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Antidiabetic activity of lycopene extracted from tomato manufacturing waste in streptozotocin (STZ)-induced diabetic rats

Haneen, H. Mouminah
hmouminah@kau.edu.sa
Food and Nutrition Department, College of Human Science and Design, King Abdulaziz University, Kingdom, Saudi Arabia.

ABSTRACT

The aim of this study is to evaluate the anti-diabetic activity of lycopene extracted from tomato manufacturing waste streptozotocin -induced diabetes in male rats. Thirty five (35) male albino rats (twenty eight diabetic and seven normal control rats) were used. The rats were divided randomized into five groups of seven rats each: G I: Normal control rats that fed only normal basal diet and water. G 2: diabetic control rats that fed only normal basal diet and water. G 3: Diabetic rats were fed on basal diet and treated with 10 mg lycopene /kg body weight. G 4: Diabetic rats were fed on basal diet and treated with 20 mg lycopene /kg body weight. G 5: Diabetic rats were fed on basal diet and treated with 30 mg lycopene /kg body weight. (G3), (G4) and (G5) were treated with lycopene orally once per day for 4 weeks. Diabetes was induced by a single intraperitoneal injection of streptozotocin 60 mg/kg body weight and it was confirmed by the elevated blood glucose ≥ 200 mg/dl after three days. Based on the obtained results, the diabetic control rats (G2) showed high blood glucose level, cholesterol, triglyceride, low-density lipoprotein (LDL-C),very low-density lipoprotein(VLDL-c) , malondialdehyde (MDA) , as well as urea, creatinine and uric acid. On the other hand, the levels of insulin production, high-density lipoprotein cholesterol (HDL-c) and antioxidant enzymes were significantly decreased in the diabetic control rats (G2) compared with the normal control rats (G1). treatment of graded doses of lycopene to diabetic rats had significantly ($P<0.05$) reduced blood glucose level, cholesterol, triglyceride, low-density lipoprotein (LDL-c), very low-density lipoprotein(VLDL-c), malondialdehyde (MDA), as well as urea, creatinine and uric acid. In addition, the levels of insulin production, high- density lipoprotein cholesterol (HDL-c) and antioxidant enzymes, such as catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST), and Glutathione-L-reduced (GSH) were significantly increased in the treated diabetic rats with lycopene extracted from tomato manufacturing waste at dose 20 mg/kg (G4) and 30 mg/kg (G5) respectively compared with the diabetic rats (G2).

Keywords: antidiabetic activity, lycopene, hypoglycaemia, insulin, renal function, antioxidant enzymes

INTRODUCTION

Diabetes mellitus is a common metabolite disorder in both developing and developed countries [1]. In this regard, the body ability to produce insulin decreased or insulin resistance occurs in the body [2] ,the main clinical complications of the diabetes mellitus are impaired cutaneous wound healing, decreased fibrinolysis activity, severe chronic atherosclerosis, dyslipidemia, hypertension, disturbance of hematological parameters including erythrocyte aggregation, erythrocyte deformability hematocrit and plasma proteins, renal failure and retinal failure [3],

[4] . Streptozotocin, which is used to trigger diabetes, is a highly toxic agent to pancreas cells especially α and β cells [5]. The waste from tomato processing consists of peel, seeds, and vascular tissue [6]. It has been reported that from tomatoes manufacture wastes makes up to 40% of the total processed tomatoes [7] .The increase of waste quantities from tomato processing industry is an important ecological and financial problem. Tomatoes processing wastes an excellent source of many nutrients and secondary metabolites that are important for human health; lycopene, β-carotene, flavonoids, chlorophyll, organic acids, phenolics, minerals, and vitamins C, E, [8]. Tomato processing pomace is considered a promising source of bioactive compounds and potential natural source of antioxidants [9] Tomato manufacture waste is a wealthy source of lycopene [10]. Bearing in mind that more than a third of tomatoes delivered to processing plants end up as processing wastes, mainly constituted by seeds and peels, the recovery of this carotenoid could represent an alternative to the by-product valorization of the tomato manufacture [11].Lycopene is a member of the carotenoid family of phytochemicals that gives plants its characteristics red color and an important fat-soluble food component with health benefits. Lycopene is a bioactive red colored pigment naturally found in tomatoes and other red fruits such as watermelon, guava and pink grapefruit [12] The interest in lycopene is increasing because its preventive properties toward numerous diseases. Studies have shown that foods rich in lycopene protect against diseases such as cancer, cardiovascular diseases, diabetes, and others [13]; [14]. The high degree of conjugation of the double bonds in the molecule of lycopene makes one of the most powerful antioxidants, with a singlet oxygen-quenching capacity twice that of β-carotene and 10 times higher than that of α-tocopherol. [15]. [16] demonstrated that lycopene extract have a good antioxidant effects against several oxidants. The aim of this study was to evaluate the antidiabetic activity of lycopene extracted from tomato manufacture waste against streptozotocin (STZ)-induced diabetic rats

