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Research Article

Amelioration of Benign Prostate Hyperplasia in Rats Through Plant Foods

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ABSTRACT

The present study was carried out to evaluate the beneficial effects of ethanolic extract of flaxseed, sesame seed, safflower seed and soybean in rat model of benign prostate hyperplasia (BPH). The whole powders of these plants were also evaluated. BPH was induced in castrated adult rats by subcutaneous injections of testosterone propioneate (3 mg/kg rat body weight) for 4 weeks. Total cholesterol (T-Ch), malondialdehyde (MDA), testosterone (TS), prostate specific antigen (PSA) and acid phosphatase were determined. Plasma creatinine and urea levels were determined as indicator of kidneys function. Aspartate transaminase and alanine transaminase activities were determined as indicator of liver function. All BPH rats administrated with different treatment showed significant reduction in plasma levels of T-Ch, TS, MDA, PSA as well as total prostatic and non-prostatic acid phosphatase activity compared with BPH rats. Flaxseeds powder was the most promising treatment in the reduction of total cholesterol and MDA levels, while flaxseeds ethanol extract showed the highest reduction of TS level compared with BPH control followed by sesame seeds ethanol extract. The plants' under investigation showed complete safety toward liver and kidney functions. In conclusion, the ethanolic extracts and whole powders of the studied plants' showed promising effect towards BPH in animal model.

Keywords: Plant foods, benign prostate hyperplasia, rats, testosterone, lipid peroxidation, prostate specific antigen.

INTRODUCTION

Benign prostate hyperplasia (BPH) and low urinary tract symptoms are common male diseases. BPH, the non-malignant enlargement of the prostate, is one of the most common urological diseases worldwide[1]. The prevalence of BPH increases with aging and may affect every three out of four men in their sixties and has become an atypical direct cause of mortality[2,4]. An estimated 612 million men will have BPH globally by 2018[5]. BPH also called benign prostate hypertrophy can be described clinically or pathologically. Clinical BPH is commonly viewed as benign enlargement of the prostate, which contributes to an array of urinary voiding difficulties among older men[6]. The hypertrophy of prostate, caused by excessive dihydrotestosterone (DHT) is estimated as the mechanism that oversupplies testosterone in blood and leads to large amount of DHT synthesis through the action of 5α-reductase in the prostate. The synthesized DHT combines with androgen receptor with consequent generation of benign prostate hyperplasia[7]. The presence of anti-androgenic phytochemicals in plant sources provides an alternative to synthetic drugs with minimal drawbacks[8]. Phytochemicals compete with the peripheral androgen receptors thus inhibit the effect of endogenous or exogenous androgens. Inhibition of 5α-reductase is considered to be a mechanism to inhibit BPH[9]. In previous research by the author's ethanol extract and whole powder of flaxseed, sesame seed, safflower seed and soybean showed promising effect as anti-androgen in growing rats[10]. So in the present research the ethanol extract and the whole powder of flaxseed, sesame seeds, safflower seeds and soybean seeds were evaluated in a model of benign prostate hyperplasia in rats.

MATERIALS AND METHODS

Materials

Plant materials: Flaxseed (*Linum usitatissimum* L.), sesame seed (*Sesamum indicum*), safflower seed (*Carthamus tinctorius*) and soybean (*Glycine max* L.) were purchased from Agriculture Research Centre, Giza, Egypt.

Animals: Male albino rats, mature, weight 206.5 ± 21.9 g were used in the present study. Animals were obtained from the animal house of National Research Centre, Cairo, Egypt. The animals were kept individually in stainless steel cages at temperature 24±2°C, a relative humidity of 55±10%, and a 12 h light cycle/12 h dark cycle. Water and food were given *ad-libitum*.

Methods

Preparation of diets: Different experimental diets were used in the study as shown in Table 1. Salt mixture and vitamin mixtures were prepared according to Briggs and Williams[11] and Morcos[12], respectively. Oil soluble vitamins were given orally in a dose of 0.1 ml/rat/week.

Preparation of plants extracts

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The air-dried powdered of flaxseed, sesame seeds, safflower seeds and soybean seeds were extracted successively in a continuous extraction apparatus (Soxhlet) until exhaustion with petroleum ether (40-60°C), then ethanol. The solvent of each extract was completely removed by evaporation under reduced pressure at a temperature not exceeding 40°C. All extracts were kept in deep-freeze till used.

Preparation of dosage form

Ethanolic extracts of different plants under study were dispersed separately in water using gum acacia to be given orally to rats. For the control, the vehicle was prepared through dissolving the same amount of gum acacia in water.

