Review Article

A SYSTEMATIC REVIEW ON PHYTOCHEMICALS HAVING VASCULAR PROTECTIVE EFFECTS

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ABSTRACT:

Vascular endothelial dysfunction, characterized by imbalances in vasodilation and constriction, deficiency of nitric oxide bioavailability, and elevated reactive oxygen species, is a key factor in cardiovascular diseases like hypertension, atherosclerosis, and diabetes. Regular consumption of medicinal plants, fruits, and vegetables can promote vascular health and lower the risk of cardiovascular diseases. Phytochemical compounds found in these resources, such as curcumin have potential therapeutic agents for vascular dysfunction due to their antioxidative mechanisms. However, further human studies are needed to confirm these effects. Also, medicinal properties against CVDs of 4 widely used plants namely ginseng, ginkgo biloba, Ganoderma lucidum, gynostemma pentaphyllum are discussed in this review to provide recent information on their vascular protective mechanisms in vivo and in vitro. However, future human studies will be necessary to confirm the clinical effects of these vascular protective mechanisms. Finally, we reviewed and reported the results of the recent clinical trials and have been conducted using these medicinal herbs with special emphasis on their efficacy, safety, and toxicity. Marketed formulations and case studies regarding to vascular protective effect are also mentioned. Our study aimed to analyse and compare monthly costs along with cost variation between Ayurveda and Allopathy medicines used to treat 2 chronic disease conditions, viz. Atherosclerosis and Hypertension. The prices of Allopathic & Ayurvedic drugs mentioned in the treatment guidelines for these 2 conditions were obtained from different sources. In the case of Allopathic drugs, the %CVD ranged from 182%for DMARDs to 1184.39% for Corticosteroids. In the case of Anti-hypertensive medicines, too, the mean %CVD ranged from 84.21% for Rasaushadhi to 353.33% for Arishta, while %CVD ranged from 150.70% for ACE inhibitors to 269.85% for Calcium channel blockers for Ayurvedic and Allopathic medicines, respectively.

INTRODUCTION:

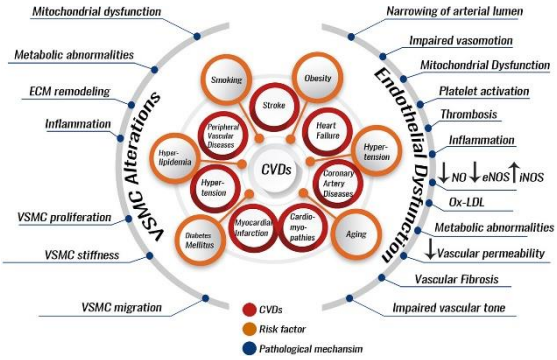
Low levels of nitric oxide gas in blood vessel walls cause endothelial disfunction, leading to coronary artery diseases, angina, chest pain, increased cardiovascular disease risk, atherosclerosis, and high blood pressure. Cardiovascular diseases (CVDs) are the leading cause of death worldwide. According to the World Health Organization (WHO), the almost 18 million deaths due to CVDs accounted for 32% of global deaths in 2019. This report also revealed that CVDs do not exclusively affect industrialized countries, as over three-quarters of CVD-related deaths occur in low- and middle-income countries. Older projections have already indicated that this number is expected to increase to over 23 million by 2030[1].

In addition to being the major cause of death worldwide, CVDs also lead to a great number of chronically ill patients, and as a consequence, to an immense socio-economic burden. Thus, there is an urgent global need for efficient CVD prevention. There are numerous established risk factors for the development and progression of CVDs.The aging process per se is a non-modifiable risk factor, as it cannot be reversed. On the contrary, other factors such as obesity, which, according to the WHO report on global health risks, is one of the major causes of ischemic heart disease, are modifiable, meaning that measures can be taken to change them and thereby reduce the risk for CVDs. Many natural substances have been used in traditional medicine in many regions of the world, often for thousands of years. In this review, we will highlight the impact of curcumin and some other phytocompounds on age-related cardiovascular dysfunction, adipose tissue, and obesity, as well as its protective effects in atherosclerosis and myocardial infarction. Cardiovascular diseases (CVDs), affecting over 17 million people annually, are the world's most common cause of death and a significant economic and health burden, accounting for 31% of annual global deaths. CVD, a condition characterized by vascular disfunction, can lead to heart failure, heart attacks, stroke, cardiomyopathies, dyslipidemias, and hypertension, causing organ damage. This