MATERIAL AND METHODS

Streptozotocin was obtained from Sigma-Aldrich Company (St. Louis, MO, USA). All kits for biochemical analysis used in this study were purchased from Cayman Chemicals and Bio Vision Incorporated, USA. Methanol, ethyl acetate and hexane were obtained from Fisher Scientific Ltd. (Loughborough, UK). All used chemicals and solvents were analytical grade.

Fresh tomato, tomato peels and tomato manufacture waste (peels and seeds approximately ratio were obtained from Gulf factory for concentrates and tomato paste, the second industrial city, Riyadh, Saudi Arabia.

Tomato manufacture waste was dried in a cabinet dryer at 50^{o}C (approximate 10% moisture content) to avoid loss of lycopene during drying, The dried tomato manufacture waste was ground and passed through 0.15mm sieves stored in air tight bags until further use.

Extraction and Purification of Lycopene

The lycopene was extracted and purified according the modified methods described by [17], [18]. The dried tomato manufacture waste were extracted with mixture of acetone, ethanol and hexane in the ratio of 1:1:2 (dried tomato waste: Solvent was 1:7) for 30 min with continuous shaking. After this deionized water was added and allowed to stand for 5min for phase separation.

The upper solvent layer was collected and concentrated using a rotary vacuum evaporator. This concentrated lycopene extract was dissolved in a mixture of both ethanol and dichloromethane in a ratio of (4:1) at 50-60°C and cooled gradually in an ice bath. This was then refrigerated overnight for crystallization. The crystals were filtered through filter paper (Whatman No.1), washed with cold ethanol and dried in freeze dryer using (LABCONCO, USA) at -50°C and 0.014 mbar for 2 days . The crystallization process was repeated to obtain crystals of higher purity levels

Experiment design

Thirty-five (35) male albino rats weighing 170-190 g (two months age) were obtained from King Fahd Center for Medical Research, King Abdulaziz University, Jeddah, Saudi Arabia. All rats' experiments were performed under protocols approved by the Institutional Animal House of King Abdulaziz University, Jeddah, Saudi Arabia.

Rats were housed in standard laboratory conditions at (25 ± 3 ^{o} C), relative humidity (50-55%) and a 12-hour light / dark cycle two weeks prior to the start of the experiment. All rats were fed standard basal diet, drinking water and libitum.

Induction of experimental diabetic rats

Diabetes rats was induced by single intraperitoneal injection of 60 mg/kg body weight dose of streptozotocin dissolved in freshly prepared 0.1 M cold citrate buffer of pH 4.5 into rats deprived of feeds 18 h but with access to water. Three days after streptozotocin administration, blood was taken from the tail artery of the rats. Animals having blood glucose levels ≥ 200 mg/dl were considered diabetic and included in the study. Thereafter, diabetic rats were randomly assigned into different groups according to the design of the study described by [19]

Thirty five (35) male albino rats (twenty eight diabetic and seven normal control rats) were used. The rats were divided randomized into five groups of seven rats each: G I: Normal control rats that fed only normal basal diet and water. G 2: diabetic control rats that fed only normal basal diet and water. G 3: Diabetic rats were fed on basal diet and treated with 10 mg lycopene /kg body weight. G 4: Diabetic rats were fed on basal diet and treated with 20 mg lycopene /kg body weight. G 5: Diabetic rats were fed on basal diet and treated with 30 mg lycopene /kg body weight. (G3), (G4) and (G5) were treated with lycopene orally once per day for 4 weeks.

