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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

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Abstract

The effect of ethanol extract of *Zapoteca portoricensis* stem on testosterone-induced benign prostate hyperplasia (BPH) in adult male albino rats was aimed at in this study. The percentage yield of the extract was determined to be 1.73% and the extract showed the presence of alkaloids, terpenoids, saponins, phenols, flavonoids, tannins, glycosides and carotenoids as phytoconstituents. A dose of 5000mg/kg body weight was found to be safe in the LD_{50} study of the extract. A total of 25 adult male albino rats (weighing 231-391g) were selected for this study and randomly divided into five groups (1, 2, 3, 4 and 5) of five animals per group. Group 1 served as the normal control, group 2 as the positive control, group 3 as the standard control groups 4 and 5 as the test groups. Animals in group 2, 3, 4 and 5 were induced with BPH via daily subcutaneous injection of testosterone propionate (3mg/kgbwt) for 14 days and group 1 received subcutaneous injection of olive oil in place of the hormone for the same duration. After the induction, groups 1 and 2 received oral administration of 2 % v/v tween 80 solution and groups 3, 4 and 5 received oral administration of finasteride (10mg/kgbwt), 100mg/kgbwt extract and 200mg/kgbwt extract respectively for 21 days. The extract treated groups also showed significant ($P < 0.05$) decrease in mean serum ALP, ALT and AST compared to those of the positive control. Mean serum total bilirubin concentrations of animals in the extract treated groups decreased non-significantly ($P > 0.05$) compared to those of group 2 animals. Mean serum creatinine and urea concentrations of animals in the extract treated groups decreased significantly ($P<0.05$) compared to those of group 2 animals. The activities of prostate acid phosphatase and 5 α reductase in sera of the treated group decreased significantly ($P < 0.05$) when compared those of group 2. From this present research, it will be logical to infer that ethanol extract of the *Zapoteca portoricensis* stem in the treatment of testosterone-induced benign prostate hyperplasia in male albino rats proffers no assault on the functional integrity of both the liver and the kidney.

Key words: Benign prostate hyperplasia, liver, kidney, *Zapoteca portoricensis*

INTRODUCTION

Medicinal plants have been identified and used throughout human history. They have the ability to synthesize a wide variety of bioactive chemical compounds that perform important biological function and have been used to make drugs (Treben, 1998). At least 12,000 of the bioactive compounds have been isolated so far, a number estimated to be less than 10% of the total number of phytochemicals known (Lai and Roy, 2004; Tapsell *et al*., 2006). These compounds including alkaloids, tannins, flavonoids, glycosides, saponins and terpenoids are the major basis of pharmacological activities of medicinal plants (Oloyede, 2005). *Zapoteca portoricensis*, commonly called white stickpea, belonging to the family of *Fabaceae* is a perennial shrub with slender unarmed branches and with small oral green leaves. The plant is a native of the West Africa, the West Indies and the Atlantic coast of America and is used in folk medicine in various countries for the treatment of toothaches, tonsilities, external wounds diarrhea and convulsion. Different parts of the plants are used in Eastern Nigeria in the treatment of constipation, convulsion, madness, prolonged labour and skin infections (Agbafor *et al*., 2011; Nwodo *et al*., 2014).

The liver is a central organ in biochemical homeostasis. Aspartate aminotransferase (AST), alanine aminotransferase and gamma-glutamyltransferase are important in diagnosis of liver damage by chemical toxicity or infection. These enzymes are located intracellularly, but leak out into the blood stream when the tissue is damaged (Burtis and Ashwood, 2003; Akubugwo and Agbafor, 2007). In spite of the tremendous strides in modern medicine, there are hardly any drugs that can stimulate liver function or offer protection to the hepatocytes from damage. Thus, many folk remedies from plants are studied for their possible hepatoprotective effect against chemically induced liver damage in experimental animals (Singh *et al*., 2010).

Chronic BPH can cause urine to back up into the kidneys and cause damage to them (Untergasser *et al*., 2005). It is well-accepted today that bladder outlet obstruction due to BPH might cause hydronephrosis and renal failure (Roehrborn, 2008). Lower urinary tract symptoms (LUTS) possibly related to benign prostatic enlargement (BPE) and benign prostatic obstruction (BPO) due to BPH interfere significantly with normal daily activities (Parsons and Kashefi, 2008). Previous study showed a much higher mortality among BPH patients who underwent surgical treatment when renal insufficiency was present at the same time. Patients with BPH also have a significantly higher risk of chronic kidney disease, probably due to an obstructive uropathy (Eman, 2013).

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Prostatic acid phosphatase (PAP), a glycoprotein synthesized by the prostate gland, is a member of a diverse group of isoenzymes, the acid phosphatases, which are capable of hydrolyzing phosphate esters in acidic medium. PAP is one of the prostatic secretions used as a marker of prostatic diseases and as an indicator of treatment progress. Elevations in PAP levels have been reported in animals treated with androgens and oestrogen and may be due to increased lysosomal activity (Jeyaraj *et al*., 2000). Steroid 5α-reductase metabolizes testosterone to 5α dihydrotestosterone (5α-DHT), which is a more potent androgen than testosterone and exerts its function in androgen-responsive tissues. The metabolite 5α-DHT is responsible for benign prostate hyperplasia (BPH) and prostate cancer (PCa), major neoplastic diseases in older men. The enzyme is produced only in specific tissues of the male human body, namely the skin, seminal vesicles, prostate and epididymis. Inhibition of 5-alpha reductase results in decreased production of DHT, increased levels of testosterone and possibly increased levels of estradiol (Atsushi *et al*., 2013). Therefore this present research determines the 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

MATERIALS AND METHODS

Plant Materials

The stems of *Zapoteca portoricensis* were collected from Orba, Nsukka, Enugu State of Nigeria. The plant materials were authenticated by Mr. Alfred Ozioko, a taxonomist at the Centre for Ethenomedicine and Drugs Development, a subsidiary of Bioresources Development and Conservation Program (BCDP), Nsukka, Enugu State.

