April 30, 2019

PharmacologyOnLine

Archives • 2019 • vol.1 • 154-165

EFFECTS OF METHANOL EXTRACT OF JATHROPHA CURCAS ROOTS ON TESTOSTERONE-INDUCED BENIGN PROSTATE HYPERPLASIA (BPH) IN MALE ALBINO RATS

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Abstract

Jathropha curcas roots extract have been claimed by traditionalist to have remedial effects on benign prostate hyperplasia (BPH). This study is aimed at evaluating the effects of methanol extract of Jathropha curcas roots on testosterone-induced benign prostate hyperplasia in male albino rats. A total of 15 male albino rats were divided into 5 groups of 3 each. The groups were a normal control, positive control, standard control (Dutasteride 0.5 mg/kg), and two test groups (50 and 100 mg/kg b.w) of the treatment extract. Benign prostate hyperplasia was induced using 25 mg/kg b.w of testosterone propionate subcutaneously for 28 days in all the groups with exception of the normal control group. This was followed by treatment with Jathropha curcas roots extracts at doses of 50 and 100 mg/kg b.w for 2 weeks daily by oral gavage. At the end of the treatment period, the animals were weighed, sacrificed and blood was collected by ocular puncture. Biochemical assays such as liver function test and antioxidant enzymes, MDA, prostate specific antigen (PSA), testosterone and zinc concentration levels were analyzed using standard procedures. Prostate weight (prostate /body weight ratio) was calculated and histological changes in the prostate were examined. The result showed non-significant ($p > 0.05$) difference in ALT, AST and ALP. There was also non-significant ($p > 0.05$) difference in MDA and SOD, however CAT significantly ($p < 0.05$) increased when group 5 was compared with group 2. Prostate specific antigen significant ($p < 0.05$) decreased when group 4 and 5 were compared with group 2.There was also a significant ($p < 0.05$) decrease in testosterone level, when group 5 was compared with group 2. Zinc concentration significantly ($p < 0.05$) increased when group 5 was compared with group 2. The relative prostate weight showed a significant ($p < 0.05$) decrease when group 5 was compared with group 2 in a dose dependent manner. Histological changes also observed in the ventral lobe of the BPH induced prostate was suppressed following treatment with the plant extract in a dose dependent manner. These results suggest that methanol extract of Jathropha curcas roots may be effectively used in the management of BPH.

Keywords: *Jathropha curcas roots, testosterone and benign prostate hyperplasia (BPH)*

Introduction

Benign prostate hyperplasia (BPH) is defined as the proliferation of prostatic stromal cells, which results in enlarged prostate gland. As a consequence, the prostatic urethra is compressed restricting the flow of urine from the bladder. This interference with urine flow may cause uncomfortable symptoms such as frequency, urgency, nocturia, intermittency, decreased stream and hesitancy in urine flow. As BPH progresses, complications, such as urine retention, urinary tract infection, and kidney blockage may develop [1].In recent years, a variety of factors have led to further increase in the number of men evaluated and/or treated for lower urinary tract symptoms. These include infectious agents, hormones, urinary reflux, metabolic syndrome, ageing process and auto immune responses [2]. These aetiologies are not completely elucidated, but for hormonal changes, the development and growth of prostate depends on androgen stimulation by dihydrotestosterone, an active metabolite found due to enzymatic conversion of testosterone by steroid 5alphareductase. Thus, production and accumulation of DHT in the prostate increases with age, resulting in the disease [3]. The prevalence of pathological BPH is 8% in the 4th decade of life, however, 50% of men develop pathological BPH between 51 and 60 years. The average weight of a prostate identified at autopsy as having BPH is 33 ± 16 g. Only 4% of the prostates in men older than 70 years weigh >100 g. Globally, benign prostatic hyperplasia affected about 210 million males in 2010 (6% of the population) [4]. It is the 5th most prevalent non-cancer-related disorder among men aged 50 years and older. Management options of benign prostate hyperplasia include, watchful waiting, drug treatment and surgical intervention. Conventional drug treatment includes 5 alpha reductase inhibitors and alpha-adrenergic antagonists. Although these drugs have great efficacy in treating patients, their adverse effects like impotence, gynecomastia, impairment of muscle growth and decreased libido for 5 alpha reductase inhibitors and orthostatic hypotension, fatigue, dizziness, abnormal ejaculation for alpha adrenergic antagonists should not be over looked. People in the developing countries have resorted to depending on herbal medicines for their health care needs due to, the adverse effects observed with the conventional drugs, long term surgical treatments which are costly as well as the risk for aged men [5]. Jatropha is derived from Greek words 'Jatros' and 'trope' (food/nutrition) which implies medicinal uses. The genus Jatropha belongs to family Euphorbiaceae and subfamily Acalyphoideae [6]. The roots back extract has shown anti-oxidant activity [7]. The roots powder has also shown anti-inflammatory activity when topically used in paste form [8]. These medicinal properties are due to the fact that, dried roots of Jatropha curcas contains, steroids, alkaloids, and saponins [9]. The presence of these phytochemicals with antioxidant and anti-inflamatory properties in the plants, suggest the roots to be used as drug for the management of BPH.