review critically assesses VEGF (vascular endothelial growth factor) therapy based on therapeutic angiogenesis and advances an alternative mechanism of vascular protection. Vascular protection involves VEGF-induced enhancement of endothelial functions, inhibiting vascular smooth muscle cell proliferation, enhancing endothelial cell survival, suppressing thrombosis, and anti-inflammatory effects. Investigation into vascular protection could help develop novel therapeutic approaches based on local VEGF gene delivery. This paper reviews phytocompounds from plants, vegetables, and fruits that offer anti-inflammatory and antioxidant properties, particularly in treating cardiovascular disorders. It also explores the mechanisms by which these compounds can improve vascular endothelial cell integrity, highlighting the potential benefits of herbal medicine over medications due to their low toxicity and clinical effectiveness. CVDs affect vessels and the heart, with atherosclerosis being a complex disease driven by low-grade inflammation. It begins with cholesterol deposition in vessel walls and chronic inflammatory reactions, leading to endothelial dysfunction in arteries prone to plaque development. Under homeostatic conditions, ROS production is counteracted by anti-oxidative systems, which are downregulated by CVD risk factors. As we age, our vascular and heart structures undergo significant changes, increasing the risk of cardiovascular events. These include endothelial dysfunction, aortic stiffening, elevated blood pressure, heart hypertrophy, and remodelling of myocardial microvasculature. [2, 3,8]

Risk factors for CVDs include hypertension, smoking, unhealthy diet, and endocrinopathies. These factors lead to pathological alterations, primarily due to endothelial dysfunction or VSMC alterations. These alterations increase the risk of atherosclerosis and hypertension, which are CVD risk factors and enhancers for other cardiovascular diseases. Vascular impairment is primarily caused by atherosclerosis, thrombosis, and high blood pressure, with common risk factors including smoking, unhealthy diet, diabetes, hyperlipidemia, and hypertension. Inflammation can impair the function of endothelial cells (ECs) in atherosclerosis, leading to the accumulation of oxidized LDL particles in the vessel wall intima.

Hypertension, a major risk factor for cardiovascular diseases (CVDs), is an independent predisposing factor for heart failure, coronary artery disease, stroke, retinopathy, nephropathy, and peripheral arterial diseases Strokes can impact cognitive and physical behaviors, potentially leading to dementia, paralysis, or even death. Vascular resistance is influenced by the sympathetic nervous system, rennin-angiotensin system, humoral factors, and local autoregulation. SNS and RAS primarily cause vasoconstriction and sodium retention through humoral mediators like endothelin, angiotensin II, catecholamines, and nitric oxide (NO), prostaglandins, and kinins. Endothelial dysfunction affects your endothelium. This thin layer of cells lines the inside of blood vessels. Dysfunction means the cells don't work the way they should. Instead of keeping blood vessels open (dilated), the cells cause your blood vessels to constrict or narrow. The condition is caused by vasospasm — a type of coronary artery disease. This means your coronary arteries become narrow even though there isn't a physical blockage. Endothelial dysfunction also increases the risk of coronary arterial disease from atherosclerosis. [2,3].

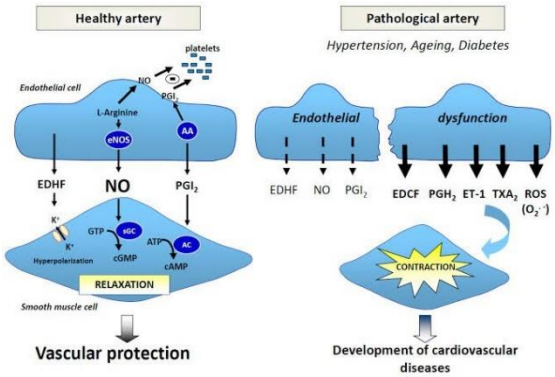


(Fig. 1.1) Pathological Processes Involved in the Development and Progression of CVDs [2]

PATHOPHYSIOLOGY:

Endothelial cells are crucial in maintaining the homeostasis of the cardiovascular system, regulating blood flow, vascular tone, angiogenesis, vascular permeability, leukocyte adhesion, and platelet aggregation. They form a semipermeable barrier that allows substances to pass through between the blood and the vascular wall. Endothelial cells secrete localized chemicals, such as nitric oxide (NO), prostacyclin, and endothelin, to control blood vessels and regulate blood flow. They also play a vital role in blood flow regulation, generating a prothrombotic and anti-fibrinolytic milieu in response to perturbations. Endothelial cells also regulate vascular tone, maintaining a balance between vasorelaxing and vaso-constricting factors in the blood. They also coordinate leukocyte trafficking during vascular injuries, facilitating the recruitment and migration of leukocytes to the subendothelial space. The development of vascular disease is dependent on the activation of vascular endothelial cells, which increase the expression of proinflammatory mediators, chemokines, and growth factors, leading to impaired vascular tone, endothelial-dependent vasodilation, and redox imbalance.

