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EFFECTS OF THE AQUEOUS SEED EXTRACT OF *HELIATHUS ANNUUS L* ON SOME BIOCHEMICAL INDICES OF PROSTATE PATHOLOGIES IN ALLOXAN-INDUCED DIABETIC RATS

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ABSTRACT

The aim of this study was to investigate the effect of the aqueous seed extract of helianthus annuus on some indices of prostate pathologies and contribute as to the relationship between diabetes mellitus and prostate pathologies. Twenty (20) Adult male wista albino rats (Rattus norvegicus) ranging from 150 to 250g weight were used in the study. Experimental diabetes was induced by single interperitoneal injection of alloxan-monohydrate dissolved in normal saline solution at a dose of 150mg /kg body weight. The rats were randomly divided into experimental and control groups of five rats each. The experimental groups (C, D) were given 400mg/kg b.w single daily dose of the aqueous extract for fifteen (15) days. Diabetes mellitus was confirmed in the experimental rats by the significant increase ($p<0.05$) in serum glucose level. Treatment with the extract showed a significant time dependant decrease ($p<0.05$). There was a significant ($p<0.05$) decrease in the serum level of prostate specific antigen and testosterone in the diabetic rats. Treatment produced a significant ($p<0.05$) increase. For oestrogen the diabetic control group rats showed significant ($p<0.05$) increase compared to the normal control group rats. The diabetic treated group rats showed a significant ($p<0.05$) increase in serum oestradiol level when compared to the diabetic control group rats. The effect of treatment was not time dependent. In conclusion Helianthus annuus L (sunflower) seed extract may have a beneficial effect in reducing risk of prostate pathology among diabetics.

Keywords: Hellianthus Annuus, Seed, Alloxan. Diabetes Mellitus, Prostate

INTRODUCTION

The term "prostate" was originally derived from the Greek word "*prohistani*", meaning 'to stand in front of and has been attributed to Herophilus of Alexandria who used the term in 335BC to describe the organ located in front of the urinary bladder [32]. The prostate is a fibromuscular and glandular organ situated in the pelvic cavity just inferior to the bladder. The function of the prostate gland is to store and secrete a thin, milky, slightly alkaline [PH 7.29] fluid called prostate fluid that usually constitutes 25%-30% of the volume of the semen along with seminal vesicle fluid. The alkalinity of semen helps neutralise the acidity of the vaginal tract, prolonging the lifespan of sperm. The prostate is also a muscle that pumps the semen out through the penis with enough force to enter into the vagina to help the sperm succeed in reaching the uterus and ensuring procreation of the species. The prostate also filters and removes toxins so that the sperm are protected, which enhances the chance of impregnation and ensures that men seed with the optimum quality of sperms. The prostate erection nerves are also responsible for erections. If these nerves, which attach to the sides of the prostate, are damaged, then erectile difficulties are guaranteed [32]. Roger and Manisha (2008) [31] mentioned three basic prostate diseases or problems; enlargement of the prostate or Benigh Prostatic Hyperplasia (BPH) which is a non- cancerous growth of the prostate gland, Prostatitis, this is essentially an infection and/or inflammation of the prostate gland and Prostate cancer. In most developed and developing countries, prostate cancer is the most commonly diagnosed malignancy affecting men beyond middle age, and is second only to lung cancer as a cause of cancer deaths in men. Diabetes mellitus is a condition in which the body does not provides enough, or properly responds to insulin, a hormone produced in the pancreas. Insulin enables cells to absorb glucose in order to turn it

to energy. This causes glucose to accumulate in the blood, often leading to various complications [29]. The incidence of diabetes mellitus in the human population has reached epidemic proportions worldwide and it is increasing at a rapid rate. There are some studies on the relationship between diabetes and prostate cancer risk, however, the results have often been discrepant and in consistent [16]. The aim of this study was to investigate the effect of the aqueous seed extract of *helianthus annuus* on some indices of prostate pathologies and contribute as to the relationship between diabetes mellitus and prostate pathologies.

