sciendo

herba polonica
International journal edited by the Institute of Natural Fibres and Medicinal Plants
Vol. 66 No. 3 2020

Received: 2020-08-23
Accepted: 2020-09-18
Available online: 2020-09-30

DOI: 10.2478/hepo-2020-0013

EXPERIMENTAL PAPER

Effects of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM) on liver function indices of benign prostatic hyperplasia (BPH) induced rats

ROBERT IKECHUKWU UROKO[1*], FATIMA AMIN ADAMUDE[2], SIMEON IKECHUKWU EGBA[1], CHARLES NNANNA CHUKWU[1], CHIDIMMA LILIAN ASADU[3], EMMANUEL CHIDERA OKWARA[1]

[1]Department of Biochemistry
College of Natural Sciences
Michael Okpara University of Agriculture
Umudike, Abia State, Nigeria

[2]Department of Biochemistry
Faculty of Medical Sciences
Federal University Lafia
Nasarawa State, Nigeria

[3]Department of Biochemistry
Faculty of Biological Sciences
University of Nigeria Nsukka
Enugu State, Nigeria

*corresponding author: phone: +2348065914471; e-mail: ir.uroko@mouau.edu.ng

Summary

Objective: This study evaluated the effects of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM) on the liver function indices of benign prostatic hyperplasia (BPH) induced rats.

Materials and Methods: The study used 30 rats divided into 5 groups, comprising normal control, BPH control, standard control, and BPH induced rats treated with 200 and 600 mg/kg/day of FAAM respectively.

Results: The BPH induction caused significant (p<0.05) increases in aspartate transaminase (AST) and alkaline phosphatase (ALP) activities of the BPH control when compared with the normal control. The BPH control also had significantly (p<0.05) reductions in the total protein, albumin and globulin concentrations

and significant (p<0.05) elevated total bilirubin and direct bilirubin concentrations relative to the normal control. The FAAM treated BPH-induced rats had non-significantly (p>0.05) reduced AST, and alanine transaminase (ALT) activities relative to the BPH control. The BPH-induced rats treated with 600 mg/kg/day of FAAM had significantly (p<0.05) reduced ALP activities relative to the BPH control. Treatment with FAAM caused significant (p<0.05) increases in the total protein, albumin, globulin concentrations and significant (p<0.05) reductions in the total bilirubin and direct bilirubin concentrations relative to the BPH control. BPH had no observable adverse effects on the liver histomorphology of the rats.

Conclusion: The findings of this study indicated that BPH impairs liver functions and treatment of BPH with combined ethanol extract of *F. africana* and *A. mauritianum* leaves restore normal liver functions in rats with BPH.

Key words: ***Funtumia africana, Abutilon mauritianum, liver marker enzymes, liver function indices, benign prostatic hyperplasia***

Słowa kluczowe: ***Funtumia africana, Abutilon mauritianum, enzymy wątrobowe, wskaźniki wątrobowe, łagodny przerost gruczołu krokowego***

INTRODUCTION

The increasing incidence of mortality due to benign prostatic hyperplasia (BPH) in ageing men globally is of serious concern and needed collective efforts to arrest it. The benign prostatic hyperplasia result from excessive growth of the prostate gland due to proliferating cells which impairs urethral functions by compressing it. Available data show 90% incidence in men aged 80–90 and about 62.3% in men aged 50–74 [1, 2]. Most treatment options for BPH come with enormous adverse health effects that largely impair urinary excretion, growth of normal cells, cause erectile dysfunction and toxic effects on vital organs like liver [3]. To minimize the adverse effects of chemotherapeutic agents, many BPH patients now use complementary and alternative medicines to manage it. Patients with chronic severe BPH have been reported to experience impaired kidney and liver functions because of BPH complications [4]. The combined *Funtumia africana* and *Abutilon mauritianum* leaves extracts are claimed by many traditional medicinal practitioners to possess high potent therapeutic effects against benign prostatic hyperplasia and various hepatic disorders without any scientific data to support their claims.

Funtumia africana (Benth.) Stapf a member of the *Apocynaceae* family has wide medical applications in traditional medicine. Its leaves possess broad antibiotic activities, antimalarial, anticancer, anti-inflammatory, antioxidative and antifungal activities [5, 6]. The plant extract has also been used to treat hepatic disorders due to its hepatic activities, as cures for persistent cough, infertility, urinary incontinence, diarrhoea in many Africana countries [6, 7]. In Nigeria, it is commonly known as akọ iré in Yoruba, and as mba-miri in Igbo language and generally known in English as false rubber tree [8]. *Abutilon mauritianum* (Jacq.) Medik belongs to the family of *Malvaceae* and is a common medicinal plant of African origin widely distributed across West African countries, especially in Nigeria. Various parts of *A. mauritianum* are used in the treatment of different ailments including fever, bacterial infections, snake bite, scabies, diarrhoea, common cold, cough, dysentery, gonorrhoea, and for labour induction [9]. *A. mauritianum* leaves are also rich in anti-inflammatory, analgesic and antipyretic activities [10]. The medicinal properties of *A. mauritianum* leaves are attributed to the bioactive phytochemicals such as saponins, tannins, terpenoids, flavonoids, and alkaloids found in high concentrations in leaves [9, 11]. This study was designed to evaluate the effects of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM) on the liver functions indices of benign prostatic hyperplasia induced rats.

