cell) dysregulation. Inflammatory stimuli initiate endothelial injury, leading to the accumulation of LDLs (low density lipids) within the vascular intima and their subsequent oxidation to oxidized LDL. The presence of oxidized LDL triggers endothelial cell activation, promoting the expression of cell adhesion molecules that attract and bind leucocytes. Activated immune cells release interleukins, cytokines, and ROS (reactive oxygen species), creating pro-inflammatory microenvironment within the arterial wall. This cascade stimulates VSMC proliferation and lipid deposition, resulting in intimal thickening and plaque development. Progressive plaque growth narrows the vessel lumen, reducing blood flow and leading to severe cardiovascular complications such as myocardial infarction, angina, stroke, and sudden cardiac death.

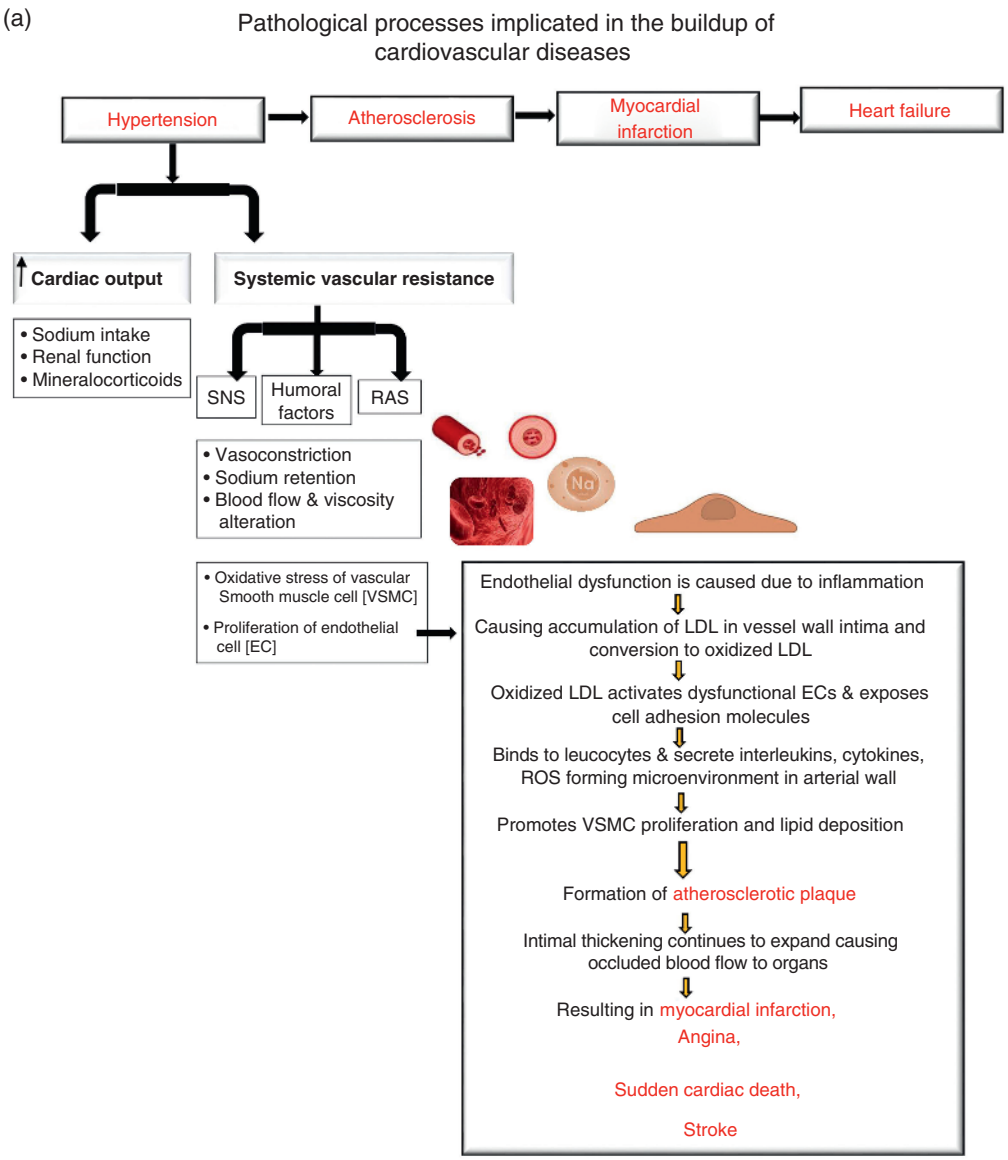



**FIGURE 1.1** (a) Core pathological events during cardiovascular diseases (CVDs); (b) pathological processes implicated in the buildup of cardiovascular diseases.

### 1.1.4.3 Coronary Artery Disease/Ischemic Heart Disease (IHD)

In this state of disease, plaque builds up in the coronary arteries, which supply the heart with sufficient blood, thereby leading to diminished blood flow.

#### 1.1.4.3.1 Pathophysiology

- Atherosclerosis and arteriosclerosis (plaque accumulation)
- Constriction of arteries resulting in diminished oxygen and blood supply
- Ischemia, angina pectoris, and myocardial infarction [29]

**Symptoms:**

- Chest discomfort (angina)
- Shortness of breath (dyspnea)
- Fatigue, with pain radiating from the shoulder to the palm
- Heart attack (blockage of an artery) [30]