MATERIALS AND METHODS

Plant Material

Helianthus annuus (sunflower) seeds were obtained form the Institute of Agricultural Research (IAR), Faculty of Agriculture, Ahmadu Bello University, Zaria. The variety was funtua oil rich type. The seeds were authenticated by the Head, oil seeds department.

Preparation of Plant Extract

The *helianthus annuus* seeds were sundried, dehulled and pounded into a fine powder using mortar and pestel. The powdery seed was poured into a beaker mixed properly with water and then placed on an electric hot plate to boil. The mixture was stirred continuously until it started boiling. It was filtered and the filtrate placed in another beaker. The filtrate was evaporated to dryness at 60^0c, and the extract was stored in a clean air-tight container in the refrigerator. It was later reconstituted in distikked water and administered.

Experimental Rats

Adult male wista albino rats (Rattus norvegicus) ranging from 150 to 250g weight were used in the study. The animals were housed in cages, allowed two (2) weeks to acclimatise and maintained on standard animals feed and drinking water *ad libitum*.

Induction of Experimental Diabetes Mellitus

Induction of diabetes was carried out by single interperitoneal injection of alloxan-monohydrate (Sigman St. Louis, M.O; USA) dissolved in normal saline solution at a dose of 150mg /kg body weight [20] . Diabetes was confirmed in alloxan induced rats by determining the blood glucose level 48hrs after injection of allaxan using one touch (R) Glucometer (Life scan Inc, 1995; Milpitas Califonia 95395, USA).

Design of the Experiment

After the induction of diabetes mellitus in the rats, the animals were randomly divided into experimental and control groups of five rats each as follows;

Group A: Normal control (positive control)
Group B: Diabetic control (negative control)
Group C: Normal treated rats
Group D: Diabetic treated rats

Treatment of Experimental Animals and Collection of Samples

Groups A and B animals were given 0.2ml of distilled water daily, while groups C and D received 400mg/kg b.w single daily dose of the dried aqueous extract for fifteen (15) days by oral intubation. Blood glucose levels were taken at five (5) days interval using one touch ® glucometer. At the end of the experiments, the rats were starved overnight before they were anesthetized and sacrificed. Blood samples were collected in clean dry centrifuge tubes, allowed to clot for 40 minutes and then spun at 5.000 rpm for 10 minutes. The sera were collected, transferred to sterile bottles and kept for analysis.

Assay of Biochemical Parameters

Parameters assayed include serum glucose assayed by the method of Trinder, 1969 [37], total Prostate Specific Antigen, PSA, by the method of Christensson *et al*, 1990 [8], Testosterone and 17β - Oestradiol, E_2, by the method of Abraham, 1981[1]. Determination of

testosterone concentration was by the method of Midgeley, 2001[25].

Statistical analysis

Data were presented as Mean ± SD of 5 replicates and analysed by one-way analysis of variance (ANOVA) using SPSS version 18 computer software package (SPSS INC, Chicago, USA). Differences at $P < 0.05$ were considered significant.

Results

Table 1: Phytochemical Screening of the Extract of *Helianthus annuus L* (sunflower) seed

Phytochemical	Aqueous Extract	Petroleum ether extract	Methanolic Extract
Alkaloids	+	-	-
Tannins	+	-	+
Anthraquinones	-	-	-
Cardiac Glycosides	+	+	-
Steroids/ Terpenes	+	+	+
Flavonoids	+	+	+
Saponins	+	-	+

KEY:-

\+ = Present

\- = Absent

The result of the phytochemical analysis as observed in Table 1 showed that the bioactive compounds found in the aqueous extract are the alkaloids, tannins, saponins, cardiac glycosides, steroids and terpenes and the flavonoids.The anthraquinones were absent. The petroleum ether extract has cardiac glycosides, steroids and terpenes only. The methanolic extract showed only the presence of tannins, steroids and terpenes, flavonoids and saponins.

