

Review Article

Medicinal Plants with antihypertensive activity. A narrative review.

Abstracts

Traditional medicine is a broad word encompassing ancient practice, culturally specific health care methods, that were used to address health issues before science was employed. Heart attacks, cerebrovascular illnesses, hypertension, and heart failure are among the cardiovascular diseases that can be managed using medicinal plants. Hypertension (HTN) increase the risk of heart attack and stroke, which makes it difficult for the heart to pump blood. This affirmation is not correct.

HTN also plays a role in atherosclerosis. There are numerous medications available to manage these disorders, but most often used antihypertensive medications come with a variety of side 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 side effects. Medicinal plants contain a number of pharmacologically active compounds that can be utilized to manage hypertension. This paper gives a general overview of a few medicinal plants whose hypotensive or antihypertensive effects have been demonstrated.

Key words: Antihypertensive, herbs, hypotensive, hypertension, medicinal plants

Herbs, Hypotensive are not a key words

Introduction

Hypertension (HTN) is a chronic medical condition that leads to elevated blood pressure (BP) in the arteries. 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 defined 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 unhealthy 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. The 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. **As 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, **(Bedane, 2018), Guwatudde et al., 2015)**. 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 **(Mv & Mwinuka, 2021); Desormais et al., 2019); 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 (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, **there is urgent** need for a long-term solution. The majority of deaths from non-communicable diseases (NCDs) are attributable to cardiovascular disorders (48%) in the **United States (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. Hypertension is 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 & 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 & 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 **(Le et al., 2012); Ferder et al., 2010)**.

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 & 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 system are compromised in 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). HTN is also caused by other illnesses that alter hormone levels, including cancer of the adrenal gland, hyperthyroidism, and hypothyroidism. In addition, metabolic disorders, pre-eclampsia during pregnancy, coarctation of the aorta, kidney disease, and other congenital defects are typical secondary causes of hypertension. 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 (Anthony & Sliwa, 2016; Tabassum & Ahmad, 2011). 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 have diabetes or kidney disease. HTN is also categorized as resistant if treatments do not bring BP down to normal levels (Viera, 2012). THIS IS NOT THE DEFINITION OF RESISTANT HTN.

Exercise-related hypertension is an abnormally high BP increase during exercise (Kovacs et al., 2017). Systolic levels during activity should be between 200 and 230 mmHg, which is considered normal (Holmqvist et al., 2012). Exercise HTN may signal a person's risk of acquiring HTN at rest (Fagard, 2011).

Pathophysiology of hypertension

Most people understand the majority of secondary HTN-related processes; on the other hand, symptoms linked with essential (primary) HTN are less characterized. 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 explained 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 (Tabassum & Ahmad, 2011); (M. Singh et al., 2010).

- Vasoconstriction, salt and water retention, and hyperactivity of the renin-angiotensin system occur. HTN is brought on by an increase in blood volume (Pimenta & Oparil, 2009).
- Heightened stress responses due to an overactive sympathetic nervous system (Takahashi, 2008); Tuck, 1986).

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 & 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 (Ghadieh and Saab, 2015) ; Sharma et al., 2012). In attempt to lessen these negative effects, the American Heart Association and other groups are now seeking for more BP goals for many persons with HTN.

Herbal drugs used for the management of hypertension

Many antihypertensive medications used to manage HTN have unwanted side effects. As a result, scientific studies advocate a variety of lifestyle changes as well as the use of appropriate medicinal plants in its management (Kamyab et al., 2021).Secondary metabolites of various herbs and spices have antihypertensive effects. Most herbal treatments control and diminish HTN by having antioxidant, anti-inflammatory, and anti-apoptotic characteristics, promoting the eNOS-NO signaling pathway, decreasing endothelial permeability, and activating angiogenesis (Liu & Huang, 2016).

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. 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. Therefore, scientific research suggests a different approach to managing hypertension through dietary changes and the use of the right phytochemistry (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 & Muhammad Asif, 2017), Rastogi et al., 2016), Nasri et al., 2014). 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 to herbal remedies in an effort to manage HTN and its complications (Sofowora et al., 2013); 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 some naturally occurring medicinal plants, which have been investigated scientifically and found to have hypotensive or antihypertensive activity, is given in this review. Table 1 summarizes the information on the types of plant part (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 medicinal plants with anti-hypertensive activity.

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

10	<i>Capparis cartilaginea</i>	Capparaceae	Shrub	Increases Calcium channels blocker	NO	(Upadhyay, 2011), (Tabassum & Ahmad, 2011)
11	<i>Carumcopticum</i>	Umbelliferae	Seeds	Increase production, Calcium channels blocker	NO	(Gilani et al., 2005)
12	<i>Cassia absus</i>	Caesalpiniaceae	Seeds	HR reduction through increased synthesis	NO	(Ahmad et al., 2018)
13	<i>Cassia occidentalis</i>	Caesalpiniaceae	Leaves	An active diuretic. preventing Ca ²⁺ influx via voltage-sensitive and receptor-operated channels as well		(Ntchapda et al., 2015)
14	<i>Coleus forskohlii</i>	Lamiaceae		Relaxation of the vascular smooth muscle (enhance NO synthesis)		(Shivaprasad et al., 2014)
15	<i>Commelina virginica</i>	Commelinaceae	Leaves	Calcium channels blockers		(Khatoon et al., 2022)
16	<i>Coptischinensis</i>	Ranunculaceae	Leaves / roots / stem	Calcium channels blocker		(Verma et al., 2021)
17	<i>Coriandrum sativum</i>	Apiaceae or Umbelliferae	Leaves	Diuretic action. By stimulating B-adrenoceptors, ROS generation is inhibited.		(Mahleyuddin et al., 2021)
18	<i>Crataeguspinnatifida</i>	Rosaceae	Leaves	Activates eNOS		(Wang, et al.,

