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Role of Nutraceuticals in the Prevention of Cardiovascular Disease

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ABSTRACT:
cardiovascular disease (CVD) is a widespread global health issue with significant impacts on health and finances. Dietary factors play a crucial role in CVD risk alongside other factors like hypertension, dyslipidemia, and lifestyle habits such as smoking and physical inactivity. Nutraceuticals, derived from combining "nutrition" and "pharmaceutical," are food components that offer medical benefits including disease prevention and treatment. Research has shown their importance in combating CVD. For example, studies demonstrate the effectiveness of berberine in lowering cholesterol levels, the beneficial effects of Coenzyme Q10 and garlic supplementation on inflammation and endothelial function, and the positive impact of curcumin on metabolic profiles and arterial stiffness. Additionally, Hydroxytyrosol found in olive oil has been linked to reduced inflammation and a lower risk of CVD events. Nutraceuticals show promise in improving therapeutic efficacy and reducing residual risk, particularly for individuals at high risk of diabetes who may not respond well to conventional treatments. While patients generally tolerate nutraceuticals well, long-term safety and efficacy data compared to clinical outcomes are often lacking, indicating a need for further research in this area.

Keywords: Dietary factors, Nutraceuticals, Hydroxytyrosol, curcumin, endothelial function.

INTRODUCTION:

Cardiovascular disease (CVD) is very prevalent; in fact, most persons over sixty tend to suffer from CVD. An estimated 20.3 million fatalities globally are attributed to CVD each year, according to data from 2022 and 2023 [1]. Additionally, morbidity is high, and cardiovascular disease (CVD) accounts for 200 billion euros of healthcare spending in Europe [2]. There are two types of risk factors for CVD: modifiable and non-modifiable. Obesity, hypertension, hyperlipidemia, diabetes mellitus, metabolic syndrome, and lifestyle risk factors including smoking, poor nutrition, and inactivity are examples of modifiable risk factors. Additionally, dietary variables have a significant impact on cardiovascular risk, either directly or indirectly, through their interactions with other risk factors such as diabetes mellitus, dyslipidemia, and hypertension [3]. Reducing risk variables in the population, particularly reducing cholesterol and blood pressure, can significantly influence CVD mortality [4].
Foods and dietary supplements have been shown to have protective effects against CVD [5], opening up

new avenues for lowering CVD risk at the population level. There is evidence to support the high promise of this strategy. As an illustration, those in the highest quintile of polyphenol consumption in the PREDIMED observational research had a 54% relative risk of CVD compared to those in the lowest quintile [6]. This review's objective is to provide an update on the most recent research on applying nutraceuticals to managing and preventing cardiovascular disease. Regretfully, not much research has quantified the relationships between the use of nutraceuticals and "hard" consequences like death. As a result, the term "atherosclerosis" refers to a serious issue: fat deposits that can potentially obstruct arteries (American Heart Association, 2017). These accumulations, known as plaque, are composed of calcium, cellular waste materials, fatty compounds, cholesterol, and fibrin, a blood clotting component. Occasionally, deposits occur in arteries that resemble sludge building within a pipe—a plumbing issue. It is not a perfect analogy, though, as accumulations can occur inside arteries and on their walls. The thickening of an arterial wall due to plaque accumulation narrows the lumen and lowers the flow of blood and oxygen to the cells. Each person experiences plaque development in a different type of artery. A plaque buildup in a big or medium-sized artery in the kidneys, legs, arms, brain, pelvis, heart, or pelvis can completely or partially stop blood flow. Once it occurs, the result is a variety of disorders. For instance, coronary heart disease is defined as plaque in the arteries that feed the heart; angina is defined as pain in the chest caused by a reduction in blood flow to the heart muscle; carotid artery disease is defined as plaque in the arteries that supply blood to the brain; peripheral artery disease (PAD) is defined as plaque in the arteries that supply the extremities, particularly the legs; and chronic kidney disease is defined as plaque in the kidneys. A heart attack or stroke may result from the aforementioned disorders.

History of the disease:

Cardiovascular diseases (CVDs) have historically been linked to the advancement of human society. Although it is difficult to identify specific historical events because of the paucity of medical knowledge and records in the past, we may follow the evolution of our understanding and approach to cardiovascular disease via significant turning points in time:

1. **Ancient Civilizations:** Ancient societies that recorded symptoms similar to cardiovascular illnesses included Egypt, Mesopotamia, China, and India. Nevertheless, their understanding was frequently derived from mystical or spiritual beliefs rather than being grounded in scientific knowledge.[7]
2. **Ancient Greece and Rome:** Hippocrates, the Greek physician, and later Roman physicians made important advances in our knowledge of cardiovascular illnesses. Hippocrates talked of palpitations and chest discomfort, most likely alluding to angina and arrhythmias.[8,9]
3. **Middle Ages:** Despite medical knowledge in Europe stagnated during the Middle Ages, Islamic scholars made significant contributions to the field. During the Islamic Golden Era, doctors such as Avicenna (Ibn Sina) wrote about the signs and potential cures for conditions that are today known as cardiovascular illnesses.[8]
4. **Renaissance and Early Modern Era:** Anatomy and physiology underwent a resurgence of interest throughout the Renaissance. The 16th-century anatomical research of Andreas Vesalius shed light on the anatomy of the heart and blood arteries.
5. **18th and 19th Centuries:** René Laennec's invention of the stethoscope in 1816 made it possible for doctors to listen to cardiac sounds and identify anomalies. This greatly enhanced the ability to diagnose cardiovascular illnesses.[9,10]

6. **20th Century:** Significant progress was made in the 20th century in our knowledge of and approach to treating cardiovascular illnesses. Important anniversaries consist of:

- **Electrocardiography (ECG):** Willem Einthoven created the first usable electrocardiogram (ECG) in 1903, making it possible to diagnose several cardiac disorders.
- **Coronary Artery Disease (CAD):** The connection between food and lifestyle and CAD was brought to light by medical researchers such as Ancel Keys in the middle of the 20th century.
- **Cardiac Surgery:** A turning point in the history of cardiac surgery was reached in 1952 when Dr. C. Walton Lillehei successfully conducted the first open-heart surgery.
- **Pharmacological Treatments:** The management of cardiovascular illnesses was transformed with the introduction of medications such as statins, ACE inhibitors, and beta-blockers.
- **Interventional Cardiology:** In the second part of the 20th century, less invasive alternatives to open heart surgery such as angioplasty and stent implantation were available.
- **21st Century:** Developments in less invasive procedures, genetics, imaging technology, and customized medicine are all influencing how cardiovascular illnesses are diagnosed and treated.
- Furthermore, preventative strategies including lifestyle adjustments and public health initiatives are receiving more attention.[11]

Cardiovascular illnesses have historically been one of the world's major causes of mortality, which has led to constant study and advancements in the field to improve the lives of those who are impacted.