Table 2: Effect of *Helianthus annuus* (Sunflower) Aqueous Seed extract on Serum Glucose Level (mmol/L) in Normal and Diabetic Rats.

Group	Initial	48hrs	Day 5	Day 10	Day 15
A	4.65±0.22	10.78±0.08[a]	11.56±0.10[a]	13.44±0.14[a]	15.24±0.12[a]
B	4.60±0.09	4.65±0.21	4.55±0.32	4.60±0.33	5.02±0.03
C	4.68±0.38	4.61±0.20[b]	5.10±0.04[b]	4.65±0.10[b]	4.53±0.17[b]
D	4.95±0.07	11.44±0.14[c]	10.78±0.10[c]	9.78±0.10[c]	8.14±0.05[c]

Values are mean ± S.D for five determinations (n=5).

KEY: A = Diabetic Control; **B** = Normal Control; **C** = Normal + Aqueous extract; **D** = Diabetic + Aqueous extract;

a = statistically significant ($p<0.05$) when compared to the normal control (NC),

b = statistically insignificant ($p<0.05$) when compared to the normal control (NC).

c = statistically significant ($p<0.05$) when compared to the diabetic control (DC).

Table.2 above shows the effect of *Helianthus annuus* (sunflower) seed extracts on serum glucose level (mmol/L) in the diabetic and normal rats groups. Induction of diabetes in the experimental rats was confirmed by the significant increase ($p<0.05$) in serum glucose level of the diabetic control rats when compared with the normal control rats. The diabetic treated group showed a significant decrease ($p<0.05$) in serum glucose level compared with the diabetic control rats group. There was no significant ($p<0.05$) difference between the normal control and the normal treated groups. For the diabetic treated groups, day15 showed a significant decrease ($p<0.05$) in serum glucose level when compared to day 5 and day 10. The effect of treatment was therefore time dependent.

Table 3: Effect of *Helianthus annuus* (Sunflower) Seed Extract on Serum Testosterone Level (nmol/L).

Group	48hrs	D5	D10	D15
A	8.40±0.13[a]	8.60±0.10[a]	10.35±0.19[a]	9.02±0.20[a]
B	18.03±0.32	18.00± 0.25	17.50± 0.30	18.06±0.15
C	18.00± 0.50	18.05±0.32[b]	18.54±0.14[b]	19.04±0.32[b]
D	8.45± 0.12	10.40±0.20[c]	15.60± 0.19[c]	12.60±0.20[c]

Values are mean ± S.D for five determinations (n=5)

KEY: A = Diabetic Control; **B** = Normal Control; **C** = Normal + Aqueous extract; **D** = Diabetic + Aqueous extract.

a = statistically significant ($p<0.05$) when compared to the normal control (NC),

b = statistically insignificant ($p<0.05$) when compared to the normal control (NC).

c = statistically significant ($p<0.05$) when compared to the diabetic control (DC).

Table.3 shows the effect of *Helianthus annuus* (sunflower) seed extracts on serum testosterone level. The result showed a statistically significant ($p<0.05$) decrease in the diabetic control group rats compared to the normal control and a statistically not significant ($p<0.05$) difference in the normal treated groups rats when compared to the normal control.

On days 5, 10 and 15 the diabetic treated group rats showed a significant ($p<0.05$) increase when compared to the diabetic control group rats.

Table 4: Effect of *Helianthus annuus* (Sunflower) Seed Extract on Serum Oestradiol Level (pm/L).

