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A Review of Medicinal Plants with Hypotensive or Antihypertensive Effects

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This review examines medicinal plants, which have been reported to have hypotensive or antihypertensive effects. It pays particular attention but not totally restricted to plants whose antihypertensive effects have been scientifically validated. The main aim of the review is to piece together information on this subject, so as to raise more awareness, prevent duplication of efforts and possibly bring more attention to medicinal plants as a veritable source of antihypertensive drug. As the review ended, it was possible to conclude that, a lot of efforts are still needed not only in the validation of the plants but also in the areas of identifying the active principles in these medicinal plants and the conduct of clinical trials in humans.

Key words: Medicinal plants sources, antihypertensive drugs, *Hibiscus sabdariffa*

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INTRODUCTION

Hypertension, for several decades, has been globally recognized as the most prevalent cardiovascular disease with potent complications such as coronary heart disease, stroke, sudden cardiac death, congestive cardiac disease, renal insufficiency and dissecting aortic aneurysm (Akinkugbe, 1996; Oates and Brown, 2001). The prevalence of the disease and its related conditions has been recognized to be increasing in the developing countries (Beevers and Prince, 1991; Akinkugbe, 1998). In Nigeria for example, the true incidence of hypertension remains unknown but its prevalence among male and female is estimated to be 11.2% with age adjusted figure of 9.3%. This translates into approximately 13.4 million Nigerian hypertensive aged 15 years and above, using the projected National population census figure of 120 million (Akinkugbe, 1998). In fact, hypertension is reported to be next to malaria as most serious health problem in developing tropical countries (Gifford, 1975; Agunwa, 1988). Thus the need to control hypertension becomes very imperative, as its complications are associated with high mortality and morbidity. The uses of conventional antihypertensive have been associated with arrays of side effects. Also, there is no cost effective monotherapeutic antihypertensive in use. Effective hypertension control has been achieved with combination therapy. Thus, in view of the a fore mentioned, it becomes imperative to continue the search for a novel drug with better-cost effectiveness and lesser side-effects (Oates and Brown, 2001).

In the last three decades, a lot of concerted efforts have been channeled into researching into local plants with hypotensive and anti hypertensive therapeutic values. The hypotensive and anti-hypertensive effects of some of these medicinal plants have been validated and others disproved (Ajayi *et al*., 1997; Ajagbonna and Adegunloye, 1998).

Attempts by the low- income group particularly the rural dwellers in the developing countries to control hypertension and its attendant complications in the face of scarce socioeconomic resources have led more people opting for herbal remedy (Farnworth *et al*., 1985; Farnworth and Soejarto, 1991; Soejarto, 1996; Lambert, 2001). However, more scientific researches are needed to be done to verify the effectiveness and elucidate the safety profile of such herbal remedies (Gamaniel, 2000; Lambert, 2001).

The increasing demand by the industrial countries for herbal remedies has put increasing pressure on the supply of raw materials available in developing countries (Lambert, 2001). It has been estimated that approximately 25% of all prescribed medications today are of natural plant sources (Gamaniel, 2000). Also, there is a clear demonstration that, the rich biodiversity of the tropical rain forests has indeed provided humanity with many important drugs.

The medicinal plants that has been scientifically studied and reported to have hypotensive or antihypertensive effects include:

Hisbiscus Sabdarifa (HS): This happens to be one of the most extensively studied plant for antihypertensive properties. The plant belongs to the botanical family *malvacae*. The leaves; calyx and corolla of this plant are use traditionally in many West African countries for various medicinal purposes and edibles. The calyx is used for making beverage soup, drink (sobo) and sauces (Bokhari and Ahmed, 1993). The antihypertensive effect of this plant extract has been variously studied. Iwuanyawu and Ayani (1994) reported from Jos, Nigeria that, the extract of HS at doses of 500 and 1000 mg kg^{-1} per oral produced a dose dependent reduction of blood pressure in spontaneously hypertensive rats. A similar result was independently produced in Lagos, Nigeria by Adegunloye *et al*. (1996). An intravenous administration of 20 mg kg^{-1} of a water extract of dry HS calyx produced a fall in the blood pressure of experimentally induced hypertensive rats. The anti hypertensive effects of the crude extract of HS has been attributed to mediation through acetylcholine and histamine like dependent mechanisms via direct vasorelaxant effects (Adegunloye *et al*., 1996). Earlier report showed that, the petal crude extract of same plant had a direct relaxant effect on the aortic smooth muscle of rats (Obiefuna *et al*., 1994). The aortic relaxant effect of the plant was recently found to be mediated through chronic nitric oxide synthetase inhibition (Dikko, 2003).

