Review Article

Medicinal Plants with antihypertensive activity. A review

Abstracts

The medical term for elevated blood pressure is hypertension (HTN). It is risky because it puts too much strain on the heart and causes atherosclerosis, which is the hardening of the arteries, in addition to raising the risk of heart disease and stroke. Other diseases like congestive heart failure, renal disease, and blindness can also arise due to HTN.Standard antihypertensive drugs frequently have a number of adverse effects. About 75-80%of the world's population, mostly in underdeveloped nations, use herbal medicines for primary health care because of its higher tolerance by the human body and fewer adverse effects.Research on native plants with hypotensive and antihypertensive therapeutic benefits has received a lot of focused attention during the past three decades.It has been prove by previous researchers that some of these medicinal herbs have hypotensive and antihypertensive properties. To evaluate the efficacy and clarify the safety profile of such herbal treatments for their antihypertensive potential, more scientific study along with Ayurveda expertise must combined with modern medicine.

Key words: Antihypertensive, hypertension, medicinal plants

Introduction

Hypertension (HTN) is a medical disorder marked by a persistent increase in arterial blood pressure.In the world, high blood pressure is the main reversible risk factor for cardiovascular disease (CVD) and all-cause mortality(Li et al., 2020), (Ge et al., 2012). There were 1.39 billion adults worldwide in 2010, and hypertension affected 31.1% of them(Mills et al., 2020), (Mills et al., 2016).HTN is defines as when the systolic and/or diastolic blood pressures are greater than 140 mmHg and 90 mmHg, respectively. The aging of the population and increased exposure to lifestyle risk factors, such as bad diets (high salt and low potassium intake and lack of physical activity), are both contributing to an increase in the prevalence of hypertension globally (Mills et al., 2020), (Samadian et al., 2016).Globally, the prevalence of hypertension has changed, although not consistently. High-income nations (HICs) had a little decline in the prevalence of hypertension during the past two decades, while low- and middle-income nations (LMICs) saw large rises (Schutte et al., 2021), (Bowry et al., 2015).

These differences in hypertension prevalence patterns indicate that LMIC health care systems may have to deal with a significant burden of infectious diseases as well as a fast rising burden of cardiovascular diseases caused by high blood pressure. One billion people worldwide suffer from hypertension, the most prevalent cardiovascular disease, which continues to be the main cause of 9.4 million deaths each year and contribute significantly to the global burden of disease (Guwatudde et al., 2015),(Bedane, 2018). The number of people with hypertension is expected to increase to 1.5 billion by 2025 from an estimated 972 million in 2000, 65% of whom resided in the developing countries (Guwatudde et al., 2015). If hypertension is not treated, it can have devastating complications, including heart attack, stroke, cardiac failure, and renal failure, among others. Many studies suggest that hypertension is a major issue in sub-Saharan Africa