**Causes: [31]**

- High lipid profiles
- Smoking
- Hypertension
- Diabetes
- Lack of exercise

**Diagnosis:**

- ECG
- Treadmill test

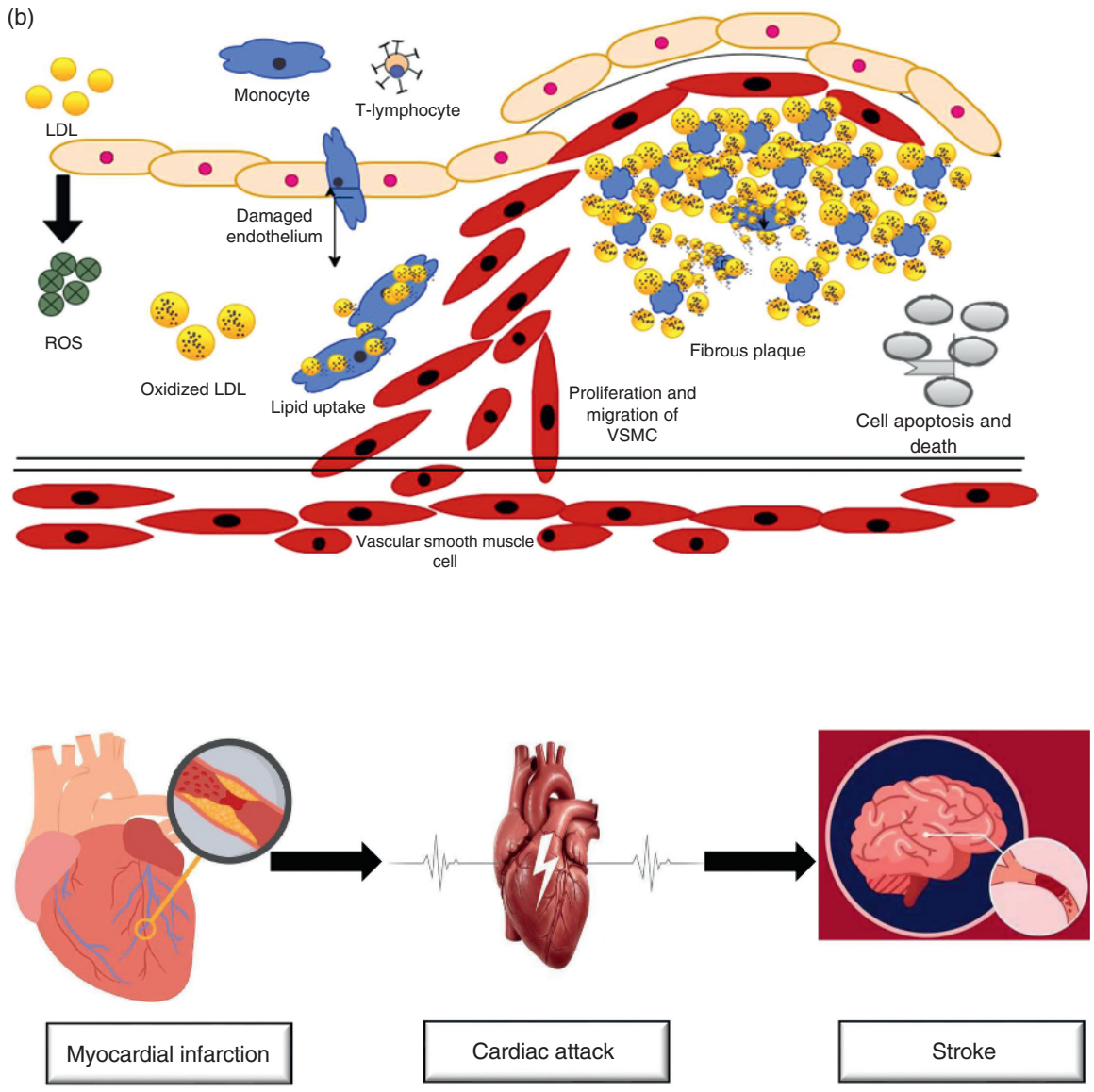



**FIGURE 1.1** (Continued)

- Coronary angiography
- Cardiac biomarkers (troponin)

### 1.1.4.4 Cerebrovascular Diseases

Stroke or transient ischemic attacks are provoked owing to influence of the blood flow and circulation to the brain, leading to temporary or permanent neurological dysfunction [32]. There are few types like

- Ischemic stroke (blockage in cerebral blood vessels)
- Hemorrhagic stroke (bleeding in and around the brain)
- Transient ischemic attack (temporary blockage and warning for stroke)

**Symptoms:**

- Numbness or weakness
- Confusion and difficulty in speaking
- Blurred vision
- Loss of balance or coordination

**Risk factors:**

- Hypertension (abnormal levels of blood pressure)
- Atrial fibrillation
- Diabetes
- Smoking
- Elevated lipid profiles

**Diagnosis:**

- Computed tomography (CT) (or) magnetic resonance imaging (MRI) of the brain
- Carotid ultrasound
- Cerebral angiography

### 1.1.4.5 Heart Failure (HF)

This is an important clinical diagnosis in which the heart cannot meet the requirements of the body, attributable to the blood-pumping efficiency of the heart.

**Types:**

- Left-sided heart failure (very common – pulmonary symptoms)
- Right-sided heart failure (peripheral edema)
- Systolic heart failure (reduced ejection fraction)
- Diastolic heart failure (preserved ejection fraction but impaired filling)

**Symptoms:**

- Dyspnea
- Somnolence
- Swelling of the legs and abdomen
- Orthopnea

**Causes:**

- CADs
- Hypertension
- Cardiomyopathy
- Valve disease
- Arrhythmias

**Diagnosis:**

- Echocardiogram
- Chest X-ray
- ECG
- BNP levels (B-type natriuretic peptide)

### 1.1.4.6 Peripheral Arterial Disease (PAD)

This is a distinguished circulatory condition in which the blood flow specifically to the legs is diminished due to narrowed arteries [33].

**Symptoms:**

- Claudication (leg pain followed by cramping during walking)
- Numbness
- Weakness
- Coldness in the foot

**Causes:**

- Atherosclerosis and arteriosclerotic diseases
- Smoking
- Diabetes
- High blood pressure and lipid profiles

**Diagnosis:**

- Doppler ultrasound
- Angiography (computed tomography (CT)/MRI)
- Ankle-brachial index

### 1.1.4.7 Rheumatic Heart Disease (RHD)

This is a chronic condition that causes damage to the heart valves as a result of rheumatic fever and streptococcal throat infection [34, 35].

**Pathophysiology:**

- Autoimmune reaction targeting the heart, joints, and brain
- Most commonly affecting the mitral and aortic valves

**Symptoms:**

- Severe breathlessness
- Chest pain
- Swelling of limbs
- Heart murmur

**Diagnosis:**

- Echocardiography [36]
- Jones criteria for rheumatic fever
- ASO titer (anti-streptolysin O)

### 1.1.4.8 Congenital Heart Disease (CHD)

This results in structural abnormalities of the heart or great vessels present at the time of birth [37].