Apart from attenuating hypertension, the chronic administration of aqueous extract of HS has been reported to reverse cardiac hypertrophy in renovascular hypertensive rats (Odigie *et al*., 2003). Chen *et al*. (2003) also reported that, HS extract inhibits the development of atherosclerosis in cholesterol fed rabbits. At a dose of 500-1000 mg kg^{-1} it lowers both systolic and diastolic blood pressure (Chen *et al*., 2003). Aqueous extract of HS given intravenously to cats, lowered blood pressure dose dependently. It relaxed rabbit aorta, uterus and diaphragm (Ali *et al*., 1999).

Clinical trials of the plant extract in human have shown reliable evidence of antihypertensive effects. A standardized dose of HS (9.6 mg per day) given to 39 patients and captopril 50 mg per day given to the same number of patients did not show

significant difference relative to hypotensive effects, antihypertensive effectiveness and tolerability (Herrera-Arellano *et al*., 2004). The evidence for efficacy of *Hibiscus sabdariffa* extract in human hypertension was provided by Haji-Faraji and Tarkhani (1999) when 31 patients with moderate essential hypertension were given HS extract for 12 days; 11.2% decrease in systolic blood pressure and 10.7% reduction in diastolic blood pressure was recorded. Another human trial was conducted by Kirdpon (1994) to buttress the therapeutic efficacy of HS extract against high blood pressure. It was observed that, the urinary excretion of creatinine, uric acid, citrate, tartrate, calcium and sodium increased when 36 men consumed HS regularly with a corresponding fall in blood pressure. Odigie and Adigun (2002) reported about the blood pressure lowering effect of HS extract in normotensive volunteers.

Rhaptopetalum coriaceum oliv (Scytopetalaceae): It has a reputation for its medicinal values. A decoition of the plant stem bark is traditionally prepared or soaked in locally distilled gin and taken as a remedy for hypertension (Keayn *et al*., 1966). Preliminary studies carried out on the plant stem bark extract showed its blood pressure lowering effects on normotensive rats (Ajagbonna and Onyeyili, 2002). In an earlier study, the stem bark extract of the plant significantly relaxed vascular smooth aortic rings from rats (Ajagbonna and Adegunloye, 1998). Recent *in vitro* studies of its vasodilatory mechanism revealed its action to be through calcium channel blockade at a concentration of 0.2 mg mL^{-1} of *R. coriaceum* extract. This was done through inhibition of Ca^{2+} release and blockade of potential sensitive channels and receptor operated channels by inhibiting noradrenaline and KCL induced Ca^{2+} influx. Result from the *in vitro* studies suggested that ethanol extract of *R. coriaceum* may be more potent as a calcium channel blocker than Nifedipine.

Allium sativum (Garlic): A plant that is indigenous to Asia but has been introduced to Africa especially the savannah areas. It is used locally in Nigeria for the treatment of respiratory infections, worms and sometimes applied topically for the treatment of skin diseases. Garlic has been used as both food and medicine in many cultures for thousands of years. One of the primary active compounds that give garlic its characteristic odour and many of its healing benefits is called Allicin (Silogy, 1994). Studies suggest that raw garlic may have beneficial cardiovascular effects, including lowered blood pressure. The same study concluded that since garlic is relatively safe and has a number of other healthful benefits, a professional herbalist may recommend 5 to 10 minced raw garlic doves per day or 300 mg of dried garlic extract three times a day for those at risk of hypertension and heart disease (Silogy, 1994).

