

Combined *Anthocleista vogelii* and *Alstonia boonei* Stem Barks Extract Alleviates Hyperlipidaemia and Renal Malfunctions in Benign Prostatic Hyperplasia-Induced Rats

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Abstract

Benign prostatic hyperplasia (BPH) is a urological disease prevalent among the ageing male population, which impairs the quality of life, including hyperlipidaemia and a decline in renal functions. Combining *Anthocleista vogelii* and *Alstonia boonei* stem bark extract has effectively managed BPH and its associated complications. This study evaluated the effects of a combined *Anthocleista vogelii* and *Alstonia boonei* stem bark extract (CAASBE) on the lipid profile and renal functions of rats induced benign prostatic hyperplasia with testosterone propionate injection. The study comprised five treatment groups, with groups 1 – 5 being the normal control, BPH control, standard control, BPH+200 mg/kg CAASBE, and BPH+400 mg/kg CAASBE, respectively. BPH was induced in the groups 2 – 4 rats by subcutaneous administration of testosterone propionate injection (5 mg/kg) for 28 days, and treatment with Finasteride and CAASBE were administered orally. The BPH control rats exhibited a significant ($p < 0.05$) increase in the total serum cholesterol, triacylglycerol (TAG), low-density lipoprotein cholesterol (LDL-C), urea, creatinine and significant ($p < 0.05$) decline in the serum high-density lipoprotein cholesterol (HDL-C) compared to the normal control. Conversely, treatment of the BPH rats with 200 and 400 mg/kg of CAASBE significantly ($p < 0.05$) reversed the altered total serum cholesterol, TAG, LDL-C, HDL-C, urea and creatinine to normal levels comparable to that of the normal control and standard control respectively. These findings show that CAASBE alleviates hyperlipidaemia and renal malfunctions in the BPH rats suggesting it could be effective in managing BPH complication.

Keywords: *Alstonia boonei*; *Anthocleista vogelii*; Benign prostatic hyperplasia; Hyperlipidaemia; Renal functions.

Abbreviations: BPH = Benign prostatic hyperplasia; TAG = Triacylglycerol; HDL-C = High density lipoprotein cholesterol; LDL-C = Low-density lipoprotein cholesterol; CAASBE = Combined *Anthocleista vogelii* and *Alstonia boonei* stem bark; *A. vogelii* = *Anthocleista vogelii*; *A. boonei* = *Alstonia boonei*.

INTRODUCTION

Among all the ailments and medical conditions affecting men's quality of life, benign prostatic hyperplasia (BPH) remains the most challenging urological disorder confronting the ageing male population worldwide. The probability of senior male increases as he attains 50 years old based on available autopsy that 42 % and 85 % of men within 51-60 and 80-above years respectively had BPH condition (Gacci et al. 2017). The increased prostate stromal and epithelial cell multiplication and proliferation in response to the high circulating testosterone and dihydrotestosterone have been implicated in the BPH pathogenesis. There is a decline in the quality of life as BPH progresses because of complications, including urinary disorder occasioned by bladder outlet obstruction and lower urinary tract

symptoms, which are difficult to manage. Genetic factors influence BPH pathogenesis as some races have an increased risk of developing BPH than others, but recently dietary habits, physical inactivity, and unhealthy lifestyle have been shown to increase the risk of BPH in ageing men (Vignozzi et al. 2014). Abnormal lipid profile, obesity, diabetes inflammatory conditions and hypertension are linked to BPH development and progression. Effective management of these common metabolic disorders in ageing men could be key to staying from BPH complications (Dahle et al. 2002). Aged men with abdominal obesity and abnormal serum lipid profile had a very low amount of high-density lipoprotein cholesterol (HDL-C), along with elevated low-density lipoprotein cholesterol (LDL-C), total cholesterol, and triacylglycerols demonstrated the increased amount of testosterone and oestradiol which

increased their risk for BPH (Adaramoye et al. 2008; Ugwu et al. 2019). The role of dyslipidaemia in the BPH pathogenesis is believed to be through stimulation of increased synthesis of androgens, including testosterone, dihydrotestosterone and oestradiol hormones that promote the growth of prostate cells. Therapeutic agents against BPH pathogenesis target and inhibit 5 α -reductase enzyme activities, thereby preventing the conversion of testosterone to dihydrotestosterone, which retard the multiplication of prostate stromal and epithelial cells and shrink the prostate size. A suitable therapeutic agent against BPH pathogenesis must be able to prevent dyslipidaemia in the subject to achieve the desired end.

