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EFFECT OF *CEIBA PENTANDRA* ON SOME BIOCHEMICAL INDICES OF RATS INDUCED BPH

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ABSTRACT

This study assessed the Anti-benign prostatic hyperplasia and biochemical effect of ethanolic extracts of *Ceiba pentandra* in rat model. Thirty-six (36) BPH induced Male rats were divided into six (6) groups of six rats each. Rats in group one served as normal control and were given rat feed only, Group two (BPH disease Control group), were administered testosterone propionate subcutaneously [3mg/kg b.w], Rats in group three in addition to testosterone propionate (3mg/kg body weight), were administered finasteride (1mg/kg b.w) orally, rats in groups four, five and six, in addition to rats feeds and testosterone propionate were given 2000mg/Kg, 1000mg/Kg and 500mg/Kg body weight extract of *Ceiba Pentandra* (CP) respectively. The rats were anaesthetized after treatment period. Blood samples were collected and serum harvested for analyses using standard methods. The oral administration of *C. pentandra* leaves extracts to testosterone induced BPH rats significantly reduced the serum PSA and cretinine concentration in a seemingly dose dependent manner compared to BPHC. The AST and ALP of HD and MD treated groups were considerably reduced compared to BPH control. It is apparent that *Ceiba pentandra* could attenuate some biochemical parameters in rats induced BPH thereby capable of ameliorating BPH in Wistar rat model.

KEYWORDS: *Ceiba pentandra*; Benign Prostatic Hyperplasia; biochemical parameters; testosterone; prostate specific antigen; liver enzyme.

1.0 INTRODUCTION

Benign prostatic hyperplasia (BPH) is a common condition in elderly Men; it is a progressive noncancerous enlargement of the epithelial cells and smooth muscle of the prostate gland accompanied by lower urinary tract symptoms (Pearson and Kashiefi 2008). BPH and kidney infection are fundamental maladies of maturing Men. Study has shown that in Nigeria, one-in-four men above the age of 40 years have symptoms suggestive of BPH (Ezeanyika *et al*., 2006). If allowed without treatment, BPH may gradually result in bladder dysfunction and ultimately lead to acute urinary retention, sepsis, toxemia and finally death (Roehrborn *et al*., 2008).

According to Kellogg (2007), the only sure way to curtail or arrest BPH development is to hold back the growth pathways of the prostate mediated by androgen by carrying out surgery or medication. Presently, various treatment options that have been adopted include: the use of drugs that have the efficacy of improving the free flow of urine (alpha blockers: *Alfuzosin, Doxazosin, Tamsulosine* and *Terazocine*d), and drugs to decrease prostate development [5-alpha reductase inhibitors: *finasteride* and *dustasteride*], and surgical treatment such as "transurethral resection of the prostate (TURP)." Upon treatment with 5-alpha reductase inhibitor the level of BPH often reduces speedily causing a decrease in the size of the prostate with time. Owing to this rationale, 5-alpha reductase inhibitors are considered as the first drugs of interest in the suppression of enlarged prostate. (Kellog, 2007;Jason *et al*., 2013). However, these treatments come with unfavorable side effects. For instance, the use of finasteride is connected with the frequency of sexual dysfunction, impotence, retrograde ejaculation, and decreased libido; the unfavorable side effect being dependent upon the duration of treatment (Robyn, 2006).

In order to bring a curative solution to the plight of BPH with optimal effectiveness and lower unfavorable side effects, research on the use of phytomedicine in remedying the challenge of BPH is currently gaining attention. In view of this, the "World Health Organization" suggested assessment of plants effectiveness in solving problems in areas of health where "safe" drugs are lacking. More so, in 2002 , the organization stated that a successful health program for growing countries cannot be realize by Western medication only, except accompanied by supplementary medicine including herbs and encourage developing countries to take advantage of exploiting their plant resources and other traditional health practices just to appreciate the hall mark of primary health care (WHO 2002).