Materials and Methods

Plant material collection

Jatropha curcas roots was used for this study. The root was collected from Ede-oballa in Nsukka, L.G.A Enugu State, Nigeria and authenticated by Mr. Alfred Ozioko of International Center for Ethno medicine and Drug Development (Inter CEDD) in Nsukka, Enugu State of Nigeria.

Animal and Housing

A total of 15 albino male rats, were used for this study, weighing 102-180 g. The rats were housed in separate standard cages in the Department of Biochemistry animal house, University of Nigeria, Nsukka, Enugu State, Nigeria under a controlled light period of 12/12 hour light/day cycle with free access to feed and water.

Induction of benign prostate hyperplasia (BPH)

Benign prostate hyperplasia (BPH) was induced by subcutaneous injection with 25 mg/kg b.w of SustanonR '250' (Testosterone esters), manufactured by Pharmatec Pakistan LTD under license from N.V. Organon OSS, The Netherlands for 28 days in male rats to be used for this study with exception of Group 1 (Normal control) [10].

Experimental design

A total of fifteen (15) albino male rats were used. They were acclimatized to laboratory conditions for

a period of one week and all rats had access to pelletized feed (Chikum feeds) and water ad libitum. They were randomly distributed into five (5) groups of three (3) animals each. The study lasted for 14 days.

The experimental groups were as follows:

Group 1: Normal Control

Group 2: Positive control

Group 3: (Standard control): Received Dutasteride 0.5 mg/kg b.w

Group 4: Received 50 mg/kg body weight of methanol extract of Jathropa curcas roots

Group 5: Received 100 mg/kg body weight of methanol extract of Jathropa curcas roots

Plant extraction method

Jatropha curcas roots were washed, dried and then ground into powder using milling machine. The powdered roots (100 g each) were soaked in 3 liters of 70% methanol for 48 hours separately. The extracts were filtered first with a muslin cloth and further filtered using Whatsman filter paper. The filtrate obtained was concentrated in a rotary evaporator at 600C, and then dried with regulated water bath at 200 C given a light brown yield of 12.5 g each.

Biochemical Assays

Alanine aminotransaminase (ALT) activity

The activity of (ALT) was determined by the Reitman-Frankel colorimetric method [11] for in vitro determination of GOT/ALT in serum using RANDOX Commercial Enzyme kit (RCA) test kit.

Aspartate aminotransferase activity

GOT (AST) activity was determined by the Reitman – Frankel colorimetric method [11] for in vitro determination of GOT/AST in serum using a RANDOX Commercial Enzyme kit (RCA) test kit

Alkaline phosphatase (ALP) activity

Phenolphthalein monophosphate method [12] for the in vitro determination of alkaline phosphatase in serum using RANDOX Commercial Enzyme kit (RCA) test kitphosphatase in water

Bilirubin using colorimetric method

Principle

Bilirubin reacts with diazotized suphanilic acid in alkaline medium to form a blue colored complex. Total bilirubin concentration is determined in the presence of caffeine, which releases albumin bound bilirubin, by the reaction with diazotized suphanilic acid. The increase in absorbance at 578 nm is directly proportional to the total bilirubin concentration [13].

Estimation of Zinc Concentration (Randox Enzyme Kit)

Principle

Zinc present in the sample is chelated by 5-Br-PAPS 2-(5-bromo-2-pyridylazo)-5-N-(N-Propyl-N-sulfopropylamino)-phenol in the reagent. The formation of this complex is measured at a wavelength of 560 nm.

Estimation of lipid peroxidation level

Lipid peroxidation was determined spectrophotometrically by measuring the level of the lipid peroxidation product, malondialdehyde (MDA) as described by [14].

