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Solanum Aculeastrum Dunal Seeds Extracts Attenuates Testosterone Propionate Induced Benign Prostatic Hyperplasia in Male Wistar Rats

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Abstract: *We investigated the effect of n-Hexane extracts of Solanum aculeastrum dunal seeds on testosterone propionate induced BPH in adult male Wistar rats. Finely ground Solanum aculeastrum seeds (1000 g) were extracted with analytical grade n-Hexane. BPH was induced in male Wistar rats weighing 280 ± 20g by injection of 10 mg/kg body weight of Testosterone Propionate for twenty eight days. Thirty six (36) male Wistar rats divided into six (6) groups of six (6) rats each was used. Group 1 served as normal control, group 2 served as BPH control, group 3 served as finasteride control while groups 4, 5 and 6 received 300 mg/kg, 450mg/kg, 600mg/kg body weight respectively of extracts for twenty eight days. All administration was by oral intubations. The animals were sacrificed and blood collected through cardiac puncture. Prostate were excised, weighed and used to determine relative prostate weight. Blood samples were analysed for serum concentrations of prostate specific antigen (PSA), 5-alpha reductase type-2 (5αRD2) and dihydrotestosterone (DHT). Qualitative and quantitative phytochemical analysis showed the presence of alkaloids (0.974 g/100g), saponins (0.236 g/100g), Flavonoids (11.07g/100g), tannins (0.310 g/100g), phenols (0.327 g/100g) and cardiac glycosides (0.0511 g/100g). The result revealed that there were significant dose-dependent decreases in prostate weights, relative prostate weights, serum PSA, 5αRD2 and DHT levels in all the test groups compared to the BPH and finasteride control groups. We conclude that the extracts showed significant anti-BPH and may be safe for use in the management of BPH.*

Keywords: *Solanum acculeastrum, Benign Prostatic Hyperplasis, Testosterone propionate, Finasteride, Wistar rats.*

1. INTRODUCTION

The efficacy of plant materials for therapeutic purposes has been widely reported, making it more acceptable both in developing countries and developed nations. Literature is replete with therapeutic potentials of plant materials, yet a plethora of these plants has remained unexploited. Interest in medicinal plants research has continued to grow because plants could provide leads for designing novel drugs [1].

Benign prostatic hyperplasia is a non-cancerous increase in size of the prostate that progresses linearly with age in all ethnic groups and is clinically identifiable in at least 50 % of men above 45 years old. It is characterized by the proliferation of prostatic tissues, prostate enlargement and lower urinary tract symptoms. It is also associated with complex histological changes involving glandular and stromal hyperplasia, fibrosis and prostatitis. The prostate gland is a major secondary endocrine organ of males whose development and growth depends on androgen stimulation especially by dihydrotestosterone (DHT), an active metabolic product from the conversion of testosterone by steroid 5-alpha-reductase

(SRD5α). It is documented that androgens and possibly estrogens constitute the primary factors responsible for prostate diseases [2]. The hormonal cascade starting by the action of 5-alpha-reductase (5AR) is known to be one of the pathways responsible for the pathogenesis of BPH [3]. BPH is diagnosed by clinical examination, assessment of urination problems, rectal examination, ultrasound examination of prostate and serum level of prostate specific antigen (PSA). The development of BPH can also be determined by measuring prostate weights. Increased relative prostate weight is used as one of the significant markers indicating the development of BPH because BPH is characterized by epithelial and stromal hyperplasia of the prostate, which results in an increase in prostate weight. When the prostate dilates, it results in the constriction of urethral canal, causing partial or complete obstruction. Due to these reasons, many studies have tested the inhibitory effects of many compounds, especially phytochemicals, on the development of BPH by measuring prostate weights. Symptoms include frequent urination, trouble starting to urinate, inability to urinate, weak stream, or loss of bladder control. Complications include urinary tract infections, bladder stones, and chronic kidney problems and these influences the patient's quality of life [4, 5].