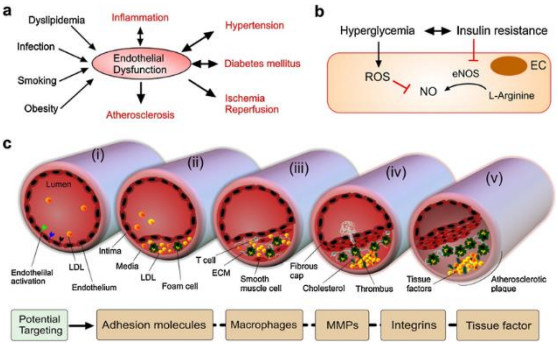
Endothelial dysfunction is a key factor in various human diseases, including PAD, cardiovascular diseases, stroke, chronic kidney failure, cancer, and infectious diseases. This coronary artery disease narrows your arteries, causing angina or chest pain. The condition increases the risk of cardiovascular disease, atherosclerosis and high blood pressure. Lifestyle changes and medications can treat it. [5,8]



(Fig. 2.1) Pathophysiology of Vascular Dysfunction

Causes

Endothelial dysfunction is a condition affecting the endothelium, a thin layer of cells that lines the inside of blood vessels. It causes blood vessels to constrict or narrow, leading to vasospasm, a type of coronary artery disease. This condition increases the risk of coronary artery disease from atherosclerosis. The endothelium controls fluids and electrolytes in the blood, helps clot blood when needed, keeps toxins out of tissues, and regulates tissue inflammation. Initially thought to be a barrier in blood vessels, endothelial dysfunction was recognized as an organ system in the late 1990s. Symptoms include narrowed blood vessels, inflammation in artery walls, increased platelet production, and porous blood vessel walls.[5]



(Fig. 2.2) Endothelial Disorder in Metabolic and Cardiovascular Diseases

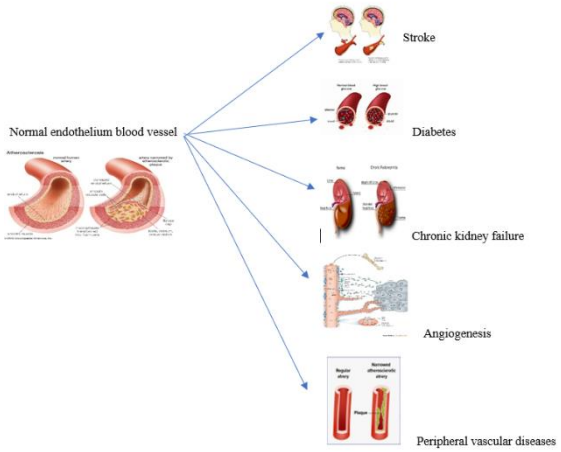
- **Symptoms**

  Angina, or chest pain, is the main symptom of endothelial dysfunction in coronary arteries. This chest pain is the result of your arteries closing when they should be open. The chest pain is often worse during physical activity. Some people develop continued angina even at rest, which can signal a heart attack. Symptoms include unrelenting chest pain, extreme fatigue and shortness of breath. This is a medical emergency that requires immediate treatment.[5]

- **Risk factors**

Certain factors may increase your risk of endothelial dysfunction. Your risk is higher if you have:

1. Diabetes.
2. High blood pressure (hypertension).
3. High blood sugar (hyperglycemia).
4. High cholesterol.
5. Metabolic syndrome.
6. Smoking.
7. Obesity [5,6]



(Fig. 2.3) Endothelial Disfunction Causing Disorders

- **Complications**

Endothelial dysfunction can lead to acute coronary syndrome. This combination of three different types of coronary artery disease increases the risk of plaque rupturing inside a blood vessel. A ruptured plaque can block blood flow to your heart muscle, causing a heart attack.[5]

- **Diagnosis and tests**

Healthcare providers use imaging tests to view blood flow through blood vessels directly. These tests let your healthcare provider check for signs of endothelial dysfunction. These tests include:

1. Electrocardiogram (EKG).
2. Angiogram, including coronary computed tomography angiogram (CCTA).
They can also use certain types of stress imaging to see if there's decreased blood flow through your blood vessels that cause decreased function in your heart. These imaging tests include:
1. Echocardiogram (echo).
2. MRI.
3. Positron emission tomography (PET) scan. [5]

