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Hypoglycemic and Hepatoprotective Activities of Coriander (*Coriandrum sativum*) Extract in Streptozocin Induced Diabetic Rats

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

The present study was designed to evaluate the role of Coriander (*Coriandrum sativum*) for management of diabetes instead of manufactured drugs, which led to many complications. Medicinal plants would be higher useful for this purpose because they are considered to be effective and non-toxic and safer than manufactured drugs. Aqueous extract of Coriander (*C. sativum*) was used to measurements their antidiabetic and hepatoprotective effects in streptozocin (STZ) induced diabetic male albino rats. Coriander (*C. sativum*) was given to the STZ induced diabetic rats at the concentration of 200 mg/kg body weight in different groups of three diabetic rats each orally once a day for 15 days. Body weight showed significant increase after 15 days of treatment with Coriander (*C. sativum*) extract compared with the normal control rats group (N). Blood glucose level on 15th day of treatment became significantly lower. The extract induced significant reduction in serum glucose, total lipids, total cholesterol, triglycerides level and

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transaminases (AST, ALT and γ-GT) activities. Liver glycogen content was significantly increased in treated animals compared to control group (N). The present data revealed insignificant changes in the serum total protein, albumin and globulin level during the experimental period. The lipid peroxidation determined was found to be decreased in plasma, liver and kidney of streptozocin induced diabetic rats treated with Coriander (*C. sativum*) extract (STZ/T) and rats group given Coriander (*C. sativum*) extract and then induced streptozocin (T/STZ), compared to control streptozocin induced diabetic rats group (STZ©). Glutathione reductase (GSH-R), glutathione peroxidase (GSH-P) and superoxide dismutase (SOD) activities were increased in liver and kidney of rat groups. These findings demonstrates that Coriander (*C. sativum*) extract have antioxidant effect for reducing lipid peroxidation in plasma and tissues and improve the liver function and antioxidant enzymes in treated rat groups compared to diabetic control rat group (STZ©). These observations revealed that the use of Coriander (*C. sativum*) extract can be recommended as natural antidiabetic, antioxidant and hypolipidemic activity agent. Findings of the present study suggest that the aqueous extract of Coriander (*C. sativum*) at the dose of 200 mg/kg body weight brings about significant beneficial effects in various biochemical parameters during diabetic and these effects are quite comparable with standard drug used to treat diabetes mellitus.

Keywords: Coriander; phytochemicals; Streptozozocin (STZ); Antidiabetic; antioxidant; rats.

1. INTRODUCTION

Diabetes mellitus (DM) consider one of the most metabolic diseases, associated with dysfunction and damage of different organs, in different areas of the world, due to abnormal metabolism of lipid, protein and carbohydrates [1] who reported “DM consider the fifth disease leading to the cause of death worldwide. DM is acute metabolic complications affecting many organs of the body and chronic vascular”. Al-lawati [2] repored that “the DM is the world’s largest endocrine disease associated with increased morbidity and mortality rates”. The chronic hyperglycemia of diabetes is the resulting of dysfunction and long-term damage of various organs [3,4] reported “the liver damage consider major causes of death in diabetes mellitus and the mortality rate from hepatic disease is greater than that from cardiovascular complications and hepatocellular carcinoma” [3,5]. “Liver plays a role in glucose and lipid homeostasis as uptake, oxidation and metabolic conversion of free fatty acids in the synthesis of cholesterol, phospholipids and triglycerides” [6]. “Chronic inflammation produced from endogenous metabolic processes are consider the most important sources of free radicals react with lipids, proteins, carbohydrates, DNA and damage all types of biomolecules” [7-9]. Other studies [10-12], indicated “the DM type 2 was increased with oxidative stress resulting oxidative damage of proteins, DNA and lipid associated with chronic degenerative diseases including diabetes, hypertension, coronary heart disease and cancer” [10,11]. Other investigator [11] showed “the free radicals produced may react with polyunsaturated fatty acids in cell membranes leading to lipid peroxidation”. “Free radicals are reactive molecules able to exist independently includes super oxide, hydroxyl radicals and hydrogen peroxide” [13]. Major cardiovascular and atherosclerosis diseases risk factors such as hypercholesterolemia are known to impair endothelial functions through increased generation of oxygen free radicals and thereby elevates lipid peroxides [10, 14] report “these free radicals initiate processes involved in atherogenesis. Oxidative stress were found to be increased with diabetes mellitus type 2 and cardiovascular disease due to free radicals, lipid peroxides and oxidation of low-density lipoproteins (LDL). “Diabetes with impaired glucose metabolism and increase hydroxyl radical production resulting lipid peroxidation” [15,16]. “Hyperglycemia and long-term complications enhanced oxidative stress and reactive oxygen species produce from metabolic process responsible for free radical generation cause disorder and reduction of the antioxidant defense activities that affecting liver, heart, kidneys, eyes, nerves and blood vessels” [5], they suggested “the most of the reactive oxygen species are scavenger by endogenous defense systems” [10]. Oral hypoglycemic therapy may not prevent the long-term complications of diabetes disorders, such as nephropathy [17], cardiovascular [18] and other side effect disorders [19]. “Some studies showed the use of synthetic anti-diabetic agents produce disturbances of the liver and kidneys side effects” [20]. Other investigators [21,11] reported that “the dietary intervention is one of the main therapies proposed in the case of type 2 diabetes

patients, and hence different substances of plant origin are gaining importance for the treatment of diabetic subjects" and in animal involving streptozotocin-induced diabetic rats [22], they found these substances have protect normal rat islets from STZ, normalize blood glucose levels and promote â-cell regeneration in islets of STZ-treated rats [23]. "Clinical and experimental studies have documented antidiabetic and antiatherosclerotic effects of plant seeds extract" [7,24]. "Current research concentrate to examine new kinds of natural products shown maintenance health and reduce risk of most chronic diseases such as coronary heart disease, cancer and diabetes" [25]. Other studies found different biological activities of substances isolated from plants origin used as antidiabetic [22,26], antihypertensive [27], anticancer activities [8,9] and cancer chemopreventive effects [3] due to their phytochemical constituents of fatty acids, flavonoid, phenolic, and polysachharides [18,28]. Phytochemicals particularly polyphenols, have considerable interest in the field of food chemistry, pharmacy and medicine due to their biological effects including antioxidant properties [29,30] they indicated that "these polyphenols may be found either free or bound to protein or plant cell walls and can bind to plasma LDL" and protect them from oxidation [14]. Bagri et al.[16] reported "plant foods have different antioxidant activity such as scavenger of free radicals and lipid peroxide cell cycle". Other investigators [17] reported "the supplementation of therapeutics with antioxidants have a chemoprotective role and act in preventing diabetes" [18]. "An increase in antioxidants materials can scavenge free radicals, to prevent atherosclerosis and heart diseases" [10,31]. Plants have been ancient extensively used for the treatment of diabetes mellitus [32,33] evidence the dietary intervention is one of the main therapies of type 2 diabetes patients or streptozotocin-induced diabetic rats. "Plant origin substances may be modulate physiological regulation that delays or prevents the long-term complications of diabetes as well as lowering blood glucose levels" [34,35]. Many plant extracts and their constituents have antioxidant activities and found to be used for treatment of many kinds of human diseases including DM [33,36]. Other investigators reported some plants have been use, in a wide variety of liver disorders, modulate of oxidative stress due to its antioxidant properties [30] and other biological activities including anticarcinogenic, antifungal, antibacterial and antioxidant effects [37]. "Recently, there is a concentrated studies are interest worldwide to identify natural antioxidant compounds have pharmacologically effective with low or no side effects to use in food industry and preventive medicine" [11, 37]. 36Alam et al. (2019) indicated that "Eruca sativa possessed a potent free radical scavenging natural antioxidants and protected against oxidative damage by increasing or maintaining the levels of antioxidant molecules and antioxidant enzyme activities". "Polysaccharide isolated from *Portulacaoleracea* prevents diabetic, vascular inflammation, hyperglycemia, and diabetic endothelial dysfunction in type II diabetic mice indication to protective effect against diabetes and vascular complications" [38]. Other studies evidence the safety and low cost of some produe materials of natural products have antioxidant activity without side effects were used in treatment of diabetes [7], Other study has been shown the plants containing antioxidant substances have scavenge free radicals and play an important role in the prevention of free radical-induced diseases [39], increase the antioxidant enzymes activity and HDL-cholesterol that reduce the risk of heart disease [40, 41]. "Antioxidants increase can scavenge free radicals and prevent atherosclerosis and carcinogenesis" [10,14]. Polyphenolic compounds enhance the stability oflow density lipoprotein (LDL) to oxidation that plays a significant rolein atherosclerosis and coronary heart disease. Several studies evidence the mechanism of action of antioxidant activity of flavonoid rich fractions from different sources have hypolipidemic [7] and hypoglycemic [7,42] activities. Phenolic compounds have potential functionofantioxidants by scavenging the superoxide anion, singlet oxygen [43], and stabilizing free radicals involved in oxidative processes due to the presence of hydroxyl groups and ring structures [44,45] used for various curative purposes in health care to prevent cancer, cardiovascular diseases and regulate lipid and carbohydrate metabolism in alloxan-induced diabetic mice [46,47]. Most studies have been shown the beneficial effects of diets rich in vegetables, fruits and grain products in reducing the risk of cardiovascular disease and certain cancers [17,31] correlate increased phenolic compounds levels in foods with reduced coronary heart disease mortality, they indicated an association between increased consumption of vegetables and fruits rich antioxidant compounds and reduced the risk of cardiovascular disease. Flavonoids consider a major group of polyphenolic compounds [37] reported "these compounds are essential

constituents of higher plant cells possess suitable chemical structure for scavenging free radicals" [48]. "High occurrence of flavonoids in fruits and vegetables used for protection against coronary heart disease" [49-51]. Zapolska-Downar et al [31] found "a dose of 15 to 50 mg/kg body mass of querstin capable of normalizing blood glucose level, augmenting liver glycogen content and reducing cholesterol and LDL concentrations in alloxan–diabetic rats". "Generally antioxidants have been identified as major health beneficial compounds reported from varieties of medicinal plants and are sources for alternative medicine. Thus the principal agents responsible for the protective effects could be the presence of antioxidant substances that exhibit their effects as free radical scavengers and hydrogen-donating compounds" [43,44,50]. The present investigation was designed to investigate the coriander (*C. sativum*) leaf extract for hypoglycemic, hepatoprotective effects and improving the antioxidant enzymes in streptozotocin-induced diabetic male albino rats.

