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Hypolipidemic and Antioxidants Properties of Methanol Leaf Extract of *Laportea aestuans* on Androgen-Induced Benign Prostatic Hyperplasia in Wistar Rats

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of article.

Abstract

Background: Benign prostate hyperplasia (BPH) is an age-related disease characterized by enlargement of the prostate gland and its associated complications.
Objectives: Phytochemicals responsible for hypolipidemic and antioxidants effects of leaf extract of *Laportea aestuans* in androgen-induced BPH Wistar rats were evaluated.
Methods: Thirty (30) male Wistar rats were divided into five groups of 6 rats each. BPH was induced by subcutaneous injection of dihydrotestosterone (DHT) and estradiol-valerate (10:1) daily for 28 days. The diseased control and drug control groups were given subcutaneous olive oil and oral finasteride (5 mg/kg.bw) respectively after induction of BPH. Rats in the test groups were given 50 and 100 mg/kg.bw of the extract orally for 28 days respectively, following disease induction. The lethal dose LD_{50} and antioxidants activity of plant extracts, lipid profile and prostate specific antigen (PSA) level of the rats were assayed using standard biochemical tests.
Results: Secondary metabolites detected were alkaloids (20.11±0.07 mg/kg), tannins (1.32±0.21), and saponins (11.41±0.14). PSA level was significantly decreased ($P<0.05$) when compared with the diseased control. The lipid profile assay revealed a significant ($P<0.05$) reduction in Triacylglycerol (62%), Cholesterol (27%) and low density lipoprotein (LDL) (19%) but high density lipoprotein cholesterol (HDL-C) concentration increased by 41%. The extracts also improved SOD (26%), catalase (38%) and reduced glutathione (36%) levels but reduced malondialdehyde (MDA) level by 28%.
Conclusion: These findings therefore provide a scientific evidence for the traditional use of *L. aestuans* in the management of complications associated with BPH which could be a function of the various phytochemicals detected in the plant.

Keywords: Antioxidant, Benign prostatic hyperplasia, Androgen, *Laportea aestuans* lipid profile

INTRODUCTION

There is an increasing interest in herbal medicine which may be due to the rise in cases of drug resistance, cost and several side effects associated with most orthodox drugs (Akomas *et al.*, 2014), and as such more wild plants are being studied. As more people come to adopt traditional herbal medicine as an alternative health care system, there is need to scrutinize the different plants use in the treatment, management and prevention of disease, especially the chronic diseases for the purpose of validating local claims on their activities.

Benign prostatic hyperplasia (BPH) is an age-related disease characterized by enlargement of the prostate with alterations in tissue histomorphology (Lee *et al*., 2012). In BPH, the prostate gland is enlarged due to increase in stromal and epithelial cellular counts leading to many health challenges in elderly men such as urinary retention, recurring urinary tract infection, urinary irritation, and possibly bladder stones (Iscaife *et al*.,2018). Factors such as excessive androgen hormones, old age and dietary lifestyle are recognized underground causes of the disease. Androgen hormones play key roles in the development of this pathological condition, although not all cases manifest with increased level of these hormones in patients. Thus the androgen hormone cannot be said to be the root cause of BPH development.

The aromatase enzyme and 5-alpha reductase is responsible for the conversion of androgens to estrogen and dihydrotestosterone (Ho and Habib, 2011). As a result, testosterone levels decreases but its metabolites (estrogen and dihydrotestosterone) increases. Dihydrotestosterone attached locally to androgen receptors in the cell nuclei, and signals the transcription of growth factors that are dangerous to the epithelial and stromal cells (Bartsch, *et al*., 2002), this effect can cause prostate hyperplasia. Therefore when the prostate muscle is weak, there is accumulation of fluid due poor excretion which causes further damages to the myofibrous tissue of the muscle (Wang-Michelitsch and Michelitsch, 2015). Because of non-proliferation of the muscle cells, collagen fibers try to repair and fill the damaged tissue which results to poor tissue function. This defective cycle of progressive muscle tissue fibrosis and fluid accumulation are the major causes of prostate enlargement in benign prostate hyperplasia (Wang-Michelitsch and Michelitsch, 2015).