From time immemorial, natural products derived from plant sources have always been the main sources of new drugs for the treatment of various diseases (Dharmani *et al*., 2006). *Ceiba pentandra*, a multi- purpose and herbaceous plant native to Obubra, Obudu, Northern parts of Nigeria and other tropical West Africa regions has been reported to have diverse medicinal and pharmacological uses. It is a plant belonging to the family *Bombacaeae*. Its promising therapeutic activities could be attributed to the presence of secondary metabolites such as polyphenol, flavonoids, alkaloid and saponins. These compounds have been identified to possess antioxidant properties; scavenging free radicals produced by oxidation – reduction reactions (Nandeesh *et al.*, 2008). Previous studies on various morphological parts of the plant have confirmed the plant to be thermogenic, diuretic, aphrodisiac, antipyretic and purgative. The plant is equally used as a hypoglycemic agent and has been found to be an effective remedy in the management of headache, dizziness, constipation and rheumatism (Ngounou *et al.*, 2000). The progression of BPH is usually monitored by assessing certain biochemical indices (Kellogg, 2007). This study investigated the ameliorative effect of *Ceiba pentandra* on relevant biochemical indices in testosterone propionate induced benign prostatic hyperplasia in Wistar rats' model.

2.0 MATERIALS AND METHODS

2.1 Materials

Fresh leaves of Ceiba pentandra were harvested from Utugwang in Obudu Local Government Area of Cross River State and authenticated by a Botanist Prof. S. Udoh of the Department of Biology, Cross River University of Technology (CRUTECH), Calabar.

2.2 Preparation of extract

The fresh leaves of the plant were washed with clean water and dried under room temperature for two weeks. The dried leaves were grinded into powdering form using mortar with pestle, before soxhlet extraction using ethanol.

2.3 Blood samples collection for analysis

5ml syringe with needle was use for the collection of blood sample through cardiac puncture into a clean plain sample tube and stored in a refrigerator for further biochemical analysis.

2.4 Experimental animals

A total of thirty six male rats (weighing 200-300 g) were obtained from the animal house of the Department of Biochemistry, Cross River University of Technology, Calabar. Prior to the

start of the experiment, the animals were allowed to acclimatize in well-ventilated standard cages with iron mesh doors for 14 days. In the course of the 21 days experimental duration, the rats were exposed to a 12-hour light/dark cycles under humid tropical conditions allowed access to grower's mash (rat chow) and clean tap water ad libitum. The animal room used for this study was well ventilated and maintained at a temperature range of 27 ^{o}C – 37 ^{o}C. The experimental procedure employed for this study was approved by the Institutional Animal Ethics Committee.

2.5 Experimental design

Thirty six male rats were divided randomly into six groups (n = 6). All the experimental groups except the normal control were induced benign prostatic hyperplasia (3 mg/Kg body weight). Rats in the Normal Control (NC) group received only feed without any special treatment, rats in the Benign Prostatic Hyperplasia Control (BPHC) group were administered 3 mg/Kg body weight testosterone propionate, rats in the Standard Control (STDC) group received 3 mg/Kg body weight testosterone + 1 mg/Kg body weight finasteride, rats in the low dose (LD) group received 3 mg/Kg body weight testosterone + 500mg/Kg body weight of *Ceiba pentandra*, rats in the medium dose group received 3 mg/Kg body weight testosterone + 1000 mg/Kg body weight of *Ceiba pentandra*,, rats in the high dose group were administered 3 mg/Kg body weight testosterone + 2000 mg/Kg body weight of *Ceiba pentandra*,. The animals in all the groups were allowed access to water and feed *ad libitum* for 21 days. Measurements of feed intake were taken daily while that of body weights was carried out on weekly basis.

2.6 Biochemical Analyses

2.6.1 Estimation of markers of hepatic function

Activities of aspartate aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP) in serum were determined based on earlier reports by [Sedlak, and Lindsay, 1968] using spectrophotometry assay kits (Randox Laboratory, United Kingdom). Total bilirubin, conjugated bilirubin and unconjugated bilirubin were estimated spectrophotometrically [Murray *et al*., 2004].