Chemicals and Assay kits

All the chemicals used in this study were of analytical grade and were used as such without further purification. Fresh distilled water was used throughout the experimental period. Assay kits used in all the analysis in this study were products of Bioscience, Cusabio, Magiwel and Randox laboratories.

Laboratory animals

Adult male abino rats (230-400 g) obtained from the animal house of Biochemistry Department, University of Nigeria, were kept under standard environmental condition of 12/12 hours light/dark cycle. They were housed in polypropylene cages (5 animals per cage), and were maintained on mouse chow (Livestock Feeds Nigeria Ltd), provided with water *ad libitum*. They were allowed to acclimatize for 7 days to the laboratory conditions before the experiment. The use and care of the animals, and the experimental protocol were in strict compliance with the Institute of Laboratory Animals Research (ILAR) guidelines on the use and care of animals, in experimental studies and approved by the local ethics committee of our institution.

Methods

Preparation of ethanol stems extract of *Zapoteca portoricensis*

Fresh stems of *Zapoteca portoricensis* were collected, cleaned and air dried before being subjected to size reduction to a coarse powder with electric grinder. The stem powder (5kg) was dissolved in 10L of 99.7% ethanol for 72hours to achieve maximum extraction. The mixture was agitated using a magnetic stirrer and filtered with Whatman No.1 filter paper. The filtrate was evaporated to dryness until constant weight of the crude extract was obtained. The concentrated crude extract (86.5g) with a percentage yield of 1.73 was stored in an air tight bottle and kept in a refrigerator at 4 °C till used.

Qualitative phytochemical analysis

Preliminary phytochemical screening was performed to identify the presence of bioactive compounds in crude ethanol stem extract of the *Zapoteca portoricensis* used in this study. The phytochemicals (such as flavonoids, glycosides, tannins, alkaloids, saponins, steroids and terpinoids) were tested for using the method of Trease and Evans (1989); modified by Sofowora (2008) and Tiwari *et al* (2011).

Acute toxicity and lethality (LD_{50}) test

The oral acute toxicity of the ethanol extract was determined according to the method described by Lorke (Lorke, 1983).

Determination of Doses

The ethanol extract of *Zapoteca portoricensis* was subjected to acute toxicity studies to determine the dose for the *in vivo* studies according to the Organization for Economic Cooperation and Development guidelines (Deora *et al*., 2010). In all cases, a 3000-mg/kg oral dose of the test extract was found to be tolerable, as no mortality was observed during the study. On the basis of this study, the doses of 100 and 200 mg/kg for the extract were selected.

Animal grouping and BPH induction

A total of 25 adult male albino rats (weighing 230-390g) were selected for this study. They were randomly divided into five groups (1, 2, 3, 4 and 5) of 5 animals each and each group housed in its own cage. Animals in Groups 2, 3, 4 and 5 were induced with BPH by exogenous administration of 10 mg/kg body weight testosterone propionate dissolved in olive oil which served as the vehicle. The administrations which were once a day by subcutaneous injection as outlined by Nandecha *et al*. (2010), Ejike and Ezeanyika (2011) and Surendra *et al*. (2011) lasted for 14 days before commencement of treatment. The normal control group (group 1) received subcutaneous injection of olive oil in place of the hormone for the same duration.

Animal grouping and BPH treatment

At the end of 14 days induction, the animals in Groups 1 (normal controls) and 2 (positive controls) were given oral doses of 2% v/v Tween 80 solution. The animals in Group 3 were given oral dose of 10 mg/kg body weight finasteride, while those in groups 4 and 5 received oral doses of 100 mg/kg and 200 mg/kg body weight extracts respectively. The oral administration was done once per day by the use of gavages for 21 days. The animals were weighed prior to the commencement of the experiment and subsequently every week till the end of the experiment as outlined by Nandecha *et al*. (2010).

Collection of sera and tissue samples for analysis

After 21 days of treatment, the rats were fasted for 12 hours, anesthetized by a brief exposure to tri chloro methane vapour, and bled exhaustively by ocular puncture. Blood samples were collected, allowed to clot and centrifuged at 2000 × *g* for 10 min. The sera were carefully separated and used for biochemical analyses.

Biochemical assays

The serum aspartate aminotransferase or serum glutamic oxaloacetic transaminase (SGOT) was determined (Reitman and Frankel 1957)**,** serum ALP was assayed with a Randox kit by the methods of Kind and King (1972), serum total bilirubin level was estimated by the method of Helga and Kenneth (1937)**,** concentrations of serum creatinine and serum urea were estimated using Randox assay kit based on the method of Tietz *et al*. (1994) and Kaplan (1965) as modified by Stephen *et al*. (2007),Prostatic acid phosphatase and Serum steroid 5 alpha reductase activities activity in serum was measured using the method of Fishman and Lerhner (1953)

Statistical analysis

Data were reported as means ± SEM, where appropriate. One-way analysis of variance (ANOVA) was used to analyse the experimental data and Duncan multiple test range was used to compare the group means obtained after each treatment with control measurements. Differences were considered significant when ($P \leq 0.05$).