Anthocleista vogelii Planch belongs to the Loganiaceae family utilised for various medicinal purposes in Africa. The stem bark has been therapeutically effective against prostate enlargement, male infertility, obesity, hyperlipidaemia, and renal and hepatic disorders (Sunday et al. 2016; Chukwu et al. 2020; Uroko et al. 2021). A phytochemical study of *Anthocleista vogelii* has revealed that it is rich in alkaloids, phenol, flavonoids, saponins, glycosides, terpenoids, steroids and tannins with minerals and vitamins (Ikpe et al. 2020). *A. vogelii* is used as a therapeutic against sleeping sickness in traditional medicine. Various experimental studies involving animal models have shown that it has anti-trypanosomal and anti-inflammatory activities (Eze et al. 2019). It has wide medicinal properties and has been useful in managing various ailments, including diabetes, jaundice, pains, venereal diseases, malaria, ulcer, and prostate enlargement (Okon et al. 2014; Chukwu et al. 2020).

Alstonia boonei De Wild is a well-known medicinal plant from the family of Apocynaceae that has demonstrated high therapeutic potential against many diseases and medical conditions confronting man. The plant is found mainly in the tropical rainforest across West African countries, but it can also be found in varying proportions worldwide. The plant extracts are pharmacologically against asthma, ulcers, toothache and impotence (Akinmoladun et al. 2007). The stem bark of *Alstonia boonei* has been reported to contain substantial amounts of phytochemicals such as flavonoids, phenols, alkaloids, tannins, cardiac glycosides, and saponins, along with high mineral contents and antioxidant vitamins, which are responsible for some of its medicinal properties (Akinmoladun et al. 2007; Oppong-Bekoe et al. 2020). Traditionally, *A. boonei* is used for treating menstrual pains, snake bites, the expulsion of residual placental in women after birth, bone remodelling, lactation induction, venereal diseases, jaundice, diabetes, rheumatism, malaria, and bacterial infections (Abbiw 1990). It has also been reported to possess anti-anaemic effects, antioxidative stress and hepatoprotective properties (Uroko et al. 2020; Okpashi et al. 2022). This study evaluated the pharmacological

impact of combined *Anthocleista vogelii* and *Alstonia boonei* stem bark extract (CAASBE) on lipid profile and renal functions of rats induced benign prostatic hyperplasia (BPH) with testosterone propionate injection.

MATERIALS AND METHODS

Plant Material

Five hundred (500) g each of the coarsely ground *A. vogelii* leaves and *A. boonei* stem barks corresponding to 1000 g of the combined plant samples were weighed into a clean, sterile container, and 2.5 L of absolute ethanol were to macerate for three days under regulation agitation. The macerated combined plant sample was filtered with a Whatman No. 1 filter paper, and the filtrate was concentrated with a Rotary Evaporator. The concentrated CAASBE was weighed, and the percentage yield was calculated as 9.78 %, corresponding to 97.8 g of CAASBE.

Experiment Animals

This study used thirty mature male Wistar albino rats within a close body range.

Chemicals and Drugs

The Finasteride, testosterone propionate injection and pentobarbital were purchased from Merck Company, USA; Health Biotech Ltd, India; and Medica Men Biotech Limited, India. The analytical grade absolute ethanol solvent and Radox commercial assay kits were purchased from Sigma Aldrich, USA, and Radox Laboratories, UK.

Study Design

Male Wistar albino rats numbering thirty with a close weight range of 160-168 g were purchased from the animal breeding unit of the Department of Zoology, University of Nigeria Nsukka, Nigeria, and kept in our animal house for seven days. The rats were provided with a standard finisher feed and drinking water and humanely handled following normal regulations and guidelines for the use of animals for an experiment. Our study design adopted five groups containing six male Wistar albino rats of similar body weight. The study groups are as follows:

- Normal control: Rats without BPH induction received only 1 ml/kg of distilled water.
- BPH control: Rats induced BPH by a subcutaneous administration of 5 mg/kg testosterone propionate injection for 28 days consecutively without any treatment.
- Standard control: Rats induced BPH by a subcutaneous administration of 5 mg/kg testosterone propionate injection and, after 60 mins, treated with oral administration of 5 mg/kg Finasteride for 28 consecutive days.

- BPH+ 200 mg/kg CAASBE: Rats induced BPH by a subcutaneous administration of 5 mg/kg testosterone propionate injection and, after 60 mins, treated with oral administration of 200 mg/kg CAASBE for 28 consecutive days.
- BPH+400 mg/kg CAASBE: Rats induced BPH by a subcutaneous administration of 5 mg/kg testosterone propionate injection and, after 60 mins, treated with oral administration of 400 mg/kg CAASBE for 28 consecutive days.

The rats fasted overnight on the 28th day of the experiment. They were anaesthetised on the 29th by the intraperitoneal injection of 25 mg/kg pentobarbital, followed by blood collection through cardiac puncture biochemical analyses and harvesting of kidney tissues for histopathological evaluation.

Determination of Lipid Profile, Serum Urea and Creatinine Concentrations

The lipid profile parameters, including total serum triacylglycerols (TAG), cholesterol, high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein-cholesterol (LDL-C), were measured following the procedures outlined in the Randox commercial assay kit for lipid profile. Also, the serum urea and creatinine concentrations were measured using the assay procedures in their respective Randox commercial assay kit.

