

A Review of Medicinal Plants with Potential Anti-Benign Prostatic Hyperplasia (Bph) Activity Used In Nigeria

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ABSTRACT

The global demand for medicines and pharmaceuticals for treatment of various diseases and industrial purposes is becoming unattainable. Thus, focus on plant research has increased in recent times all over the world and results have shown an immense potential of some of these plants. The Benign prostatic hyperplasia (BPH) also called Benign enlargement of the prostate (BEP) is a common part of aging and constitutes a lot of health burden for adult men. Prevalence statistics on BPH is well documented in developed world but not so in Africa, especially Nigeria. The cause of BPH is not well elucidated and no definite information on risk factors exists. Factors chiefly age, genetics, lifestyle, hypertension, obesity, diabetes and insulin resistance have been linked to the development of BPH. The androgen-testosterones, its metabolite, dihydroxytestosterone (DHT) and estrogen are believed to play a role in the development of BPH. BPH in most cases is treated with surgical procedures that allow normal voluntary expression of urine. Medications such as alpha-blockers and 5 α -reductase among others which target the reduction of prostate gland or relaxation of the muscle tone are used to manage BPH. The use of medicinal plants in management and treatment of BPH has been reported and has shown some promises. This work therefore reviewed some common medicinal plants used by traditional medicinal practitioners in Nigeria for management of BPH. Plant parts used, phytochemical constituents and other activities were reported.

Keywords: BPH, medicinal plants, Nigeria, Phytochemicals

INTRODUCTION

Benign prostate hyperplasia (BPH) also called benign enlargement of the prostate (BEP) is a progressive pathologic condition associated with aging in men and characterized by proliferation of prostatic tissues, prostate enlargement and lower urinary tract symptoms (LUTS) [1].

In BPH the prostate often enlarges to the point where urination is difficult and sometimes impossible for some people. However, experts consider BPH as hyperplasia (increase in the number of cells) or hypertrophy (a growth in the size of individual cells) of the prostatic stromal epithelial cells, which results in the formation of a large or discrete nodule in the preurethral region of the prostate [2]. When sufficiently large, the nodules compress the urethral canal to cause partial or sometimes complete obstruction

of the urethra and thus interfere with the normal flow of urine [3]. Studies have shown that as men age, the active testosterone in the blood decreases leaving a higher proportion of estrogen. In addition, the accumulation of DHT, a metabolite of testosterone, in the prostate may encourage the growth of cells. These are supported by the fact that castrated individuals do not develop BPH when they age. Although prostatic specific antigen (PSA) levels may be elevated in cases of BPH due to inflammation and sometimes urinary tract infections, BPH does not lead to cancer or increase the risk of cancer [4]. BPH in most cases is treated with surgical procedures that allow normal voluntary expression of urine. Medications such as alpha-blockers and 5 α -reductase which are adrenoceptor antagonists

(Terazosin and Doxazosin) and 5-alpha-reductase inhibitors (finasteride and dutasteride) and some forms of combination therapies (e.g. finasteride and doxazosin, or dutasteride and terazosin) among others are used to manage BPH. They target the reduction in the mass of prostate gland or relaxation of the muscle tone [5]. These have been observed to have their efficacy compromised by numerous side effects such as dizziness and decreased blood pressure.

Nigeria has a rich biodiversity and enormous number of indigenous medicinal plants. The practice of traditional medicine has long been in use alongside orthodox medicine but mainly for primary health care. The use of herbal medicine has been reported to be on the increase in many developing and industrialized countries. This new development stems from the fact that these alternative medical services are often affordable and accessible to the vast rural population and therefore serve as

Medicinal Plants with Reported Potential Anti-BPH Activity

Celosia argentea

Celosia argentea F. Cristata(L), commonly called cocks comb or African egg plant, Lagos spinach or "YOKOTO" in (Yoruba) Western Nigeria and "ALAYYAFO" in (Hausa) Northern Nigeria. It is a tender annual herbaceous plant of tropical origin, in the family Amaranthaceae. The leaves and flowers are edible and one of the commonly consumed vegetables in Nigeria. *C. argentea* leaves, seeds, roots and stems are traditionally employed as antipyretic, anti-inflammatory, antioxidant, antidiabetic, antidiarrheal, anti metastatic and antihelminthic. Ethanol extracts of the leaves yielded alkaloids, flavonoids, saponins, glycosides and tannins [11]. In addition, some of the chemical constituents of *C. argentea* include 2-descarboxy-betanidin, 3-methoxytyramine, 4-O-β-D-apifuranosyl-(1→2)-β-D-glucopyranosyl-2-hydroxy-6-methoxyacetophenone, amarantin, betalamic acid, celogenamide A, celogentin, celosian, celosin, cristatatin, dopamine, lyciumin, moroidin, nicotinic acid and (S)-tryptophan [12]. An evaluation of effect of the leaves of *C. argentea* on antioxidant status, PSA and hematological parameters

