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Evaluation of Ginger Rhizomes Extract Effect on Glucose Level, Lipid Profile and Liver Function in Induced Alloxan Diabetic Mice.

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ABSTRACT

In recent years, plant extracts have been witnessed a special attention due to the unique properties of these types of extracts to act as antioxidants, antimicrobials, antitumor and antidiabetic agents. This study was aimed to establish the effect of ginger rhizomes extract toward hyperglycemia, hyperlipidemia, liver function and kidney function in alloxan diabetic mice. Ethanolic ginger extract was prepared from Ginger rhizomes using 70% ethanol as extraction solvent. Alloxan monohydrate was used to induce diabetes by a dose of 150 mg/ kg body weight (BW). Forty healthy mice have been divided into four groups. The first group includes 10 normal mice that were injected with 0.1 ml (5% W/V) of physiological saline (negative control, NC). 30 mice were injected with 0.1 ml of alloxan (150 mg/kg BW) to induce diabetes, which were subdivided into three groups, which represent, second group, third group and fourth group. Second group represents diabetic control (positive control, PC). Group3 and group 4 represent the diabetic groups that were treated with 50 mg/kg and 100 mg/kg of ginger extract for 30 days, respectively. Blood samples were collected by heart puncture at the end of treatment period with ginger extract. Glucose, insulin, total antioxidants (TAO), GOT, GPT, ALP, TC, TGs, HDL, creatinine, urea and uric acid were evaluated in all the studied groups. The results revealed that ginger extract was lowered the levels of glucose, TAO, TGs, urea and raised the level of HDL to the normal level in comparison with both negative and positive control groups. Also, ginger extract was reduced the levels of TC, GOT, GPT, ALP and raised insulin level toward the normal value in compared to the normal control. The results confirmed the potential role of ginger extract toward hyperglycemia, hyperlipidemia together with improvement of liver function and kidney function in alloxan induced diabetic mice.

Keywords: ginger rhizomes extract, hyperglycemia, hyperlipidemia, alloxan diabetic mice

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INTRODUCTION

At last two decades, plant extracts have more attention in medicinal applications [1, 2]. Ginger rhizomes have a numerous medical applications like gastrointestinal disorders and anti-inflammatory effect [3, 4]. A cheap and easy holistic approach is required to apply for acceptability by all categories of people due to increase of global prevalence of diabetes mellitus [5]. The effects of ginger extract in alloxan-induced diabetes and propylthiouracil-induced hypothyroidism in rats was studied and referred to that the activity of ginger extract in hypothyroidism rats was more than in diabetic rats in reducing LDL and TC, in addition to Glucose levels which were found to be reduced in ginger- treated diabetic groups [6].

In recently study, the effect of ginger extract against diabetes induced heart abnormalities in rats, the study was concluded that ginger extract reduced structural heart abnormalities in diabetes rats, these results had been attributed to the improvement of liptin, C-reactive protein, cathepsin G, homocystein, apolipoprotein A and B levels [7]. Another study that conducted by Khandouzi N, et al which elucidated the effect of ginger extract on type 2 diabetes patients, the study confirmed that the ginger extract improve glycated hemoglobin A1c, blood sugar, malondialdehyde and apolipoproteins A,B [8].

The effects of cinnamon, cardamom, saffron and ginger rhizomes extract on diabetic patients type 2 were investigated as supplementary remedies; the results of this investigation were explained that the herbal remedies had considerably beneficial effects on cholesterol rather than other measurements of oxidative stress, glycemic control and inflammation [9]. More recently, it was reported that the activity of ginger extract as anti-diabetic material was recommended as an important dietary supplements for patients suffering from diabetes type 2 due to the active ginger components, gingerols, shogaols and paradols, paradol considers a major metabolite of shogoal. Shogoal play a key role in reducing of blood glucose, cholesterol and body weight in case of high-fat diet-fed mice [10].

Efficiency of ginger rhizome in treatment of diabetes was investigated via randomized clinical trials, it was recorded that blood glucose and HbA1c can be lowered by ginger root supplementation; furthermore, it may be effective factor for managing diabetes mellitus when combined with dietary and life style elements [11]. In more recent study, the aqua-alcoholic extract of Zingier effect was estimated toward retina in diabetic rats in term of arginase activity. The study was elucidated that ginger extract might be a promising therapeutic substance for diabetic retinopathy disorder [12].

The aim of the present study is to investigate the effect of hydro-alcoholic extract of ginger rhizomes on hyperglycemia, lipid profile, liver function and kidney function in induced alloxan diabetic mice.