The study of antioxidant chemistry has become of importance because of the production of excess free radicals by oxidation reactions which can start chain reactions that destroy cells which could result to various disease conditions such as cancer stroke, Parkinson's disease, atherosclerosis amongst others. Antioxidants agents quench free radicals and their intermediates thereby inhibiting the free radicals chain reactions. Polyphenols, thiols, superoxide dismutase, glutathione, catalase are some of the examples of antioxidant agents. Free radicals are mostly generated during oxidative respiration due to mitochondria leakage of unpaired oxygen specie, which in turn cause a chain of reactions that result in cellular damage. Antioxidants thereby act by eliminating this chain of reactions by quenching free radical intermediates, stopping further oxidation reactions in the process (Lawal *et al*. 2016).

The specie *L. aestuans*, is a native of western India and belong to the family *Utricaceae*. It is synonymous with *Fleurya aestuans* (Linn) and *Fleurya aestuans* Gaud. They appear as a weed and in new cultivations. It is 1.5 m long and widespread in the African and Asians tropics. The leaf is used traditionally as laxatives, pain-killer and stomach troubles. The crushed stem is employed as anti-inflammatory agent. The leaf and flower parts are used in medicine to cure diarrhea and dysentery (Elujoba *et al*., 2005). Although information on the pharmacological activities of the plant remains inadequate, it is now known that its essential oil contains methyl salicylate and has significant antioxidant and antimicrobial effects (Oloyede and Ayanbadejo, 2014). Essiet *et al*., (2011) also reported that concoction of the root and leaf is taken for the treatment of poison. This study was therefore designed to evaluate the hypolipidemic and antioxidant effects of leaf extract of *L. aestuans* in androgen induced prostate hyperplastic rats.

METHODOLOGY

Collection and Preparation of plant sample

Leaves of *Laportea aestuans* were collected from Ikwuano Local Government Area of Abia State. Plant

samples were authenticated by taxonomist in the herbarium section of the Department of Forestry and Environmental Management, Michael Okpara University of Agriculture Umudike (MOUAU). Voucher specimen number (MOUAU/FEM/BCH/054) was kept in the herbarium of the Department for referral. The samples were properly washed, cut into pieces, shade dried to a constant weight and processed into fine powder using a laboratory sized electric blender. The resulting powder was transferred into an airtight container and stored at room temperature until use. 100 g of the *L. aestuans* as macerated in a 250 mL of methanol for 48 hours and filtered with Whatman No. 1 filter paper. Then the filtrate was evaporated to dryness at 45ºC using water bath to obtain the crude extract.

Phytochemical screening

The crude methanol extract obtained was used to test for the presence of the following plant secondary metabolites; alkaloids, flavonoids, steroids, saponins, phenols, tannins, glycosides, anthraquinones, carbohydrates, resin and cardiac glycosides (Harborne, 1998)

Animals

Thirty adult albino male rats (120-160 g) obtained from the Animal house of the University of Nigeria, Nsukka were used. All rats were housed at 25°C in stainless steel cages under normal daylight/dark cycle and humid tropical condition and were fed with standard rat feed, with water *ad libitum* but starved for 12 hr prior to the commencement of experiment.

Acute toxicity studies

This study was done to determine the median lethal dose (LD_{50}) of the methanol extract of *L .aestuans*. A total of 15 albino rats of both sexes were used for the study following the methods of Chinedu *et al.,* (2013). The LD_{50} was calculated using the formula; $LD50 = (Mo + M1) \div 2$

Where: M_0 = highest dose that gave no mortality. M_1 = lowest dose that gave mortality.

Induction of Benign Prostatic Hyperplasia

The animals were fasted for 12 hours (with free access to water) and BPH was induced using a mixture of Dihydrotestosterone (DHT) and Estradiol valerate (ratio 10:1) following the methods of Ejike and Ezeanyika, (2011). Dose for induction of BPH was formulated as 9 mg/kg body weight of DHT and 0.9 mg/kg body weight estradiol valerate given by subcutaneous injection every other day for 28 days. Stock was prepared by dissolving 1g of DHT and 0.1 g Estradiol valerate in 100 ml of olive oil.