			/ roots.	and inhibits platelet aggregation and thrombosis.	2011),
19	Crinum glaucum	Amaryllidaceae	Leaves	Boost NO production. Reduce systolic and diastolic pressure.	(Ndjenda Ii et al., 2021)
20	Crocus sativus	Iridaceae	Roots / leaves	Blocks Ca ²⁺ Channels	(Hosseini et al., 2018), (Srivastava et al., 2010)
21	Cymbopogon citratus	Poaceae or Gramineae	Leaves	Inhibits Ca ²⁺ Influx. Increases NO bioavailability	(Dzeufiet et al., 2014)
22	Daucus carota	Umbelliferae	Arial part	Blockade of calcium channels	(Gilani et al., 2000)
23	Desmodium styracifolium	Leguminosae	Leaves	Stimulate cholinergic receptors.	(Tabassum & Ahmad, 2011)
24	Fuchsia magellanica	Onagraceae	Leaves	ACE inhibitor. Acts as a diuretic.	(Hansen et al., 1995), (Kamyab et al., 2021)
25	Gossypium barbadense	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 Ca ²⁺ channels. Decrease plasma Na ⁺ Levels. Direct vasorelaxant actions that mediate through acetylcholine	(Baradaran et al., 2014), (Tabassum & Ahmad, 2011)

				and histamine-like dependent mechanism.	
27	<i>Jatropha gossypifolia</i>	Euphorbiaceae		Calcium channels blocker.	(Silva et al., 2011), (Wu et al., 2019)
28	<i>Laelia autumnalis</i>	Orchidaceae	Roots	Calcium channels blocker	(Vergara-Galicia et al., 2010)
29	<i>Lavandula stoechas</i>	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 & Ahmad, 2011), (Lim, 2014).
30	<i>Lepechinia caulescens</i>	Lamiaceae	Roots	Nitric oxide liberation	(Talha et al., 2011)
31	<i>Lepidium latifolium</i>	Cruciferae	Leaves	It exerts diuretic action in rat	(Wright et al., 2007)
32	<i>Lumnitzera racemosa</i>	Combretaceae	Leaves	Calcium channels blocker. Enhance NO synthesis	(Das et al., 2022), (Manohar, 2021)
33	<i>Lycopersicon esculentum</i>	Solanaceae	Tomato fruits	Antioxidant activity. Slow the progress of atherosclerosis.	(Phachonpai, 2020)
34	<i>Mammea africana</i>	Calophyllaceae	Bark	Ca ²⁺ antagonists	(Nguelefack-Mbuyo et al., 2008)
35	<i>Moringa oleifera</i>	Moringaceae	Leaves	Diuretic action, ACE inhibitor	(Kumolosasi et al., 2021), (Ma et al., 2021)
36	<i>Musangacecropiodes</i>	Cecropiaceae	Leaves	Vasorelaxant action,	(Kamyab et al., 2021)
37	<i>Ocimum basilicum</i>	Lamiaceae	Leaves	. Eugenol's effects on the cardiovascular system are linked to its	(Baradaran et al., 2014), (Tabassum & Ahmad, 2011)

				ability to inhibit calcium channels.	
38	<i>Olea europaea</i>	Oleaceae	Leaves	Angiotensin II inhibition	(Ivanov et al., 2018), (Susalit et al., 2011)
39	<i>Phyllanthus niruri</i>	Euphorbiaceae	Leaves	Vasorelaxation and a drop in blood pressure are both mediated by α -adrenoceptor activation.	(Bello et al., 2020),
40	<i>Pinus pinaster</i>	Pinaceae	Bark	ACE I	(Maimoona et al., 2011)
41	<i>Pueraria lobata</i>	Fabaceae	Roots	Vasodilation and antioxidant action	(Ng et al., 2011), (Bebrevska et al., 2010)
42	<i>Punicagranatum</i>	Lythraceae	Fruits	Reduces ACEI action	(Mayasankaravalli et al., 2020)
43	<i>Rauwolfia serpentina</i>	Apocynaceae	Leaves / Roots	Deplete catecholamine	(Kaur, 2017), (Shah et al., 2020)
44	<i>Rhaptopetalum coriaceum</i> liver	Scytopetalaceae	Stem bark	Calcium channel blocker	(Tabassum and Ahmad, 2011)
45	<i>Salvia cinnabarina</i>	Lamiaceae	Leaves	Nitric oxide production	(Sultana & Muhammad Asif, 2017)
46	<i>Sesamum indicum</i>	Pedaliaceae	Seeds	Antioxidant activity	(Elleuch et al., 2011), (Mushtaq et al., 2020)
47	<i>Solanum sisymbriifolium</i>	Solanaceae	Roots	Diuretics	(Ibarrola et al., 2022)
48	<i>Tanacetum vulgare</i>	Asteraceae	Leaves	Diuretic action. NO production enhancer	(Babich et al., 2023)
49	<i>Theobroma cacao</i>	Malvaceae	Cacao powder	Antioxidant and calcium channels blocker	(Ishaq & Jafri, 2017)
50	<i>Uncaria rhynchophylla</i>	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. This study highlights the efficacy of some “herbal” which is an ancient tradition, used in the management of hypertension. This ancient concept should be carefully investigated especially the bioactive phytochemicals in the light of modern medical science and can be utilized for potential development of anti-hypertensive drugs that have little side effect and easily accessible.

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