Casteration of rats

Castration was induced in rats as described by Van Coppenolle *et al*.[13].

Design of the experimental study

Sixty male rats were divided into two groups. Group one (6 rats) was served as normal healthy control. Group two (54 rats) was served as benign prostate hyperplasia (BPH) rat model (First stage). To prevent the influence of intrinsic testosterone, rats of BPH group were castrated 3 days prior to the administration of testosterone propionate. BPH was induced in castrated adult rats by subcutaneous injections of testosterone propioneate (3 mg/kg rat body weight) for 4 weeks according to the method of Jang *et al*.[14]. At the end of the first stage (induction of BPH in rats), the rats of BPH group were divided into nine sub-groups each of 6 rats (second stage). So the groups in the second stage were normal healthy rats, which served as normal control. Group two (the first sub-group) was BPH control. Group one and two were fed on balanced diet. Group 3 was fed on balanced diet and given daily oral dose of sesame seeds ethanol extract (300mg/kg rat body weight). Group 4 was fed on balanced diet and given daily oral dose of soybean ethanol extract (300mg/kg rat body weight). Group 5 was fed on balanced diet and given daily oral dose of safflower seeds ethanol extract (300mg/kg rat body weight). Groups 6 was fed on balanced diet and given daily oral dose of flaxseed ethanol extract (300mg/kg rat body weight). Group 7 was fed on balanced diet containing 20% of sesame seeds powder. Group 8 was fed on balanced diet containing 20% of soybean powder. Group 9 was fed on balanced diet containing 20% of safflower seeds powder. Group 10 was fed on balanced diet containing 20% of flaxseed powder. At the end of this experiment (an additional 4 weeks after BPH induction) blood samples were collected from all rats after an overnight fast for the determination of plasma total cholesterol (T-Ch)[15], plasma malondialdehyde (MDA) as indicator of lipid peroxidation[16], plasma testosterone (TS) using ELISA technique[17], plasma prostate specific antigen (PSA)[18], acid phosphatase as indicator of prostatic activity[19]. The plasma levels of creatinine[20] and urea[21] were determined as indicator of kidney function, while the activity of aspartate transaminase (AST) and alanine transaminase (ALT)[22] were determined as indicator of liver function. The entire prostate was removed from all animals and weighed. Animal procedures were performed in accordance with the Ethics Committee of the National Research Centre, Cairo, Egypt, and followed the recommendations of the National Institutes of Health Guide for Care and Use of Laboratory Animals (Publication No. 85-23, revised 1985).

Statistical analysis

The results of animal experiments were expressed as the Mean ± SE and they were analyzed statistically using the one-way analysis of variance ANOVA followed by Duncan's test. T-test was used for comparison of normal rats and BPH rats in the first stage.

RESULTS

Nutritional parameters of normal rats and BPH rat's model are shown in table 2. Final body weight, body weight gain, total food intake and feed efficiency ratio showed significant reduction in BPH rat model compared with normal control. Nutritional parameters of different experimental groups are illustrated by table 3. Final body weight, body weight gain, total food intake and feed efficiency ratio showed significant reduction in BPH control compared with normal control. Feeding BPH rats' diet containing sesame seeds powder or flaxseed powder or oral administration of sesame seeds ethanol extract showed significant improvement in body weight gain, total food intake and feed efficiency ratio compared with BPH control, but showed non-significant changes compared with normal control. Table 4 showed total cholesterol, testosterone, lipid peroxidation and prostate weight of different experimental groups. After injection of testosterone propionate for 4 weeks to induce BPH, prostate weight were consistently higher in BPH control relative to normal rats group, the increase was nearly twice that of normal rats group. The present results indicate that BPH was successfully induced through subcutaneous injection of testosterone propionate. As also can be seen, in the groups administrated with different treatments, flaxseed ethanol extract was the best treatment; the indices of prostate weight were reduced by 44% compared with BPH control group.

Plasma total cholesterol level of BPH control group showed significant elevation compared with normal control rats and also compared with all BPH treated groups. All "BPH" rats administrated with different treatments showed significant reduction in plasma cholesterol level compared with BPH control. BPH rats fed on diet containing 20% flaxseed powder showed significant reduction of total cholesterol level to reach about of normal level.

Testosterone plasma level of BPH control was elevated significantly compared to that of normal control. All BPH rats administrated with different treatment showed significant reduction of plasma testosterone level compared with BPH control but still higher than normal control. Flaxseed ethanol extract showed the highest reduction in testosterone level compared with BPH control followed by sesame seeds ethanol extract.