Experimental Design

A complete randomized experimental design comprising of five treatment groups replicated thrice with each replicate having three rats was used for the study. All administration after induction of BPH was done orally for duration of 28 days as follows: Group I: Normal; received distilled water orally and labeled NC. Group II: BPH disease control; received olive oil (1 ml/kg) and labeled HC. Group III: BPH; received finasteride (5 mg/kg) and labeled DC. Group IV: BPH; received 50 mg/kg.bwt of *L. aestuans* extract and Group V: BPH; received 100 mg/kg.bw of *L. aestuans* extract. The sublethal dosage used for this study was obtain by dividing the LD_{50} (5000 mg/kg) by a factor (100) for the initial dose and subsequent dose was doubled. After 28 days, the rats starved overnight were sacrificed the next day by cervical dislocation and the blood samples of the respective rats were collected by cardiac puncture into sample bottle. The blood was collected by cardiac puncture into a sterile plain tube without anticoagulant for lipid profile, PSA and antioxidant enzymes assay.

Lipid Profile Studies

A portion of each blood sample was centrifuged at 1200 rpm for 5 minutes at room temperature to collect plasma which was used to estimate total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triglycerides (TAG) using commercial kits obtained from Randox Laboratories, UK

Determination of Prostate Specific Antigen

After anesthetizing the rats, blood samples were collected from their hearts and sent to an associate laboratory to evaluate free prostate specific antigen (PSA) in the blood using the PSA enzyme-linked immunosorbent assay (ELISA) kit (BioCheck Inc., USA) by strictly following manufacturer's instructions. The value was expressed in nano grams per ml (ηg/ml) of serum.

Determination of antioxidants biomakers

The Superoxide dismutase (SOD) was determined by the method of Zou *et al*., (1986). One unit of SOD activity was defined as the quantity of SOD required to inhibit 50% of protien and expressed as mg/100 g. The activity of catalase (CAT) was analyed according to the method of Greenwald (1985) using

H_2O_2 as substrate. The enzyme was measured following the dissappearance of H_20_2 at 570 nm and expressed as mole of H_20_2 consumed/min/mg protein. Glutathione (GSH) level was determined by the procedure of Ellaman (1959). The activity was expressed as mole NADPH consumed/min/mg protein. Malondialdehyde (MDA) was measured spectrophotometrically at 535nm and expressed as µmol/mL

RESULTS

Table 1 showed the phytochemical composition of *L. aestuans* .The result showed that the extract of *L. aestuans* leaves has high concentration of alkaloid, saponin and flavonoid.

Table 1: Photochemical constituent of methanol extract of the leaves of *L. aestuans*

Phytochemicals (mg/100 g)	Conc. ± SD
Alkaloid	20.11±0.07
Flavonoid	16.72±0.07
Tanin	1.32 ± 0.21
Saponin	11.41± 0.14
Phytate	3.07 ± 0.14
Crude glycoside	5.52 ± 0.21
Oxalate	0.49 ± 0.14

Table 2 showed the result for the LD_{50} of the extract on rats. *L. aestuans* extract was not toxic because no mortality and behavioral sign of toxicity was recorded at the highest dose of 5000 mg/kg except for loss of appetite

Table 2: Result of LD_{50} of the Methanol extract of *Laportea aestuans* leaves

	Dose(mg/kg)	No. of animals	Mortality/sign of toxicity
Stage1	200	1	0
	600	1	0
	800	1	0
	1000	1	0
Stage	1500	1	0
	2000	1	0
	3000	1	0
Stage3	3500	1	0
	4000	1	0
	5000	1	0

The results of mean body weight of animals treated with leaf extract of *L. aestuans* are showed in **Table 3.** The mean body weight of the animals treated with 100 mg/kg. bw of *L. aestuans* extract had less significant gain ($p<0.05$) in weight after 28 days of treatment compared with the normal control.

Table 3: Effect of Methanol extract of *L. aestuans* on body weight changes

Treatment	Initial Weight (G)	Final Weight (G)	%Weight Gain/Loss
Normal control	91.6 ± 7.67	136.3 ± 16.3	32.8^{c}
Disease control	106.6 ± 0.42	144.5 ±22.1	26.2^{b}
Drug control	113.1 ± 2.4	150.8 ±26.6	25.0^{ab}
50 mg/kg *L.aestuans*	120.8 ± 1.1	170.5 ±13.3	29.1^{bc}

Mean with different superscript (a-b-c) are significantly different at ($P<0.05$) along the columns.