Several community-based epidemiological studies have documented varying prevalence of BPH. In developing countries, the prevalence of the disease reaches 86 % by the age of 81 - 90 years old. Ezeanyika *et al*. [6] reported a prevalence of 25.30 % in Nsukka, South-Eastern Nigeria, which is similar to figures from the United Kingdom (25.3 %) and Spain (24.94 %). Adegun and Popoola [7] reported a prevalence of 88 % in Ado-Ekiti, South-West Nigeria, which is comparable to 84.4% in another hospital-based study in Ethiopia [8]. In Port-Harcourt, South-South Nigeria, the prevalence of BPH was 72.2 % using the international prostate symptoms score (IPSS), and 60 % using digital rectal examination [9]. In another study in Odi/Osi Local Government Area, another rural setting in South - West Nigeria, the prevalence rate of 23.7 - 45.3 % per 1000 men was reported [10]. In the US, it is estimated that each year about 1.7 million people visit to hospital is due to manifestations of this disease [11]. It is a significant health care problem due to its high prevalence and the cost associated with its treatment.

Current methods of BPH treatment include the use of hormonal products, androgen antagonists, 5-alpha reductase inhibitors (finasteride), α-1- adrenergic blockers (alfuzosin, doxazosin, tamsulosin and terazosin) and surgery. The 5α-reductase inhibitors inhibit the enlargement of BPH by reducing the production of DHT while the α-1-adrenergic antagonists work by relaxing the smooth muscle in the prostate and the neck of the bladder [12]. These conventional medications are not only too costly but have severe side-effects such as erectile dysfunction, impotence and gynecomastia. The α-1-adrenergic antagonists cause orthostatic hypotension, fatigue, dizziness and abnormal ejaculation. These side effects are due to the drugs structural similarities to steroidal hormones. Additionally, the required long-term drug treatment and surgical treatments are expensive and risky for aged men hence the shift in focus to herbal remedies with less severe or no side effects [13, 14].

Plants and plants derived products that have been reported to show some level of anti-BPH activities. *Pygeum africanum* extracted from the bark of the African plum tree has been used in Europe since 1969 in the treatment of symptomatic BPH [15]. The consumption of tomatoes and tomato products significantly reduced plasma prostate specific antigen (PSA) levels in patients with BPH [16]. The extract of *Urtica dioica* (Urticaceae) roots has been used for the treatment of BPH [17]. Herbal preparations from saw palmetto and cernilton are registered pharmaceutical product in Korea, Western Europe, Japan and Argentina used to improve symptoms of BPH [18]. Also, Herbal remedies from *Saxifraga stolonifera*, *Zi-Shen Pill (ZSP)*, *Orbignya speciosa*, *Phellodendron amurense*, *Ganoderma lucidum*, *Serenoa repens*, *Lepidium meyenii* and *Telfairia occidentalis* extracts have shown some improvements on BPH [19, 20]. However, there is currently no available information on the effects of *Solanum aculeastrum* dunal on the treatment or management of BPH, hence the need to explore these plant materials for possible pharmacological and biochemical influence on the pathology of BPH.

Solanum aculeastrum dunal (Solanaceae) commonly known as *Omotobo* by the *Abagusii* community of Kenya is also known as soda apple or goat bitter apple or poison apple [21]. In Nigeria, the *Efiks*/*Ibibios*, the fourth largest ethnic group in the country, it is commonly referred to as *Nditot Ekpo* or *Nkeŋhe nditot* [22] The species name *aculeastrum* refers to the thorns that adorn most parts of the shrub. It is a shrub or small tree native to tropical Africa down to South Africa. It grows in a wide range of soil terrain and climatic conditions. It occurs naturally in grassland, woodland and in forest margins.

