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Effect of Biscuits Fortified with Pumpkin, and Sunflower Seeds, on Alloxan-Induced Diabetic Rats

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Abstract:
Edible seeds have been used to reduce the symptoms of diabetes because they contain natural antioxidants that can protect cell function caused by diabetes. This study aims to investigate the effect of biscuits fortified with pumpkin and sunflower seeds and metformin (antihyperglycemic medication) on diabetic rats. Eight groups of six adult male albino rats, each weighing (150±10g), were used in this study. For 28 days, biscuits fortified with pumpkin and sunflower seeds and metformin were gradually added to the basal diet at a rate of 2.5 and 5 %, and 250mg/kg, respectively. Alloxan (150 mg/kg body weight) was injected subcutaneously into diabetic rats. At the end of the experiments, serum glucose levels, lipid profiles of triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL-c), very low-density lipoprotein (VLDL-c), and high-density lipoprotein (HDL-c), the activities of the liver enzymes ALT & AST, and the kidney functions of creatinine, uric acid, and urea levels were evaluated. The results indicated that consumption of biscuits fortified with pumpkin and sunflower seeds, as well as metformin significantly ($P \leq 0.05$), improved the level of glucose in the serum blood of rats, increased HDL-c significantly, and improved liver and kidney functions by decreasing ALT, AST, creatinine, uric acid, and urea in the rats compared to the positive group. In conclusion, the most significant thing to add is biscuits fortified with pumpkin and sunflower seeds to our snack diet to reduce glucose in the blood.

Keywords*: Plant seeds, Rats, Glucose, Metformin, Biochemical analysis*

Introduction

According to the World Health Organization, diabetes mellitus (DM), is a severe, chronic illness that develops when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it creates. Therefore, it is a serious public health problem (1). It is a hazardous metabolic disorder. Insufficient insulin production or peripheral tissues' inability to react to the presence of insulin can lead to chronic hyperglycemia (2). It is a metabolic condition that affects people of all racial and ethnic backgrounds equally and has become the leading cause of mortality globally, is spreading like an epidemic. It has many kinds that are categorized according to diverse pathophysiology and is defined by excessive amounts of glucose in the blood. The hallmark of type 1 diabetes, also known as insulin-dependent diabetes, is insulin insufficiency brought on by autoimmune disease. Type 2 diabetes, also known as non-insulin-dependent diabetes, is caused by a combination of insufficient insulin production and resistance to insulin action (3). Insulin shortage or relative deficit is the root cause of diabetes. Due to cells' inability to absorb glucose, there is a shortage of intracellular glucose despite an abundance of external glucose, which raises blood glucose levels (4). The main contributor to diabetes complications and the onset of diabetes vascular illnesses, particularly cardiovascular disease, is hyperglycemia (5).

The biguanide class of drug Metformin (MET) is an oral antihyperglycemic medication that is commonly used to treat type 2 diabetes (6). In addition to inhibiting hepatic glycogenolysis and gluconeogenesis, metformin also limits the amount of glucose that may enter the bloodstream from the gut, improves peripheral tissue insulin sensitivity, and increases muscle tissue uptake of glucose. MET was discovered to improve beta cells' ability to secrete insulin (7).

The pumpkin plant (*Cucurbita maxima*), which has its origins in Asia, is now widely cultivated throughout many temperate and tropical parts of the world. There are several different types of pumpkins, including Cucurbita pepo, *Cucurbita maxima*, and *Cucurbita stilbo*. In terms of medicine, a pumpkin is described as round, orange in color, and having long vines and a flowering stage, similar to other winter squash (8). In many nations, people like pumpkins. Polyunsaturated fatty acids, proteins, phytosterols, vitamins, trace elements like zinc, and antioxidant substances including tocopherol, phenolic compounds, flavonoids, and carotenoids were all abundantly present in its seeds. Many health advantages were provided by pumpkin seed oil (9). Vitamins, oil (37.8-45.4%), particularly Omega 6 fatty acids, and protein (25.2–37%) are all present in pumpkin seeds (10). D-chiro-inositol, which was isolated from pumpkin, has been associated with its antidiabetic activity and was once thought to be an insulin action mediator (insulin sensor) (10). Pumpkin seed powder and oil can help diabetic rats' insulin levels and general health, as well as reduce the negative effects of diabetes. One diet that decreased blood glucose levels and lipid profiles in diabetic rats was pumpkin seed powder and oil (12).

