Toxicological evaluation of the effects of serial extracts of *Solanum aculeastrum* seeds on testosterone propionate induced benign prostatic hyperplasia in male wistar rats.

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**ABSTRACT**

The effect of serial extracts of *Solanum aculeastrum* seeds on liver, kidney and haematological parameters in Wistar rats induced with Benign Prostatic Hyperplasia (BPH) was investigated. Finely ground *Solanum aculeastrum* seeds (1000 g) were extracted with hexane, chloroform, benzene, ethylacetate and ethanol respectively using serial exhaustive extraction technique. Male Wistar rats weighing 280 ± 20g were injected with 10 mg/kg body weight of Testosterone Propionate through intraperitoneal route for twenty eight days to induce BPH. The animals were divided into eight (8) groups of six (6) rats each. Group 1 (Normal control) was not induced with BPH and served as normal control, group 2 was induced and not treated and served as BPH control, group 3 (Finasteride control) was induced and received standard drug, finasteride while groups 4 (Hexane extract treated group), 5 (Chloroform extract treated group), 6 (Benzene extract treated group), 7 (Ethylacetate extract treated group) and 8 (Ethanol extract treated group) were induced and treated orally with 300 mg/kg body weight of hexane, chloroform, benzene, ethylacetate and ethanol extracts respectively for twenty eight days. The animals were sacrificed and blood collected through cardiac puncture. Biochemical studies were conducted using standard procedures. The results revealed significant (P < 0.05) decreases in serum ALT, AST and ALP activities in all the treated groups compared to the BPH control. The decrease in ALT activity was however not significant compared with the finasteride control whereas the decrease in both AST and ALP activities in all the extracts treated groups were significant compared to the finasteride control. There was no significant (P < 0.05) changes in serum urea concentration but creatinine concentration in the treated groups were significantly reduced when compared to the BPH control and finasteride control. Equally, there were significant increases in RBC, WBC, Hb, LYM and PLT counts in groups 3, 4, 5 and 8 compared to the BPH control. The observed biochemical effects were found to be solvent dependent and compared favourably with the standard drug, finasteride. The results suggest that the serial extracts may be safe for use in medicinal purposes. These findings support the therapeutic use of the fruit berries by the herbalists in treating inflammatory diseases. However, further studies using different doses of each extract should be conducted in order to establish the dose-dependent effects of the extracts.