2.6.2 Estimation of markers of renal function

Serum concentrations of urea and creatinine were evaluated using Randox assay kits (Randox Laboratory, United Kingdom). An automatic analyser ROCHE module Cobas 6000 (C-501 and C-601) (Roche diagnostics, North America) was employed for this analysis.

2.6.3 Estimation of Prostate Specific Antigen (PSA) in the Serum: PSA was estimated using a two-step enzyme immunoassay sandwich method combined with Enzyme- Linked Fluorescence Assay (ELFA) (BioMerieux /France).

2.7 Statistical analysis

The data are presented as mean ± SEM (n = 6). Data obtained were analysed using one-way ANOVA followed by least square difference (LSD) post-hoc comparison test to evaluate significant difference between the mean values of the experimental and control groups. Differences at $P < 0.05$ were regarded as significant. Graphpad prism version 7 and SPSS software package version 23.0 were used for the statistical analyses.

3.0 RESULTS AND DISCUSION

3.1 RESULTS

The results shown below are the effects of *Ceiba pentandra* leaf on selected biochemical parameters in testosterone propionate-induced benign prostatic hyperplasia in wistar rats. Differences at $P < 0.05$ were regarded as significant.

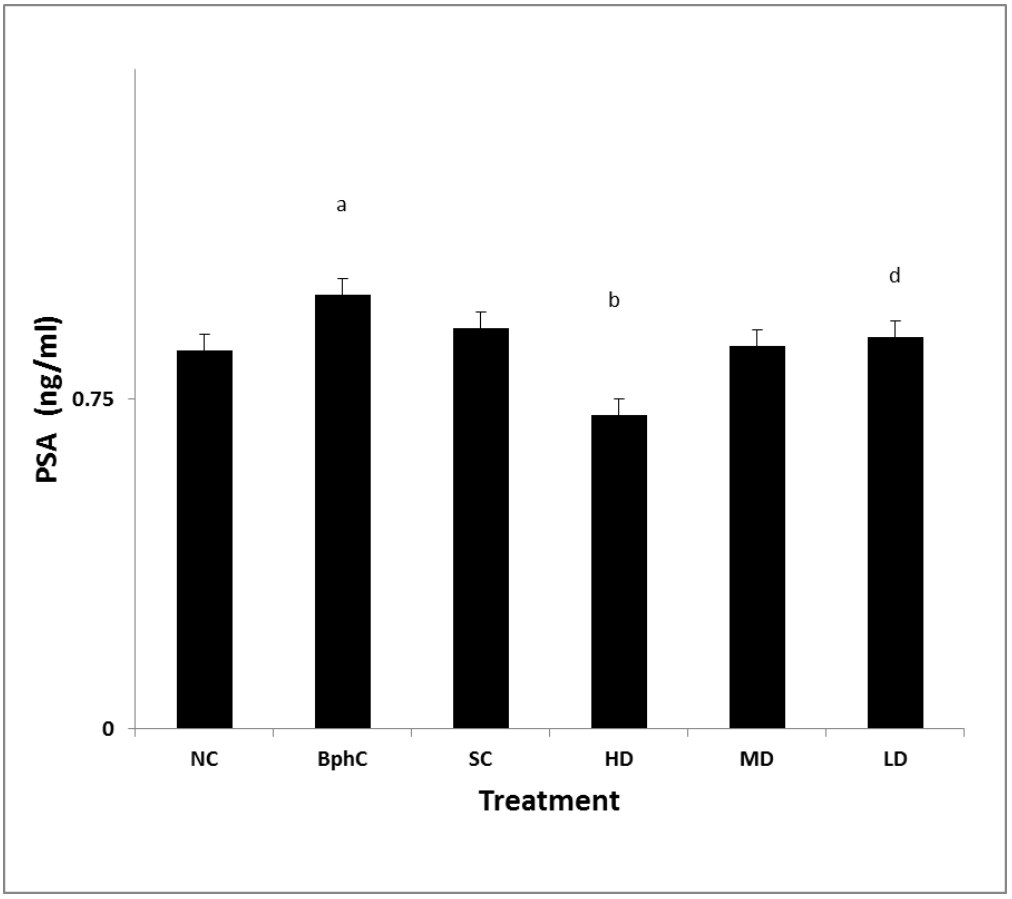

Figure 1: Effect of Treatment of *Ceiba pentandra* on Prostate Specific Antigen (PSA).