2. MATERIALS AND METHODS

2.1 Materials

a. A fresh coriander (*Coriandrum sativum*) as whole plant was washed with tap-water followed by distilled water and cut into small pieces.
b. Streptozocin (STZ) used as a diabetogenic agent and all other chemicals used were purchased from Sigma chemical company (USA).
c. Twenty eight male albino rats (*Rattus norvgicus*) were purchased from Biological Products of National Research Center, Cairo, Egypt. After two week of acclimatization, the rats were then divided into four groups, 7 rats each, on the basis of their body weight, housed in wire screen cages.

2.2 Methods

2.2.1 Preparation of extract

A known weight of fresh coriander (*Coriandrumsativum*) was ground in a food grinder (mincer) and mixed well with hot water (1:1 v/v) twice using a homogenizer for 5 min. The homogenate was filtered through cheesecloth and WhatmanNo.1 filter paper. The obtained filtrate was used for the determination of total phenolic, flavonoid, fatty acids and used for oral administration to the diabetic rats [28]. The solid residue was dried and stored in desiccators till used.

2.2.2 Analytical methods

Protein concentration was measured according to the method of Lowry et al. [52] using bovine serum albumin as a standard. Lipids were extracted with chloroform-methanol mixture (2:1 V/V), according to the method described by Folch et al. [53]. Total carbohydrate value was also estimated [54]. Ashes were quantified gravimetrically after incineration in a muffle oven at 550 °C. Phenolic and flavonoid were extracted with 80 % methanol, ultrasonic bath for 20 min and centrifuged for 5 min at 15000 rpm. [55].Total phenolic content (TPC) was estimated [56,57].Total flavonoid contents (TFC) was estimated spectrophotometrically [58].Flavonoids was identified using apigenine, quercetin and catechin as standard [59,60]. The lipid peroxidation inhibitory activity was determined [61], compated the results with standard quercetin.

2.2.3 Induction of experimental animal

The intraperitoneal injection of Streptozotocin (60 mg/kg body weight) exerts direct toxicity and causes a permanent hyperglycemia within 48 – 72 h [16]. A freshly prepared solution of streptozocin (60 mg/kg) dissolved in 0.1mol/L citrate buffer, pH 4.5 was injected intraperitoneally in rats in a volume of 1 mL/kg. After 72 h of streptozocin (STZ) administration (Streptozocin diabetic rats), Blood was obtained and plasma glucose of all groups was measured. Diabetes was confirmed by the determination of fasting glucose concentration on the third day post administration of streptozocin (STZ). Rats with plasma glucose level exceeding 300 mg/dl were considered as STZ diabetic rats (hyperglycemia). All normal and STZ diabetic rat (hyperglycemic rats) groups were taken for the present experiment. After 45 days of experiments, initial and final body weights were recorded.

Twenty eight male albino rats (*Rattusnorvgicus*) weighing about 160.40 g ±1.40 were purchased from Biological Products of National Research Center, Cairo, Egypt. The rats were fed with a normal commercial pellet diet and given water ad libitum. After two week of acclimatization, the rats were then divided into four groups, 7 rats each, on the basis of their body weight, housed in wire

screen cages. The first group was used as normal rats group (N) and given distilled water daily. The second and third groups were injected intraperitoneally with STZ (60 mg/kg body weight), the second group maintains without any treatment over experimental period (30 days) and they were given distilled water only and used as STZ diabetic control rats (STZ), The third STZ diabetic group (STZ) was orally treated with extract (200 mg/kg body weight) for 30 days (STZ/T) and the fourth group (T/STZ) were treated orally with coriander (*C. sativum*) extract daily for 15 days once a day [62] and then they were injected intraperitoneally with STZ (60 mg/kg). After 45 days, the food was removed and rats were anesthetized and blood samples were obtained. Heart, kidney and liver of each rat were immediately removed, washed using saline (0.9%), drying using filter paper, weighed and stored till used.

2.2.4 Protein and lipid digestibility

During the feeding period (6 weeks), the rat faeces were collected and dried in an oven at 105°C, collected, weighed and tested. Weight gain and food intake were also calculated [7,30].

2.2.5 Blood and tissue samples

At the end of 6 weeks, and an overnight fasting, seven rats from each group were anesthetized with sodium nesdonal (60 mg/kg body weight). Blood samples were collected using capillary tubes from retro-orbital venous plexus of rats and plasma was obtained by centrifugation at 10000g for 20 min using cooling centrifuge (Sigma 2K15) and used for estimation of glucose and different parameters. Stored plasma samples at - 60ºC were analyzed for glutathione (GSH) and the activities of glutathione-S-transferase (GSH-T), glutathione peroxidase (GSH-P), glutathione reductase (GSH-R), superoxide dismutase (SOD) and thiobarbituric acid reactive substances (TBARS). Liver, kidney and heart tissues were removed immediately, weighed and washed using saline (0.9%) and stored at -70°C till used. Tissues were minced and homogenized (10% W/V) separately with cold sodium potassium phosphate buffer (0.01 M, pH 7.4) using homogenizer (Mechanika Precyzyjna Warszawa model MPW-309, Poland). The homogenates were centrifuged at 10000g for 20 min at 4ºC, and the resultant supernatants were used for estimation of antioxidant enzyme activities and the levels of TBARS (as marker of lipid peroxidation).

2.2.6 Biochemical assays

Blood glucose level was estimated according to the method of Trinder [63]. Protein concentration was measured as previous [52]. Serum albumin level was measured according to the method of Doumas et al., [64]. Globulin was calculated by subtracting albumin form total protein. Total lipid (TL) was assayed by the method of [65] Knight et al. [65] and for total cholesterol (TC), by the method of Trinder [66]. High density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) and triacylglycerols (TAG) levels were also estimated [67,68]. Plasma VLDL was isolated by precipitation using MgCl2 and phosphotungstate (Sigma Chemical Company) according to the method of Burstein et al. [69]. Very low density lipoprotein cholesterol (VLDL-C) was determined with enzymatic method using Bio-diagnostic kit [67]. Alkaline phosphatase (ALP), Alanine amionotransferase (ALT) and aspartate amino transferase (AST) activities were measured according to the method of Reitman and Frankel [70]. γ-Glutamyl Transpeptidase (GGT) was also determined [71]. Glutathione S-transferase (EC 2.5.1.18), Glutathione peroxidase (EC1.11.1.9) activity in plasma and homogenates of liver, kidney, and heart tissues were assessed [72]. Superoxide dismutase (EC 1.15.1.1) activity was measured by the NADH oxidation procedure, as described by Elstner et al. [73]. Glutathione reductase (EC 1.6.4.2), was assayed using the method of Goldberg and Spooner [74]. Lipid peroxidation (LP) was estimated by measuring thiobarbituric acid reactive substances (TBARS) concentrations using malondialdehyde (Sigma com.) as a standard according to the methods of Quintanilha et al. [75] and Esterbauer and Cheeseman [76]. Glycogen content was determined by the anthrone method as described by Carrol et al. [77]. One unit of enzyme was defined as an amount of GST needed to catalyze formation of 1nmol of thioester/min and the specific activity is expressed as nmole/min/mg of tissues or nmol/min/ml of plasma.

2.2.7 Statistical analysis

The obtained data for various biochemical parameters were statistically analysed using student t-test [78]. Results were expressed as mean value ± SE and a difference of $P < 0.05$and $P < 0.01$were considered significant (*) and higher significant (**).

significant at $p < 0.05$and high significant at $p < 0.01$.

3. RESULTS AND DISCUSSION

3.1 Chemical Analysis of Coriander (*C. sativum*) Extract

Plants which are consider a part of human culture used by ancient peoples as food or medicine [79] evidence they have nutritional quality and health. Coriander is recognized as one of the most important spices in the world and is of great significance in international trade. Coriander (*C. sativum*) has been used by ancient people in various regions all over the world. Coriander (*C. sativum*) was used in food and medical industries as considered non-toxic and have biological activity in the treatment of most diseases [80,82], they reported different parts of plant have been common among people and pharmaceutical industry. Current research concentrates heavily on novel antidibetic and anticancer drugs development [37,81,82] they reported certain plant materials might be useful as chemopreventive agents [83]. Epidemiological investigations indicated that certain plant componds provide a means of chemoprevention due to phytochemical constituents. Moreover, traditional plant remedies have been used for centuries in the treatment of the diabetes [30,84] but only a few have been scientifically evaluated. Treatments of diabetes mellitus (DM) have been recorded using different traditional plant as onion [85,86].The leaves are used as antidiabetic agent [87]. Aqueous extract of *Morus alba* leaves was reported as hypoglycemic as well as hypolipidimic agent [88].Coriander (*C. sativum*) extract contains suitable amounts of carbohydrate(56.24±1.80g%),protein(14.40±0.60 %), lipid (12.10±0.20g%) and polyphenols (4.02±0.01g%). The levels of phenolic and flavonoid contents were 2.80±0.01 and 0.80±0.001 g/100g respectively (Table 1).These results are similar to those reported by Sohail et al.[82]