(SSA), where it has been reported to be as high as 38% in some groups (Guwatudde et al., 2015), (Ogah and Rayner, 2013). Ten to twenty million of the over 650 million people in SSA are thought to suffer hypertension (Desormais et al., 2019), (Mv & Mwinuka, 2021), (Guwatudde et al., 2015). But many SSA nations still lack comprehensive fundamental information on the prevalence of hypertension and how it is spread among the various SSA populations(Guwatudde et al., 2015). Several studies have also examined the prevalence of pre-hypertension and the percentage of people with hypertension who are aware of their condition. In Nigeria, there were an estimated 20.8 million cases of hypertension among adults aged at least 20 in 2010. The prevalence was 28.0% (24.6, 31.9), with men and women experiencing 30.7% (24.9, 33.7) and 25.2% (22.7, 31.9), respectively, of the disease(Ajayi et al., 2019), (Adeloye et al., 2015).Also, it is predicted that by 2030 there will be 39.1 million cases of hypertension among adults aged at least 20 years, with prevalence rates of 30.8% (24.5, 33.7) for both sexes - 32.6% (27.3, 38.2) for men and 29.0% (21.9-32.2) for women(Ajayi et al., 2019). Thus, the urgent need for a long-term solution. The majority of deaths from non-communicable diseases (NCDs) are attributable to cardiovascular disorders (48%) in the US. Raised blood pressure is one of the top physiological and behavioral risk factors for mortality, and it is responsible for 13% of all deaths worldwide. According to reports, hypertension ranks fourth among causes of early death in industrialized nations and seventh in underdeveloped nations. According to earlier studies, hypertension is one of the main causes of death and disability and is fast becoming more common in emerging nations. Hypertensionis classified as either primary (essential) or secondary. Essential or primary HTN is the most common type of HTN, affecting 90 to 95% of hypertensive patients(Princewel et al., 2019), (Khan et al., 2016). Despite the lack of a clear cause, there are numerous contributing factors, including a sedentary lifestyle, stress, visceral obesity, and potassium deficiency (hypokalemia)(Tabassum and Ahmad, 2011). Age-related risk is also higher(Barton et al., 2016),the presence of certain inherited genetic variants and a family history of HTN (Zhu et al., 2018), (Tabassum and Ahmad, 2011). An additional risk factor is an increase in renin, an enzyme released by the kidney (Nandhini, 2014) similar to overactive sympathetic nervous system(Saxena et al., 2018). Insulin resistance may also influence HTN, which is a part of syndrome X, generally known as the metabolic syndrome. High fructose corn syrup-containing diets may raise one's risk of acquiring HTN(Ferder et al., 2010), (Le et al., 2012).The other 5 to 10% of instances, known as secondary HTN, are brought on by additional disorders that affect the kidneys, arteries, heart, or endocrine system(Tabassum and Ahmad, 2011). By definition, secondary HTN has a known cause. Since this type is treated differently from essential HTN by addressing the underlying cause of the raised BP. The pathophysiological mechanisms that control blood plasma volume and cardiac function, including the hormone-regulatory endocrine systemare compromisedin HTN. Some common and well-known secondary causes of HTN include Cushing's syndrome, in which the adrenal glands generate too much of the hormone cortisol (Tabassum and Ahmad, 2011).Furthermore, pre-eclampsia during pregnancy, aortic coarctation, kidney disease, sleep apnea, obesity are common secondary causes of hypertension(Hegde et al., 2023), (Zhang et al., 2022). Chronic HTN is a major contributor to chronic kidney failure and one of the risk factors for stroke, heart attack, heart failure, and arterial aneurysm(Tabassum and Ahmad, 2011), (Anthony and Sliwa, 2016). Life expectancy is decreased with moderate arterial BP increase. Changes in food, lifestyle, and medication can all

help to control blood pressure better and lower the chance of any ensuing health issues. The systolic and diastolic BPs are another factor used to categorize HTN. The blood pressure in vessels while the heart is beating is known as systolic blood pressure. The pressure between heartbeats is known as diastolic BP. A person is categorized as having pre-HTN or HTN if their systolic or diastolic blood pressure readings are higher above the considered normal ranges for their age. HTN is divided into a number of subcategories, including stage I, stage II, and isolated systolic HTN (Tabassum and Ahmad, 2011). Individual systolic HTN, which is frequent in senior people, is defined as having a high systolic pressure with a normal diastolic pressure. A patient's resting blood pressure readings from two or more clinic visits are averaged to arrive at these groupings. If a person's blood pressure is continuously at least 140 mmHg systolic or 90 mmHg diastolic and they are older than 50, they are considered to have HTN. Further treatment is necessary for patients whose blood pressure is greater than 130/80 mmHg and who alsohave diabetes or kidney disease.

Pathophysiology of hypertension

Most people understood the majority of secondary HTN-related processes; on the other hand, symptoms linked with essential (primary) HTN less characterized. What is known is that early in the disease's progression, cardiac output is elevated with normal total peripheral resistance (TPR). Eventually, cardiac output returns to normal levels, while TPR rises. Three theories have been put out to explain this, and they are as follows:

• Lack of sodium excretion by the kidneys causes the release of natriuretic factors like atrial natriuretic factor, which raises TPR as a side effect(M. Singh et al., 2010), (Tabassum and Ahmad, 2011).