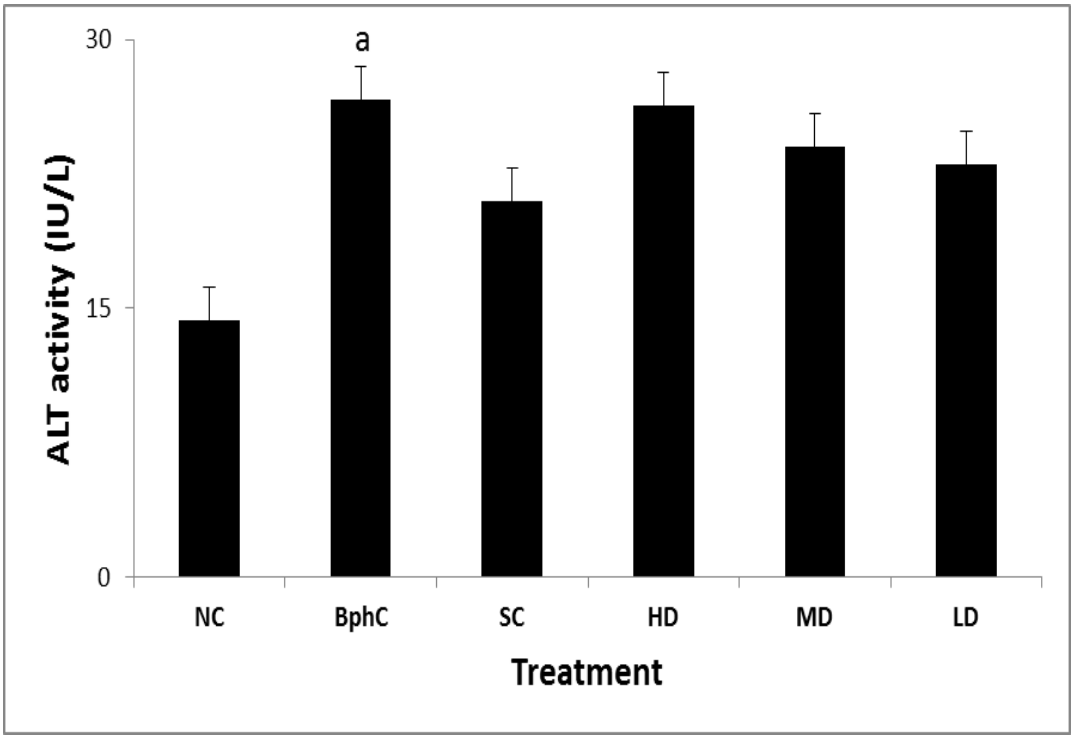

Figure 2: Effect of Treatment of *Ceiba pentandra* on Alkaline phosphatase (ALT).