Types of cardiovascular disease:

Cardiovascular diseases (CVDs) encompass a range of disorders affecting the heart and blood vessels. These illnesses can be roughly divided into many categories:

1. **Coronary Artery Disease (CAD):** The most prevalent kind of cardiovascular illness, coronary artery disease (CAD), is brought on by a buildup of plaque that causes the coronary arteries, which feed blood to the heart muscle, to narrow or block (atherosclerosis). Angina (chest discomfort) or heart attacks (myocardial infarctions) may result from this.[12,13]
2. **Hypertensive Heart Disease:** This disorder is brought on by persistently high blood pressure, or hypertension, which can harm the heart's blood arteries, valves, and muscles. Heart failure and left ventricular hypertrophy, or enlargement of the left pumping chamber of the heart, are two disorders that may show symptoms of it.[13]
3. **Heart Failure:** When the heart cannot pump enough blood to fulfill the body's demands, heart failure results. Cardiomyopathy, hypertension, and CAD are a few of the underlying disorders that can cause it (disease of the heart muscle).[12,14]
4. **Arrhythmias:** Heart rhythm irregularities, or arrhythmias, can result in the heart beating too rapidly (tachycardia), too slowly (bradycardia), or irregularly. Atrioventricular block, ventricular tachycardia, and atrial fibrillation are examples of arrhythmia types.[14]
5. **Valvular Heart Disease:** The heart valves, which regulate blood flow within the heart, are aberrant or diseased with this illness. Aortic stenosis, or constriction of the aortic valve, mitral valve prolapses, and infective endocarditis are examples of disorders that fall under the category of valve disease.
6. **Peripheral Artery Disease (PAD):** A narrowing or blockage of the arteries outside the heart, usually in the legs, causes PAD. Symptoms like cramping in the legs and a reduction in blood flow to the extremities may result from this.[12,14]

7. **Congenital Heart Disease:** Birth defects in the heart are referred to as congenital heart disease. These flaws can impact the heart's blood arteries, valves, or chambers and range greatly in severity from very minor issues to potentially fatal flaws.[12,15]
8. **Stroke and Transient Ischemic Attack (TIA):** Strokes and TIAs (mini-strokes) are closely linked because they both entail interruptions of blood flow to the brain, even though they are not specifically cardiovascular disorders. Hemorrhagic strokes are caused by bleeding into the brain, whereas ischemic strokes are caused by blockages in the blood arteries supplying the brain.[12-15]

These are a few of the main categories of cardiovascular disorders; each has unique risk factors, symptoms, causes, and modes of treatment. For these illnesses to be managed and prevented, early identification, lifestyle changes, and the right medical therapies are crucial.

Symptoms of cardiovascular disease:

Conditions that impact the heart and blood vessels are known as cardiovascular diseases (CVDs). Depending on the particular form of CVD, symptoms might vary, however, some typical ones include:

1. **Chest Pain (Angina):** A feeling in the chest that is similar to pressure, tightness, or squeezing. Moreover, pain may radiate to the back, neck, jaw, shoulders, or arms. Physical activity or mental stress can cause angina, which is often eased by resting or taking medicine. [12-15]
2. **Shortness of Breath (Dyspnea):** Breathing difficulties, particularly when exercising or when lying flat. A buildup of fluid in the lungs brought on by diseases like pulmonary edema or heart failure can cause dyspnea.
3. **Palpitations:** - Heartbeat awareness, erratic heart rhythms, or the sensation that certain beats are "skipping". Palpitations may cause lightheadedness, dizziness, or fainting.
4. **Fatigue:** Extended fatigue or weakness that does not go away with enough rest. Reduced blood supply to tissues and organs as a result of illnesses such as peripheral artery disease or heart failure can lead to fatigue.
5. **Swelling (Edema):** Swelling in the abdomen, feet, ankles, or legs. Fluid retention, frequently as a result of heart failure or venous insufficiency, leads to edema.
6. **Dizziness or Fainting (Syncope):** - Moments of dizziness, fainting, or almost fainting. Reduced blood supply to the brain, usually as a result of arrhythmias or structural cardiac issues, can cause syncope.
7. **High Blood Pressure (Hypertension):** - High blood pressure, is usually characterized as a diastolic pressure of more than 80 mmHg or a systolic pressure of more than 130 mmHg. Although hypertension frequently shows no symptoms at first, if treatment is not received, it might result in consequences such as heart attack, stroke, or renal damage.
8. **Leg Pain or Numbness (Peripheral Artery Disease):** - Leg pain, cramping, or numbness, particularly when exercising. Narrowed arteries in the legs cause peripheral arterial disease (PAD), which reduces blood flow to the lower limbs.
9. **Cyanosis:** Bluish discoloration of the lips, nail beds, or skin. When tissues don't get enough oxygen, it can cause cyanosis, which might be a sign of heart or lung troubles.
10. **Symptoms Specific to Heart Attack or Stroke:** Sudden chest pain, dyspnea, nausea, perspiration, and pain or discomfort in the arms, back, neck, jaw, or stomach are some of the signs of a heart attack. Sudden weakness or numbness in the face, arm, or leg (usually on one side of the body) are common stroke symptoms. Other symptoms include blurred or lost vision, severe headaches, dizzin-

ess, or trouble speaking or comprehending speech. [12-17]

It's crucial to remember that different people may suffer various symptom combinations and intensities, and certain CVDs, like hypertension, may not initially exhibit any symptoms at all. Should any alarming signs appear, it is imperative to seek immediate medical attention because prompt identification and treatment might enhance the prognosis of patients with cardiovascular conditions.

Diagnosing cardiovascular disease:

Diagnosing cardiovascular disease (CVD) typically involves a combination of medical history assessment, physical examination, diagnostic tests, and imaging studies. The specific diagnostic approach may vary depending on the suspected type of CVD and the patient's risk factors.

1. **Medical History and Physical Examination:** The patient's medical history, including any family history of cardiovascular disease, risk factors (such as diabetes, smoking, or high blood pressure), and any symptoms that may indicate a cardiovascular condition, will be reviewed by the healthcare practitioner. Peripheral edema, irregular pulses, abnormal heart sounds (murmurs), and other indications of heart or vascular illness may be discovered during a comprehensive physical examination. [19]
2. **Blood Tests:** In situations of suspected heart attacks, blood tests can give important information regarding blood sugar, cholesterol, and signs of heart muscle injury (like troponin). To evaluate inflammation and cardiac function, respectively, other tests such as brain natriuretic peptide (BNP) and C-reactive protein (CRP) may be performed. [20]
3. **Electrocardiogram (ECG/EKG):** - An electrocardiogram (ECG) captures the electrical activity of the heart and is useful in identifying cardiac anomalies, evidence of prior myocardial infarctions, and irregular heart rhythms (arrhythmias). [18-20]
4. **Echocardiography:** - Echocardiography, or "echo," creates pictures of the anatomy and function of the heart using ultrasonic waves. It is capable of assessing chamber dimensions, pumping efficiency (ejection fraction), and heart valve function. [18-19]
5. **Stress Testing:** Stress testing assesses how the heart reacts to pharmacological or physical stress. Nuclear stress testing (using radioactive tracers), stress echocardiography, and exercise treadmill testing might all be used.
6. **Cardiac Catheterization and Angiography:** - During a cardiac catheterization, a thin, flexible tube called a catheter is inserted into blood arteries and passed through to the heart. During catheterization, angiography (also known as coronary angiography) visualizes the coronary arteries and detects blockages or narrowing using contrast dye and X-rays. [21-23]
7. **Computed Tomography (CT) Angiography:** - CT angiography uses contrast dye and X-rays to create finely detailed pictures of the heart and blood arteries. It is capable of evaluating aortic pathology, cardiac anatomy, and coronary artery disease. [21]
8. **Magnetic Resonance Imaging (MRI):** - Cardiac MRI creates finely detailed pictures of the anatomy and physiology of the heart using radio waves and magnetic fields. In addition to evaluating blood flow and cardiac viability, it can identify anomalies such as cardiomyopathy or congenital heart problems. [18-21]
9. **Holter Monitoring and Event Recorders:** - These devices enable the diagnosis of intermittent arrhythmias by constantly recording the heart's electrical activity over time (Holter monitor) or in response to symptoms (event recorder). [19-22]

10. **Coronary Calcium Scoring:** This non-invasive imaging test helps determine the risk of coronary artery disease (CAD) by measuring the quantity of calcium in the coronary arteries using computed tomography (CT).