It has also been recorded from gentle to steep slopes on various soil types such as sandy soils, reddish brown clay-loam and brown sandy loam. The petals are white to pale violet and the flower has a bitter, sour smell. At maturity, the fruits or berries are about 4 to 5 cm in diameter, becoming greenish-yellow when ripe [23, 24, 25]. The fruits, both matured and immatured, contain the alkaloid solanine. The leaves and berries of *Solanum aculeastrum* contain mainly straight-chain aliphatic hydrocarbons [26, 27, 28]. Among the *Abagusii* community of Nyamira County of Kenya, the fruits and leaves of *Solanum aculeastrum* are used fresh, dried, boiled, or charred for the treatment of jigger infestations and wounds (*Tungiasis*), swollen joints in fingers, gangrene, toothaches, gonorrhea, bronchitis and rheumatism [21, 26, 27]. They are also used as eyewash. A decoction of the root bark is used in Kenya for the treatment of sexually transmitted bacterial diseases, including gonorrhea as well as acne [21, 29]. The *Efik/Ibibios* of Nigeria use decoction of the ripe berries for the treatment of splenomegaly [22]. Ethnobotanical survey revealed that the berries are used in the treatment of breast cancer [26, 27]. Methanol and aqueous extracts of the berries have been shown to have moderate antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aureginosa* and *Bacillus subtilis* bacteria [25, 28, 30]. The present study investigated the effect of n-hexane extracts of air-dried *Solanum aculeastrum* dunal seeds on testosterone propionate induced BPH.

2. MATERIALS AND METHODS

Plant Materials

Samples of ripe fruit berries of *Solanum aculeastrum* dunal were obtained from locations in Itu Local Government Area of Akwa Ibom State in Nigeria and authenticated by a taxonomist at the Department of Botany, Akwa Ibom State University, Nigeria. The samples were washed under clean gently running tap water to remove dirt on the fruits. Thereafter the fruits were kept for two hours for the water to dry off, a sharp stainless steel knife was used to cut open the fruits, in order to remove the seed. The seeds were freed from the mesocarp and pericarp and air-dried at room temperature (25 ± 2 ^{o}C) until a constant weight was obtained. After drying, the seeds were ground using a desk top grinder (Model No: QBL-18L40, Turinar Corp, Shang-Hai, China) into fine particles and stored in different plastic containers with screw cap.

Figure1. *photos of intact Solanum aculeastrum dunal plant and ripe berries*

Preparation of Extracts

The *Solanum aculeastrum* dunal seeds extracts were prepared using the modified methods of Nidal *et al*. [31]. The finely ground *Solanum aculeastrum* dunal seeds (1000 g) were soaked in 1000 ml n-hexane at room temperature (25 ^{o}C) for 24 hours in a 2000 ml separating funnel with continuous shaking. After

that, the filtrate was obtained by running the tap of the separating funnel. The sample residue in the separating funnel was re-extracted with another 1000 ml n- hexane. The combined filtrate was collected and kept in a labeled pre-weighed volumetric flask at room temperature. The filtrate collected in weighed volumetric flasks was placed in a Büchi rotary evaporator at 40 ^{o}C in order to recover the solvents, and to obtain the crude extracts. The weights of the crude extracts were determined by calculating the difference in the weights. The extracts were kept in different sterile brown bottles and stored at – 4 ^{o}C in the refrigerator.

Phytochemical screening

Qualitative and quantitative phytochemical screening was carried out according to the method

described by Tiwari *et a*l. [32].

Animal Treatment

Thirty six (36) matured male Wistar rats weighing 200 - 280 ± 20.0 g were used in this work. The animals were obtained from the animal house, Biochemistry Department, University of Uyo, Uyo, Akwa Ibom State. The animals were housed in well ventilated cages in the experimental room at a temperature of 25 ± 4 °C and relative humidity of 65 ± 5 % with an alternating 12 hours light and dark cycle for three days to acclimatize. They were allowed access to food (grower's mash from Vital Feeds, Jos, Plateau State, Nigeria) and water *ad libitum.* All animals handling and experiments were carried out in line with the guidelines of institutional animals' ethical committee. Sacrifice of animals was performed under full anaesthesia and the carcasses were properly disposed by burying.