**Keywords:** *Solanum aculeastrum*, BPH, Finasteride, Liver, Kidney, Haematology

**INTRODUCTION**

Toxicity studies are considered a vital and integral part of drug development considering the fact that herbal medicines are often used erratically without due consideration for the potential adverse effects that could possibly be associated with the use of such herbs (WHO, 1987; WHO, 2000). Plants have been used for medicinal purposes since the beginning of human history and are the basis of modern medicine. The World Health Organization (WHO) estimated that 80% of the world’s population in developing countries depended on plants and traditional medicine practitioners to meet their primary health care needs (WHO, 2002; WHO, 2018). Wild edible plants have always been an important source of therapeutics in traditional folk medicine (Omalu and White, 2011). According to ethnobotanical sources, whole plant extracts contain multiple molecules with activities that could be beneficial to health (Solowy et al., 2014). Also, a variety of local herbs and vegetables are believed to contribute significantly to the improvement of human health, in terms of prevention, and/or cure of diseases (Roberts and Tyler, 1999). Plants are important source of new chemical substances with potential therapeutic effects (Farnsworth, 1989; Akpanabiatu et al., 2006; Edem, 2009a; Akpanabiatu et al., 2012). Consequently, there is an increasing focus on the use of plant bioactive agents as a source of medicine all over the world and a large body of evidence has been accumulated to show their immense potentials in various traditional systems. *Solanum aculeastrum* (Solanaceae) commonly known as *Omotobo* by the Abagusiti community of Kenya is also known as soda apple or goat bitter apple or poison apple (Laban et al., 2015). In Nigeria, the Efiks/Ibibios, the fourth largest ethnic group in the country, it is commonly referred to as *Nditot Ekpo* or *Nkeyhe nditot*. The species name *aculeastrum* refers to the thorns that adorn most parts of the shrub (Kodu et al., 2006b). The fruits, both matured and immatured, contain the alkaloid solanine (Hutchings et al., 1996). The leaves and berries of *Solanum aculeastrum* contain mainly straight-chain aliphatic hydrocarbons.
(Koduru et al., 2006a). Among the Abagusii community of Nyamira County of Kenya, the fruits and leaves of *Solanum aculeastrum* are used fresh, dried, boiled, or charred (ashed) for the treatment of jigger infestations and wounds (*Tungiasis*), swollen joints in fingers, gangrene, toothaches, gonorrhea, bronchitis, rheumatism and in ringworm in cattletes (Koduru et al., 2006a; Koduru et al., 2007a; Laban et al., 2015). They are also used as eyewash (Laban et al., 2015). A decoction of the root bark is used in Kenya for the treatment of sexually transmitted bacterial diseases, including gonorrhea as well as acne (Kokwaro, 2009). The Efik/Ibibios of Nigeria use decoction of the ripe berries for the treatment of splenomegaly (Ubon, 2019). Ethnobotanical survey revealed that the berries are used in the treatment of breast cancer (Koduru et al., 2006a; Koduru et al., 2007a). Methanol and aequous extracts of the berries have been shown to have moderate antimicrobial activity against *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis* bacteria (Wanyonyi et al., 2002; Wanyonyi et al., 2003; Wabwoba et al., 2010). 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 (Iweala and Ogidigo, 2015a). It is characterized by the proliferation of prostatic tissues, prostate enlargement and lower urinary tract symptoms (Briganti et al., 2009). It is also associated with complex histological changes involving glandular and stromal hyperplasia, fibrosis and prostatitis (Chapple and Smith, 1994; Barnes, 2002). 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 (Lee, 2019). Current methods of treatment include the use of hormonal products, androgen antagonists, 5-alpha reductase inhibitors (finasteride), α-1 adrenergic blockers (alfuzosin and terazosin) and surgery (Gravas and Oelke, 2010; Iweala and Ogidigo, 2015b). However, in aged people, there can be associated underlying conditions, thus surgical intervention cannot be performed in all cases. Some of these conventional medications are not only too costly but can cause severe side-effects such as erectile dysfunction and gynecomastia due to its structural similarities to steroidal hormones hence the shift in focus to herbal remedies (Rankin et al., 2006; Ezeanyika et al., 2006; Berhanu, 2008; Adegun and Popoola, 2011; Ngalie et al., 2019; Madersbacher et al., 2019). Several community-based epidemiological studies have documented varying prevalence of BPH in both developing and developed countries with rates reaching 86 % by the age of 81 - 90 years old (Wei et al., 2005; Ezeyuenike et al., 2006; Berhanu, 2008; Adegun and Popoola, 2011; Bock-Oruma, 2013; Ojewola et al., 2017). It is a significant health care problem due to its high prevalence and the cost associated with its treatment. The increased demand for herbal products coupled with the erroneous impression by the people that herbal products are natural and thus less harmful to the body have raise concerns and fear over the quality, efficiency and safety of some of herbal remedies (Rankin et al., 2006; Sharif et al., 2013). There have been confirmed cases of renal failure and liver diseases associated with herbal medicine consumption in some country Nigeria inclusive (Calixto, 2000 and Etuk et al., 2009). It is therefore necessary to investigate the safety of serial extracts of *solanum aculeastrum* seeds in relation to its therapeutic application in the treatment of Testosterone Propionate induced Benign Prostatic Hyperplasia (BPH) in Wistar rats. This work shall investigate the subacute effects of the extract with special attention to liver, kidney and haematological parameters of the experimental rats model.

II. MATERIALS AND METHODS

Collection of 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 between November, 2017 and January 2018, and authenticated by a taxonomist at the Department of Botany and Ecological Studies, University of Uyo, Uyo, Nigeria. A voucher specimen with number ‘Ubon, UUH 2687 ‘Itu’ was deposited in the herbarium of the University of Uyo, Uyo, Nigeria. The samples were washed under clean gently running tap water to remove dirt on the fruits. After the fruits were kept for 2 hrs 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 °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.