• Vasoconstriction, salt and water retention, and hyperactivity of the renin-angiotensin system occur. HTN is brought on by an increase in blood volume(Pimenta and Oparil, 2009).

• Heightened stress responses due to an overactive sympathetic nervous system(Tuck, 1986), (Takahashi, 2008).

Another well-known fact about HTN is that it is highly heritable and polygenic (produced by multiple genes), and a few potential genes have been proposed as the disease's etiological factors (Sharma et al., 2012), (Tabassum and Ahmad, 2011).The study of the connection between prolonged endothelium injury and essential HTN has gained favor recently among experts on the disease. To what extent long-term increased BPs or whether they occur before the onset of HTN is yet unknown cause endothelial alterations. For coronary artery disease, stroke, and renal failure, HTN is a significant independent risk factor. The risk of a fatal coronary event doubles for every 20 mmHg rise in systolic blood pressure and 10 mmHg rise in diastolic blood pressure over the range of 115/75 to 185/115 mmHg (Sharma et al., 2012), (Ghadieh and Saab, 2015). In attempt to lessen these negative effects, the American Heart Association and other groups are now urging more aggressive BP goals for many persons with HTN. Diuretics, calcium channel blockers, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, vasodilators, and other medications are frequently used to treat HTN.

Anti-hypertensive drugs.

There are both pharmaceutical and non-pharmacological methods for managing hypertension. While non-pharmacologic therapies involve changing one's way of life to manage high blood pressure, pharmacologic treatment involves the use of anti-hypertensive medications to lower blood pressure. To obtain optimal blood pressure control, one must alter one's lifestyle and take the right prescription combinations and dosages of antihypertensive medications (Mancia et al., 2014), (Düsing, 2006).The severity and prevalence of the disease have led to the development of numerous synthetic medications for the management of hypertension. Although the majority of these medications have shown to be more effective, they are not without negative effects as shown in table 1. Therefore, scientific research suggests a different approach to managing hypertension through dietary changes and the use of the right phytomedicine(Ajayi et al., 2019), (Singh et al., 2015). A growing number of people are turning to herbal remedies due to their accessibility, cultural acceptance, safety, efficacy, lack of adverse effects, and cost-effectiveness. Herbal remedies have recently received attention as alternate medicines for the treatment and prevention of cardiovascular issues(Sultana and Muhammad Asif, 2017), (Rastogi et al., 2016), (Nasri et al., 2014). Despite the availability of many modern antihypertensive medications, the majority of individuals still rely on complementary and alternative therapies, but some believe that combining these therapies with conventional therapies improves outcomes (Abubakar et al., 2015). Intensive study into local plants with hypotensive and antihypertensive therapeutic benefits has been conducted over the past three decades. Due to the lack of socioeconomic resources, low-income individuals in developing nations, particularly those who live in rural areas, have turned more and more to herbal remedies in an effort to manage HTN and its complications (Farnsworth et al., 1985).However, additional scientific investigation is required to confirm the efficacy and clarify the safety profile of such herbal therapies. An overview of the naturally occurring medicinal plants that have been investigated scientifically, and found tohave hypotensive or antihypertensive properties is given in this review.Table 2 summarizes the information on the types of extracts, as well as the mechanisms of action, and references pertaining to the plants that have been studied or reported to have antihypertensive activity in animal studies.