Result of relative organ weight of experimental animals represented in **Table 4** showed no significant (P<0.05) difference in relative weight of liver, heart, and kidney of all the experimental animals. However, the relative prostate weight in disease control increased significantly (P<0.05) when compared with other experimental groups.

Table 4: Effect of methanol extract of *L. aestuans* leaf on relative organ weight of rats

Treatment	Heart	Kidney	Liver	Prostate
Normal control	0.58 ± 0.05[a]	1.15 ± 0.29[a]	5.71 ± 0.8 [a]	0.39 ± 0.11[c]
Drug control	0.53 ± 0.09[a]	1.11 ±0.08[a]	5.8 ± 0.77 [a]	0.43 ± 0.16[b]
Disease control	0.56 ± 0.08[a]	1.14 ±0.14[a]	5.78 ± 0.3 [a]	0.71 ± 0.08 [a]
50mg/kg*L. aestuans*	0.57 ± 0.09[a]	1.14 ± 0.08[a]	5.65 ± 0.5 [a]	0.48 ± 0.09[b]
100mg/kg*L.aestuans*	0.58 ± 0.08[a]	1.12 ±0.04[a]	5.71 ± 0.72[a]	0.46 ± 0.04[b]

N = 4 animals, mean with different superscript (a-b-c) are significantly different at (P<0.05) along the columns.

Figure 1 showed a significant decrease (p<0.05) in serum Cholesterol, triglycerides and LDL-C, in groups administered the plant extract when compared with the diseased control group. HDL-C level in the treatment groups increased significantly (P<0.05)

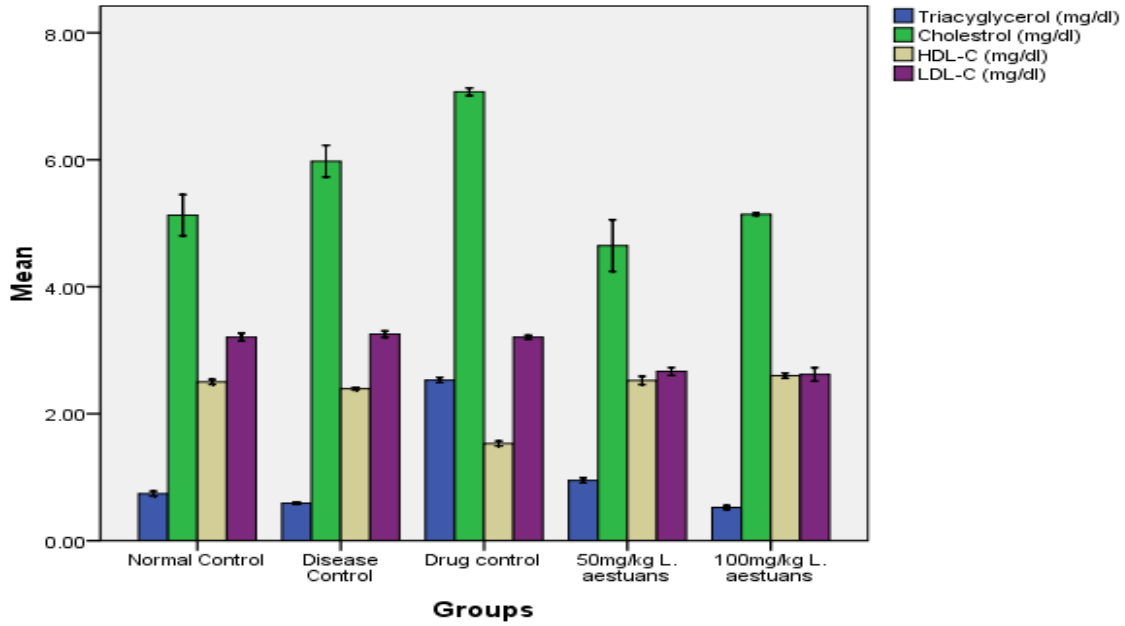

Figure 1: Effect of methanol extract of *Laportea aestuans* leaf on lipid profile of rats

The result in **Figure 2** showed a significant (P< 0.05) increase in PSA in diseased control group. Administration of the plant extract showed marked decreased in PSA level when compared with the diseased group.