MDA plasma level as indicator to lipid peroxidation was increased significantly in BPH control rats compared with normal control. This elevation in MDA level revealed that BPH is associated with significant elevation of lipid

peroxidation and oxidative stress. Administration of different treatments to BPH rats showed significant reduction in MDA level. Flaxseed powder was the most promising treatment in the reduction of MDA.

Table 5 showed acid phosphatase activity and PSA of different experimental groups. Plasma levels of total, prostatic and non-prostatic acid phosphatase activity increased significantly in BPH control compared with normal rats group. Also PSA plasma level was elevated significantly in BPH control when compared with normal control. Administration of different studied treatments showed significant reduction of plasma levels of PSA, total, prostatic and non-prostatic acid phosphatase activity compared with BPH control.

Liver and kidneys function of different experimental groups are shown in table 6. Plasma levels of creatinine and urea, as indicator to kidneys function and activity of ALT and AST showed non-significant changes in all experimental groups. Non-significant changes of liver and kidneys function in different experimental groups revealed the complete safety of the studied plants in form of extracts and powder.

DISCUSSION

BPH was induced in castrated adult male rats by subcutaneous injection of testosterone propionate (3 mg/kg rat body weight). External testosterone increases the development of an immature prostate, castration before maturity prevents prostatic growth and testosterone administration to castrated adult male rat induce growth in the gland to normal size[23]. Castration of adult male rats causes extensive atrophy of prostate with induction of apoptosis, majorly of the ventral prostate epithelial cells[24]. Further administration of testosterone exogenously to castrated rats caused suppression of apoptosis and prevents epithelial cell atrophy. Tissue androgens, testosterone and DHT, stimulates prostate enlargement[25].

In the present study induction of BPH in rats reduced final body weight, body weight gain, total food intake and feed efficiency ratio significantly. Significant reduction in body weight gain in BPH model is in agreement with the results of Kim *et al*.[25].

BPH rat model in the present study increased prostate weight, plasma levels of testosterone, T-Ch, MDA as indicator to lipid peroxidation, PSA and acid phosphatase (total, prostatic and non-prostatic).

The elevation in testosterone plasma level and prostate weight in BPH rat model in the present study is in agreement with the results of Kim *et al*. and Yang *et al*.[25,26] who reported that BPH rat model exhibited increases in prostate size and testosterone level.

In the present study induction of BPH in rats elevates plasma total cholesterol level. The prostate synthesizes cholesterol at a level similar to the liver and accumulates it in a deposit within the gland in an age-dependent manner. It was reported that cholesterol content in the prostate of BPH subjects was twice that in a normal prostate[27]. Nandeesha *et al*.[28] reported that circulating total and HDL cholesterol were associated, in a castrated/testosterone and normal manner, respectively, with prostate enlargement in a series of 50 symptomatic BPH cases and 38 controls. Moyad and Lowe[29] also reported that high level of total cholesterol, LDL-cholesterol, triglyceride and low level of HDL-cholesterol increased the risk of BPH, and cholesterol-lowering medication may reduce the risk of BPH.

Srivastava and Mittal[30] suggested that decline in antioxidant system favors accumulation of free radical. They reported that oxidant-antioxidant imbalance may be one of the main reasons responsible for the development of BPH. The generation of free radicals as reflected by increased MDA levels in BPH patients could be one of the causes leading to the development of cancer. Aydin *et al.* and Aryal *et al*.[31,32] also reported that in BPH, increased lipid peroxidation and decreased levels of antioxidants have been observed.

The acid phosphatase includes all phosphatases after surgery or anti-androgen therapy the levels slowly approach normal, with a subsequent rise if the treatment is unsuccessful. The levels of this enzyme are also elevated in patients with BPH. Elevated serum prostatic acid phosphatase (PAP) may be elevated in some benign conditions such as BPH[33].

PSA is a protein produced merely in the prostate gland in large amount. The PSA level in the blood can vary by about 20% from day to day[34]. Lakhey *et al*.[35] also reported that PSA is used in the diagnosis and management of patients with prostate cancer and other prostatic diseases such as BPH. Serum PSA correlates with prostate volume, and men who have large prostates and high serum PSA are at higher risk of experiencing more significant symptoms, including progression to acute urinary retention LUTS include bladder storage symptoms such as nocturia[6].