“These results are in accordance with those reported by other investigators” [30,89]. “Polyphenolic compounds have been reported to exert an inhibitory effect on growth rate by decreasing protein digestibility. Polyphenol and flavonoid are very important plant constituents because of their antioxidant activity” [86,90]. “The antioxidant activity of phenolic compounds is mainly due to their properties which play an important role as free radical scavengers, reducing agents, and complexes of pro-oxidant metals” [91]. “In this experiment, the intake of coriander (*C. sativum*)extract rich in polyphenolic compounds significantly affect body weight gain. Similar results were obtained by other investigators using different plants” [80,81]. “Chromatographic analysis revealed that there are different values of individual flavonoids (quercetin>apigenin>catechen) in coriander (*C. sativum*) extract. Similar results were obtained by other investigators” [37,82,92]. The result obtained from the estimation of total polyphenol and flavonoid contents showed that water are better solvents for the extraction of phenols and flavonoids. These results are in agreement with the study by Tsao and Deng [93] which showed that phenolic and flavonoids are generally better extracted using water or a mixture of water and alcohols. Lipids were analyzed for determination of fatty acids composition using Gas Liquid Chromatography. Results showed Coriander (*C. sativum*) have both unsaturated and saturated fatty acids (14.20 % and 85.80 % respectively). The percentages of monounsaturated fatty acids and polyunsaturated fatty acids were 26.60 % and 59.20 % respectively. These results are in agreement with those reported by 81Sriti et al. [80,81] and Moharib and Tadrus[94] who reported that the coriander and Apiaceae family plants extract was ranged from 0.30 to 82 %. Results are consistant with those reported by Jukanti et al. [79] who found low amounts in chickpea (4.50–6.00g oil/100g). Polyunsaturated fatty acid constituents of coriander (*C. sativum*) are higher than that of saturated fatty acid showed the predominance of polyunsaturated to saturated fatty acids in the present samples. These results are in agreement with those obtained by other investigators [37,95] found the polyunsaturated constituents were predominants than that of saturated constituents of perilla extracts. Daniewski et al. [96] reported higher value for polyunsaturated to saturated fatty acids was found for safflower extract. Similar results were obtained with other investigators [79,94] found saturated fatty acids content was ranged from 6.90 % to 9.20 % [80,83]. However polyunsaturated fatty acids plays an important role in the regulation of biological functions. Bachir and Bellil [97] and Shyamapada and Manisha [98] reported plant containing phytochemicals could be used in preventive strategies to reduce the risk of most diseases including cancer (99Dharmalingam and Nazni 2013). Different kinds of plants have antioxidant substances capable of scavenging free superoxide radicals protecting biological systems

against the harmful effects of oxidative processes on macromolecules [12,36]. Recent study has shown that some extracts intake cause improve in some biochemical parameters of oxidative stress and exhibited reduce the risk of some diseases [37,44]. Plants components can be considered as bioactive molecules in medicine have been demonstrated to have chemopreventive effects [82,83]. Plant-derived compounds, were found to be used in treatment of diabetes [51,82,98], cardiovascular [7,17] and other various diseases [100].

"Streptozocin (STZ) is known for its cell toxicity and has been extensively used in induced diabetes mellitus in animals. STZ induced hyperglycemia in models was previous used" by Vasconcelos et al. [101]. STZ induces hyperglycemia in experimental animals and used to induce diabetes in rats" [102]. "Intraperitoneal injection of STZ increased plasma glucose level gradually to reach its maximum level within 14 days. Flavonoid had significantly maintained blood glucose level and antagonizing the effect of STZ on diabetes militus. Diabetics and experimental animal models exhibit high oxidative stress due to persistent and chronic hyperglycemia, which thereby depletes the activity of antioxidative defense system and thus promotes de novo free radicals generation" [28,30,103]. "In the present study, STZ was associated not only with hyperglycemia but also with low antioxidant enzymes activity"[17]. Sharma et al. [90] found a natural antioxidant drug that reduces hyperglycemia in STZ-induced diabetes and prevents reactive oxygen damage. Oral administration of plant extract markedly reduced the blood sugar level of normal, glucose-fed hyperglycemic and streptozocin induced diabetic rats when compared with control animals [30,103]. Other investigators use single oral administration of of *Eqisetummyrio - haetum* water extract at doses of 7 and 13 mg/kg and butanol extract at doses of 8 and 16 mg/kg for treatment streptozotocin-diabetic rats [51, 82,104]. A different flavonoid, used in doses of 15–50 mg/kg body mass was capable of normalizing blood glucose level, augmenting liver glycogen content and significantly reducing serum cholesterol and LDL concentration in STZ–diabetic rats [16,32]. However, the beneficial effects of flavonoids on DNA adduct levels, oxidative damage to DNA and chromosomal aberrations in human could not be demonstrated. Administration of some plants significantly diminished the hyperglycemia in mildly diabetic mice [44,90,98]. Other studies reported ten percent of plant extract produced a significant decrease in plasma glucose levels in normal and streptozotocin induced diabetic rats when administered by intraperitoneal injection or gastric tube [4,12,18]. Moreover,, the researchers conducted decades over last has shown plant and plant based therapies have a potential to control and treat diabetes and its complications [82,103]. The present study was undertaken to determine the effect of dose of coriander (*C.sativum*) extract on antioxidant and blood glucose concentration in STZ induced diabetic rats.

3.2 Body Weight

Diabetes in general characterized by weight loss and it was seen in the present study. Streptozocin (STZ) administration brought about marked reduction in body weight of rats and this reduction was found to be statistically significant when compared with normal rat group (N). These reduced body weights were found to be increased when compared to their respective diabetic control group (STZ©) and this increase was found to be statistically significant in rats treated with coriander (*C. sativum*) extract (Table 2). However, coriander (*C. sativum*) extract seems to be more effective in maintaining body weight.

Table 1. Chemical composition of coriander (*C. sativum*) extract

Components	Dry weight (g/100g)
Protein	14.40±0.60
Lipid	12.10±0.20
Ash	9.20±0.40
Total carbohydrate	56.24±1.40
Total polyphenol	4.02±0.01
Total phenol	2.80±0.01
Total flvonoid	0.80±0.001

Mean of five samples (Mean ±SE)

Table 2. Body weight, body weight gain and organ weights of experimental rats

Parameters	Experimental groups			
	N	STZ ©	STZ / T	T / STZ
Body weight (g)	210.60±2.20	180.80±4.20**	190.50±3.20*	196.80±2.40*
Weight gain (g)	50.20±0.20	20.40±0.80**	40.10±0.60**	44.40±.0.40**
Liver weight (g)	10.20±1.20	8.60±0.80	9.02±0.86	9.40±0.84
Kidney weight (g)	1.60±0.04	1.34±0.06	1.50±0.02	1.58±0.20
Heart weight (g)	0.90±0.01	0.84±0.02	0.86±0.01	0.88±0.01

(Mean values for 7 rats/ each 2 weeks/ group)
** Significant (P<0.05) ** Higher significant (P<0.01)*

Results in Table (2) show the body weight and body weight gain were significantly lower in treated rats as compared to normal rat group (N) as shown in Table 2. It can be observed that the STZ decreased weight gain significantly (20.40±1.20) than that of N rat groups (50.20±2.10). Body weight values in rats given dose of coriander (*C. sativum*) extract were lower also than that of N rat group but higher significantly increases as compared to those of STZ © [7,37].The weight gain of rat groups received coriander (*C.sativum*) extract before and after STZ dose (T/STZ and STZ/T respectively) was significantly increased (40.10±1.40 and 44.40±1.60 respectively) than those of STZ © rat group. These results are consistent to other studies [30,35], which have previously suggested that date waste, sugar beet, and cellulose had lowering effects on growth rate of rats. It can be concluded, that these differences are definitely relatable to the presence of different types and constituents of phytochemical compounds in the dose of coriander (*C.sativum*) extract [82,94]. However, polyphenolic compounds have been reported to exert an inhibitory effect on growth by decreasing protein digestibility [17,89]. Coriander (*C. sativum*) extract did not cause any significant change in organs weight of treated rat groups compared to N control group. However, treatment with coriander (*C. sativum*) extract resulted in treatment and protection against the STZ-induced reduction of body weight (Table 2). The decreased in body weight due to STZ observed in the present study have been previously reported by [7,14,26]. The weight loss of animals treated with STZ can be at least partially due to the drug toxicity which accelerates the water elimination in urine. Also, STZ-induced weight loss might be due to gastrointestinal toxicity and thereby reduced ingestion of food [4,9,33]. The nephrotoxicity induced by STZ in the present study is established by a number of observations and the increased relative kidney weight is one of those observations. Thus in the present study, the results suggest that coriander (*C.sativum*) extract is bioavailable, and possesses significant potential to prevent STZ-induced toxicity and weight loss.

3.3. Protein and Lipid Digestibility

Protein and lipid digestibility was lowered by 14% and 19 % respectively (Fig 1) in rats group STZ © as compared to those of normal rat group (N). The rat groups received coriander (*C. sativum*) extract (STZ/T and T /STZ) showed higher significant increase in protein and lipid digestibility (96.80±0.20, 92.40±0.42 and 94.40±0.20, 94.20±0.40 respectively) as compared to those of STZ © but lower than that of normal rat group (98.20±0.40 and 96.80±0.44 respectively). These results showed that the consumption of protein and lipids was similar in the all rat groups, whereas fecal protein and lipids contents were respectively increased by 14 % and 29 %, in rats given coriander (*C.sativum*) extract compared with rats of STZ ©.These effects may be attributed to the presence of soluble carbohydrate associated polyphenols. The present results are in the range with those reported by other workers [30,34]. Similar results were reported by other workers [96,92,82,89].