**Types:**

- Atrial septal defect
- Ventricular septal defect
- Tetralogy of Fallot
- Patent ductus arteriosus (PDA)
- Coarctation of the aorta

**Symptoms:**

- These symptoms vary based on type and severity
- Cyanosis (bluish skin)
- Poor feeding or growth
- Shortness of breath
- Heart murmur

**Diagnosis:**

- Prenatal ultrasound (fetal echo)
- Echocardiography
- Cardiac catheterization

#### 1.1.4.9 Deep Vein Thrombosis and Pulmonary Embolism

The condition of deep vein thrombosis is associated with a blood clot [38] in deep veins (typically in the legs), showing symptoms like swelling, pain, redness, and warmth, and possible risks are immobility, surgery, and inherited clotting disorders.

In pulmonary embolism, a clot from deep vein thrombosis travels to the lungs, causing severe blockage [39], and the symptoms observed are sudden chest pain, shortness of breath, and a rapid heart rate, which can be life-threatening.

**Diagnosis:**

- D-dimer test
- Venus Doppler ultrasound
- CT pulmonary angiography

## 1.2 CONVENTIONAL MANAGEMENT OF CARDIOVASCULAR DISEASES

Conventional management of heart diseases refers to the standard medical practices and important therapies implemented to prevent, treat, and manage different CVDs [9]. All these approaches were established and endorsed by international guidelines, in particular those from the American Heart Association, the European Society of Cardiology, and the World Health Organization. Contemporary healthcare regulations focus on preventing and minimizing the likelihood of heart disease [40], minimizing adverse outcomes, and addressing the major risk factors of cardiovascular disorders. For instance, in the condition of atherosclerosis, therapeutic approaches focus on modulating hemostasis, controlling hyperlipidemia, or modulating thrombotic complications [41]; hence, they rely on reducing LDLs using statins [40, 42, 43] or combinational drugs depending on patients' response. Modern and multiple antihypertensive drugs are employed to control elevated blood pressure in hypertensive patients [44]. Due to the availability of numerous antihypertensive agents, physicians are able to prescribe highly effective drug combinations for reducing blood pressure and protecting target organs [45].

### 1.2.1 GOALS OF MANAGEMENT [46]

- Reduce morbidity and mortality
- Prevent disease progression
- Relieve symptoms (angina, dyspnea)
- Improve quality life
- Prevent complications (heart failure, stroke)

### 1.2.2 MAJOR ASPECT OF TRADITIONAL CARDIOVASCULAR DISEASE MANAGEMENT

#### 1.2.2.1 Lifestyle Modification

This is implemented along with pharmacological therapy for the prevention of CVD. In this, dietary management is much needed to improve an individual's lifestyle [47] by suggesting low-sodium, low-fat diets, reducing saturated fats, increasing fiber intake, and encouraging the individuals to opt for nourishing foods like fruits, veggies, and whole grains, thereby curbing convenience foods and added sugars.

The individual is advised to increase physical activity through moderate exercise for three hours per week and complete cessation of smoking, thus reducing the risk of recurrent CVD [48]. Alcohol intake is very much restricted for men and women, with a limitation of one drink per day, along with increasing mindfulness, incorporating relaxation techniques, and seeking therapy for anxiety and depression, thereby reducing unwanted stress.

#### 1.2.2.2 Pharmacological Management

This is very important and particularly is prescribed based on the type and severity of CVDs.

a. **Antihypertensives**:
These are the medicaments used to control abnormally high blood pressure, which is a key factor in CVD. Beta-blockers (e.g., Metoprolol) lower the blood pressure and heart rate [49], inhibitors like calcium channel blockers (like amlodipine) dilate blood vessels, angiotensin-converting enzyme inhibitors (such as losartan) reduce afterload and mortality, and diuretics (e.g., hydrochlorothiazide) help by reducing fluid overload [50].

b. **Antiplatelet and anticoagulant therapies:**
This class of drugs is used to prevent clot formation and recurrent events. Aspirin is considered the cornerstone for secondary platelet prevention [51]. Clopidogrel–ticagrelor dual therapy is used after stenting or acute coronary syndrome, and Warfarin [52] is used for deep vein thrombosis, atrial fibrillation, and pulmonary embolism.

c. **Lipid lowering drugs:**
These class of drugs are used to manage hyperlipidemia, statins (atorvastatin, rosuvastatin) lower LDL cholesterol and stabilize plaques [53]. Ezetemibe and PCSK9 (proprotein convertase subtilisin/kexin type 9) inhibitors are mainly employed in statin-intolerant patients showing significant reduction of bad LDLs.

d. **Antianginal and antiarrhythmic drugs:**
These are mainly used against all types of angina pectoris [54] and CADs and are also used to treat arrhythmias. Nitrates [55–57], including nitroglycerine, act as a vasodilator, and quinidine and amiodarone are used to control arrhythmias [58–60].

Figure 1.2 presents an overview of major pharmacological classes used in managing cardiovascular disorders, including

