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Protective Effects of Ginger in Streptozotocin-Induced Diabetes Mellitus in Rats

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Abstract

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder characterized by a high blood glucose resulting from defects in insulin secretion and action, which also effect on lipid metabolism. Previous studies revealed that maybe ginger has hypoglycemic activity in diabetic animals in addition to control cholesterol and triglycerides levels in STZ induced diabetic rats.

Method: This study is an experimental research which was done in the first half of 20205. Firstly, the extracts of Fresh rhizomes of ginger (zingiber officinalis) were prepared. Then DM was induced by using streptozotocin (STZ). Rats have fasted for 12 hours before induction of diabetes, IP injection of 45 mg/ Kg body weight STZ. The animal was Ginger extract was started Two weeks before the induction of diabetes and was continued for Two weeks after induction. The control group was injected IP with equivalent amount of buffer. In the next step blood sampling were collected and biochemical analysis was performed. Having collected the data, SPSS 24 was used for the statistical analyses. Descriptive statistics and one–way analysis of variance (ANOVA) followed by DUN can's multiple range test (DMRT) was run to analysis.

Results: STZ injection induced significant hyperglycemia and dyslipidemia in diabetic rats. Treatment with ginger extract, administered before and after diabetes induction, significantly reduced blood glucose, total cholesterol, LDL, and triglyceride levels, while increasing HDL levels. These results suggest that ginger extract has a protective effect against STZ-induced metabolic disturbances and may serve as a potential therapeutic agent for managing diabetes and its complications.

Conclusion: This study demonstrated that ginger extract significantly reduced blood glucose and improved lipid profile in STZ-induced diabetic rats, suggesting its potential ant diabetic and protective effects. Further studies are needed to explore its mechanisms and therapeutic applications.

Key word: Ginger, Diabetes, Blood glucose, Lipid profile

I. Introduction:

Diabetes mellitus is a chronic metabolic disorder characterized by a high blood glucose resulting from defects in insulin secretion and action, which also effect on lipid metabolism [(1)]. The world health organization (WHO)

predicts that the number of cases worldwide will touch 366 million or more by the year 2030 [2]. DM is classified into two major categories type 1 which accounts for 5-10% of cases and type 2 which accounts for more than 90% of diabetes and is associated with metabolic disorders of lipids and carbohydrates [3] . Dyslipidemia is a frequent complication of DM and is characterized by low level of high-density lipoprotein (HDL) and high level of low-density lipoproteins (LDL) and triglycerides (TG) [4]. Diabetes mellitus can be treated by using different drugs including insulin, biguanides, sulfonylureas, and thiazolidinediones' available treatments cause glucose regulation, but fail to prevent lipid alterations this may expose the patients to cardiovascular complications [5]. Insulin therapy reduces hyperglycemia and glycosylated hemoglobin, and delays some diabetes-related morbidity [6]. However, even with insulin therapy, some secondary complications associated with diabetes including heart disease, neuropathy, and hypertension remain overwhelming conditions in diabetic patients [7]. Different traditional medicinal plants have been used for their beneficial effects in combating diabetes and the related complications without side effects. Naturally derived anti-oxidants appear more favorable for reducing diabetes-induced side effects in diabetic patients[8].Among these plants that are scientifically evaluated to have beneficial effects in diabetes are spices such as cinnamon and cloves, others such as ginger, green tea, and mulberry leaves [9]. Previous studies indicated that ginger has better hypoglycemic effects in combination with cinnamon, garlic, and clove [10]. Ginger is an underground rhizome of plant Zingiber officinale belonging to the family Zingberaceae. It has a long history of use as herbal medicine to treat a variety of purposes including anti-migriane, antithrombotic, anti-arthrirtic, anti-inflammatory, anti-nauseal properties, indigestion, and cold induced syndrome [11].Ginger and its active components are strong anti-oxidants agents and have remarkable effects in the treatment of metabolic syndrome abnormalities [12]. Several studies revealed that ginger has hypoglycemic activity in diabetic animals in addition to control cholesterol and triglycerides levels in STZ induced diabetic rats. It is investigated that GLP-1 levels can be regulated through gingerol effect on insulin release [13]. Previous studies demonstrated that oral administration of up to 2 gm/Kg of ginger extract for a long period has wide margin of safety and did not cause any mortality or affect general condition or hematological parameters in male and female rats [14].

II. Aim of the study:

To observe the influence of ginger roots on lipid abnormalities and blood glucose levels in STZ- diabetic rats.