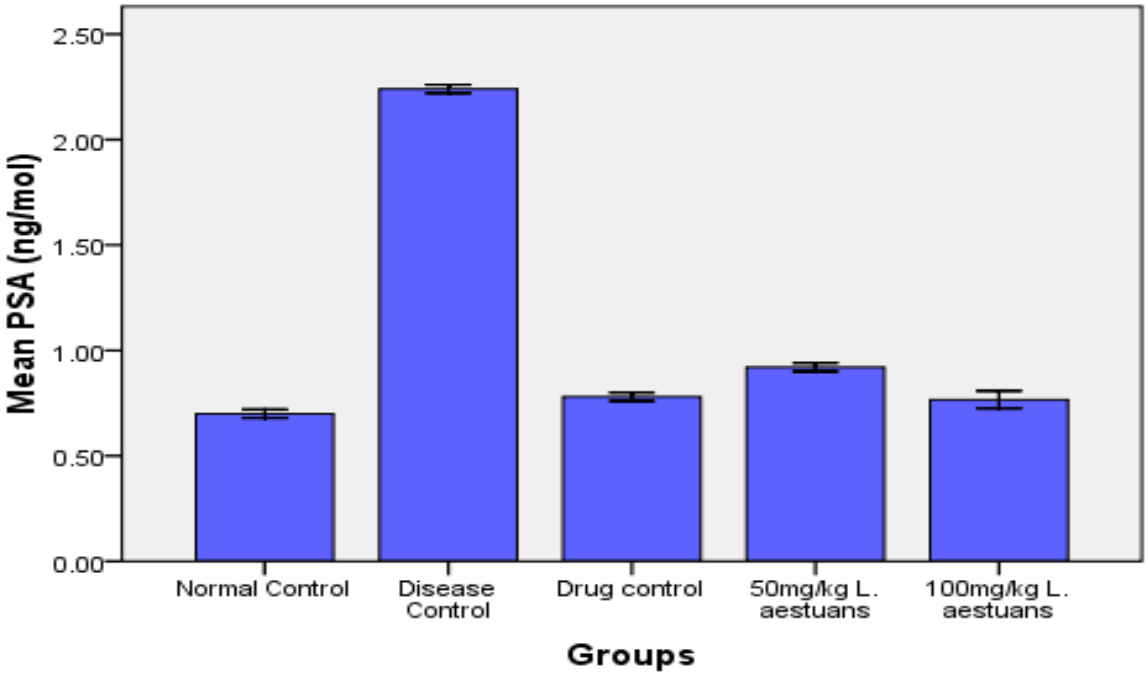

Figure 2: Effect of methanol extract of *L. aestuans* leaf on PSA level of rats

The antioxidant effect of the methanol extract of *L. aestuans* is shown on **Table 5**. Results revealed a significant ($p < 0.05$) increase in SOD, CAT and GSH level and decrease in MDA concentrations in the treatment groups when compared with the diseased control group

Table 5: Effect of methanol extract of *L.aestuans* on Antioxidant properties in rats

Groups	SOD (mg/dl)	CAT(mg/dl)	GSH(mg/dl)	MDA (mol/mL)
Normal control	11.18 ±0.23^{c}	2.83 ± 0.09^{bc}	5.42 ±0.340^{c}	10.20 ±0.3^{d}
Disease control	8.36 ±0.45^{a}	2.12 ±0.27^{a}	3.56 ±0.42^{a}	19.98± 0.25^{a}
Drug control	11.38 ±0.18^{c}	3.10 ±0.24^{c}	4.80 ±0.18^{b}	12.20±0.75^{b}
50 mg/kg.bwt	10.56 ±0.21^{b}	2.74 ± 0.28^{b}	4.35 ± 0.29^{b}	15.05± 0.53^{c}
100 mg/kg.bwt	11.30 ±0.16^{c}	3.46±0.83^{d}	5.61 ± 0.30^{c}	14.30± 0.30^{c}

Values with different superscripts are significantly ($p < 0.05$) different N = 4 animals.