Blood sample collection or Sample preparation for biochemical analysis

After the last day of treatment (28th day) , the animals were anaesthetized with ethyl ether and sacrificed by simple incision of the jugular vein, the blood samples were collected into clean, dry, sample bottles for serum analyses. Blood samples were left undisturbed to clot at room temperature for 30 minutes and then centrifuged at 4000 rpm for a period of 15 minutes. After centrifugation, the serum samples were aspirated using a Pasteur's pipette. The serum samples were stored in a freezer at - 5oC until further analysis

Analytical Chemical and biochemical

Total lycopene content of samples was determined spectrophotometrically using the method of [20].

Fasting blood glucose level was determined by collection of blood sample from the tail artery of the rats at interval of 0 week, 1st week, 2nd week, 3rd week and 4th week of the treatment period respectively. The rats were not fed for 16 h before collecting their blood samples. Serum glucose after fasting was measured by glucose-oxidase principle as described by [21], using digital glucometer (Accuchek Advantage) and was expressed as mg dL Determination of insulin by enzyme linked immunosorbent assay ELISA method as described by **[22].**

Determination of serum cholesterol according to the method described by [23]. Serum triglycerides (TG) were estimated by Enzymatic colorimetric GPO-PAP kit according to the method described by [24]. High- Density Lipoprotein Cholesterol (HDL-c) was estimated calorimetrically according to the method described by [25]. Low -Density Lipoprotein Cholesterol (LDL-c) and Very Low - Density Lipoprotein Cholesterol (VLDL-c), were calorimetrically determined according to the method described by [26].

Determination of Renal Functions

Renal function parameters; uric acid, urea and creatinine, were estimated calorimetrically as methods described by [27], [28], and **[29]**, respectively.

The malondialdehyde (MDA) was determined calorimetrically following the method of [30]. Enzymatic antioxidants parameters including glutathione reductase (GR), Glutathione-S-transferase (GST), Glutathione peroxidase (GPx), and catalase (CAT) activities were determined calorimetrically in serum according to [31], [32], [33], and [34] respectively

Statistical analysis:

Statistical analysis was done by using the Statistical Package for (SPSS) for the Social Sciences for Windows, version 22 (SPSS Inc., Chicago, IL, USA). Collected data was presented as mean± standard error (SE). Analysis of Variance test (ANOVA) was used for determining the significances among different groups according to [35]. The values of $p < 0.05$ were considered as significant.

RESULTS AND DISCUSSION

Lycopene content in various raw materials is presented in Table (1). The results showed that, the tomato peel had the highest lycopene content 48.75 mg/100g followed by tomato manufacturing waste 43.92mg/100g and fresh tomatoes 7.33 mg/100g on wet basis. These data are consistent with the results of studies conducted by other scientists [36], [37] and [38], who found that the lycopene content of fresh tomatoes ranged from 0.88 to 7.74 mg/100 g of product. These findings are confirmed with [11] who found that tomato peels contain high amounts of lycopene compared to tomato manufacturing waste. While, the tomato manufacturing waste includes seeds and peels, which may lead to a decrease in lycopene content in tomato processing waste [17].

Table (1). Lycopene content in various raw materials

Raw Materials	Lycopene content (mg/100g)
Fresh tomato	7.33 ± 0.66^{c}
Tomato manufacturing waste	32.92 ± 1.12^{a}
Tomato peels	48.75 ± 1.05^{b}

Values with different letters in the same column are significantly different at P<.0.05.