The patient's symptoms, risk factors, and the probable kind of CVD all influence the diagnostic tests that are used. Healthcare professionals can effectively identify cardiovascular disease (CVD), assess its severity, and create a suitable treatment plan with the help of a thorough diagnostic examination. [18-22]

CAUSES OF CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) includes various conditions that impact the heart and blood vessels. The causes of CVD are multifactorial and often involve a combination of genetic, lifestyle, and environmental factors. Here are some key factors contributing to the development of cardiovascular disease:

1. **High Blood Pressure (Hypertension):** One of the main risk factors for CVD is hypertension. Chronically elevated blood pressure can cause artery damage, which can result in heart failure, atherosclerosis (hardening and constriction of the arteries), and other problems.[22]
2. **High Cholesterol Levels:** High triglyceride and low-density lipoprotein (LDL) cholesterol ("bad cholesterol") levels can aggravate atherosclerosis and coronary artery disease (CAD) by causing plaque to develop in the arteries.[22-23]
3. **Smoking/Tobacco Use:** One of the main risk factors for CVD is smoking. Tobacco smoke contains chemicals that cause blood vessel damage, decrease oxygen flow to tissues, raise blood pressure, and encourage blood clot formation—all of which are factors in cardiovascular disease.[15,17,22]
4. **Diabetes Mellitus:** A higher risk of CVD is linked to diabetes, especially type 2 diabetes. Elevated blood sugar levels have the potential to harm neurons and blood vessels, resulting in hypertension, atherosclerosis, and an increased risk of heart attack and stroke.[18,22]
5. **Obesity and Physical Inactivity:** Several CVD risk factors, including hypertension, dyslipidemia (abnormal lipid levels), insulin resistance, and inflammation, are associated with excess body weight, especially abdominal obesity. These hazards are further increased by physical inactivity.[18,13]
6. **Unhealthy Diet:** CVD is a result of diets heavy in processed foods, cholesterol, trans fats, saturated fats, and sodium (salt). These food-related variables have the potential to elevate blood pressure, and cholesterol, and induce oxidative stress and inflammation in the body.[18]
7. **Family History and Genetics:** A person's risk is increased by a family history of cardiovascular disease (CVD), especially if a close relative had the disease while they were young—before the age of 55 for men and 65 for women. Certain people are also predisposed to CVD for genetic reasons.[18,22,23]
8. **Stress and Mental Health:** Extended periods of stress, depression, and social distancing have been associated with a higher risk of CVD. These variables have a direct impact on cardiovascular function and can also lead to harmful habits including smoking, overeating, and inactivity.[15,17,18]
9. **Alcohol Consumption:** Drinking too much alcohol is linked to a higher risk of cardiovascular disease, especially when ingested in significant amounts. Excessive alcohol consumption has been linked to hypertension, obesity, and an increased risk of cardiac arrhythmias and cardiomyopathy.[18]

10. **Environmental Factors:** By encouraging inflammation, oxidative stress, and endothelial dysfunction, exposure to environmental contaminants, such as air pollution and second-hand smoking, can exacerbate cardiovascular disease (CVD).[15,22]
11. **Other Risk Factors:** Age (risk increases with age), gender (men tend to have a higher risk at a younger age, whereas women's risk evens out with age), and certain medical disorders (e.g., chronic renal disease, sleep apnea) are other variables that may raise the risk of CVD.[13,15,17,18,22,23]

The prevention and treatment of cardiovascular disease need to address modifiable risk factors through lifestyle changes (such as eating a healthy diet, exercising often, and quitting smoking) and medical interventions (such as prescription pharmaceuticals for high blood pressure and cholesterol). Furthermore, lowering the total burden of cardiovascular disease can be achieved by early identification and treatment of CVD risk factors.

RISK FACTORS OF CARDIOVASCULAR DISEASES

Numerous risk factors might have an impact on the complicated disorders known as cardiovascular diseases (CVDs). These risk factors fall into two general categories: those that are changeable and those that are not. Non-modifiable risk factors are unchangeable, but modifiable risk variables can be controlled by dietary adjustments or medical procedures. The following are the main cardiovascular disease risk factors:

Modifiable Risk Factors:[24-28]

a. **High Blood Pressure (Hypertension):** One of the main risk factors for CVD is hypertension. It may cause artery damage, raising the risk of heart attack, stroke, and atherosclerosis (artery narrowing).
b. **High Cholesterol Levels:** Hypertension is one of the primary risk factors for CVD. It could damage arteries, increasing the chance of atherosclerosis (artery narrowing), heart attacks, and strokes.
c. **Smoking/Tobacco Use:** The chemicals in tobacco smoke cause blood vessel damage, inflammation, elevated blood pressure, and a higher risk of atherosclerosis, heart disease, and stroke.[15]
d. **Diabetes Mellitus:** Diabetes, especially type 2 diabetes, raises the risk of atherosclerosis, heart disease, and stroke in addition to being linked to insulin resistance and elevated blood sugar.
e. **Obesity and Overweight:** Dyslipidemia, insulin resistance, hypertension, and inflammation are associated with excess body weight, especially abdominal obesity, and these conditions raise the risk of cardiovascular disease (CVD).[12,21]
f. **Unhealthy Diet:** Diets heavy in processed foods, cholesterol, trans fats, saturated fats, and sodium (salt) can raise blood pressure, cause obesity, and raise cholesterol, all of which raise the risk of cardiovascular disease (CVD).
g. **Physical Inactivity:** Diabetes, insulin resistance, dyslipidemia, obesity, and hypertension are all linked to inactivity regularly, which increases the risk of cardiovascular disease.
h. **Excessive Alcohol Consumption:** Excessive drinking can worsen blood pressure, increase the risk of cardiomyopathy, arrhythmias, and stroke, and lead to obesity.[18]
i. **Stress:** Prolonged stress and poor coping strategies (such as binge eating or smoking) might raise the risk of CVD, hypertension, and inflammation.

Non-Modifiable Risk Factors:[24-28]

a. **Age:** As people age, their risk of cardiovascular disease rises, especially after menopause for women and after age 55 for men.

b. **Gender:** While women's risk of CVD decreases with age, men often have a higher risk at a younger age. But after menopause, women are more vulnerable.
c. **Family History:** An individual's risk is increased if there is a family history of CVD, especially if a close relative had the disease when they were young.
d. **Genetics:** Individuals may be predisposed by genetic factors to diseases such as familial hypercholesterolemia, which raises the risk of CVD with an early start.

For the prevention and management of cardiovascular disease, it is essential to recognize and address these risk factors through lifestyle changes (such as eating a healthy diet, getting regular exercise, and quitting smoking) and medical interventions (such as taking medication for hypertension or cholesterol-lowering medicines). Furthermore, lowering the total burden of cardiovascular disease can be achieved by early identification and treatment of CVD risk factors.

COMPLICATION OF CARDIOVASCULAR DISEASE

There are several potentially fatal complications associated with cardiovascular disease (CVD). Depending on the kind and degree of the cardiovascular disease, several problems may arise. The following are a few typical issues linked to cardiovascular disease:

1. **Heart Attack (Myocardial Infarction):** When blood flow to a portion of the heart is restricted, generally due to a blood clot, a heart attack takes place. This may cause harm to the heart muscle and cause symptoms including nausea, shortness of breath, and chest discomfort.[29]
2. **Stroke (Cerebrovascular Accident):** An ischemic stroke happens when a blood clot blocks blood flow to the brain, or a hemorrhagic stroke happens when a brain hemorrhage occurs. Severe headache, trouble speaking or comprehending speech, and abrupt weakness or numbness on one side of the body are some of the symptoms.[16,22]
3. **Heart Failure:** Heart failure occurs when the heart is unable to pump enough blood to meet the body's needs. It can result from conditions such as coronary artery disease, high blood pressure, or cardiomyopathy. Symptoms include shortness of breath, fatigue, swelling in the legs and abdomen, and difficulty exercising.[11,13]
4. **Arrhythmias:** Heart failure, coronary artery disease, and electrolyte abnormalities are just a few of the cardiovascular diseases that can cause arrhythmias or irregular heartbeats. Sudden cardiac arrest, palpitations, and fainting can result from severe arrhythmias.[22,13]
5. **Peripheral Artery Disease (PAD):** Narrowed arteries in PAD cause less blood to reach the limbs, primarily the legs. It can produce weakness, numbness, cramping in the legs, and especially while exercising. Tissue damage and non-healing wounds (gangrene) can result from severe PAD.[29,22]
6. **Aneurysm:** A weak spot or bulging in the wall of a blood vessel, generally in the cerebral arteries or the aorta (the body's major artery), is called an aneurysm. Aneurysms have the potential to burst, causing internally fatal hemorrhage.[13,29]
7. **Pulmonary Embolism:** When a blood clot enters the lungs and stops blood flow, it is known as a pulmonary embolism. If left untreated, it can cause sudden death, dyspnea, and chest discomfort. It can also be a consequence of disorders like deep vein thrombosis (DVT).[16,22]
8. **Endocarditis:** An infection of the inner lining of the heart's chambers and valves is known as endocarditis. It can happen when germs or bacteria enter the circulation and adhere to broken heart valves or other cardiac tissues. Fever, exhaustion, and heart valve damage are all possible outcomes of endocarditis.[29]