DISCUSSION

There is an established correlation between the use of medicinal plants and decrease incidence of disease. This is possible because of the presence of natural antioxidants and phytochemicals such as alkaloids, flavonoid, saponins and taninns contain in these plants which have been reported to have various pharmacological effects (Iweala and Ogidigo, 2015). This study showed that the plant *L. aestuans* contain large concentration of phytochemicals that have pharmacological properties. The result is in agreement with the result of Omotosho *et al*., (2018) that also reported high concentrations of these compounds in *L. aestuans* leaves. It is therefore possible that the leaves of *L. aestuans* may possess active substances which scavenge the free radicals of protein glycation, oxidative degeneration and exerts hypolipidemic effects. `

To study the safety or toxicity of plant extract, evaluation of biomarkers of organs integrity is very important because it gives an insight on the adequate diagnostic and prognostic information as well as pathological condition of animals exposed to the text substance (Lawal *et al*., 2014). In the present study, there was no observed mortality observed at the dose of 5000 mg/kg.bw. This shows that *L. aestuans* could be generally regarded as safe (GRAS). This finding is

in agreement with Umar *et al*., (2019), who reported that any compound or drug with oral LD_{50} estimates greater than 1000 mg/kg body weight could be considered to be of low toxicity and safe.

Prostatic hyperplasia is a high-prevalence urinary tract disease in elderly men. Testosterone induces hyperplasia in simple epithelial cells by causing frequent inflammation of the epithelial cells over time, which leads emergency urination with frequent urination and poor urine flow (Iscaife *et al*., 2018). In this study, a significant increase ($P<0.05$) was observed in prostate weight in the diseased group when compared with the normal and other treatment groups which could be due to growth in the quantity of cellular numbers in the prostate tissue. This result is in line with the findings of Wang and Olomi, (2011) that also reported increase in prostate weight in BPH conditions. Thus, increased prostate weight is used as one of crucial markers of BPH according to previous studies (Bisson *et al*.,2007). Also, Ugwu, *et al*., (2018) has proven that administration of the aqueous extract of *Vernonia amygdalina* to rats induced with BPH has protective effects against the development of BPH as seen in the reduction of prostate weight.

The result of the PSA level shows a significant ($P<0.05$) reduction in the groups treated with different doses of *L. aestuans* leaves when compared with the diseased control group. Serum PSA correlates with prostate volume, and men with large prostates and high serum PSA are at higher risk of showing significant symptoms which including progression to acute urinary retention, lower urinary tract symptoms and nocturia (Roehrborn, 2011). A decrease in PSA is linked to a reduction in prostatic hyperplasia due to inhibition of 5α-reductase, an enzyme that convert testosterone to dihydrotestosterone (DHT) which has been implicated in the development of BPH (Ho and Habib, 2011). There is strong evidence that phytochemicals agents are effective inhibitors of 5α-reductase that consequently leads to reduction in DHT concentrations and slows down BPH proliferation (Ejike and Ezeanyika, 2011)

Hypercholesteromia and hypertriglyceridemia have been reported to occur in BPH condition (Kosova *et al*., 2014). This study showed a significant ($P<0.05$) decrease in LDL-C, triglycerides and total cholesterol. However, there was a significant increase in HDL-C in the test groups when compared with the BPH induced group without treatment ($P < 0.05$). This is in agreement with the findings of Omotosho *et al*., (2018) that reported significant reduction in LDL-C, triglycerides and cholesterol in rats treated with *L. aestueans* leaves. LDL-C is known as a factor in coronary occlusion. On the contrary, HDL-C is protective cholesterol and is responsible for transportation of cholesterol from peripheral tissues to the liver and other tissues. The effects of *L. aestuans* on the lipid components means that it can be assumed a potential hypolipidemic agent, which will be a great advantage in BPH conditions

The result of the study shows that there was significant increase ($P<0.5$) in SOD, catalase and reduced GSH following administration of the extract when compared with the diseased control rats. Apart from the function of the 5-alpha reductase enzyme, oxidative stress plays an important role in the development of prostatic hyperplasia (Gupta-Elera *et al*., 2012). Oxidative stress is caused by an imbalance between antioxidants and reactive oxygen species (ROS) which increases the active radicals thus decreasing the efficient functioning of body's immune system (Khandrika *et al*., 2009). In the present study, oxidative stress was observed in the diseased group without treatment evidenced by decreased level of SOD, GSH and catalase. Endogenous testosterone is converted to DTH in prostate stromal cells which is far more active than testosterone and causes changes in androgen receptor cells on the surface of epithelial cells, which alters DNA transcription causing mitochondrial leakage and free radical production.