Preparation of Extracts

The *Solanum aculeastrum* seeds extracts were prepared through serial exhaustive extraction technique using the modified methods of Nidal et al. (2015), Pandey and Tripathi (2014) and Azmir et al. (2013). The finely ground *Solanum aculeastrum* Dunal seeds (1000 g) were soaked in 1000 ml n-hexane at 25 °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-weighted volumetric flask at room temperature. The residue was air-dried and the process of extraction was repeated as described four more times with chloroform, n-benzene, ethylacetate and finally with ethanol. The filtrates of each solvent extraction was collected and kept in labeled weighed volumetric flasks at room temperature. The different filtrates collected in weighed volumetric flasks were separately placed in a Büchi rotary evaporator at 40 °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 °C in the refrigerator.

Animal Treatment

Forty eight (48) matured male Wistar rats weighing 180 - 200 ± 3.0 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.
Experimental Design

The animals were weighed and randomly selected into eight (8) groups of six (6) animals each. Beningn prostatic hyperplasia was induced by intraperitoneal injection of testosterone propionate (10 mg/kg body weight) for twenty eight (28) days (Ejike and Ezeaniya, 2011; Iweala and Ogídipo, 2015b; Mbaka et al., 2017; Cai et al., 2018). Finasteride (Proscar®), a 5-a reductase inhibitor, was purchased from Amela Pharmacy, 34 Nwaniba Road, Uyo; Akwa Ibom State and was used as the standard anti-BPH drug, for twenty eight days.

Group 1 were normal animals fed with grower’s mash and water ad libitum alongside with 0.40 ml olive oil administered orally throughout the experimental period. Group 2 were given 10 mg/kg body weight of Testosterone Propionate (TP) intraperitoneally for twenty eight days without any form of treatment afterwards. Group 3 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.30 ml of Finasteride orally for another twenty eight (28) days. Group 4 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.40 ml of the hexane extract orally for another twenty eight (28) days. Group 5 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.50 ml of the chloroform extract orally for another twenty eight (28) days. Group 6 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.50 ml of the n-benzene extract orally for another twenty eight (28) days. Group 7 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.54 ml of the ethylacetate extract orally for another twenty eight (28) days. Group 8 were given 10 mg/kg body weight of Testosterone propionate (TP) intraperitoneally for twenty eight (28) days and thereafter treated with 0.60 ml of the ethanol extract orally for another 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.

<table>
<thead>
<tr>
<th>Group</th>
<th>Name</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Normal Control</td>
<td>Normal animals + 0.40 ml Olive oil</td>
</tr>
<tr>
<td>2</td>
<td>BPH Control</td>
<td>BPH induced rats without treatment</td>
</tr>
<tr>
<td>3</td>
<td>Finasteride Control</td>
<td>BPH + finasteride (5 mg/kg b. wt.).</td>
</tr>
<tr>
<td>4</td>
<td>Hexane Extract Treated</td>
<td>BPH + hexane extract (300 mg/kg body wt.).</td>
</tr>
<tr>
<td>5</td>
<td>Chloroform Extract Treated</td>
<td>BPH + chloroform extract (300 mg/kg body wt.).</td>
</tr>
<tr>
<td>6</td>
<td>Benzene Extract Treated</td>
<td>BPH + n-benzene extract (300 mg/kg body wt.).</td>
</tr>
<tr>
<td>7</td>
<td>Ethylacetate Extract Treated</td>
<td>BPH + ethylacetate extract (300 mg/kg body wt.).</td>
</tr>
<tr>
<td>8</td>
<td>Ethanol Extract Treated</td>
<td>BPH + ethanol extract (300 mg/kg body wt.).</td>
</tr>
</tbody>
</table>

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. All animals handling and experiments were carried out in line with the guidelines of institutional animals’ ethical committee as approved by the Post-Graduate School, University of Uyo, Nigeria. Sacrifice of animals was performed under full anaesthesia and the carcasses were properly disposed by burying.

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.
Determination of Biochemical and hematological parameters

The serum levels of AST, ALT, ALP, BUN and creatinine were estimated using standard laboratory assay kits obtained from Randox Laboratories Ltd. 55 Diamond Road, Crumlin, County Antrim, UK. Full blood counts (FBC) was determined according to the method described by Jain (1986) using sysmex® automated haematology analyzer, KX- 21n (non- cyanide haemoglobin analysis method), Sysmex corporation, Kobe - Japan.

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.

