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REVIEW ARTICLE
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REVIEW ON PROTECTIVE EFFECT OF MEDICINAL PLANTS ON HYPERTENSIVE PATIENTS

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ABSTRACT-
Blood pressure, which is the force of circulating blood on blood vessel walls, is one of the vital indicators. The pressure that blood exerts on blood vessel walls increases when the major arteries lose their inherent strength and flexibility and the smaller ones narrow. A major cause of death in every country, high blood pressure is perilous and extremely destructive to the heart and blood vessels. Since many patients are worried about the negative effects of chemical medications, they frequently choose herbal medicines to control their blood pressure. The safety and effectiveness of a single herb or combination of herbal items in decreasing blood pressure have been the subject of much investigation; some studies have produced positive results, while others have produced negative ones. There is additional scientific proof that certain herbs, such as quince, green and white mulberries, garlic, saffron, and grape seed, can lower blood pressure. The scientific literature of clinical trials and animal research that assessed the safety and efficacy of herbs in decreasing blood pressure was thoroughly reviewed in this study.

Keywords-Hypertension, Medicinal plants,

Introduction-

Cardiovascular diseases (CVDs) are a serious public health concern since they are a primary cause of weakness and premature death[1].
It is an extremely dangerous medical condition that can raise the risk of renal, brain, heart, and other disorders. Globally, it is a leading cause of premature mortality. Even if clinical hypertension is managed with a number of contemporary medications, there are a number of negative effects linked to this condition [2].
Hypertension is a major threat to health, especially for older people. Over one-fourth of all death among the elderly people is due to high blood pressure and its complications. It is usually asymptomatic until the development of complications such as heart failure, stroke and kidney failure [3]
The medications suggested for the treatment of hypertension aims to bring SBP and DBP less than 140/90 mmHg which also reduces the associated cardiovascular complications [4].
Predisposing factors to high blood pressure include genetics, stress, low levels of physical exercise, smoking, alcohol, diet, and obesity[5].

The two main categories of hypertension: primary and secondary hypertension
"Essential Hypertension" is another name for primary hypertension. 95% of all cases of hypertension worldwide are of this type. It is a form of hypertension for which there is no discernible secondary etiology [6].
To treat hypertension, the FDA has approved a number of synthetic medications. These medications have been categorized into classes based on how they work: α-blockers, β-blockers. Blockers of the angiotensin receptor, diuretics, inhibitors of angiotensin converting enzymes and blockers of calcium channels

Risk factors
The following risk factors are associated with high blood pressure:
• Age increases the risk of hypertension. Around age 45, or early middle age, is when men's hypertension becomes more common. Women are more likely than men to exhibit hypertension after the age of 65.
• Obesity: More oxygen and nutrients must be delivered to the body through the bloodstream in fat people. Pressure on the arterial wall will increase in tandem with the volume of blood in circulation.
• Physical inactivity: Additionally, a decrease in physical activity increases the risk of obesity, which can result in hypertension.
• Smoking: Chemicals from tobacco may damage the artery walls, causing the vessels to narrow and perhaps resulting in hypertension.
• High salt intake: Consuming a lot of salt in the diet keeps fluids in the body, which raises blood pressure.
• Low consumption of potassium in the diet: Potassium helps to keep the amount of Na+ in the tissues constant. An excessive sodium concentration in the blood can occur if a person is unable to consume enough potassium through their food or maintain an adequate potassium level.
• Low dietary intake of Vit D There is currently no evidence linking low vitamin D intake to high blood pressure. Blood pressure-altering renal enzymes may be influenced by vitamin D.
• High intake of alcohol. Excessive alcohol drinking may harm the heart.
• Anxiety " Anxiety plays a significant role in raising blood pressure as well. Anxiety, smoking, and excessive alcohol use can all lead to hypertension.
• Definite long lasting circumstances. A number of illnesses, including sleep apnea, renal disorders, and pregnancy, might increase the risk of hypertension[7].
Pharmacotherapy of hypertension
There are following drugs which are used in the treatment of hypertension [8].

• **Thiazide diuretics**
Thiazide as well as thiazide-like diuretics has been a base of treatment of primary/essential hypertension. The most familiar drug in this group, hydrochlorothiazide, was conventionally utilized in doses of 50-100 mg/day. These doses were related with metabolic or electrolytic issues. Low-dose treatment has since been established to be effective and has least side effects. The hypotensive effect is achieved by reduction of cardiac output and plasma volume. However, the reduction in BP is impaired by renin-angiotensin system leading to hypovolemia.