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RESULTS

Preliminary phytochemical screening of *Zapoteca portoricensis* stem extract from aqueous and different organic solvents carried out reported relative presence of various phytoconstituents such as alkaloids, terpenoids, saponins, phenols, flavonoids, tannins, glycosides and carotenoids (Table 1). The LD_{50} result of the ethanol extract of *Zapoteca portoricensis* stem on adult mice showed that the extract was safe at a dose of 5000 mg/kg body weight since there was no record of death during the study. Fig. 1 shows a significantly ($p < 0.05$) lower alkaline phosphatase (ALP) activity of animals in group 2, group 4 and group 5 compared to the ALP activity of normal control animals (group 1). The ALP activity of group 3 animals was observed to be non-significantly ($p > 0.05$) higher compared to ALP activity of the normal control animals. However ALP activity of animals in group3, group 4 and group 5 was significantly ($p < 0.05$) lower compared to that of the positive control (group 2) animals and there was significantly ($p < 0.05$) higher ALP activity of animals in extract treated groups compared to that of the group 3 animals (Fig. 1). The data in Fig. 2 shows a significantly ($p< 0.05$) higher alanine aminotransferase activity of animals in the induced groups (group 2, group 3, group 4 and group 5) compared to the enzyme (ALT) activity of animals in normal control group (group 1). Animals in the induced and treated groups (group 3, group 4 and group 5) had significantly ($p < 0.05$) lower alanine amino transferase activity compared to that of animals in the induced and non-treated group or positive control group (group 2) as shown in Fig. 2. However, the increase in alanine aminotransferase activity of animals in the extract treated group (group 4) was non-significant ($p > 0.05$) compared to the ALT activity of the finasteride treated group (group 3) (Fig. 2).

The data in Fig. 3 reveal that there are significant ($P < 0.05$) increases in the aspartate amino- transferase (AST) activities of group 2, group 3, group 4 and group 5 animals compared to the AST activity of normal control animals (group 1). Fig. 3 shows also that there are significantly ($p < 0.05$) lower AST activities of animals in group 3, group 4 and group 5 (the induced and treated groups) compared to the AST activity of group 2 (the induced and non-treated group). It also shows that there is a significantly ($p < 0.05$) higher aspartate aminotransferase (AST) activity of group 4 animals compared to the AST activity of the standard control animals (group 3) and a significantly ($p < 0.05$) lower AST activity of animals in group 5 compared to the AST activity of standard control animals (group 3). The serum total bilirubin concentrations of animals in the extract treated groups (groups 4 and 5) were significantly ($p<0.05$) lower compared to that of the positive control animals treated with testosterone propionate only (group 2). There was no significant difference ($p>0.05$) observed in serum total bilirubin concentrations of the extract treated animals (groups 4 and 5) compared to those of group 1 and group 3 animals and in between the extract treated groups (Fig. 4). The mean serum creatinine concentration were significantly ($p<0.05$) lower in the extract treated groups (groups 4 and 5) compared to the mean serum creatinine concentration of the positive control animals (group 2). It was non-significantly ($p>0.05$) and significantly ($p<0.05$) lower in group 4 and group 5 respectively compared to the standard control group (group 3). There was no significant difference ($p>0.05$) in creatinine concentration of group 4 compared to that of the normal control group (group 1) while that of group 5 was non-significantly ($p>0.05$) lower compared to those of group 1 and group 4 (Fig. 5). The mean serum urea concentrations of the extract treated groups (groups 4 and 5) were non-significantly ($p<0.05$) higher compared to that of the normal control group (group 1). However, there were significantly ($p<0.05$) lower mean serum urea concentrations of animals in the extract treated groups (groups 4 and 5) compared to that of the animals in positive control group (group 2) and non-significantly ($p>0.05$) lower mean serum urea concentrations compared to that of group 3 animals. There was non-significantly ($p>0.05$) lower mean serum urea concentration of animals in group 5 compared to mean serum urea concentration of animals in group 4 (Fig. 6). The mean serum prostatic acid phosphatase (PAP) activities of animals in extract treated groups (groups 4 and 5) were observed to be significantly ($p<0.05$) lower compared to mean serum PAP activity of positive control animals (group 2). There were non-significantly ($p>0.05$) lower activities of mean serum PAP observed in the extract treated groups (groups 4 and 5) compared to that of the normal control group animals (group 1). However, mean serum PAP activities of the extract treated groups were significantly ($p<0.05$) higher compared to that of the finasteride treated group (group 3) and there was no significant difference ($p>0.05$) in mean serum PAP activity of group 5 (200 mg/kg body weight) animals compared to the activity observed in group 4 (100 mg/kg body weight) animals (Fig. 7). There were non-significantly ($p>0.05$) higher activities of mean serum steroid 5 alpha reductase of animals in the induced and treated groups (group 3, group 4 and group 5) compared to the mean serum steroid 5 alpha reductase activity of animals in the normal control group (group 1) (Fig. 8). However, it was observed that animals in the induced and non-treated (positive control) group (group 2) had significantly ($p<0.05$) higher mean serum steroid 5 alpha reductase activity compared to the mean serum steroid 5 alpha reductase activity of animals in the normal control group (group 1). The mean serum steroid 5 alpha reductase activities of animals in the extract treated groups (group 4 and group 5) were observed to be non-significantly ($p>0.05$) lower compared to the mean serum steroid 5 alpha reductase activity of animals in the finasteride treated (standard) group (group 3). The induced and extract treated groups showed significantly ($p<0.05$) lower mean serum steroid 5 alpha reductase activities compared to the activity observed in the induced and non-treated (positive control) animals (group 2). There were non-significantly ($p>0.05$) lower mean serum 5 alpha reductase activities of animals in group 4 and group 5 compared to that of group 3 animals and no significant difference ($p>0.05$) was observed in the activity between group 4 and group 5 animals (Fig. 8).