Group	48hrs	Day 5	Day 10	Day 15
A	123.00±1.14[a]	127.06±0.23[a]	125.25±0.53a	120.17±0.05[a]
B	90.20±3.06	93.56±1.17	91.53±2.05	90.50±0.56
C	90.050±.60	92.05±0.71[b]	89.17±2.35[b]	91.77±0.32[b]
D	125.00±0.20	133.66± 0.11[c]	137.70±0.65[c]	125.11±0.71[c]

Values are mean ± S.D for five determinations (n=5)

KEY: A = Diabetic Control; **B** = Normal Control; **C** = Normal + Aqueous extract; **D** = Diabetic + Aqueous extract.
a = statistically significant ($p<0.05$) when compared to the normal control (NC),
b = statistically insignificant ($p<0.05$) when compared to the normal control (NC).
c = statistically significant ($p<0.05$) when compared to the diabetic control (DC).

Table. 4 shows the effect of *Helianthus annuus* (sunflower) seed extracts on serum oestradiol level (pm/L). The diabetic control group rats showed significant ($p<0.05$) increase compared to the normal control group rats. The difference between the normal treated group rats and the normal control group rats was statistically not significant ($p<0.05$).
On days 5, 10 and 15 the diabetic treated group rats showed a significant ($p<0.05$) increase in serum oestradiol level when compared to the diabetic control group rats. The effect of treatment was not time dependent.

Table 5: Effect of *Helianthus annuus* (Sunflower) Seed extract on Serum Total Prostate Specific Antigen (PSA) Level.

Group	48hrs	Day5	Day10	Day15
A	0.93 ± 0.01^{a}	0.93 ± 0.02^{a}	0.95 ± 0.03^{a}	0.92 ± 0.04^{a}
B	1.26 ± 0.67	1.25 ± 0.07	1.24 ± 0.05	1.26 ± 0.02
C	1.24 ± 0.23	1.24 ± 0.08^{b}	1.23 ± 0.03^{b}	1.27 ± 0.01^{b}
D	0.94 ± 0.02	0.90 ± 0.04^{c}	0.90 ± 0.07^{c}	0.88 ± 0.06^{c}

Values are mean ± S.D for five determinations
KEY: A = Diabetic Control; **B** = Normal Control; **C** = Normal + Aqueous extract; **D** = Diabetic + Aqueous extract.
a = statistically significant ($p<0.05$) when compared to the normal control (NC),
b = statistically insignificant ($p<0.05$) when compared to the normal control (NC).

c = statistically significant ($p<0.05$) when compared to the diabetic control (DC).

Table. 5 shows the effect of the *Helianthus annuus* (sunflower) seed extracts on serum total prostate specific antigen level. The result showed a statistically significant ($p<0.05$) decrease in the diabetic control group rats compared to the normal control and a statistically no significant ($p<0.05$) difference in the normal treated groups rats when compared to the normal control. On days 5, 10 and 15 the diabetic treated groups rats showed a significant ($p<0.05$) decrease in serum total prostate specific antigen level when compared to the diabetic control group rats.

DISCUSSION

The preliminary phytochemical screening of the aqueous extract of *H*elianthus *annuus* (sunflower) seed (Table 1) showed the presence of alkaloids, tannins, cardiac glycosides, steroids, terpenes, flavonoids and saponins while the petroleum extract showed the presence of cardiac glycosides, steroids, terpenes and saponins only. Erah (1994) [11] reported that the hypoglycaemic activity of the leaves of higher plants were associated with their alkaloid component. He also reported that flavonoids are frequently found in plants with hypoglycaemic activity. The potent antioxidant and free radical scavenging activities of flavonoids [15, 2] could counteract the free radical generation responsible for alloxan-induced diabetes, and may contribute to the potency of the aqueous extract. Also, heterogeneous phytoconstituents of crude extracts have been reported to have synergistic effect [24, 2]. Ivorra *et al.*, (1989) [17] and Swanston-Flatt *et al.*, (1990) [35] reported that hypoglycaemic phytochemicals include alkaloids, cardiac glycosides, flavonoids, saponins, tannins, steroids and terpenes and so on. The hypoglycaemic effects of *Helianthus annuus* (sunflower) seed extract may therefore also be partly due to the presence of these bioactive constituents. Medicinal plants which exhibit anti-diabetic activities usually possess active substances which are able to mimic