III. RESULTS

Effects of serial extract of Solanum aculeastrum seeds on serum ALT, AST and ALP activities of testosterone propionate induced BPH in male Wistar rats

The results of the effects of serial extracts of Solanum aculeastrum seeds on the liver function enzymes of BPH induced male Wistar rats are presented in Table 2. The results indicate that induction of BPH resulted in a significant (p < 0.05) increase in serum ALT, AST and ALP activity of the BPH control compared to the normal control. However, treatment with serial extracts of Solanum aculeastrum seeds and the standard drug, finasteride resulted in significant (P < 0.05) decreases in ALT, AST and ALP activities in all the treated groups compared to the BPH control. The decrease in ALT activity was however not significant compared with the finasteride control. In contrast, the decrease in both AST and ALP activities in all the extracts treated groups were significant compared to the finasteride control.

Effects of serial extract of Solanum aculeastrum seeds on serum urea and creatinine levels of testosterone propionate induced BPH in male Wistar rats

The oral administration of serial extracts of Solanum aculeastrum seeds to BPH induced male Wistar rats was associated with changes in some kidney biochemical parameters (Table 3). The data showed that induction of BPH in rats resulted in a significant (p < 0.05) decrease in serum urea and creatinine concentrations compared to the normal control. Treatment with serial extracts of Solanum aculeastrum seeds and finasteride produced no significant (P < 0.05) changes in serum urea concentration but the creatinine concentration in both the extracts and finasteride treated groups were significantly reduced when compared to the BPH control. These decreases in the extracts treated groups were also significant compared to the finasteride control group.

Table 2. Effects of Serial Extracts of Solanum aculeastrum seeds on Liver Function Enzymes Activity of BPH induced male Wistar rats.

<table>
<thead>
<tr>
<th>GROUP NAME</th>
<th>ALT (U/L)</th>
<th>AST (U/L)</th>
<th>ALP (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Control</td>
<td>6.42 ± 0.17</td>
<td>20.13 ± 1.07</td>
<td>260.65 ± 2.59</td>
</tr>
<tr>
<td>BPH Control</td>
<td>8.73 ± 0.30a</td>
<td>323.00 ± 0.78a</td>
<td>323.00 ± 8.59a</td>
</tr>
<tr>
<td>BPH + Finasteride</td>
<td>5.68 ± 0.49ab</td>
<td>210.00 ± 0.64ab</td>
<td>22.00 ± 3.67ab</td>
</tr>
<tr>
<td>BPH + Hexane Extract</td>
<td>6.16 ± 0.32b</td>
<td>266.00 ± 0.74ab</td>
<td>18.00 ± 3.97bc</td>
</tr>
<tr>
<td>BPH + Chloroform Extract</td>
<td>6.20 ± 0.14b</td>
<td>252.00 ± 0.71bc</td>
<td>38.00 ± 3.66abc</td>
</tr>
<tr>
<td>BPH + Benzene Extract</td>
<td>5.53 ± 0.39b</td>
<td>256.00 ± 10.05ab</td>
<td>12.38abc</td>
</tr>
<tr>
<td>BPH + Ethyl acetate Extract</td>
<td>6.05 ± 0.42b</td>
<td>247.00 ± 97.00a ± 0.52abdef</td>
<td>02 ± 7.42abc</td>
</tr>
<tr>
<td>BPH + Ethanol Extract</td>
<td>6.30 ± 0.22b</td>
<td>280.00 ± 30.00 ± 0.71cdg</td>
<td>9.46acefg</td>
</tr>
</tbody>
</table>
Values are expressed as Mean ± SEM, n = 6 ; a = Test groups compared with normal control; b = Groups 3, 4, 5, 6, 7 and 8 compared with group 2; c = Groups 4, 5, 6, 7 and 8 compared with group 3; d = Test groups compared with group 4; e = Test groups compared with group 5; f = Test groups compared with group 6; g = Test groups compared with group 7.

Table 3. Effects of serial extracts of Solanum aculeastrum seeds on kidney function parameters of BPH induced male Wistar rats.