Ikeyi and Ugwoke forerunner in primary health care. The World Health Organization [6] estimated that four billion people (about 80 percent of the world population) use herbal medicine for some aspect of primary health care. Thus, encourages developing countries to supplement their health care programs with traditional herbal preparations, provided they are proven to be non-toxic [7].

The use of complementary and alternative medicine in the management and treatment of BPH has shown some promises and is gaining popularity. It is estimated that about 30% of men diagnosed of BPH use complementary and alternative medicine [8] [9]. The non-occurrences and limited side effects have made herbal treatment to be safer and cheaper alternatives. Hence, many plants with ethno pharmacological properties have been screened for anti-BPH properties and have produced some encouraging results [10].

in prostatic rats, showed a significant decrease in PSA levels with considerable improvement in prostatic histology. This Study suggests, *C. argentea*-supplemented diet prevented or suppressed the development of BPH in rats [13].

Citrullus lanatus

Citrullus lanatus(Thunb.) var. *lanatus*) commonly called water melon and Kankana in (Hausa) northern Nigeria, is a scrambling and trailing vine, in the annual flowering plant of family Cucurbitaceae. The large fruit is a modified berry called *pepo* with a thick rind (exocarp) and fleshy center (mesocarp and endocarp). Most commonly, the inside can be red or pink, fleshy, juicy and sweet. *C. lanatus* seeds, leaves and rind are commonly used in traditional medicine with increasing acclaimed efficacy. The seeds have both nutritional and pharmacological importance in the management of Diabetes mellitus and Prostate disorders. Phytochemical screening of the seed extracts of *C. lanatus* indicated the presence of steroids, alkaloids, flavonoids, phenols, terpenoids, saponins, anthraquinones, tannins and reducing sugar [14]. It is also rich in proteins and essential amino acids like

arginine, glutamine and aspartic acid, vitamins and minerals such as zinc, vitamins C, B2, riboflavin and essential fatty acids and carbohydrate and thus may contribute to its antioxidant and anti-inflammatory properties [15]. Treatment of experimentally induced BPH in rats with methanol extracts caused a significant decrease in the enlarged prostate- prostates weight, PSA level, seminal vesicle and testes sizes in a dose related manner ($P < 0.05$) compared to the hormone treated control. Histological examination of the prostate revealed significant changes in its histo-architecture with an increase in the fibro muscular layer, decrease in prostatic acini size, shrinkage of epithelium, and no infolding of the epithelium into the lumen, compared to the hormone treated control [16].

Croton membranaceus

Croton membranaceus commonly called Croton or Rushfoil is a perennial plant of the family Euphorbiaceae. It is found in the moist bush vegetation and savannah at low elevations of West tropical Africa -Ghana, Cote d'Ivoire and Nigeria. The plant roots and leaves are used to treat urinary retention caused by an enlarged prostate, measles and to improve food digestion. The root bark contains scopoletin and julocrotine, a glutarimide alkaloid and calcium oxalate crystals [17].

A reduction in prostate gland size, prostate symptoms scores and PSA values have been observed in studies involving men, 40-year-old and above, upon treatment with *C. membranaceus* extracts [18]; [19]. In another study, histological examination in experimentally induced BPH animal models treated with *C. membranaceus* extracts showed reduction of stromal and epithelial cell growth [20].

Cucurbita pepo

Cucurbita pepo (*C. pepo* L. var. *pepo* L. Bailey) commonly called Pumpkin, 'ugboguru' or 'anyu' is one of the most common pumpkins in the eastern part of Nigeria. It is one of the species or varieties of the pumpkin in family Cucurbitaceae. In Nigeria, *C. pepo* is rarely found growing in the wild but cultivated for the edible leaves, stem, fruits, pulp and seeds [21]. Studies have indicated that *C. pepo* seeds

are good alternative sources of proteins, lipids and minerals (Mg, Ca, Zn, P and Fe). In addition to bioactive compounds with ant fatigue, hepatoprotective, anti-diabetes, anticancer, and anti-obesity properties [22]. The seeds and oil from pumpkin seeds are used in traditional medicinal practices for the relief of difficulties associated with an enlarged prostate gland (BPH) and micturition problems related to overactive bladder. In rats experimentally induced with BPH, treatment with pumpkin seeds significantly ($P < 0.05$) inhibited enlarged prostate at high concentrations (10%) of the seed. Studies in individuals with BPH reported pumpkin seeds decreased protein-binding prostate (PBP) levels, weight of ventral prostate size and improved histology of testis [23] and inhibited prostate hyperplasia induced by testosterone, and improved the histology of the prostate [24]. Results from a narrative review showed that the use of pumpkin seeds in the management of patients affected by LUTS-BPH improved the symptoms and their quality of life [25].