the activity of insulin or which exert similar effects on the beta cells of the pancreas causing them to synthesize and secret insulin [16]. Although the mechanism of the anti-diabetic effect of *Helianthus annuus* (sunflower) seed extract is not yet established, it is likely that they act in a manner typical of other medicinal plants that influence glucose uptake and metabolism. Table 2 shows the effect of *Helianthus annuus* (sunflower) seed extracts on serum glucose level in diabetic and diabetic treated rats. Experimental diabetes was induced by a single intraperitoneal injection of alloxan monohydrate at a dose of 150mg/kg b.w [20, 36]. Diabetes was confirmed in the experimental rats after 48hours by the significant increase ($P<0.05$) in serum glucose level of the diabetic control group rats when compared to the normal control group rats. The diabetic rats treated with *Helianthus annuus* (sunflower) seed extract showed a significant decrease ($P<0.05$) in serum glucose level compared with the diabetic control group rats. Similarly, those treated with the standard diabetic drug also showed a significant decrease ($P<0.05$) in serum glucose level compared with the diabetic control group rats. The result obtained in this study indicates that the aqueous extract of *Helianthus annuus* (sunflower) seed produced significant hypoglycaemic effects in alloxan induced diabetic rats.

This is consistent with the findings of Al-Attar, (2012) [3]. It is possible that the plant extracts may reverse the catabolic features of insulin deficiency, decrease the release of glucagon or increase that of insulin, stimulate directly glycolysis in peripheral tissues, increase glucose removal from the gastrointestinal tract [23]. Hypoglycaemic effect of Sunflower (*Helianthus annuus*) seed extract could also possibly, be due to increased peripheral glucose utilization. Inhibition of the proximal tubular reabsorption mechanism for glucose in the kidneys, if any, can also contribute towards blood sugar lowering effects [33]. For all the treated groups day 15 showed a significant decrease ($P<0.05$) in serum glucose level when compared to days 5 and 10. This implies that the

treatment was time dependent for serum glucose level. Table 3 showed a statistically significant decrease ($P<0.05$) in serum testosterone (TTS) level in the diabetic rats compared to the normal rats. This result is consistent with other research findings. Low serum testosterone level is reported to be associated with a variety of comorbidities, including insulin resistance, obesity and type 2 diabetes [12]. A link between testosterone deficiency and diabetes has also been suggested with the demonstration that men with type 2 diabetes have lower testosterone levels than weight-match nondiabetic control subjects [17]. In addition, six large progressive studies have shown that low testosterone levels predict development of type 2 diabetes in men [17]. Birkeland *et al* (1993) [6] and Haffner *et al*., (1994) [14] in their studies demonstrated a positive relation between total testosterone levels and insulin sensitivity in normal and diabetic men. Furthermore, a number of cross-sectional epidemiological studies have reported an association between low testosterone and type 2 diabetes [18]. Evidence also suggests that a close inverse relation exist between serum levels of testosterone and the degree of obesity in men [40, 28]. Specifically, abdominal or central obesity has been inversely related to total and free testosterone and it has also been reported that subcutaneous fat accumulation in the trunceal area is highly predictive of low plasma concentration of free testosterone [18] .

The obesity cycle hypothesis suggests an explanation for these inverse associations between testosterone and obesity and insulin resistance. According to this hypothesis, testosterone is metabolized to 17b-estradiol (E_2) by aromatase located in excess adipocytes; the lower testosterone levels then allow for increased lipoprotein lipase activity, resulting in increased fatty acid uptake and triglyceride storage in adipocytes. This, in turn, results in an increase in fat mass, which correlates with increased insulin resistance and greater breakdown of testosterone and increase in serum oestrdiol level. Decreased level of TTS and increasing level of E_2 correlates with the incidence of impotence among diabetics. This