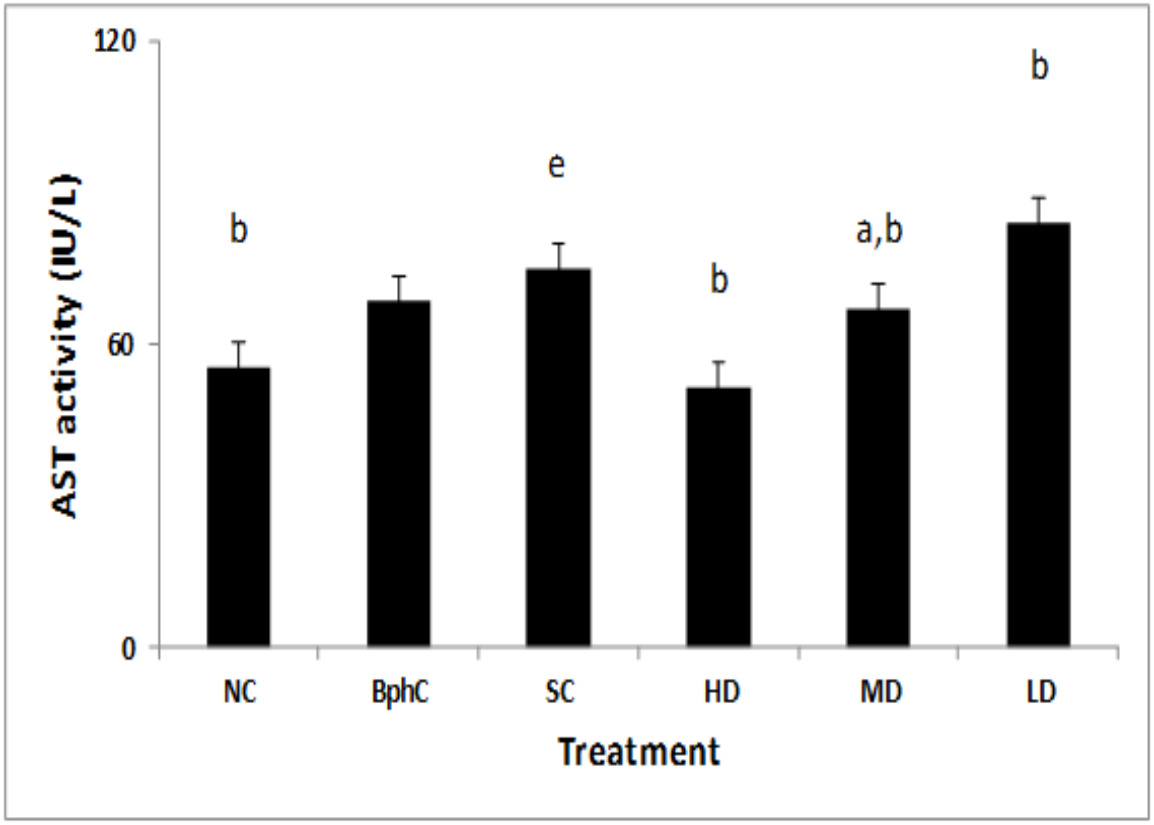

Figure 3: Effect of Treatment of *Ceiba pentandra* on Aspartate Aminotransferase activity of testosterone induced BPH Wistar rats.