Histopathological Examination of Kidney Tissues

The kidney sections collected from each of the five groups for the histopathological examination were fixed in 10% phosphate-buffered formalin for two days. The tissues were dehydrated in four different alcohol strengths in ascending order. The histopathological examination of the kidney sections was carried out

according to the procedures outlined by Uroko *et al.* (2020).

Ethics Approval

The study design was reviewed by the ethical board of the Department of Physiology, Biochemistry, and Pharmacology, Michael Okpara University of Agriculture, Umudike and approved with reference number: MOUAU/VPP/EC/18/005.

Statistical Analysis

All the data generated from the study were compared and analysed for statistically significant differences with the Duncan multiple range comparison test and one-way analysis of variance (ANOVA) using Statistical Products and Service Solutions version 22. Mean with a p-value < 0.05 are considered statistically different, while a mean with a p-value > 0.05 indicated no significant difference.

RESULTS AND DISCUSSION

RESULTS

Effects of CAASBE on the Serum TAG Concentrations of BPH-induced Rats

Figure 1 indicated a substantial elevation in the TAG concentration of the BPH control compared to the normal control. The standard control and BPH rats, which received 200 and 400 mg/kg CAASBE, showed no significant decline in serum TAG concentrations relative to the normal control. Conversely, the standard control that received 5 mg/kg Finasteride and BPH rats that received 200 and 400 mg/kg CAASBE showed significantly reduced serum TAG concentrations compared with the BPH control.

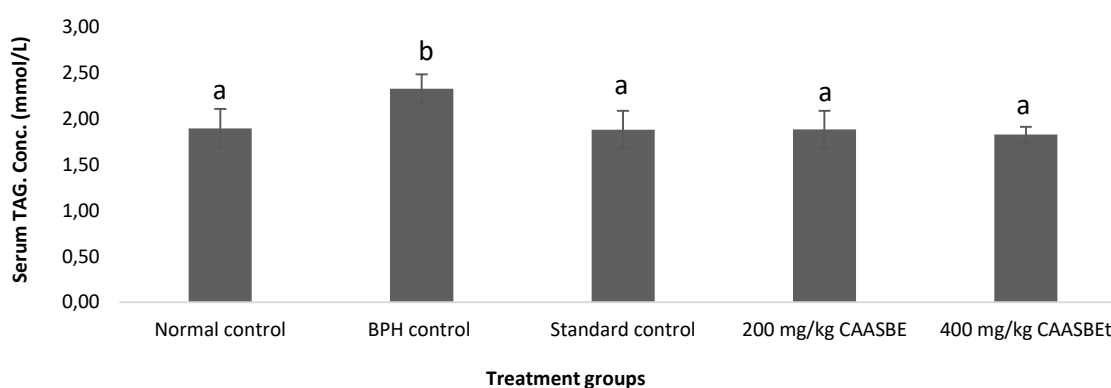


Figure 1. Serum TAG concentrations of BPH rats treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Serum HDL-cholesterol Concentrations of BPH rats

The result in Figure 2 showed a significant reduction in the serum HDL-cholesterol concentration of the BPH

control relative to the normal control. The standard control administered Finasteride, and BPH rats that received 200 and 400 mg/kg CAASBE, respectively, demonstrated no significant decline in the serum HDL-

cholesterol concentrations compared to the normal control. Conversely, the serum HDL-cholesterol concentrations in the standard control and BPH rats that

received 200 and 400 mg/kg CAASBE, respectively, exhibited a significant increase in the serum HDL-cholesterol concentration compared to the BPH control.

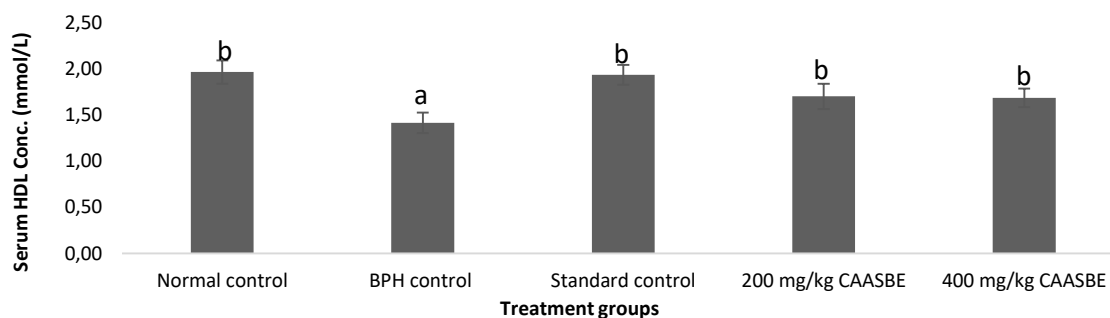


Figure 2. Serum HDL concentrations in BPH rats treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Total Serum Cholesterol Concentrations of BPH -induced Rats

Figure 3 showed a significantly elevated total serum cholesterol concentration in the BPH control compared with the normal control. However, there was no significant variation in the total serum cholesterol

concentration in the standard control and BPH rats that received 200 and 400 mg/kg CAASBE, respectively, compared with the normal control. Conversely, the total serum cholesterol concentrations in the standard control and BPH rats treated with 200 mg/kg CAASBE decreased significantly compared to the BPH control.