probably accounts for erectile dysfunction (or importance) in diabetic suffers. Many studies have shown that testosterone therapy has beneficial effects on insulin sensitivity and markers of obesity [32, 4, 18]. A number of potential hypotheses have been derived to explain these observations. Studies on the direct effects of testosterone on cultured adipocytes and adipose tissue suggest that androgen treatment may decrease adipogenesis and increase lipolysis [7] by a number of different mechanisms. Testosterone has been reported to inhibit lipid uptake and lipoprotein lipase activity in adipocytes, along with stimulating lipolysis through an increased in the number of beta-adrenergic receptors, and also inhibiting the differentiation of precursor adipocytes . Further evidence for the negative effect of testosterone on adipocyte differentiation was provided by Singh *et al.*, (2003) [34] who reported that the treatment of isolated stem cells with testosterone promoted the development of myocytes rather than adipocytes and that testosterone deficiency favored the development of adipocytes over cells of myocyte lineage. Consequently, testosterone treatment may directly reduce visceral fat mass and increase muscle mass, resulting in decrease in waist circumference, which, in turn, has a direct effect on circulating fatty acids and insulin resistance. Another potential mechanism for the beneficial effect of testosterone in diabetic men may be to increase the metabolic rate and promote the acquisition of energy from fat stores.

Pitteloud *et al.*, (2005) [29] describe an inverse relationship between testosterone levels and mitochondrial function, with low testosterone levels being associated with reduced muscle mitochondrial oxidative phosphorylation. Consequently, testosterone may increase the metabolic rate and promote the acquisition of energy from fat stores. These observations support the low energy levels in diabetics generally. Insulin resistance is associated with reduced testosterone secretion by the Leydig cells of the testis. Hormonal changes, associated with diabetes, which may result in the

low testosterone level, has been suggested as the basis of the relationship between a lower risk of prostate cancer among diabetics[13]. In this study, treatment with *Helianthus annuus* (sunflower) seed extract improves the serum levels of testosterone significantly ($P<0.05$). The significant increase ($P<0.05$) in the diabetic treated rats may be due to the effect of treatment on the diabetic state. Table 4 shows that the diabetic rats had a significant increase in serum oestradiol (E_2) level compared to the normal rats. Studies suggest that men with *diabetes mellitus* have a reduced risk of developing prostate cancer and a number of theories exist to explain this protective phenomenon, but the most prevalent argues that *diabetes mellitus* may lower prostate cancer risk through a reduction of essential serum growth factors-insulin, insulin-like growth factor (IGF-1) and testosterone [19] .

Decrease in testosterone levels are accompanied by a concomitant rise in oestradiol levels [19] which could explain why *diabetes mellitus* paradoxically increases the risk of endometrial and breast cancer in women while reducing the risk of prostate cancer in men. In men, increase in oestradiol and decrease in testosterone as a result of conversion of testosterone (TTS) to oestradiol by the enzyme aromatase (acyp 4501819) is a risk factor for benigh prostate hyperplasia(BPH) and proliferation of prostate cancer cells. The paradox may arise from the fact that aromatase is domicile in fat cells and diabetic patients lose both protein and fat (i.e they lose body weight) and are lean. Men lose TTS as they age at the rate of 1%/year from about 40 years. Age and stress may risk factors to BPH and prostate cancer.

The increase in serum oestradiol level in diabetes is supported by the obesity cycle hypothesis. The diabetic treated rats showed further significant increase ($P<0.05$) compared to the normal rats. That is even after treatment with *Helianthus annuus* (sunflower) seed extracts the serum levels of oestradiol remained higher than that of the normal rats. The reason for this is not clear. The effect

