



# Radical Scavenging and Antioxidant Effects of Garlic Oil and Vitamin E in Streptozotocin-Induced Diabetic Rats

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## ABSTRACT

The antioxidant, antidiabetic, radical scavenging activity of garlic oil, Vit E, and their combination were investigated in male albino Wistar rats. Forty rats were divided into five groups (n=8). One group was considered as the negative control (G1), and the rest were injected with streptozotocin for inducing diabetes and divided into 4 groups as follows. group (G2): as the positive control, (G3): treated with garlic oil, (G4): treated with Vit E, and (G5): treated with a mixture of both garlic oil and Vit E. The streptozotocin positive control group (G2) showed decreased antioxidants, high-density lipoprotein, blood glucose, lipid peroxidation, cholesterol, and triglycerides, as well as decreased lipoprotein-cholesterol densities. The treatment of diabetes in G3, G4, and G5 by garlic oil, Vit E, and their mixture, respectively enhanced the antioxidant and decreased the blood glucose, lipid profile, and lipid peroxidation. In G5, the garlic oil and Vit E combination showed better protection against streptozotocin-induced diabetes than either garlic oil or Vit E, separately.

**Key Words:** Garlic oil, Vit E, Antioxidants, Streptozotocin, Diabetes

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## INTRODUCTION

Diabetes mellitus (DM) is an epidemic worldwide as a metabolic disease where hyperglycemia is resulted through the defection in insulin secretion or action [1, 2]. It is initially characterized by a loss of glucose homeostasis and in the disorders of carbohydrates, proteins, lipids, and essential elements' metabolisms, leading to endothelial destructions and several micro- and macro-vascular complications [3]. About half a billion people worldwide have diabetes and reducing death could be doubled during periods 2005 to 2030 [4].

In addition, common chronic diseases as diabetes are an outcome of oxidative stress and oxidative damages to tissues [5, 6]. Moreover, chronic diabetics are reported to have elevated indices of oxidative stress [7], which is accompanied by the decrease of antioxidant effects which increase deleterious effects of free radicals [8]. Antioxidants protect the body against damage through ROS and their roles and the organisms can utilize

enzymatic and non-enzymatic endogenous antioxidant defense system [9].

Based on its toxic effect on pancreatic  $\beta$ -cells, streptozotocin is commonly used for inducing diabetes mellitus [6, 10]. Diabetes mellitus induced with Streptozotocin generates reactive oxygen species leading to oxidative damage. This causes the activity of the antioxidant defense system to deplete, which promotes the generation of de novo free radicals [5, 6, 11].

Nowadays, antidiabetic drugs such as biguanide and sulfonylurea are more available for reducing hyperglycemia in diabetes mellitus, but unfortunately, available drugs have many side effects on diabetic cases [12]. Therefore, several patients in many cases use a combination of herbal remedies and oral hypoglycemic agents [4]. Also, nutrition with therapeutic effects may be useful and improve lifestyle depending on reducing disease infections [5, 13]. Recently, new natural therapies and alternative medicines have stimulated a new method

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for ethnopharmacology, and several medicinal herbs are used as treatments for diabetes [5, 14].

Garlic (*Allium sativum* L.) is widely used as a condiment and spice and as noted in previous investigations [15], it has several health-promoting effects including antidiabetic, hyperinsulinemia, hypocholesterolemia, hypotriglyceridemia, anti-glycation, anti-lipid peroxidation, anti-oxidant level, and stimulating catalase activity potentials [16, 17].

Naturally occurring Vit E exists in 8 forms. The most biological activity is related to  $\alpha$ -tocopherol that is considered as the main antioxidant agent and is a powerful chain-breaking for restraining peroxy radicals [18, 19]. It was found that Vit E terminates the chain reactions of lipid peroxidation in lipoproteins and membranes. Investigating Vit E protective in many biological studied models of the injury became very interested in recent investigations [19, 20].

Our investigation aimed to determine the probable changing of oxidant/antioxidant status in diabetic rats and illustrated the radical scavenging characteristics of garlic oil and Vit E.

## MATERIALS AND METHODS

### *Herbal materials*

Garlic oil is purchased from native herbal shops in Jeddah, Saudi Arabia.