MATERIALS AND METHODS

Plant material

Fresh leaves of *Funtumia africana* (Benth.) Stapf and *Abutilon mauritianum* (Jacq.) Medik leaves were collected from Forestry Research Institute of Nigeria, Eastern Station, Ahia Eke, Ndume, Umuahia, Abia State a farm located in at Ahiaeke, Ndume Umuahia and used for the study. Fresh leaves of *F. africana* and *A. mauritianum* were properly identified and authenticated by a taxonomist, Dr Ndukwe K. Ibeh

at the Herbarium unit of the Department of Forestry, Michael Okpara University of Agriculture, Umudike, Abia State, Nigeria. *F. africa*na and *A. mauritianum* leaves were identified with voucher numbers 2694-5 (Preuss 1899) and Jones FHI 13749, respectively.

Preparation of combined ethanol extract of FAAM

The *F. africana* and *A. mauritianum* leaves were handpicked, washed in running tap water, sliced into smaller pieces to increase their surface areas and dried under shade for 3 weeks respectively. The dried leaves samples were pulverised into coarse powder and 250 g of each plant sample (1:1 *w/w*) equivalent to 500 g of combined plant samples was weighed into conical and 1.5 l of absolute ethanol was added. It was allowed to stand for 72 h with intermittent shake to ease the extraction of the polar phytoconstituents of the combined extract before it was filtered after 72 h with mesh cloth. It was further filtered with Whatman No. 1 filter paper and the filtrate was concentrated in a water bath at 65°C to allow the ethanol solvent evaporate completely. Next, the percentage yield was calculated.

Experimental animals

Thirty (30) male Wistar albino rats weighing 115–150 g used for this study were purchased from the Animal House, Department of Zoology and Environmental Sciences, Faculty of Biological Sciences, University of Nigeria, Nsukka, Enugu State, Nigeria. The rats were kept at the Animal House of the Department of Biochemistry, Michael Okpara University of Agriculture Umudike for 2 weeks with free access to a standard laboratory diet (Vital feed) and water *ad libitum* and acclimatized to laboratory conditions under a 12 h light/dark cycle. After 2 weeks of acclimatization, the rats were used experimental study.

Experimental design

Thirty (30) rats were randomly distributed into five groups containing 6 rats each as follow:

Group 1 (Normal control):	Rats without BPH induction that received 2 ml/kg/day of distilled water for 28 days.
Group 2 (BPH control):	BPH-induced rats without any treatment for 28 days.
Group 3 (Standard control):	BPH-induced rats treated with 5 mg/kg/day of finasteride for 28 days
Group 4 (BPH + 200 mg/kg/day FAAM):	BPH-induced rats treated with 200 mg/kg/day of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM) for 28 days.
Group 5 (BPH + 600 mg/kg/day FAAM):	BPH-induced rats treated with 600 mg/kg/day of combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum leaves* (FAAM) for 28 days.

Benign prostatic hyperplasia (BPH) was induced in the rats by subcutaneous injection of testosterone propionate in olive oil (5 mg/kg/day) for 28 days consecutively. Treatments were given to the rats 1 hour after testosterone propionate (TP) administration for consecutive 28 days. After the last administration of testosterone propionate and treatments on the 28th day, the rats fasted overnight. Blood samples were withdrawn from the rats, livers were collected and weighed accordingly and stored in 4% formaldehyde for histological examination.

Biochemical analyses

The aspartate transaminase (AST) and alanine transaminase (ALT) activities were assayed according to the methods of Reitman and Frankel [12]. The alkaline phosphatase activities were assayed according to the method described by Englehardt [13]. Total bilirubin and direct bilirubin concentrations were determined using the methods of Jendrassik and Grof while total protein, albumin and globulin concentrations were determined with the method described by Reinhold [14, 15].

Histopathological examination

Sections of livers were collected for histopathological examination at the end of the study period. The samples were fixed in 10% phosphate-buffered formalin for a minimum of 48 hours before tissue preparation. The tissues were subsequently trimmed, dehydrated in 4 ascending grades of alcohol (70%, 80%, 90% and 100%), cleared in 3 grades of xylene

and embedded in molten wax, following the method described by Disbrey and Rack [16]. The photomicrographs were taken using a Motic™ 5.0 megapixels microscope camera at x100, x160 and x400 magnifications.

Ethical issues

The study fully adhered to the Regulations of the Research Ethics Committee of Iranian Ethical Guidelines for the use of animals in research and the guidelines of the Research Ethics Committee of Michael Okpara University of Agriculture Umudike (MOUAU) for animal experiments. Ethical clearance for this study was obtained from the Ethical Committee of the Department of Physiology and Pharmacology, College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike under the Ethical Number: MOUAU/VPP/EC/18/003.

Statistical analysis

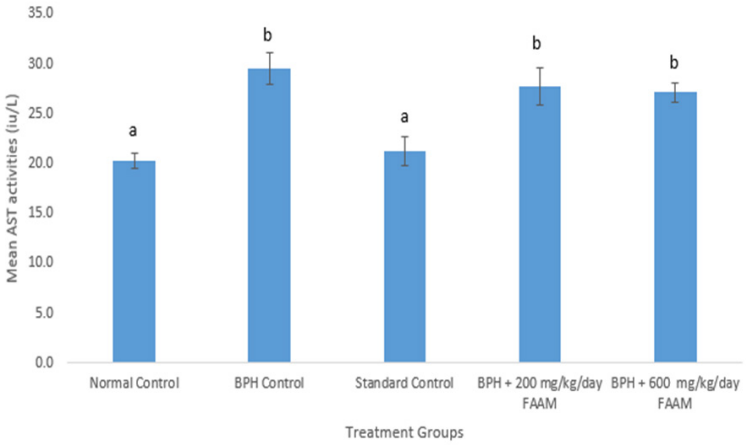
The data obtained were statistically analysed with a Statistical Products and Service Solutions (SPSS) v. 22 by one-way analysis of variance (ANOVA). The means of the various treatment groups were compared with Duncan multiply range comparison test and levels of statistical significance difference were established at $p<0.05$. The results were presented as mean ± standard deviation (n=6).