Determination of Enzyme Antioxidant

Estimation of superoxide dismutase (SOD)

Superoxide dismutase activity was assayed by the method of Xin et al. [15]. The method implores xanthine and xanthine oxidase to generate superoxide radicals which reacts with 2-(4 iodophenyl)-3-(4nitrophenol)-5-phenyl tetrazolium chloride (I.N.T) to form a red formazan dye. The superoxide dismutase activity is then measured by the degree of inhibition of this reaction. One unit of SOD is that which causes a 50 % inhibition of the rate of reduction of INT under the conditions of the assay.

Estimation of catalase activity

The activity of catalase was assayed by the method of Aebi [16]. Dichromate in acetic acid was reduced to chromicacetate, when heated in the presence of hydrogen peroxide with the formation of perchromic acid as an unstable intermediate. Chromic acetate form was measured at 570 nm. Catalase was allowed to split hydrogen peroxide for

a different period of time. The reaction was stopped at different intervals by the addition of dichromate acetic acid mixture and the remaining hydrogen peroxide was determined by measuring chromate acetate colorimetrically.

Plasma testosterone using ELISA technique

Principle

Plasma testosterone using ELISA techniquewas determined according to the method of Tietz [17]. It uses competitive enzyme immunoassay (type 7) principle which uses reagents such as antibody, enzyme-antigen conjugate and native antigen.

Mixture of biotinylated antibody, enzyme-antigen conjugate and a serum containing the native antigen leads to a simultaneous reaction between the biotin attached to the antibody and the streptavidin immobilized on the micro well (a competitive reaction of conjugate for a limited number of antibody binding sites). This affect the separation of the antibody bound fraction after decantation or aspiration.

EnzAg + Ag +AbBtnAgAbBtn + EnzAgAbBtn

Plasma prostate specific antigen (PSA) was determined according to Stowel et al., [18]

Principle

Immunoenzymometric Assay (Type 3)

The essential reagents required for an immunoenzymometric assay include high affinity and specificity antibodies (enzyme and immobilized), with different and district epitope recognition, immobilization takes place during the assay at the surface of a microplate well through the interaction of streptavidin coated on the well and exogenously added biotinylated monoclonal anti-PSA antibody.

Upon mixing monoclonal biotinylated antibody, the enzyme labeled antibody and a serum containing the native antigen, reaction results between the native antigen and the antibodies without competition or steric hindrance to form a soluble sandwich complex.

The interaction is illustrated by the following equation

EnzAb(p) + AgtPSA + BtnAbEnzAb(P)-AgtPSA-BtnAb(m)

BtnAb(m = biotinylated antibody (excess Quantity)

AgtPSA = Native Antigen (variable Quantity)

EnzAb(p) = Enzyme labeled Antibody (excess Quantity)

EnzAb(P)-AgtPSA-BtnAb(m) = Antigen Antibody Complex

Ka =Rate Constant of Association

K-a = Rate constant of dissociation

After equilibrium is attained, the antibody bound fraction is separated from unbound antigen by decantation or aspiration. The enzyme activity in the antibody bound fraction is directly proportional to the native antigen concentration. By utilizing several different serum references of known antigen values, a dose response curve can be generated from which the antigen concentration of an unknown can be ascertained.

Prostate weight to body weight ratio (Prostate index)

Prostate weight to body weight ratio were calculated by dividing prostate weight with that of animal body weight multiplied by 100 for the individual study group animal [19].

Percentage increase in prostate weight

The percentage increase was calculated by dividing the prostate weight of the individual test groups with that of the positive control and multiplied by 100.

Percentage inhibition of increase in prostate weight

Percentage of inhibition was calculated as follows:

100 – {[(PW of treated group-PW of negative control)/(PWof positive group-PW of negative control)]×100}

Where PW: Prostate Weight [20].

Histological examination of the prostate

After blood collection, the prostate was carefully dissected out from the abdominal region, fixed in 10% formalin solution for 72 hours and sliced into a thickness of 2.1 mm. The tissues where dehydrated with alcohol of graded concentration and treated with paraffin wax and thereafter cast into blocks as described by Drury et al. [21].Sections of the tissues where then cut using microtone to 5 µm. These where later attached to the slide and allowed to dry. The sample slice where subsequently stained in haematoxylin-eosin. Tissue section of the organ collected from the animals in group 1-5 were prepared for histopathological examination using standard techniques. The slide section where examined using Motic© light microscope and the photomicrographs where taken using Motic© microscope camera.