- **Management and treatment**

If you have coronary or peripheral artery disease due to endothelial dysfunction, your healthcare provider may also recommend medications, such as:
1. Aspirin or medications to prevent blood clots.
2. Blood pressure medicines like calcium channel blockers.
3. Cholesterol-lowering drugs like statins.
4. Nitrates to open up blood vessels.
If you have endothelial dysfunction, you can also minimize your symptoms with dietary and lifestyle changes. These include:
1. Eating a heart-healthy diet and getting regular exercise.
2. Limiting alcohol consumption.
3. Losing weight (if needed) and maintaining a healthy weight.
4. Finding healthy ways to manage stress.
5. Getting help to quit smoking and avoiding second hand smoke.
6. Managing conditions like high blood pressure, diabetes and high cholesterol. [5]

3. PHYTOCOMPOUNDS:

Ginseng

Ginseng, an ancient plant native to Asia and North America, is commonly used in oil extracts, tea, tablets, capsules, and dried roots. Extracts have been shown to have anti-obesity, anti-hyperglycemic, anti-hypertensive, insulin sensitization, and anti-hyperlipidemic effects.

MOA

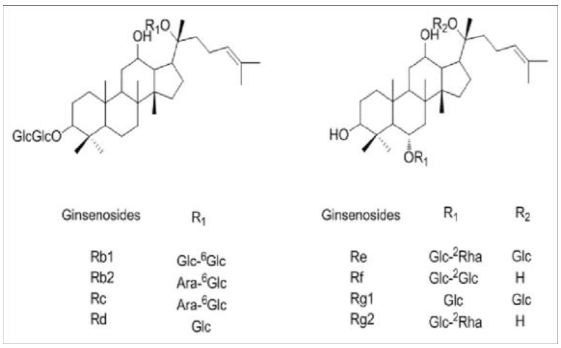
Ginseng enhances eNOS expression, NO production, and NO-dependent vasorelaxation, improving vascular tone by inhibiting arginase activity, increasing NO generation, and enhancing eNOS dimer formation.

Ginseng to the clinic

Clinical trials have investigated the cardio-protective and beneficial effects of Ginseng and its constituents in CVD treatment, with a significant number focusing on hypertension, arterial occlusive diseases, and strokes. One trial found that Panax Ginseng extract (PGE) decreased serum

triglycerides and total cholesterol levels while increasing HDL levels due to its potent antioxidant effects.

Ginseng Plant



Chemical Structure of Ginseng
(Fig. 4.1)

Safety, toxicity, and side effects of ginseng

Ginseng extracts have minimal side effects, with few adverse effects reported after prolonged use. However, a young man experienced hypertension, shortness of breath, dizziness, and concentration issues after three years of Ginseng supplementation. [2, 7,9]

Ginkgo biloba

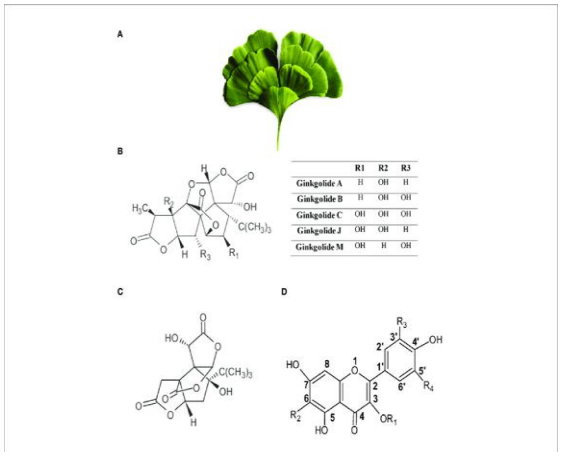
Ginseng extracts have minimal side effects, with few adverse effects reported after prolonged use. However, a young man experienced hypertension, shortness of breath, dizziness, and concentration issues after three years of Ginseng supplementation.

MOA

Ginkgo biloba (GBE) is known for its antioxidant and anti-inflammatory properties, which are beneficial in various diseases. Its vasodilatory and antihypertensive properties can improve cardiovascular health. GBE also exhibits ACE inhibitory activities, cholinergic pathway activation, endothelial health improvement, and serum lipid-lowering activities. It can limit LPS-induced proliferation of VSMCs, regulate inflammatory response in blood vessels, and reduce adipogenesis and lipolysis, leading to lipid accumulation suppression.