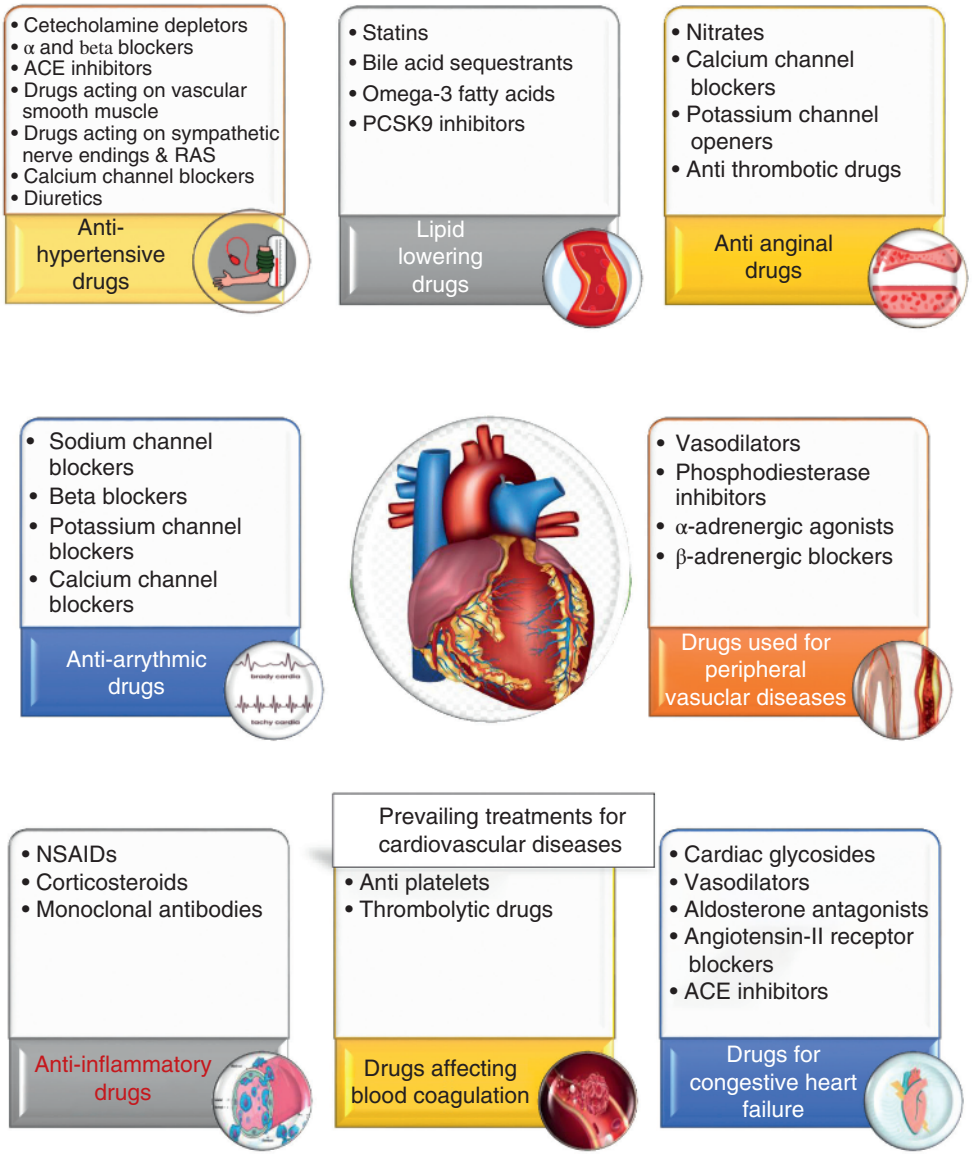



**FIGURE 1.2** Pharmacological treatment strategies for cardiovascular diseases.

antihypertensives, antianginal agents, anticoagulants, and lipid-lowering drugs.

### 1.2.2.3 Surgical and Interventional Management

**a. Percutaneous coronary intervention (PCI):**
This includes angioplasty and stenting, used in acute coronary syndrome as well coronary artery stenosis [61, 62].

**b. Coronary artery bypass grafting (CABG):**
This surgical technique is for open-heart surgery to bypass blocked arteries and is also performed in multivessel disease or in diabetic patients [63, 64].

**c. Valve repair or replacement:**
This is specific to surgical or transcatheter aortic valve replacement [65] and also for valvular stenosis or regurgitation.

**d. Implantable devices:**
These include pacemakers for AV block or bradycardia, and implantable cardioverter defibrillators [66], which are opted for perilous arrhythmic patients.

**e. Cardiac resynchronization:**
This therapy is advantageous for patients with heart failure associated with dyssynchrony [67, 68].

**f. Thrombolytic therapy:**
This is used for the emergency treatment of ischemic stroke and myocardial infraction [68]. Drugs like streptokinase and alteplase are advised.

**g. Cardiac rehabilitation:**
This is a designed program, wherein training exercises and counseling are specified for patients to reduce unwanted stress and strain and to support individuals in making behavioral changes, resulting in improved outcomes in

patients with CVD. It improves outcomes after myocardial infarction, bypass grafting, or heart failure hospitalization [69–71].

h. **Long-term monitoring**:
Continuous monitoring of blood pressure, glucose levels, and lipid profiles, along with periodical checkups, with the physicians and following patient's education on warning signs and symptoms helps the individuals from CVDs [72].

#### 1.2.2.4 Challenges in Conventional Management

There are few challenges that are highly focused on [73, 74]:

- Poor medication
- Underdiagnosis in early stages
- Polypharmacy in elderly patients
- Gender disparities with reference to diagnosis and treatment
- Limited access in rural or low-income settings

#### 1.2.2.5 Limitations of Conventional Therapies

Lifestyle modifications, pharmacological treatment, and different surgical procedures are the conventional therapies that have acquired clinical importance in reducing the burden of various CVDs [74]. However, these approaches are not without limitations, which can hinder patient outcomes in certain populations, as well as in long-term disease control.

a. **Control of incomplete risk factor:**
Several patients may not achieve optimal control of hypertension, hyperlipidemia, and diabetes despite their treatment. This is due to individual variation in drug response, mainly pharmacogenetics, which leads to suboptimal outcomes.

b. **Medication-related limitations:**

- Therapeutic drugs may have few side effects, and tolerability varies among individuals. Patients receiving statins experience myopathy and elevated liver enzymes. Similarly, patients treated with beta-blockers and ACE blockers may experience fatigue, depression, erectile dysfunction, cough, angioedema.
- Polypharmacy is very common in elderly or comorbid patients and may lead to drug–drug interactions, noncompliance, and possible increased risk of adverse effects.
- Lifelong medication regimens result in poor adherence in about 50% of population. Other reasons include cost, side effects, complex dosing schedules, and lack of symptoms.

c. **Surgical or interventional therapy limitations:**
CABG and PCI are invasive with high risks of bleeding, infection, and other complications. In angioplasty, restenosis can occur even with stenting, and device failures, like pacemaker malfunction, require close monitoring and immediate replacement. Low- and middle-income individuals have limited accessibility because of the high cost and long waiting period for surgery in public health systems.

d. **Lifestyle modification barriers and lack of personalization:**
These are very difficult to implement and sustain with various behavioral changes in this real-world setting. The individuals dietary habits are shaped by factors such as socioeconomic status, education, mental health and cultural food preferences. Limited access to nutritious foods can further challenge their ability to maintain proper dietary compliance. The acceptable conventional therapy "one-size fits all" does not account for individual genetic differences and disease progression, resulting in a lack of personalization.

e. **Limitations of psychosocial factors and certain populations:**
Lack of mental health support and poor outcomes related to depression, anxiety, and stress integration result in underdiagnosis and undertreatment in cardiac management [75]. Often certain populations like women, elderly, and frail patients cannot tolerate standard doses or aggressive therapies. Ethnic disparities in treatment cause barriers due to genetics, access-related, and cultural limitations.