RESULTS

Biochemical analyses

The result of aspartate transaminase (AST) activities of BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves showed significant ($p<0.05$) increase in the AST activities observed in BPH control when compared with normal control rats (fig. 1). Likewise, the BPH-induced rats treated with low and high doses (200 and 600 mg/kg/day, respectively) of the combined extract showed significant ($p<0.05$) increase in AST activities as compared with normal control rats. However, the standard control that was BPH-induced but treated with 5 mg/kg of finasteride showed no significant ($p<0.05$) increase in the AST activities as compared with normal control. The standard control had significantly ($p<0.05$) lower AST activities relative to BPH control, while there was no significant ($p<0.05$) decrease observed in the AST activities of BPH-induced rats treated with low and high dose (200 and 600 mg/kg/day, respectively) of combined extract, as compared with BPH control.

The data in figure 2 show that alanine transaminase (ALT) activities in BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The result showed that there was no significant ($p<0.05$) increase in the ALT activities of the BPH control and BPH-induced rats treated with 200 mg/kg/day of the combined extract when compared with the normal control. Also,



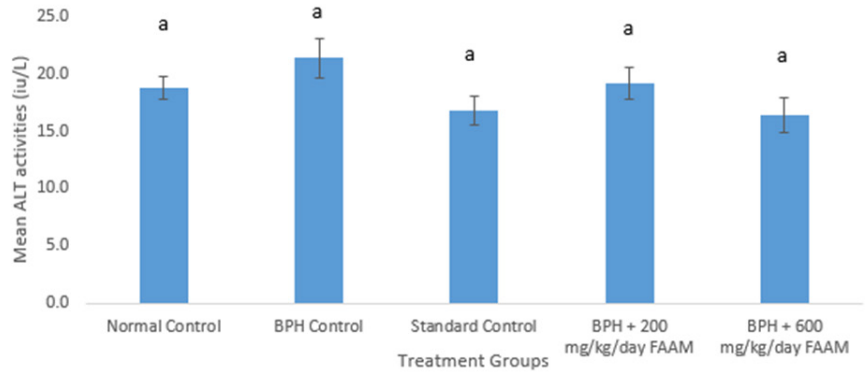
Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly ($p<0.05$) different between any pair of means.

Figure 1

Aspartate transaminase (AST) activities of BPH-induced rats treated with combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)

standard control group treated with 5 mg/kg/day of finasteride and BPH-induced rats treated with 600 mg/kg/day of the combined extract showed no significant (p<0.05) decreases in the ALT activities relative to normal control. Furthermore, the standard control and BPH-induced rats treated with 200 and 600 mg/kg of combined extract formulation respectively showed no significant (p<0.05) decrease in the ALT activities when compared with the BPH control. Additionally, all the combined extract (200 and 600 mg/kg/day) treated BPH-induced rats showed no significant (p<0.05) decreases in ALT activities when compared with the standard control.

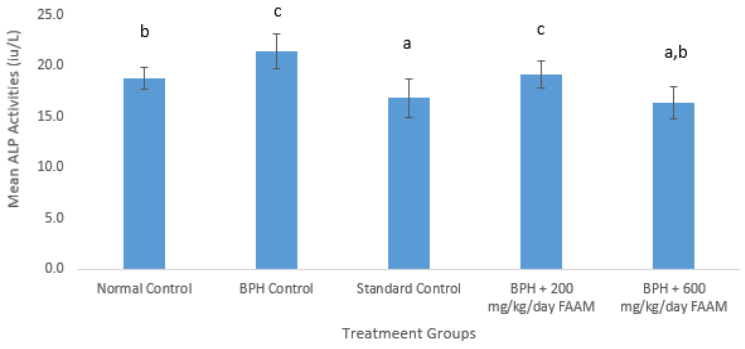
The data in figure 3 show the alkaline phosphatase (ALP) activities of BPH-induced rats treated with combined ethanol extract of *F. africna* and *A. mauritianum* leaves. The result showed that there were significant (p<0.05) increase in the ALP activities of BPH control and BPH-induced rats treated with 200 mg/kg/day of the combined ethanol extract when compared with the normal control. However, the standard control treated with 5 mg/kg/day of finasteride showed significant (p<0.05) decrease in the ALP activities relative to normal control, while BPH-induced rats treated with the combined extract at a dose of 600 mg/kg/day of showed no significant (p<0.05) decrease in the ALP activities as compared with normal control. Furthermore, the standard control and BPH-induced rats treated with 600 mg/kg/day of the combined ethanol extract



Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 2

Alanine transaminase (ALT) activities of BPH-induced rats treated with combined extract *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)