Table 1: Preliminary analysis of phytochemicals in aqueous and different organic stem extract of *Zapoteca portoricensis*

S. No.	Phytochemicals	Inference in different extracts				
		A	B	E	EA	M
1	Alkaloids	+	++	++	+++	++
2	Anthraquinone	−	−	−	−	−
3	Carotenoids	+	+	++	+	+
4	Flavonoids	−	−	++	+	−
5	Glycosides	++	+	++	+	++
6	Phenols	+	+	+	−	+
7	Reducing sugar	−	−	−	−	−
8	Saponins	++	+	+++	+	++
9	Steroids	−	+	−	−	−
10	Tannins	−	−	+	−	+
11	Terpinoids	−	++	++	−	++

Key: A = Aqueous extract, B = Butanol extract, E = Ethanol extract, EA = Ethyl acetate extract, M = Methanol extract, − = Not detected, + = Present in low concentration, ++ =Present in moderate concentration and +++ = Present in high concentration.

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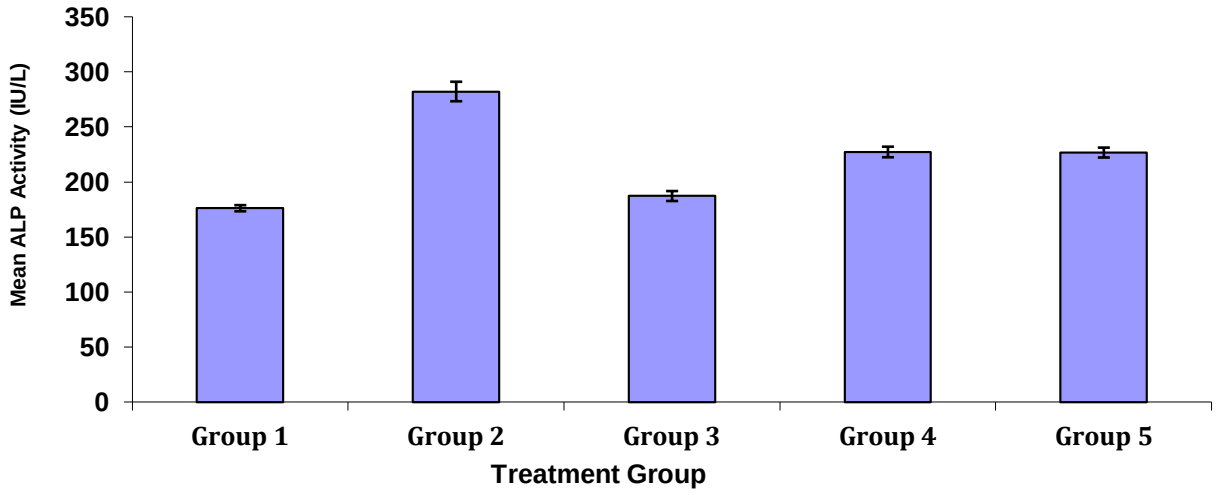

Fig. 1: Effect of ethanol extract of *Zapoteca portorensis* stem on the alkaline phosphatase activity of normal and testosterone-induced male albino rats

Group 1 = Normal control
Group 2 = Positive control (Testosterone-induced BPH non-treated)
Group 3 = Standard control (BPH + finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

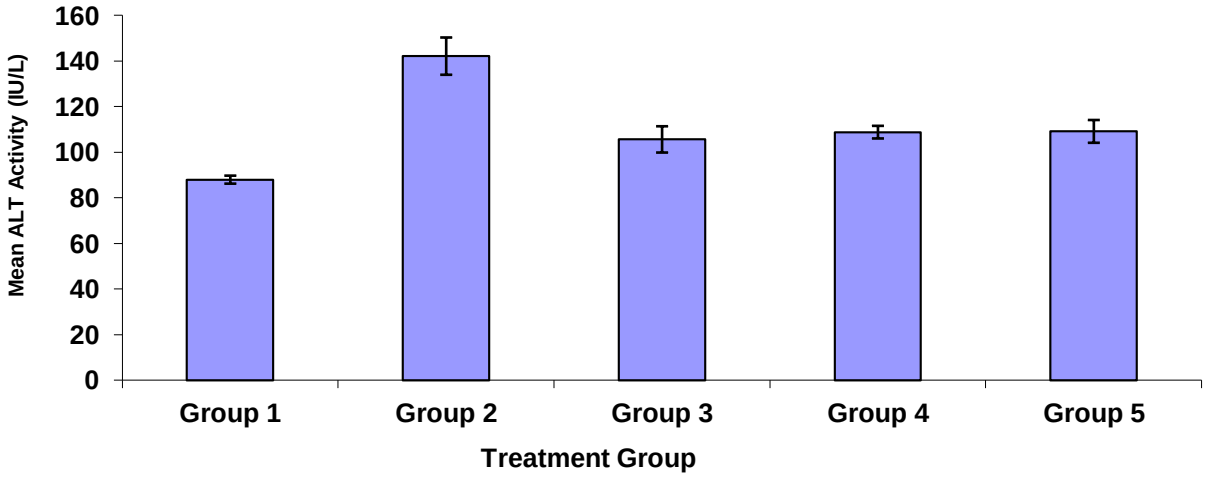

Fig. 2: Effect of ethanol extract of *Zapoteca portorensis* stem on the alanine aminotransferase activity of normal and testosterone-induced male albino rats

Group 1 = Normal control
Group 2 = Positive control (Testosterone-induced BPH non-treated)
Group 3 = Standard control (BPH + finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