9. **Cardiac Arrest:** An abrupt cessation of heart function, commonly brought on by an electrical heart problem, is known as cardiac arrest. It causes respiration to stop and pulse and consciousness to fade. A cardiac arrest is a medical emergency that has to be treated right away with defibrillation and CPR.[13,22]
10. **Sudden Cardiac Death:** In people with or without established heart disease, sudden cardiac death refers to an unanticipated death from cardiac causes that often occurs within an hour of the beginning of symptoms. Arrhythmias like ventricular fibrillation frequently cause it.

These consequences underscore how critical it is to identify cardiovascular illness early, treat it appropriately, and take preventative actions to lessen its burden and the dangers that go along with it. Medication, surgery, lifestyle changes, and cardiac rehabilitation are all possible forms of treatment that can enhance results and lower the chance of problems.[11,13,16,22,29]

PATHOPHYSIOLOGY OF CARDIOVASCULAR DISEASE

1. **Initiating Factors:** Endothelial dysfunction and inflammation inside the arteries are caused by risk factors such as genetic susceptibility, high blood pressure, smoking, diabetes, obesity, and high cholesterol.[30,31]
2. **Endothelial Dysfunction:** Oxidative stress, inflammation, and other conditions cause the endothelial cells that line the arteries to malfunction. Increased permeability, circulating leukocyte adhesion, and compromised vasodilation are the results of dysfunction.[12,32,33]
3. **Atherosclerosis Development:** Lipids, particularly low-density lipoprotein (LDL) cholesterol, build up in the artery wall after penetrating the injured endothelium. Foam cells are created when monocytes or macrophages penetrate the artery wall and absorb lipids. Smooth muscle cells go from the media into the intima, multiply, and help the fibrous cap that covers the lipid-rich plaque to develop. [34,35,12]
4. **Plaque Formation:** The build-up of inflammatory cells, lipids, foam cells, and extracellular matrix proteins results in the formation of an atherosclerotic plaque in the artery wall. Three factors lead to plaque destabilization: oxidative stress, weakening of the fibrous cap, and inflammation.[30-35]
5. **Complications:** Platelet activation and thrombus formation are caused by plaque rupture or erosion, which exposes thrombogenic material. Myocardial infarction, unstable angina, and sudden cardiac death are examples of acute coronary syndromes that can occur when a thrombus partly or obstructs the artery.[33,34]
6. **Coronary Artery Disease (CAD):** Atherosclerotic plaque causes the coronary arteries to gradually constrict or block, which causes myocardial ischemia and myocardial infarction. Silent myocardial ischemia or stable angina pectoris are two possible signs of chronic ischemia.[30-33]
7. **Heart Failure (HF):** Prolonged volume overload (such as valvular heart disease) or pressure overload (such as hypertension) causes left ventricular hypertrophy and poor diastolic relaxation. Systolic dysfunction with decreased ejection fraction (heart failure with reduced ejection fraction, or HFrEF) can be brought on by the advancement of CAD, myocardial infarction, or persistent hypertension. Impaired ventricular filling and relaxation may result in diastolic dysfunction and preserved ejection fraction, or heart failure with preserved ejection fraction, or HFpEF.[12,21,30-35]

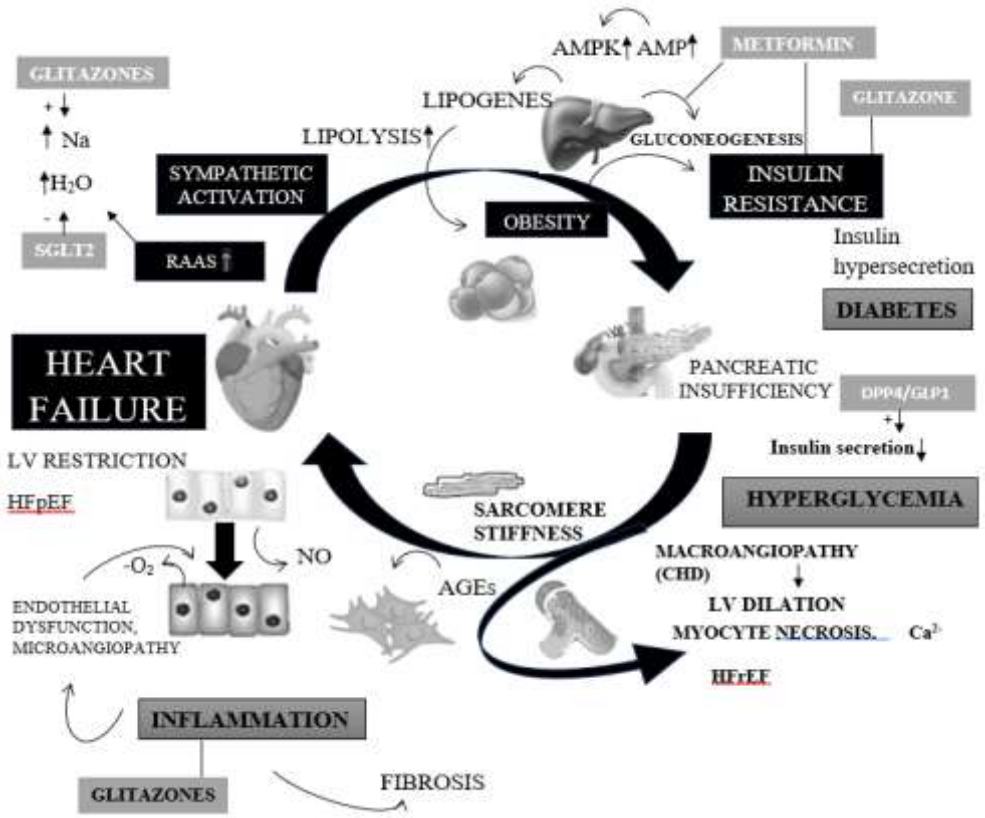

FIG:1 DIFFERENT ASPECTS OF HEART FAILURE ALLOPATHIC REMEDIES:[36-41]

Allopathic remedies, also known as conventional or mainstream medicine, encompass a wide range of drugs used to treat cardiovascular diseases. These drugs are classified into several categories based on their mechanisms of action and therapeutic effects. Here's a general classification of allopathic remedies commonly used in cardiovascular disease treatment:

Antihypertensive drugs:[11]

1. **Angiotensin-converting enzyme (ace) inhibitors:** Examples include enalapril, lisinopril, and ramipril. They work by inhibiting the conversion of angiotensin I to angiotensin II, thereby reducing vasoconstriction and aldosterone secretion.
2. **Angiotensin ii receptor blockers (arbs):** Examples include losartan, valsartan, and irbesartan. They block the effects of angiotensin II on blood vessels, leading to vasodilation.
3. **Beta-blockers:** Examples include metoprolol, carvedilol, and atenolol. They lower blood pressure and heart rate by obstructing the effects of adrenaline on the heart and blood arteries.
4. **Calcium channel blockers:** Examples include amlodipine, verapamil, and diltiazem. They inhibit the influx of calcium ions into vascular smooth muscle cells, leading to vasodilation and decreased cardiac contractility.
5. **Diuretics:** Examples include hydrochlorothiazide, furosemide, and spironolactone. They increase the excretion of sodium and water by the kidneys, reducing blood volume and blood pressure.