### *Animals and experimental design*

Experimental work of this research was performed under approved protocol from The Bioethics Committee of King Abdulaziz University at King Fahad Medical Research Center, Jeddah, KSA for six weeks. The experimental animals fed a standard diet before starting our investigation for excluding undercurrent infections. Animals were randomly divided into 5 groups, every one contained 8 rats as G1 (negative control), which fed basal diet and intravenously injected by 0.05mol/l citrate buffer merely. The remained 32 rats were received fresh streptozocin (50mg/kg BW) in 0.05 mol/l citrate buffer. After 7days of injections, rats with a fast blood glucose level of >200mg/dl were considered as diabetics [21]. Glucose measurement was done by taking blood from the vein of the rat tail using a normal glucose monitoring meter. We started our investigation 1 week after STZ injections. Later, rats were divided into 4 groups of G2 as a positive diabetic, which fed the normal basal diet, G3 diabetic group, treated with 200 mg/kg BW of garlic oil by using oral gavage [22], and G4 diabetic group, treated with 300 mg/kg BW of Vit E oil by using oral gavage [23]. The fifth group was the diabetic group treated with a

combination of Vit E and garlic oil as in the 3<sup>rd</sup> and 4<sup>th</sup> groups by using oral gavage.

### *Sample collection*

#### *Blood samples and serum separation*

Rats fasted overnight and blood samples were collected from the optical vein under anesthesia and centrifuged (3,000rpm/10min) to separate serum and kept at -20°C pending assay. Serum was used for the determination of fasting blood glucose, insulin, lipid profile, liver profile, and kidney profile. The antioxidant and malondialdehyde were estimated in the liver tissue homogenate.

#### *Dissection and kidney homogenate preparation*

Rats were sacrificed under ether anesthesia and the cervical dislocation and pieces of the liver were separated and kept on ice for the preparation of homogenates.

#### *Preparation of liver tissue homogenate*

The ice-cold liver tissue of each rat was perfused with PBS, pH 7.4, containing 0.16mg/ml heparin for removing clots and RBCs. Tissues were homogenized on 5-10ml/g tissue of cold buffer. Homogenates were centrifuged (4,000 rpm/15 minutes/4°C) and the supernatant was used for determining the criteria of samples.

### *Biochemical analysis*

#### *Glucose and insulin determination*

Glucose was assayed by using a Human kit -Germany (CAT.NO:10260) and Insulin level was assayed by using insulin ELIZA kit (CAT.NO: E-EL-R2466) from Elabscience, USA.

#### *Lipid peroxidation (MDA) determination*

Serum lipid peroxidation assaying MDA in the liver tissue homogenate by MDA assay kit (CAT.NO: ab118970) by Abcam

#### *Antioxidant enzyme activity*

The antioxidant parameters were tested in the liver tissue homogenate through Superoxide Dismutase (SOD) activity and estimated in the serum using SOD colorimetric Assay kit by Elabscience (CAT.NO: E-BC-K020). Catalase (CAT) activity was estimated in the serum using a colorimetric/fluorometric testing kit (CAT.NO: ab83464) by Abcam. The glutathione-S-transferase activity was evaluated in the serum using a colorimetric assay kit (CAT.NO: E-BC-K029). Glutathione peroxidase (GPx) was estimated in serum using a colorimetric testing Kit (CAT.NO: ab102530) and glutathione (GSH) was estimated by a fluorometric assay kit (CAT.NO: ab65322).

**Lipid profile**

Serum cholesterol was estimated using a Cholesterol kit (CAT.NO: 10017) by Human-Germany. Serum triglycerides were estimated using triglycerides kit (CAT.NO: 10720P) by Human-Germany and the serum LDL was estimated using LDL cholesterol kit (CAT.NO: 10094) by Human-Germany. Also, the very low-density cholesterol (VLDL) was estimated by multiplying the triglycerides by 0.2 (mg/dl) according to the Friedewald equation (LDL = Total cholesterol - HDL - Triglyceride/5).

**Kidney profile**

Urea activity was estimated by using the Enzymatic colorimetric test (CAT.NO: 14601) by the Medichem Middle East and creatinine was estimated by using creatinine Colorimetric kit (CAT.NO: 235 001) by SPECTRUM.