Worldwide cultivation and consumption of sunflower (*Helianthus annuus*) seeds is a result of their high nutrient content, which includes fiber, protein, unsaturated fats, selenium, copper, zinc, iron, vitamin E, and several other nutrients, antioxidants, minerals, and vitamins that are crucial in the prevention or treatment of various diseases, diabetes being one of them. Because they contain chlorogenic acid, quinic acid, caffeic acid, glycosides, and phytosterols, these seeds have anti-diabetic characteristics. These sulfur-rich proteins are suitable for human intake since they aid in carrying out their metabiological tasks, such as muscle cell formation and insulin generation, and they also contain 20% of proteins that give Sulphur and nitrogen (13). Sunflower seeds, for example, can be used to treat type 2 diabetes

by lowering blood sugar levels. Sunflower seeds' chlorogenic acid and seco-isolariciresinol diglucosoid, two of these seeds' bioactive ingredients, were used to treat insulin resistance and to produce insulin (2). Conjugated linoleic acid isomers like cis-9 and trans-10, which are contained in these seeds, play a role in restoring normal glucose tolerance in both humans and animals. Because they block the activities of oxygen-reactive species that contribute to the induction of pathways that ultimately result in diabetes, natural anti-glycates and antioxidants are more advantageous for treating and preventing diabetes (14).
This study aims to evaluate the effects of various doses of biscuits fortified with pumpkin and sunflower seed on blood glucose level in diabetic rats induced by alloxan.

Materials and methods

Materials:

Pumpkin (*Cucurbita maxima*) and sunflower (*Helianthus annuus*) seed were obtained from local market, Shibin El-Kom City, Menoufia Governorate, Egypt. Alloxan, also known as 5, 5-dihydroxyl pyrimidine-2, 4, 6-trione, is an organic molecule, urea derivative, carcinogen, and cytotoxic glucose derivative obtained by Al-Gomhoria Company for Trading Drugs, Chemicals, and Medical Instruments in Cairo, Egypt. SIGMA Chemical Company, USA provided pure white crystalline cholesterol powder and saline solutions. Casein, cellulose, choline chloride powder, and DL methionine powder, were obtained from Morgan Co. Cairo, Egypt. 50 mature normal male albino rats of the Sprague Dawley strain, weighing 140±10g were purchased from the Vaccine and Immunity Organization, Ministry of Health, Helwan Farm, Cairo, Egypt. Chemical kits for the determination of TC, TG, HDL-c, ALT, AST, ALP, urea, uric acid, creatinine, and alloxan were obtained from Al-Gomhoria Company for Chemical, Drugs Trading and Medical Instruments, Cairo, Egypt.
Wheat flour (72 % extraction) was provided from The South Cairo mills company, Cairo government, Egypt. Sucrose, butter, fresh whole eggs, skim milk powder, baking powder, vanilla powder, and water are all ingredients in the dough for biscuits dough. These items were purchased in Cairo, Egypt, at a local market.