BPH Induction

Adult male Wistar rats weighing 200 - 280 ± 20.0 g were induced with BPH by intraperitoneal injection of testosterone propionate (10 mg/kg body weight) for twenty eight (28) days [33].

Experimental Design

The animals were selected into six (6) groups of six (6) animals each and treatment regimen conducted as shown in Table 1. All treatment lasted for twenty eight (28) days. The animals had free access to feed and water *ad libitum* throughout the period of experiment and their body weights were measured weekly throughout the period of the experiment.

Table1. *Animal Grouping and Treatment*

Group	Name	Treatment
1.	Normal Control (NC)	Normal animals + 0.40 ml Olive oil
2.	BPH Control (BPHC)	BPH induced rats without treatment
3.	Finasteride Control (FinC)	BPH + finasteride (5 mg/kg b. wt.).
4.	Treatment group I	BPH + n-hexane extract (300 mg/kg body wt.).
5.	Treatment group II	BPH + n-hexane extract (450 mg/kg body wt.).
6.	Treatment group III	BPH + n-hexane extract (600 mg/kg body wt.).

Animal Sacrifice and Preparation of Sera for Analysis

All experimental animals were anaesthetized using chloroform fumes 24 hours after the last administration of the extract. Blood samples for sera preparation was collected by cardiac puncture into sterile plain tubes and EDTA (0.77M) bottles for haematological analysis. The liver, kidneys and prostates were harvested from scarified rats, washed with ice-cold saline solution (0.9% w/v), blotted, and weighed. Serum samples were extracted from the clotted blood into sterile plain tubes after centrifugation at 2000 rpm for 10 minutes using a bench top centrifuge (MSE Minor, England). The sera were stored in the refrigerator for analyses while the whole blood samples were used in determining haematological indices.

Drugs and Chemicals

All chemicals and reagents used for this research were of analytical grade and were obtained from Sigma-Aldrich, St. Louis, USA. Testosterone Propionate (TP) was obtained from Tokyo Chemical Industry, Tokyo, Japan.

Assay for PSA, DHT and 5αRD2

The Enzyme-linked immunosorbent assay (ELISA) kits for the estimation of PSA, DHT and 5αRD2 were obtained from Uscn Life Science Inc. Wuhan 430056, Peoples Republic of China were adopted for their estimation following the procedure on the manufacturers' manual.

Relative Prostate Weight

The relative prostate weight (RPW) otherwise called prostatic index or prostate weight to body weight ratio was calculated by dividing prostate weight with that of animal body weight [34].

Statistical Analysis

Statistical analysis was carried out using window SPSS version 23.0. One way analysis of variance (ANOVA) was adopted for comparison and results were subjected to post hoc test using Turkey multiple comparison test. The data were expressed as means ± standard error of the mean (SEM) and values with $p < 0.05$ were considered significant.

3. RESULTS

Phytochemical Screening of n-hexane extracts of *Solanum aculeastrum* dunal seeds

The result of the qualitative and quantitative analyses of n-hexane extracts of *Solanum aculeastrum* dunal seeds is presented in Tables 2 and 3. The results show that alkaloids, saponins, flavonoids, tannin, phenols and cardiac glycosides, were detected (Table 2). Quantitative phytochemical analysis (Table 3) indicates that flavonoids contents (g/100 g) was the highest (11.07), followed by phenols (0.327), tannins (0.310), saponins (0.236), alkaloids (0.0974) and cardiac glycosides (0.0511).