Ginkgo biloba to the clinic

Clinical trials have been conducted to test different formulations and doses of Ginkgo biloba leaf extract (GBE) in various diseases, with 7 out of 88 trials focused on vascular diseases. Several ongoing trials assess GBE's protective effects in CVDs. A Phase 3 trial evaluated Rinexin®, an anti-platelet agent for peripheral artery disease, while a Phase 4 trial assessed Ginkgo biloba pills for CHD patients with impaired glucose regulation.



(Fig. 4.2)Ginkgo Biloba with its Chemical Structure

Safety, toxicity, and side effects of ginkgo biloba

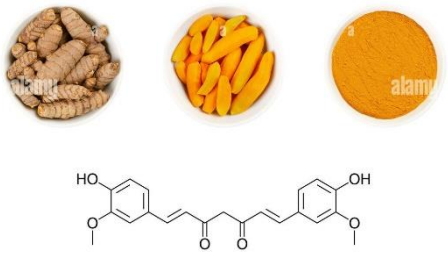
Ginkgo biloba leaf extracts can cause mild adverse effects, such as gastrointestinal upset, headache, dizziness, constipation, and allergic skin reactions. High dosages can cause restlessness, diarrhoea, nausea, vomiting, and weakness. GBEs should be stopped at least 2 weeks before surgical procedures and used with caution during pregnancy, labour, and lactation. They can also decrease plasma concentrations of omeprazole, ritonavir, and tolbutamide and interact with other medications. [2,9]

Curcumin

Curcumin, is a flavonoid compound which is obtained from roots of plant 'Curcuma longa' which is a major component of turmeric. Curcumin is beta-diketone group of carbon double bond with number hydroxy group and methoxy substituent.

MOA

Curcumin basically helps to protect endothelial cells from negative vascular effects which are stimulated by TNF-alpha which modulates P38, signal transducer and activator of transcription-3 (STAT-3) nuclear factor KAPPA-B (NFKB) and C-Jun N-terminal kinase in endothelial cells. It is also reported that Curcumin significantly inhibited TNF-alpha induced lectin like oxidised LDL receptor 1 (LOX-1) and supressed endothelial disfunction against TNF-alpha.
Basically, the authors also determined that curcumin treatment inhibited the formation of ROS along with IKB-alpha and translocation of NF-B. curcumin simultaneously induces eNOS to produce sufficient production and availability of nitrous oxide (NO) for optimal endothelial function. Additionally, it is also found that curcumin reduced the production of ICAM-1 mRNA and its associated protein in human umbilical vein endothelial cells (HUVECs). Curcumin also helps to inhibit the adhesion of leukocyte.
Leukocyte recruitment and adhesion are the hallmarks for vasculature and probably. The first stage in atherosclerotic plague development. When leukocyte adhered to endothelial cells then development and stabilization of local inflammation occurs.



(Fig. 3.3)
Curcumin and its Chemical Structure

Curcumin to the clinic

Brachial artery flow-mediated dilation and aortic pulse-wave velocity are commonly used to assess impaired endothelium-dependent dilation and increased large elastic artery stiffness, which are associated with cardiovascular events and mortality. Curcumin, a polyphenol found in turmeric, has been shown to activate antioxidant transcription, suppress

inflammation, and reduce proliferation, and improve kidney histology in ADPKD models.

Safety, toxicity, and side effects of curcumin

Both turmeric and its main active ingredient, curcumin, are generally considered safe and without any serious side effects. However, some people may experience side effects when they take them in large doses as supplements.

Digestive issues. People may experience mild digestive issues such as bloating, acid reflux, flatulence, and diarrhoea at daily doses exceeding 1,000 mg.

Headache and nausea. Doses of 450 mg or higher may cause headache and nausea in a small number of people.

Skin rash. People have reported a skin rash after taking a dose of 8,000 mg of curcumin or more, but this seems to be very rare [2,3,9]

Ganoderma lucidum

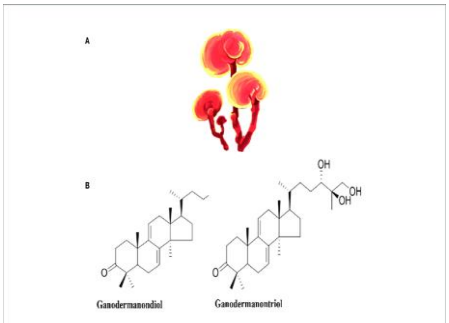
Ganoderma lucidum, also known as lingzhi or reishi, is a mushroom with various bioactive compounds including immunomodulation, anti-oxidation, liver protection, anti-proliferation, and anti-angiogenesis. Its triterpenoids have hepatoprotective, anti-hypertensive, hypo-cholesterolemic, anti-histaminic, anti-tumour, and anti-angiogenic effects.