Methods

Biscuit Processing:

Biscuits samples were processed from doughs containing 2.5 and 5% Pumpkin and sunflower seed powder as substituting levels for wheat flour according to the method described by **(15)**. The formula used was as follows: 200 g wheat flour, 60 g sugar, 50 g shortening, 2 g sodium chloride, 0.8 g sodium bicarbonate, 3 g ammonium bicarbonate, 4 g dextrose, 4 g skimmed milk powder and 40 - 42 ml water. The ground powder sugar and fat were creamed in a Hobart mixer (N-50) with a flat beater for 3 min at 61 rpm (speed 1). Sodium bicarbonate, sodium chloride and ammonium bicarbonate were dissolved in water and added. Skimmed milk powder was made into suspension with water and transferred to the cream. The contents were mixed for 6 min at 125 rpm (speed 2) to obtain a homogenized and creamy texture. Sieved flour was added to the cream and mixed for 2 min at 61 rpm (speed 1). The dough pieces were sheeted to a thickness of 3.5 mm, cut using a circular mould (51 mm diameter) and baked at 205°C for 8-9 min. After baking, biscuits were left to cool at room temperature and were wrapped tightly with polypropylene pouches and kept until further analysis.

The induction of diabetes:

According to **(16)** method, diabetes was induced in normal healthy male albino rats by injecting 150 mg/kg body weight of alloxan intraperitoneally. Fasting blood samples were taken one week after alloxan injections to measure fasting serum glucose 200 mg/dl in diabetes rats, according to **(17)**.

Experimental design:

The study was carried out and approved at Animal House, Department of Nutrition and Food Science, Faculty of Home Economics, Menoufia University, Egypt.

In this experiment, 48 adult male white albino rats, "Sprague Dawley" strain, 10 weeks old, weighing (150±10g), were used. For adaptation, all rats were fed a basal diet (casein diet) prepared according to **(18)** for 7 days. After this adaptation period, rats were divided into 8 groups, six rats per each as follows: group (1): Rats fed on basal diet only as negative control. Group (2): Diabetic rats fed on basal diet only as a positive control group. Group (3): Diabetic rats fed on basal diet and biscuits fortified with pumpkin seeds as powder by 2.5% of diet. Group (4): Diabetic rats fed on basal diet and biscuits fortified with pumpkin seeds as powder by 5% of diet. Group (5): Diabetic rats fed on basal diet and biscuits fortified with sunflower seeds as powder by 2.5% of diet. Group (6): Diabetic rats fed on basal diet and biscuits fortified with sunflower seeds as powder by 5% of diet. Group (7): Diabetic rats fed on basal diet and mixture (1:1) of biscuits fortified with pumpkin and sunflower seeds by 2.5% of diet. Group (8): Diabetic rats fed on basal diet and mixture (1:1) of biscuits fortified with pumpkin and sunflower seeds by 5% of diet. The experiment continued for 28 days, at the end of the experimental period each rat weight separately, then slaughtered and blood samples were collected.

Blood sampling

At the end of the experiment period (28 days), rats were fasted for 12-h then rats were scarified. Blood samples were collected from the portal vein into dry clean centrifuge tubes for serum separation, blood samples centrifuged for 10 minutes at 4000 rpm to separate, the serum according to **(19)**. Serum samples were frozen at -18 ˚C until chemical analysis.

Biochemical analysis

Enzymatic determination of serum glucose and was carried out calorimetrically according to the method of **(20)**. Total cholesterol, Triglycerides (T.G), High Density Lipoprotein (HDL-c), Low Density Lipoprotein (LDL-c), and Very Low Lipoprotein (VLDL-c) were determined according to **(21, 22 and 23)**. Determination of serum alanine aminotransferase (ALT), serum asparatate aminotransferase (AST), serum alkaline phosphatase (ALP) was carried out according to the method of **(24**, **25 and 26)**, respectively. Serum urea and serum creatinine were determined by enzymatic technique according to **(27 and 28)**. In contrast, serum uric acid was measured calorimetrically using the method of **(29)**.

Statistical analysis

The data were analyzed using a completely randomized factorial design **(30)** when a significant main effect was detected; the means were separated with the Student-Newman-

Keuls Test. Differences between treatments of ($P \le 0.05$) were considered significant using Costat Program. Biological results were analyzed by One Way ANOVA.