3.4 Blood Parameters

Streptozocin (STZ) causes destruction of pancreas cells and increase in blood glucose levels. It is evident from the present investigation that STZ administration at the dose of 60 mg/kg body weight causes diabetes in male albino rats. Glucose levels in STZ© diabetic rats was raised to more than 3 fold (372.6 ±4.20) as compared to N rats (120.60 ±2.10) on 3 day. Interestingly, the increase in glucose levels in diabetic groups was found to be higher significantly as compared to N rat group (Fig 2). These raised levels of blood glucose in diabetic rats were decreased significantly after oral administration of coriander

(*C. sativum*) extract. Blood glucose levels were found to be decreased from 367.60±4.20 to 131.80±2.13 and 122.20±1.80 mg/dl after oral administration of coriander (*C. sativum*) extract in treated group (STZ/T and T/STZ respectively) compared to those of diabetic rats (STZ ©). Coriander (*C. sativum*) extract treatment also decreased blood glucose levels from 367.60 ±4.20 mg/dl in STZ © to 122.20±1.80 mg/dl T/STZ. This decline in blood glucose levels of treated groups compared with their respective diabetic (STZ ©) was found to be higher statistically significant [4,18,33] The reduction of glucose level after administering coriander (*C. sativum*) was 66.80%.These results are attributed to the presence of suitable amounts of polyphenol and flavonoid (5.92±0.10 and 0.58±0.20g/100g respectively) in coriander (*C. sativum*) extract (Fig 2). A significant decrease in the concentration of plasma glucose was noted after administration of different doses of aqueous and alcoholic extract of different pants [30,33], showed that the aqueous extract contain nearly 50 mg/100g of flavonoids possessed anti hyperglycemic activity [16,51] they proved the insulin-stimulatory effect of *Punica granatum*, and *Syzygium alternifolium* from existing β-cells in diabetic rats [8,9,82]. Results showed that the coriander (*C. sativum*) extract that contain nearly 0.80 g/100g of flavonoids and 4.02g/100g polyphenol possessed anti hyperglycemic activity [9,12,51]. Hence it has proved highly effective in causing significant anti-hyperglycemic response in rats. Oral administration of aqueous extract from *Balanitesa egyptiaca* for 30 days to normal senile diabetic rats induced a highly significant decrease of serum glucose level compared to normal control group (N) as the present results (Fig 2). Oral administration of the extracts of *Retamaraetam* and *Melastomamala bathricum*on blood glucose levels both in normal and streptozocin (STZ) diabetic rats led to significant decrease of blood glucose level [22, 39,90]. It is evident from these results that reduction in glucose levels brought by aqueous coriander (*C. sativum*) extract is encourage comparable with reduction brought about by other different plant. The administered extract of *Swertiacory mbosa* produced significant lowering in the serum glucose level [9,14,26], reported that the extract of *Swertiacory mbosa* induced a stimulation of islet insulin release and potentiated the glucose stimulation to insulin secretion. Other investigators [16,18] suggested that the hypoglycemic activity of aqueous extract may be generally mediated through enhancement of peripheral metabolism of glucose and an increase in insulin release.Hypoglycemic activity may be due to the effect of extract on intestinal reduction of the absorption of glucose. Moreover, oral administration of aqueous and ethanolic (50% v/v) extract of *Punica granatum*led to significant blood glucose lowering effect in normal, glucose fed hyperglycemic and alloxan-induced diabetic rats [12,33].

In the present study, some aspects of carbohydrate, protein and lipid metabolism and liver function parameters were studied in the normal and diabetic rats treated with aqueous coriander (*C. sativum*) extract at a dose of (200mg/kg body weight).

Fig (2) illustrate that the activities of transaminases (ALT and AST) are significantly decreased in diabetic rats given the aqueous extract of coriander (*C. sativum*) after 30 days of treatment compared to control and STZ rat groups : Similar decrease in γ-GT activity was observed in diabetic rats received aqueous extract of coriander (*C. sativum*) for 30 days. Diabetes mellitus (DM) is a syndrome initially characterized by a loss of glucose homeostasis [16,30,33]. Administration of water extract of coriander (*C. sativum*) revealed a significant decrease in the activities of serum alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma aminotransferase (γ-GT) of diabetic rats compared to control and STZ rat groups. The decreases of transaminases activity with the treatments have been attributed to improved liver function [38 37,44]. The results (Fig 2) showed higher significant increase in the levels of ALP in diabetic rat group (STZ ©) after administration with 50 mg/kg STZ (266.45±3.97 IU/L) compared to those of normal N control rat group (140.10±3.14 IU/L). The levels of ALP in treated rat groups (STZ /T and T/STZ) were found to be significantly decreases (144.04±2.30 and 133.10±2.20 IU/L) compared to those of STZ © (263.45±3.97 IU/L). Aspartate and alanine transaminases (AST and ALT) levels exhibited higher significant in STZ © (98.40±0.98 and 96.85±1.59 U/ml respectively) compared to those of N control rat group (65.80±1.58 and 58.90±1.01 U/ml respectively). Results in Fig (2) showed significant decreases in the levels of AST and ALT in treated rat groups (STZ /T and T/STZ) compared to those of N and STZ © rat groups. The present results also showed higher significant in the levels of γ-GT (22.84±1.60 and 24.40±1.04 U/l) in treated rat groups (STZ /T and T/STZ) compared to those of diabetic STZ ©

(78.42±1.40 U/l). Transaminases are the most sensitive biomarkers directly implicated in the extent of cellular damage and toxicity because they are cytoplasmic in location and are released into the circulation after cellular damage. Alterations in AST and ALT are reported in hepatic disease and in myocardial infarction [19,33,37]. On the other hand, treatment with STZ significantly increased plasma AST, and ALT activities compared to control. The presence of coriander (*C. sativum*) extract with STZ minimized its toxic effect on plasma and liver enzymes to reach the control levels (Fig 2). The significant disturbance in the activities of plasma AST and ALT has been previously reported by other investigators [15,22,36] stated the ability of STZ to cause alterations in the activity of these enzymes could be a secondary event following STZ-induced liver damage with the consequent leakage from hepatocytes. Treatment of the diabetic rats with the aqueous extract of some plants (*Lupinus albus* and *Zygophyllum coccineum*) restored the activities of the AST, ALT, ALP and LDH to their normal level in plasma, liver and testes in induced diabetic rats [7,18, 49], they reported the medicinal plants control the release of glucose form the liver. Generally, liver toxicity of STZ is characterized by elevation of serum transaminases [3,18]. In the present study, elevation in the plasma levels of transaminases are indicators of impaired liver functions and is further emphasized by the significant decrease in the activity of transaminases (Fig 2). This effect of coriander (*C. sativum*) extract pretreatment supports the antioxidant activities of coriander (*C. sativum*) extract [12,80]. Aqueous extract of coriander (*C. sativum*) showed insignificant change of total protein, albumin and globulin in plasma of diabetic rats after 30 days of treatment compared to that corresponding N and STZ © value as illustrated in Fig (3). The obtained data indicated that aqueous coriander (*C. sativum*) extract of produced no-significant effect on serum total protein, albumin and globulin concentration of diabetic rats after 30 days. These results suggested that the administration of coriander (*C. sativum*) extract might adversely interfere with glycaemic in diabetic rats. Extract of coriander (*C. sativum*) slightly improved serum protein and albumin concentration in comparison with diabetic rats. Moreover, SZC-induced decrease in total protein and albumin.

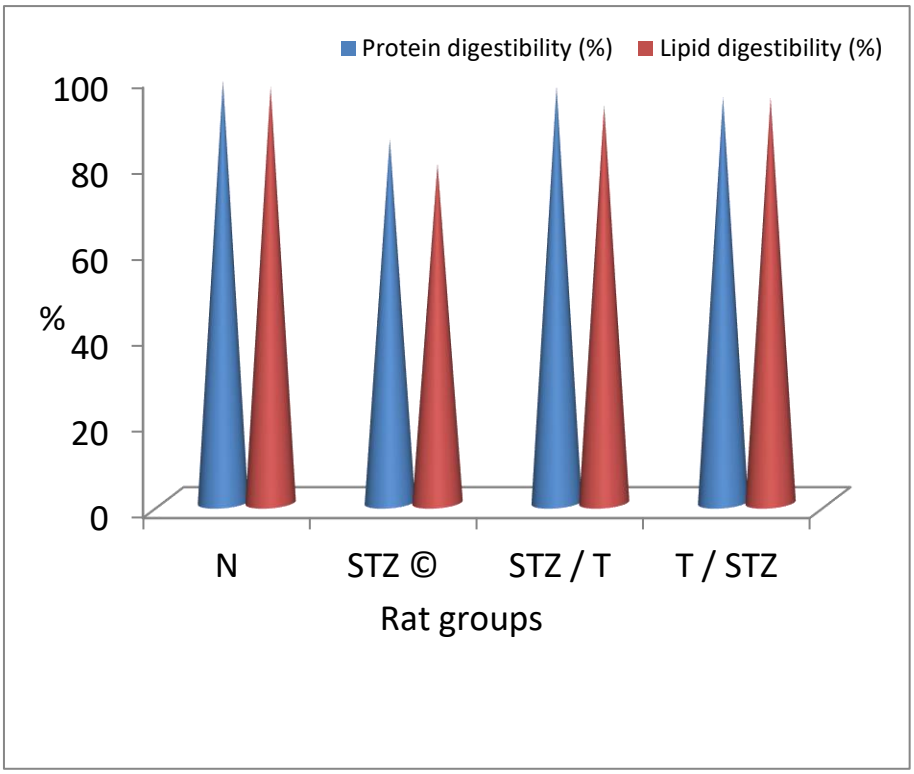


Fig. 1. Protein and lipid digestibility of experimental rat groups
(Mean values for 7 rats / group)
** Significant (P< 0.05) ** Higher significant (P< 0.01)*