Raphia hookeri

Raphia hookeri (G. Mann & H.A. Wendl.) - Raphia palm, West African Wine Palm, Ivory Coast raphia palm, Raphia (En), Ráfia (Fr) is an evergreen monoecious palm tree with an unbranched stem in the family Areaceae/Palmaceae. It is found abundantly in freshwater zone of the Niger Delta, Nigeria. In Africa including Nigeria, India, Malaysia and Singapore, it is generally harvested from the wild and occasionally cultivated. It is one of the most economically useful plants in Africa and a major source of firewood, raffia, piassava fibres, fermented palm wine, starch and oil. The fruit is edible when cooked but poisonous when eaten raw. Studies have shown that mineral composition of Raphia palm exudates include: Calcium, Magnesium, Sodium, Potassium, Manganese, Cobalt and Iron, and anti-nutrients -Hydrocyanic acid, oxalates and Phytic acid [26]. The oily mesocarp of fruit is used in traditional medicine as laxatives, for stomach ache and as liniment for pains [27]; [28]. The seed extract is used in traditional medicinal practice along with other concoctions to

treat symptoms similar to that exhibited in BPH [29]. Studies have shown that ethanol seed extract of *R. hookeri* effectively reduced the size of the enlarged prostate gland, induced in adult male rats and photomicrograph of prostate showed extensive shrinkage of glandular tissue. Thus, the extract attenuated hyperplasia and showed to be good prophylaxis against BPH. [30].

Secamone afzelii

Secamone afzelii is a scandent shrub and climber belonging to the family Asclepiadaceae. It is widespread in Southern Nigeria, West and Central Africa and occurs in secondary forest and savanna thickets. It is also common in abandoned fields and field boundaries, growing in a wide range of climatic conditions particularly in the sun or in light shade [31]. *S. afzelii* contains a high concentration of flavonoids, saponins, reducing sugars, coumarins and the triterpenoid [32]. Its leafy twig infusion is used in treatment of sexually transmitted diseases, diabetes and schistosomiasis [33]. Also, gonorrhoea, cough and catarrh as well as galactagogue [34]. Its leaf extract is used singly and in combination with other herbs to treat BPH. The efficacy of *S. afzelii* leaves used locally to manage BPH showed that the extract caused marked decrease in prostate weight, PSA level, testosterone level, significant decrease of glandular tissue by causing extensive shrinkage of glands and stroma of experimentally induced BPH in rats [35].

Solanum macrocarpon

Solanum macrocarpon L. commonly called African eggplant, 'Igbagba' (yoruba), 'Dauta' (hausa) and 'Anara/ afufa' (igbo) [36], is a tropical perennial plant of the family Solanaceae [37]. In Nigeria, the fruits and leaves are usually eaten raw as vegetables. It is used in traditional medicinal practice in the treatment of anemia, gout, rheumatism, angina, tumors, cancerous tissues and Parkinson's disease. It possesses anti-inflammatory, anti-glaucoma, anti-asthmatic, anti-allergic and anti-viral properties [38] and protective effect against hepatotoxicity [39]. It has bioactive antioxidant agents including flavonoids, phenols, alkaloids, saponins,

tannins, cardiac glycosides and terpenoids [40] [41]. Studies with albino rats induced with BPH showed that PSA levels decreased significantly ($p < 0.05$) in groups fed with *S. macrocarpon* leaves. The histological studies also showed a considerable improvement in the prostatic histo-architecture. Thus, the use of *S. macrocarpon* in the management of disorders associated with inflammation, and its non-toxicity may explain its potentials in the management of BPH [42].