**Liver profile**

ALT was determined in the liver tissue using Human testing Kit (Germany) (CAT.NO: EC2612). Aspartate Aminotransferase (AST) was assessed in the serum by a Human kit (Germany) (CAT.NO: EC261).

**Physiological evaluation**

Bodyweight was measured every 10 days as BWG and BWG%.

**Statistical analysis**

The data was analyzed by SPSS Inc., USA/ 24 for calculating t-test and M±SD and after that using ANOVA (p<0.05) [24].

**RESULTS AND DISCUSSION**

**Diabetic parameters**

**Table 1** displays the effect of the use of Vit E and garlic oil for 6 weeks on serum insulin and blood glucose levels in diabetic animals. Diabetes induction in G2 increased significantly (p<0.001) and serum FBS and insulin were compared with G1. Diabetic rats treated with garlic oil, Vit E, and their mixture in G3, G4, and G5, (p<0.001), respectively decreased either serum FBS or insulin compared to the G3. In G3, rats treated with garlic oil had efficiently higher Vit E in G4. On the other hand, the mixture of Vit E and garlic oil in G5 was much more efficient than garlic oil in G3 and Vit E in G4.

**Antioxidant enzymes and lipid peroxidation**

**Table 1** also displays the effect of garlic oil and Vit E for 6weeks on antioxidant enzymes in liver tissue homogenate of diabetic rats. The mean±SD of catalase, superoxide dismutase, reduced glutathione, and glutathione peroxidase in liver samples of positive control decreased significantly (p<0.001) compared to G1. In G3 and G4, treated diabetic rats showed no significant increase in antioxidant criteria compared to those in positive control. Mean antioxidants in G5 were increased (P<0.05) compared to the G3.

Administering Vit E and garlic oil affects the lipid peroxidation levels in the liver tissue homogenate in diabetic rats for 6 weeks. Inducing diabetes in G3 (p<0.001) significantly increased the mean value of MDA in liver tissue homogenate in G3 compared to G1. The mean value of liver tissue homogenate MDA in G3 was slightly lower than that of G3, the differences were non-significant. Treating diabetic rats in G4 and G5 with garlic oil and Vit E, respectively showed significant (p<0.001) decrease in the mean value of liver tissue homogenate MDA compared to G3 and a combination of Vit E and garlic oil in G5 was much more efficient in lowering lipid peroxidation than garlic oil in G3 and Vit E in G4 (**Table 1**).

**Table 1.** The Effect of 6-Week Administrating Garlic Oil and Vit E for on Antioxidant Enzymes, Lipid Peroxidation, Blood Glucose and Insulin in the Liver of Diabetic Rats

Antioxidants	Statistics	Groups				
		G1 (-) Control	G2 (+) Control	G3 Garlic Oil	G4 Vit E	G5 Combination
Catalase (CAT)	Mean±SD	0.443±0.09 <sup>a</sup>	0.274±0.09 <sup>c</sup>	0.301±0.11b <sup>c</sup>	0.277±0.07 <sup>c</sup>	0.381±0.08 <sup>ab</sup>
	LSD 0.05=0.088					
	T-test	-	4.385 <sup>***</sup>	-0.564 <sup>NS</sup>	-0.098 <sup>NS</sup>	-2.269 <sup>*</sup>
Superoxide dismutase (SOD)	Mean±SD	582.07±107.27 <sup>a</sup>	476.62±124.01 <sup>b</sup>	511.16±52.92 <sup>a</sup>	472.46±99.28 <sup>a</sup>	534.96±61.92 <sup>a</sup>
	LSD 0.05=96.614					
	T-test	-	4.042 <sup>***</sup>	-0.638 <sup>NS</sup>	0.065 <sup>NS</sup>	-1.034 <sup>NS</sup>
Glutathione reductase (GSST)	Mean±SD	76.23±12.91 <sup>a</sup>	69.83±18.93 <sup>a</sup>	74.42±10.90 <sup>a</sup>	75.96±6.89 <sup>a</sup>	81.72±17.64 <sup>a</sup>
	LSD 0.05=14.72					
	T-test	-	1.036 <sup>NS</sup>	-0.638 <sup>NS</sup>	-0.955 <sup>NS</sup>	-1.265 <sup>NS</sup>