MOA

G. lucidum, an antioxidant, has been shown to protect against oxidative stress in model organisms like Caenorhabditis elegans and treat hypertension. It also contains ACE inhibitory peptides (ACEIPs) that can inhibit ACE activity. G. lucidum's water extract can reduce body weight, inflammation, and insulin resistance in HFD-fed mice. In a study, G. lucidum spores (GLSP) were found to decrease cholesterol and triglycerides in diabetic rats, attenuating oxidative stress levels and upregulating genes related to lipid metabolism.

Ganoderma lucidum. (A) Ganoderma lucidum (from https://pngtree.com/freepng). (B) Examples of the chemical structure of two Triterpenes from Ganoderma lucidum.[13].

Ganoderma Lucidum and its Chemical Structure (Fig. 3.4)



Ganoderma lucidum to the clinic

Antioxidants are potential therapeutic substances that can prevent atherosclerosis and other diseases. Preclinical studies have shown that G. lucidum constituents possess antioxidant activities, but evidence for their activities in human subjects was lacking. A follow-up study showed an enhancement of plasma total antioxidant markers status and improvement of CHD biomarkers after 10 days of supplementation. A crossover human intervention study found that plasma total antioxidant power was enhanced after the administration of a single dose of G. Lucidum extract. G. lucidum PsP was also examined for its antioxidant properties, showing increased SOD, decreased MDA levels, and reduced counts of circulating endothelial cells and endothelial progenitor cells. A randomized clinical trial found no effect on glycosylated hemoglobin and fasting plasma glucose, and increased risk of mild events. A prospective double-blind, placebo-controlled trial found that G. lucidum failed to provide benefit against cardiovascular disease (CVD) in patients with the metabolic syndrome and not effective in treating elevated blood pressure.

Safety, toxicity, and side effects of ganoderma lucidum

The safety of polysaccharides extracted from G. lucidum fruiting bodies was evaluated in Wistar rats, with no abnormal symptoms, death, or significant differences in body weight or food intake. High doses of G. lucidum polysaccharides modulated immune responses, but did not significantly affect phagocytic function or macrophages. A 12-week trial on 23 dyslipidemic and mild hypertensive volunteers found no effect on clinical chemistry parameters, but symptoms like headache and influenza/running nose were found. Further studies are needed to assess the toxicity, side effects, and safety of G. lucidum for human consumption. [2,9]

Gynostemma Pentaphyllum

Gynostemma pentaphyllum, also known as Jiaogulan, is a climbing vine found in subtropical China, Japan, Myanmar, and India. It is used as a health supplement in beverages, biscuits, face washes, and bath oils. The herb has low genetic diversity and high variation among populations. Its biological effects range from antimicrobial, antioxidant, anticancer, anti-inflammatory, antidiabetic, antilipidemic, neuroprotective, and anti-obesity effects. It has been used to treat hepatitis and hypertension.

MOA

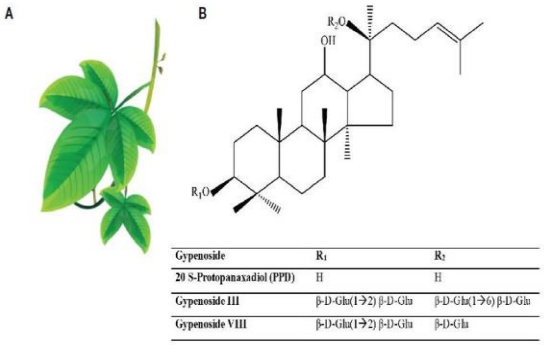
Inflammation can contribute to atherosclerosis and other cardiovascular disease risk factors, making reducing inflammation a protective factor. Gypenoside XLIX from G. pentaphyllum has been studied for its anti-inflammatory properties, inhibiting NF-kB activation through a PPAR-a dependent pathway. However, it also attenuated NF-kB activation and suppressed NO production by inhibiting iNOS activity. Combine, a flavonoid from G. pentaphyllum, has been found to be involved in lipid metabolism, reducing intracellular concentrations of triglyceride and cholesterol, and decreasing lipogenic gene expression.