Antiplatelet agents:

1. **Aspirin (acetylsalicylic acid):** Inhibits platelet aggregation by irreversibly inhibiting cyclooxygenase, thereby reducing the risk of blood clot formation.
2. **P2y12 inhibitors:** Examples include clopidogrel, prasugrel, and ticagrelor. They inhibit the

P2Y12 receptor on platelets, reducing platelet activation and aggregation.

Anticoagulants:

1. **Vitamin K antagonists (vkas):** Examples include warfarin. They inhibit the synthesis of vitamin K-dependent clotting factors (II, VII, IX, X).
2. **Direct oral anticoagulants (doacs**): Examples include dabigatran, rivaroxaban, apixaban, and edoxaban. They directly inhibit specific clotting factors (e.g., thrombin or factor Xa), preventing the formation of blood clots.

Cholesterol-lowering drugs:

1. **Statins:** Examples include atorvastatin, simvastatin, and rosuvastatin. They inhibit HMG-CoA reductase, the rate-limiting enzyme in cholesterol synthesis, thereby reducing LDL cholesterol levels.
2. **Ezetimibe:** Inhibits cholesterol absorption in the small intestine, reducing LDL cholesterol levels.

Cardiac glycosides:

1. **Digoxin:** Increases myocardial contractility and reduces heart rate by inhibiting the sodium-potassium ATPase pump.

Vasodilators:

1. **Nitroglycerin:** Dilates coronary arteries and veins, reducing myocardial oxygen demand and relieving angina symptoms.

Antiarrhythmic drugs:

1. **Class I (sodium channel blockers):** examples include procainamide, quinidine, and lidocaine. They inhibit sodium channels, delaying depolarization and reducing excitability.
2. **Class ii (beta-blockers):** As mentioned earlier, they also have antiarrhythmic properties by reducing sympathetic activity.
3. **Class iii (potassium channel blockers):** Examples include amiodarone, sotalol, and dofetilide. They prolong the action potential duration and refractory period.
4. **Class IV (calcium channel blockers):** As mentioned earlier, they also help control certain types of arrhythmias by slowing conduction through the AV node.

NUTRACEUTICAL MANAGEMENT IN THE CARDIOVASCULAR SYSTEM:

In 1989, Stephen DeFelice, the founder and head of the Foundation for Innovation in Medicine, coined the word "nutraceuticals." "Food, or parts of a food, that provide medical or health benefits, including the prevention and treatment of disease" is the definition of a nutraceutical (7). The concept includes pharmaceuticals derived from natural sources. A quick summary of the nutraceuticals with the strongest evidence is provided below. Several nutraceutical classes have been suggested to offer potential advantages in the treatment of CVD. Any substance that is regarded as food and has health advantages, such as illness prevention or health promotion, is referred to as a nutraceutical. It refers to any safe dietary ingredient that has been shown to improve health via scientific research, including the prevention or treatment of disease. The nutraceutical product's functional ingredient needs to be standardized and made using excellent manufacturing techniques.

Table 1: Potential cardiovascular benefits of nutraceuticals in human studies

Nutraceutical	Cardiovascular health benefits
	◆ Reduce lesion volume

Allicin	◆ Short-term reduction in levels of serum LDL, total cholesterol, and triacylglycerols but no long-term benefits
Dietary fiber e.g. butyrate	◆ The trend for reduced risk of CVD - events, which were no longer significant after controlling for other confounding variables ◆ Reduced risk of peripheral arterial disease, hemorrhagic stroke, CVD - events
Flavonoids	◆ Reduced circulating LDL levels and the expression of pro-inflammatory cytokines ◆ Increased vasodilation and enhanced endothelial function ◆ Enhanced flow-mediated dilation in patients with congestive heart failure
Hydroxytyrosol	◆ Reduced risk of CVD-event and subclinical atherosclerosis in high-risk patients by decreasing serum oxidative LDL levels, total cholesterol levels, and the expression of inflammatory biomarkers ◆ Improved endothelial function
ω- 3 puffs	◆ Reduced atherothrombotic risk, the number of CVD -events, and the number of sudden cardiac deaths ◆ Increased plaque stability and reduced levels of pro-inflammatory cytokines ◆ Increased endothelial function and reduced arterial stiffness
ω - 6pufas	◆ Increased arterial stiffness and serum CRP levels ◆ Reduced serum LDL, total cholesterol, and triacylglycerol levels
Phytosterols	◆ Reduced serum LDL levels ◆ Reduced levels of serum LDL, but no change in serum CRP levels
Vitamin C & e	◆ Vitamin C reduces the risk of CVD event, the prevalence of CAD ◆ Vitamin C increases vasodilatation and endothelial function ◆ Vitamin E reduces the serum oxidative LDL and the risk of non-fatal CVD - events ◆ Combined vitamin C and E supplementation improved arterial stiffness, flow-mediated dilation, and oxidative stress levels

Polyphenols and flavonoids:

Polyphenols, which comprise molecules from the flavonoid (Anthocyanins, flavan-3-ols, flavanols, flavanones, flavones, and isoflavones) and non-flavonoid (phenolic acids and stilbenes) families, are the most prevalent secondary metabolites in the kingdom of plants.

Consuming foods and beverages high in polyphenols, such as various fruits, vegetables, chocolate, red wine, grape juice, and tea, has been linked in numerous studies to a lower risk of cardiovascular illnesses. Naturally occurring in fruits, vegetables, tea, and red wine, flavonoids are a class of phenolic chemicals with anticarcinogenic and cardioprotective qualities. Numerous studies have shown that flavonoids' anti-inflammatory and antioxidant qualities may also enhance vascular functioning. Furthermore, a high dietary intake of flavanols has been linked to a lower risk of coronary heart disease mortality, and an increased intake of tea and flavonoids may help prevent ischemic heart disease.[42-44]

While flavonoids have been shown in numerous trials to have cardioprotective properties, there are also contradictory data.[45] Studies have not ruled out the idea that flavonoids may have a preventive impact on established coronary disease, but there is little assurance about the relationship between flavonoid consumption and total coronary disease.[46] Flavonoids found in food can improve endothelial function in patients with coronary artery disease, following heart transplantation, or in healthy volunteers with or without cardiovascular risk factors when consumed acutely and repeatedly.[47,48] Nitric oxide synthase's enhanced activity is thought to have a role in the vascular actions of flavonoids, according to experimental research conducted on people and animals.[49,50] Soy isoflavones are also members of the flavonoid class, and studies in animal models have indicated that consuming a diet high in these compounds can enhance endothelial function, induce vasodilation, and lower blood pressure. Because of experimental bias, the outcomes in human trials have not been dependable.