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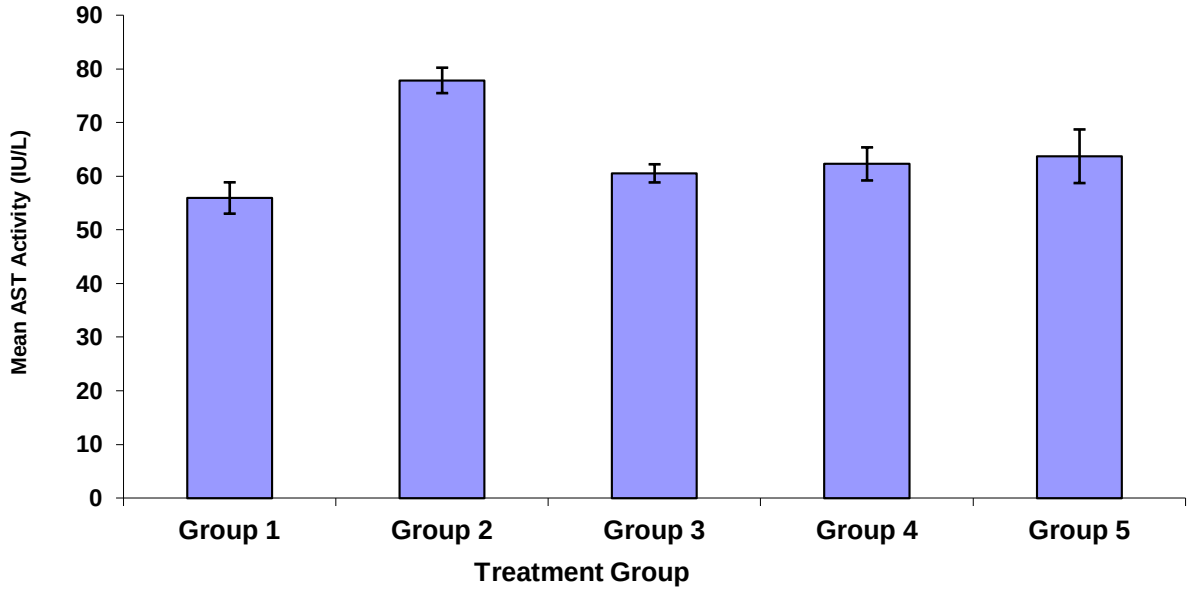

Fig. 3: Effect of ethanol extract of *Zapoteca portorensis* stem on the aspartate aminotransferase activity of normal and testosterone-induced male albino rats

Group 1 = Normal control
Group 2 = Positive control (Testosterone-induced BPH non-treated)
Group 3 = Standard control (BPH + finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

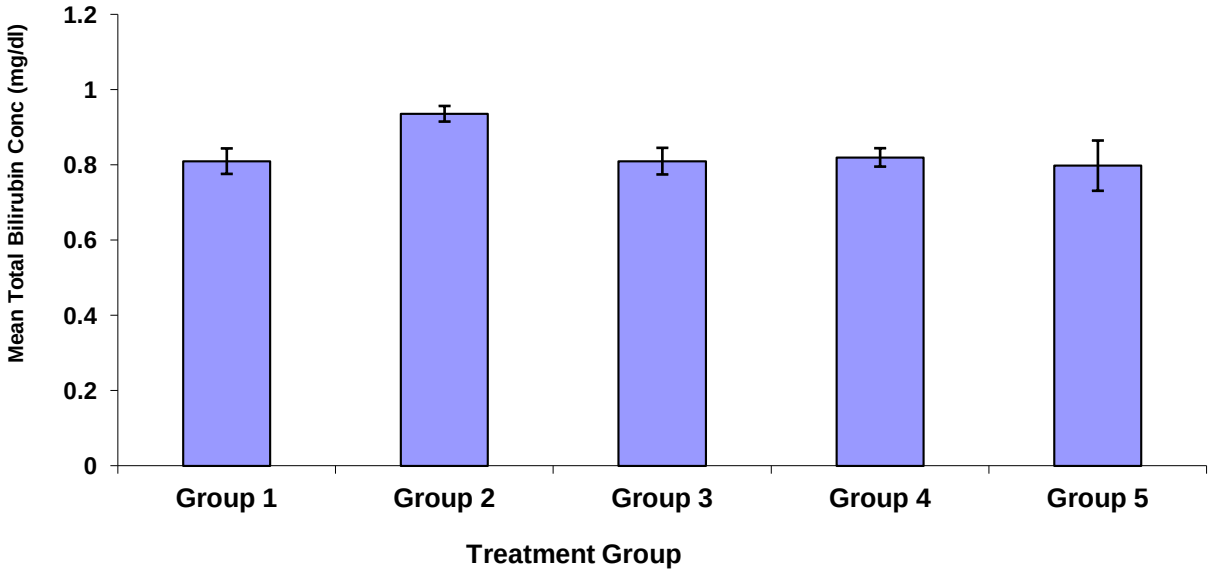

Fig. 4: Effect of ethanol extract of *Zapoteca portorensis* stem on the total bilirubin concentration of normal and testosterone-induced male albino rats

Group 1 = Normal control
Group 2 = Positive control (Testosterone-induced BPH non-treated)
Group 3 = Standard control (BPH + finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