Reduced Glutathione (GSH)	Mean±SD	1.14±0.37 <sup>a</sup>	0.802±0.11 <sup>a</sup>	0.938±0.332 <sup>a</sup>	0.937±0.288 <sup>a</sup>	1.151±0.42 <sup>a</sup>
	LSD 0.05= 0.32					
	T-test	-	2.773 <sup>**</sup>	-1.020 <sup>NS</sup>	-1.168 <sup>NS</sup>	-2.637 <sup>**</sup>
Glutathione peroxidase (GPX)	Mean±SD	161.56±31.41 <sup>ab</sup>	148.39±42.96 <sup>b</sup>	63.66±37.69 <sup>ab</sup>	162.31±26.26 <sup>ab</sup>	194.33±48.48 <sup>a</sup>
	LSD 0.05=37.96					
	T-test	-	0.644 <sup>NS</sup>	-0.620 <sup>NS</sup>	-0.694 <sup>NS</sup>	-2.383 <sup>*</sup>
MDA	Mean±SD	0.879±0.171 <sup>c</sup>	1.215±0.301 <sup>a</sup>	1.028±0.076 <sup>b</sup>	0.850±0.049 <sup>d</sup>	0.790±0.056 <sup>e</sup>
	LSD 0.05=0.145					
	T-test	-	-3.081 <sup>**</sup>	1.830 <sup>NS</sup>	3.440 <sup>**</sup>	4.486 <sup>***</sup>
Blood glucose	Mean±SD	70.25±17.06 <sup>c</sup>	142.75±34.16 <sup>a</sup>	100.37±19.77 <sup>b</sup>	113.37±25.73 <sup>b</sup>	88.50±20.46 <sup>bc</sup>
	LSD0.05=25.07					
	T-test	-	-4.778 <sup>***</sup>	3.552 <sup>***</sup>	2.316 <sup>*</sup>	3.723 <sup>***</sup>
Insulin	Mean±SD	0.329±0.052 <sup>ab</sup>	0.376±0.092 <sup>a</sup>	0.287±0.068 <sup>bc</sup>	0.302±0.059 <sup>bc</sup>	0.261±0.042 <sup>c</sup>
	LSD0.05=0.057					
	T-test	-	-1.559 <sup>NS</sup>	2.696 <sup>**</sup>	1.863 <sup>NS</sup>	3.661 <sup>***</sup>

Significance level: <sup>\*</sup>P<0.05, <sup>\*\*</sup>P<0.01, <sup>\*\*\*</sup>P<0.001. ANOVA: within each row, means with different superscripts (a, b, c, d, or e) are significantly different at P<0.05, means superscripts with the same letters mean that there is not any significant difference at P<0.05.

#### Kidney function

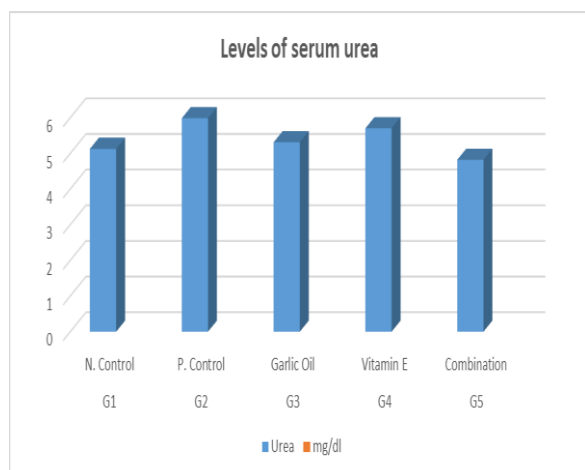
Administration of garlic oil and Vit E for 6 weeks affects kidney function in diabetic animals. Diabetes inductions in G2 had increased (p<0.001) in ±M urea compared to negative control as shown in **Figure 1**. In G4, ±M were lower than G3 and showed non-significant differences. Treating diabetic rats in G3 and G5 were high and significantly (p<0.001) reduced the mean value of urea in comparison to G3 (**Table 2**).

in G2, the ±M of creatinine increased significantly in the positive control compared to G1 as shown in **Table 3**. In G4, the mean value was lower than that of G3 and showed non-significant differences. Treating diabetic rats in G3 and G5 with garlic oil and the combination of garlic oil and Vit E, respectively were high and significantly (p<0.001) reduced the mean values of urea compared with G3 (**Table 2**). Similar to the previous results, the combination in G5 was more efficient than garlic oil or Vit E alone in G3 and G4, respectively.

