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

JOSEPH ANNA UBON[1*], MONDAY ISAIAH AKPANABIATU[2], JUSTINA IME UDOTONG[3] and UDEME EDEDEM OKON[4]

[1*]Research Scholar [2]Professor of Biochemistry [3]Senior Lecturer [4]Research Scholar

[1*] Department of Biochemistry, Faculty of Basic Medical Sciences, College of Health Sciences, University of Uyo, Akwa Ibom State, P.M.B. 1017, Uyo, Akwa Ibom State, Nigeria.

[2]Department of Biochemistry, Faculty of Science, University of Uyo, Akwa Ibom State, P.M.B. 1017, Uyo, Akwa Ibom State, Nigeria.

[3]Department of Biochemistry, Faculty of Science, University of Uyo, Akwa Ibom State, P.M.B. 1017, Uyo, Akwa Ibom State, Nigeria.

[4]Department of Clinical Biochemistry, Faculty of Natural and Applied Sciences, Michael Okpara University of Agriculture, Umudike, Abia State, P.M.B. 7267, Umuahia, Abia State, Nigeria.

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 acculeastrum*, 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 medical 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 (Olaku and White, 2011). According to ethno-botanical sources, whole plant extracts contain multiple molecules with activities that could be beneficial to health (Solowey *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 *Abagusii* 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 *Nkeŋhe nditot*. The species name *aculeastrum* refers to the thorns that adorn most parts of the shrub (Koduru *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 cattles (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 aqueous extracts of the berries have been shown to have moderate antimicrobial activity against *Staphylococcus aureus, Escherichia coli, Pseudomonas aureginosa* 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 with less severe or no side effects (Vaughan *et al*., 2002; Forley and Kirby, 2003; Saigal and Joyce, 2005; Chinedu *et al*., 2011; Nyamai *et al*., 2016; Ngulde *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; Ezeanyika *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 has raise concerns and fear over the quality, efficiency and safety of some of herbal remedies (Rankin *et al* ., 2002; 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 ^{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.

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 ^{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 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 ^{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.

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 Ezeanyika, 2011; Iweala and Ogidipo, 2015b; Mbaka *et al*., 2017; Cai *et al*., 2018). Finasteride (Proscar®), a 5- α 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 I 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 1: Animal Grouping and Treatment

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

GROUP	GROUP NAME	ALT (U/L)	AST (U/L)	ALP (U/L)
1.	Normal Control	6.42 ± 0.17	20.13 ± 1.07	260.65 ± 2.59
2.	BPH Control	8.73 ± 0.30a	21.00 ± 0.78a	323.38 ± 8.59a
3.	BPH + Finasteride	5.68 ± 0.49ab	16.33 ± 0.64ab	210.22 ± 3.67ab
4.	BPH + Hexane Extract	6.16 ± 0.32b	17.72 ± 0.74ab	266.18 ± 3.97bc
5.	BPH + Chloroform Extract	6.20 ± 0.14b	19.16 ± 0.71bc	252.38 ± 3.66abc
6.	BPH + Benzene Extract	6.53 ± 0.39b	17.10 ± 0.59ab	256.99 ± 12.38abc
7.	BPH + Ethyl acetate Extract	6.05 ± 0.42b	14.97 ± 0.55abdef	247.02 ± 7.42abc
8.	BPH + Ethanol Extract	6.30 ± 0.22b	20.30 ± 0.71cdfg	280.60 ± 9.46acefg

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.

GROUP	GROUP NAME	UREA (mmol/L)	CREATININE (µmol/L)
1.	Normal Control	5.01 ± 0.07	238.51 ± 8.81
2.	BPH Control	4.59 ± 0.12a	222.88 ± 7.11a
3.	BPH + Finasteride	4.33 ± 0.07a	162.36 ± 8.97ab
4.	BPH + Hexane Extract	4.56 ± 0.17a	93.40 ± 1.69abc
5.	BPH + Chloroform Extract	4.48 ± 0.15a	91.17 ± 4.74abc
6.	BPH + Benzene Extract	4.87 ± 0.11ce	87.28 ± 1.63abc
7.	BPH + Ethyl acetate Extract	4.89 ± 0.11ce	84.50 ± 0.98abc
8.	BPH + Ethanol Extract	4.48 ± 0.12afg	105.26 ± 2.67abcefg

Values are expressed as Mean ± SEM, n = 6; a = Test groups compared with normal control; b= Groups 3, 4, 5, 6, 7 and 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.

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

ROUP	BC x10^3/µL)	BC x10^6/µL)	b g/dL)	HCT (%)	CV fL)	CH pg)	CH (g/)
C	2.80 ± 1.35	.66 ± 0.27	5.72 ± 0.43	7.47 ± 2.10	0.53 ± 0.30	6.50 ± 0.28	7.27 0.37
PHC	4.43 ± 0.44a	.29 ± 0.29	4.28 ± 0.46a	2.40 ± 1.51a	0.73 ± 1.01	6.65 ± 0.22	7.40 0.32
inC	8.38 ± 1.56ab	.92 ± 0.11b	5.78 ± 0.25b	4.48 ± 0.83	1.68 ± 0.48	6.98 ± 0.19	7.55 0.35
ETG	5.18 ± 0.27ac	.90 ± 0.17b	5.60 ± 0.32b	3.74 ± 1.11	1.14 ± 1.12	6.88 ± 0.25	7.62 0.23
ETG	4.52 ± 0.18ac	.08 ± 0.24b	5.62 ± 0.70b	3.90 ± 1.75	9.36 ± 1.20c	7.00 ± 0.71	8.58 0.70
ETG	7.77 ± 0.56abe	.70 ± 0.22	4.77 ± 0.28	0.25 ± 1.66ac	8.35 ± 0.18abc	6.30 ± 0.17	7.87 0.30
aETG	5.35 ± 1.11ac	.83 ± 0.10	4.52 ± 0.14a	0.28 ± 0.28ac	6.52 ± 0.60abc	6.60 ± 0.07	9.38 0.47
HETG	7.53 ± 1.40abe	.72 ±0.24abc	5.65 ± 0.24b	3.85 ± 1.34	7.15 ± 0.89abc	6.52 ± 0.10	8.80 0.47

Values are expressed as Mean ± SEM, n = 6; a = Test groups compared with normal control; b = Groups 3, 4, 5, 6, 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 mpared 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. 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

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, nephroprotective activity may be attributed to the presence of biologically active compounds such as flavonoids, saponins, tannins and terpenoids (Palani *et al*., 2009, Gulnaz *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 erythropoietin 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 following the treatment with *Solanum aculeastrum* seeds extracts may be a reflection of the leucopoetic 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 phagocytocis, 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 consequents 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 acculeastrum* 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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