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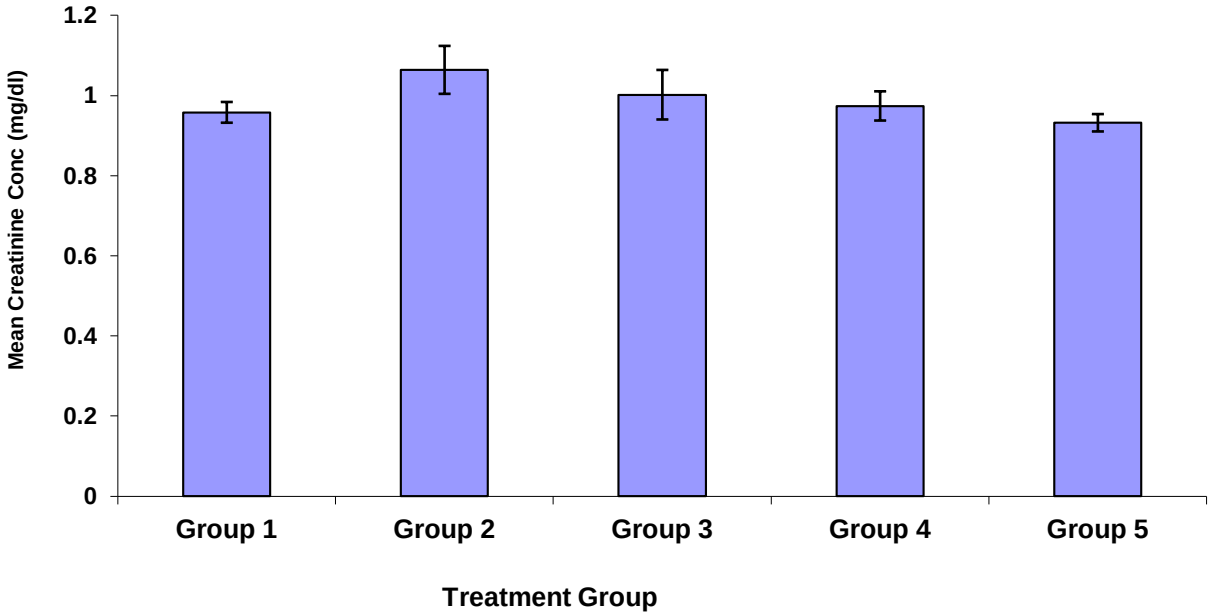

Fig. 5: Effect of ethanol extract of *Zapoteca portorensis* stem on the creatinine concentration of normal and testosterone-induced male rats

Group 1 = Normal control (Vehicle only)
Group 2 = Positive control (Testosterone-induced BPH only)
Group 3 = Standard control (BPH + 10 mg/kg finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight
Group 5 = BPH + extract treated (200mg/kg body weight)

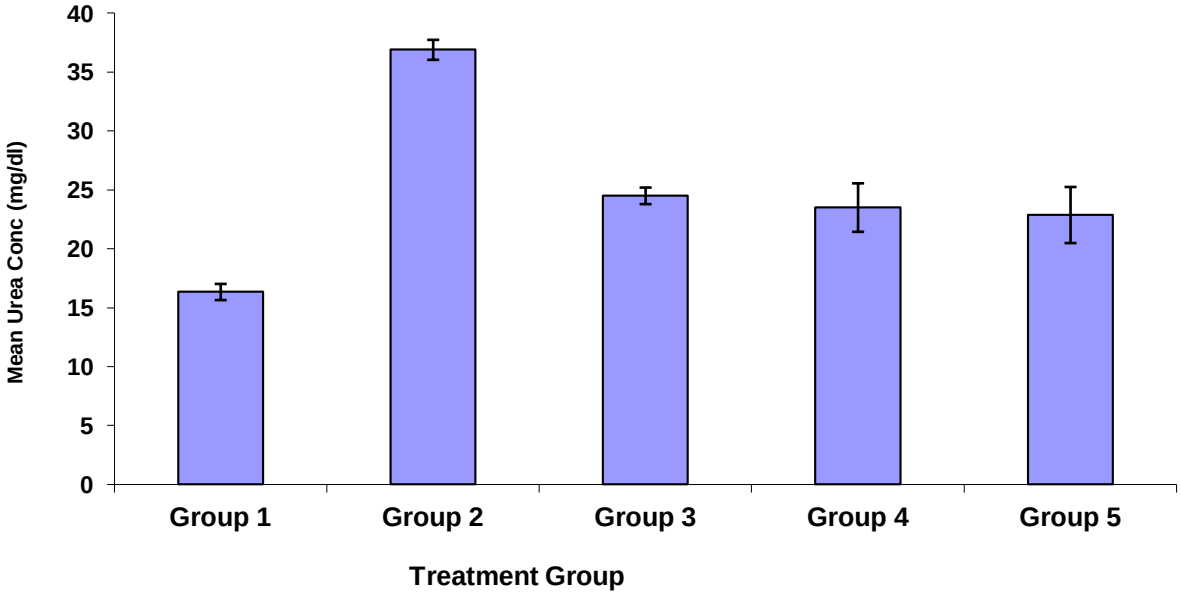

Fig. 6: Effect of ethanol extract of *Zapoteca portorensis* stem on the urea concentration of normal and testosterone-induced male albino rats

Group 1 = Normal control (Vehicle only)
Group 2 = Positive control (Testosterone-induced BPH only)
Group 3 = Standard control (BPH + 10 mg/kg finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