**Table 2.** The Effect of Administrating Garlic Oil and Vit E for 6 Weeks on Kidney and Liver Functions in Diabetic Rats

Parameters	Statistics	Groups				
		G1 (-) Control	G2 (+) Control	G3 Garlic Oil	G4 Vit E	G5 Combination
Urea	Mean±SD	5.129±0.46 <sup>a</sup>	5.986±0.66 <sup>b</sup>	5.311±0.67 <sup>c</sup>	5.704±0.69 <sup>a</sup>	4.820±0.60 <sup>d</sup>
	LSD 0.05= 0.548					
	T-test	-	-5.122 <sup>***</sup>	3.828 <sup>**</sup>	1.801 <sup>NS</sup>	3.366 <sup>**</sup>
Creatinine	Mean±SD	3.975±2.18 <sup>c</sup>	4.837±2.22 <sup>a</sup>	4.178±2.19 <sup>b</sup>	4.573±2.20 <sup>a</sup>	3.905±1.79 <sup>d</sup>
	LSD 0.05= 0.561					
	T-test	-	-5.136 <sup>***</sup>	3.728 <sup>***</sup>	1.801 <sup>NS</sup>	2.618 <sup>**</sup>
ALT	Mean±SD	23.53±4.35 <sup>d</sup>	54.07±12.92 <sup>a</sup>	43.15±7.73 <sup>b</sup>	37.84±9.78 <sup>e</sup>	27.87±6.40 <sup>c</sup>
	LSD 0.05= 9.66					
	T-test	-	-5.418 <sup>***</sup>	1.685 <sup>NS</sup>	2.258 <sup>*</sup>	5.038 <sup>***</sup>
AST	Mean±SD	44.47±8.61 <sup>d</sup>	75.41±4.96 <sup>a</sup>	62.16±6.70 <sup>b</sup>	53.45±11.25 <sup>c</sup>	45.65±7.42 <sup>e</sup>
	LSD 0.05= 8.98					
	T-test	-	-8.619 <sup>***</sup>	12.780 <sup>***</sup>	5.158 <sup>***</sup>	8.421 <sup>***</sup>

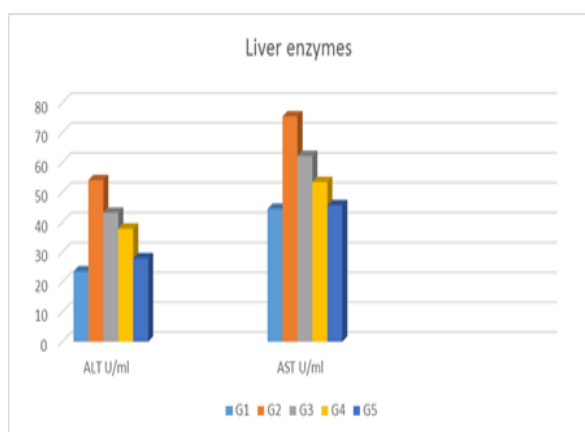
\*significant at P<0.05, \*\*\*: significant at P<0.001. ANOVA: within each row, means with different superscript (a, b, c, d, or e) are significantly different at P<0.05.



**Figure 1.** The Effect of Garlic Oil, Vit E, and their Combination on Serum Urea in Streptozotocin-induced Diabetic Rats

### Liver function

**Table 2** also shows the administration effects of Vit E and garlic oil for 6 weeks on liver function in rats. Induction of diabetes in G2 significantly ( $p < 0.001$ ) increased ALT and AST in G2 compared to that of G1 as shown in **Figure 2**. Treating the diabetic rats with garlic oil (G3) decreased ALT and AST in the positive control group. The differences were non-significant when compared to G3. The mean values of ALT and AST in G4 were significantly ( $p < 0.05$ ) lower than that of positive control, whereas in G5 they were significantly high ( $p < 0.001$ ) decreased when compared with G3.