## 1.3 HERBAL MEDICINE

Despite the ubiquitous existence of therapeutic regimens for scaling down cardiovascular events, their probably critical adverse effects are still areas of concern. Thus, this has evoked the exploration of alternative and complementary therapies for the enhanced oversight of CVDs [2]. There is an expanding awareness of the role of herbs in anticipating their use [76]. Herbal medicine, also termed as phytotherapy or botanical medicine, specifically refers to the use of plants or plant-derived substances to prevent or cure various diseases and maintain proper health. This is one of the ancient forms of medicine and remains a key element of traditional and complementary medicinal systems in the world. This herbal medicine includes whole-plant (leaves, seeds, fruit, bark, and roots) extracts, tinctures [77], and herbal formulations (teas, ointments, etc.).

### 1.3.1 HISTORICAL BACKGROUND

Historically herbs are interpreted as any form of plants or plant products [78]. Plants with healing properties were first medicaments used, and extracts from plants served as the foundation of the foremost drugs [79]. Herbal medicine is one of the most ancient medicinal systems, which can be tracked thousands of years ago [80], and has been practiced for many years across different civilizations.

Indisputably, nature is a paramount source in discovering new drugs that lead the way for the treatment of various diseases [81]. The chronicles of natural drug inception were established in Mesopotamia (nearly 2600 BC) and demonstrated the utilization of around 100 plant-acquired compounds. The Egyptian Ebers Papyrus (from 1500 BC) provides one of the best records of the use of more than 700 natural medicines. Fifty-two natural medicinal preparations from the Chinese *Materia Medica* (1100 BC) (for example, ginseng and liquorice root) and 800 natural extracts (Ashwagandha, turmeric) were recorded in the Indian Ayurvedic record [81, 82]. Greek medicine and indigenous medicine systems were also accomplished across Africa, America, and Australia. In 1985, the WHO estimated that about 65% of the world's inhabitants would depend on herb-derived traditional medicaments and identified 122 compounds, with different host countries using 94 plant species for ethnomedicinal treatment [83]. Despite favorable outcomes of bringing natural products into practice, the focus of drug discovery shifted due to the proceedings in combinatorial chemistry [81]. Nonetheless, naturally derived compounds are the major sources of new drugs due to the elucidation of contemporary published scientific data, technological breakthroughs, and research trends [82, 84].

### 1.3.2 PRINCIPLES OF HERBAL MEDICINE

- Herbal medicine operates based on several principles like holistic approach, which considers lifestyle, environment, and emotional aspects of whole person, and mainly aims to restore balance and support the individual's healing capacity.
- Herbal medicine provides synergistic action [2], with different active constituents present in the whole plant potentiating its therapeutic effect and reducing toxicity compared with a single-compound drug.
- Herbal medicine treatment is often tailored to individual needs as per the symptoms and constitution and is often prevention-oriented, supporting immunity, promoting general wellness, and improving resistance to stress.
- Herbal and plant remedies not only contain thousands of bioactive compounds with therapeutic significance but are also considered economical [85].

### 1.3.3 FORMS OF HERBAL PREPARATIONS

- Chamomile is available in the forms of teas and infusions
- Ginger root is available in decoction form
- Echinacea is available in the form of tincture
- *Ginkgo biloba* is available in the form of tablets and capsules
- Arnica is best used in the form of ointments and cream for skin or joints

### 1.3.4 ROLE AND SAFETY OF HERBAL MEDICINE IN MODERN WORLD

The role of herbal medicine in the modern era is increasing tremendously over synthetic drugs due to prospective natural remedies with no side effects. The WHO supports amalgamation of traditional and herbal medicines into national healthcare systems. Some important pharmaceuticals which are derived from plants include aspirin from willow bark, digoxin from foxglove, and artemisinin from *Artemisia annua*. It is a very well-known fact that not all herbs and medicinal plants are safe [1], few may be toxic or interact with conventional drugs like ephedra. Further, the quality-control aspects, along with the standardization process, remain a big challenge in the manufacturing of herbal drugs. Important regulatory bodies, like the United States Food and Drug Administration (USFDA), the European Medicines Agency (EMA), and many countries' pharmacopeias, have classified these herbs as dietary supplements and listed them as herbal formulations.

### 1.3.5 ADVANTAGES, CHALLENGES, AND LIMITATIONS OF HERBAL MEDICINE

Notable advantages of herbal medicine are

- Natural and generally well-tolerated
- Rich source of bioactive compounds
- Can mark chronic or functional disorders (stress and digestion)
- Affordable and accessible, especially in rural or developing areas

However, these are a few challenges and limitations ahead for these herbal medicines, which include:

- Lack of clinical trials for many herbal formulations
- Risk regarding misidentification, contamination, or adulteration
- Herb–drug interactions [1]
- Dosage and potency

### 1.3.6 HERBAL MEDICINE IN CARDIOVASCULAR HEALTH

CVDs like hypertension, atherosclerosis, arteriosclerosis, myocardial infarction, cardiac arrhythmias, cardiac failure, and stroke are the leading causative factors for death worldwide. Conventional therapies, though effective, have limitations, with side effects, cost, and drug resistance [86]. The role of herbal medicine is gaining popularity as an integrative and revolutionary approach to effective CVD therapy due to its natural origin, multi-target effects, and fewer side effects when used meticulously.