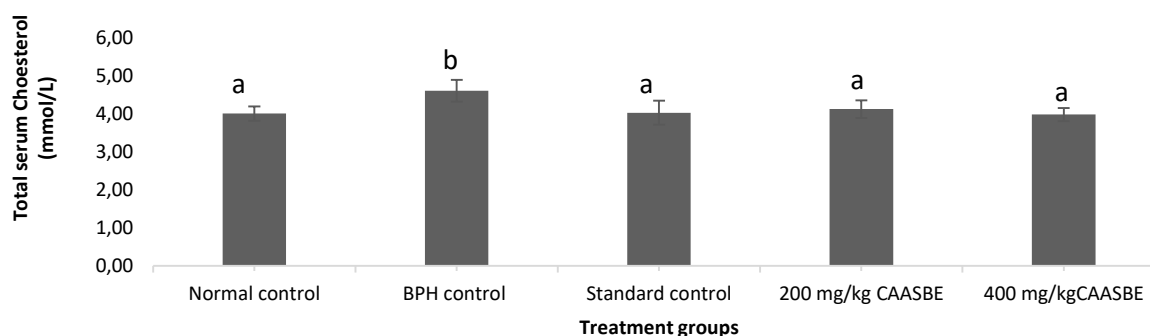


Figure 3. Total serum cholesterol concentrations of BPH rats treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Serum LDL-cholesterol Concentrations of BPH Rats

Figure 4 demonstrated a significant rise in the serum LDL-cholesterol concentration of the BPH control rats compared to the normal control. Contrarily, the standard control and BPH rats that received 200 and 400 mg/kg

CAASBE, respectively, showed no significant increase in the serum LDL-cholesterol concentration relative to the normal control. The level of serum LDL-cholesterol in the standard control and BPH rats treated with 200 and 400 mg/kg CAASBE were significantly reduced compared to the BPH control.

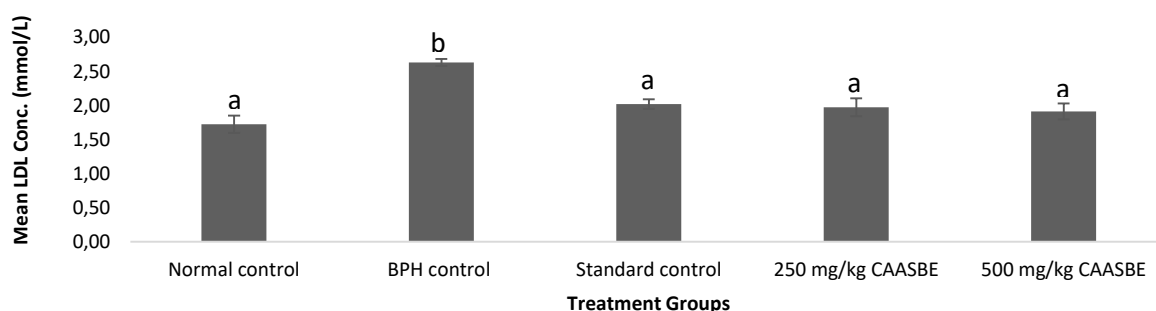


Figure 4. Serum LDL-cholesterol concentrations of BPH treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Serum Urea Concentrations of BPH Rats

Figure 5 indicated a significant increase in the serum urea concentration of the BPH control compared to the normal control. There were mild variations in the serum urea concentrations of the standard control and BPH rats

treated with 200 and 400 mg/kg CAASBE, respectively, compared to the normal control. The serum urea concentrations of the standard control and BPH rats administered varying doses of CAASBE showed significant reduction compared with the BPH control.