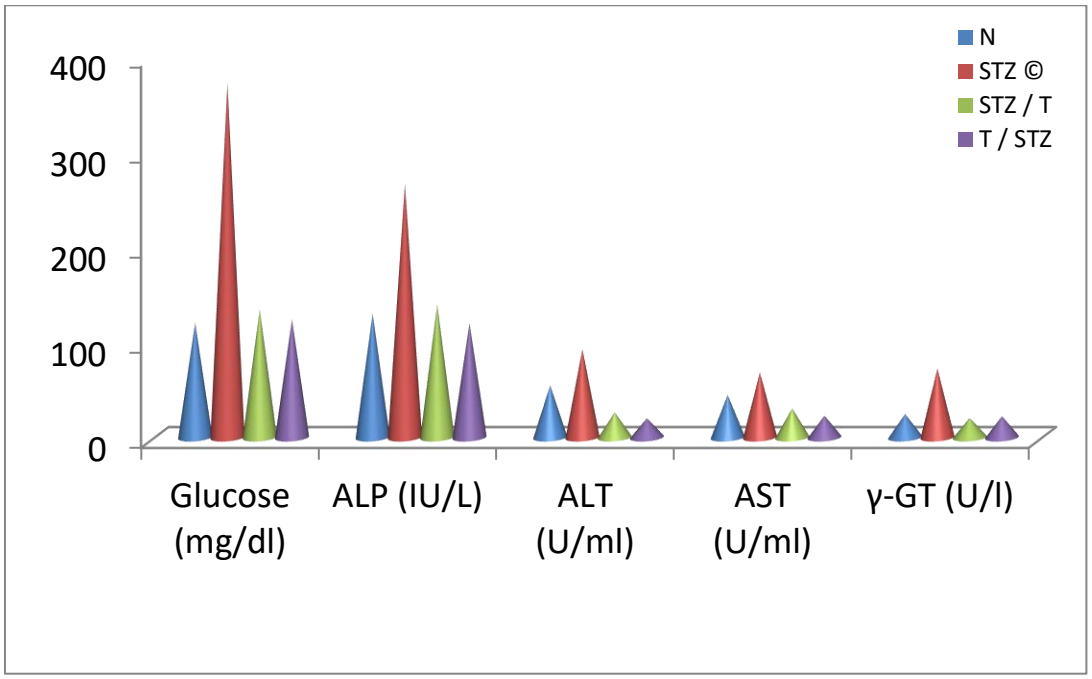


Fig. 2. Glucose, ALP, ALT, AST and y-Gt levels in plsma of experimental rat groups

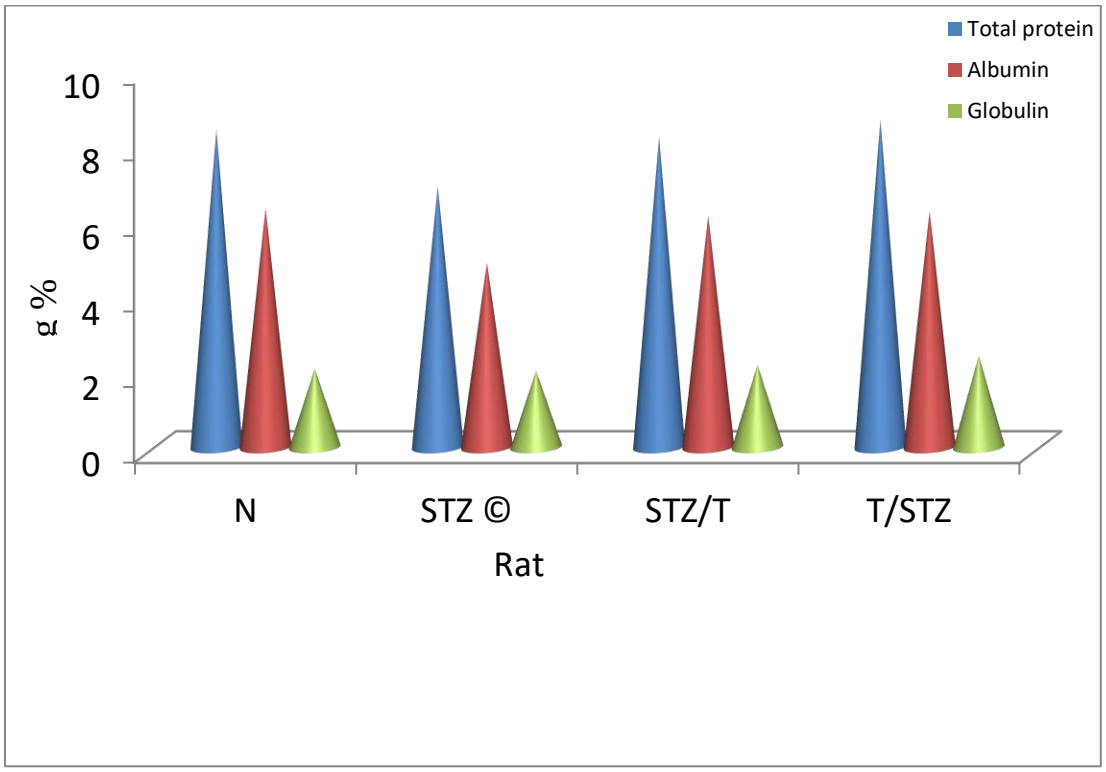


Fig. 3. Total protein, albumin and globulin levels in sera of experimental rat groups.

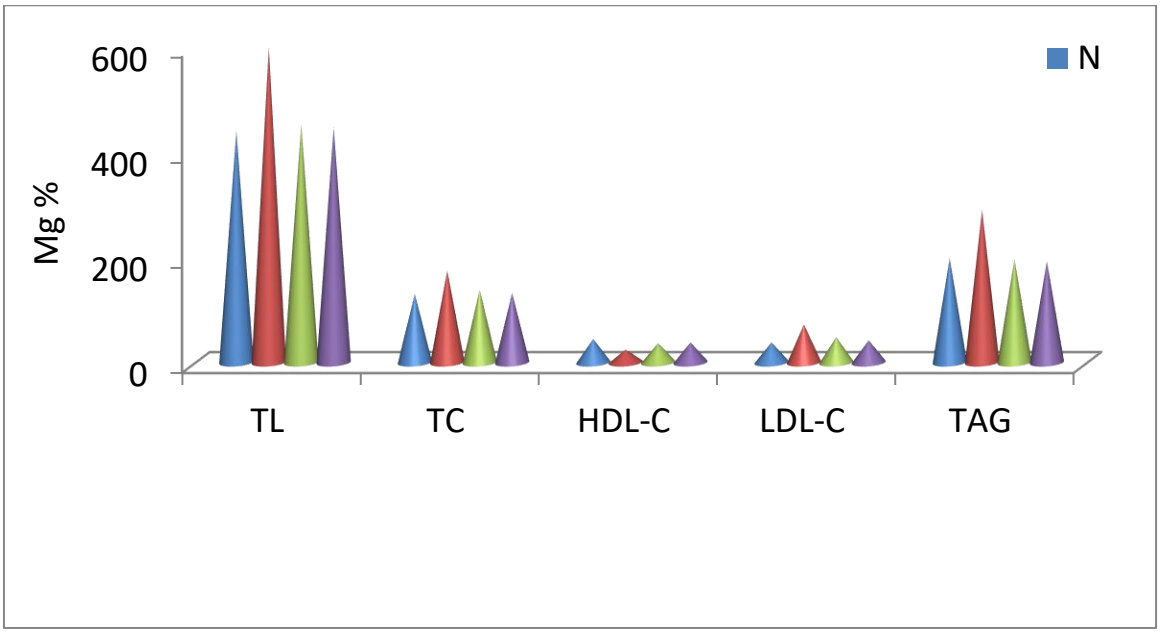


Fig. 4. TL, TC, HDL-C, LDL-C andTAG levels in plasma of experimental rat groups.