Gynostemma Pentaphyllum to the Clinic

Few human trials have investigated the therapeutic effects or safety of G. pentaphyllum extracts. Only four studies have used G. Actiponin, an extract of G. pentaphyllum, has been used for weight loss in obese individuals, with no adverse effects. Another study found that G. pentaphyllum water extract inhibited platelet aggregation, suggesting potential for preventing cardiovascular diseases. Anxiety disorders have been linked to an increased risk of developing cardiovascular diseases, and G. pentaphyllum ethanol extract has shown anti-anxiety effects on mice exposed to chronic stress. Studies have shown that G. pentaphyllum tea can improve insulin sensitivity and glycemia in T2DM patients, with no adverse side effects. The current data indicates that G. pentaphyllum is effective in improving insulin sensitivity and blood sugar levels if administered alone and may be enhanced when combined with other medications.

Safety, toxicity and side effects

A study on G. pentaphyllum extract's toxicity on female Sprague-Dawley rats found no toxicity or abnormalities. Long-term administration of a dose up to 750 mg/kg body weight also showed no toxicity. A Phase I clinical trial found no major immune adverse events or biochemical parameters affected by G. pentaphyllum extract. A randomized, double-blind, placebo-controlled clinical trial in 72 healthy adults found no adverse side effects of the ethanolic extract. Overall, G. pentaphyllum consumption seems safe at the doses required for therapeutic effect. [2,9].



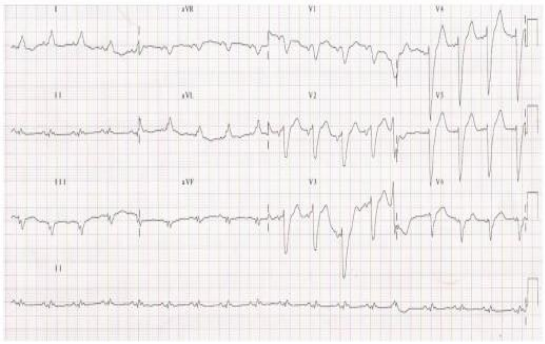
Gypenoside	R_1	R_2
20 S-Protopanaxadiol (PPD)	H	H
Gypenoside III	β-D-Glu(1→2) β-D-Glu	β-D-Glu(1→6) β-D-Glu
Gypenoside VIII	β-D-Glu(1→2) β-D-Glu	β-D-Glu

(Fig. 3.5)
Gynostemma Pentaphyllum with Chemical Structure

CASE STUDY

1st case study

A 67-year-old woman with ischemic heart disease was admitted to the hospital due to chest pain and shock. She was diagnosed with myocardial infarction in April 2009, and was diagnosed with hypertension, diabetes mellitus, dyslipidemia, and smoking. After the infarction, she underwent coronary angiography, which revealed 70% obstruction in the right coronary, anterior descending, and circumflex arteries. Echocardiogram revealed ventricular dysfunction with diffuse hypokinesis. The patient's evolution was asymptomatic until October 2009, when she had a cerebrovascular accident with motor sequela. On December 30, 2009, she experienced severe chest pain for one hour. Laboratory tests revealed hemoglobin, hematocrit, leukocytes, total cholesterol, total cholesterol, triglycerides, CK-MB mass, troponin I, urea, creatinine, sodium, potassium, bicarbonate, and base excess. After cardiac arrest, she had seizures and cardiac arrest, which was reversed in five minutes. A new cardiac arrest occurred 20 minutes later, which was also reversed. After half an hour, a new episode of cardiac arrest occurred, which was irreversible, and the patient died.[11].



(Fig . 4.1)

Electrocardiogram - Sinus rhythm, low voltage of the QRS complex in the frontal plane, electrically inactive area in the inferior wall and left bundle branch block.

2nd case study

Barry, a 47-year-old male with a family history of heart problems and diabetes, was diagnosed with cardiovascular disease (CVD) risk factors such as increased alcohol consumption, poor diet, and slightly elevated cholesterol. His health check was delivered by a white British female PN, who had 8 years of experience and preferred JBS3 over QRISK2. Barry's 10-year risk was 3.1%, and his heart age was estimated at 54, 7 years older than his actual age. The main recommendations were to reduce chocolate biscuit consumption and increase fruit and vegetable intake. Barry implemented these changes three weeks post-health check, and his cholesterol fell to within the normal range. Barry expressed concerns about the health check's depth and the level of understanding it provided. He also expressed concerns about the PN's confidence in delivering the 10-year CVD risk, as he could not fully understand the information. The consultation would have been improved to better understand Barry's situation and provide more comprehensive information. The patient's heart condition was influenced by a misinterpretation of the discussion about event-free survival age, leading to a misconception of his survival age of 73. The practitioner's VSR interview revealed the same misinterpretation. Barry was also confused by the PN's attempt to demonstrate small changes can be effective.[12].