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Effect on fasting Blood Glucose Levels

The effect lycopene extracted from tomato manufacturing waste on fasting blood glucose levels of streptozotocin - induced diabetic rats during 4-weeks shown is as in (Fig 1). Results indicated that, the diabetic control rats(G2) had a significantly($P < 0.05$) increased in fasting serum glucose level after three days of streptozotocin injection by 252.63 % when compared with normal control rats (G 1). treatment of diabetic rats with lycopene extracted from tomato manufacturing waste at dose 10, 20 and 30 mg/kg of body weight showed a had significantly ($P<0.05$) decreased in serum glucose level by 65.52, 73.56 and 77.01 % for (G 3), (G 4) and (G 5) respectively compared with diabetic control rats at the end of the experiment (after 4 weeks from study). These results are coincide with [39] they mentioned that, the ability of lycopene to reduce blood glucose levels in diabetic rats may be due to its ability to protect vital biomolecules including lipids, protein, and beta-cell DNA from free radicals or as a result of its antioxidant activity through scavenging of free radicals released from glucose autoxidation resulting from sustained hyperglycemia. Results also indicated that, the lycopene extracted from tomato manufacturing waste showed a significantly effect on fasting blood glucose level and significantly decreased during the experimental period, compared to the diabetic control. The increased of the lycopene (extracted from tomato manufacturing waste) doses from 10 mg to 30 mg /kg of body weight per day was a significantly increased its hypoglycemic effect from 3rd week until the end of the experiment. The same trend was obtained by [40], [41] and [42].

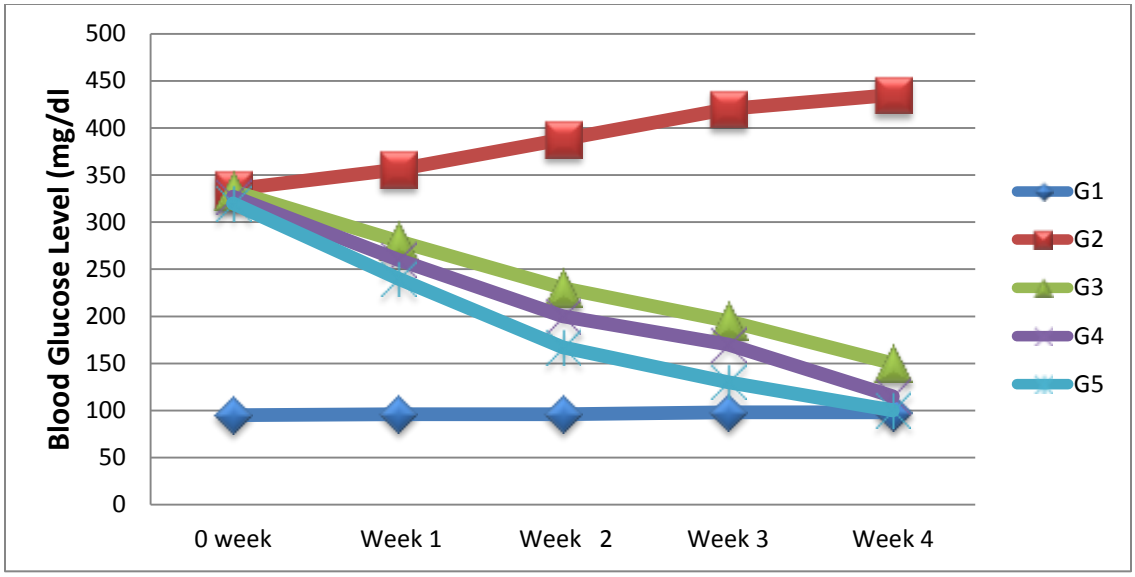

Fig (1) Effect of lycopene extracted from tomato manufacturing waste on fasting blood glucose level in streptozotocin - induced diabetic rats.