Glutathione protects the cell by reducing the level of free radicals while superoxide dismutase (SOD) is an enzyme that also exhibit antioxidant role. Therefore, by lowering the level of these enzymes, the body cells are more likely to be damaged by active radicals (Ahmed *et al*., 2019). High levels of nitrate radicals have also been found in prostatic hyperplasia which confirms the important role of antioxidants in the fighting against the disease (Arsova-Sarafinovska *et al*., 2009).This extract is rich in saponins, tannins, alkaloids, flavonoid and other phytochemical contents which have antioxidant and anticancer characteristics. It is therefore reasonable to attribute the medicinal activities of this plant to the combined effects of these phytochemicals and other bioactive components contained in the plant.

CONCLUSION

Alkaloids, tannins, saponins and flavonoids were the major secondary plant metabolites found in *L. aestuans*. The study demonstrated the hypolipidemic effect of *L. aestuans* by reducing the levels of total cholesterol, triglycerides, LDL-C and also antioxidant properties. It also revealed its ability to reduce the PSA level and prostate weight of androgen induced begin prostatic hyperplasia. These combined effects can subsequently play a vital role in preventing the incidences of premature occurrence of BPH.

ETHICAL APPROVAL

Ethical approval for the study (MOUAU/EC/21/029) was obtained from the MOUAU Committee on Animal Use and Care. All investigations were conducted in accordance with the accepted principles for laboratory animal use and care (NRC, 2011).

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REFERENCES

Ahmed, Amar, S.A., Eryilmaz, R., Demir, H., Aykan, S., Demir, C. (2019). Determination of oxidative stress levels and some antioxidant enzyme activities in prostate cancer. *Aging Male* 22(3):198–206

Akomas, S.C., Okafor, A.I., Ijioma, S.N. (2014). Hypoglycemic, Hematologic and Hypolipdemic activity of *Mucuna pruriens* ethanol leaf extract in alloxan diabetic rats. *Annual Research and Review in Biology*; 4(24): 4284-4292

Arsova-Sarafinovska, Z., Eken, A., Matevska, N., Erdem, O., Sayal, A., Savaser, A *et al.* (2009). Increased oxidative/nitrosative stress and decreased antioxidant enzyme activities in prostate cancer. *ClinBiochem* 42(12):1228–1235

Bartsch, G., Rittmaster, R., and Klocker, H. (2002) Dihydrotestosteron und die Rolle der 5α-Reduktasehemmerbei der benignen Prostata hyperplasie.*DerUrologeA*; 41(5):412–424

Bisson, J.F., Hidalgo, S., Rozan, P and Messaoudi, M. (2007) Therapeutic effect of ACTICOA powder, a cocoa polyphenolic extract on experimentally induced prostate hyperplasia in Wistar-Unilever rats. *Journal of Medicinal Food*, 10:628-635.

Chinedu E., Arome, D. and Ameh F. S. (2013).A New Method for Determining Acute Toxicity in Animal Models. *Toxicological International*, 20(3):224-226

Ejike, C.E.C.C and Ezeanyika, L.U.S. (2011). Management of experimental benign prostatic hyperplasia in rats using food-based therapy containing *Telfairia occidentalis* seeds. *Afri.J.Tradit Complement Altern Med:* 8(4); 398-404

Elujoba, A. A., Odeleye, O. M and Ogunyemi, C. M. (2005)Traditional medical development for medical and dental primary health care delivery system in Africa. *African journal of Traditional Complement and Alternative Medicine*. 2:46-61

Ellman. G. L. (1959) Tissue sulfhydryl groups. Archives of Biochemistry and Biophysics, 82:70- 77

Essiet,U A., Edet, N.I and Bala, D. N.(2011) "Phytochemical and physiochemical analysis of the leaves of *Laportea aestuans*(Linn) Chew and *Laportea aestuans*(Schumach) Chew (male and female)", *Asian Journal of Plant Science and Research,* 1(2):PP: 35 – 42.

Greenwald, R.A (1985) CRC Handbook of Methods for oxygen Radical Research. *CRC Press*. Boca Raton, ISBN-13: 9780849329364, PP: 267-278

Gupta-Elera, G., Garrett, A.R, Robison, R.A. and O'Neill, K. L (2012) The role of oxidative stress in prostate cancer. *European Journal of Cancer Prev* 21(2):155–162

Harborne, J.B., (1998). Phytochemical Methods-A Guide to Modern Techniques of Plant Analysis. *Chapman and Hall, London*, pp: 182-190.