### 1.3.6.1 Mechanism of Action of Cardiovascular Herbs

The herbal medicines used in CVDs exhibit different mechanisms by targeting pathophysiological processes and exerting synergistic effects. The primary mechanism of these cardiovascular herbs are as follows:

i. **Antioxidant activity:** Oxidative stress plays crucial role in the pathogenesis of atherosclerosis and myocardial infraction. Herbs like turmeric, green tea, and grapes seed extract, which are very rich in polyphenols, flavonoids, and curcuminoids, neutralize free radicals reducing LDL cholesterol, and protecting endothelial cells from damage, thereby improving nitric oxide availability for vasodilation [87].

ii. **Anti-inflammatory effect:** Chronic inflammation is a key factor in CVDs, including atherosclerosis and hypertension. Herbs like turmeric, boswellia, and ginger [87] inhibit enzymes such as tumor necrosis factor-alpha (TNF-α), interleukin 6 (IL-6), and ERP, pro-inflammatory cytokines, and cyclooxygenase 2 (COX-2), as well as nuclear factor-kappa B (NF-κB) pathways.

iii. **Hypolipidemic effect:** Several herbs [1] reduce plasma cholesterol and triglyceride levels, supporting dyslipidemia management. Garlic and guggul lower total and LDL cholesterol, increase high-density lipoprotein (HDL) levels, inhibit HMG Co-A (3-hydroxy-3-methylglutaryl-coenzyme A reductase) reductase, and enhance bile acid excretion.

iv. **Antihypertensive effect:** Many herbs exhibit vasodilatory and diuretic activities to help control high blood pressure [88]. *Hibiscus sabdariffa*, garlic, and olive leaf [89] exhibit angiotensin-converting enzyme inhibition, calcium channel-blocking property, enhanced nitric oxide synthesis, and promotion of renal sodium excretion (natriuresis).

v. **Antiplatelet and anticoagulant activity:** Thrombosis and platelet aggregation [90] are the two factors that contribute to myocardial infraction and stroke. Few herbs act as natural blood thinners; for example, garlic, ginger, and *G. biloba* inhibit platelet aggregation, suppress thromboxane $A_2$ synthesis, and enhance fibrinolytic activity [91] with potential interactions with all connectional anticoagulants.

vi. **Vasodilatory and endothelial effects:** Herbs like ginseng, hawthorn improve vascular tone and endothelial function by enhancing blood flow and reducing vascular resistance [92]. These herbs increase endothelial nitric oxide production, inhibit endothelin-1, and protect VSMCs from any possible vascular stress.

vii. **Cardiotonic effect:** *Terminalia arjuna* increases myocardial contractility, supporting the management of mild to moderate heart failure. This herb strengthens heart muscle contraction and improves cardiac output [93], providing digitalis-like effects with improved safety.

viii. **Antiarrhythmic effect:** Herbs like motherwort (*Leonurus cardiaca*) and arjuna (*T. arjuna*) stabilize cardiac rhythm by acting on ion channels or by reducing myocardium excitability [94, 95]. These two medicinal herbs modulate calcium and potassium channels and exhibit mild sedative effects, thereby reducing stress-induced arrhythmias.

ix. **Diuretic effect:** Dandelion and celery seed are herbs with natural diuretic properties [96] helping in the management of hypertension and fluid retention. These two medicinal herbs promote excretion of sodium and water, reducing blood volume and pressure.

x. **Anti-atherosclerotic activity:** Turmeric, garlic, and guggul are medicinal herbs that inhibit plaque formation, enhance lipid clearance [97], and reduce vascular inflammation. These herbs enhance cholesterol efflux [98] from macrophages and inhibit foam cell formation.

Figure 1.3 presents selection of medicinal plants that are traditionally and scientifically recognized for their beneficial effects on the cardiovascular system. The illustration emphasizes the integrated role of plant-derived compounds in preserving endothelial function, enhancing myocardial performance, and preventing vascular damage associated with oxidative stress and inflammation. The illustration underscores the significance of traditional medicinal knowledge as a foundation for developing natural, plant-based cardioprotective therapies.

### 1.3.6.2 Clinical Evidence and Research

Various medicinal herbs have shown different clinical evidence that supports future research.

- **Garlic (*Allium sativum*):** Meta-analysis shows significant reductions in blood pressure and LDL cholesterol, and it also exhibits a mild antiplatelet effect.
- **Hawthorn (*Crataegus* spp.):** Clinical trials suggest this drug is beneficial in mild heart failure with improvements in exercise capacity and symptom relief.
- **Turmeric (*Curcuma longa*):** This herb is shown to reduce inflammatory markers (C-reactive protein (CRP), TNF-α) and improve endothelial function in some small clinical studies.
- **Green tea (*Camellia sinensis*):** Due to its antioxidant and lipid-lowering properties, long-term consumption of green tea reduces cardiovascular mortality [99].
- **Arjuna (*T. arjuna*):** In heart failure patients, this herbal medicine demonstrated significant improvement in left ventricular ejection fraction in a few Indian clinical trials.

The findings outlined in Table 1.1 represent the different plant species used in the management of various CVDs.

Table 1.1 summarizes various medicinal plants employed in the prevention and treatment of cardiovascular disorders. It lists the herbs and their therapeutic roles, collectively