Effects of lycopene extracted from tomato manufacturing waste on insulin in diabetic rats are shown in Fig (2). Results of biochemical analyses revealed that, the diabetic control rats (G2) showed a significantly decreased by 66.60% for insulin compared with normal control rats (G 1). Results of present work indicate that, at the end of the experiment (after 4 weeks from study), the treatment of diabetic rats with lycopene extracted from tomato manufacturing waste at the dose 10, 20 and 30 mg/kg of body weight showed had significantly increased in serum insulin by

44.21, 91.58 and 178.53 % for (G 3), (G 4) and (G 5) respectively when compared with diabetic control rats (G 2). The results shown herein are consistent with [41],[42] and [43] who revealed that, the hypoglycemic effect of lycopene has been attributed to a number of processes, including increased insulin production, increased beta cell repair and proliferation, enhanced effects of insulin and adrenaline, and increased antioxidant capacities

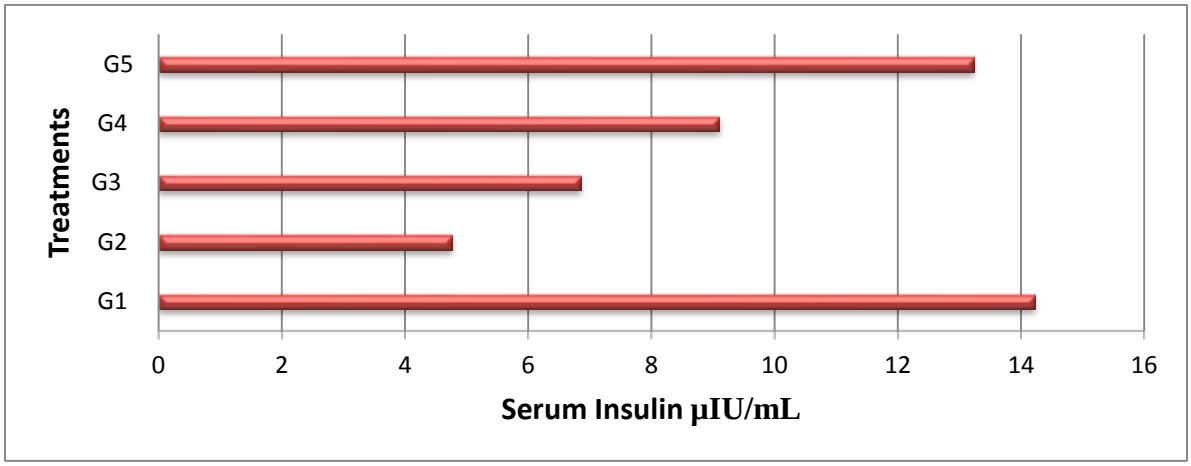

Fig (2) Effect of lycopene extracted from tomato manufacturing waste on insulin in streptozotocin - induced diabetic rats.

Effects of lycopene extracted from tomato manufacturing waste on serum lipid profile in streptozotocin-induced diabetic rats are shown in table (2). Results of present work indicate that, the diabetic control rats (G2) showed significantly ($P<0.05$) increased levels of total cholesterol (TC), triglyceride (TG), low-density lipoprotein cholesterol (LDL-c), low-density lipoprotein cholesterol (VLDL-c) and significantly ($P<0.05$) decreased in high-density lipoprotein cholesterol (HDL-c) when compared with normal control rats (G1). Diabetic rats treated with lycopene extracted from tomato manufacturing waste showed a significant ($P<0.05$) decreased in the levels of TC, TG, LDL-c, VLDL-c and significantly ($P<0.05$) increased in high-density lipoprotein cholesterol (HDL-c) when compared with diabetic control rats (G2). These results confirmed with [44], they reported that, lycopene mainly prevents endothelial damage, inhibits cholesterol synthesis by inhibiting 3-hydroxy-3-methylglutarylA reductase, inhibits low-density lipoprotein cholesterol (LDL) oxidation, restores HDL functions, lowering level of triglyceride (TG), and low density lipoprotein cholesterol. It is evident from these results that, diabetic rats was treated with lycopene extracted from tomato manufacturing waste at dose 20 mg/kg of body weight per day (G4) showed a significant ($P<0.05$) decrease in the levels of TC, TG, LDL-c ,VLDL-c by 28.73, 42.96, 62.67 and 42.96% respectively when compared with diabetic control rats (G2). In addition, the diabetic rats were treated with lycopene extracted from tomato manufacturing waste at doses 10, 20 and 30 mg/kg of body weight per day (G3), (G4) and (G5) showed a significantly ($P<0.05$) increased in the levels of HDL-c by 20.23, 40.45 and 52.59% respectively when compared with diabetic control rats (G2). These obtained results also confirmed with [45], who found that lycopene reduces cholesterol levels, triglycerides (TG) and

low- density lipoprotein cholesterol (LDL.c) and increases high- density lipoprotein cholesterol (HDL.c) in diabetic rats. These findings also are concomitant with [46], who found that, lycopene possesses lipid-lowering effects that prevent oxidation for total cholesterol (TC), triglyceride (TG) and low- density lipoprotein cholesterol (LDL.c) and increased the formation of high- density lipoprotein cholesterol (HDL.c).