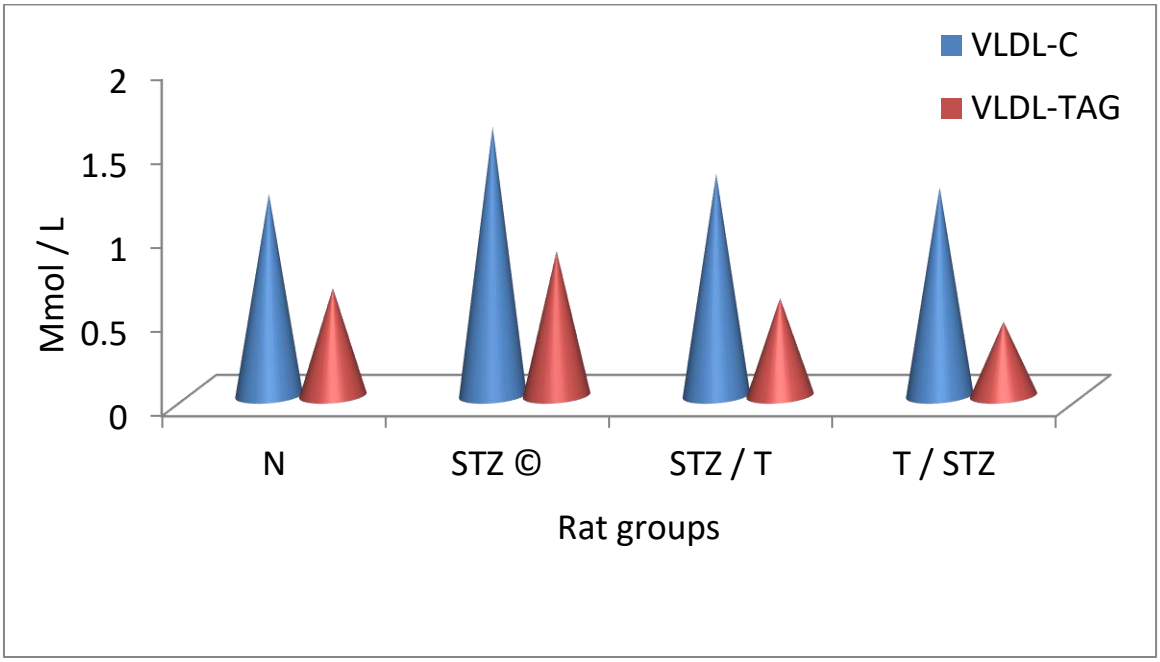


Fig. 5. VLDL-C and VLDL-TAG levels in plasma of experimental rat groups

Plasma lipid responses of N, STZ ©, STZ/T and T/STZ groups of rats are given in Fig (4). Diabetic rats treated with aqueous extract of coriander (C. sativum) induced a significant decrease in serum total lipids, total cholesterol and triglyceride level after 30 days. Different changes were observed in plasma TL, TC, HDL-C, LDL-C, VLDL-C, TAG and VLDL-TG. The present results showed that the rat treatment with STZ (STZ ©) caused higher significant increase in the levels of TL, TC, LDL-C, VLDL-C, TAG and VLDL-TG compared to N control rat group. While, rats were treated with coriander (C. sativum) extract showed significant decreases in the levels of plasma TL,TC, HDL-C, LDL-C, VLDL-C, TAG and VLDL-TG when compared to normal control rat group (N) and the rat group received STZ © (Figs 4,5). The rat were

treatment with dose of coriander (C. sativum) extract (STZ/T and T/STZ) have a significant increases in the level of plasma HDL-C (12.82% and 18.79 % respectively). Several investigators [3, 4,11,28], strongly suggested the consumption of purified components, which could be beneficial in terms of reducing hypercholesterolemia, hyperlipidemia, Higher significant decreases were observed in plasma TL (22.41-25.20%) and TC (24.80-28.60%) of rats received coriander (C. sativum) extract. Both animal and clinical studies have previously suggested that psyillum and rhubarb maybe potentially a hypocholesterolemic agent [31]. Consistent with these finding, the cholesterol lowering effect (22-25%) of coriander (C. sativum) extract used was elucidated in this study (Figs 4, 5). Higher significant decrease was observed in the level of TG (32.60-37.70%) of rats given coriander (C. sativum) extract. Positive correlation exists between the incidence of coronary atherosclerosis andplasma LDL-C concentration, which may act as cardiovascular risk factor, as stated by other workers [11,37]. Therefore, higher reduction in LDL-C levels (26.32-32.46%) in plasma of treated rat groups (STZ /T and T/STZ) means that coriander (C. sativum) extract had lowering effects on the incidence of coronary atherosclerosis and reduce the risk factor of cardiovascular diseases [10,16,31]. The present study examined polyphenol might improve the lipid components level and oxidative damage resulting STZ-induced in rats (14,16,90]. The dose of coriander (C. sativum) extract lowered plasma TC by about 28%. These doses also results the significant attenuation in the VLDL-C concentrations (23-26.40%) observed in rat groups treatment (STZ /T and T/STZ respectively). Moreover, TC/HDL-C ratio which is a marker of dyslipidemia was about 2,3-fold lower in STZ /T and T/STZ rat groups compared to STZ © rat group. Contrary to these findings [15] reported that some extract had no significant effects on serum TC in rats. Choi et al. [41] reported that the diet induced hypercholesterolemia is almost always useful for the assessment of agents that interfere with absorption, degradation and excretion of cholesterol. The reasons for the lower plasma VLDL-C contents in rats received coriander (C. sativum) extract may have been elevated of the VLDL uptake by the liver. The present results showed that the rats were received coriander (C. sativum) extract (100mg/kg) have higher plasma HDL-C content (46.80 and 50.20 mg/dl) than those of STZ © (control group). Moharib [37] reported that the cholesterol was carried from peripheral tissues to the liver. Coriander (C. sativum) extract doses significantly lowered plasma TG by about 32.6-37.7% and VLDL-TG by 31 - 44% compared to N and STZ © rats. These effects may be due to the effect of enzyme involved plasma VLDL-TG hydrolysis. The present results are in the range with those reported by other investigators [10,14,16].The coriander (C. sativum) extract (100mg/kg) decreased significantly in plasma TC level (24.80-28.60%) and VLDL-C (23-26.40%) as compared to those of N and STZ ©. TC/HDL-C ratio were lower2.30 and 3.01-fold in rat groups (STZ/T and T/ STZ respectively) received parsley (Petroselinum sativum) extract (100mg/kg) compared to STZ © control rats. TG content (32.60% and 37.70%) and VLDL (31% and 44%) were reduced in plasma of rat groups (STZ/T and T/STZ respectively) compared to STZ © rats group. Plasma protein and albumin values were nearly similar in all rat groups. These effects may be attributed to the presence of polyphenol. Several studies have been established that phenolic substances exert preventing development of atherosclerosis [39,40]. Treatment of diabetic rats in the present study, with coriander (C. sativum) extract produced marked decreases of serum total lipids total cholesterol and triglyceride concentration as compared with the normal rats. This may be due to the role of coriander (C. sativum) in increase over mobilization of lipids from blood vessels to liver or decrease lipogenesis mechanism in liver and decrease the mobilization of lipids from liver to the blood vessels [18,20,37]. The reduction of total lipids, cholesterol and triglycerides in diabetic rats of the present study may be attributed to increased clearance and decreased production of the major transporters of endogenously synthesised total cholesterol and triglycerides [15,30]. All these observations indicated the hypolipidemic effect of coriander (C. sativum). A similar affect was reported by Nabi et al. [4]. Cholesterol-lowering effects of coriander (C. sativum) extract may be due to increased utilization of cholesterol for bile synthesis in the liver [30,96].Another possibility is that the extract may effects cholesterol synthesis which seems to be decreased as a result of inhibition in hydroxy methyl glutaryl co-enzyme a reductase [12,16,28]. It is also possible that it exerts its effect on cholesterol esters of polyunsaturated fatty acids [7,37] which are more rapidly metabolized by liver and other tissues, which might enhance their rate of turnover and excretion. The reason for triglyceride-lowering effect of coriander (C. sativum) extract could be contributed to a reduced availability of free fatty

acid for hepatic uptake and triglyceride synthesis release with subsequent hypotriglyceridemia [12,14,37]. Liver plays a major role in glucose and lipid homeostasis. It participates in the uptake, oxidation and metabolic conversion of free fatty acids and in the synthesis of cholesterol, phospholipids and triglycerides. Hyperlipidemia is one of the major risk factors of atherosclerosis and endothelial dysfunction [15,31]. The glutathione-S-transferase (GST) family of enzymes comprises a long list of cytosolic, mitochondrial, and microsomal proteins [37,82,104]. Diabetic rats treated with aqueous extract of coriander (C.sativum) induced a significant decrease in serum total lipids, total cholesterol and triglyceride level compared to those reported by other investigators (30,33,51). Similar decreases in serum total lipids, total cholesterol and triglycerides were also observed in normal rats treated with plant extract [37, 82].

3.5 Plasma and Tissues TBARS Contents

Plasma and tissues TBARS concentrations are shown in Fig (6). The coriander (C. sativum) extract treated rat groups (STZ/T and T/STZ) led to low plasma TBARS contents (75%) compared to those STZ© rats. TBARS concentrations in liver and kidneys were markedly reduced by 41% and 65% respectively in group of treated rats (STZ/T and T/STZ) compared to rats received STZ©. The results also showed the treated rats (STZ/T and T/STZ) resulted in a decrease of TBARS in all tissue. These data suggest that the coriander (C. sativum) extract treated groups (STZ/T and T/STZ) are less susceptible to peroxidative damage of oxidative stress such as STZ©. These effects are due to the presence of parsley (Petroselinum sativum) extract containing polyphenol [30,39]. Increased superoxide anion production in hypercholesterolaemic vessels contributes to the atherosclerotic process [31,38,82], reported that hypercholesterolemic and atherosclerosis were associated with increased tissue content of a lipid peroxidation product. It is well known that plant polyphenols act as free radical scavenger in vitro [30,40,90]. Results also showed that the plasma TBARS concentrations were significantly lower in the coriander (C. sativum) extract treated rats groups (STZ/T and T/STZ) compared with those of STZ© rat group (Fig 6). Other invesyigators [30,47,90,98] reported that the increases plasma lipid peroxidation and TBARS concentrations were detected in hypercholesterolemic and hypertriglyceridemicrats,Free radicals generation is positively correlated with plasma TC and TG concentrations in rabbits [12,16,98]. In present investigation, rats treated with coriander (C. sativum) extract (STZ/T and T/STZ) had lower plasma TC and TG contents and a positive correlation between plasma TBARS and TG contents was observed.