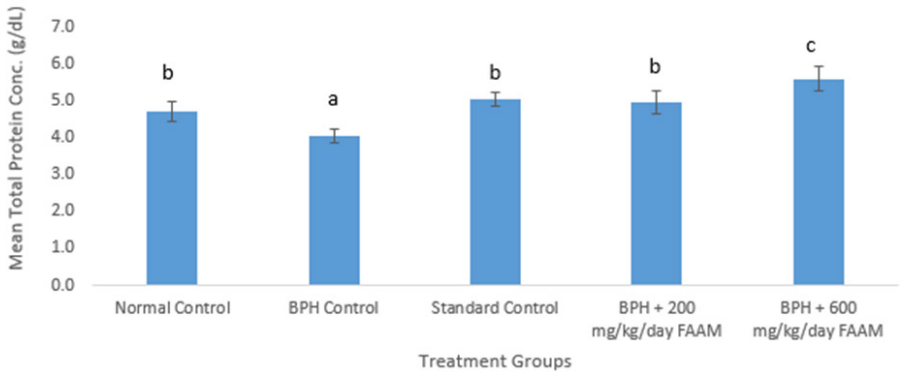
Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 3

Alkaline phosphatase activities of BPH-induced rats treated with combined ethanol extract of*Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)

showed significant (p<0.05) decrease in ALP activities as compared with BPH control. Additionally, the BPH-induced rats treated with 200 mg/kg/day of the combined extract showed significant (p<0.05) increase in the ALP activities relative to standard control while the BPH-induced rats treated with 600 mg/kg/day of the combined ethanol extract showed no significant (p<0.05) decrease in the ALP activities as compared with the standard control.

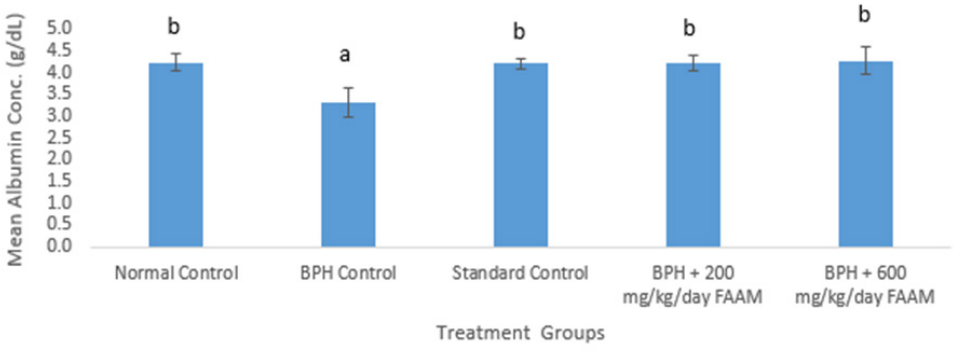
Figure 4 shows total protein concentrations of BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The result indicated no significant (p<0.05) increases in total protein concentrations of the standard control treated with 5 mg/kg/day of finasteride and BPH-induced rats treated with 200 mg/kg/day of the combined ethanol extract when compared with the normal control. On the contrary, the BPH-induced rats treated with 600 mg/kg/day of the combined ethanol extract showed significant (p<0.05) increase in the total protein concentration relative to the normal control while the total protein concentration of the BPH control was significantly (p<0.05) reduced when compared with the normal control. The standard control and BPH-induced rats treated with 200 and 600 mg/kg/day of the combined extract, respectively showed significant (p<0.05) increases in the total protein concentrations when compared with the BPH control. Besides, the BPH-induced rats treated with



Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 4

Total protein concentrations of BPH-induced rats treated with combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)



Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 5

Albumin concentrations of BPH-induced rats treated with combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)

200 and 600 mg/kg/day of the combined ethanol extract had no significant (p<0.05) decrease and significant (p<0.05) increase in the total protein concentrations respectively relative to the standard control.

The result in figure 5 shows the albumin (ALB) concentrations in BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The result showed no significant (p<0.05) decreases in the albumin concentrations of standard control treated with 5 mg/kg/day of finasteride and BPH-induced rats treated with 200 mg/kg/day of the combined extract when compared with the normal control. The BPH control showed a significant (p<0.05) reduction in the albumin concentration relative to the normal control while the BPH-induced rats treated with 600 mg/kg/day of the combined extract showed no significant (p<0.05) increase in the albumin concentration when compared with the normal control. Furthermore, the standard control and BPH-induced rats treated with 200 and 600 mg/kg/day of the combined extract respectively showed significant (p<0.05) increases in the albumin concentrations when compared with the BPH control.

The result in figure 6 shows the globulin concentrations of BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The result showed no significant (p<0.05) decrease in the globulin concentration of the standard control and BPH induced rat treated with 200 mg/kg/day of the combined extract as compared with normal control. The BPH control showed significant (p<0.05) decrease in the globulin concentration relative to the normal control while the BPH-induced rat treated with 600 mg/kg/day of the combined extract showed significant (p<0.05) increase in the globulin concentration when compared with the normal control. Furthermore, the BPH-induced rats treated with 200 and 600 mg/kg/day, respectively, of the combined extract showed significant (p<0.05) increase in the globulin concentrations relative to the BPH control. Contrary, the standard control showed no significant (p<0.05) increase in the globulin concentration when compared with the BPH control.

The data in figure 7 show total bilirubin concentrations in BPH-induced rats treated with combined extract of *F. africana* and *A. mauritianum* leaves. The result indicated that the standard control and BPH-induced rats treated with 200 and 600 mg/kg/day of the combined extract, respectively showed significant (p<0.05) decrease in the total bilirubin concentrations when compared with the normal control while the BPH control showed significant (p<0.05) increase in the total bilirubin relative to the normal control. Furthermore, the BPH control and the BPH-induced rats treated with 200 and 600 mg/kg/day respectively showed significant (p<0.05) decrease in the total bilirubin concentrations when compared with the BPH control. Similarly, the BPH-induced rats treated with 200 and 600 mg/kg/day, respectively, showed non-significant (p<0.05) increase and decrease in total bilirubin concentrations as compared with standard control.