According to Prof. Maurice Iwu, it has been established that, extracts of Garlic possessed a demonstrable cholesterol lowering and antihypertensive properties. In a feeding experiment with rabbits, the animals given Garlic had very less marked increase in blood cholesterol than those given the same diet but without Garlic. The oil extracted from Garlic prevents fat induced hypercholesterolemia and sucrose induced hyperlipidaemia and enhances fibrinolytic activity. The extract has been shown in 5 consecutive cases of hypertension to reduce the blood pressure to satisfactory levels (Maurice, 1993).

Musanga cecropioides: Is a rapidly growing plant belonging to the Cecropaicea family, ubiquitous to the tropical rain forests particularly of West Africa. It is known as the umbrella three or corkwood in English, *parasoiler* in French; Aga or Agbawo in Yoruba; Onru in Igbo and Uno in Efik. Traditionally, preparations from various parts of the plant such as leaves, latex, stem bark and roots are used as remedy for various illnesses especially hypertension, typanosomiasis, leprosy, chest infections and rheumatism (Bouquet, 1969).

Several workers have demonstrated the scientific efficacy of the latex and the leaves extract as a vaso-relaxant and therefore hypotensive agent (Ebeigbe *et al*., 1991; Dongmo *et al*., 2002). Ayinde *et al*. (2003) reported about the hypotensive effect of *Musanga cecropioides* stem bark extract in rabbits. The water extract of the stem bark produced a dose-related reduction in mean arterial blood pressure. The mean arterial blood pressure fell by 4.51±0.5 mm Hg at 10 mg kg^{-1} and 65.23±6.28 mm Hg at 40 mg kg^{-1}. The hypotensive effect of the extract was not affected by prior administration of either atropine (0.5 mg kg^{-1}) or promethazine (0.25 mg kg^{-1}). In a similar, studies on the stem bark extract of the plant. Adeneye (2005) reported that, a graded doses of the extract (0.5 to 5 mg kg^{-1} body weight) produced a dose dependent fall in the mean arterial pressure of Sprague-Drawley rats.

Cassia occidentalis: A member of the family Caesalpiniaceae. Usually, a small tree growing 5-8 m in height. The leaf of this plant is used in local folk medicine as an antihypertensive agent (Oliver, 1960; Sadique, 1987; Ajagbonna *et al*., 2001). *In vitro* studies done to investigate the pharmacological and biological effects of

the aqueous leaf extract of *Cassia occidentalis* revealed its relaxant effects in aortic rings with or without endothelium. The studies revealed that, the *cassia* extract may be relaxing smooth muscle and reducing blood pressure by inhibiting Ca^{2+} influx through receptor operated channel and voltage sensitive channel showing its non-selectivity on these Ca^{2+} channels.

Vitex dodiana: It is used in Nigerian Herbal Medicine to treat, dysentery, diarrhoea and sometimes mixed with species to induce labour. Okoye and Ladeji (1996) investigated the effect of oral administration of this extract on blood pressure of rats. The extract exerted hypotensive effect. Both the systolic and diastolic blood pressure were significantly reduced 45 min following oral administration of the extract and remain so for the next 75 min. The blood pressure began to return to normal from about 2 h later.

Phyllanthus amarus (Eurphobiaceae): Amaechina and Omogbai (2004) reported that, intravenous administration of the aqueous extract of the leaves of this plant (5 to 80 mg kg^{-1}) to anaesthetized male rabbits produced significant fall in the diastolic, systolic and mean arterial pressure of normotensive rabbit in dose dependent manner. The hypotensive effect of the extract was blocked by Atropine (1 mg kg^{-1}) while promethazine at the same dose potentiated its action. A comparative screening of the effect of the extract to that of verapamil a conventional antihypertensive agent showed that 40 mg kg^{-1} of the extract cause a fall in mean arterial pressure of 17.435.9 mmHg, which is comparable to the 16.893.3 mmHg produced by 0.20 mg kg^{-1} maximal dose of verapamil, a calcium slow channel blocker.