Table 1 Some conventional antihypertensive drugs

S/N	Classification	Types / Examples	Common Side effects
1.	Diuretics:	• Loop diuretics(Furosemide)	Dry mouth, Headache, Dizziness Nausea and vomiting.
		• Thiazide diuretics(Hydrochlorothiazide)	Hypokalemia, frequent urination, constipation, diarrhea, headache, erectile

			dysfunction, vision problems, and weakness/ muscle spasms.
		• Potassium-sparing diuretics(Spironolactone)	Hyperkalemia, Nausea and vomiting. Abdominal discomfort. Headache. Drowsiness. Confusion. Ataxia (loss of control on bodily movements due to lack of coordination between muscles and brain).
2.	Adrenergic receptor antagonists:	• Beta blockers(Atenolol, Metoprolol)	weakness, dizzy or lightheadedness (these can be signs of a slow heart rate), Difficulties sleeping or nightmares. Erectile dysfunction.
		• Alpha-blockers(Prazosin, Doxazosin).	Dizziness, headaches, drowsiness, weakness, palpitations, and nausea, Swollen feet, ankles or fingers, Urinary tract infection (UTI) or cystitis.
		• Mixed Alpha + Beta-blockers(Carvedilol, Labetalol).	Fatigue, dizziness, nausea, and constipation, erectile dysfunction
3.	Adrenergic receptor agonists:	• Alpha-2 agonists(Clonidine,	Drowsiness, headache. lack of

		Methyldopa).	energy
4.	Calcium channel blockers:	• Dihydropyridines (Amlodipine, Nifedipine)	Constipation. Dizziness. Fast heartbeat (palpitations) Fatigue. Flushing. Headache. Nausea. Rash.
		• Non-dihydropyridines (Diltiazem, Verapamil).	Chest pain, Coughnoisy breathing, dizziness, faintness, or lightheadedness dizziness.
5.	ACE inhibitors:	• Captopril, Enalapril, Fosinopril, Lisinopril.	Dry cough, hyperkalemia Fatigue. Dizziness, Headache, Loss of taste.
6.	Angiotensin II receptor antagonists:	• Valsartan, Candesartan, Losartan, Telmisartan.	Headache, fainting, Dizziness, Fatigue, vomiting and diarrhea, back pain, Leg swelling.
7.	Aldosterone antagonists:	• Eplerenone, Spironolactone.	Cough. Dizziness. Headache. Diarrhea, hyperkalemia.
8.	Vasodilators:	• Sodium nitroprusside, Hydralazine.	Rapid heartbeat (tachycardia) Heart palpitations. Fluid retention (edema) Nausea. Vomiting. Headache.
9.	Centrally acting adrenergic drugs:	• Clonidine, Guanabenz, Methyldopa, Moxonidine.	Slow heart rate. Constipation. Dizziness. Drowsiness. Dry mouth. Fatigue.

			Fever. Headache.

Table 2 Some medicinal plants with anti-hypertensive activity.

S/N	Names of plants	Family	Part used	Mechanism of action	References
1	Achilleamillefolium	Asteraceae	Flower	Calcium channel blockers and ACE inhibitors	(Arias-Durán et al., 2021)
2	Allium sativum	Alliaceae	Rhizome	Enhance nitric oxide production	(Nwokocha et al., 2011), (El-Saber Batiha et al., 2020)
3	Andrographis paniculata	Acanthaceae	Herbs	Increases NO, Inhibit ACE, Block calcium channels	(Cahyawati, 2021), (Verma et al., 2021)
4	Annona muricata	Annonaceae	Leaves, fruits	Reduce peripheral vascular resistance	(Sokpe et al., 2020), (Adefegha et al., 2015)
5	Apiumgraveolens	Apiaceae	Seeds	Calcium channels blocker.	(Makarova et al., 2022),
6	Aristolochiamanshuriensis	Aristolochiaceae	Leaves	Diuretic	(Tabassum and Ahmad, 2011)
7	Artocarpusaltilis	Moraceae	Leaves	ACE Inhibitors	(Siddesha et al., 2011)
8	Blond psyllium	Plantaginaceae	Roots / leaves	Lower systolic blood pressure	(Sharma et al., 2012)
9	Camellia sinensis (green Tea extracts)	Theaceae	Leaves	Inhibits ACE (AT1 receptor), Increases NO	(Xingfei et al., 2020)
10	Cappariscartilaginea	Capparaceae	Shrub	Calcuim channels blocker	(Upadhyay, 2011), (Tabassum & Ahmad, 2011)