The result in figure 8 shows the direct bilirubin (D. BIL) concentrations of BPH-induced rats treated

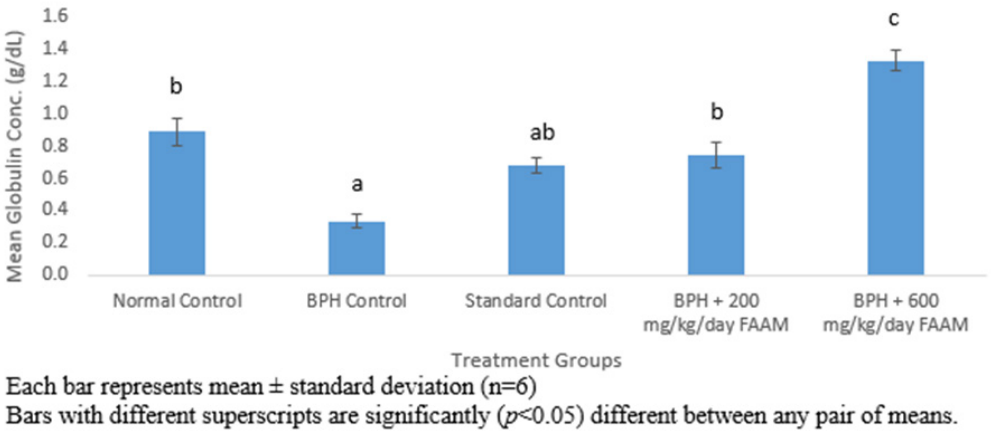
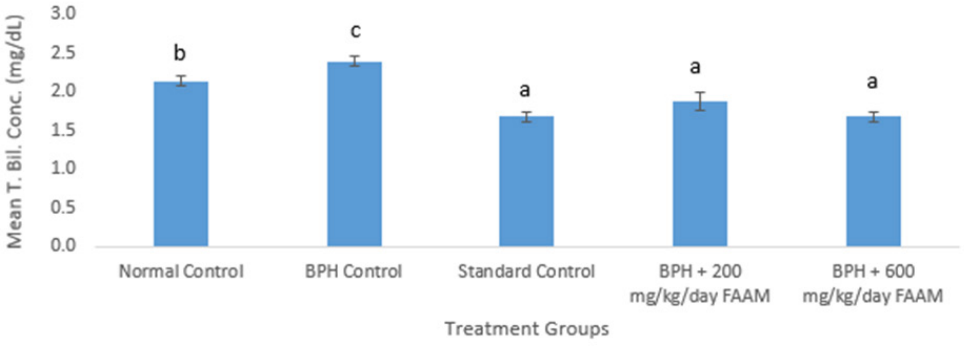


Figure 6

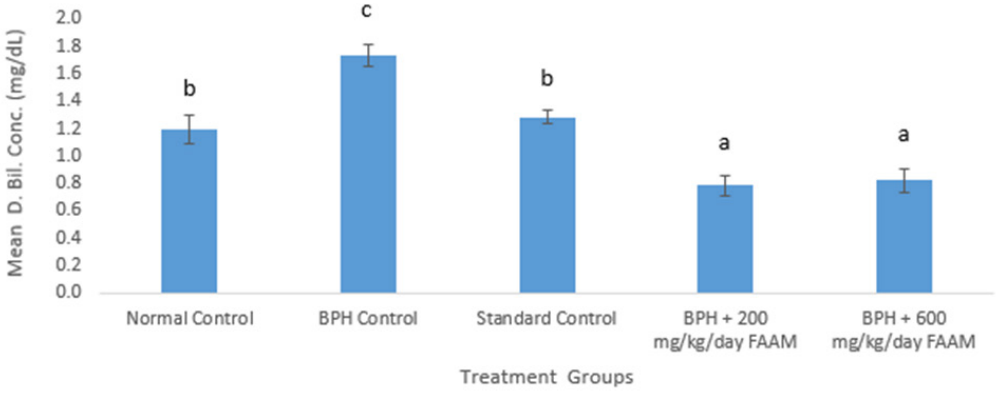
Globulin concentrations of BPH-induced rats treated with combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)



Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 7

Total bilirubin concentrations BPH-induced rats treated with combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)



Each bar represents mean ± standard deviation (n=6)
Bars with different superscripts are significantly (p<0.05) different between any pair of means.

Figure 8

Direct bilirubin concentrations of BPH-induced rats treated with the combined ethanol extract of *Funtumia africana* and *Abutilon mauritianum* leaves (FAAM)

with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The result showed significant (p<0.05) decreases in the direct bilirubin concentrations in the BPH-induced rats treated with combined ethanol extract at a dose of 200 and 600 mg/kg/day, respectively, as compared with the normal control. However, the BPH control showed significant (p<0.05) increase in direct bilirubin concentration relative to normal control, while the standard control treated with finasteride at a dose of 5 mg/kg/day showed no significant (p<0.05) increase in the direct bilirubin concentration as compared with normal control. Furthermore, the standard control and the BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves at a dose of 200 and 600 mg/kg/day, respectively, showed significant (p<0.05) reductions in a direct bilirubin concentration, as compared with BPH control. Additionally, the BPH-induced rats treated with combined extract at a dose of 200 and 600 mg/kg/day showed significant (p<0.05) decreases in the direct bilirubin concentrations, as compared with standard control.