A meta-analysis of randomized controlled trials was conducted to ascertain the impact of a soy-based diet on blood pressure. The results indicated that soy-derived isoflavones lower blood pressure in hypertensive individuals but not in normotensive individuals; further trials were necessary to corroborate these findings. As a result, information regarding how soy isoflavones affect blood pressure is still unreliable. [52-54]

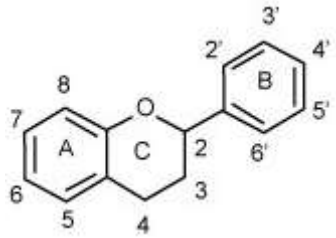

FIG 2 STRUCTURE OF FLAVONOIDS.[55]

TABLE:2 FLAVANOIDS CLASSES AND FOOD SOURCES.[55]

Flavonol	Onion, broccoli, cherry, apple, raspberry, red wine
Flavone	Honey, red pepper, celery, parsley
Isoflavone	Soy flour, soymilk, soybeans
Flavan-3-ol	Cocoa, green tea, cherry
flavanone	Citrus fruits
Anthocyanidin	Grape, cherry, raspberry, blueberry

Flavonoid intake lowers the risk of CVDs, according to a systematic review and meta-analysis that found an inverse relationship between the dietary intake of flavonoid subclasses and CVD risks. However, this meta-analysis was based on observational studies, which may have introduced biases such as dietary classification errors or the presence of unmeasured or uncontrolled risk factors. Extra virgin olive oil is another food high in flavonoids. Consumption of extra virgin olive oil was linked to higher diastolic and systolic blood pressure in an inverse manner. When compared to placebo, hypertensive twins treated with an olive leaf extract at a dose of 500–1000 mg daily for 1–8 weeks likewise showed a decrease in blood pressure[56]. By raising plasma nitrite/nitrate and lowering serum asymmetric dimethylarginine (ADMA), which is an endogenously generated molecule that can impede the generation of nitric oxide (NO), extra virgin olive oil may also help lower blood pressure. All things considered, a polyphenol-rich diet may help to enhance endothelial function by increasing the

bioavailability of NO.[57] High concentrations of polyphenols have also been found in grape seed and red wine extracts, and consuming these substances has been linked to positive health outcomes. Because grape and wine polyphenols suppress platelet aggregation, lower oxidative stress, and decrease LDL oxidation, they may be able to lower high blood pressure and improve cardiovascular illnesses.[58] The extract from grape seeds may have antioxidant properties that reduce the quantity of reactive oxygen species (ROS), even if the exact mechanism of action of grape seeds is yet unknown.[42] This capacity shows promise in cardiovascular and metabolic illnesses (CVD), as these conditions are frequently associated with high ROS. There is a lot of data showing how flavonoids affect the cardiovascular system; however, additional research is required to determine the right quantity of flavonoid consumption required to have meaningful and safe benefits. Determining which particular flavonoid subclasses provide these desired effects and for which particular diseases they might be advantageous is also important.[51]

Vitamins:

Patients with hypertension respond to oxidative stress more than usual and produce more reactive oxygen species (ROS).[59,60] Furthermore, the hypertensive patient has compromised endogenous and exogenous antioxidant defense systems. Antioxidant deficiencies have been linked to cardiovascular illnesses and hypertension, according to several epidemiological studies. Because of the antioxidant elements they contain, such as ascorbic acid (vitamin C), a range of foods are of interest and have been examined in light of the epidemiological increase of chronic non-communicable illnesses like diabetes mellitus and cardiovascular events.[61,62] Although the significance of vitamin consumption is well acknowledged, little is understood about how exactly vitamins affect cardiovascular health.[63] Decreased plasma vitamin E levels have been linked to an increased risk of cardiovascular disease, according to many studies. In a similar vein, a higher risk of cardiovascular events was linked to lower plasma levels of ascorbic acid or vitamin C. Human blood pressure is correlated with higher blood concentrations of vitamin C. An inverse association between plasma ascorbate levels and diastolic and systolic blood pressure was verified in a 17-week controlled diet depletion-repletion trial of vitamin C.[64,65] This study also indicated that vitamin C may be associated to the beneficial effects of fruits and vegetables on blood pressure reduction. Furthermore, tissue ascorbic acid concentrations can be crucial for preserving low blood pressure. Thus, it is advised to maintain a serum level of plasma ascorbate of at least 100 mcmol/L to get a positive impact on blood pressure. To validate this conclusion, though, further long-term intervention studies need to be carried out. Without changing the AT1 receptor's maximum binding capacity or the AT2 receptor's binding affinity for angiotensin II, ascorbic acid lowers the AT1 receptor's binding affinity.[666,67] Given that the AT1 receptor mediates the majority of the angiotensin II-induced cardiovascular effects, including vascular contraction, aldosterone secretion, and cardiovascular cell growth and proliferation, among others, these findings offer a mechanistic explanation for the ascorbic acid's reported blood pressure-lowering effect. The disruption of ATR1 disulfide bridges appears to be the cause of this decrease in the AT1 receptor's affinity for angiotensin II.[68,69] In response to research suggesting that vitamin E or vitamin C may lower the risk of cardiovascular disease, 14641 US male physicians who were initially 50 years of age or older participated in a randomized, double-blind, placebo-controlled factorial trial of vitamin E and vitamin C between 1997 and 2007. [70-74]At randomization, 754 of the men had prevalent cardiovascular disease. Few long-term trials have assessed men who were initially at low risk of

cardiovascular disease, and no prior trial in males has looked only at vitamin C's role in preventing cardiovascular disease, claim the study's authors. Consequently, neither vitamin E nor vitamin C treatment decreased the incidence of significant cardiovascular events in this extensive, long-term experiment among male doctors. [75,76]

These findings did not support the use of these supplements in middle-aged and older men to prevent cardiovascular disease [46]. In a different research, vitamin C's effects led to a drop in blood pressure and a rise in nitric oxide, which enhanced arterial compliance and endothelial function. In young individuals in good health, the inverse association between plasma ascorbic acid and blood pressure was noted in the attenuation of blood pressure rises that decreased the risk of related vascular events. Even in young individuals who are in good health, this study indicates that vitamin C may have a significant role in blood pressure management [53]. Consuming vitamin C-rich foods seems to be beneficial for decreasing blood pressure, but further long-term research with patients of all ages and hypertension stages is required to determine which people may benefit. Vitamin D is another crucial vitamin linked to cardiovascular illnesses. This vitamin is mostly found in some kinds of fish and is produced by the skin in response to sun exposure. It is also absorbed through the food [54]. Upon entering the body, vitamin D undergoes a rapid conversion to its primary circulating form, 25-hydroxyvitamin D (25 (OH) D) [55]. In addition to its traditional function in maintaining calcium-phosphate balance, vitamin D also seems to have immunoregulatory and anti-inflammatory properties [56]. Numerous studies [12,57,58] report inverse relationships between low sun exposure, or low serum 25(OH)D levels, and elevated risks of stroke, myocardial infarction, peripheral vascular diseases, and heart failure. They also suggest a strong correlation between vitamin D deficiency and cardiovascular disease. In addition, greater activation of inflammatory pathways at the epicardial adipose tissue (EAT) level is associated with both systemic and local vitamin D insufficiency in patients with coronary artery disease (CAD), and its accumulation may be a risk factor for CAD [66]. Despite being the first to link vitamin D and EAT-level inflammation in humans, Dozio and colleagues were unable to determine if vitamin D administration may prevent local EAT inflammation in these individuals. In addition, it suggests that vitamin D supplementation reduces inflammatory processes and promotes anti-inflammatory responses in EAT.[77,78] Gunasekar and colleagues used an animal model to demonstrate that vitamin D deficiency increases both the recruitment of M1 macrophages and the pro-inflammatory expression of adipokine in the EAT. In animal models, vitamin D3 supplementation can significantly increase HDL-C levels as well as macrophage pro-inflammatory polarization, which protects against the development of atherosclerosis. Vitamin D deficiency can also promote the progression of atherosclerosis and decrease plasma HDL-C levels. Through several processes, including blood pressure regulation, vascular smooth muscle cell activity, modulation of vascular tone, and maintenance of a healthy endothelium, vitamin D has a significant protective impact on the heart. Vitamin D's anti-inflammatory and anti-mitotic properties contribute to endothelium stability, which at least partially explains its cardiovascular benefits.[79-85] There is no proof of randomized clinical studies showing that vitamin D supplementation prevents CVDs, despite several indications linking vitamin D insufficiency to endothelial dysfunction and CVDs. To enhance target therapies and expand the data supporting the beneficial effects of vitamin D replacement on cardiovascular health, there is still a considerable need to understand how mediates cardiovascular function.