Statistical Analysis

The results were expressed as mean ± standard error of mean (SEM) and test of statistical significance was carried out using one-way analysis of variance (ANOVA).The data obtained were analyzed using IBM Statistical Products and Service Solutions (SPSS), version 16. Values with $p < 0.05$ were considered statistically significant.

Results

The AST activities showed a non-significant ($p > 0.05$) difference when the test groups were compared with controls. ALT showed a significant ($p < 0.05$) decrease when group 4 and 5 were compared with group 1. ALP concentration in group 4 significantly ($p < 0.05$) decreased compared with group 1 and 2. Group 5 also revealed a significant ($p < 0.05$) decrease when compared group 1. Total bilirubin showed a significant ($p < 0.05$) decrease when group 4 and 5 were compared with group 1.

The Malondialdehyde (MDA) concentrations of animals treated in group 4 and 5 showed non-significant ($p > 0.05$) difference when compared with controls. Superoxide dismutase activities (SOD) significantly ($p < 0.05$) decreased when group 4 and 5 were compared with group 3. Catalase activities was significantly ($p < 0.05$) increased when group 5 was compared with group 1, 2 and 4.

There was no significant ($p > 0.05$) difference in PSA level following administration of 25 mg/kg b.w of testosterone for 28 days, however treatment with Jathropha curcas roots extract showed a significant ($p < 0.05$) decrease when groups, 4 and 5 were compared with group 2 and 3. Testosterone significantly ($p < 0.05$) decreased when group 5 was compared with group 2 and 3.. Also a significant ($p < 0.05$) decrease in zinc was observed when group 4 was compared with groups 1, 2 and 3.Group 5 significant ($p < 0.05$) increased in zinc when compared to 2,3 and 4.

The prostate weight significantly decreased when group 5 was compared with group 2. Prostatic index also showed a significant decrease when group 5 was compared with group 2. Group 3 (80.0 %) and 4 (87.3%) had the highest percentage increase in prostate weight.. The effects of Jathropha curcas roots extracts inhibited prostate growth at different doses tested with group 5 (60.5%) having the highest percentage inhibition while group 4 (21.43%) had the least.

Sections of the prostate gland collected from group 1 showed the normal histomorphometric features. The sections showed prostate gland parenchyma composed of multiple round to ovoid or irregularly shaped alveoli (A) of varying sizes seperated by vascularized thin fibromuscular stroma (S). Sections of the prostate gland collected from the animals in group 2 showed histological changes consistent with severe widespread prostatic hyperplasia. It show prostatic alveolar epithelia lined by crowded low columnar cells (white arrow) with foamy eosinophilic cytoplasm and basal euchromatic nuclei with prominent nucleoli.

Sections of the prostate gland collected from the animals in group 4 showed widespread histopathological lesions consistent with prostate hyperplasia. See group 2 for details. Alveoli (A); Fibromuscular Stroma (S); Hyperplastic alveolar epithelium (arrow). A wide area of the tissue section collected from the animals in group 5 showed a relatively normal histomorphology of the prostate gland. See Group 1 for details.

Discussion

BPH does not have effects on the liver function, however, analyses of the activities of some basic liver function enzymes in the plasma or serum can be used to indirectly access the integrity of tissues after being exposed to certain pharmacological agent(s). These enzymes are usually biomarkers whose plasma concentrations above the homeostatic limits could be associated with various forms of disorders which affect the functional integrity of the liver tissues [22]. Although, serum levels of both AST and ALT become elevated when disease processes affect the liver integrity, ALT is the more liver specific enzyme and therefore generally more specific to changes in activity levels than AST [22]. There was non-significant ($p > 0.05$) difference in liver function parameters when all the treatment groups were compared with group 2. Even if there had been an elevation in ALP upon extract administration, it could still not have confirmed liver damage because according to Odutola [23], ALP and AST originate from different tissues such as the liver, bones, intestine and placenta.

Malondialdehyde (MDA) levels in plasma or serum provides a convenient in vivo index of lipid peroxidation and represents a noninvasive biomarker of oxidative stress often clinically employed to investigate radical-mediated physiological and pathological conditions [24]. Circulating MDA levels were found to be significantly higher in BPH patients than in healthy donors [25] and strongly correlated with prostate-specific antigen levels. However, other works found circulating MDA levels in BPH patients similar to those in controls [27].