Effects of combined ethanol extract of *F. africana* and *A. mauritianum* leaves on the liver histomorphology of benign prostatic hyperplasia induced in rats

The sections of the liver presented in figure 9 showed normal hepatic histomorphology for laboratory rodents. Normal hepatic lobules consisting of normal hepatocytes arranged in interconnecting cords around the central veins were observed. The hepatic cords are separated by hepatic sinusoids and

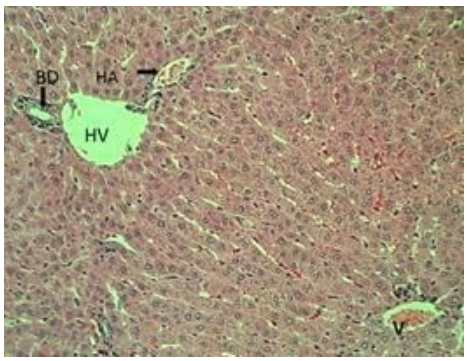


Figure 9

Histomorphology of liver section from normal control rats that were not induced benign prostatic hyperplasia.`

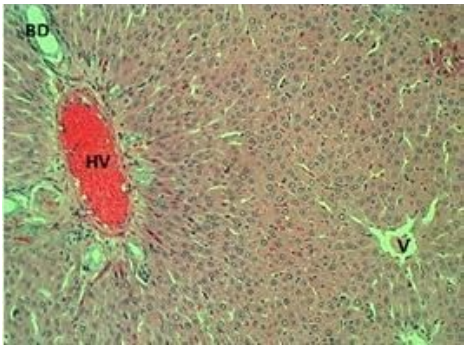


Figure 10

Histomorphology of liver section from benign prostatic hyperplasia induced untreated rats.`

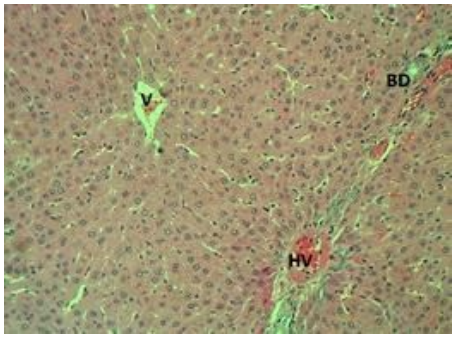


Figure 11

Histomorphology of liver section from benign prostatic hyperplasia induced rats treated with 5 mg/kg/day of finastride (standard drug).

are radially arranged around central veins, terminating at the portal areas in each hepatic lobule which contains the branches of the hepatic artery, hepatic vein and the bile ducts. Similarly, the sections of livers from BPH-induced untreated rats (fig. 10), BPH-induced rats treated with finasteride (i.e.

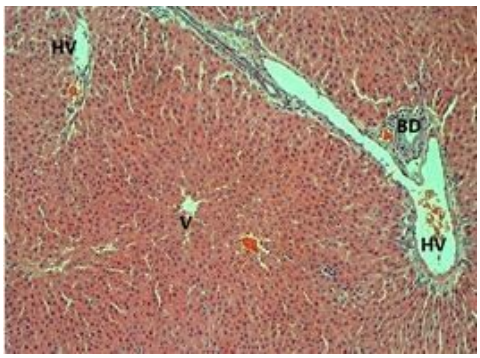


Figure 12

Histomorphology of liver section from benign prostatic hyperplasia induced rats treated with 200 mg/kg/day of FAAM.

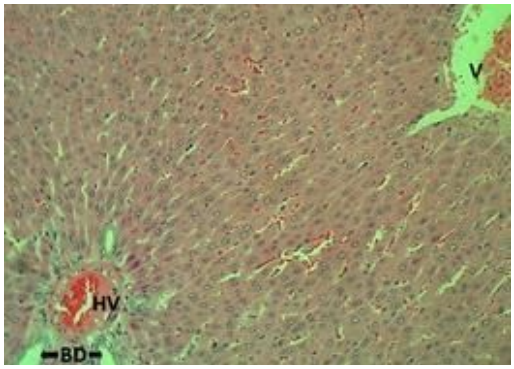


Figure 13

Histomorphology of liver section from benign prostatic hyperplasia induced rats treated with 600 mg/kg/day of FAAM.

standard control) in fig. 11, BPH-induced rats treated with polyherbal extract at a dose of 200 mg/kg and 600 mg/kg/day as shown in figure 12 and 13, respectively, showed normal liver histomorphology of normal rodents. The (V); (HV); (HA); and (BD) in figures 9 and 10 represent central vein, hepatic vein, hepatic artery and bile duct. H&E x160.