11	Carumcopticum	Umbelliferae	Seeds	Increase NO production, Calcium channels blocker	(Gilani et al., 2005)
12	Cassia absus	Caesalpiniaceae	Seeds	HR reduction through increased NO synthesis	(Ahmad et al., 2018)
13	Cassia occidentalis	Caesalpiniaceae	Leaves	An active diuretic. preventing Ca2+ influx via voltage-sensitive and receptor-operated channels as well	(Ntchapda et al., 2015)
14	Coleus forskohlii	Lamiaceae		Relaxation of the vascular smooth muscle (enhance NO synthesis)	(Shivaprasad et al., 2014)
15	Commelinavirginica	Commelinaceae	Leaves	Calcium channels blockers	(Khatoon et al., 2022)
16	Coptischinensis	Ranunculaceae	Leaves / roots / stem	Calcium channels blocker	(Verma et al., 2021)
17	Coriandrumsativum	Apiaceae or Umbelliferae	Leaves	Diuretic action. By stimulating B-adrenoceptors, ROS generation is inhibited.	(Mahleyuddin et al., 2021)
18	Crataeguspinnatifida	Rosaceae	Leaves / roots.	Activates eNOS and inhibits platelet aggregation and thrombosis.	(Wang, et al., 2011),
19	Crinum glaucum	Amaryllidace	Leaves	Boost NO	(Ndjenda Ii et

		ae		production. Reduce systolic and diastolic pressure.	al., 2021)
20	Crocus sativus	Iridaceae	Roots / leaves	Blocks Ca2+ Channels	(Hosseini et al., 2018), (Srivastava et al., 2010)
21	Cymbopogoncitratus	Poaceae or Gramineae	Leaves	Inhibits Ca2+ Influx. Increases NO bioavailability	(Dzeufiet et al., 2014)
22	Daucuscarota	Umbelliferae	Arial part	Blockade of calcium channels	(Gilani et al., 2000)
23	Desmodiumstyracifolium	Leguminosae	Leaves	Stimulate of cholinergic receptors.	(Tabassum and Ahmad, 2011)
24	Fuchsia magellanica	Onagraceae	Leaves	ACE inhibitor. Acts as a diuretic.	(Hansen et al., 1995), (Kamyab et al., 2021)
25	Gossypiumbarbadense	Malvaceae	Leaves	Reduced the tension in an isolated guinea pig aorta induced by phenylephrine.Anti oxidant activity.	(Rawat et al., 2016), (Baradaran et al., 2014), (Mans et al., 2010)
26	Hibiscus sabdariffa	Malvaceae	Leaves	Increases NO, Blocks Ca2+ channels. Decrease plasma Na+Levels. Direct vasorelaxant actions that mediate through acetylcholine and histamine-like dependent mechanism.	(Baradaran et al., 2014), (Tabassum and Ahmad, 2011)
27	Jatropha gossypiifolia	Euphorbiacea e		Calcium channels	(Silva et al., 2011), (Wu et