Results and Discussion

Data tabulated in table (1) show the effect of biscuits fortified with pumpkin, sunflower and metformin, on glucose levels of diabetic rats. The obtained data revealed that the positive control group had a higher glucose level, whereas the negative control group had a lower level, with a significant difference ($P \le 0.05$). The mean values were 273.50 and 102.50 mg/dl, respectively.

Diabetic rats fed on basal diet with 500mg/kg metformin had the lowest glucose levels when compared to the control positive group, with a significant difference ($P \le 0.05$), the average level was 115.50 mg/dl. The highest glucose level in diabetic rats was reported for biscuits + 2.5 % sunflower seeds with a significant difference ($P \le 0.05$) being 155.0 mg/dl. These results corroborated those of (31) who discovered that Metformin treatment led to maintained good glycemic control and improved neuropathy and pancreatic lesions in female fatty rats. The fatty rat is useful for the development of novel anti-diabetic agents that show potential to improve glucose metabolic disorders in the liver.

Also, (32), found that diabetic rats who fed cakes enhanced with both fresh pumpkin and varying amounts of whole pumpkin seeds showed a significant improvement ($P \le 0.05$) in their glucose and insulin levels compared to diabetic rats who fed control cakes, and that this improvement increased with increasing the amount of whole pumpkin seeds in cakes. These results are returned to a result of the higher phenolic and flavonoid content of pumpkin seeds than wheat flour.

Diabetes mellitus is treated with medication, although multiple studies have demonstrated that eating lowers blood glucose levels in diabetic individuals. By reducing blood sugar levels, sunflower seeds, for instance, can be used to treat type 2 diabetes. The bioactive elements of these seeds, like the chlorogenic acid present in sunflower seeds, have been utilized to treat insulin resistance and increase the generation of insulin (2).

Table (1): Effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on glucose level of diabetic rats

Treatments Groups	Glucose (mg/dl)
G1 C (-)	$102.50^{g} \pm 2.50$
G2 C (+)	$273.50^{a} \pm 5.50$
G3 (Biscuits +2.5% Pumpkin seeds)	$144.00^{c} \pm 1.00$
G4 (Biscuits +5% Pumpkin seeds)	$133.50^{d} \pm 1.50$
G5 (Biscuits +2.5% Sunflower seeds)	$155.00^{b} \pm 1.00$
G6(Biscuits +5% Sunflower seeds)	$146.50^{c} \pm 1.50$
G7 (Biscuits +250 mg/kg Metformin)	$126.00^{e} \pm 3.00$
G8 (Biscuits +500 mg/kg Metformin)	$115.50^{f} \pm 2.50$
LSD ($P \le 0.05$)	4.643

Each value represents the mean ± SD of three replicates.
Means in the same column with different letter are significantly different (P<0.05).

The effect of biscuits enriched with pumpkin, sunflower seeds, and metformin on the serum liver functions (ALT, and AST) of diabetic rats is shown by the data presented in table (2). It is clear to notice that there was a significant difference (P≤0.05) between the (ALT) values recorded by the positive and negative control groups. The mean values were 57.50 and 26.00 U/L, respectively.

Serum ALT was highest in the group fed biscuits + 250 mg/kg metformin and lowest in the group fed biscuits + 5% pumpkin seeds, with a significant difference (P≤0.05), which were 48.00 and 28.50 U/L, respectively.

With regard of serum AST, the positive control group had a significantly (P≤0.05) higher value when compared to the negative control group, which were 172.50 and 117.00 U/L, respectively. The group fed biscuits +250 mg/kg metformin had the highest serum AST, whereas the biscuits +5% pumpkin seeds had the lowest, with a significant difference (P≤0.05), which were 136.00 and 108.00 U/L, respectively. These results are in line with (33), which discovered that biscuits supplemented with pumpkin seed powder and oil can be employed as functional foods for the treatment of fatty liver brought on by amitriptyline. Reduced serum AST and ALT activity and lower fat levels are indicators of the protective impact. The bioactive elements and overall antioxidant content of pumpkin seeds may be to blame for this. Therefore, adding pumpkin seed powder and oil to various dietary products is advised for potential resistance against fatty liver.