Lepidium Latifolium (Cruciferae): A specie used in folk medicine in the Canary Islands. known locally as rompepiedra meaning stone breaker because of its effect on renal lithiasis. It has been found to have hypotensive effect through its diuretic action in rats (Navarro *et al*., 1994). The aqueous leaf extract given in doses of 50 and 100 mg kg^{-1} via intraperitoneal and oral routes respectively produced significant and dose dependent diuretic and hypotensive activities. The extract was more potent as a diuretic when administered per oral than through intra-peritoneal route. The study went further to extrapolate the diuretic action of the extract from rats to man, using the activity of furosemide in both cases as a guideline. The standard daily recommended dose for *Lepidium latifolium* in man was 3-5 g per day in the form of tea, which is equivalent to 43-71 mg kg^{-1} body weight in a 70 kg subject (Navarro *et al*., 1994) . Also *Raphanus Sativus* (Cruciferae) has also been found to have the same pharmacological activities (including the mean urinary output) as *Lepidium latifodium.*

In another study, the Orissa Villagers in the Phillippines were reported to have used the decoition of the root of *Abutilon indicum* as an anti-hypertensive and health promotion tonic to the pregnant women (Hansawasdi *et al*., 2000). In China, the dry vine of *Aristolochia mansihuriensis* is being used as a diuretic and antiphlogistic for the treatment of Oedema and rheumatic pain. The plant extract was found to possess magnoflorine which has a hypotensive effect (Hansawasdi *et al*., 2000) . The dry fruit of *Crataegus pinnatifida* (Fructus Cattaegi family) or *C. cuneata* has equally been used in China as a decoction for treatment of hypertension for thousands of years (Ren and Chen, 1986). Pharmacological and Clinical trials have shown that, it lowers blood pressure. For example, in experiments with anaesthetized rabbits, intravenous administration of the extract preparation lowered the blood pressure for up to 3 h (Bensky and Gamble, 1990). Grataegic acid was identified as one hypotensive principle (Ren and Chen, 1986). Bensky and Gamble (1990) in a similar study demonstrated the cardiovascular effects of *Desmodium styracifolium*, which is officially listed in the *Chenese pharmacopoenia* and used as a diuretic. Preparations from the plant dry leaves and stems injected intravenously into anaesthetized dogs, increased coronary circulation, lowered arterial blood pressure, slowed the heart rate and decreased the oxygen consumption of the heart (Bensky and Gamble, 1990).

The dry root of *Pueraria lobata* is officially listed and used in China as a muscle relaxant, antipyretic and for the treatment of dysentery and hypertension (Tang and Eaisenbrand, 1992). The total isoflavones from the ethanol extract of its roots had hypotensive effect on anaesthetized dogs and unanesthetized hypertensive dogs (Tseng *et al*., 1974). The isoflavone, peurarine has in clinical trials with patients suffering from hypertension or angina pectoris, showed that when administered intravenously at a dose range of 100-200 mg, there was a decrease in blood Catecholamine levels, blood pressure and heart rate (Zeng *et al*., 1979).

A methanol extract of the hooks of an Uncaria species was found to have a potent and long-lasting hypotensive effect in rats and the activity was different from that of *Uncaria rynchophylline* and its analogue.

Further studies of the extract resulted in the isolation of 3-indole alkaloid, glycoside, cadambine, dihydrocadambine and isodihydro-Cadambine. The later two were found to be the hypotensive principles whereas caddambine was inactive (Endo *et al*., 1983).

In India, *Fuchsia magellanica* locally called Chiko or tilco; infusion of the leaf extract reduces body temperature, acts as a diuretic and lowers blood pressure (Hougnton and Manby, 1985). Schmeda-Hirschmann *et al.* (1992) investigated the ethanol/aqueous extracts of this species in normotensive rats and found a reduction in the mean arterial pressure. In another species, S. Polytamus, Schmeda-Hirschmann *et al.* (1992) found a moderate to strong reduction in the arterial pressure in normotensive rats.