MARKETED FORMULATIONS: [13]

Table. 5.1. Cost of gluco-corticosteroids:

Drug	Dosage	Minimum cost	Maximum Cost
Prednisolone	5mg	4.12	156
	10mg	9.84	66.62
	20mg	17.2	90.00
	40mg	33.81	51.17

Table. 5.2 Cost of anti-hypertensive drugs

Drug	Dosage	Minimum Cost	Maximum Cost
Amlodipine	2.5mg	6.50	27.60
Diltiazem	60mg	20.03	50.40
Atenolol	50mg	6.77	23
Enalapril	5mg	17.95	33.71
Losartan	25mg	16.50	38.35
Valsartan	80mg	41	86
	40mg	70	152.50
Labetalol	100mg	100	137
Olmesartan	20mg	34	116.70
Prazosin	2.5mg	94.60	125.80

COMPARATIVE STUDY

Modern medicine management focuses on minimizing the risk of cardiovascular diseases (CVDs) by addressing major risk factors and minimizing adverse outcomes. In atherosclerosis, traditional therapeutic approaches aim to control hypertension and hyperlipidemia or modulate hemostasis to avoid thrombotic complications. Current conventional therapeutic approaches rely on lowering LDL levels using statins, but pro-protein convertase subtilisin/kexin type 9 (PCSK9) inhibitors have been approved for use in patients with heart problems. The CANTOS clinical trial (2017) suggests that a combination therapy of statins and canakinumab may be necessary for patients with elevated inflammation. Complementary and alternative medicine (CAM), including herbal remedies, have already tackled the inflammatory aspect of atherosclerosis earlier than the CANTOS study. Modern therapy regimens for hypertension involve controlling BP elevations using multiple antihypertensive drug agents.

Traditional medicine and ethnomedicine have been around since human history, relying on natural resources as medications. Herbal and plant products have been a common source of medications, including aspirin, digoxin, ephedrine, lovastatin, taxol, and reserpine. These plants have been used to find new drugs for treating diseases, such as hypertension treatment. The earliest records of natural drugs, found in Mesopotamia around 2600 BCE, describe the use of around 1000 plant-derived compounds. The Egyptians' Ebers Papyrus, Chinese Materia Medical record, and Indian Ayurvedic record all document the use of natural extracts in therapy. Around 65% of the world population relied on plant-derived traditional medicines in 1985. The

WHO identified 122 compounds from 94 plant species used for various ethnomedical treatments. Commercially, drug production from natural products is a viable commodity, with 39% of new drugs approved between 1983 and 1994 being natural compounds or derived from natural compounds. However, advances in combinatorial chemistry shifted focus from natural products to synthesis at the laboratory bench. Despite this, natural products as drugs or discovery platforms are still alive, with traditional herbal and plant-derived extracts becoming more mainstream.[14].

CONCLUSION

Natural herbs are rich sources of potential therapeutic candidates for various diseases including cardiovascular diseases, neurodegenerative disorders, and metabolic dysregulation. Reprocessing the existing medications for alternative applications is an important way to discover new therapies with known safety profiles. For cardiovascular diseases, the vital components of pathogenesis are ROS production and inflammation, which are targeted by many phytocompounds and existing medications. Although extensive studies have been carried out to determine the vascular protective effects of active phytocompounds reviewed in this paper, there are ongoing developments and research studies on other human diseases. Active phytocompounds isolated from natural resources often face challenges in bioavailability and stability. Thus, improving extraction and formulation techniques to maintain biological activities is crucial. Furthermore, biosafety, long-term bioactivity, degrading properties, interactions with immune cells, the ability to sustainably circulate in humans, and excretion must be thoroughly evaluated before consumption. In addition, further research is needed to minimize the cost of industrial-scale manufacturing, develop better methods for synthesis or extract, and discover the optimal route of administration. New phytochemical agents to treat cardiovascular diseases particularly vascular endothelial cells are expected to surface with the progress of research. This review discusses the therapeutic properties of various plants in treating cardiovascular diseases (CVDs). While these plants have potent properties, clinical benefits have not been confirmed. Safety and toxicity concerns have raised concerns, such as Gingko Biloba. Future studies and clinical trials should investigate the role of different medicinal plants and their mechanisms in CVDs.

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