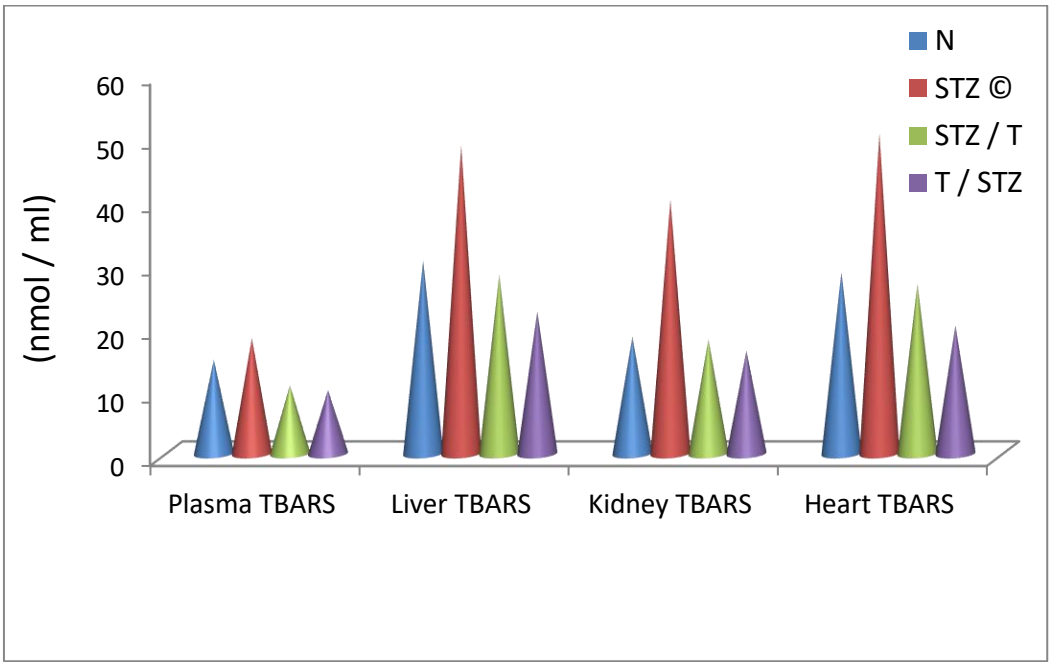


Fig. 6. TBARS of plsama, liver, kidney and heart levels of experimental rat groups

The antioxidant effect of an aqueous extract of plant used in Ayurvedic medicine in different countries, were studied in rats with streptozocin-induced diabetes. Oral administration of plant extract (200mg/kg body weight) for 45 days resulted in a significant reduction in thiobarbituric acid reactive substances and hydroperoxides [16,47,92]. The extract also causes a significant increase in reduced glutathione in the liver and kidneys of rats with STZ-induced diabetes. To determine the lipid peroxidation, malondialdehyde (MDA) levels were measured in serum and tissues homogenates (liver, kidney and heart). Both serum and tissues homogenates MDA were increased considerably in the STZ© rats in comparison with normal N control (Fig 7). Serum MDA was also decreased significantly (12-33%) by dose of coriander (C. sativum) extract (Fig 7). Oral administration of 50 mg/kg/day of parsley (P. sativum) extract to rats diminished the tissues homogenate MDA level markedly by 72%. Serum MDA was also decreased significantly (Fig 7). The levels of MDA equivalents, was significantly increased in liver, heart and kidneys of the rats in the control group (Fig 7). But this increase was significantly reduced to the normal control level in rats administered coriander (C. sativum) extract containing flavonoids [15,86,90]. Lipid peroxide is an important pathogenic event in myocardial infarction and the accumulated lipid peroxides reflects the various stages of the disease and its complications [90,87,103]. Increases the level of lipid peroxides injure blood vessels, causing increasing adherence and aggregation of platelets to the injured sites [12,16]. Both serum and tissues homogenate revealed increased in MDA levels in the rats (STZ /T and T/STZ) in comparison with N rats (Fig 7). However, the dose of 200 mg/kg produced higher protection against lipid peroxidation. Recent reports show that TBARS in the gastric mucosa, an index of lipid peroxidation, were increased by ethanol injury, but the increase was inhibited by the administration of 50 mg/kg coriander (C. sativum) extract through decrease of reactive oxygen metabolites [30,98,105] when used different doses of extract. Administration of coriander (C. sativum) extract at a dose of 10mg / kg body weight /day could effectively lower the levels of lipid peroxides and MDA equivalents in rats. [6,12,16,17]. Concerning liver glycogen content, there was higher significant increase due to oral administration of aqueous coriander (C. sativum) compared to control as shown in Fig (7). The elevation of hepatic glycogen observed in treated rats, indicates increased glucose storage as a result of increased insulin glycogenesis induced by high level of glycogen [27,30,105]. Other researcher stated the effect of plant leaf extract on plasma glucose and hepatic glycogen content in streptozocin-induced diabetic rats [27,30]. Moreover, the hypoglycemic effect of aqueous coriander (C.sativum) extract may be attributed to increase in the time course of glucose absorption from the intestine [15,23].

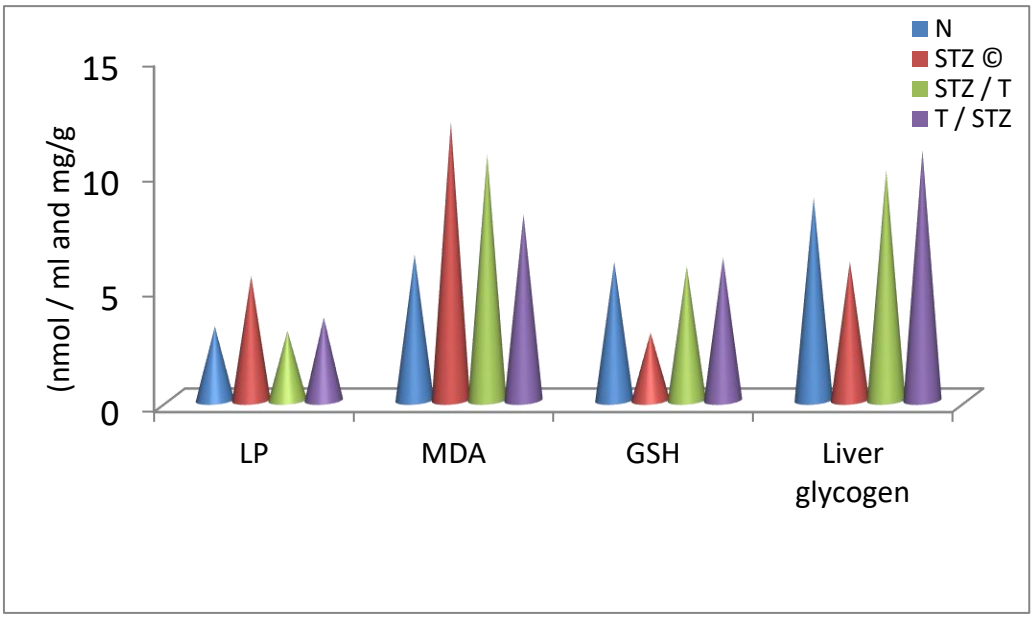


Fig. 7. Lp, MDA, GSH and liver glycogen levels in experimental rat groups

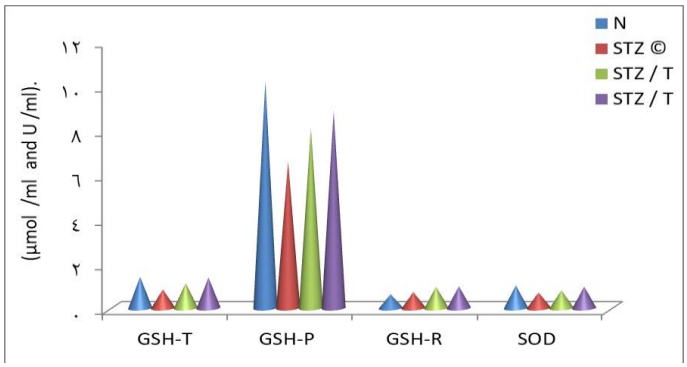
3.6 Antioxidant Enzymes Activities

The coriander (*C. sativum*) extract recorded high phenol and flavonoid contents. There was a linear correlation between the antioxidant activity and total phenol and flavonoid contents of T. foenum graecum [14,24,29]. This suggests that the phenolic compounds contributed significantly to the antioxidant capacity of plant species. The result was consistent with the findings of other workers [90,91,98] who reported positive correlation between total phenols and scavenging activity. The present study was undertaken to determine the effect of dose of coriander (C. sativum) extract containing polyphenol and flavonoids on antioxidant status and blood glucose concentration in STZ induced diabetic rats. Treated rats showed a significant decrease in activitiesof glutathione-S-transferase (GSH-T), glutathione peroxidase (GSH-P) and glutathione reductase (GSH-R) in heart [16,94]. The activities of glutathione dependent enzymes were restored at near normal in rats pretreated with coriander (C. sativum) extract (T/STZ). Glutathione reductase and glutathione peroxidase are essential for maintaining constant ratio reduced glutathione to oxidized glutathione in the cell [16,98]. Decreased glutathione levels in rat administration may be due to its increased utilization in protecting SH containing proteins from lipid peroxides. Reduces availability of glutathione also reduces the activity of glutathione peroxidase and glutathione-S-transferase in rat administration [17,37,103].they reprted inactivation of glutathione reductase in the heart, leads to accumulation of oxidized glutathione which inactivates enzymes containing SH groups and inhibits protein synthesis. Coriander (C. sativum) extract pretreatment restores glutathione level and increases the activities of glutathione peroxidase and glutathione-S-transferase. SOD activity was decreased on coriander (C. sativum) extract administration in accordance with the observation of [12,91,98]. During myocardial infarction, superoxide radicals generated at the site of damage modulates SOD, resulting in the loss of activity and accumulation of superoxide radical, which damages myocardium [29,91]. Coriander (C. sativum) extract pretreatment increases the activity of SOD and it scavenges superoxide radicals and reduces myocardial damage caused by free radicals [98,103]. However, the dose of 200 mg/kg/day produced protection against lipid peroxidation. A slight increase produced by the extract (50 mg/kg/day) in glutathione-S-transferase (GST) activities in the liver tissue in all studied groups. Activities of scavenging enzyme SOD was significantly decreased in liver, heart and kidneys of rats (Fig 7).