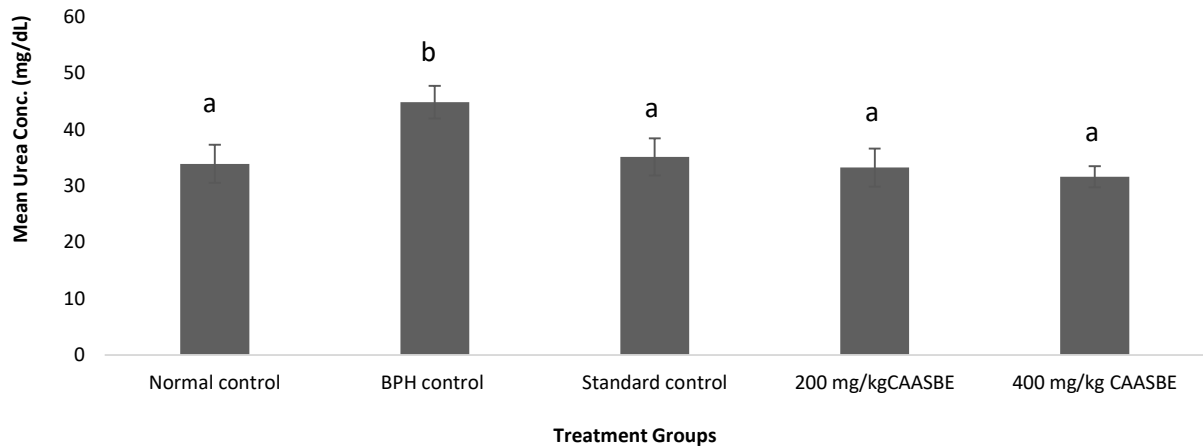


Figure 5. Serum urea concentrations of BPH rats treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Serum Creatinine Concentrations of BPH Rats

The serum creatinine concentration in the BPH control was significantly elevated compared to the normal control, standard control and BPH rats administered 200

and 400 mg/kg CAASBE, respectively (Figure 6). In contrast, the standard control and BPH rats treated with 200 and 400 mg/kg CAASBE showed no significant difference in their serum creatinine concentrations relative to the normal control.

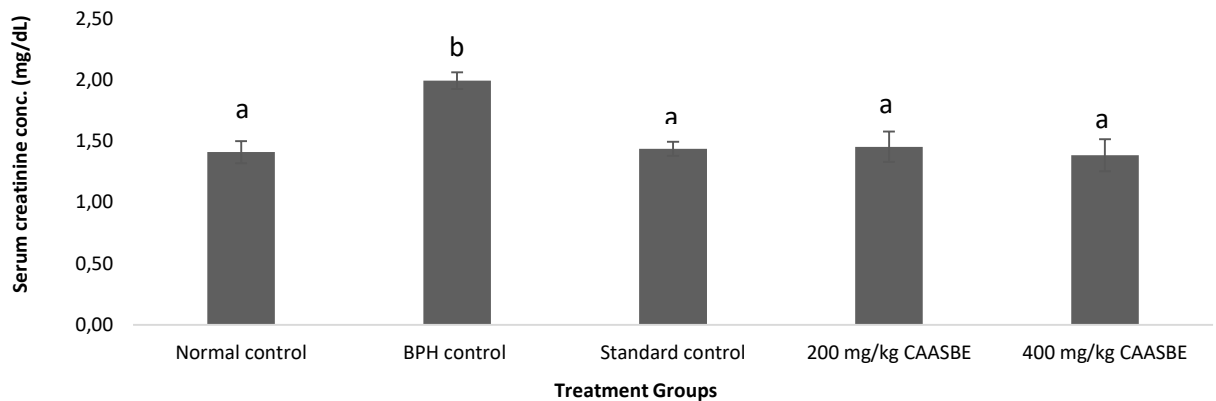
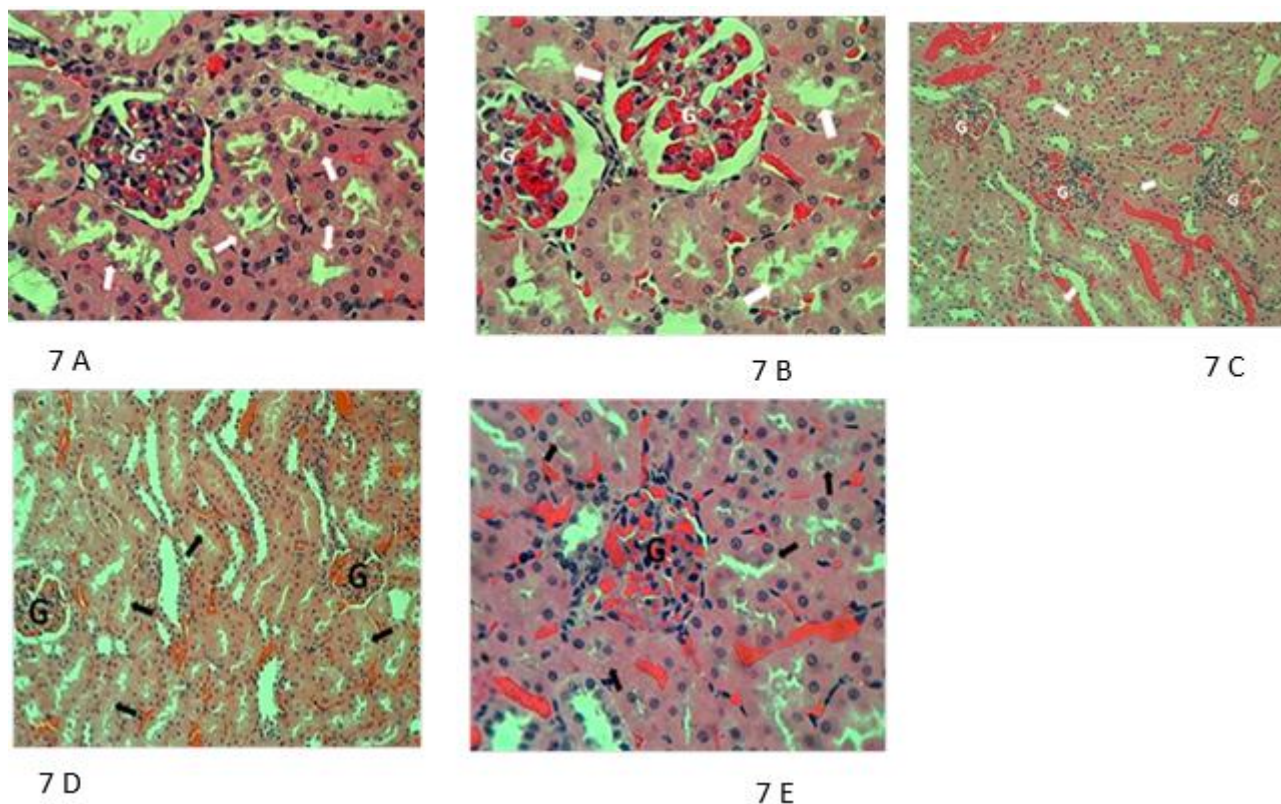