**Figure 2.** The Effect of Garlic Oil, Vit E, and their Combination on Liver Enzymes in streptozotocin-induced Diabetic Rats

### Lipid profile

Administration impacts of Vit E and garlic oil for 6 weeks on lipid profile in diabetic rats are shown in **Table 3**. Mean values of total cholesterol, triglycerides, VLDL, and LDL were enhanced ( $P < 0.001$ ), and HDL was

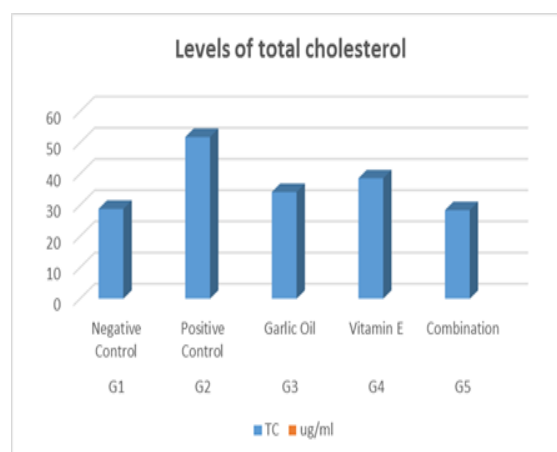
reduced compared to G1. Treating rats in G3, G4, and G5 had a higher reduction in total cholesterol, triglycerides, VLDL, and LDL, and enhancing HDL compared with G3. Moreover, G5 was more efficient compared to G3 and G4. **Figure 3** indicates the impact of garlic oil, Vit E, and their combination on serum total cholesterol.

### Total body weight

Administration of garlic oil and Vit E for 6 weeks affects the total BW in diabetic rats (**Table 4**). In G2 at all experiment stages, diabetes nonsignificantly decreased the bodyweight in comparison to the negative control except after 20 days which was highly significant ( $P < 0.01$ ). Treating the diabetic rats with garlic oil and Vit E in G3 and G4, respectively, significantly reduced the body weight compared to G2 in different levels of significance. On the other hand, using garlic oil and Vit E in G5 led to a nonsignificant increase in the total BW compared to G2.

### Physiological evaluation

Administration effects of garlic oil and Vit E for 6 weeks on physiological evaluation in diabetic rats (**Table 4**). The body weight gain per day (BWG/day) and the bodyweight gain per 30 days (BWG/30 days) were decreased in the G2 as a result of induction of diabetes. Treating with garlic oil and Vit E (G3, G4) decreased the BWG/day, whereas their combination in G5 increased it. The body weight gain percentage (BWG%) non significantly increased in G2 compared to G1. Treating with garlic oil in G3 nonsignificantly decreased the BWG%, whereas Vit E in G4 and their combination in G5 nonsignificantly increased the BWG% in comparison to the positive control group.



**Figure 3.** The Effect of Garlic Oil, Vit E, and their Combination on Serum Total Cholesterol in Streptozotocin-induced Diabetic Rats