• **Beta blockers**
Such medicines lessons the burden on cardiac along with the dilatation of the arteries, in this way heart starts beating at slower rate and this causes less force on walls of the blood vessels. Beta blockers show better results when used in combinations especially when used in adults.

- **Angiotensin-converting enzyme (ACE) inhibitors**

Pharmacological mechanism of these drugs is to dilate arteries via stopping the production of those usual compounds which narrow arteries. Such drugs are usually used by those patients who are also suffering from persistent renal disorders.

- **Angiotensin II receptor blockers (ARBs)**

This class of medicine relaxes blood vessels by inhibiting their narrowing. Patients having compromised kidney state can get benefits from ARBs by using them like among their medications.

- Calcium channel blockers Such medicines are helpful in soothing the muscles of arteries. It has been observed that calcium channel blockers give better result than ACE inhibitorts in aged patients.

- **Renin inhibitors**

Enzyme like rennin is synthesized by renal system which initiates a series of compound reations that elevates BP. Aliskiren (Tekturna) decreases synthesis of enzyme renin.

Traditional medicine has only partially been successful in lowering the prevalence of this serious illness among its patients in recent years. There are a number of natural treatments that can assist lower the number of patients who have hypertension.

Research on natural treatments for high blood pressure is conducted annually in large numbers.

The following are some benefits of using natural medicine instead of medication:

- In comparison, natural therapy is less expensive than contemporary cures and therapies. There is easy access to complementary therapies.
- There are no undesirable side effects associated with natural or traditional therapies that use herbs, vegetables, and fruits, in contrast to allopathic cures.
- Natural remedies don't work unless the prescribed dosage isn't taken as directed.
- Because natural remedies are less likely to interfere with other body systems, they are generally harmless [10].

Pathophysiology of hypertension-

Increasing vascular resistance, which is mainly recognized by decreasing vascular diameter as a result of increased arterial remodeling and vascular contraction, is one of the pathophysiological processes that lead to the development of hypertension.

Numerous factors, including elevated renin-angiotensin-aldosterone system (RAAS), sympathetic nervous system stimulation, vasopressin, impaired G protein-coupled receptor signaling, inflammation, different T-cell functions, and the range of vasoactive peptides secreted by smooth muscle and other endothelial cells, contribute to the pathophysiology of hypertension.

Increased arterial reactivity brought on by dysregulation of pro-oxidant enzymes and endothelial nitric oxide synthase (eNOS), elevated basal and activated calcium levels via calcium channels, and the co-occurrence of vascular smooth muscle cell (VSMC) hyperplasia and hypertrophy can all lead to enhanced vasoconstriction. Management of Blood Pressure Blood volume, cardiac output, arterial tone balance, and other features of the cardiovascular system can all be used to calculate blood pressure. To maintain healthy blood pressure levels, a complex interplay between the immune system, sympathetic nervous system (SNS), endothelial cells, renin-angiotensin-aldosterone system (RAAS), natriuretic peptides, and other elements of an integrated neurohumoral system is required. Any imbalance among the elements of this integrated neurohumoral system might either directly or indirectly result in an increase or reduction in the average blood pressure level. (figure 1) (2).