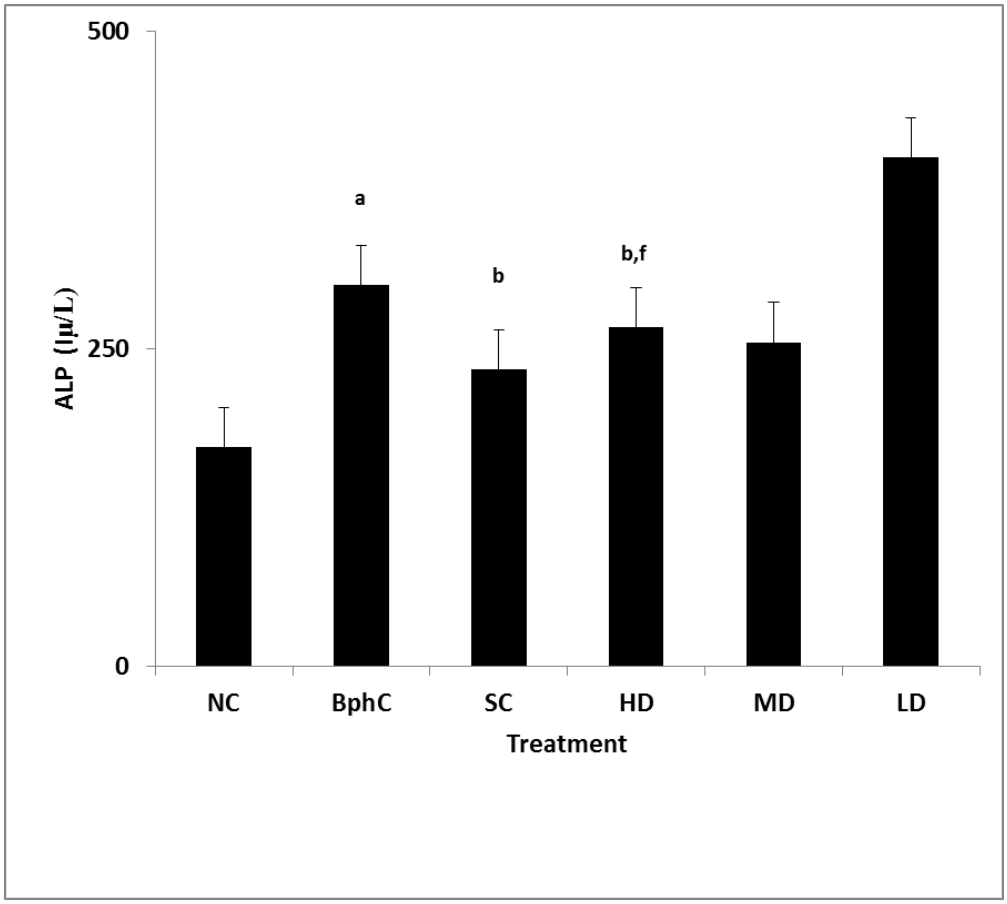

Figure 4: Effect of Treatment of *Ceiba pentandra* on Alkaline Phosphatase of testosterone propionate induced BPH Wistar rats.

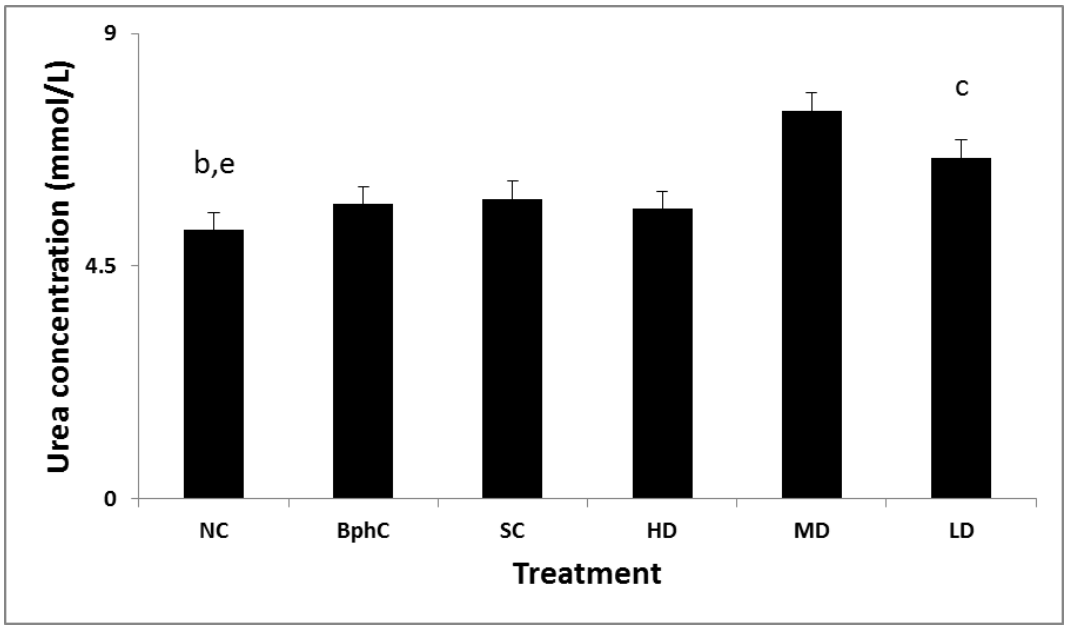

Figure 5: Effect of Treatment of *Ceiba pentandra* on Urea concentration of testosterone induced BPH Wisatr rats medium dose showed no significant (p>0.05) compared to SC (standard control) group (Fig 6).