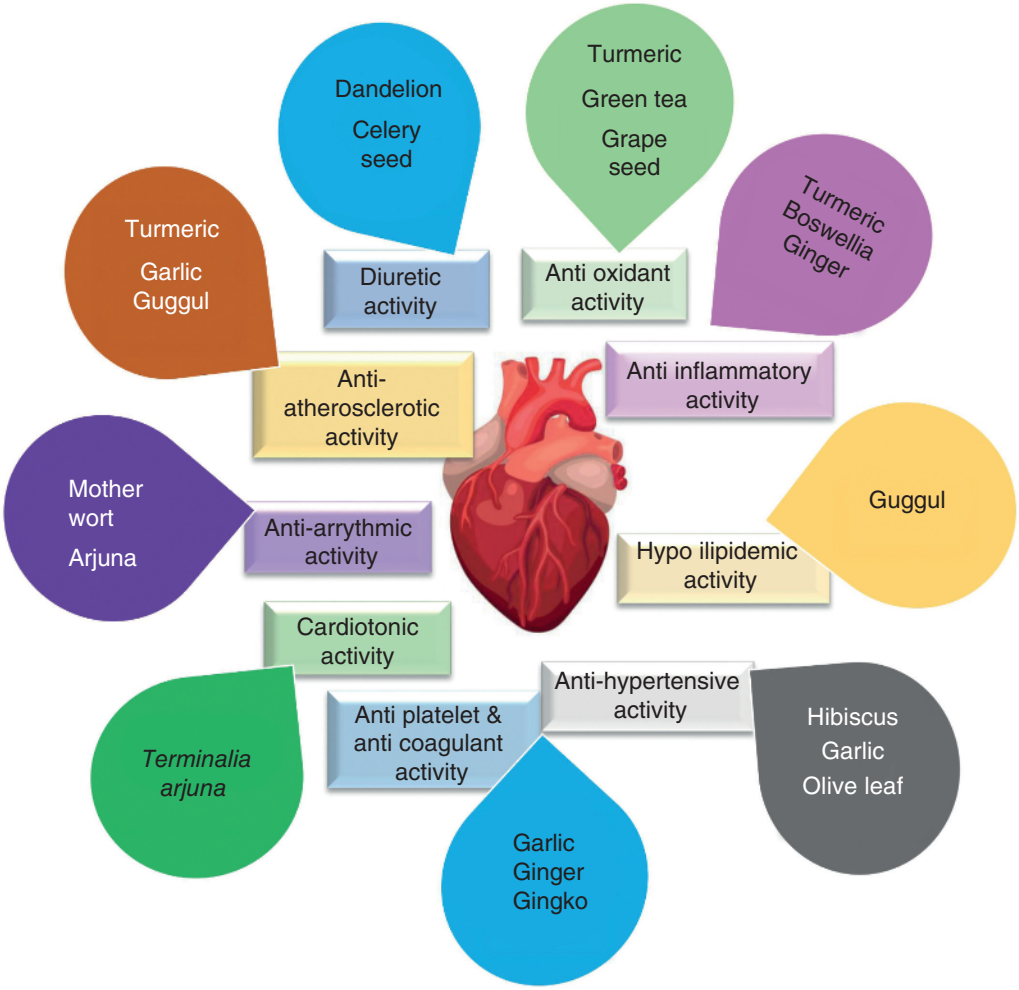



**FIGURE 1.3** Significance of traditional medicinal knowledge for their therapeutic effects on the cardiovascular system.

demonstrating the potential of phytotherapy as a complementary approach to conventional cardiovascular treatment.

### 1.3.6.3 Advantages of Herbal Medicine in Cardiovascular Diseases

Several herbal medicines offer many advantages, including multi-target actions [100], better affordability and accessibility, exhibiting mild side effects, and cultural acceptability in traditional medicinal systems like Ayurveda and traditional Chinese medicine [101].

### 1.3.6.4 Safety Concerns and Limitations

- Proper attention needs to be focused on the safe use of herbal medicines in terms of herb–drug interactions. The examples are:
  - Garlic + anticoagulants – increased bleeding risk
  - *G. biloba* + aspirin – risk of intracranial hemorrhage
- There is a great concern related to herbal medicine standardization issues with variations in active compound content, dosage, and formulation between the products.
- The wide usage of herbal medicines is limited due to a lack of large-scale trials and the possibility of misuse and overdose, particularly in self-medication.

### 1.3.6.5 Assimilation with Conventional Therapy

This herbal medicine is best used as a complementary therapy for critical interventions. The use of phytopharmaceuticals [102] and standardized extracts is being developed to bridge the gap between herbal medicine and conventional drugs.

Collaboration between herbalists, pharmacists, and physicians is essential to ensure safe and effective use.

### 1.3.6.6 Conjunctional and Anticipation in Cardiovascular Health

i. **The need for integrative approaches:** Despite significant advancements in modern medicine, CVD remains the leading cause of mortality and morbidity worldwide. This has led to growing interest in integrative healthcare models that unify conventional medicine, herbal medicine, lifestyle interventions, technological innovations like digital health and artificial intelligence, and finally precision and personalized medicine [102].

**Table 1.1** Plant species used in the treatment of various CVDs.

| Cardiovascular condition | Plant species |
|---|---|
| Reduction of blood pressure | • *Achillea millefolium* (common yarrow)<br>• *Allium sativum* (garlic)<br>• *Berberis integerrima* (barberry)<br>• *Olea europaea* (olive tree)<br>• *Silybum marianum* (milk thistle) |
| Management of angina | • *Camellia sinensis* (green tea)<br>• *Panax spp.* (ginseng)<br>• *Ginkgo biloba* (ginkgo)<br>• *Medicago sativa* (alfalfa) |
| Antioxidant activity | • *Boerhavia diffusa* (hogweed)<br>• *Tamarindus indica* (tamarind)<br>• *Terminalia arjuna* (arjuna)<br>• *Curcuma zedoaria* (white turmeric)<br>• *Zingiber zerumbet* (shampoo ginger) |
| Treatment of blocked arteries | • *Anthemis gayana* |
| Cardiomyopathies | • *Apium graveolens* (celery) |
| Congenital heart disease | • *Strychnos nux-vomica* (poison nut) |
| Heart attack prevention | • *Carthamus tinctorius* (safflower)<br>• *Inula helenium* (elecampane) |
| Reduction of blood lipid levels | • *Coriandrum sativum* (coriander)<br>• *Lactuca sativa* (lettuce)<br>• *Mentha spicata* (spearmint)<br>• *Senna alexandriana* (Alexandrian senna),<br>• *Sesamum indicum* (sesame)<br>• *Trigonella foenum-graecum* (fenugreek) |
| Cardiac arrhythmias | • *Ulmus glabra* Hudson |
| Improvement of venous blood flow | • *Melilotus indicus* |
| Anti-inflammatory (cardioprotective support) | • *Curcuma longa* (turmeric)<br>• *Withania somnifera* (Ashwagandha)<br>• *Ocimum sanctum* (holy basil)<br>• *B. diffusa* (punarnava)<br>• *Tinospora cordifolia* (guduchi) |
| Heart failure (cardiotonic) | • *Nerium indicum* (oleander)<br>• *Crataegus oxyacantha* (hawthorn)<br>• *A. sativum* (garlic)<br>• *Emblica officinalis* (amla) |

ii. **Integration of herbal medicine in cardiovascular care:** The complimentary use of important herbs like garlic, hawthorn, turmeric, and arjuna have demonstrated beneficial effects in hypertension, IHD, and heart failure. When integrated appropriately, these herbal medicines can enhance conventional therapies, reduce side effects, and improve quality of life [103]. The implementation of structured, evidence-based integrative protocols safely combines herbal and pharmaceutical treatments. A key factor is effective collaboration between herbalists, cardiologists, and pharmacists. The use of standardized herbal extracts and the development of phytopharmaceuticals ensure dose accuracy, safety, and regulatory compliance. Standardized herbal medicines may act as adjuncts to statins, beta-blockers, and angiotensin-converting enzyme inhibitors [104].