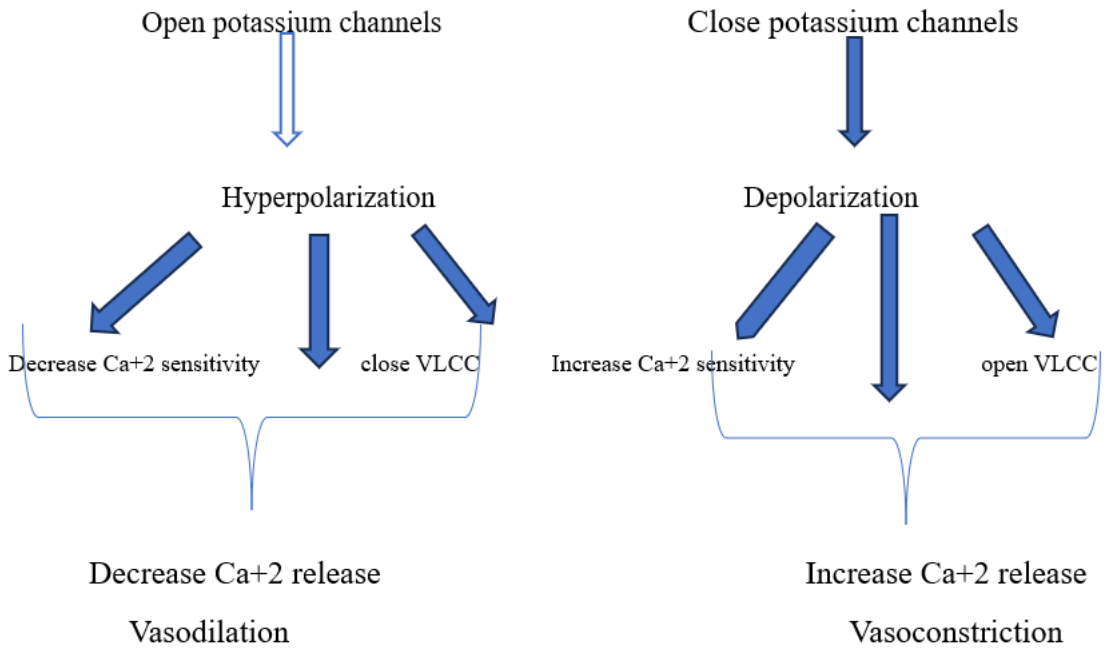


Fig.1 Effect of potassium channels blood vascular system

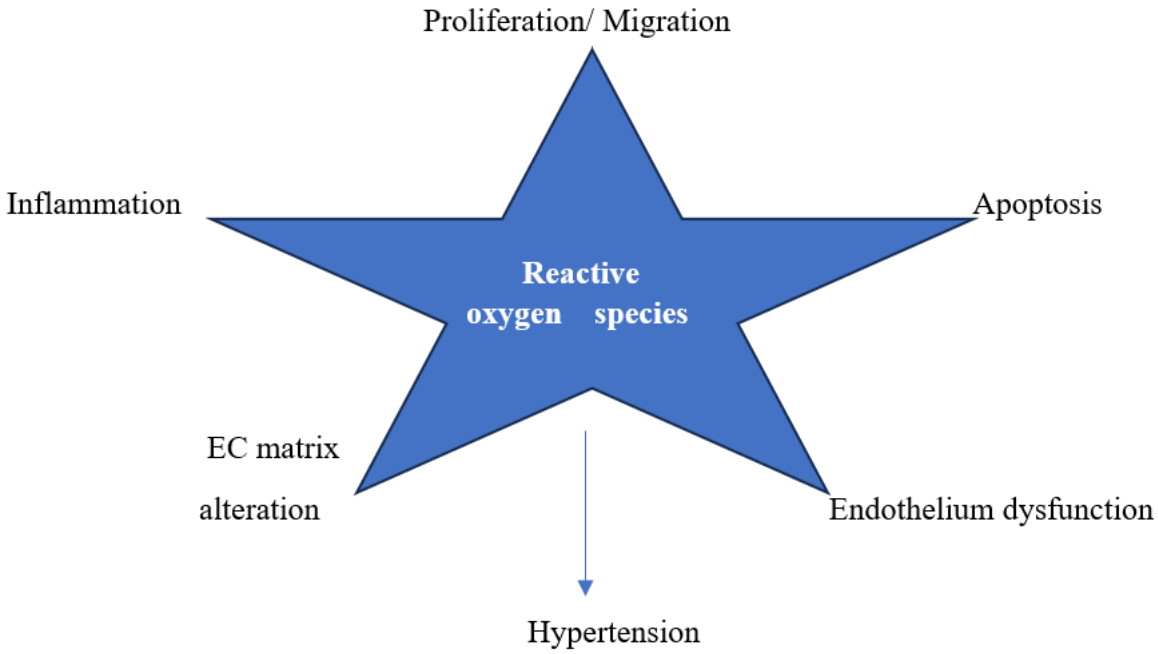


Fig. 2 Effect of reactive oxygen species on blood vascular system

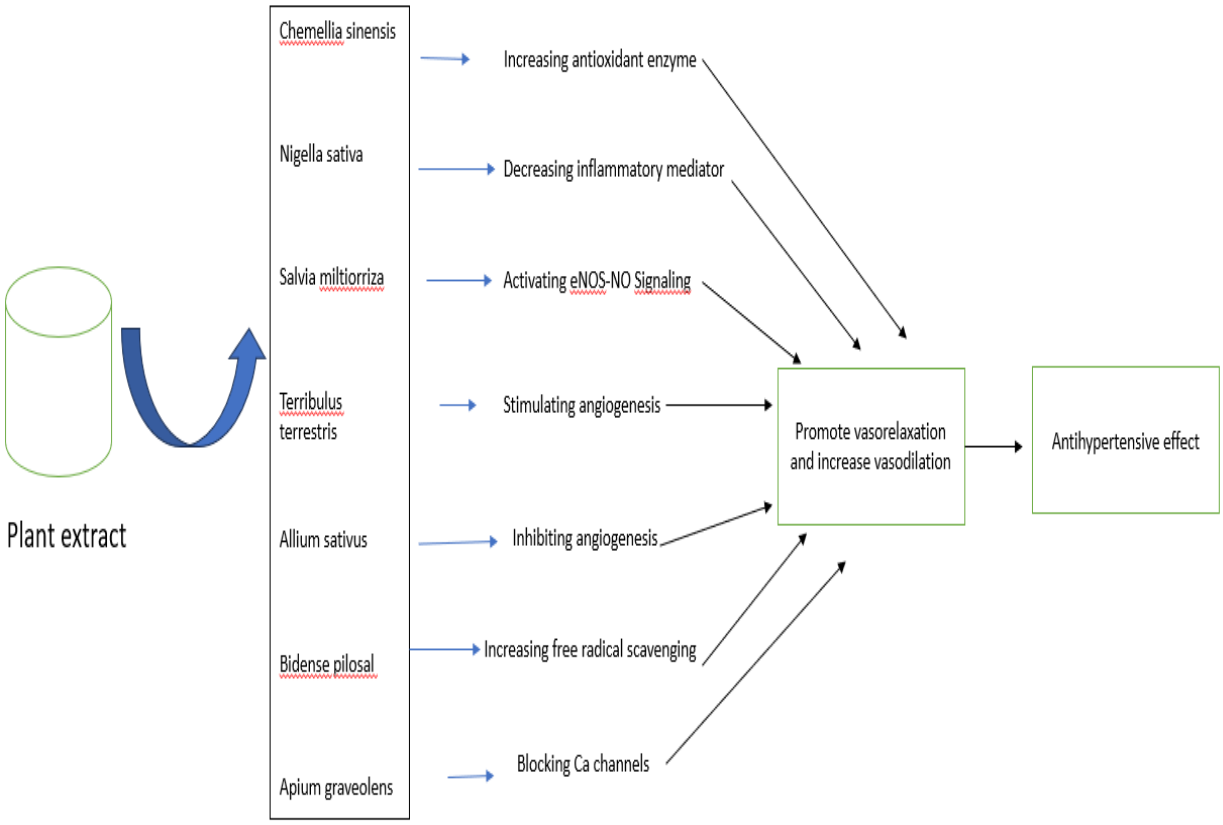
Medical plants used in treatment for hypertension

Secondary metabolites from a number of plants and spices have antihypertensive properties. Most herbal medicines contain anti-inflammatory, anti-apoptotic, and antioxidant properties that assist control and reduce hypertension. They also induce angiogenesis, restrict endothelial permeability, and activate the eNOS-NO signaling pathway.

It has been demonstrated that certain Medicinal plant extracts used to treat hypertension work in the following ways shown table 1.