of duration of treatment is not consistent. Prostate specific antigen (PSA) is a glycoprotein produced primarily by the epithelial cells of the prostate gland, and its regulation is under the control of androgens and progestins. The physiological function of PSA is not yet entirely understood, its well- known and accepted physiological function is that PSA proteolyticaly cleaves seminogelins and fibronectin present in seminal plasma and thus cause liquefaction of the seminal clot after ejaculation. This process does promote the release and motility of sperms cells [21, 22, 8] .Other potential functions of the activity of PSA, imply its role as a cell growth inhibitor, and anticarcinogenic/antiagiogenic molecule, or inducer of apoptosis. PSA is the most valuable prostatic cancer marker that is used for population screening, diagnosis, and monitoring of patients with prostate cancer. Elevated serum PSA concentrations are known to be connected with the three most common prostatic diseases, that is, prostate cancer, benigh prostatic hyperplasia (BPH) and prostatitis.

Results from this study (Table 5) showed a statistically significant ($p<0.05$) decrease in serum PSA level in the diabetic control group rats compared to the normal control group rats. Fukui, *et al.*, (2008) [12] reported that serum PSA levels were lower in diabetic men than in healthy men, David *et al.*, (2006) [10] also found for men a similar decrease in mean PSA .In another study, David *et al.*, (2006) [10] examined the association between diabetes and prostate specific antigen levels. The results show that the predicted geometric mean PSA values was lower in the diabetic group than in the nondiabetic group and was lowest in men who had diagnosis with diabetes more than ten years previously. The trend for decreased PSA by diabetes status was statistically significant. Muller, *et al.*, (2009) [26] also supported the hypothesis that more severe forms of diabetes are associated with lower PSA levels. These results are consistent with a lower risk of prostate cancer among diabetics. Results from epidemiologic studies on the relationship between diabetes and

prostate cancer risk are often inconsistent and confusing. Patients with diabetes have been reported to be at increased risk of prostate cancer [12] , however recent studies suggest a lower risk of prostate cancer and BPH among diabetics [21,10], but it is paradoxical that PSA and type 2 diabetes increases with age and prostate cancer risk is associated with increase in oestradiol (E_2). In the meta-analysis of Kasper and Giovannucci, (2006) [19], an overall prostate cancer risk reduction of 16% was shown for diabetic patients. The basis of this relationship is unclear. The mechanism of the association may involve the regulation of PSA by androgens. Diabetic men have lower androgen levels than nondiabetic men, and this may particularly explain their lower PSA levels [31] .Two important pathways might be involved in the association of diabetes and both PSA and prostate cancer. Lower testosterone levels in diabetic men might be responsible for their reduced PSA levels, as PSA is regulated by androgens. Nevertheless, prostate cancer risk is not associated with serum testosterone levels at the same time. However, PSA cleaves insulin-like growth factor binding protein-3, which is the major binding protein for insulin-like growth factor-1 .This might lead to increased serum insulin-like growth factor-I, which is an important risk factor of prostate cancer [31]. However, it is not clear whether the complex regulation of these mechanisms leads to a parallel reduction of PSA and prostate cancer in diabetic men or not [26].

Diabetes might also alter PSA values through impaired kidney function or as a consequence of diabetic medication use. Serum PSA concentration is age dependent, that is, it tends to increase with age because the prostate enlarges with years and contain more PSA-producing tissue. Even though an inverse association between diabetes and PSA levels was observed in several studies, PSA levels seem to be influenced by a number of demographic, lifestyle, and health characteristics, which might deserve careful attention in the interpretation of test results. Furthermore, the role of severity, duration, and therapy of diabetes are yet to be exposed as more

detail data are still lacking [26]. Treatment with *Helianthus annuus* (sunflower) seed extract further reduced significantly ($P<0.05$) the serum levels of PSA in the diabetic treated group rats compared to the diabetic control. The serum levels of PSA in the diabetic treated, however still remain below that of the normal control rats. This effect was not time dependant.

CONCLUSION

Based on the results of this study, particularly the effect on indices of prostate pathologies, *Helianthus annuus* (sunflower) seed extract may have a beneficial effect in reducing risk of prostate pathology among diabetics.

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