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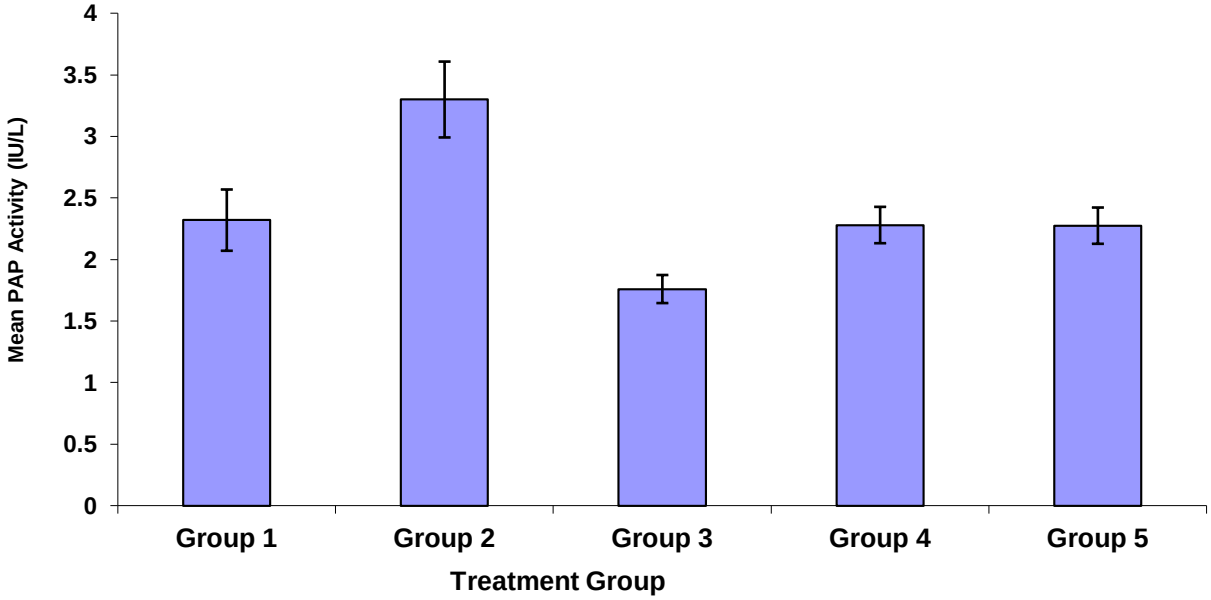

Fig. 7: Effect of ethanol extract of *Zapoteca portorensis* stem on the prostatic acid phosphatase activity of normal and testosterone-induced male albino rats

Group 1 = Normal control (Vehicle only)
Group 2 = Positive control (Testosterone-induced BPH only)
Group 3 = Standard control (BPH + 10 mg/kg finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

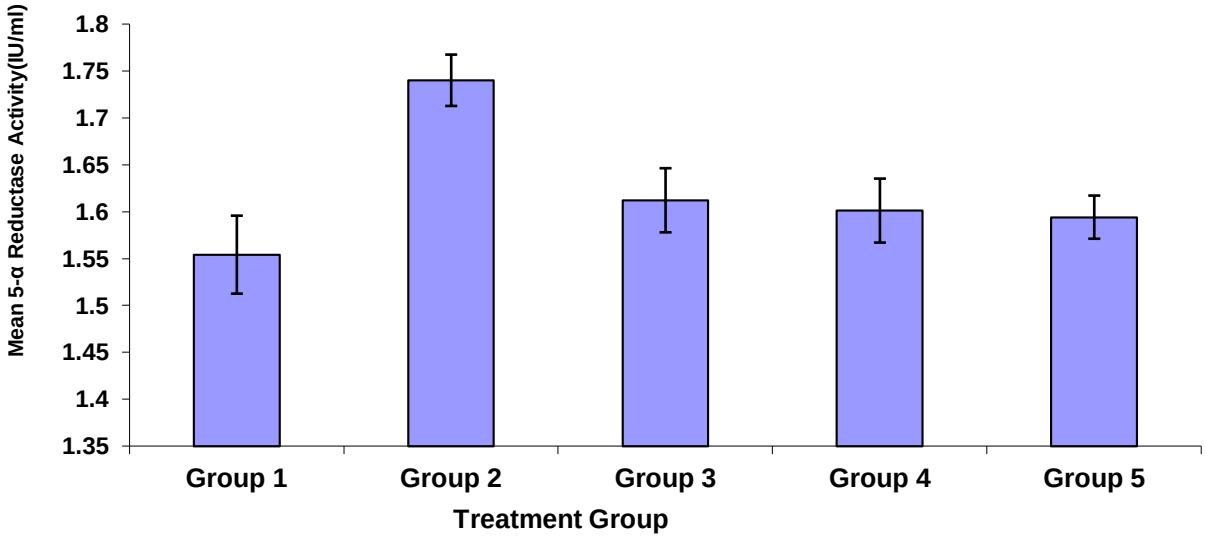

Fig. 8: Effect of ethanol extract of *Zapoteca portorensis* stem on the 5-alpha reductase activity of normal and testosterone-induced male albino rats

Group 1 = Normal control (Vehicle only)
Group 2 = Positive control (Testosterone-induced BPH only)
Group 3 = Standard control (BPH + 10 mg/kg finasteride-treated)
Group 4 = BPH + extract treated (100mg/kg body weight)
Group 5 = BPH + extract treated (200mg/kg body weight)