**Table 3.** The Effect of 6-Week Administration of Vit E and Garlic Oil on Lipid Profile in Diabetic Rats

Lipid profile	Statistics	Groups				
		G1 (-) Control	G2 (+) Control	G3 Garlic Oil	G4 Vit E	G5 Combination
TC	Mean±SD	28.80±6.22 <sup>c</sup>	51.80±2.94 <sup>a</sup>	34.20±1.09 <sup>b</sup>	38.60±2.40 <sup>d</sup>	28.40±2.60 <sup>e</sup>
	LSD 0.05= 4.514					
	T-test	-	-15.16 <sup>***</sup>	10.40 <sup>***</sup>	6.82 <sup>***</sup>	12.40 <sup>***</sup>
TG	Mean±SD	13.80±1.92 <sup>b</sup>	32.20±6.37 <sup>a</sup>	14.20±3.89 <sup>c</sup>	15.00±1.87 <sup>d</sup>	12.60±1.14 <sup>e</sup>
	LSD 0.05= 4.579					
	T-test	-	-5.25 <sup>***</sup>	7.81 <sup>***</sup>	5.95 <sup>***</sup>	7.53 <sup>***</sup>
HDL	Mean±SD	33.80±13.86 <sup>a</sup>	13.60±3.20 <sup>b</sup>	13.80±3.89 <sup>a</sup>	9.80±1.30 <sup>b</sup>	14.40±1.51 <sup>a</sup>
	LSD 0.05= 8.317					
	T-test	-	3.23 <sup>**</sup>	-.078 <sup>NS</sup>	2.179 <sup>*</sup>	-.691 <sup>NS</sup>
LDL	Mean±SD	15.40±1.52 <sup>b</sup>	20.34±2.17 <sup>a</sup>	15.26±0.94 <sup>c</sup>	15.14±2.76 <sup>d</sup>	15.24±1.94 <sup>e</sup>
	LSD 0.05= 2.801					
	T-test	-	-5.50 <sup>***</sup>	3.69 <sup>**</sup>	3.19 <sup>**</sup>	3.05 <sup>**</sup>
VLDL	Mean±SD	2.76±0.38 <sup>b</sup>	6.44±1.27 <sup>a</sup>	2.84±0.77 <sup>c</sup>	3.00±0.37 <sup>d</sup>	2.52±0.22 <sup>e</sup>
	LSD 0.05= 0.935					
	T-test	-	-5.25 <sup>***</sup>	7.81 <sup>***</sup>	5.65 <sup>***</sup>	7.53 <sup>***</sup>

Significance level: \*\*: at P<0.01, \*\*\*: P<0.001. ANOVA: within each row, means with different superscript (a, b, c, d, or e) are significantly different at P<0.05.

**Table 4.** The Effect of 6-Week Administration of Garlic Oil and Vit E on the Total Body Weight and Biological evaluation in Diabetic Rats

parameters	Statistics	Groups				
		G1 (-) Control	G2 (+) Control	G3 Garlic Oil	G4 Vit E	G5 Combination
After 10 day	Mean±SD	260.50±25.18 <sup>a</sup>	240.12±40.42 <sup>a</sup> <sup>b</sup>	187.87±17.51 <sup>c</sup>	188.62±23.38 <sup>d</sup>	227.87±18.81 <sup>e</sup>
	LSD 0.05= 27.755					
	T-test	-	1.66 <sup>NS</sup>	3.83 <sup>***</sup>	2.52 <sup>**</sup>	0.70 <sup>NS</sup>
After 20 day	Mean±SD	280.87±22.88 <sup>a</sup>	245.12±51.23 <sup>b</sup>	183.75±25.35 <sup>c</sup>	199.87±31.94 <sup>e</sup>	252.87±25.90 <sup>d</sup>
	LSD 0.05= 33.838					
	T-test	-	2.27 <sup>**</sup>	4.07 <sup>***</sup>	1.65 <sup>NS</sup>	-.337 <sup>NS</sup>
After 30 day	Mean±SD	294.50±26.46 <sup>a</sup>	269.00±55.33 <sup>a</sup>	220.50±20.80 <sup>b</sup>	222.37±25.88 <sup>a</sup>	272.87±30.29 <sup>d</sup>
	LSD 0.05= 34.380					
	T-test	-	1.49 <sup>NS</sup>	2.35 <sup>*</sup>	1.815 <sup>NS</sup>	-0.152 <sup>NS</sup>
Before surgery	Mean±SD	313.75±26.43 <sup>a</sup>	291.87±56.49 <sup>a</sup>	220.87±28.35 <sup>b</sup>	231.25±27.57 <sup>b</sup>	293.25±33.03 <sup>a</sup>
	LSD 0.05= 34.906					
	T-test	-	1.43 <sup>NS</sup>	3.41 <sup>**</sup>	2.40 <sup>**</sup>	-0.05 <sup>NS</sup>
BWG g/day	Mean±SD	1.775±0.379 <sup>a</sup>	1.725±0.692 <sup>a</sup>	1.100±0.818 <sup>a</sup>	1.420±0.812 <sup>a</sup>	2.197±1.007 <sup>a</sup>
	LSD 0.05= 0.761					
	T-test	-	0.197 <sup>NS</sup>	1.646 <sup>NS</sup>	1.314 <sup>NS</sup>	-0.972 <sup>NS</sup>
BWG	Mean±SD	53.25±11.37 <sup>a</sup>	51.75±20.77 <sup>a</sup>	33.00±24.54 <sup>a</sup>	42.62±24.36 <sup>a</sup>	65.37±30.22 <sup>a</sup>