Table 2 showed non-significant ($p > 0.05$) difference in malondialdehyde levels when group 4 and 5 were compared with the group 2 (Positive control) after the 14 days treatment. Interest in oxidative stress with relation to the development of disease has gained large attention during the last decade. Lipid peroxidation is a major mechanism of cell injury in tissues and organs subjected to oxidative stress that has been studied extensively [27]. The control of lipid peroxidation is of special significance in biology because of its particular importance in relation to membrane damage [28]. The antioxidant activity of phenolic compounds is mainly due to redox properties, which allow them to act as reducing agents, hydrogen donors, singlet oxygen quenchers, heavy metal chelators and hydroxyl radical quenchers [29]. Superoxide dismutase activities (SOD) had non-significant ($p > 0.05$) difference when the treatment groups were compared with group 2(Positive control). Catalase activities was significantly ($p < 0.05$) increased when group 5 was compared with group 2(Table 2).

The effects of administration of Jathropha curcas extract on testosterone level showed a significant ($p < 0.05$) decrease. This decrease indicates the corresponding effects of the plant extract on total cholesterol lowering levels, since cholesterol is a possible substrate for testosterone synthesis and the presence of steroids in the plant prevented the absorption of cholesterol in the intestines. Zinc concentration in serum of BPH rats were observed in this study. This is in line with the work of Chyan et al. [30] who reported that at high tissue concentrations of zinc, this trace element inhibits the transformation of testosterone to dihydrotestosterone and plays an important role in maintaining the physiological function and normal tissue structure of the prostate.

Elevated levels of PSA are usually associated with prostate disorders such as BPH. A decrease in PSA is linked to a reduction in prostate hyperplasia due to inhibition of prostatic 5α-reductase. The 5α-reductase is the enzyme that converts testosterone to dihydrotestosterone (DHT) which is implicated in development of BPH [1]. Several plants have been reported to have 5α-reductase inhibitory activity and hence prevent the development of BPH [31, 10]. There is strong evidence that phytochemical agents are effective inhibitors of 5α-reductase that consequently leads to reduction in DHT concentrations and slows down BPH [32]. Hence treatment with Jathropha curcas roots extract also showed a significant ($p < 0.05$) decrease.

Subcutaneous injection of testosterone in rats exhibited enlargement of prostate as a consequence of progressive hyperplasia of glandular and stromal tissue of prostate gland clearly confirmed influence of androgen on prostate growth. Treatment with Jathropha curcas roots

extracts significantly decreased the prostate weight in a dose dependent manner. Group 5 significantly ($p < 0.05$) decreased when compared with group 2 indicating the plant potentials in management of BPH. Prostatic enlargement is used as an important marker for the disease. The prostatic index in this study also significantly ($p < 0.05$) decreased when group 5 was compared with group 2 as shown in table 5. This confirmed the effects of the plant on prostate and body weight reduction observed in this study and also in line with the work of Bhavin et al. [33]. The plant potentials in management of BPH, further gave a prostate weight inhibition of 60% in group 5 following treatment for 14days, indicating the plant rich phytochemicals in a dose dependent manner.

Histopathological examination of prostate sections of rats following the 14 days post administration of Jathropha curcas was consistent with the other biochemical results. Normal control showed the normal histomorphometric features. The sections showed prostate gland parenchyma composed of multiple round to ovoid or irregularly shaped alveoli (A) of varying sizes seperated by vascularized thin fibromuscular stroma (S). The alveolar epithelia were lined by single layer of cuboidal to low columnar cells (white arrow) with hypereosinophilic cytoplasm and basal euchromatic nuclei. Infolding of the epithelium into the alveolar lumen were infrequently observed. Group 5 showed a relatively normal histomorphology of the prostate gland. See Group 1 for details. However, a few alveoli (involving mostly the alveoli at the periphery of the glands) showed histological changes consistent with prostate hyperplasia. Alveoli (A); Fibro-muscular stromal (S); Cuboidal alveolar epithelium (Arrow).

Conclusion

Jathropha curcas (L) roots were found to be potent plant, this may be attributed to the levels of phytochemicals contained in the plant. These phytochemicals may be responsible for the various antioxidant activities, testosterone reduction, zinc supplementation, PSA and prostate weight reduction in male albino rats induced with benign prostate hyperplasia. This therefore suggests the two plant extracts may be used for the management of BPH.