Figure 6. Serum creatinine concentrations in BPH rats treated with CAASBE. Each of the bars indicated mean \pm standard deviation ($n = 6$), and any of the results with unlike superscripts are significantly ($P < 0.05$) different from the paired mean.

Effects of CAASBE on the Kidney Histomorphology of BPH Rats

The kidney section from the normal control rats indicated a normal renal histomorphology for laboratory rodents, containing normal glomeruli (G) in the cortex containing intact renal tubules indicated by the arrow. The renal tubules also contain unaltered outer and inner

medulla, as shown in Figure 7 A. Similarly, the sections of kidneys from BPH control rats (Fig. 7B), standard control (Fig. 7 C), and BPH induced rats treated with 200 mg/kg and 400 mg/kg of CAASBE in Fig. 7 D and Fig. 7 E, respectively, showed normal kidney histomorphology of normal rodents.



Figures 7. A - E. Histomorphology of kidney section from normal control rat, BPH control rat, Standard control, BPH rats treated with 200 mg/kg CAASBE, and BPH rat treated with 400 mg/kg CAASBE, respectively.

DISCUSSION

The combined *A. vogelii* and *A. boonei* stem bark (CAASBE) is a potent therapeutic agent against BPH and several diseases in traditional medicine across south-eastern Nigeria. It has little scientific data on its effects on other biochemical and physiological functions. The BPH is a medical condition common in the ageing male population worldwide but with increased occurrence in males of African origin. It is caused by prostate enlargement occasioned by the rapidly dividing and proliferating prostate stromal and epithelial tissues in response to the stimulatory actions of increased dihydrotestosterone (DHT) concentration (Gacci et al. 2017). This study evaluated the effects of a combined CAASBE on the lipid profile and renal functions in benign prostatic hyperplasia (BPH) induced rats. In this study, the BPH induction without administration of any therapeutic agent resulted in a significant elevation of the serum TAG, cholesterol, LDL, urea and creatinine concentrations along with a significantly reduced HDL concentration in the BPH control compared to the normal control.

The significantly elevated serum TAG concentration in the BPH control relative to the control indicates the adverse effect of BPH on lipid metabolism, which promoted hyperlipidaemia in the BPH rats. The elevated serum TAG level in the BPH control agrees with Ugwu et al. (2019) that high serum TAG level is associated with BPH pathogenesis. The BPH control rats could

have experienced impaired carbohydrate catabolism and conversion of excess amount of free fatty acids resulting in increased serum TAG concentration due to the decline in the transport of TAG to the liver for catabolism because of the inadequate amount of HDL needed for the vehicle. The BPH rats could have suffered acute pancreatic inflammation that impaired carbohydrate metabolism and elevated serum TAG concentration. The BPH induction might have impaired the metabolism of TAG ingested from dietary sources that could have contributed to the increased circulating serum TAG concentration. The effect of BPH on TAG indicates that increased serum TAG is associated with BPH progression, which predisposes the BPH patient to the increased risk of arteriosclerosis, cardiovascular dysfunction and paralysis of some parts of the body. This finding agrees with Güven and Gökhan (2022) report that hyperlipidaemia could accelerate BPH progression. The substantially reduced serum TAG concentration in all the BPH rats administered CAASBE relative to the BPH control but comparable to the normal control and standard control, respectively, could be attributed to the antihyperlipidemic effects of CAASBE. The CAASBE might be rich in bioactive phytoconstituents such as flavonoids, alkaloids, terpenoids and vitamins that could be responsible for lowering the serum TAG concentrations in the BPH rats. The low serum TAG concentrations in the CAASBE-treated BPH rats indicated improved carbohydrate

metabolism and efficient transport of TAG to the liver for catabolism which might have contributed to reduced risk of stroke, hypertension and heart diseases which are associated with abnormal serum TAG levels in line with Güven and Gökhan (2022).