Flaxseed ethanol extract was the best treatment in reduction prostate weight, reduced plasma levels of total cholesterol, testosterone, MDA, PSA and acid phosphatase followed by sesame seeds ethanol extract and flaxseed powder. The significant reduction observed in these parameters may be attributed to the presence of lignans and isoflavones. Lignans, a class of phytoestrogens, are biologically active compounds with weak estrogenic or anti-estrogenic, antioxidant, and antitumor properties, mediated through inhibition of growth signal factors and modulation of enzymes involved in the hormone metabolism that can influence prostate metabolism[36,37].

BPH rats feeding on balanced diet containing 20% flaxseed powder showed considerably higher reduction of cholesterol. This may be due to its high content of dietary fiber as mentioned by Pereira *et al*.[38] who reported that dietary fibers of flaxseed lowering blood cholesterol and thus protect against coronary heart disease. Also Demark-Wahnefried *et al*.[39] reported that flaxseed-supplemented (30 g/day) diet for 6 month significantly decreased the cholesterol levels in BPH subjects.

Administration of different plants extracts and plants powder under investigation reduced MDA in BPH rats with different degrees. Various herbal extracts reduce oxidative stress in BPH rats[40-42]. Flaxseed is a nutritional whole grain, containing numerous chemical constituents and lignans that possess antioxidant activity[43]. Flaxseed

Table 1: Composition of different experimental diets (g/100g).

Ingredients	Diets				
	Balanced	Sesame	Soybean	Safflower	Flaxseed
Casein	12	8.16	3.76	8.36	8.41
Corn oil	10	-	5.8	4.54	2.09
Sucrose	23.5	21.4	20.98	19.9	20.7
Starch	47	42.94	41.96	39.7	41.3
Salt mix.	3.5	3.5	3.5	3.5	3.5
Vitamin Mix.	1	1	1	1	1
Fiber	3	3	3	3	3
Sesame seeds	-	20	-	-	-
Soybean	-	-	20	-	-
Safflower seeds	-	-	-	20	-
Flaxseed	-	-	-	-	20

Table 2: Nutritional parameters of normal and BPH groups in the first stage (Mean ± SE).

Parameters	Normal control	BPH control
Initial body weight(g)	206.5^{a}±10.87	206.5^{a}±9.31
Final body weight (g)	251.9^{a}±8.77	219.0^{b}±9.50
Body weight gain (g)	45.1^{a}±4.99	12.6^{b}±3.11
Total Food Intake (g)	360.0^{a}±11.10	315.0^{ab}±20.37
Feed Efficiency Ratio	0.13^{a}±0.01	0.04^{b}±0.01

In column different letters means significant difference at 5% probabilities (p<0.05).

Table 3: Nutritional parameters of different experimental groups in the second stage (Mean ± SE)

Groups	Initial body weight (g)	Final body weight (g)	Body weight gain (g)	Total food intake (g)	Feed efficiency ratio
Normal control	251.6^{a}±8.77	283.5^{a}±8.66	31.9^{a}±1.62	315.7^{a}±1.89	0.10^{a}±0.005
BPH control	219.0^{b} ±9.50	229.5^{b}±9.87	10.5^{c}±0.81	288.3^{b}±9.10	0.04^{c}±0.002
BPH sesame seeds ethanol extract	219.0^{b}±14.09	247.7^{b}±13.38	28.7^{a}±1.41	320.8^{a}±8.21	0.09^{a}±0.005
BPH soybean seeds ethanol extract	217.5^{b}±7.08	233.8^{b}±7.89	16.3^{bc}±1.89	307.8^{ab}±3.88	0.05^{bc}±0.01
BPH safflower seeds ethanol extract	220.7^{b}±7.23	235.0^{b}±6.19	14.3^{bc}±2.27	315.8^{a}±5.07	0.05^{bc}±0.01
BPH flaxseeds ethanol extract	219.5^{b}±8.12	233.8^{b}±9.03	14.3^{bc}±3.39	304.2^{ab}±6.11	0.05^{bc}±0.01
BPH sesame seeds powder	216.2^{b}±3.52	241.8^{b}±3.06	25.7^{a}±2.50	300.8^{ab}±8.41	0.09^{a}±0.01
BPH soybean seeds powder	219.3^{b}±11.16	235.3^{b}±12.05	16.0^{bc}±2.72	305.8^{ab}±6.11	0.05^{bc}±0.01
BPH safflower seeds powder	217.0^{b}±10.89	236.0^{b}±11.89	19.0^{b} ± 3.10	309.7^{a}±6.93	0.06^{b}±0.01
BPH flaxseeds powder	217.2^{b}±4.50	243.2^{b}±4.41	26.0^{a} ±1.57	311.7^{a}±5.43	0.08^{a}±0.005