Additionally, treatment with pumpkin and sunflower seeds improved transaminase activity in alloxan-diabetic rats. This effect may have occurred due to the seeds' high flavonoid and phenolic content, which protects liver cells from harm (34).

Table (2): Effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on liver functions of diabetic rats

Treatments Groups	ALT (U/L)	AST (U/L)
G1 C (-)	$26.00^{d} \pm 1.00$	$117.00^{cde} \pm 6.00$
G2 C (+)	$57.50^{a} \pm 2.50$	$172.50^{a} \pm 2.50$
G3 (Biscuits +2.5% Pumpkin seeds)	$37.00^{c} \pm 1.00$	$126.00^{c} \pm 4.00$
G4 (Biscuits +5% Pumpkin seeds)	$28.50^{d} \pm 4.50$	$108.00^{e} \pm 8.00$
G5 (Biscuits + 2.5% Sunflower seeds)	$44.00^{b} \pm 1.00$	$123.00^{cd} \pm 4.00$
G6(Biscuits +5% Sunflower seeds)	$33.50^{c} \pm 1.50$	$110.50^{e} \pm 5.50$
G7 (Biscuits +250 mg/kg Metformin)	$48.00^{b} \pm 4.00$	$136.00^{b} \pm 4.00$
G8 (Biscuits +500 mg/kg Metformin)	$38.00^{c} \pm 4.00$	$115.50^{de} \pm 2.50$
LSD (P ≤ 0.05)	4.896	9.122

Each value represents the mean ± SD of three replicates.

Means in the same column with different letter are significantly different (P<0.05).

The effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on serum total cholesterol and triglycerides in diabetic rats is shown in table (3). The findings revealed a significant difference (P≤0.05) between the cholesterol levels of the positive control group and the negative control group. The mean values were 139.00 and 88.00 mg/dl, respectively. With a significant difference (P≤0.05), the group given the biscuits +5% pumpkin seeds had the lowest cholesterol levels while the group given the biscuits +250 mg/kg metformin had the highest. The mean values were 97.0 0and 131.00 mg/dl, respectively.

On the other hand, a significant difference (P≤0.05) was found between the triglyceride values of the positive control group and the negative control group. The mean values were 120.00 and 70.50 mg/dl, respectively. The group that consumed biscuits with 5% pumpkin seeds had the lowest triglyceride levels, whereas the group that consumed biscuits with 250 mg/kg of metformin had the highest levels, with a significant difference (P≤0.05). The mean values were 89.00 and 117.0 mg/dl, respectively. These outcomes support the findings of (35) who claimed that consuming pumpkin seeds induced a decrease in TC, TG, and LDL-c values. The presence of unsaturated fatty acids in the seeds contributed to this impact.

Both pumpkin and sunflower seeds have a large amount of phytosterols and phenolic components and are fatty seeds. According to reports, phytosterols have a hypocholesterolemic impact by preventing the absorption of cholesterol (36).

Table (3): Effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on serum total cholesterol and triglycerides in diabetic rats

Treatments Groups	Total Cholesterol (mg/dl)	Triglycerides (mg/dl)
G1 C (-)	$88.00^{g} \pm 6.00$	$70.50^{e} \pm 1.50$
G2 C (+)	$139.00^{a} \pm 3.00$	$120.00^{a} \pm 1.50$
G3 (Biscuits +2.5% Pumpkin seeds)	$110.50^{e} \pm 1.50$	$108.00^{bc} \pm 1.00$
G4 (Biscuits +5% Pumpkin seeds)	$97.00^{f} \pm 1.00$	$89.00^{d} \pm 3.50$
G5 (Biscuits + 2.5% Sunflower seeds)	$125.00^{c} \pm 2.00$	$112.00^{b} \pm 2.00$
G6(Biscuits +5% Sunflower seeds)	$114.50^{de} \pm 2.50$	$106.50^{c} \pm 2.50$
G7 (Biscuits +250 mg/kg Metformin)	$131.00^{b} \pm 2.00$	$117.00^{a} \pm 3.00$
G8 (Biscuits +500 mg/kg Metformin)	$118.50^{d} \pm 3.50$	$105.50^{c} \pm 4.50$
LSD (P ≤ 0.05)	5.711	4.839