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Table 1: Effects of methanol extracts of *Jathropha curcas* roots on some liver parametersin serum of benign prostate hyperplasia (BPH) induced male albino rats

Groups	AST(iu/L)	ALT (iu/L)	ALP(iu/L)	T.BIL (mg/dl)
1	40.33 ± 3.18^{ab}	76.33 ± 3.18^{bc}	15.63 ± 1.23^{c}	0.72 ± 0.30^{b}
2	34.33 ± 0.88^{a}	60.00 ± 1.15^{ab}	13.30 ± 0.17^{b}	0.66 ± 0.11^{ab}
3	35.33 ± 4.91^{a}	60.66 ± 4.37^{ab}	12.33 ± 0.72^{ab}	0.44 ± 0.05^{ab}
4	38.33 ± 3.18^{a}	54.00 ±7.81^{a}	10.63 ± 0.45^{a}	0.31 ± 0.02^{a}
5	45.00 ± 3.46^{ab}	59.00 ± 0.58^{ab}	12.30 ± 1.10^{ab}	0.32 ± 0.01^{a}

Values are expressed as mean ± SEM;(n =3). Values with different letters as superscript are considered statistically significant at $p < 0.05$

Keys: Group 1: Normal control, Group 2: Positive control, Group 3: Dutasteride 0.5 mg/kg,
Group 4: *Jathropha curcas* roots extract 50 mg/kg b.w, Group 5: *Jathropha curcas* roots extract 100 mg/kg b.w

Table 2: Effects of methanol extracts of *Jathropha curcas* roots on MDA and some antioxidant parameters inbenign prostate hyperplasia (BPH) induced male albino rats

Groups	MDA (mg/ml)	SOD (iu/l)	CAT (iu/l)
1	0.53 ± 0.23^{a}	9.62 ± 0.58^{ab}	8.14 ± 2.92^{abc}
2	1.85 ± 0.12^{ab}	10.15 ± 0.06^{ab}	2.95 ± 1.04^{a}
3	2.10 ± 1.21^{ab}	13.13 ± 1.78^{bc}	11.55 ± 1.33^{cd}
4	2.30 ± 0.54^{ab}	8.69 ± 0.67^{a}	5.10 ± 2.48^{ab}
5	1.28 ± 0.39^{ab}	10.11 ± 0.08^{ab}	12.81 ± 1.21^{cd}

Table 3: The effects of methanol extracts of *Jathropha curcas* roots on prostate specific antigen (PSA) in benign prostate hyperplasia (BPH) induced of male albino rats.

Groups	PSA (ng/ml)	
	Day 1(No Treatment)	Day 14(Treatment)
1	0.81 ± 0.04	1.01 ± 0.07^{bc}
2	1.14 ± 0.01	1.25 ± 0.01^{d}
3	1.18 ± 0.05	1.09 ± 0.12^{cd}
4	1.33 ± 0.17	0.84 ± 0.03^{ab}
5	1.21 ± 0.07	0.85 ± 0.04^{ab}

Table 4: Effects of methanol extracts of *Jathropha curcas* roots on testosterone and zinc in serum of benign prostate hyperplasia (BPH) induced albino male rats

Groups	Testosterone (ng/ml)	Zinc (mg/dl)
1	1.75 ± 0.03^{ab}	192.15 ± 15.10^{d}
2	2.00 ± 0.09^{b}	162.83 ± 4.67^{b}
3	1.90 ± 0.05^{b}	166.30 ± 6.50^{bc}
4	1.62 ± 0.10^{ab}	136.46 ± 6.55^{a}
5	1.57 ± 0.26^{ac}	188.50 ± 14.29^{cd}

Table 5: Effects of methanol extracts of *Jathropha curcas* roots on prostate weight parameters in benign prostate hyperplasia (BPH) induced male albino rats

Groups	PW(g)	PW Index (g)	% Increase in PW	% Inhibition of PW
1	0.40 ± 0.14^{a}	0.25 ± 0.09^{a}	-	-
2	0.96 ± 0.052^{c}	0.72 ± 0.05^{c}	-	-
3	0.77 ± 0.047^{bc}	0.61 ± 0.05^{bc}	80.0	33.93
4	0.83 ± 0.03^{bc}	0.63 ± 0.07^{bc}	87.3	21.43
5	0.60 ± 0.12^{ab}	0.49 ± 0.12^{b}	63.1	60.5

Plate 1: Photomicrographs of the prostate from animals in groups 1 to 5. H and E x 60