Table (2). Effect of lycopene extracted from tomato manufacturing waste on Total cholesterol (TC), Triglycerides (TG), high- density lipoprotein cholesterol (HDLc), low-density lipoprotein cholesterol (LDLc) and very low density lipoprotein cholesterol (VLDLc) in streptozotocin-induced diabetic

Treatments	Cholesterol (mg/dL)	Triglyceride (mg/dL)	HDL.c (mg/dL)	LDL.c (mg/dL)	VLDL.c (mg/dL)
G1	75.38 ± 6.44^{e}	128.85 ± 2.96^{c}	68.46 ± 2.65^{a}	18.85 ± 0.83^{d}	11.93 ± 0.62^{e}
G2	155.22 ± 9.53^{a}	230.45 ± 7.44^{a}	42.27 ± 1.32^{e}	66.86 ± 5.93^{a}	46.09 ± 1.84^{a}
G3	120.45 ± 7.42^{b}	140.22 ± 6.38^{b}	50.82 ± 1.75^{b}	41.59 ± 0.90^{b}	28.04 ± 1.42^{b}
G4	110.62 ± 6.48^{c}	131.46 ± 5.22^{c}	59.37 ± 2.38^{c}	24.96 ± 1.63^{c}	26.29 ± 1.30^{c}
G5	105.93 ± 5.33^{d}	110.32 ± 4.10^{d}	64.50 ± 3.65^{d}	19.37 ± 1.87^{d}	22.06 ± 0.88^{d}

Values with different letters in the same column are significantly different at P<.0.05.

Renal functions of Streptozotocin - induced diabetic rats treated with lycopene extracted from tomato manufacturing waste are shown in Table (3). Results obtained data indicated that, the diabetic control rats (G 2) showed high significant ($p<0.05$) increased in renal function when compared with normal control rats (G 1) by 105.45, 142.35 and 45.95% for urea, creatinine and uric acid respectively. Treatment of diabetic rats with lycopene extracted from tomato manufacturing waste at dose 10 mg/kg of body weight per day had significantly ($P<0.05$) decreased by 29.64, 17.29, and 19.13% % for urea, creatinine and uric acid respectively when compared with diabetic control rats (.G2). In addition the treatment of diabetic rats with lycopene extracted from tomato manufacturing waste at dose 30 mg/kg of body weight per day showed high significantly ($P<0.05$) decreased by 44.41, 47.05, and 57.67% for Urea, Creatinine and Uric acid respectively when compared with diabetic control rats (G2). It is evident from these results that, lycopene extracted from tomato manufacturing waste restored renal functions of diabetic rats by treated with different dose of lycopene when compared with diabetic control rats. The lycopene extracted from tomato manufacturing waste caused amelioration on Urea, Creatinine and Uric acid. These findings are confirmed with [47] and [48], who revealed that lycopene prevents diabetes-induced renal impairment by increasing antioxidant defense and improving renal function in diabetic rats. Moreover, lycopene significantly lowered creatinine in diabetic rats preventing the formation of diabetic nephropathy as well as improving kidney function in diabetic rats.

Table (3). Effect of lycopene extracted from tomato manufacturing waste on renal functions (Urea, Creatinine and Uric acid) in streptozotocin-induced diabetic rats.