Table 1 Herbal remedies for treatment of hypertension

Common name	Botanical name	Family	Part used	Chemical constituents
Snake root	Rauwolfia serpentina	Apocynaceae	Root	Ajamaline, rescinnamine, serpentine, sarpagine, deserpidine, and chandrine
Garlic	Alium sativum	Liliaceae	bulbils	Sulfur containing compounds allin, ajoene, diallylsulfide, dithiin, S-allylcysteine,
Turmeric	Curcuma longa	Zingiberaceae	rhizomes	curcumin and curcuminoids
Ginger	Gingiber officinalis	Zingiberaceae	Rizomes	Volatile oils; 3sesquiterpines:-bisaboline, zingiberene and zingiberol
Tomato	Lycopersicon esculentum	Solanaceae	Whole	Lycopene
Coriander	Coriandrum sativum	Umbelliferae	seeds	Citronellal, citral, geraniol and citronellyl acetate
Ajwain	Trachyspermum ammi	Apiaceae.	seeds, essential oils	thymol, Carvacrol, p-cymene, Beta-pinene, Terpinene-4-ol
Ginseng	Panax ginseng	Araliaceae	root	Ginsenoside
Flaxseed	Linum usitatissimum	Liliaceae	seeds	α-linolenic acid
Onion	Allium cepa	Amaryllidaceae	Bulbs, extract	Quercetin, Rutin, Cysteine sulfoxides
Cinnamon	Cinnamomum zeylanicum	Lauraceae	barks	Cinnamaldehyde, Cinnamic acid, Eugenol
Arjuna	Terminelia arjuna	Combretraceae	bark	Tannins, triterpenoid saponins, flavonoids, gallic acid, ellagic acid, phytosterols, calcium, magnesium, zinc, copper.
Ginko	Ginko biloba	Ginkgoaceae	Seed, leaf	Phenolic acids; ginkgolic acid, hydroginkgolic acid, gingolides flavonoids. Bioflavonoids; sciadopitysin, ginkgetin, bilobetin.



1.Rauwolfia (Rauwolfia serpentina)- It belongs to the family Apocynaceae and is an evergreen shrub [11]. Reserpine is the most significant primary active ingredient among the approximately 80 alkaloids that have been identified from Rauwolfia species. Reserpine (3,4,5-trimethyl benzoic acid ester of reserpic acid, an indole derivative of 18-hydroxy yohimbine type) is responsible for the antihypertensive effects of Rauwolfia roots. Of all the alkaloids, it is the most common and is mostly used as a natural tranquilizer [12].

The mechanism of action of reserpine is well researched and well documented. Reserpine binds to protein receptors called *vesicular* monamine transporters *(*VMATs) in the organelle membranes of specialized secretory vesicles of presynaptic neurons [13].

Reserpine prevents intracellular neurotransmitters from binding to VMAT proteins and stops secretory vesicles from uptaking neurotransmitters [14,15].

Figure-1

2. Garlic (Allium sativum)-

A wide range of illnesses can be treated with the bulb of garlic. Menstrual disorders, age-related vascular alterations including atherosclerosis, hypertension, hyperlipidemia, earaches, and chronic fatigue syndrome (CFS) are all treated with garlic [16].

The main active compound property is garlic odor, and allicin has positive therapeutic benefits. Platelet aggregation is thought to be strongly inhibited by garlic. Lower blood pressure encourages the production of the relaxing factor derived from endothelium (EDRF), which results in smooth muscle relaxation and the anticipated induction of vasodilation.

Garlic is one of the most popular supplements because of its capacity to combat bacteria and free radicals. This is due to the high quantities of the compound allicin that garlic contains. Garlic is one of the complementary therapies that is used the most frequently for the regulation of blood pressure, with estimates indicating that between 50 and 75 per cent of individuals who have hypertension make use of it. Garlic's blood-pressure-lowering effects have been connected to its active sulfur components. To accomplish this, Nitric Oxide (NO) and Hydrogen Sulphide (H2S) production is enhanced. However, the most important featureis garlic's ability to block the action of the Angiotensin Converting Enzyme (ACE) [17, 18].

Figure-2

3.Turmeric (curcuma longa)-

Another name for turmeric is curcumin, which has anti-inflammatory and anti-cancer qualities.

CVDs including hypertension are helped by curcumin. Curcumin inhibits SP1/AT1R DNA binding, which reduces AT1R-mediated vasoconstriction and artery-specific AT1R expression, hence delaying the onset of hypertension [19].

Figure -3

4.Ginger (zingiber officinale)-

Potassium-containing ginger extract is utilized as an alternative medicine. Because it prevents renin-angiotensin from being released, more water and sodium are excreted, blood pressure is lowered, and less salt and water are retained in the circulation.

Ginger is a herbal therapy with several health benefits that can be used as a treatment for high blood pressure.

It acts as a therapeutic agent that boosts the cardiovascular system and supports the immune system by lowering levels of low-density lipoprotein and cholesterol, which can have negative effects on the heart. Because it is a vasodilator, ginger can help lower blood pressure and increase blood circulation [20].