The HDL cholesterol is a very important type of cholesterol that maintains a healthy balance of lipid profile via its role in moving LDL-cholesterol, potentially unhealthy cholesterol, to the liver for catabolism and elimination from blood circulation. Aside from the clearance of LDL-cholesterol from clogging the arterial walls, many researchers have suggested that HDL possesses antioxidant, anti-inflammation and anticoagulant properties. The significantly decreased serum HDL-cholesterol concentration in the BPH control showed the adverse effects of BPH on the serum HDL-cholesterol concentration. The reduction in the HDL level in the BPH control suggests that alterations in lipid profile, especially the serum HDL-cholesterol concentration, are associated with the BPH pathogenesis, and adequate regulation or restoration of altered lipid profile could play an important role in alleviating the adverse effects of BPH on general body functions. The reduced HDL-cholesterol level in the BPH control is in line with the findings of Gacci et al. (2017) that lower HDL-cholesterol level is associated with prostate enlargement and that hyperlipidaemia could accelerate BPH progression by promoting prostate cell inflammation. The low serum HDL-cholesterol concentration in the BPH control has great health consequences as there could be a decline in the transport of LDL-cholesterol and other cholesterol molecules to the liver for metabolism and clearance, which will increase the risk of narrowing the arterial walls and heart diseases as earlier reported by Uroko et al. (2021). However, the significantly increased serum HDL-cholesterol concentrations in the BPH rats treated with Finasteride and CAASBE, respectively, compared to the BPH control showed the anti-dyslipidaemia effects of the CAASBE against BPH-associated alterations in the lipid profile. The high serum HDL-cholesterol level in the CAASBE-treated BPH rats is indicative that there would be effective extraction of LDL-cholesterol from the blood vessels to the liver for breakdown, thereby freeing the arteries from the deposition of LDL-cholesterol, narrowing, increased blood pressure and complications that might result in heart diseases. Thus, treating BPH rats with CAASBE improves serum HDL-cholesterol levels and prevents adverse health effects associated with its low blood level. The increased HDL in the CAASBE-treated BPH rats agrees with Gacci et al. (2017).

Cholesterol is an important lipid profile component in synthesising bile acids and many steroid hormones, including gonadal and adrenal steroid hormones, and maintaining membrane structure and integrity. Still, its high serum concentration could accelerate the risk of

developing cardiovascular diseases. The substantially increased serum cholesterol concentration in the BPH control compared to the normal control demonstrated that BPH progression is linked to the abnormally elevated serum cholesterol concentration. The increased serum cholesterol level in the BPH control aligns with previous findings that increased serum cholesterol level, including in the prostate tissues, is associated with the pathogenesis of benign and malignant prostatic diseases (Rohrmann et al. 2005; Yat-Ching et al. 2011). Increased circulating cholesterol could induce signalling pathways that enhance BPH pathogenesis. The elevated serum cholesterol concentration in the BPH control suggests that there is an increased likelihood of the high serum cholesterol being deposited on the blood vessel walls, thereby forming arterial clots and hindering blood flow which might increase the blood pressure and heart diseases that would adversely affect the survival of the BPH control rats. In contrast, the substantially reduced serum cholesterol concentration of the BPH rats treated with 200 and 400 mg/kg CAASBE showed the anti-hypercholesterolaemia effects of the phytoconstituents present in the CAASBE. The anti-hypercholesterolaemia effects demonstrated by CAASBE in this study were comparable to the Finasteride effect in the standard control, suggesting that CAASBE possesses high therapeutic potential against BPH and its associated health complications. The drastically reduced cholesterol coupled with the low serum LDL-cholesterol level in the CAASBE-treated BPH rats showed a low risk of atherosclerosis and cardiovascular diseases in the BPH rats treated with CAASBE. The substantial reduction in the serum total cholesterol level in the BPH rats treated with CAASBE aligns with previous findings that inhibiting cholesterol synthesis by therapeutic agents could reduce BPH progression and that hypercholesterolaemia aggravates BPH progression (Rohrmann et al. 2005).