Each value represents the mean ± SD of three replicates.
Means in the same column with different letter are significantly different (P<0.05).

Data presented in table (4) show the effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on serum lipid profiles of diabetic rats. The results revealed that the HDL-c of negative control rats group recorded the higher value when compared with positive control group with significant difference (P≤0.05). The mean values were 58.00 and 29.00 mg/dl, respectively. While the highest HDL-c of treated group recorded for group fed on biscuits +5% sunflower seeds but, the lowest value recorded for group fed on biscuits +250 mg/kg metformin with a significant difference (P≤0.05). The mean values were 52.50 and 43.00 mg/dl, respectively.

On the other hand, the LDL-c of positive control rats group recorded the higher value when compared with negative control group with a significant difference (P≤0.05). The mean values were 58.90 and 15.90 mg/dl, respectively. While the highest LDL-c of treated group recorded for group fed on biscuits +250 mg/kg metformin but, the lowest value recorded for group fed on biscuits +5% pumpkin seeds with a significant difference (P≤0.05). The mean values were 64.60 and 28.60 mg/dl, respectively.

As for VLDL-c, the positive control rats group recorded the higher value when compared with negative control group with a significant difference (P≤0.05). The mean values were 24.00 and 14.10 mg/dl, respectively. While the highest VLDL-c of treated group recorded for group fed on biscuits +250 mg/kg metformin but, the lowest value recorded for group fed on biscuits +5% pumpkin seeds with significant difference (P≤0.05). The mean values were 23.40 and 17.80 mg/dl, respectively. These findings are in line with those of (32) who found that pumpkin polysaccharides dramatically decreased TG, TC, and LDL levels as well as increased HDL levels in diabetic mice. These results are also consistent with (37) who found that, as compared to diabetic animals, animals treated with various pumpkin seed extracts showed significantly higher rates of HDL and significantly lower values of TC, TG, LDL, and VLDL.

Additionally, the groups that included pumpkin and sunflower seeds had lower levels of the lipid profile parameters, which is consistent with the findings of (38) who discovered that adding pumpkin and apricot oils to supplement diets reduced triglyceride, total cholesterol, and LDL-cholesterol levels.

Table (4): Effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on lipid profiles of diabetic rats

Treatments Groups	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)
G1 C (-)	$58.00^{a} \pm 3.00$	$15.90^{g} \pm 2.10$	$14.10^{c} \pm 2.10$
G2 C (+)	$29.00^{d} \pm 5.00$	$58.90^{a} \pm 2.90$	$24.00^{a} \pm 1.90$
G3 (Biscuits +2.5% Pumpkin seeds)	$45.00^{c} \pm 1.00$	$43.90^{d} \pm 2.60$	$21.60^{ab} \pm 4.40$
G4 (Biscuits +5% Pumpkin seeds)	$50.50^{b} \pm 0.50$	$28.60^{f} \pm 2.40$	$17.80^{bc} \pm 1.10$
G5 (Biscuits + 2.5% Sunflower seeds)	$49.50^{b} \pm 1.50$	$53.10^{c} \pm 2.10$	$22.40^{a} \pm 2.00$
G6 (Biscuits +5% Sunflower seeds)	$52.50^{b} \pm 2.50$	$40.70^{e} \pm 1.30$	$21.30^{ab} \pm 2.00$
G7 (Biscuits +250 mg/kg Metformin)	$43.00^{c} \pm 2.00$	$64.60^{b} \pm 1.40$	$23.40^{a} \pm 1.80$
G8 (Biscuits +500 mg/kg Metformin)	$46.00^{c} \pm 3.00$	$51.40^{c} \pm 2.60$	$21.10^{ab} \pm 2.80$
LSD (P ≤ 0.05)	3.421	2.837	4.325