Table2. *Qualitative phytochemical screening of n-hexane extracts of Solanum aculeastrum dunal seeds.*

Phytochemicals	Hexane Extract
Alkaloids	+
Saponins	+
Flavonoids	+
Tannin	+
Phenols	+
Cardiac glycosides	+

+ = Present

Table3. *Quantitative phytochemical screening of n-hexane extracts of Solanum aculeastrum dunal seeds.*

Phytochemicals	Percentage composition (g /100 g)
Alkaloids	0.974
Saponins	0.236
Flavonoids	11.07
Tannins	0.310
Phenols	0.327
Cardiac glycosides	0.0511

Effects of n-hexane extracts of *Solanum aculeastrum* dunal seeds on body weights, organ weights and prostatic index of BPH induced male Wistar rats

The animals exhibited significant weight loss after four weeks of BPH induction. Treatment with the extracts and finasteride resulted in progressive weight. The results indicate that there was a significant ($p < 0.05$) increase in body weights of animals in all the treatment groups compared to the BPH control as well as the normal control groups (Table 4). The results also indicate a significant decrease in liver weights in groups 5 and 6 compared to the BPH control. The results in Table 4 also reveals a significant increase in prostate weight in the BPH control compared to the normal control; and a corresponding significant decrease in prostatic weight in the finasteride treated group as well as treatment group 5 compared to the BPH control. There were also significant decreases in the relative prostate weights (RPW) of all the treatment groups compared to the BPH control.

Effects of n-hexane extracts of *Solanum aculeastrum* dunal seeds on serum PSA, 5αRD2 and DHT concentration of BPH induced male Wistar rats

The results of the effects of n-hexane extracts of *Solanum aculeastrum* dunal seeds on serum PSA, 5αRD2 and DHT concentration of BPH induced male Wistar rats are presented in Table 5. The results show that induction of BPH significantly ($p < 0.05$) increased the serum PSA levels compared to the normal control. In contrast, there were significant dose-dependent decreases in serum PSA levels of all the *Solanum aculeastrum* seeds extracts and finasteride treatment groups compared to the BPH control. The results also show that induction of BPH significantly ($p < 0.05$) increased the serum 5αRD2 and DHT levels compared to the normal control. Again, there were significant dose-dependent decreases in serum 5αRD2 and DHT levels of all the *Solanum aculeastrum* seeds extracts and finasteride treatment groups compared to the BPH control. The decrease in serum 5αRD2 levels in the treatment groups were significant when compared to the finasteride treated group.

Table4. *Effects of n-hexane extracts of Solanum aculeastrum dunal seeds on organ weights and prostatic index of BPH induced male Wistar rats.*

GROUP	GROUP NAME	Body wt. (g)	Liver wt. (g)	Kidney wt. (g)	Prostate wt. (g)	RPW (g)
1	Normal Control	229.67 ± 3.72	6.30 ± 0.37	1.09 ± 0.12	0.35 ± 0.02	0.00150 ± 0.08
2	BPH Control	226.00 ± 1.90	6.74 ± 0.26	1.17 ± 0.09	0.41 ± 0.03[a]	0.00180 ± 0.12[a]
3	BPH + Finasteride	274.00 ± 3.15[a]	6.03 ± 0.28	1.07 ± 0.01	0.35 ± 0.01[b]	0.00129 ± 0.04[b]
4	BPH + n-hexane extract (300mg/kg bd.wt.)	273.20 ± 3.15[a]	6.46 ± 0.26	1.06 ± 0.03	0.38 ± 0.02	0.00141 ± 0.07[b]
5	BPH + n-hexane extract (450mg/kg bd.wt.)	289.50 ± 6.81[ab]	5.36 ± 0.23[ab]	0.99 ± 0.07	0.33 ± 0.02[b]	0.00113 ± 0.07[ab]
6	BPH + n-hexane extract (600mg/kg bd.wt.)	292.00 ± 3.56[ab]	5.55 ± 0.26[b]	1.11 ± 0.09	0.38 ± 0.02	0.00130 ± 0.05[b]

Values are expressed as Mean ± SEM, n = 6

a = $p < 0.05$ (Test groups compared with normal control).

b = $p < 0.05$ (Groups 3, 4, 5 and 6 compared with group 2).

c = $p < 0.05$ (Groups 4, 5 and 6 compared with group 3).