DISCUSSION

This study evaluated the liver function indices of BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves. The benign prostatic hyperplasia disorder has been reported to alter liver functions and increased serum hepatic enzyme activities including alanine transaminase and alkaline phosphatase [17, 18]. The significantly elevated hepatic enzyme activities including aspartate transaminase (AST) and alkaline phosphatase (ALP) in the BPH-induced untreated

rats are an indication of liver injury and increased leakage of hepatic enzymes to extrahepatic tissues due to increased liver membrane permeability. However, no significant increase of alanine transaminase (ALT) activity in the BPH-untreated rats indicated that the liver injury in rats was not sufficient to cause much leakage of ALT out of the liver to the extrahepatic tissues. The BPH probably elicited no liver injury, because a significant increase in ALT is more specific to liver injury than significant increases in the AST and ALP activities, as they could have arisen from other organs and tissues outside hepatic tissues [19]. The dose-dependent non-significant reductions in AST and ALT activities in the BPH-induced rats treated with combined ethanol extract of *F. africana* and *A. mauritianum* leaves relative to BPH control indicated hepatoprotective and non-hepatotoxic effects of combined ethanol extract. Furthermore, the BPH-induced rats treated with the combined ethanol extract of *F. africana* and *A. mauritianum* leaves at a dose of 600 mg/kg/day compared with BPH control showed that the combined ethanol extract possesses hepatoprotective effects that decreased leakage of ALP to extrahepatic tissues. The significant alterations in liver marker enzymes activities of BPH-induced rats in this study were in disagreement with findings of Mohamed *et al*., who reported non-significant alterations in the ALT and AST activities of BPH-induced rats [20].

The significant reductions in the total proteins, albumin and globulin concentrations in BPH-induced untreated rats showed that rats suffered from impaired liver functions that reduced the biosynthetic ability of livers. This adversely affected the level of proteins including albumin and globulins synthesized by the liver. The impaired liver functions in BPH-induced untreated rats will invariably increase the negative effects of BPH in rats and reduce their survival chances. The significant reductions in serum albumin and globulin levels could be attributed to their decreased synthesis in the liver but could also occur due to malabsorption and nephrotic syndrome. The significantly elevated total protein, albumin and globulin concentrations in BPH-induced rats treated with graded doses of combined ethanol extract of *F. africana* and *A. mauritianum* leaves relative to BPH control indicated that combined extract ameliorated the adverse effects of BPH on liver functions. Proteins are needed in sufficient concentrations in the body to maintain adequate biochemical functions such as transport of chemical substances including minerals and lipids. They play an essential role in the regulation of blood pressure and inflammatory reactions and their sufficient concentrations in the combined ethanol extract of *F. africana* and *A. mauritianum* leaves treated BPH-induced rats will promote normal biochemical functions and improve their survival chances. Albumin is synthesized in the liver and functions to transport minerals, bilirubin, chemical signals (hormones), vitamins, drugs, lipids, and thus prevents hyperlipidaemia and atherosclerosis [21, 22]. Globulins are also mainly synthesized in the liver but very little concentration can be produced by plasma cells. The increased albumin and globulin levels in BPH-induced rats treated with combined extract further suggest the improved capacity of liver cells to synthesize enough globulin and decreased the loss of protein through kidney which mostly occurs in nephrotic syndrome associated with BPH. Low globulin level in BPH untreated rats could adversely affect their immune system, as globulins are integral part of immunological responses in the body, while the increased globulin levels in combined ethanol extract of *F. africana* and *A. mauritianum* leaves would promote effective immune functions. These findings are in line with reports of Alavi-Shoushtari *et al.*, on the role of globulins in immunological responses [23].

Bilirubin is a metabolic breakdown product of haemolysis with antioxidant and anti-inflammatory properties [24]. The significantly increased serum total bilirubin and direct bilirubin concentrations in BPH-induced untreated rats relative to the normal control and BPH-induced rats treated with the combined ethanol extract of *F. africana* and *A. mauritianum* leaves showed that BPH has negative effects on the liver functions. The elevated total bilirubin and direct bilirubin could be attributed to increased red blood cell haemolysis, reduced albumin level to enhance hepatic uptake of bilirubin and impaired ability of the body to conjugate bilirubin to ease detoxification and agrees with the findings of Tarantino *et al.,* that liver injury or disease reduces the hepatic clearance of bilirubin [25]. However, lower total bilirubin observed in BPH-induced rats treated with graded doses of combined ethanol extract of *F. africana* and *A. mauritianum* leaves indicated hepatoprotective effects of combined extract that prevented the adverse effects of BPH on liver cells. The BPH-induced rats treated with combined extract retained their normal liver integrity and functions and were able to detoxify bilirubin effectively with improved clearance rate. High albumin levels in serum in combined ethanol of *F. africana* and *A. mauritianum* leaves treated BPH-induced rats

enhanced the hepatic uptake and detoxification of bilirubin in line with findings of Inoue *et al*. [26]. The normal liver histomorphology of BPH-induced untreated, and BPH-induced rats treated with finasteride and combined ethanol of *F. africana* and *A. mauritianum* leaves, respectively, indicated that BPH induction caused no observable injury to liver histo-architecture, though, there was massive impair of liver functions in the rats.

CONCLUSION

The findings of this study showed there are impaired liver functions associated with benign prostatic hyperplasia in rats and treatment with combined ethanol extract of *F. africana* and *A. mauritianum* leaves could effectively prevent it. The combined ethanol extract of *F. africana* and *A. mauritianum* leaves possesses hepatoprotective properties needed to reverse liver injury and integrity and restore full hepatic function but requires further studies to identify and isolate its bioactive constituents.

Funding/support: the authors affirmed no external funding for this study.

Conflicts of interest: authors declare no conflicts of interests.

REFERENCES

1. Chokkalingam AP, Yeboah ED, Demarzo A, Netto G, Yu K, Biritwum RB, et al. Prevalence of BPH and lower urinary tract symptoms in West Africans. Prost Canc Prost Dis 2012; 15(2):170-176.