Several other medicinal plants has been listed in literature and claimed to be useful in the treatment of blood pressure disorders both in the African and Asian folkloric medicine. These claims are yet to be scientifically evaluated. Elizabeth Kafar, listed *Viscum album* (mistletoe) to be excellent for the treatment of stress induced hypertension. Its combination with *Passiflore incanata* is said to stop the headache associated with hypertension and induce sleep. Other medicinal plants associated with reduction in blood pressure include; *Veronica officinalis* (speed well), *Allium Urinum* (Ramsons), *Verbena Hastata* (Vervain) and *Lycopodium claraton* (Common Club Moss).

Crataegus Species (Hawthorn), a member of the rose family, which was formerly used as an evil spirit repellent in the middle ages. American physicians recognized its medicinal properties in the early 19th century. Although hawthorn has not been studied specifically for hypertension, considerable evidence supports the cardiovascular benefits of this herb. Reports indicate that hawthorn can be taken safely by people with hypertension who are taking blood pressure medications. The two main substance that contribute to hawthorn's beneficial effects on the heart are flavonoids and oligomeric procyanidins which are potent antioxidant agents (Mashour and Freshman, 1998). There exists an alkaloid known as rynchophilline in cat's claw. This alkaloid has been studied at the Shangai College of Traditional Chinese Medicine. According to their findings, rynchophilline has demonstrated an ability to inhibit platelet aggregation and thrombosis, which suggest that, it may be useful in preventing strokes and reducing the risk of heart attack by lowering blood pressure, increasing circulation and inhibiting both the formation of plague on arterial walls and formation of blood clots in the brain, heart and arteries.

According to Chinese theory, Celery is effective for hypertension because it acts upon the liver; one type of hypertension is associated with the liver. In Mainland China; Celery was useful in reducing hypertension in 14 out of 16 patients (Somanadhan *et al.*, 1999). The Juice was mixed with equal amount of honey and about 8 ounces was taken orally three times each day for up to one week. Fresh Celery juice can be mixed with vinegar to relieve dizziness and headache and shoulder pain associated with hypertension. It is also administered in hypertension associated with pregnancy and climacteric (Ang-lee *et al.*, 2001).

Ginger root is commonly used in Asian cooking. Ginger acts to improve blood circulation and relaxes muscles surrounding blood vessels. Ginger is also a powerful digestive herb that helps alleviate uneasiness and nausea. The olive leaf from olive tree is native to the Mediterranean region. Olive leaf extract helps in lowering blood pressure and combats arrhythmias, or irregular heartbeat (Fugh-Berman, 2000). *Agathosma betulina* (Buchu) is one of the South Africa's medicinal plants and has been used by the indigenous peoples of the area for centuries to treat a wider range of ailments. It is an effective diuretic and anti-inflammatory agent. Early Dutch settlers use buchu to make a brandy tincture which is still used today to treat many disorder (Ang-lee *et al.*, 2001).

Flaxseed or linseed (*Linium usitatissumum*) is derived from the flax plant, an annual herb believed to have originated in Egypt. Flaxseed and its oil are rich in alpha linolenic acid, an essential fatty acid that appears to be beneficial for heart diseases, inflammatory bowel disease, arthritis and other health problems. Alpha linolenic acid belongs to a group of substance called Omega-3 fatty acids: Several studies suggest that diets rich in Omega-3 fatty acids lower blood pressure significantly in people with hypertension (Ang-lee *et al.*, 2001).

The renewed interest in the search for new drugs from natural sources, especially from plant sources, has gained global attention during the last two decades (Soejarto, 1996). The tropical rain forests have become an important point of this activity, primarily due to the rich biodiversity they habour, which promises a high diversity of chemicals with potential novel structures. However, of this rich biodiversity, only a small portion has been studied for its medicinal potential (Soejarto, 1996). At the same time, there is a sense of urgency in studying these forests so as to unveil their pharmaceutical secrets before deforestation takes its toll with the loss of species diversity, hence, the chances of finding novel drugs are improved upon (Lambert, 2001).

The rich biodiversity of the forest is found in the tropical belt, where most of the world's developing countries are located. It is these developing countries, most of which are poor in biotechnology, who are the owners of the threatened plant genetic diversity. It is hopes that, researches in this field will continue to explore the rich biodiversity of these forest for the benefit of humanity as a lot is still needed to be done.

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