Table5. *Effects of n-hexane extracts of Solanum aculeastrum dunal seeds on serum PSA, 5αRD2 and DHT concentration of BPH induced male Wistar rats.*

GROUP	GROUP NAME	PSA (pg/ml)	5αRD2 (ng/ml)	DHT (ng/ml)
1	Normal Control	0.36 ± 0.03	5.11 ± 0.22	63.92 ± 0.70
2	BPH Control	0.52 ± 0.06[a]	7.31 ± 0.36[a]	82.91 ± 0.91[a]
3	BPH + Finasteride	0.35 ± 0.01[b]	4.92 ± 0.14[b]	66.33 ± 0.77[b]
4	BPH + n-hexane extract (300mg/kg bd.wt.)	0.39 ± 0.02[b]	5.66 ± 0.07[bc]	70.50 ± 1.52[ab]
5	BPH + n-hexane extract (450mg/kg bd.wt.)	0.37 ± 0.02[b]	5.46 ± 0.14[bc]	68.78 ± 2.42[ab]
6	BPH + n-hexane extract (600mg/kg bd.wt.)	0.34 ± 0.06[b]	5.40 ± 0.21[bc]	67.01 ± 1.50[ab]

Values are expressed as Mean ± SEM, n = 6

a = $p < 0.05$ (Test groups compared with normal control).

b = $p < 0.05$ (Groups 3, 4, 5 and 6 compared with group 2).

c = $p < 0.05$ (Groups 4, 5 and 6 compared with group 3)

4. DISCUSSION

Phytochemicals have gained extensive attention because of their numerous therapeutic activities. They exhibit structure related biochemical and pharmacological actions capable of reducing the risk of multiple diseases. Their effectiveness depends on the synergicity and phytochemical load and the yield depends on the effectiveness of the extraction method [35, 36, 37].

The result of the present study indicated that n-hexane extracts of *Solanum aculeastrum* seeds contains alkaloids (0.974 g/100g), saponins (0.236 g/100g), Flavonoids (11.07g/100g), tannins (0.310 g/100g), phenols (0.327 g/100g) and cardiac glycosides (0.0511 g/100g) which could serve as potential source of bioactive agents in herbal medicine (Tables 2 and 3). Phytochemical constituents of medicinal plants possess numerous therapeutic activities. Flavonoids have been utilized to improve human health via their multiple biological functions including anti-inflammatory, antimicrobial, antioxidant, anticancer activities and the prevention of osteoporosis [38, 39]. Alkaloids have been used as an analgesic, antispasmodic or bactericidal agents. They are known to inhibit certain mammalian enzymic activities such as those of phophodiesterase, prolonging the action of cAMP. They also affect glucagons and thyroid stimulating hormones [40, 41, 42]. Saponins have been reported to be useful in reducing inflammation of upper respiratory passage and also chiefly as foaming and emulsifying agents and detergents [43, 44]. Tannins have astringent properties that hasten the healing of wounds and prevention of decay. Tannin compounds have antimicrobial activities and are responsible for preventing and treating urinary tract infections and other bacterial infections [45, 46].

Our investigation reveals that induction of BPH resulted in significant weight loss and treatment with the extracts and finasteride resulted in progressive weight gain overtime. The results indicate that there was a significant ($p < 0.05$) increase in body weights in all the treatment groups compared to the BPH control as well as the normal control (Table 2). The results also indicate a significant decrease in liver weights in groups 5 and 6 compared to the BPH control. The results in table 2 also reveals a significant increase in prostate weight in the BPH control compared to the normal control; and a corresponding significant decrease in prostatic weight in the finasteride group as well as group 5 compared to the BPH control group. There were also significant decreases in the relative prostate weight of all the treatment groups compared to the BPH control. This indicates that the extract might have caused a marked decrease in prostate weight of BPH induced rats comparative to the orthodox drug. Omotosho et al. [5] reported that decrease in prostate weight and relative prostate weight are indicative of BPH amelioration. Therefore, our extract may be effective for treatment of prostate enlargement.