2. Singh RP, Agarwal R. Mechanisms of action of novel agents for prostate cancer chemoprevention. Endocrine-Related Canc 2006; 13:751-778.

3. Chan SW. Pathology and medical therapy of benign prostatic hyperplasia. Hong Kong Med Diary 2011; 16(6):4-8.

4. Ezugwu CH, Joshua PE, Chilaka FC, Nwodo OFC, Dasofunjo K, Ezugwu MU. Effect of ethanol extract of *Zapoteca portoricensis* stem on liver, kidney and prostatic biomarkers of testosterone-induced benign prostate hyperplasia (BPH) in male albino rats. Austr J Basic Appl Sci 2018; 12(10):19-27.

5. Ramadwa TE, Elgorashi EE, McGawa LJ, Ahmed AS, Eloff JN. Antimicrobial, anti-inflammatory activity and cytotoxicity of *Funtumia africana* leaf extract fractions and the isolated methyl ursolate. South Afr J Bot 2017; 108:126-131.

6. Uroko RI, Egba SI, Uchenna ON, Orjiakor CA, Agbafor A, Alaribe CC. Therapeutic effects of methanolic extract of *Funtumia africana* leaves on antioxidants and haematological indices of carbon tetrachloride-induced oxidative stress in rats. Drug Invent Today 2019; 12(1):114-122.

7. Soro D, Koné MW, Kamanzi-Attindehou K. Evaluation des activités antimicrobiennes et anti-radicaux libres de quelques taxons bioactifs de Côte d'Ivoire. Eur J Sci Res 2008; 40(2):307-317.

8. Burkill HM. The useful plants of West Tropical Africa. 2nd ed., vol. 4. Families M-R. Royal Botanic Gardens, Kew, Richmond 1997.

9. Banso A, Adeyemo S. Phytochemical screening and antimicrobial assessment of *Abutilon mauritianum, Bacopa monnifera* and *Datura stramonium*. Biokemistri 2006; 18(1):39-44.

10. Akapa TC, Kehinde AO, Beatrice OO, Olajide OJ. Antipyretic activity of *Abutilon mauritianum* (Jacq.) roots in Wistar rats. Intern J Pharm Sci Res 2014; 5:42-46.

11. Achigan-Dako EG. *Abutilon mauritianum* (Jacq.) Medik. In: Brink M, Achigan-Dako EG. (Editors), PROTA, Wageningen 2010:24-25.

12. Reitman S, Frankel S. A colourimetric method for the determination of serum glutamic oxaloacetic and glutamic pyruvic transaminase. Am J Clin Path 1975; 28:56-63.

13. Englehardt A. Measurement of alkaline phosphatase. Aerztl Labor 1970; 16:42-43.

14. Jendrassik L. Grof P. Determination of total bilirubin. Biochemistry 1930; 279:81-89.

15. Reinhold JG. Total protein, albumin and globulin. Standard Meth Clin Chem 1953; 1:88-97.

16. Disbrey BD, Rack JH. Histological Laboratory Methods. Livingstone 1970.

17. Harvey PW, Everett DJ, Springall CJ. Adverse effects of prolactin in rodents and humans: breast and

prostate cancer. J Psichopharmacol 2008; 2:2-7.

18. Meludu SC, Ezenwelu VI, Manafa PO, Onah CE, Ekuma-Okereke O. Biochemical characteristics of liver enzymes, prolactin, zinc and selenium in benign prostatic hyperplasia and cancer of the prostate patients attending urology clinic at Nnamdi Azikiwe University Teaching Hospital, Nnewi. Imper J Interdiscipl Res 2017; 3(7):223-232.

19. Akubugwo IE, Agbafor KN. Hepatotoxical evaluation of water and salt from Okposi and Uburu salt lakes, Nigeria. Estudos de Biologia 2007; 29:99-104.

20. Mohamed DA, Rashed MM, Shallan M, Fouda K, Hanna LM. Amelioration of benign prostate hyperplasia in rats through plant foods. Interna J Pharmacogn Phytochem Res 2016; 8(12):2063-2070.

21. Savory J, Hammond J. Measurement of proteins in biological fluids. In: Sonnenwirth AC, Jarett L (eds.). Gradwohl's Clinical Laboratory Methods and Diagnosis, St Louis 1980.

22. McPherson RA. Specific Proteins. In: Henry JB (ed.). Clinical Diagnosis and Management, Philadelphia 1984.

23. Alavi-Shoushtari SM, Asri-Rezai S, Abshenas J. A study of the uterine protein variations during the oestrus cycle in the cow: a comparison with the serum proteins. Animal Reprod Sci 2006; 96(1-2):10-20.

24. Shen H, Zeng C, Wu X, Liu S, Chen X. Prognostic value of total bilirubin in patients with acute myocardial infarction: A meta-analysis. Medicine (Baltimore) 2019; 98(3):e13920.

25. Tarantino G, Colao A, Capone D, Conca P, Tarantino M, Grimald E, et al. Circulating levels of cytochrome C, gamma-glutamyl transferase, triglycerides and unconjugated bilirubin in overweight/obese patients with non-alcoholic fatty liver disease. J Biol Reg Homeo Agents 2011; 25(1):47-56.

26. Inoue M, Hirata E, Morino Y, Nagase S, Chowdhury JR, Chowdhury NR, Arias IM. The role of albumin in the hepatic transport of bilirubin: studies in mutant analbuminemic rats. J Biochem 1985; 97(3):737-743