Telfairia occidentalis

Telfairia occidentalis (Hook. f) commonly called fluted gourd, fluted pumpkin, ugu (Igbo), and ikong-ubong (Efik/Ibibio), Iroko (Yoruba), of the family cucurbitaceae is a tropical perennial, vine grown in Nigeria for its edible leafy vegetable and seeds in soups and herbal medicines. The leaves are rich in minerals such as iron, potassium, sodium, phosphorus, calcium and magnesium. It has antioxidants such as thiamine, riboflavin, nicotinamide, ascorbic acid and amino acids such as alanine, aspartate, glycine and leucine and phytochemicals such as tannins, terpenoids, flavanoids and saponins [43]. The seeds are high in protein and fat, and therefore, contribute to a well-balanced diet when boiled and eaten whole, or fermented and added to 'ogili' while the shoots and leaves are consumed as vegetables. It is used to treat sudden attack of convulsion, malaria, and anemia, atherosclerotic cardiovascular disorders, high blood pressure, hyperglycemia, dyslipidemia, arthritis, liver problems and inflammatory conditions [44]. Studies have reported shrinking of enlarged prostate gland and reduction of the associated prostatitis in induced BPH in Wistar rats, treated with the seeds and leaves extracts of *T. occidentalis* [23]. *T. occidentalis* incorporated in a test diet reduced the mass and secretory activity of the enlarged prostate. Thus, *T. occidentalis* could have a positive role to play in the non-surgical management of BPH [10].

Trichosanthes cucumerina

Trichosanthes cucumerina. var. *anguina*, commonly called 'snake gourd/ serpent gourd or long tomato/African snake tomato, is a tropical or subtropical

monoecious annual vine in the family Cucurbitaceae [1]. The shoots, tendrils, and leaves are consumed as greens. The immature fruits are edible but become too bitter to eat as it reaches maturity. However, on maturity, it does contain a reddish pulp that is used in Africa as an economic substitute for tomatoes. The leaves of the plant are used in folklore for headache, alopecia, fever, abdominal tumours, bilious, boils, acute colic, diarrhoea, haematuria, skin allergy, abortifacient, vermifuge, stomachic, refrigerant, purgative, malaria, hydragogue, hemagglutinant, emetic, cathartic, bronchitis and anthelmintic.. The preliminary chemical screening of the aqueous extract revealed the presence of carbohydrates, flavonoids, saponins, flavonolglycoside and triterpenoid, carotenoids, phenolic acids which makes the plant pharmacologically and therapeutically active [23]; [24]. The cucurbitacins and are particularly known in folk medicine for their strong purgative, anti-inflammatory, and hepatoprotective activities thus *T. cucumerina* is used in the treatment of inflammatory conditions. [31]. This may explain the use of *T. cucumerina* in traditional medicinal practice in the management of BPH. Results from a study on the effect of methanol extract of *T. cucumerina* seed on experimentally induced BPH in adult male Wistar rats showed a reversal in seminal vesicles (glandulaevesiculosae) or vesicular glands

CONCLUSION

From the result of this study, it is evident that these plants have some significant anti-BPH activity in animal models. The plant extracts appear to be non-toxic, even at relatively high concentrations. They also contain bioactive and antioxidant agents such as flavonoids, terpenoids, saponins and steroids which contribute to its anti-inflammatory properties and hence its anti-BPH activities.

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Ikeyi and Ugwoke weight [8] and in PSA values after the administration of the extract [19]. In addition, histological studies showed a reversal to the normal state, and reduction in the number of prostatic acini and tubules after administration of the extract [23]. In another study, preliminary results showed that *T.cucumerina* had antiproliferative and aromatase inhibitory effects in the LNCaP cells and H295R cells. Thus, natural compounds present in the *T.cucumerina* may have delayed prostate cancer progression [40].

Zapoteca portoricensis

Zapoteca portoricensis, (Jacq.) H.M. commonly called white stick pea and popularly known as "ELUGELU" in eastern Nigeria is a perennial flowering plants in the legume family Fabaceae. Its roots and leaves contain phytochemical agents of pharmacological importance. The aqueous and alcoholic extracts of the roots and leaves are used traditionally to treat tonsillitis, convulsion, diarrhea and other gastrointestinal disorders. [37] documented that methanol extracts of the roots has an anti-ulcer activity while the antimicrobial potentials of different leaves extracts from the plant have been reported [30]. The terpenoids and steroids obtained from the root extracts have significant anti-inflammatory activity [23]. Thus, traditional use of *Z. portoricensis* root extract in the management of disorders associated with inflammation may explain its use in the management of BPH.

Research must be towards purifications and characterization of the extracts for their chemical and bio-pharmacological activities.

There is the need therefore for clinical trials to confirm the efficacy and effects of these medicinal plants on BPH in humans.

It is hoped that these medicinal plants would serve as a useful tool for the development of novel, safer, potent and cost effective drugs.

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