In column different letters means significant difference at 5% probabilities (p<0.05) for treated groups but for BPH group was in comparison of normal control.

lignans possess their antioxidant properties through inhibition of lipid peroxidation or direct hydroxyl radical scavenging activity[44]. Due to flaxseed properties as lipophilic antioxidant so it easily pass the blood testis barrier and may induce direct antioxidant activity[43]. It was reported by Jeng and Hou[45] that sesame lignans have the activity to scavenge reactive oxygen spices.

BPH rats given oral administration of ethanol extract of flaxseed, sesame seeds and soybean showed significant reduction in prostate weight with different degrees. Bisson *et al*.[37] reported that lignan-rich extract from flaxseed hulls significantly reduced the prostate weight of BPH rats models compared to normal control animals. Also, Ren and Huang[46] reported that soybean isoflavone reduced the prostate weight of BPH rat's models.

BPH rats given oral administration of ethanol extract of sesame seed and flaxseed ethanol extract showed higher reduction of PSA, total, prostatic and non-prostatic acid phosphatase levels. Also all the BPH rats feeding on balanced diet containing 20% of the studied plants' powder showed reduction in PSA plasma levels with different degrees. Cereals and legumes are good source of dietary fiber. Preliminary clinical evidence suggests that dietary fiber may lower PSA and slow the growth of proliferative benign prostate tissue[47]. Demark-Wahnefried *et al*.[39] reported that flaxseed-supplemented (30 g/day) diet for 6 month significantly decreased the PSA levels in BPH subjects. Zhang *et al*.[48] evaluated the ability of flaxseed lignan extract containing 33% secoisolariciresinoldiglucoside (SDG) to alleviate LUTS and found that dietary flaxseed lignan extract appreciably

Table 4: Total cholesterol, testosterone, lipid peroxidation and prostate weight of different experimental groups (Mean ± SE).

Groups	T-Ch (mg/dl)	Testosterone (ng/ml)	MDA (nmol/ml)	Prostate weight (g)
Normal control	91.7^{bc}±2.47	1.47^{e}±0.15	10.33^{f}±0.32	0.75^{e}±0.02
BPH control	117.0^{a}±5.90	2.50^{a}±0.22	20.09^{a}±0.75	1.58^{a}±0.06
BPH sesame seeds ethanol extract	98.4^{bc}±1.91	1.65^{de}±0.08	16.40^{bcd}±0.65	0.97^{cd}±0.04
BPH soybean seeds ethanol extract	99.8^{bc}±1.18	1.85^{cd}±0.08	17.05^{bc}±1.37	1.08^{bc}±0.05
BPH safflower seeds ethanol extract	100.5^{b}±1.27	1.97^{bcd}±0.09	18.43^{ab}±0.99	1.05^{bc}±0.05
BPH flaxseeds ethanol extract	96.6^{bc}±2.91	1.48^{e}±0.06	14.54^{cde}±0.41	0.88^{de}±0.03
BPH sesame seeds powder	96.1^{bc}±2.14	2.07^{bc}±0.10	17.05^{bc}±1.18	1.12^{bc}±0.05
BPH soybean seeds powder	96.2^{bc}±1.47	2.15^{bc}±0.10	13.76^{de}±1.06	1.13^{b}±0.05
BPH safflower seeds powder	96.1^{bc}±2.75	2.23^{ab}±0.08	13.90^{de}±0.67	1.17^{b}±0.07
BPH flaxseeds powder	91.3^{c}±2.44	1.95^{bcd}±0.04	12.86^{e}±0.84	1.08^{bc}±0.05

In column different letters means significant difference at 5% probabilities (p<0.05) for treated groups but for BPH group was in comparison of normal control.

Table 5: Acid phosphatase and PSA of different experimental groups (Mean ± SE).