<table>
<thead>
<tr>
<th>GRO UP</th>
<th>GROUP NAME</th>
<th>UR EA (mol/L)</th>
<th>UR NINE (μmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Normal Control</td>
<td>5.0</td>
<td>238.5 ± 0.07</td>
</tr>
<tr>
<td>2.</td>
<td>BPH Control</td>
<td>4.5</td>
<td>222.88 ± 0.12</td>
</tr>
<tr>
<td>3.</td>
<td>BPH + Finasteride</td>
<td>4.3</td>
<td>162.36 ± 0.07</td>
</tr>
<tr>
<td>4.</td>
<td>BPH + Hexane Extract</td>
<td>4.5</td>
<td>93.40 ± 0.17</td>
</tr>
<tr>
<td>5.</td>
<td>BPH + Chloroform Extract</td>
<td>4.4</td>
<td>91.17 ± 0.15</td>
</tr>
<tr>
<td>6.</td>
<td>BPH + Benzene Extract</td>
<td>4.8</td>
<td>87.28 ± 0.11</td>
</tr>
<tr>
<td>7.</td>
<td>BPH + Ethyl acetate</td>
<td>4.8</td>
<td>84.50 ± 0.11</td>
</tr>
<tr>
<td>8.</td>
<td>BPH + Ethanol Extract</td>
<td>4.4</td>
<td>105.26 ± 0.12</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM, n = 6; a = Test groups compared with normal control; b = Groups 3, 4, 5, 6, 7 and 8 compared with group 2; c = Groups 4, 5, 6, 7 and 8 compared with group 3; d = Test groups compared with group 4; e = Test groups compared with group 5; f = Test groups compared with group 6; g = Test groups compared with group 7.

Effects of serial extract of Solanum aculeastrum seeds on haematological indices of testosterone propionate induced BPH in male Wistar rats

The results presented in Table 4 reveals that the induction of BPH in rats resulted in significant increases in WBC and LYM counts and significant decreases in Hb, HCT and PLAT counts compared to the normal control. Treatment with finasteride resulted in significant increases in WBC, RBC, Hb, LYM and PLAT counts compared to the normal control. In the same vein, treatment with Solanum aculeastrum seeds extracts resulted in significant increases in WBC, RBC, Hb, MCV, LYM and PLAT counts compared to the BPH control. However when compared to the finasteride control, there were significant increases in WBC in groups 3 and 7; RBC in group 8; HCT, MCV and MCHC in groups 6, 7 and 8.
In our study, the significant increases in serum ALT, AST and ALP activities in rats treated with serial extracts of *Solanum aculeastrum* (et al., 2006). The results of our study revealed significant decreases in serum AST, ALT and ALP activities in rats treated with serial extracts of *Solanum aculeastrum* seeds. A similar trend was also observed in the finasteride-control group. These suggest that the extracts were most likely safe and the liver impairments likely induced male Wistar rats.

### Table 4: Effects of serial extracts of *Solanum aculeastrum* dunal seeds on haematological indices of BPH induced male Wistar rats.