g /30 days	LSD 0.05= 22.789					
	T-test	-	0.19 <sup>NS</sup>	1.64 <sup>NS</sup>	1.31 <sup>NS</sup>	-0.97 <sup>NS</sup>
	Mean±SD					
BWG %	LSD 0.05= 12.211	20.68±5.01 <sup>a</sup>	21.23±5.76 <sup>a</sup>	17.97±14.60 <sup>a</sup>	23.59±15.53 <sup>a</sup>	29.02±14.69 <sup>a</sup>
	T-test	-	-0.18 <sup>NS</sup>	0.59 <sup>NS</sup>	-0.63 <sup>NS</sup>	-1.36 <sup>NS</sup>

\*: significant at P<0.05, \*\*: significant at P<0.01, \*\*\*: significant at P<0.001. ANOVA: within each row, means with different superscript (a, b, c, d, or e) are significantly different at P<0.05.

Streptozotocin-induced diabetes causes immense harm to pancreatic  $\beta$ -cells and consequently decreases insulin secretion and increases blood glucose [5, 6, 14]. However, the pancreatic  $\beta$ -cells may remain functional in type-II DM, and different oral hypoglycemic agents that stimulate insulin secretion can be utilized to control hyperglycemia [25].

The decreased insulin secretion and increased FBS in the positive control diabetic groups are associated with streptozotocin-induced diabetes [6]. In addition, lipid peroxidation, total cholesterol, triglycerides, kidney function parameters (creatinine and urea), liver function parameters (AST and ALT) were increased, whereas insulin levels, HDL, and all evaluated antioxidants decreased due to the induction of diabetes [4, 13]. Streptozotocin-induced diabetes causes high oxidative stress typical to diabetes, damaging endothelium tissues, increasing blood cholesterol levels, promoting lipid peroxidations, and worsens blood platelet functional disorder [26]. Pancreatic  $\beta$ -cells had poor antioxidant capacities, and susceptible to oxidative stress might be modifying the cellular proteins and lipids either structures or functions, led to dysfunction, apoptosis, and necrosis of  $\beta$ -cells, and affected insulin secretions or functions [27, 28].

Treating the diabetic rats in G3, G4, and G5 with garlic oil, Vit E, and their combination, respectively succeeded in alleviating diabetes by decreasing oxidative stress as revealed by the increase in the antioxidant parameters and the HDL, as well as the decrease in lipid peroxidation, total cholesterol, triglycerides, kidney function parameters (creatinine and Urea), and liver function parameters (AST and ALT), and increase in insulin levels, HDL, and all studied antioxidants due to their free radicals scavenging activity. This result is consistent with the previous investigation [21, 29].

Vit E has been considered as an antioxidant in previous investigations in animal models of diabetes. It decreases several cellular markers of oxidative stress, protects against lipid peroxidation, and prevents increasing plasma glucose levels [19, 21, 29].

Studies have concluded that to minimize the negative effects on healthy cells, garlic may act by decreasing

activity on ROS or by interacting with them. According to standardization procedures adopted and chemical structure, the antioxidative potency of various garlic compounds differs [30, 31].

Total body weight and physiological evaluations were also affected by streptozotocin-induced diabetes and alleviated by treating these altered parameters in G3, G4, and G5 with garlic oil, Vit E, and their combinations [32, 33].

## CONCLUSION

Vit E, Garlic oil, and their combination succeeded to have a remarkable antioxidant and antidiabetic activity. The combination of both Vit E and garlic oil was more efficient for the treatment of streptozotocin-induced diabetes.

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