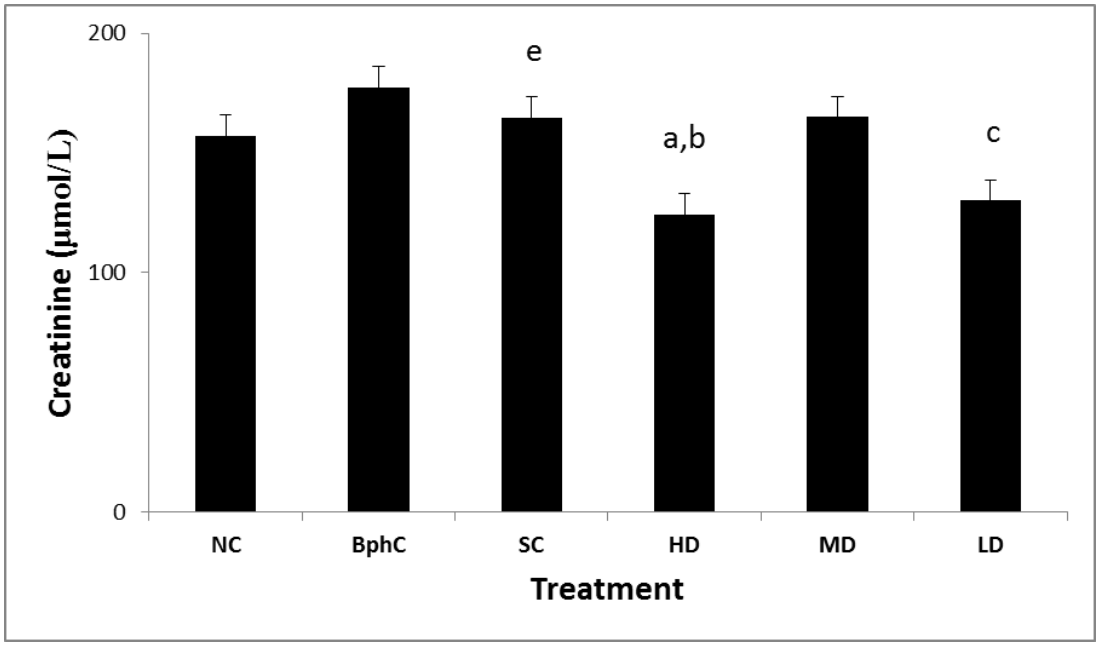

Figure 6: Effect of Treatment of *Ceiba pentandra* on serum Creatine of testosterone induced BPH Wistar rats.

3.2 DISCUSSION

BPH tends to be more severe and progressive in African-American men, possibly because of the higher testosterone levels, 5-alpha-reductase activity, androgen receptor expression, and growth factor activity in this population. It is no doubt that in older/aging men, BPH is the prevalent benign diseases and main cause of lower urinary tract symptoms. Testosterone is an important hormone for prostate growth, enlargement and maintenance of functional integrity. Testosterone has important effects on cardiovascular and liver disease as well as mental health.

The PSA level of rats treated with high dose of plant extract decreased significantly ($p<0.05$) compared to BPH control group. Prostate specific antigen is a serene protease produced by both benign and malignant prostatic epithelium. High serum concentration of PSA implies that noncancerous enlargement of the prostate and inflammation (Balk et al., 2003), the reduction in the concentration of PSA observed here could be attributed to secondary metabolites such as polyphenol, flavonoids, alkaloid and saponins present in *Ceiba pentandra* leaf. The PSA of the BPH control group increased significantly compared to the normal control. This increase could potentially result to BPH and it is dependent on the potent androgen (Dihydrotestosterone DHT). In prostate gland, type II 5-alpha reductase metabolizes circulating testosterone into DHT which works locally, not systematically. DHT

binds to androgen receptors in the cell nuclei, potentially resulting in BPH. In comparison with the result of Ekeyi *et al*. (2021), a total percentage increment of 63.3% was recorded with testosterone induction. This however contradicts the 14.51% increase recorded in this research. This variation could be due to short duration of administration of the treatment.