MATERIALS AND METHODS

Ginger rhizomes extraction

Ginger rhizomes, which were obtained from the local market, were washed well and cut off into small pieces and left to dry at room temperature for two weeks, then the small dried pieces were grinded by agate mortar and pestle to obtain fine powder of ginger rhizomes. 100 grams from ginger rhizomes powder were extracted with 500 ml of 70% ethanol solvent. The mixture was mixing by magnetic stirrer at room temperature for 24 hrs. Then, it was filtrated and the filtrate was poured into a wide dish to evaporate. The dried extract was scraped and placed in a sealed vial and stored in a dark place.

Animals care

Forty healthy mice have been used in this study. They were purchased from animal house/ biotechnology center in al-Nahrain University. The animal age is three months old; the weight of each one is about 30 grams. The animals were lived in clean cages that washed weekly with soap and tap water and sterilized with 70% ethanol along study period. Mice were exposed to 12 hours light program at room temperature of $24\pm2\ ^{\circ}$ C.

Induction of diabetes

Mice were induced with diabetes by injection (IP) of alloxan monohydrate in physiological saline (5% w/v) at a dose of 150 mg/kg body weight in a volume of 0.1 ml. The diabetic state was confirmed through a period of 48 hours after alloxan injection by weight loss and hyperglycemia.

Experimental groups

Four groups of mice consisting ten mice for one were classified as follows:

Group 1: normal mice injected with 0.1 ml (5% w/v) of physiological saline (negative control, NC).
Group 2: normal mice injected with alloxan (0.1 ml) to induce diabetic mice (positive control, PC)
Group 3: diabetic mice treated with 50 mg/ml of ginger rhizomes extract for 30 days after injection with alloxan (treated diabetic group 3).
Group 4: diabetic mice treated with 100 mg/ml of ginger rhizomes extract for 30 days after injection with alloxan (treated diabetic group 4).

General method:

Blood samples were collected occasionally by heart perforation at the end of treatment period with ginger rhizomes extract. The mice fasted over night and killed by cervical dislocation.

Biochemical measurements:

All the studied biochemical parameters were estimated using agape diagnostics kits. Serum glucose level was determined using (GOD-POP) method [13]. Total cholesterol TC), triglyceride (TGs) and high density lipoprotein (HDL) were determined by GPO-TOPS methods [14-16]. Activities of SGOT, SGPT were estimated according to Reitman S and Frankel S. [17] while ALP had been determined by Kind and King Method [18]. Creatinine was determined according to Atriss, J.D et al method [19]. Urea and uric acid were evaluated depending on urase/GLDH and uricase TOPS methods respectively [20, 21]. Total antioxidants were estimated as reported in [22].

Statistical analysis:

All the studied parameters data in this work are expressed as mean ± SD. Data were evaluated statistically using analysis of variance [ANOVA] by SPSS program version 17 [23]. $P < 0.05$ was taken to indicate of the significant differences.

RESULTS AND DISCUSSION

Table (1) shows the results of serum glucose, insulin and total antioxidants (TAO) levels of all the studied groups. The level of fasting blood sugar in positive control (diabetic control, G2: 188.53±16.94mg/dl) was higher than other groups due to induce the diabetes by alloxan action. The level of glucose was decrease in both treated groups with ginger extract (G3: 122.65±11.74, G4: 100.33±9.80mg/dl) in comparison to the positive control, at the same time, the results showed that glucose level in group 4 was reached to the normal level of glucose in compare to the negative control (98.44±10.52 mg/dl) by the action of ginger extract dose, 100 mg/kg weight. In contrast, the action of ginger extract dose (50 mg/ml) on glucose level was decrease the upper glucose value (188.53±16.94 mg/ml) to 122.65±11.74 mg/dl in comparison with the higher dose (100 mg/dl), but not reached to the normal value (98.44±10.52 mg/ml) of fasting blood glucose.

The results also showed the effect of ginger extract on insulin level. The level of insulin was increased in both the treated groups with ginger extract (G3 74.52±8.06:, G4: 74.28±6.91 µIU/ml) in comparison to the positive control, but not reached to the normal value in compare to the negative control (90.34±8.05 µIU/ml).

In contrast of glucose and insulin levels, total antioxidants (TAO) values in both treated groups (G3: 0.32±0.012, G4: 0.33±0.010 mM) was increased up to the normal value (G1: 0.34±0.018 mM) in compare with negative and positive controls, respectively (G1: 0.34±0.018, G2: 0.22±0.011 mM). This result referred to that

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both doses of ginger extract (50 and 100 mg/kg weight) gave the similar effect on TAO activity of the treated groups, in other word, in the case of total antioxidants activity in induced alloxan diabetic mice, the minimum dose (50 mg/kg) enough to treated the disorder of TAO to the normal value. This finding revealed that ginger extract possesses a good antioxidants property among other phytochemicals.