				blocker.	al., 2019)
28	Laeliaautumnalis	Orchidaceae	Roots	Calcium channels blocker	(Vergara-Galicia et al., 2010)
29	Lavandulastoechas	Lamiaceae	Leaves	The crude extract's antihypertensive and bradycardia effects may be mediated by a mechanism or mechanisms that are comparable to those of acetylcholine.	(Baradaran et al., 2014), (Tabassum and Ahmad, 2011), (Lim, 2014).
30	Lepechiniacaulescens	Lamiaceae	Roots	Nitric oxide liberation	(Talha et al., 2011)
31	Lepidiumlatifolium	Cruciferae	Leaves	It exert diuretic action in rat	(Wright et al., 2007)
32	Lumnitzera racemose.	Combretaceae	Leaves	Calcium channels blocker. Enhance NO synthesis	(Das et al., 2022), (Manohar, 2021)
33	Lycopersiconesculentum	Solanaceae	Tomato fruits	Antioxidants activity. Slow the progress of atherosclerosis.	(Phachonpai, 2020)
34	Mammea Africana	Calophyllacea e	Bark	Ca2+ antagonists	(Nguelefack-Mbuyo et al., 2008)
35	Moringaoleifera	Moringaceae	Leaves	Diuretic action, ACE inhibitor	(Kumolosasi et al., 2021), (Aekthammarat et al., 2019), (Ma et al., 2021)
36	Musangacecropiodes	Cecropiaceae	Leaves	Vasorelaxant action,	(Kamyab et al., 2021)
37	Ocimumbasilicum	Lamiaceae	Leaves	. Eugenol's effects on the cardiovascular system are linked to its ability to inhibit calcium	(Baradaran et al., 2014), (Tabassum and Ahmad, 2011)

				channels.	
38	Oleaeuropaea	Oleaceae	Leaves	Angiotensin II inhibition	(Ivanov et al., 2018), (Susalit et al., 2011)
39	Phyllanthusniruri.	Euphorbiaceae	Leaves	Vasorelaxation and a drop in blood pressure are both mediated by -adrenoceptor activation.	(Bello et al., 2020),
40	Pinuspinaster	Pinaceae	Bark	ACE I	(Maimoona et al., 2011)
41	Puerarialobate	Fabaceae	Roots	Vasodialation and antioxidant action	(Ng et al., 2011), (Bebrevska et al., 2010)
42	Punicagranatum	Lythraceae	Fruits	Reduces ACEI action	(Mayasankaravalli et al., 2020)
43	Rauwolfiaserpentine	Apocynaceae	Leaves / Roots	Deplete catecholamine	(Kaur, 2017), (Shah et al., 2020)
44	Rhaptopetalumcoriaceumoliver	Scytopetalaceae	Stem bark	Calcium channel blocker	(Tabassum and Ahmad, 2011)
45	Salvia cinnabarina	Lamiaceae	Leaves	Nitric oxide production	(Sultana and Muhammad Asif, 2017)
46	Sesamumindicum	Pedaliaceae	Seeds	Antioxidant activity	(Elleuch et al., 2011), (Mushtaq et al., 2020)
47	Solanumsisymbriifolium	Solanaceae	Roots	Diuretics	(Ibarrola et al., 2022)
48	Tanacetumvulgare	Asteraceae	Leaves	Diuretic action. NO production enhancer	(Babich et al., 2023)
49	Theobroma cacao	Malvaceae	Cacao powder	Antioxidant and calcium channels blocker	(Ishaq & Jafri, 2017)
50	Uncariarhynchophylla	Rubiaceae	Herbs	Calcium channel blocker	(Loh et al., 2017), (Ndagijimana et al., 2013)
51	Viscum album	Santalaceae	Leaves	Enhances NO production	(Poruthukaren et al., 2014)

52	Zingiberofficinale	Zingiberaceae	Rhizome	Calcium channel blocker. Inhibits lipid peroxidation	(Yeh et al., 2014), (Dhanik et al., 2017)

Conclusion

In recent years, there has been a resurgence of interest in the quest for novel medications derived from natural sources, particularly plant sources. Tropical rain forests have grown to be a key area of this activity, mostly because of the abundant biodiversity they support, which promises a wide variety of compounds with potentially unique structures. Nonetheless, only a small percentage of this diverse biodiversity has been investigated for its potential as medicine. As a result, in the future, we may be able to treat HTN with medications derived from plants and herbs that are naturally occurring and have fewer side effects and greater absorption.

Significance Of The Study:

The study highlights the efficacy of "herbal" which is an ancient tradition, used in some parts of India. This ancient concept should be carefully evaluated in the light of modern medical science and can be utilized partially if found suitable.

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