Treatments	Urea (mg/dL)	Creatinine (mg/dL)	Uric acid (mg/dL)
G1	4.22 ± 0.06^{d}	1.23 ± 0.02^{d}	4.25 ± 0.09^{d}

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G2	8.67 ± 0.09^{a}	2.55 ± 0.07^{a}	10.30 ± 0.30^{a}
G3	6.10 ± 0.13^{b}	2.11 ± 0.09^{b}	8.33 ± 0.21^{b}
G4	5.29 ± 0.11^{c}	1.72 ± 0.05^{c}	6.82 ± 0.13^{c}
G5	4.82 ± 1.17^{d}	1.35 ± 0.03^{d}	4.36 ± 0.11^{d}

Values with different letters in the same column are significantly different at P<.0.05.

Serum malondialdehyde of streptozotocin - induced diabetic rats treated with lycopene (extracted from tomato manufacturing waste) are shown in Fig (3). Results of present work indicated that, at the end of the experiment (after 4 weeks from study), the diabetic control rats (G 2) showed high significantly increased by 145.60% in serum malondialdehyde (MDA) levels when compared with normal control rats (G 1). Results, also indicated that, treatment of graded doses of lycopene extracted from tomato manufacturing waste to diabetic rats had significantly ($p<0.05$) decreased in levels of malondialdehyde (MDA) concentration. Treatment of diabetic rats with lycopene extracted from tomato manufacturing waste at 10, 20 and 30 mg/kg of body weight had a significantly decreased in serum malondialdehyde (MDA) levels by 20.52, 38.44 and 57.44 % for (G 3), (G 4) and (G 5) respectively when compared with diabetic control rats (G 2). The same trend was obtained by [49] who found that, lycopene treatment at all doses in diabetic rats had significantly ($P<0.05$) decreased malondialdehyde (MDA) levels in the blood. The largest reduction of malondialdehyde (MDA) levels was observed in diabetic rats treated with 40 mg/kg body weight of lycopene. [50], who revealed that, treatment of diabetic rats with lycopene given once daily for three months attenuated oxidative stress by significantly lowering the serum malondialdehyde (MDA) level.

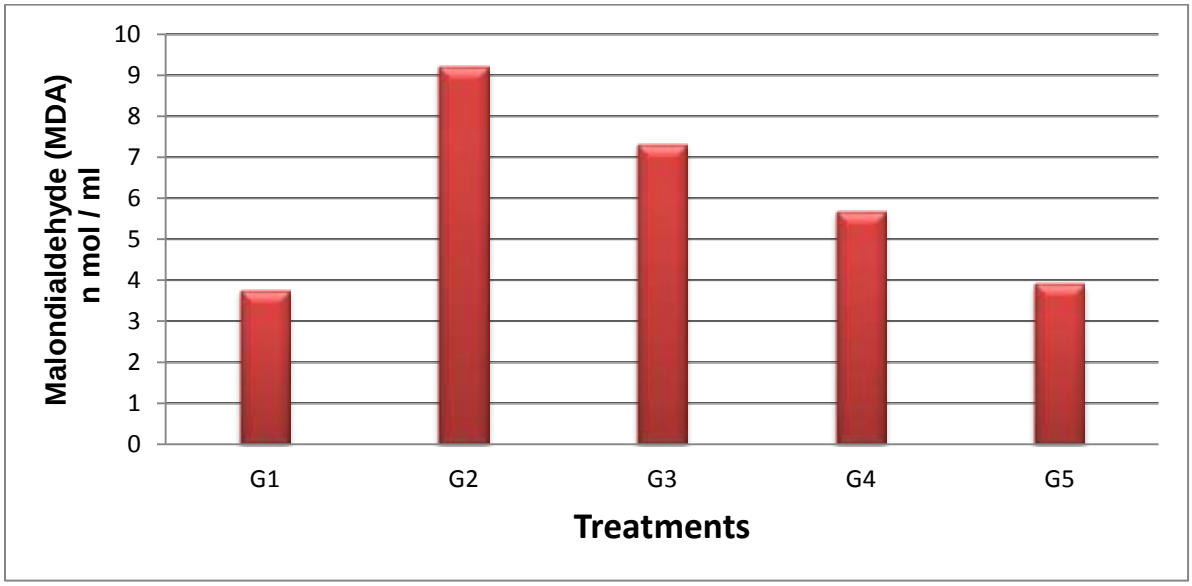

Fig (3). Effects of lycopene extracted from tomato manufacturing waste on serum malondialdehyde (MDA) concentration in streptozotocin-induced diabetic rats.