The LDL-cholesterol is one of the components of the lipid profile parameters commonly evaluated to monitor one's lipid profile status. The elevation in the serum LDL-cholesterol indicates impending health consequences, mostly when there is a substantially low serum HDL-cholesterol level (Kang et al. 2015). LDL-cholesterol is the main lipid deposited on the arteries, which clogs and narrows the arterial area, thereby increasing the blood flow pressure that has a far-reaching implication on heart functions and general wellbeing. The significantly elevated serum LDL-cholesterol in the BPH control showed that BPH caused an imbalance in the lipid profile composition of the rats, exposing them to the increased health risk of accumulation of LDL-cholesterol in the arteries, which agrees with the findings of Uroko et al. (2021). The decline in the serum HDL-cholesterol needed to remove and transport LDL-cholesterol from the blood vessels to the liver could be responsible for the elevated serum LDL-cholesterol in the BPH control. The high serum

LDL-cholesterol level in the BPH control agrees with Güven and Gökhan (2022) findings that increased LDL-cholesterol is linked with BPH progression. Conversely, the substantial decrease in the serum LDL-cholesterol concentrations in the Finasteride and CAASBE treated BPH rats, respectively, relative to the BPH control, showed each therapeutic agent's ability to restore the altered LDL-cholesterol to the normal level. The power of CAASBE to lower LDL-cholesterol indicates that it could promote normal biochemical and physiological functions aside from restoring an enlarged prostate to normal size, as Uroko et al. (2021) and Güven and Gökhan (2022). This finding suggests that CAASBE could play a key role in preventing and managing high blood LDL-cholesterol, arteriosclerosis and cardiovascular disorders.

Evaluating the serum urea level is a very reliable indirect method of ascertaining the renal function status and serves as a guide for taking necessary action to restore normal renal functions. Urea is an excretable end product protein and nitrogenous base metabolism that is filtered by the glomerular of the kidney and excreted with excess fluid in the body. The high serum urea concentration points to renal dysfunction. The elevated serum urea concentration in the BPH control relative to the normal control suggested an impaired renal glomerular filtration and excretion of urea from the circulating blood. The substantially elevated serum urea concentration in the BPH control finding agrees with the previous findings that increased serum urea levels in BPH rats are associated with impaired renal functions (Weinstein *et al.*, 2009; Uroko *et al.*, 2021). The persistent rise in the serum urea level could lead to various adverse health complications, including hypertension and cardiac dysfunctions. This finding suggests impaired glomerular filtration rate and increased serum urea level may be associated with BPH progression if not effectively managed. In contrast, the significantly reduced serum urea level in the standard control and all the CAASBE-treated BPH rats showed that treatment with Finasteride and CAASBE alleviated the adverse effects of BPH on renal functions, according to the findings of Uroko *et al.* (2021). The ability of CAASBE to drastically restore the elevated serum urea level in the BPH rats similar to the normal control could be attributed to the therapeutic effects of the bioactive constituents in the combined extract, which is an indication that CAASBE could be used to manage renal disorders.

The serum creatinine level is the metabolic waste product of creatine catabolism that is regularly filtered from the blood by the renal glomerular and eliminated from the body via urine. The serum creatinine level, like serum urea level, reflects the glomerular filtration rate and the renal function status. The sensitivity of serum creatinine level as a measure of renal function status is very reliable when coupled with the serum urea level.

The high serum creatinine level in the BPH control relative to the normal control could be attributed to impaired creatinine filtration and clearance by the renal glomerular in line with Weinstein *et al.* (2009). The high serum creatinine level in the BPH control indicated impaired removal of excess wastes in the circulating blood via urinary excretion, which could adversely affect the regulation of biochemical and physiological activities in the body. Contrarily, the significantly reduced serum creatinine level in the BPH rats treated with CAASBE suggests that the combined extract relief the adverse effects of BPH induction by testosterone propionate injection and restored the ability of the renal glomerular to filter and remove excess creatinine from the blood in line with the findings of Uroko *et al.* (2021). The very low serum creatinine level showed that CAASBE could be used as a therapeutic agent against renal disorders, which agrees with the earlier reports by Reshma et al. (2014).

The normal renal histomorphology observed in the BPH control, standard control, and BPH rats treated with 200 and 400 mg/kg CAASBE, respectively, compared to the renal histomorphology of the normal control, showed that it caused no renal injury in the rats. These suggest that BPH interfered with renal functions and reduced the glomerular filtration rate and clearance of wastes out of the body. The absence of observable alterations in the renal histomorphology is in order because the testosterone propionate injection administered to induce BPH is not nephrotoxic. The increased serum urea and creatinine concentrations indicated impaired renal functions due to stress associated with BPH pathogenesis and complications rather than renal injury. The absence of histomorphological alterations of the kidney sections of the BPH control and the BPH rats treated with Finasteride and CAASBE are consistent with Uroko *et al.* (2021).

CONCLUSIONS

The findings of this study showed that treatment of BPH rats with CAASBE significantly restored the altered lipid profile to a normal level. The CAASBE-treated BPH rats had considerably reduced serum urea and creatinine concentrations compared to the BPH control but no alterations in the renal histomorphology. The findings suggest that treatment with CAASBE could prevent hyperlipidaemia and renal malfunctions in BPH rats.

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