Tomato and lycopene:

Red fruits and vegetables such as watermelons, tomatoes, papayas, and red peppers contain lycopene, a carotenoid. In addition to their well-known culinary flexibility, tomatoes also add nutritious value to diets. Lycopene accounts for over 90% of the total carotenoids found in tomatoes, while other components include carotene, folate, phenolic compounds, and vitamins C and E.[86-89] Research attention has increased on the relationship between tomato and lycopene consumption and lower risk of cardiovascular disease.

The risk of myocardial infarction, coronary insufficiency, and angina pectoris is strongly inversely correlated with lycopene intake, according to the Framingham Heart Offspring Study. Furthermore, decreased plasma levels of lycopene were reported in cases of atherosclerosis, hypertension, acute myocardial infarction, and stroke. Lycopene, the most potent antioxidant among the main carotenoids, is crucial in avoiding cardiovascular disease in people [84]. Although lycopene bioavailability in supplements has not been investigated as much, it is still a crucial topic for investigation. Tomato supplementation for three months induced alterations in miRNA expression and decreased oxidative stress, according to an experimental investigation conducted on Wistar rats. Furthermore, these modifications seem to be in charge of the improvement of diastolic function and decrease in the cross-sectional area of left ventricular myocytes. [90-93]Nevertheless, further research is required to determine the precise roles that tomatoes and lycopene may play in the prevention and treatment of cardiovascular illnesses. Additionally, the positive effects of these nutrients on the heart that have not yet been explored must be clarified. Endothelial function is well recognized as a good indicator of vascular health (CITE). Moreover, coronary or peripheral vascular endothelium dysfunction appears to be an independent predictor of cardiovascular events, and endothelial dysfunction contributes to the development of atherosclerosis. One potential contributing factor to endothelial dysfunction is increased oxidative stress. Remarkably, an 8-week lycopene supplementation has been demonstrated to enhance the positive effects of oxidative stress biomarkers in a randomized, double-blind, placebo-controlled research (by decreasing oxidative DNA damage and raising plasma superoxide dismutase enzymatic activity).[94-98] Additionally, because endothelial function is closely linked to inflammatory indicators, their antioxidant actions may be very important in enhancing endothelial function. These outcomes show how consuming lycopene regularly is helpful. Numerous studies have linked lycopene and tomatoes to decreased rates of cardiovascular disease incidence. However, the impact of lycopene supplementation is yet unknown and unproven. Even though lycopene makes up over 90% of all carotenoids in tomatoes, further research is necessary to fully comprehend the advantages of the other bioactive substances that are present. It is also advised to eat fruits and vegetables high in natural carotenoids until more studies clarify and validate the noteworthy advantages of lycopene supplementation in people.[99,100]

Garlic:

Allium sativum, or garlic, has been used for food and medicine for a very long time. Water makes up the majority of garlic's composition (65%), along with fructose, sulfur compounds, proteins, and free amino acids.[101,102] Garlic's nutritional and therapeutic properties are attributed to sulfur compounds that are either produced or present in it. Recent research has demonstrated that allicin, often referred to as diallelic thiosulfate, is partially responsible for the cardiovascular health advantages of garlic. C-S-lyase (alliinase) operates on alliin (S-allyl-L-Cysteine sulfoxide) and transforms it into allicin (allylthiosulfinate) when the cellular structure of garlic is disrupted. Using non-enzymatic reactions,

allicin produces several sulfides, such as methyl allyl trisulfide (MATS), diallyl sulfide (DAS), diallyl disulfide (DADs), and diallyl trisulfide (DATS) (Ariga & Seki, 2006), all of which have strong antiplatelet properties. Consuming garlic can improve vasodilatation and fibrinolysis in both people and animals, as well as prevent platelet aggregation in humans.[103,104]

Aged garlic extract (AGE), which is made by preserving sliced raw garlic in an ethanol solution for 20 months at room temperature, is a significant and thoroughly researched garlic preparation. To determine the effectiveness of this garlic preparation, more research is necessary. Future research might look at a combination of antioxidants over a longer period and look at a diabetic cohort with a greater cardiovascular risk, including those with existing cardiac illness, to better explore the characteristics of AGE. Apart from AGE, there exist several forms of garlic, like oil, powder, and oil, which might have advantageous effects.[105,106] Garlic was discovered to have additional cardiovascular benefits, including cardioprotective effects supported by H2S, which is created when garlic derivatives are converted into human erythrocytes. H2S has anti-inflammatory, antioxidant, and antiapoptotic properties that protect the heart. H2S has a variety of physiological activities in mammalian tissues and is a gas-signaling molecule that is cardioprotective. It is critical to cellular function and guards against necrosis, oxidative stress, and apoptosis. In mice with murine lesions and ischemia/reperfusion, treatment with exogenous H2S is feasible and might lead to a notable decrease in the extent of myocardial infarction [101]. The idea that eating garlic has a substantial

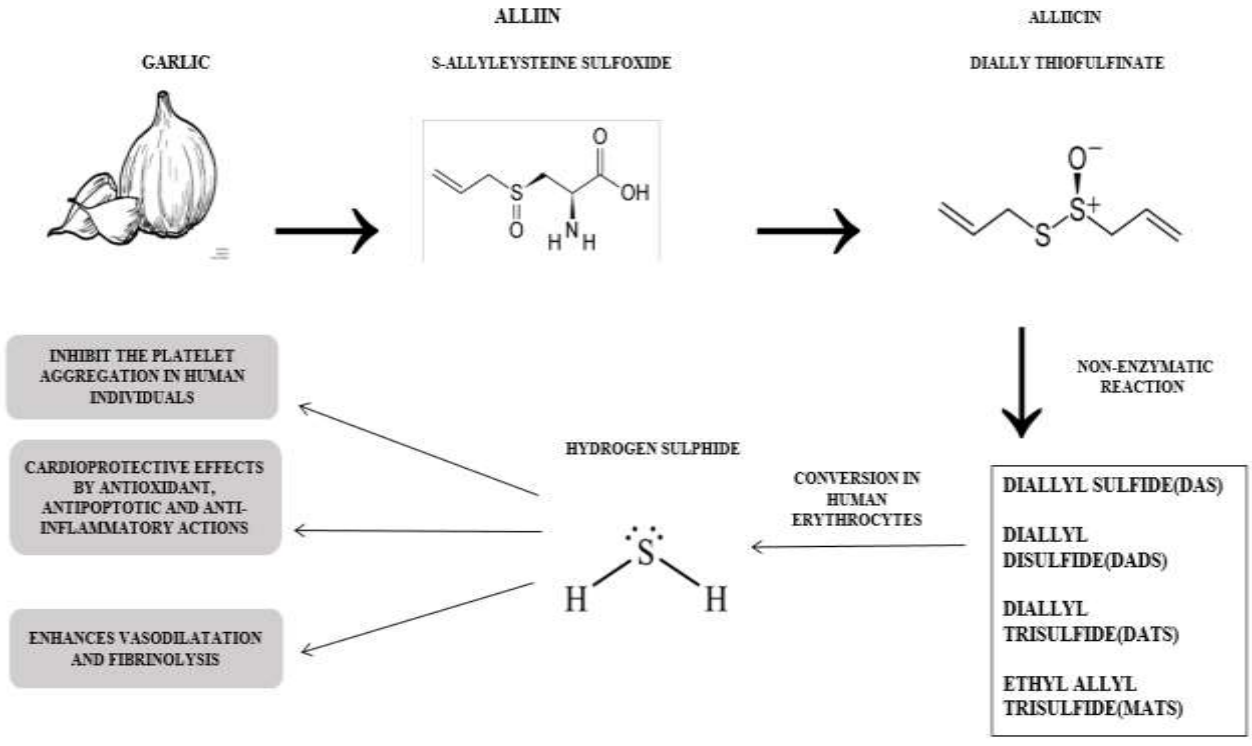

FIG 3 NUTRACEUTICAL FORMULATIONS OF GARLIC [55]

cardioprotective impact is backed by an enormous body of scientific research [102]. Following extremely encouraging in vitro research demonstrating the therapeutic benefits of garlic, clinical trials were conducted to assess the effects of garlic on cardiovascular disorders. Nevertheless, many of these trials were equivocal.