Effect of lycopene extracted from tomato manufacturing waste on antioxidant enzymes in streptozotocin-induced diabetic rats shown is as in Table (4). Results of present work indicate

that, the diabetic control rats (G 2) showed significantly decreased by 27.36, 71.91, 62.30, 68.90 and 68.03% for catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST), and Glutathione-L-reduced (GSH) respectively when compared with normal control rats (G 1). The results of this study showed that, Diabetic rats was treated with lycopene extracted from tomato manufacturing waste showed that were significant increased on antioxidant enzymes activities; catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST), and Glutathione-L-reduced (GSH) when compared with diabetic control rats (G2). The same trend was obtained by [43], who reported that lycopene extracted from tomatoes significantly increased antioxidant enzyme activities such as catalase, superoxide dismutase and glutathione peroxidase in streptozotocin-induced diabetic rats. Results, also indicated that, the diabetic rats treated with lycopene (extracted from tomato manufacturing) at dose 30, 20 and 10 mg/kg had a significantly increased in antioxidant enzymes by (32.45% 25.44 and 12.60%) for catalase enzyme (CAT), (221.76% 154.92 and 100.0%),for glutathione reductase (GR) and (65.22% ,141.30 and 177.17%),for glutathione peroxidase (GPx) for group G5, G4 and G3 respectively, when compared with diabetic rats G2. On the other hand, the diabetic rats treated with lycopene at dose 10, 20 and 30mg/kg had a significantly increased by(105.56% 153.47 and 200.59%)for glutathione-S-transferase (GST) and (98.72% 198.72 and 262.92%),for glutathione-L-reduced (GSH)) in for group G3, G4 and G5 when compared with diabetic control rats G2 respectively These findings could be due to the significant medicinal benefits of tomato lycopene as an antioxidant which is a powerful antioxidant that effectively scavenges free radicals and increased of antioxidant enzymes activities [51].

Table (4).Effect of lycopene extracted from tomato manufacturing waste on antioxidant enzymes catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST), and Glutathione-L-reduced (GSH) in streptozotocin-induced diabetic rats

Treatments	(CAT) U/L)	(GR) µmol/mg protein/min	(GPx) µmol/mg protein/min	(GST) µmol/mg protein/min	(GSH) µmol/mg protein/min
G1	110.64±0.53^{a}	6.87 ± 0.20^{a}	2.44 ± 0.16^{a}	4.63 ± 0.15^{a}	4.88 ± 0.24^{a}
G2	80.37± 0.73^{d}	1.93 ± 0.28^{e}	0.92 ± 0.09^{d}	1.44 ± 0.20^{e}	1.56 ± 0.20^{e}
G3	90.25± 0.43^{c}	3.87 ± 0.17^{d}	1.52 ± 0.06^{c}	2.96 ± 0.09^{d}	3.10 ± 0.09^{d}
G4	100.82±0.53^{b}	4.92 ± 0.12^{c}	2.22 ± 0.07^{b}	3.65 ± 0.20^{c}	4.66 ± 0.12^{c}
G5	106.45±0.63^{b}	6.21 ± 0.26^{b}	2.55 ± 0.12^{b}	4.33 ± 0.25^{b}	5.10 ± 0.25^{b}

Values with different letters in the same column are significantly different at P<.0.05.

CONCLUSION

Treatment with graded doses of lycopene had significantly reduced blood glucose level, cholesterol, triglyceride, low-density lipoprotein (LDL-c), very low-density lipoprotein (VLDL-c), malondialdehyde (MDA), as well as urea, creatinine and uric acid in streptozotocin induced

diabetic rats. It also increased the levels of insulin production, high- density lipoprotein cholesterol (HDL-c) and antioxidant enzymes, such as catalase (CAT), glutathione reductase (GR), glutathione peroxidase (GPx), glutathione-S-transferase (GST), and Glutathione-L-reduced (GSH)

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