HDL-c = High density lipoprotein cholesterol, LDL-c = Low density lipoprotein cholesterol, VLDL -c = Very low-density lipoprotein cholesterol. Each value represents the mean ± SD of three replicates.
Means in the same column with different letter are significantly different (P<0.05).

Data given in table (5) show the effect of white mulberry, fig leaves and their mixtures on kidney functions of diabetic rats. The obtained results indicated that the urea level of positive control rats group recorded the higher value when compared with negative control group with a significant difference (P≤0.05). The mean values were 57.50 and 31.00 mg/dl, respectively. While the highest urea level of treated group recorded for group fed on biscuits +250 mg/kg metformin but, the lowest value recorded for group fed on biscuits +5% sunflower seeds with a significant difference (P≤0.05). The mean values were 51.50 and 39.50 mg/dl, respectively.

On the other hand, the uric acid level of positive control rats group recorded the higher value when compared with negative control group with no significant difference (P≤0.05). The mean values were 7.50 and 4.15 mg/dl, respectively. While the highest uric acid level of treated group recorded for group fed on biscuits +250 mg/kg metformin but, the lowest

value recorded for group fed on biscuits +5% pumpkin seeds with no significant difference ($P \leq 0.05$). The mean values were 6.90 and 6.15 mg/dl, respectively.
When it came to creatinine, the positive control rats had a greater value than the negative control rats, although there was no significant difference ($P \leq 0.05$). The average values were 0.59 and 0.37 mg/dl. While the greatest creatinine level of the treated group was found in the group fed on biscuits +250 mg/kg metformin, the lowest value was found in the group fed on biscuits + 2.5% sunflower seeds, with no significant difference ($P \leq 0.05$), which were 0.51 mg/dl and 0.35 mg/dl, respectively. These findings are consistent with the findings of (39), who discover that they recommended many medicinal plants used already in traditional medicine, experimental and clinical, and nephroprotective effects among them are flax and pumpkin seeds mixture rich in PUFAs and antioxidant compounds in animals.
(40) discovered that rats given a high-fat diet along with pumpkin seed oil had considerably lower renal function results than rats given a high-fat diet alone. As the percentage of whole pumpkin seeds in cakes grew, the decline in urea and creatinine readings also increased. Additionally, (41) pointed out that the effect of sunflower oil on kidney function (serum uric acid and creatinine) demonstrated a significant improvement in kidney function levels when compared to the control group. This reflects the potent therapeutic effect of feeding rats stock seed and sunflower oil for the treatment of hyperlipidemia in rats.

Table (5): Effect of biscuits fortified with pumpkin, sunflower seeds, and metformin on kidney functions of diabetic rats

Treatments / Groups	Urea (mg/dl)	Uric Acid (mg/dl)	Creatinine (mg/dl)
G1 C (-)	$31.00^{f} \pm 3.00$	$4.15^{c} \pm 0.55$	$0.37^{cd} \pm 0.03$
G2 C (+)	$57.50^{a} \pm 2.50$	$7.30^{a} \pm 0.10$	$0.59^{a} \pm 0.05$
G3 (Biscuits +2.5% Pumpkin seeds)	$47.50^{bc} \pm 4.50$	$6.55^{bc} \pm 1.15$	$0.40^{cd} \pm 0.00$
G4 (Biscuits +5% Pumpkin seeds)	$41.00^{de} \pm 1.00$	$6.15^{c} \pm 0.15$	$0.40^{cd} \pm 0.10$
G5 (Biscuits + 2.5% Sunflower seeds)	$41.50^{de} \pm 3.50$	$6.85^{abc} \pm 0.85$	$0.35^{d} \pm 0.05$
G6 (Biscuits +5% Sunflower seeds)	$39.50^{e} \pm 1.50$	$6.30^{bc} \pm 0.3$	$0.50^{ab} \pm 0.00$
G7 (Biscuits +250 mg/kg Metformin)	$51.50^{b} \pm 1.50$	$6.90^{ab} \pm 0.3$	$0.51^{ab} \pm 0.00$
G8 (Biscuits +500 mg/kg Metformin)	$46.00^{cd} \pm 4.00$	$6.40^{bc} \pm 0.10$	$0.45^{bc} \pm 0.05$
LSD ($P \leq 0.05$)	5.220	0.722	0.085