Ho, C.K and Habib, F.K (2011). Estrogen and androgen signaling in the pathogenesis of BPH. *Nat Rev Urol*8(1):29

Iscaife, A., Anjos, G., Barbosa, N. C., Nahas, W.C., Srougi, M. and Antunes, A. A. (2018) The role of bladder diverticula in the prevalence of acute urinary retention in patients with BPH who are candidates to surgery. *International Brazilian journal of Urology*, 44(4):765–770

Iweala, E.E.J. and Ogidigo, J.O. (2015). Prostate Specific antigen, antioxidant and hematological parameters in prostatic rats fed *Solanum macrocarpon* L. leaves. *Asia journal of biological sciences*; 8(1); 30-41

Khandrika, L., Kumar, B., Koul, S., Maroni, P and Koul, H. K (2009) Oxidative stressin prostate cancer. *Cancer Letters* 282(2):125–136

Kosova, F., Temeltaş, G., Arı, Z. and Lekili, M. (2014). Possible relations between oxidative damage and apoptosis in benign prostate hyperplasia and prostate cancer patients. *Tumor Biology* 35(5):4295–4299

Lawal, B., Oluwatosin, K. Shittu., Florence, I. Oibiokpa., Eustace, B. Berinyuy. andHadiza Mohammed. (2016) African natural products with potential antioxidants and hepatoprotective properties: a review. *Clinical Phytoscience* (2016); 2:23

Lawal, B., Ossai, P.C., Shittu, O. K and Abubakar, A.N. (2014).Evaluation of phytochemicals, proximate, minerals and anti-nutritional compositions of yam peel, maize chaff and bean coat. *International Journal of Applied Biological Research*, 6(2), 01-17.

Lee, M.-Y., Shin, I.-S., Seo, C.-S., Lee, N.-H., Ha, H.-K., Son, J.-K., and Shin, H.-K. (2012). Effects of *Melandrium firmumm* ethanolic extract on testosterone-induced benign prostatic hyperplasia in Wistar rats.*Asian Journal of Andrology*, 14(2), 320–324.

NRC (2011). Guide for the Care and Use of Laboratory Animals. Eighth Edition, Committee for the Update of the Guide for the Care and Use of Laboratory Animals, Institute for Laboratory Animal Research, National Research Council (NRC), The National Academic Press, Washington DC, USA.

Oloyede, G. K. and Ayanbadejo, O. E. (2014) Phytochemical, toxicity, antimicrobial and antioxidant screening of extracts obtained from Laportea aestuans (Gaud). *Journal of medical science*, 14(2)51-59

Omotosho Omolola E, Oladipupo O.Ogunlade and Biodun O Salako(2018) Phytochemical screening and antioxidant parameters data in prostatic rats fed with *Laportea aestuans* leaves *Elsevier Inc*2352-3409

Roehrborn, C. G. (2011) Male lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). *Med. Clinical. North America*., 95: 87–100.

Ugwu, M. N., Mgbekem, M.A and Eteng, M. U. (2018) Effect of Aqueous extract of *Vernonia amygdalina*on biochemical indices of prostate functions in hormonal induced enlarged prostate in rats. *Journal of Complementary and Alternative MedicalResearch*,6(1):1-12.

Umar, I. S., Yusuf, A.A., Alawode, A.R., Obiekezie, C. I, Okunlola, B.M., Abdulrazaq, O.M, Ariyeloye, S.D and Lawal, B. (2019). Phytochemical compositions and biochemical effect of *Phyllanthus amarus* in albino rat. *GSC Biological and Pharmaceutical Sciences*, 8(1), 128-133.

Wang, Z, and Olumi, A.F (2011) Diabetes, growth hormone-insulin-like growth factor pathways and association to benign prostatic hyperplasia. *Differentiation*; 82(4–5):261–271

Wang-Michelitsch, J and Michelitsch, T.M (2015) Tissue fibrosis: a principal proof for the central role of Misrepair in aging. arXiv preprint

Zou, Guolin, GuiXingfen, Zhong Xiaoling, *et al.* (1986) Improvements in pyrogallol autoxidation method for the determination of SOD activity. *Prog BiochemBiophys*, 13(4):71

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