<table>
<thead>
<tr>
<th>R</th>
<th>BC</th>
<th>BC</th>
<th>b</th>
<th>CT</th>
<th>CV</th>
<th>CH</th>
<th>CH</th>
</tr>
</thead>
<tbody>
<tr>
<td>O</td>
<td>x10^3/μL</td>
<td>x10^6/μL</td>
<td>g/dL</td>
<td>%</td>
<td>mL</td>
<td>pg</td>
<td>(g/L)</td>
</tr>
<tr>
<td>U</td>
<td>P</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>2.80 ± 1.35</td>
<td>.66 ± 0.27</td>
<td>5.72</td>
<td>7.47</td>
<td>0.53 ± 0.30</td>
<td>6.50</td>
<td>7.27 ± 0.37</td>
</tr>
<tr>
<td>P</td>
<td>4.43 ± 0.43a</td>
<td>.29 ± 0.29</td>
<td>4.28</td>
<td>2.40</td>
<td>0.73 ± 1.01</td>
<td>6.65</td>
<td>7.40 ± 0.32</td>
</tr>
<tr>
<td>H</td>
<td>0.44a</td>
<td>0.46a</td>
<td>1.51</td>
<td>2.80</td>
<td>4.28</td>
<td>6.52</td>
<td>0.60ab</td>
</tr>
<tr>
<td>C</td>
<td>8.38 ± 1.56ab</td>
<td>.92 ± 0.11b</td>
<td>5.78</td>
<td>4.48</td>
<td>1.68 ± 0.48</td>
<td>6.98</td>
<td>7.55 ± 0.35</td>
</tr>
<tr>
<td>C</td>
<td>5.18 ± 0.25b</td>
<td>.90 ± 0.83</td>
<td>5.60</td>
<td>3.74</td>
<td>1.14 ± 1.12</td>
<td>6.88</td>
<td>7.62 ± 0.23</td>
</tr>
<tr>
<td>E</td>
<td>0.27ac</td>
<td>0.17b</td>
<td>0.32b</td>
<td>1.11</td>
<td></td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>E</td>
<td>4.52 ± 0.18ac</td>
<td>.08 ± 0.24b</td>
<td>5.62</td>
<td>3.90</td>
<td>9.36 ± 1.20c</td>
<td>7.00</td>
<td>8.58 ± 0.70</td>
</tr>
<tr>
<td>E</td>
<td>0.70b</td>
<td>1.75</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.71</td>
</tr>
<tr>
<td>E</td>
<td>7.77 ± 0.56ab</td>
<td>.70 ± 0.22</td>
<td>4.77</td>
<td>0.25</td>
<td>8.35 ± 0.18ab</td>
<td>6.30</td>
<td>7.87 ± 0.30</td>
</tr>
<tr>
<td>G</td>
<td>e</td>
<td>0.28</td>
<td>1.66a</td>
<td>1.14</td>
<td></td>
<td></td>
<td>0.17</td>
</tr>
<tr>
<td>a</td>
<td>5.35 ± 1.11ac</td>
<td>.83 ± 0.10</td>
<td>4.52</td>
<td>0.28</td>
<td>6.52 ± 0.60ab</td>
<td>6.60</td>
<td>9.38 ± 0.47</td>
</tr>
<tr>
<td>E</td>
<td>0.14a</td>
<td>0.28a</td>
<td>0.07</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>G</td>
<td>1.90ab</td>
<td>±0.24</td>
<td>5.65</td>
<td>3.85</td>
<td>7.15 ± 0.89ab</td>
<td>6.52</td>
<td>8.80 ± 0.47</td>
</tr>
<tr>
<td>G</td>
<td>e</td>
<td>abc</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.10</td>
</tr>
</tbody>
</table>

Values are expressed as Mean ± SEM, n = 6; a = Test groups compared with normal control; b = Groups 3, 4, 5, 6 and 7 and 8 red with group 2; c = Groups 4, 5, 6, 7 and 8 compared with group 3; d = Test groups compared with group 4; e = Test groups compared with group 5; f = Test groups compared with group 6; g = Test groups compared with group 7;NC = Normal Control; BPHC = Benign Prostatic Hyperplasia Control; FinC = Finasteride Control; HETG = Hexane Extract Treated Group; CETG = Chloroform Extract Treated Group; BETG = Benzene Extract Treated Group; EaETG = Ethyl acetate Extract Treated Group; OHETG = Ethanol Extract Treated Group.

### IV. DISCUSSION

Renal and hepatic function analyses are very useful for the screening of the toxicity of drugs and plant extracts, as both are important for the survival of an organism (Olorunnisola et al., 2012). Liver is a vital organ actively involved in many metabolic and biochemical processes, and is the target for many toxins (Meyer and Kulkarni, 2011). Hepatic damages are linked to alterations in the metabolic functions of this organ (Wolf, 1999). In our study, the significant increases in serum ALT, AST and ALP activities in the BPH control compared to the normal control suggests the likelihood that the induction of BPH caused cell membrane damage in the liver (Table 2). However, increased ALP activity is needed during stress to produce adequate amount of phosphate groups for oxidative phosphorylation leading to ATP generation. This in turn, is required for the phosphorylation of some biomolecules, such as ethanolamine and choline to form phosphatidyl ethanolamine and choline, which are vital to the stability of cellular plasma membrane (Adebayo et al., 2006). The results of our study revealed significant decreases in serum AST, ALT and ALP activities in rats treated with serial extracts of *Solanum aculeastrum* seeds.
caused by BPH induction may have been attenuated by the serial extracts of Solanum aculeastrum seeds. This corroborate the findings of Adesina et al. (2019) who reported a decreasing trend in serum liver enzymes activities in rats administered with ethyl acetate and petroleum ether extracts of Bridelia micrantha and Mitracarpus villosus.