iii. **Personalized and precision medicine:** Genomic studies are revealing genetic predispositions to CVD, and future directions include pharmacogenomics, which identifies patients who may benefit from specific medicinal herbs. Biomarker-guided herbal formulations are helpful in targeting of information, oxidative stress, and lipid metabolism [105].

iv. **Technological integration:**

   a. **Digital health and monitoring:** Digital devices can track heart rate, blood pressure, ECG, and physical activity, helping herbal and lifestyle interventions [106]. Mobile apps and telemedicine can guide the use of herbal supplements and diet.

   b. **Artificial intelligence:** Artificial intelligence models can analyze the patients' data to recommend personalized integrative treatment plans [106]. Further, machine learning can identify synergistic herb–drug combinations and predict adverse interactions.

v. **Emerging research and innovations:** The recent trends and innovations include:

- Nanotechnology [107], which is being explored to enhance the bioavailability and targeted delivery of herbal compounds.
- Medicinal herb-based nutraceuticals, which are being designed to serve as both food and medicine.

Examples include cardioprotective teas and fortified oils.

- Active research, which is focused on herb combinations with synergistic effects (polyherbal formulations).

vi. **Regulatory and education framework:** WHO guidelines are very crucial, particularly for the global harmonization of herbal medicine standards.

- Pharmacovigilance systems [108] should be enhanced to monitor herb–drug interactions and different adverse events.
- Intensive training for medical practitioners should be provided to facilitate safe and more effective use in integrative cardiology practice.

vii. **Challenges and rationale**
According to the data presented in Table 1.2, the major challenges associated with the use of herbal medicines in cardiovascular care, along with the rationale supporting their continued exploration, are being demonstrated [86]. The table emphasizes the need for standardized formulations and improved quality control measures to enhance the credibility and therapeutic reliability of herbal products in CVD management.

viii. **Future vision:**
Proper focus and attention are needed on the following aspects [109]:

- Holistic cardiovascular care model including
  - Conventional pharmacotherapy
  - Standardized herbal treatments
  - Lifestyle medicine (diet, exercise, stress management)
  - Digital tools (apps, artificial intelligence algorithms)
- Continuous focus on preventive cardiology using herbal medicines and dietary phytochemicals.
- Cross-disciplinary research involving botany, pharmacology, genomics, and artificial intelligence will define CVD management.

**Table 1.2** Major challenges associated with the use of herbal medicines in cardiovascular care.

| Principal drawbacks | Scientific rationale |
|---|---|
| Insufficient safety and efficacy evidence | Herbal products are introduced into the market without rigorous preclinical or clinical validation to establish safety and therapeutic efficacy in contrast to conventional pharmaceutical agents. |
| Use in vulnerable populations | Clinical evaluation of herbal formulations in pediatric and pregnant populations is largely absent. Consequently, their administration is discouraged in children, pregnant or lactating women, and those planning conception due to potential risk of adverse outcomes. |
| Contamination and unintentional substitution | Instances of product mislabeling, where listed botanicals are replaced with alternative or incorrect plants, have been documented. Furthermore, contamination with synthetic drugs or other adulterants poses additional safety concerns. |
| Inconsistent active constituents | The pharmacologically active components of many herbal preparations remain unidentified, and in cases where they are known, their concentration may exhibit significant variability among different formulations. |
| Absence of specific antidotes | Improper use of herbal medicines such as excessive dosing or prolonged administration can result in serious toxic effects or organ damage. Currently, no specific antidote therapies are available to mitigate such toxicities. |

## 1.4 CONCLUSION

Millions of people worldwide are affected by a broad spectrum of cardiovascular disorders with distinct pathophysiological mechanisms, risk factors, and clinical presentations. However, risk factors such as hypertension, smoking, obesity, and physical inactivity are commonly shared. Understanding, addressing, and analyzing both adaptable and unalterable risk factors are very crucial in preventing and controlling CVDs. Different public health policies through integrated health systems and educating the individuals might reduce the risk components of these diseases. The conventional management of CVDs is based on a well-established combination of lifestyle interventions, pharmacological therapy, surgical procedures, and continuous clinical monitoring. The emergence of futuristic therapies like gene therapy and artificial intelligence-based models and the traditional methods remain core strategies in reducing cardiovascular morbidity and mortality. Though conventional therapies are the backbone of CVD management, they still have a few limitations in terms of effectiveness, accessibility, and long-term adherence. These gaps highlight the need for innovative, integrative, and personalized approaches like smart drug delivery systems, digital health monitoring, and genomics. All these strategies are effectively being explored in futuristic CVD management.

Herbal medicine is a highly valuable healthcare source with potential therapeutic use. This interest in integrity and complementary medicine, ensuring scientific validation, quality assurance, and safe practice, is essential for the effective implementation into the mainstream medicine. Herbal medicine acts as a promising adjuvant in CVD management, particularly in prevention and early intervention. There are several herbs that show clinical relevant benefits and the need for high-quality research, standardization of products, and confirmation of safety and efficacy. Professional collaboration is essential for these medicines. As might be expected, the entire future lies in

modern approaches that combine the strengths of herbal and modern medicine.

The therapeutic application of herbal medicines in the management of CVDs remains insufficiently supported by robust scientific evidence. Although certain herbal agents exhibit activity on biological pathways associated with cardiovascular function, existing clinical investigations are generally limited by small sample size and lack statistically significant effects on major clinical outcomes. Consequently, the current body of evidence is inadequate to endorse the clinical use of herbal medications for cardiovascular conditions. Furthermore, potential adverse effects, including drug–herb interactions, contamination and substitution with other compounds, present additional safety concerns. It is therefore imperative that physicians enhance their understanding of herbal pharmacology to critically evaluate their clinical implications, effectively counsel patients regarding their potential risks and benefits, and emphasize that natural origin does not inherently equate to safety. Further well-structured clinical studies with larger participant samples are essential to clarify the therapeutic potential and mechanistic pathways of various medicinal plants in CVDs.

Amalgamating herbal medicine into mainstream cardiovascular care holds transformational potential, with advancements in innovative technology, pharmacology, and data science. The future of cardiovascular health lies in holistic scaffolding that values both tradition and innovation.

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