Each value represents the mean ± SD of three replicates.
Means in the same column with different letter are significantly different (P<0.05).

Conclusion

In comparison to the positive group, rats who consumed biscuits fortified with pumpkin, sunflower seeds and metformin had significantly improved hyperglycemia, HDL-c, liver, and kidney function. The best addition to our snack diet for lowering blood sugar levels is biscuits fortified with pumpkin and sunflower seeds.

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تأثير البسكويت المدعم ببذور القرع العسلى وعباد الشمس على الفئران المصابة بالسكر المستحث بالألوكسان

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الملخص العربي:
استخدمت البذور الصالحة للأكل لتقليل أعراض مرض السكر لاحتوائها على مضادات الأكسدة الطبيعية التي يمكن أن تحمي وظيفة الخلايا التي يسببها مرض السكر. تهدف هذه الدراسة إلى معرفة تأثير البسكويت المدعم ببذور القرع العسلى وعباد الشمس وكذلك الميتفورمين على الفئران المصابة بمرض السكر. تم استخدام ٤٨ فأرفي هذه الدراسة وتقسيم الفئران إلى ثماني مجموعات كل مجموعة ستة ذكور فئران بالغة ، وزن كل منها (١٥٠±١٠ جم). تمت إضافة البسكويت المدعم ببذور القرع العسلى وعباد الشمس وكذلك الميتفورمين إلى النظام الغذائي الرئيسي. بمعدل ٢,٥٪ ، ٥٪ لمدة ٢٨ يومًا ، 250 ، ٥٠٠مجم / كجم على التوالي. تم حقن الألوكسان بجرعة (١٥٠ مجم / كجم من وزن الجسم) تحت الجلد في الفئران المصابة بمرض السكر. في نهاية التجربة ، تم قياس مستويات الجلوكوز في سيرم الدم ، صورة دهون الدم مثل الدهون الثلاثية (TG) ، والكوليسترول الكلي (TC) ، والبروتين الدهني منخفض الكثافة (LDL-c) ، والبروتين الدهني منخفض الكثافة جدا (VLDL-c) ، والبروتين الدهني مرتفع الكثافة (HDL-c) ونشاط إنزيمات الكبد ALT & AST ووظائف الكلى مثل مستويات الكرياتينين وحمض البوليك واليوريا. أشارت النتائج إلى أن استهلاك البسكويت المدعم ببذور القرع العسلى وعباد الشمس وكذلك الميتفورمين أدى إلى تحسن معنوي (P≤0.05) من مستوى الجلوكوز في دم الفئران وزيادة مستوى HDL-c بشكل ملحوظ وتحسين وظائف الكبد والكلى عن طريق خفض ALT، AST ، الكرياتينين ، حمض البوليك ، واليوريا في الفئران مقارنة بالمجموعة الضابطة الموجبة. في الختام ، يفضل اضافة البسكويت المدعم ببذور القرع العسلى وبذور عباد الشمس إلى نظامنا الغذائي للوجبات الخفيفة لخفض مستوى الجلوكوز في الدم.

الكلمات المفتاحية: بذور النباتات، الفئران، السكر ، ميتفورمين، التحاليل الكيميائية الحيوية .