Serum urea, creatinine and electrolytes concentration as well as histological examination of the organ, are considered as markers of renal dysfunction (Imo et al., 2018). Nephrotoxicity is indicated by significant elevation in serum level of urea and creatinine (Imo and Uhegbu, 2015; Imo et al., 2019). Serum urea level differs directly with protein intake and inversely with the rate of excretion (Adesina et al., 2019). Creatinine is the waste product formed in the muscles by its metabolism and is synthesized in the liver, passes into the circulation and is taken up almost entirely by the skeletal muscles (Sottas et al., 2013). An increase in serum creatinine reflects the extent of tubular necrosis (Solez, 1982). The decrease in serum urea and creatinine levels in this study indicates a possible neproprotective property of serial extracts of Solanum aculeastrum seeds (Table 3). The possible mechanisms could be due to their potent antioxidant property, inhibition of lipid peroxidation in renal tissues, prevention of protein and nucleic acid degradation as well as anti-inflammatory actions (Madhan et al., 2016). Moreover, neproprotective activity may be attributed to the presence of biologically active compounds such as flavonoids, saponins, tannins and terpenoids (Palani et al., 2009, Gulpaz et al., 2010 and Pathan et al., 2013). The lack of adverse effect of serial extracts of Solanum aculeastrum seeds on renal function indices in rats may suggest that the typical functioning of the nephrons at the glomeruli level was not affected. This is consistent with the findings of Tanuja et al. (2016). Haematological studies provide information on various infections, necrosis of visceral organs and the presence of stress factors. They provide important clinical data on states of infections, malignancies and immune derangements hence: they play critical roles in the diagnosis, prognosis and management of various diseases and disorders (Saunders et al., 2001; Lawal et al., 2015). The results of this study revealed that induction of BPH in rats resulted in significant increases in WBC and LYM counts and significant decreases in Hb, HCT and PLAT counts compared to the normal control (Table 4). Treatment with finasteride resulted in significant increases in WBC, RBC, Hb, LYM and PLAT counts compared to the normal control. Similarly, treatment with Solanum aculeastrum seeds extracts resulted in significant increases in WBC, RBC, Hb, MCV, LYM and PLAT counts compared to the BPH control and normal control. Red blood cell are major indices for evaluating circulatory erythrocytes and are significant in the diagnosis of anaemia and also serve as useful indices of the bone marrow capacity to produce RBC (Peters et al., 2011; Ozkan et al., 2012). The significant increase in RBC and Hb following oral administration of Solanum aculeastrum seeds extracts is an indication of erythropoiesis stimulation by the extract. The extract may have increased the rate of erythropoetin release in the kidney, which is the humoral regulator of RBC production (Mishra and Tandon, 2012). Infection or acute stress causes a rise in WBC count. However, the significant increase in the WBC and LYM counts observed in the treatment with Solanum aculeastrum seeds extracts may be a reflection of the leukopoietic and possible immunomodulatory effects of the extracts which augmented the production of more WBC and LYM (Bashir et al., 2015). This is capable of increasing the animal’s capability of generating antibodies in the process of phagocytosis, a high degree of resistance to diseases; enhance adaptability to local environmental and disease prevalent conditions (Okunlola et al., 2012). The significant decrease in PLT count observed in the BPH control may be an indication of anti-thrombopoetin activity, meaning that the blood clotting mechanism of the animals may have been compromised with consequent effects of high loss of blood in case of injury (Lawal et al., 2015). However, treatment with Solanum aculeastrum seeds extracts showed significant improvements in most of the hematological parameters compared to the BPH control and finasteride control groups. The result of this study agrees with earlier findings by Berinyuy et al. (2015).

V. CONCLUSION

The findings of this study revealed that consecutive intraperitoneal injection of testosterone propionate for twenty eight days in rats caused significant increases and untoward effects in the levels of liver, kidney and haematological parameters. These effects were significantly attenuated by all the serial extracts of Solanum aculeastrum seeds. Therefore, our findings may suggest that the extracts were largely non-toxic, and may be safe for use in the management of BPH. However, further studies using different doses of each extract should be conducted in order to establish the dose-dependent effects of the extracts. Investigations on the genotoxicity and reproductive toxicity of the extracts are also recommended.

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VII. DECLARATION OF CONFLICTING INTEREST

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