III. Methodology

This study is an experimental research which was done in the first half of 20205. Firstly, Fresh rhizomes of ginger (zingiber officinalis) were obtained from the local market of herbs in Iraq. The extract was prepared by soaking 15 gm of rhizome slides in 500 ml of boiling water for 30 minutes and then filtered and cooled at room temperature and kept in clean drinking bottles then dispensed to the animals orally. The extract was freshly prepared daily for the period of the experiment. 30 healthy adult male Wistar Albino rats weighing between 150-200 gm were housed in cages at controlled temperature(22C) with 12:12 light: dark cycle and had free access to tap water and standard pellet diet for one week adaptation period before the experiment. Rats were housed (5 animals per cage) in standard plastic cages with wood chip bedding. DM was induced by using STZ. It was freshly dissolved in 0.0M citrate buffer, pH 4.5 for intraperitoneal injection (IP). It was prepared in 1 gr vials and kept in cold store and refrigerator temperature (2-8 C) away from light.

Rats have fasted for 12 hours before induction of diabetes, IP injection of 45 mg/ Kg body weight STZ. The animal was allowed to drink a 5% glucose solution overnight to overcome the drug- induced hypoglycemia. The animals were considered as diabetic if their blood glucose levels were above 150 mg/dL on the third day of STZ injection. Ginger extract was started 2 weeks before the induction of diabetes and was continued for 2 weeks after induction. The control group was injected IP with equivalent amount of buffer.

Experiment protocol

The experimental animals (30 rats) were divided into 3 groups; each group contained 10 animals.
Group NC: Normal control rats.
Group DC: Diabetic control without treatment. .

Group DGI: Diabetic rats administered GI extract.
NC and DC groups (control and diabetic without treatment) were supplied with water and fresh food daily for a period of the experiment. DGI group were supplied by ginger, instead of water for the period of the experiment.

Blood sampling

Rats were anesthetized with diethyl ether; the blood samples were collected from orbital venous plexus after overnight fasting. A total of 1 mL was put in small heparinized tubes and serum was obtained by centrifuging each blood sample at 3000 rpm for 10 minutes. Serum was used for the estimation of glucose of rats by enzymatic kits using a spectrophotometer. The treatment continued for 4 weeks. Blood samples were collected from each rat on the 1st and 4th week of the experiment for determination of blood glucose and lipid profile.

Biochemical analysis:

Glucose determination was carried out according to the method of Trinder, 1969 [(15)], While cholesterol was determined by enzymatic method described by Richmond, 1973[(16)]. Triglycerides were determined by colorimetric method as described by Young, 2001[(17)]. HDL is determined in a method described by Lopes-Virella, 1977[(18)].

Statistical analysis

Having collected the data, SPSS 24 was used for the statistical analyses. Descriptive statistics (percentage, mean, and standard deviation) were used to describe the data. Inferential statistics including the Kolmogorov–Smirnov test along with a test of normality was also used. The one–way analysis of variance (ANOVA) followed by DUN can's multiple range test (DMRT) was run to analysis. Statistical comparisons were performed by A p-value < 0.05 was considered statistically significant.

IV. Results of the Study

This chapter presents the finding of the data analysis in tables according to the objectives of the study:

Table (1): Levels of blood biochemical indicators obtained in the control and experimental groups

Parameters Mg/dl	Normal group NC	Diabetic group STZ DC	Pretreated group STZ and ginger DGI	P-value
Glucose	105.8 + 6	353	153.6	0.023
Triglycerides	63	197	98	0.045
Cholesterol	74	106	72	0.001
LDL	35	49	23	0.001
HDL	56	49	83	0.033
				0.017

As shown in Table 1, serum glucose levels in the diabetic control (DC) group, which received no treatment, continued to rise significantly over the course of the experiment compared to other groups. In contrast, diabetic rats treated with ginger extract exhibited a significant reduction in blood glucose levels during the treatment period compared to untreated diabetic rats. Pre-treatment with ginger extract effectively regulated fasting blood glucose, resulting in a marked decrease to 153.6 mg/dl compared with the diabetic control group.

Regarding lipid profile parameters, STZ injection led to a notable increase in total cholesterol and low-density lipoprotein (LDL) levels, while high-density lipoprotein (HDL) levels were significantly decreased compared to normal rats. Pretreatment with ginger extract ameliorated these lipid abnormalities, significantly lowering cholesterol and LDL levels and increasing HDL levels compared to untreated diabetic rats. Specifically, cholesterol decreased from 106 mg/dl in diabetic controls to 72 mg/dl in the ginger-treated group, LDL was reduced from 49 mg/dl to 23 mg/dl, and HDL was markedly elevated from 49 mg/dl to 83 mg/dl. Additionally,

triglyceride levels, which increased from 63 mg/dl in normal rats to 197 mg/dl in diabetic controls, were reduced to 98 mg/dl after ginger treatment, indicating improved lipid metabolism.