When compared to a placebo, a comprehensive review and meta-analysis of hypertensive patients receiving treatment with garlic-only formulations showed a drop in blood pressure. Garlic may lower blood pressure in hypertensive individuals, according to a new study. This effect is comparable to that of common blood pressure medications such as diuretics, angiotensin II receptor blockers, calcium channel blockers, and angiotensin-converting enzyme inhibitors. Additionally, studies should be conducted to determine whether garlic may have an anti-hypertensive effect in pre-hypertensive individuals, as this would be crucial in preventing the progression of hypertension. Garlic preparations supplementation may be a supplemental treatment option for hypertension. Garlic showed promising effects in individuals with moderate hypertension in a meta-analysis; however, not enough data was obtained to support therapeutic therapy recommendations, and research on the relationship between blood pressure and garlic preparations have yielded conflicting findings.

Other nutraceutical management:[107-117]

1. **Omega-3 fatty acids**: It has been demonstrated that omega-3 fatty acids, namely the fish oil constituent's docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA), are advantageous to cardiovascular health. They can decrease blood pressure, lessen inflammation, and cut lipid levels. People who are at risk of cardiovascular disease or have excessive triglycerides are frequently advised to take omega-3 supplements.
2. **Antioxidants:** Coenzyme Q10 (CoQ10), vitamins C and E, and other antioxidants can help lower oxidative stress and inflammation, which are linked to the onset of cardiovascular disease. A well-balanced diet full of fruits, vegetables, nuts, and seeds can provide these nutrients, or in certain situations, supplements can be used to receive them.
3. **Plant sterols and stanols:** It has been demonstrated that plant sterols and stanols, which are present in fruits, vegetables, nuts, and seeds, can help reduce LDL cholesterol levels. They function by preventing the intestines from absorbing cholesterol. Supplements containing plant sterol and stanol are readily accessible and can be used in a cholesterol-lowering program.
4. **Fiber:** Dietary fiber, especially the soluble kind that is present in fruits, vegetables, legumes, and oats, can help decrease LDL cholesterol and strengthen heart health. For those who find it difficult to obtain adequate fiber from their diet, psyllium husk supplements may be suggested.
5. **Magnesium:** Magnesium helps to control heart rate and blood pressure. If a person has a magnesium shortage or is at risk of cardiovascular disease, magnesium supplements may be advised.
6. **Vitamin D:** Elevated risk of cardiovascular disease has been linked to low vitamin D levels. Supplementing with vitamin D may be advantageous, particularly for people with low vitamin D levels or little sun exposure.
7. **Lifestyle modifications:** The treatment of cardiovascular disease using nutraceuticals should be complemented by lifestyle changes such as eating a heart-healthy diet, getting regular exercise, quitting smoking, managing stress, and keeping a healthy weight. These lifestyle choices can improve the overall health of the cardiovascular system and increase the efficacy of nutraceutical treatments.

Table3: The stages of atherosclerosis development at which different nutraceuticals exert their potential beneficial effects:

Nutraceuticals	LDL OXIDATION	PRO-INFLAMMATORY GENE EXPRESSION	MONOCYTE RECRUITMENT	FOAM CELL FORMATION	PLAQUE STABILITY
Nutraceuticals and the stages of atherosclerosis Development at which they exert beneficial effects	Hydroxy Tyr Flavonoid Vitamin C	Omega-3 PUFAs Omega-6 PUFAs Hydroxytyrosol Allicin Flavonoid Dietary fiber	Dietary Fiber Allicin Omega-6 PUFAs Omega-3 PUFAs	Phytosterols Allicin Omega-3 PUFAs	Dietary Fiber Omega-6 PUFAs

In a recent randomized controlled pilot study, thirty menopausal healthy women with mild hyperlipidemia who lived in rural communities (ages 45 to 65) were divided into two experimental groups and randomly assigned to one of two treatments: either one received daily treatments of cucumber (100–125 g) or curry leaf powder (5 g) for 45 days.[118-120] Triacylglycerol (TAG), total cholesterol (TC), and low-density lipoprotein-cholesterol (LDL-C) were all much lower in the groups that received curry leaf powder and cucumber treatment. The level of high-density lipoprotein-cholesterol (HDL-C) was only substantially higher in the group that received curry leaf powder treatment. This finding raises the possibility of curry leaves and cucumbers serving as nutraceuticals in the treatment of CVD. [121-126]To determine if adding beet juice to a regular diet would result in a measurable drop in blood pressure, a double-blind, randomized, placebo-controlled crossover research including thirty independent persons was conducted. 500 g of either placebo juice (PL) or beetroot and apple juice (BJ) were randomly assigned to the volunteers. [127-133]An ambulatory blood pressure monitor was used to measure the volunteers' blood pressure (ABPM) at baseline and at least hourly for 24 hours after they consumed juice. According to the findings of this study, men's blood pressure can be lowered by consuming beetroot juice as part of a regular diet in healthy, independent people. Allium cepa (onion) nutraceutical formulations are recommended for the treatment of several acute and chronic illnesses. The effects of a quercetin-rich onion skin extract on 24-hour ambulatory blood pressure and endothelial function in overweight-to-obese patients with (pre-)hypertension were assessed in a 12-week treatment period followed by a 6-week washout period. The trial included sixty-eight subjects (thirty-four males and thirty-four females) and was double-blinded, placebo-controlled, and cross-over. The results of this study indicate that quercetin (162 mg/day) from onion skin extract supplements decreases ambulatory blood pressure in hypertension patients, indicating quercetin's potential cardioprotective impact. Nutraceutical management in cardiovascular disease involves the use of specific nutrients, dietary supplements, and dietary modifications to support heart health, manage risk factors, and potentially reduce the progression of cardiovascular conditions.[134,135] This approach aims to

complement conventional medical treatments and lifestyle modifications to optimize cardiovascular health.

CONCLUSION

Nutraceuticals play a vital role in the prevention of cardiovascular disease (CVD) by offering alternative and complementary approaches to traditional pharmaceutical interventions. These compounds, derived from food sources, possess therapeutic properties that target multiple cardiovascular risk factors, including hypertension, dyslipidemia, inflammation, and endothelial dysfunction. Through extensive research, various nutraceuticals such as berberine, Coenzyme Q10, garlic supplementation, curcumin, and hydroxytyrosol have demonstrated efficacy in improving cardiovascular health markers and reducing the incidence of CVD events.

One of the key strengths of nutraceuticals lies in their ability to address not only individual risk factors but also their interactions, providing a holistic approach to CVD prevention. Additionally, nutraceuticals offer the advantage of being generally well-tolerated by patients, with fewer adverse effects compared to some pharmaceutical medications. This makes them particularly suitable for individuals who may not respond well to conventional therapies or who prefer natural interventions. However, despite their promise, the widespread adoption of nutraceuticals in CVD prevention faces several challenges. These include the need for further research to establish optimal dosages, formulations, and combinations, as well as to ensure long-term safety and efficacy. Moreover, regulatory issues and limited awareness among healthcare professionals and the general public may hinder their integration into clinical practice.

In conclusion, nutraceuticals represent a promising adjunctive strategy in the prevention of cardiovascular disease. Their multifaceted benefits, coupled with their favorable safety profile, position them as valuable components of comprehensive CVD prevention programs. Moving forward, concerted efforts are needed to bridge the gap between research and practice, facilitating the incorporation of nutraceuticals into evidence-based guidelines and promoting their widespread use to reduce the global burden of cardiovascular disease.

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