The rats treated with coriander (C. sativum) extract containing phenolic and flavonoids showed significant elevation in the activity of SOD when compared with normal rats (80,90,91]. In the case of reduced glutathione, a significant decrease was observed in liver, heart, kidney and blood of rats as shown in Fig8 (a, b,c,d). Activities of GSH-R, GSH-P and GSH-T were significantly reduced in liver, heart and kidney of rats as shown in Fig 8 (a. b. c,). Several reports have shown that hyperlipidemia diminishes the antioxidant defense systems [37,51,82,96], decreasing the activities of SOD and thereby elevating the lipid peroxide contents, resulting in the production of toxic intermediate. The decreased activity of GSH-R should normally result in a decreased concentration of reduced glutathione. The treatment with coriander (C. sativum) extract containing flavonoids has elevated the levels of these parameters in tissues of experimental rats [12,90,91] reported natural flavone, induced a significant increase in Sharma et al. activity. In the present study, the activities of SOD in tissues of rats were significantly decreased when compared to the normal rats (N). The administration of coriander (C. sativum) extract containing phenolic amd flavonoids to the rats showed significant elevation in the activities of antioxidantenzymes.

3.7 Oxidative stress and Antioxidant Potential of Coriander (*C. sativum*) Extract against STZToxicity

Treated animals revealed a significant elevation in plasma, heart, kidney and liver thiobarbituric acid reactive substances (TBARS), while the activities of antioxidant enzymes (GSH-T, SOD and GSH-P) were decreased. On the other hand, plasma total protein and albumin, and body weight were significantly decreased. SZC-induced decrease the activities of antioxidant enzymes, total protein and albumin [17,21,23].



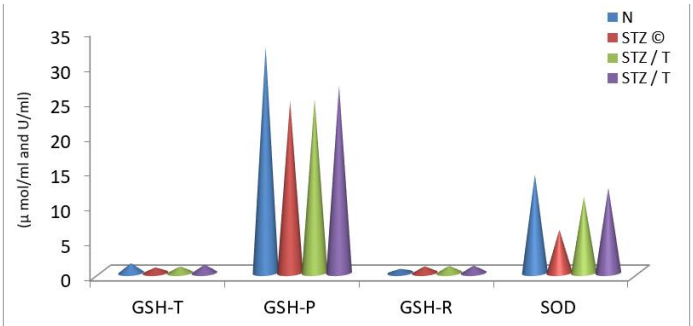


Figure (8b) : GSH-T, GSH-P, GSH-R and SOD activities in liver.

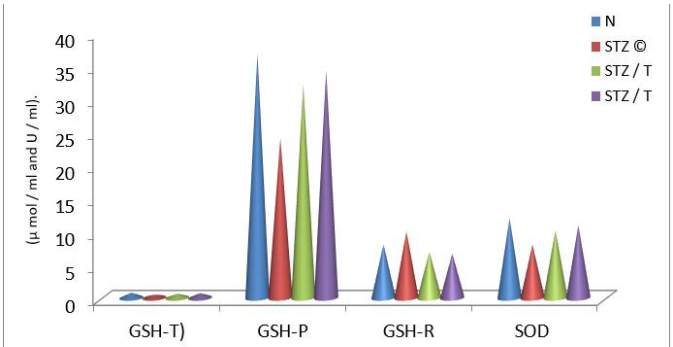


Figure (8 c) : GSH-T, GSH-P, GSH-R and SOD activities in kidny.

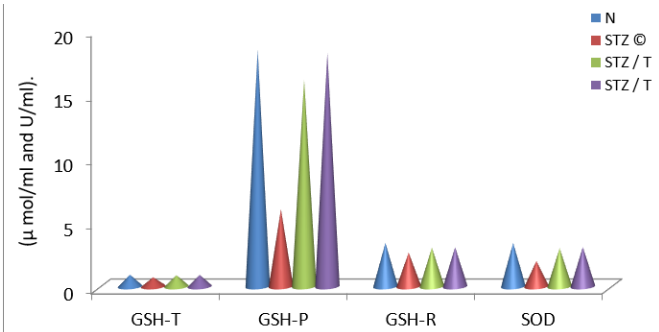


Figure (8d) : GSH-T, GSH-p, GSH-R and SOD activities in heart.

Fig. 8 (a, b, c, d). Activities of of antioxidant enzymes (GSH-T, GSH-P, GSH-R and SOD) in plasma and tissue homogenates (liver, kidney and heart) of male albino rats
(Mean values for 7 rats / group)

Coriander (C. sativum) extract was enhanced superoxide dismutase (SOD) activity by 38 and 64% in liver and kidney respectively. Glutathione reductase (GSH-R) activity was increased by 17% and 30% in liver and kidney in rat groups (STZ/T and T/STZ) compared to those of STZ © rats. Glutathione peroxidase (GSH-P) activity increased significantly in liver and kidney. The present results show that the rats received coriander (C. sativum) extract exhibited higher SOD activity in liver and kidney as compared to those of STZ© rats. Free radicals are the source of lipid peroxidation derived from oxygen and the first line of defense against them is SOD [30,39,90]. Hence, the increased SOD activity in liver (28%) and kidney (64%) suggests that the absence of accumulation of superoxide anion radical might be responsible for decreased lipid peroxidation in these tissues [16,91,103]. This is also evident from the fact that relatively higher decrease in lipid peroxidation in the liver and kidney of rats given coriander (C. sativum) extract being accompanied by the relatively higher increase in SOD activity in these tissues [30,44,82] demonstrated alterations in the liver antioxidants in hyperlipidemic rats. Moreover, GSH-P is responsible for most of the decomposition of lipid peroxide in cells and may thus protect the cell from the effects of peroxides. In the present investigation, higher GSH-P and GSH-R activities in liver and kidney were observed in rats adminstered coriander (C. sativum) extract compared to those of STZ© rats as shown in Fig. 8 (a,b,c,d). The enhanced GSH-P activity with a concomitant increase in GSH-R activity in the liver and kidney from rats received coriander (C. sativum) extract indicates the over activation of glutathione oxidation/reduction cycle [30,37]. Other studires [16,91,98] indicated the aqueous coriander extract exhibiting considerable antioxidant activity. Other studies demonstrate decreases GSH-P activity in the liver of rats received plant extract [37]. In heart tissue, however, enhanced lipid peroxidation in rats received coriander (C. sativum) extract compared to those of STZ© rats may be due to lower GSH-P and GSH-R activities. It can be hypothesized that the reasons for decrease GSH-P and GSH-R activities in heart tissue of of rat group given coriander (*C. sativum*) extract may be inactivate GSH-P which leads to inactivate SOD. Therefore, it is possible that the low GSH-P activity in heart tissue of rat group given coriander (C. sativum) extract (T/STZ and STZ/T) might be due to a loss in total glutathione. It can be concluded that the coriander (C. sativum) extract capable of decreasing plasma TC, TG and VLDL and improve dyslipidemia. Moreover, it also improves antioxidant status by lowering lipid peroxidation and enhancing antioxidant enzymes. Therefore, the hypolipidemic effect of coriander (C. sativum) extract in rats was observed in the present investigation could be valuable for the protection against hyperglycemia, and cardiovascular diseases induced STZ. Coriander (C. sativum) extract rich polphenols may be improve and reduce cholesterol absorption. The chemical analyses of coriander (C. sativum) extract revealed the presence of higher contents of polyphenol and flavonoids.

Flavonoids present in coriander (C. sativum) extract have been reported to have antioxidant and hypocholesterolemic activities [12,14,17], Previous efforts have shown that these flavonoids inhibit oxidation of low density lipoprotein. Therefore, it may be suggested that the hypolipidemic and antioxidant activity of coriander (C. sativum) extract might be correlated to these compounds.t However, there was a linear correlation between the antioxidant activity and total phenol and flavonoid contents. The present result was consistent with the findings of other investigators [91,103] who reported positive correlation between total phenols and scavenging activity. Superoxide anion is harmful to cellular components and scavenging ability of the extracts may be due to the presence of flavonoids [82,90]. The present study examined possible usefulness of coriander (C. sativum) containing mainly quercetin to protect the rat against diabetic effect of STZ and its effect on some antioxidant enzymes (SOD and GSH-P) which can protect cell against oxidative stress in DM. Natural product are rich in polyphenolic and flavonoids exhibits high antioxidant activity and are able to scavenge the radicals of hydroxyl, peroxyl, superoxide. Some studies [82,91,105], reported the hypoglycemic action of the extract in diabetic rats may be possible through the stimulation of glucose uptake by peripheral tissue, inhibition of endogenous glucose production or activation of gluconeogenesis in liver. Therefore, the present results revealed that the extract of coriander (C. sativum) showed a protective effect against SZC toxicity. The role and use natural antioxidants is mainly for preventing oxidative damage in DM [90.98]. The present results indicate that the preventive effects of coriander (C. sativum) may be due to inhibition of lipid peroxidation by its antioxidant nature. Results could provide the potential utility of C. sativum as a source of raw

material for industrial utilization of phenolic. Many investigaors [80,91,98] suggesting that this coriander (C. sativum) extract considered as a a source of natural antioxidants used as substitute of synthetic antioxidants in food industry. The most significant findings of the present study is that the aqueous extract of coriander (C. sativum) at the dose of 200 mg/kg body weight for 30 days have shown beneficial effect not only on blood glucose levels but also on body and organs weight in streptozocin induced diabetic rats.

4. CONCLUSION

Coriander (*C. sativum*) is commonly consumed foods, have a long history consumption of diet ingredients with no record of harm. Coriander (*C. sativum*) extracts containing different components possess bioactivities appears of potential effects on the risk factors of cardiovascular, cancer and infectious diseases due to its contents of polyphenol and flavonoid. The present results suggest the intake of coriander (*C. sativum*) extract containing polyphenol and flavonoid as antioxidant compounds in certain doses is useful to improve the lipid status of STZ-induced hyperglycemic and hyperlipidemic rats, inhibiting lipid peroxidation and activating antioxidant enzymes that may be used for treatment and reduces the death from different diseases.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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