Groups	Acid phosphatase (U/L)			PSA (ng/ml)
	Total	Prostatic	Non-prostatic	
Normal control	31.1^{f}±1.05	19.4^{d}±0.49	11.7^{d}±0.74	25.2^{e}±1.51
BPH control	48.9^{a}±0.62	27.9^{a}±0.67	21.0^{a}±0.94	54.0^{a}±1.18
BPH sesame seeds ethanol extract	36.9^{e}±0.90	21.9^{cd}±1.50	15.0^{c}±1.18	41.8^{d}±1.30
BPH soybean seeds ethanol extract	43.3^{bc}±0.96	25.1^{ab}±1.17	18.2^{ab}±0.62	46.7^{bc}±0.88
BPH safflower seeds ethanol extract	45.6^{b}±1.67	25.4^{ab}±1.39	20.2^{ab}±1.26	47.8^{b}±0.70
BPH flaxseeds ethanol extract	39.2^{de}±1.34	21.9^{cd}±0.67	17.4^{bc}±1.04	42.0^{d}±1.00
BPH sesame seeds powder	42.5^{bc}±0.80	24.1^{bc}±1.04	18.4^{ab}±0.70	46.5^{bc}±0.92
BPH soybean seeds powder	43.9^{bc}±0.98	24.7^{bc}±0.61	19.2^{ab}±0.94	47.8^{b}±1.19
BPH safflower seeds powder	45.09^{b}±0.65	25.3^{ab}±0.34	19.8^{ab}±0.58	48.7^{b}±0.88
BPH flaxseeds powder	41.2^{cd}±1.00	23.3^{bc}±0.72	17.9^{b}±1.20	44.2^{cd}±1.01

In column different letters means significant difference at 5% probabilities (p<0.05) for treated groups but for BPH group was in comparison of normal control.

Table 6: Kidneys and liver functions of different experimental groups (Mean±SE).

Groups	Creatinine (mg/dl)	Urea (mg/dl)	AST (IU/l)	ALT (IU/l)
Normal control	0.60^{a}±0.03	28.6^{a}±0.74	68.3^{a}±1.82	24.7^{a}±1.69
BPH control	0.65^{a}±0.02	31.9^{a}±1.44	74.8^{a}±2.15	27.2^{a}±1.64
BPH sesame seeds ethanol extract	0.59^{a}±0.02	29.4^{a}±0.69	70.7^{a}±3.49	25.5^{a}±1.59
BPH soybean seeds ethanol extract	0.62^{a}±0.02	29.7^{a}±0.56	71.8^{a}±3.33	27.7^{a}±0.56
BPH safflower seeds ethanol extract	0.61^{a}±0.02	29.1^{a}±1.79	71.5^{a}±1.98	24.7^{a}±1.26
BPH flaxseeds ethanol extract	0.60^{a}±0.02	29.9^{a}±1.37	70.8^{a}±4.52	25.3^{a}±1.33
BPH sesame seeds powder	0.58^{a}±0.03	30.1^{a} ±1.00	71.7^{a}±1.56	27.2^{a}±1.47
BPH soybean seeds powder	0.57^{a}±0.03	29.3^{a}±1.20	72.8^{a}±2.39	27.0^{a}±1.53
BPH safflower seeds powder	0.58^{a}±0.03	28.8^{a}±0.97	72.5^{a}±7.10	25.3^{a}±0.88
BPH flaxseeds powder	0.61^{a}±0.03	29.4^{a}±1.06	74.5^{a}±4.69	25.5^{a}±1.54

In column different letters means significant difference at 5% probabilities (p<0.05).

improved LUTS in BPH subjects. Also flaxseed powder effect may be due to its high content of linolenic acid which has been found to be useful to BPH patients. Yan and Spitznagel[49] and Xiao and Singh[50] reported that administration of essential fatty acids linoleic and linolenic to BPH patients showed improvement in their status. β-sitosterol[51] and certain unsaturated fatty acids such as gamma-linolenic acid, α-linolenic acid, linoleic acid, myristoleic acid, and oleic acid[52] have been found to inhibit 5α-reductase activity to varying degrees. Natural sources are an alternative treatment with minimal drawbacks to synthetic drugs for BPH[53].

The effect of sesame seed may be due to their high content of β-sitosterol which has been found to inhibit BPH and improve LUTS in BPH subjects[54,55]. Also *in vitro* and animal studies have shown that sesame seed is one of the richest sources of lignan, which may have protective effect against hormone-related disease such as breast cancer and BPH (56). The mechanisms by which the plant extracts protect against BPH rat model may be also due to the high

levels of phenolic compounds present in the plants under the study as shown from the present study. A variety of polyphenols are known to have the ability to inhibit testosterone 5α-reductase activity and so prevent BPH[57].

CONCLUSION

The ethanolic extracts and whole powders of the studied plants' showed promising effect towards BPH in animal model. All the studied extracts' and plants' powders showed complete safety towards liver and kidney function.

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