Ginger's high potassium concentration makes it possible to reduce both excessive blood pressure and heart rate.When administered intravenously (1.75–3.5 mg/kg) or orally (70–140 mg/kg). Tri-phasic blood pressure profiles, which are defined by a quick drop in blood pressure, an intermediate rise, and a protracted decline in blood pressure, are produced by the bioactive ingredients (6)-gingerol and (6)-shogoal in ginger.(6)-gingerol is a recently discovered angiotensin II type 1 receptor antagonist. There is proof that ginger helps reduce lipid levels, such as LDL, VLDL, triglycerides, and cholesterol. Furthermore, it inhibits angiotensin-converting enzyme-1 activity [21-24].

Figure-4

5.Tomato

Many studies have demonstrated that tomatoes can help treat a variety of non-communicable diseases, such as diabetes, high blood pressure, heart disease, and high cholesterol. Throughout the world, one of the most well-liked and extensively consumed vegetable crops is the tomato, or Lycopersicon esculentum L. The complex mixture of heart-healthy carotenoids found in tomatoes includes lutein, β-carotene, and lycopene (35–96% of total lycopene, mostly in all forms of trans-isomers, and 1–22% cis-lycopene) [25].

Figure-5

6.Coriander

"Geranyl acetate, linalool, and gamma-terpinene are the three primary chemical constituents of coriander. Citral and citronellyl acetate (1.36% each), citronellol (1.31%), m-cymene (1.27%), a-farnesence (1.22%), citronellal (1.96%), and geraniol (1.87%) are also present in trace levels. Numerous studies have found that coriander has antioxidant qualities and inhibits the b-adrenoceptor from generating reactive oxygen species (ROS). However, its effects on blood pressure have not yet been investigated in clinical trials.

Due to the Ca2+ antagonist, the seeds' aqueous methanolic extract (1–30 g/ml) reduces mean arterial blood pressure, diastolic blood pressure, and systolic blood pressure. Evidence suggests that coriander extract acts as a diuretic, assisting the body in eliminating excess water and sodium. This may assist

if your blood pressure is elevated. Some research have connected coriander to lower cholesterol levels [26-29].

Figure-6

7. Ajwain

Ajwain, commonly known as carom or carom seed, is a component of Indian cooking.

Thymol, found in large quantities in carom seeds, has been shown to have the ability to block calcium channels. Because they stop calcium from making cardiac muscle cells contract, Ca2+ entry blockers relax and widen blood vessels, lowering blood pressure. Ajwain and verapamil, a calcium channel blocker, both had comparable blood pressure-lowering effects in experimental mice [30].

Figure-7

8. Ginseng

One of the most popular herbal remedies is ginseng. According to clinical research, ginseng may help cure diabetes, erectile dysfunction, and weariness. Ginseng's pharmacological characteristics and potential benefits for blood pressure (BP) management have been the subject of numerous studies. Administering ginsenoside to human endothelial cells has been demonstrated to enhance the production and release of nitric oxide (NO) and to cause the overexpression of endothelial nitric oxide synthase (eNOS), which leads to vasodilation [31].

Larger doses of ginseng lower blood pressure, whereas smaller ones cause it to rise. Therefore, in hypotensive patients, ginseng lowers blood pressure, most likely via modifying vascular function, autonomic nervous system modulation, or arterial baroreflex. [32-34].

Figure-8

9.Flaxseed

It is believed to be an annual herb that originated in Egypt. Rich in α-linolenic acid, an essential fatty acid, linseed and its oil can aid with a number of conditions, including inflammatory bowel disease, heart disease, and arthritis. α-linolenic acid belongs to the group of substances called omega-3 fatty acids. Numerous studies have shown that eating a diet rich in omega-3 fatty acids significantly lowers blood pressure in people with hypertension. Flaxseed lowers blood cholesterol, platelet aggregation, and inflammatory markers. It also works as an antioxidant and enhances glucose tolerance, all of which may help prevent atherosclerotic cardiovascular disease. Consuming 15 to 50 g of ground flaxseed daily can gradually reduce the concentrations of low-density lipoprotein and total cholesterol without altering triglycerides or high-density lipoprotein cholesterol. However, the precise mechanism is unknown [35].