Overall, these findings indicate that ginger extract administration, both before and after diabetes induction, exerts a protective effect by significantly improving hyperglycemia and dyslipidemia in STZ-induced diabetic rats. This suggests a potential therapeutic role for ginger in managing diabetes and its associated metabolic complications.

V. Discussions:

This study represents an animal model of insulin-dependent DM. Injection of STZ caused severe hyperglycemia and lipid profile disorders thorough out the study. This results support previous investigation in which the STZ induced diabetes in rats that showed significant higher levels of fasting blood sugar levels compared to normal control rats [19]. The present results demonstrate that the oral administration ginger extract for 2 weeks before diabetes induction and 2 weeks after induction lowered the blood glucose level significantly compared to diabetic rats. Several experimental studies reported that long term administration of ginger extract significantly decreased blood glucose level in type I induced diabetic animals [20, 21]. A number of animal studies supported the hypoglycemic effect of ginger extract in type 2 DM. Clinical trials revealed that long period of ginger supplementation for patients with Type 2 DM lowered blood glucose, improved insulin sensitivity and lipid profile. Akhani et al 2004 observed that ginger juice exhibits hypoglycemic effect in both normal and STZ - induced diabetic rats [22]. Mascolo et al 1989 reported significant hypoglycemic effect in normal rabbits at different times at variety of doses [23].

In vitro studies reported that the possible mechanism of ginger hypoglycemic action may be due to enhance insulin sensitivity as a result of increasing the glucose uptake by skeletal muscles and this is related to 6-gingerol [24]. Other studies revealed that this effect was due to reduction of glucose absorption from intestine [25] and its effect on the activities of glycolytic enzymes. Several studies demonstrated that ginger can antagonize the suppression effect of serotonin receptors on insulin. Other possible mechanism explained the effect of ginger extract as hypoglycemic agent by its inhibition of glucose reabsorption in proximal tubules [26]. Hyperlipidemia is a metabolic complication of DM characterized by elevated levels of cholesterol, triglycerides, and phospholipids [27]. The results demonstrated that there was a significant increase in total cholesterol, triglycerides, LDL- cholesterol, and decrease in HDL cholesterol in STZ – induced diabetic rats. These findings similar to previous studies that confirm disorders in lipid profile in STZ induced diabetes in rats. Hyper cholesteremia in this model is due to increased intestinal absorption and synthesis of cholesterol (11).Oxidative stress may be the cause of hyperlipidemia in diabetic rats due to formation of High level of free radicals and lipid peroxides that play important role in the development of atherosclerosis [14]. Ginger extract inhibits oxidative stress and inflammation by enhancing antioxidant enzymes and TNF-alpha activity in STZ- induced diabetic rats [17]. The antioxidant activity may be due to high polyphenol content in ginger .Ginger also may elevate the activity of hepatic enzyme that is responsible for conversion of cholesterol to bile acids [18]. Presence of niacin in ginger causes increased clearance of VLDL, lower TG levels, increase hepatic uptake of LDL, and inhibition of cholestrogenesis. When ginger added to the animal diet, a considerable increase in the pancreatic and intestine lipase that have role in lipid digestion.

VI. Conclusions:

The results of the present study showed that induction of diabetes using STZ led to a significant increase in blood glucose levels and lipid profile disturbances, including elevated cholesterol and LDL levels and reduced HDL levels in laboratory rats. However, administration of ginger extracts before and after diabetes induction significantly reduced blood glucose levels and improved the lipid profile. These findings suggest that ginger may possess antidiabetic and protective effects against the metabolic complications associated with diabetes. Given the promising results of this study, it is recommended that further research be conducted using different doses of ginger extract over longer time periods and on other animal models and human subjects, in order to better understand the underlying mechanisms of its antidiabetic effects. Additionally, investigating the effects of

ginger on other parameters such as inflammatory markers, oxidative stress, and tissue changes in diabetes may open new avenues for its therapeutic use in managing diabetes and preventing its complications.

Ethics approval

The study was approved by the Research Deputy and Research Ethics Committee of Al-Bayan University.

Conflict of interest

The author declares no competing interests.

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