The attenuation percentage from the initial BPH untreated group using the highest dose treatment with *Cebia pentandra* recorded about 27.7%. Ekeyi *et al*. (2021), showed a total of 57% using *Cassia sieberiana*. This was on different dose administration. Omolola *et al*. (2018) also showed that the PSA value decrease from 0.3325-0.153ng/ml using *Tetracarpidum conophorum* leaf extracts. This value is relative to *Cebia pentandra* of 0.986-0.712ng/ml. a study from oral administration of *Juniperus communis* L extract is able to prevent testosterone induced BPH in rats (Avicenna, 2008). *Juniperus communis* L. is an evergreen tree or shrub was traditionally used for urinary retention and intermittency urination (Mahdavi *et al*., 2019; Avicenna, 2008). The mechanism of attenuation of testosterone induced BPH by these plants is the inhibition of 5-alpha reductase which blocks production of DHT, ultimately slowing down the development of prostate cells and tissues.

Most testosterone booster/pills post common side effect including liver damage/failure (Ocampo, 2018). Testosterone adversely affects liver function (Saad, 2009). High level of ALT may indicate liver damage from hepatitis, infection or testosterone pills (Medline Plus, 2020). Although liver enzymes have more significance in the liver, heart, kidney, brain, skeletal muscles and red blood cells. 70% of PSA in serum is complexed to anti-proteases and the clearance of complexed PSA from serum is thought to be through the liver (Ahdogan et al., 2002). Decrease testosterone levels are associated with chronic liver disease and may cause paradox decrease in PSA levels due to suppression of its production (Akdogan *et al*., 2002).

The ALT level of rats when treated with testosterone increases by almost two folds from 14.33IU/l to 26.67IU/l. However, ALP was significantly lowered in standard control and the high dose of *Cebia pentandra* compared to the untreated group with the treatment groups showing a dose-dependent decrease. The serum activities of these markers are indicators of liver damage and their concentrations may be elevated in the bloodstream (Mimae, 2017).

Testosterone reduces protein and nitrogen loss. The effect of testosterone on hepatic urea synthesis in humans has not been studied. In this study, administration of *Ceiba pentandra* in

medium and low doses increased the urea concentration compared to other groups, this agrees with the findings of Lam *et al*. (2017).

Creatinine is a marker of renal function. The serum creatinine level was observed to increase swiftly from 157.20µmol/l to 177.40µmol/l when administered with testosterone. The association between testosterone administration and creatinine level are likely to reflect a complex balance between muscle and renal function that varies with age (Samoszuks et al., 2020). The result also revealed a sharp decrease when the treatment (*Cebia pentandra* leaf extract) was administered. This shows that *Cebia pentandra* is a potent remedy for renal diseases

4.0 CONCLUSION

The results shown in this work suggest that the ethanol extract of *Ceiba pentandra* leaf has potential for use in the management of BPH.

Conflict of interest

The authors declare no conflict of interest.

A declaration of the liability

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by us.

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Contributions

MO-A conceived and supervised the scientific work. JOE and MO-A designed the work. The animal procedure was done by POE. JOE and SOO carried out the laboratory and biochemical analyses. SOO and POE statistically analysed and interpreted the data. The manuscript was drafted and prepared by JOE and SOO. All authors made a critical revision of the manuscript for important intellectual content before approving its final copy.

Consent for publication

Not applicable

Abbreviations

ANOVA: Analysis of variance

BPH: Benign Prostatic Hyperplasia

GFR: Glomerular filtration rate

LSD: Least square difference

SPSS: Statistical package for social sciences

TURP: Transurethral Resection of the Prostate

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