The results of the effects of n-hexane extracts of *Solanum aculeastrum* dunal seeds on serum PSA, 5αRD2 and DHT concentration of BPH induced male Wistar rats are presented in table 3. The results show that induction of BPH significantly ($p < 0.05$) increased the serum PSA levels compared to the normal control. In contrast, there were significant dose-dependent decreases in serum PSA levels of all the treatment groups compared to the BPH control. However, the decrease in the extracts treatment groups were not significant when compared to the finasteride control group. The results also show that, there were significant dose-dependent decreases in serum 5αRD2 and DHT levels of all the treatment groups compared to the BPH control. The decrease in serum 5αRD2 levels in the treatment groups were significant when compared to the finasteride treated group. However, the decrease in serum DHT levels in the treatment groups were not significant when compared to the finasteride treated group.

Serum PSA correlates with prostate volume and is a reliable marker for BPH and prostate cancer. It is and usually elevated in prostate disorders. A decrease in PSA is associated with reduced prostate hyperplasia as a direct consequence of 5α-reductase inhibition or anti-BPH actions [47]. Dihydrotestosterone (DHT) has an important role in the development of BPH. Testosterone, the precursor of DHT, is synthesized in the testes and adrenal glands, and is converted to DHT via the action of the enzyme, 5-alpha reductase which is mainly present in prostate, epididymis, hair follicle, and liver tissue. DHT has substantially greater affinity for androgens receptors (AR) than testosterone does, and binding of DHT to AR in the prostate results in the production of proteins such as PSA as well as regulatory proteins that induce cell proliferation, resulting in BPH [48]. DHT is important for the development of the prostate. However, it is also responsible for the pathologic growth of the prostate. DHT binds to androgen receptors with subsequent modulation of target genes causing BPH and its related cancer [47]. To arrest BPH and the further development of cancer, 5-α-reductase

inhibitors are administered to act as pathologic substrates of the disease, thereby arresting the disease, reducing the prostate volume, and improving symptoms [48]. *Solanum aculeastrum* is rich in a wide variety of phytochemicals - saponins, steroids, alkaloids, flavonoids and phenols which may be responsible for the reduction in PSA level [49, 50]. The mechanism could possibly be through stimulation of androgen receptors within the prostatic stromal cells [13]. These findings are consistent with our earlier observations showing lower prostate weights, thus strongly buttressing that the *Solanum acculeastrum* seed extracts might possess anti-BPH properties.

5. CONCLUSION

Our findings reveal that n-hexane extracts of *Solanum acculeastrum* seeds significantly attenuated BPH in Wistar rats. We conclude that the extracts may be safe for use in the management of BPH. The use of *Solanum acculeastrum* seeds in folk medicine for the treatment of spleenomegaly and other inflammatory conditions are justifiable. Investigations on the hepatotoxicity, nephrotoxicity and genotoxicity of the extracts are on-going in our laboratory.

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ETHICAL APPROVAL

Ethical approval for the study was obtained from Faculty of Biological Sciences Research and Ethics Committee, Akwa Ibom State University.

CONTRIBUTION OF AUTOURS

We declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by the authors. “All authors contributed to the study conception and design. Bright Frank Archibong authenticated the plant material and supervised the phytochemical analysis. Udeme Ededem Okon confirmed the clinical induction of BPH in Wistar rats. Joseph Ubon, Rose Esen and Utibe Evans conducted the biochemical analysis, collected, analyzed and interpreted the data while Joseph Ubon wrote the manuscript. All authors read, corrected and approved the manuscript for publication.

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