Figure-9

10.Onion

In rats with normotension, onions were observed to reduce blood pressure when administered fructose and anesthesia. Blood pressure has been linked to organo-sulfur compounds because they maintain the major arteries' elasticity and reduce blood viscosity, which prevents blood clotting. Quercetin, the substance most frequently linked to onions, can lower blood pressure by an average of 5 mm Hg by improving vascular function and lowering oxidative stress through its interaction with free radicals. Aqueous extracts of onions (400 mg/kg/d) increased eNOS while suppressing VCAM-1 expression. Because they increase the antioxidant kinetics of SOD and glutathione peroxidase (GPX) enzymes and decrease NADPH oxidase activity, onions seem to have antioxidant properties.

Figure-10

11.Cinnamon

Cinnamon belongs to the genus Cinnamomum, which is a member of the Lauraceae family. The leaves and bark of the cinnamon tree are important due to their tasty and aromatic properties, and they are commonly used as a spice in cooking or to create essential oils. The effect of C. cassia on ischemic heart disease was evaluated in a rat model using Sprague Dawley rats. The active components, cinnamon aldehyde and cinnamic acid, are thought to have cardioprotective properties because they produce vasorelaxant nitric oxide. Cinnamon aldehyde, a component of cinnamon, has been linked to

a vasorelaxative action via blocking L-type calcium channels. However, an in vivo experiment supported the hypothesis that its impact on KATP channels in the vascular smooth muscles was what produced the drop in blood pressure. Research on cinnamon's impact on diabetes is extensive, but little is known about how it affects blood pressure regulation. In dogs and guinea pigs, it results in peripheral vasodilation, which lowers blood pressure. Cinnamon dramatically lowered both systolic and diastolic blood pressure readings, according to a meta-analysis of three trials; however, the exact mechanism by which it does this is still unknown. An further study with fifty-nine subjects demonstrated that cinnamon dietary supplements successfully reduced systolic blood pressure [36-39].

Figure-11

12.Arjuna bark

In India, Terminalia arjuna is a deciduous tree. The use of its bark in Ayurvedic medicine dates back more than three centuries. Among Terminalia's active components include triterpenoid saponins, flavonoids, gallic and ellagic acids, OPCs, phytosterols, calcium, magnesium, zinc, and copper 5. Many studies have shed light on the relationship between terminalia and certain heart disorders, such as hypertension, coronary artery disease, and congestive heart failure. A significant decrease in systolic blood pressure and a 50% decrease in angina episodes were two indicators that it was helpful for individuals with stable angina, according to a study on its effects on patients with unstable and stable angina [40-42].

Figure-12

13.Ginkgo

The ginkgo tree's fruit and leaves are commonly used to treat dementias, including mixed dementia, Alzheimer's, and vascular dementia. Ginkgo leaf is also used to treat symptoms associated with cerebral vascular insufficiency, especially in older persons, such as headaches, tinnitus, vertigo, dizziness, mood swings, memory loss, and hearing issues. The ginkgo tree's fruit and leaves are commonly used to treat dementias, including mixed dementia, Alzheimer's, and vascular dementia. Additionally, ginkgo leaf is used to treat symptoms associated with cerebral vascular insufficiency, especially in older persons, such as depression, mood swings, migraines, tinnitus, vertigo, dizziness, memory loss, and hearing issues. Among the herb's main active components are flavonoids and glycosides. Both ginkgo and its plant compounds are sold separately and in combination. Additionally, ginkgo has a little decreasing influence on blood pressure. Research indicates that ginkgo leaf extract

appears to slightly lower blood pressure and enhance pancreatic beta-cell activity in response to glucose loading.

Figure-13

Conclusion

Many conservation studies are currently being conducted on medicinal plants to ascertain whether their traditional uses are based on true pharmacological qualities or on folklore. Comparing herbal medicines to synthetic ones, the former are less costly and do not have any adverse effects. Since ancient times, people have employed botanicals to treat a wide range of illnesses, including heart problems. It is not surprising that they have shown effectiveness in lowering blood pressure and improving heart function. It is true that nature is the source of inspiration for or the production of all novel, little chemical entities used as medications throughout degeneration. This could be the reason that more people are turning to herbal therapy for CVD treatment instead of allopathic medicine. In this review, the most often used plants for the management and treatment of hypertension were examined. Furthermore, it is advised that patients be well educated on the use of herbs like coriander and black cumin that have been used for a long time.

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