DISCUSSION

The extent of hepatic damage is assessed by the levels of serum marker enzymes activity like alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) which were significantly ($p<0.05$) lowered by administration of ethanol extract of *Zapoteca portoricensis* stem (group 4 and group 5) compared to the activities of ALP, ALT and AST of the non-treated (positive control) groups. This suggests that the ethanol extract of *Zapoteca portoricensis* stem has hepatoprotective effect, since the serum level of ALT and AST were increased in good correlation with the severity of hepatic injury (Collen *et al*., 2003). Similarly, bilirubin is excreted by the liver; hence its level in the blood is an index of liver function (Collen *et al*., 2003). Thus, mean serum total bilirubin level which was also significantly ($p<0.05$) elevated by BPH induction, but remarkably reduced by treatment with *Zapoteca portoricensis* extract strongly suggest that the stem extract protected the rat liver against BPH-induced damage as much as finasteride did. High level of bilirubin in the serum suggests haem degradation resulting from destruction of red blood cells (Collen *et al*., 2003) due to BPH induction. Therefore, the non-significantly ($p>0.05$) and

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significantly ($p<0.05$) lower levels of total bilirubin in *Zapoteca portoricensis* stem extract-treated groups respectively suggest the potency of the extract to alleviate or protect damage to red blood cell membrane when compared to the induced and non-treated positive control. The results of this study on the liver function are in agreement with those obtained from the report of Lee *et al*., (2012) where there was decrease in activity of the serum toxicity marker enzymes of the BPH treated animals compared to those of the non-treated group. The activity of *Zapoteca portoricensis* stem on liver function tests can also be supported by the report of Agbafor *et al.*, (2014) on hepatoprotective property of *Zapoteca portoricensis* leaf extract.

This study demonstrates the effects of BPH on renal function test when compared with the normal control by increasing significantly both mean serum urea and mean serum creatinine level. Chronic BPH can cause urine to back up into the kidneys and cause damage to them (Untergasser *et al*., 2005). It is well-accepted today that bladder outlet obstruction due to BPH might cause hydronephrosis and renal failure (Roehrborn, 2008). Lower urinary tract symptoms (LUTS) possibly related to benign prostatic enlargement (BPE) and benign prostatic obstruction (BPO) due to BPH interfere significantly with normal daily activities (Parsons and Kashefi, 2008). Previous study showed a much higher mortality among BPH patients who underwent surgical treatment when renal insufficiency was present at the same time. Patients with BPH also have a significantly higher risk of chronic kidney disease, probably due to an obstructive uropathy (Eman, 2013). The significantly ($p<0.05$) lower mean sera urea and creatinine concentrations in the induced BPH and non-treated positive control compared to that of the non-induced group (normal control) buttress these facts. This is also supported by the significantly ($p<0.05$) lower concentrations of mean sera urea and creatinine observed in the induced and treated groups compared to that of the induced and non-treated positive control. These results being in agreement with the study carried out by Eman (2013) suggest a protective role of *Zapoteca portoricensis* stem extract against BPH-induced renal failure.

Prostatic acid phosphatase (PAP), a glycoprotein synthesized by the prostate gland, is a member of a diverse group of isoenzymes, the acid phosphatases, which are capable of hydrolyzing phosphate esters in acidic medium (Moul *et al*., 1998). PAP is one of the prostatic secretions used as a marker of prostatic diseases and as an indicator of treatment progress (Bauer, 1988). Elevations in PAP levels have been reported in animals treated with androgens and estrogen and may be due to increased lysosomal activity (Jeyaraj *et al*., 2000). The higher values received for mean serum PAP activities of animals in BPH induced groups corroborate the increase in secretory activity (due to hyperplasia) especially in the positive control animals with significant ($p<0.05$) value . This study is in agreement with studies carried out by Ejike and Ezeanyika (2011) and Surrendra *et al*. (2011). The reduction in mean sera PAP activities of the induced and extract-treated groups to near normal when compared to the mean serum PAP activity of the induced and non-treated (positive control) group suggests a positive effect of the stem extract on serum PAP activity, which is essential for the normal functioning of the prostate gland. This efect also buttresses its effectiveness in forestalling aberrant growth of the prostate and is in tandem with the report of Ejike and Ezeanyika (2011). However, the significantly ($p< 0.05$) lower PAP activity (standard control) animals compared to that of the normal control animals may be due to adverse effect of finasteride in BPH treatment with regard to prostatic secretions (Irwig and Kolukula, 2011).

The steroid 5α-reductase metabolizes testosterone to 5α dihydrotestosterone (5α-DHT), which is a more potent androgen than testosterone and exerts its function in androgen-responsive tissues. The metabolite 5α-DHT is responsible for benign prostate hyperplasia (BPH) and prostate cancer (PCa), major neoplastic diseases in older men (Atsushi *et al*., 2013). The enzyme is produced only in specific tissues of the male human body, namely the skin, seminal vesicles, prostate and epididymis. Inhibition of 5-alpha reductase results in decreased production of DHT, increased levels of testosterone and possibly increased levels of estradiol. Finasteride is the first 5alpha-reductase inhibitor that received clinical approval for the treatment of human benign prostatic hyperplasia (BPH) and androgenetic alopecia (male pattern hair loss). These clinical applications are based on the ability of finasteride to inhibit the Type II isoform of the 5alpha-reductase enzyme, which is the predominant form in human prostate and hair follicles and the concomitant reduction of testosterone to dihydrotestosterone (DHT). However, in rodents both isoforms are inhibited by the finasteride (Atsushi *et al*., 2013). These processes may support the significant decrease in the enzyme's activity of animals in the induced and treated groups compared to its activity in the induced and non- treated animals. This reduction in the steroid 5α-reductase activity of the extract treated groups which was also observed in that of the finasteride-treated group may be attributed to the inhibitory effect of the extract on testosterone-induced BPH.

CONCLUSION

From this present research, it will be logical to infer that ethanol extract of the *Zapoteca portoricensis* stem in the treatment of testosterone-induced benign prostate hyperplasia in male albino rats proffers no assault on the functional integrity of both the liver and the kidney.

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