Table 1: shows glucose, insulin and total antioxidants (TAO) levels in all the studied groups.

Groups	glucose level (mean ± SD) mg/dl	insulin level (mean ± SD) µIU/ml	TAO level (mean ± SD) Mm
Group 1 negative control	98.44±10.52[a]	90.34±8.05[a]	0.34±0.018[a]
Group 2 positive control treated with alloxan	188.53±16.94[b]	64.48±6.55[b]	0.22±0.011[b]
Group 3 treated with alloxan + 50 mg/kg of ginger extract	122.65±11.74[c]	74.52±8.06[c]	0.32±0.012[a]
Group 4 treated with alloxan + 100 mg/kg of ginger extract	100.33±9.80[d]	74.28±6.91[c]	0.33±0.010[a]

A,b,c,d are significant differences for each parameter in the same column

The values of total cholesterol (TC), triglycerides (TGs) and high density lipoprotein (HDL) were recorded for all the studied groups as shown in table (2). It was observed that TC level in positive control (206.07±21.08 mg/ml) was increased in compare to the negative control (171.20±19.21 mg/ml) due to the action of alloxan on this group, while, its level in both treated groups (G3: 185.84±18.57, G4: 176.73±19.08 mg/ml) was decreased toward normal value in comparison with both positive and negative controls due to the action of ginger extract doses of 50 and 100 mg/kg body weight on both group 3 and group 4 (G3: 185.84±18.57, G4: 176.73±19.08 mg/ml), respectively.

The results also showed that the level of TGs in diabetic control (G2:123.34±11.75 mg/ml) was higher than negative control (G1:112.66±14.280). After the treatment by ginger extract, the level of TGs was decreased to the normal value in treated groups, group 3 and group 4 (G3: 116.20±13.29, G4: 115.09±10.32 mg/dl), respectively.

Table 2, also, showed decreasing in HDL level in diabetic group (G2: 39.21±6.58 mg/ml) than negative control (G1: 48.08±5.40 mg/ml), whereas its level increasing toward the normal value after treatment with ginger extract in both treated groups (G3: (47.08±4.87, G4: 47.55±5.72 mg/ml), thus, the effect of ginger extract on triglycerides was observed at both doses (50 and 100 mg/kg body weight) that returned the abnormal value of HDL to the normal condition in both treated groups.

Table 2: shows total cholesterol (TC), triglyceride (TGs) and high-density lipoproteins (HDL) levels in all the studied groups.

Groups	TC level (mean ± SD) mg/dl	TGs level (mean ± SD) mg/ml	HDL level (mean ± SD) mg/ml
Group 1 negative control	171.20±19.21[a]	112.66±14.28[a]	48.08±5.40[a]
Group 2 positive control treated with alloxan	206.07±21.08[b]	123.34±11.75[b]	39.21±6.58[b]
Group 3 treated with alloxan + 50 mg/kg ginger extract	185.84±18.57[c]	116.20±13.29[a]	47.08±4.87[a]
Group 4 treated with alloxan + 100 mg/kg ginger extract	176.73±19.08[d]	115.09±10.32[a]	47.55±5.72[a]

a, b, c, d are significant differences for each parameter in the same column

The effect of ginger extract on GOT, GPT and ALP in all the studied groups was observed in table 3. The results showed decreasing in levels of GOT, GPT and ALP in both treated groups (G3:44.38±5.37,

58.33±7.27, 223.75±18.96 G4: 42.65±4.91, 57.09±6.33, 221.85±20.48 U/L) respectively, in comparison with the positive control (diabetic control: 67.08±8.04, 72.06±7.85, 277.90±22.18 U/L) respectively, but not to normal values of GOT, GPT and ALP as shown in table 3, this means a limited impact of the ginger extract on these disorders. In another word, ginger extract was improved the levels of these enzymes toward the normal condition.

Table 4 revealed levels of creatinine, urea and uric acid in all the studied groups. The results showed no effect on each of creatinine and uric acid disorders when both diabetic groups treated with ginger extract (G3: 161.85±16.88, 7.33±1.74 and G4: 159.22±16.37, 6.59±0.89) respectively. Whereas the level of urea was decreased at both doses in the treated groups (G3: 23.65±4.08 and G4: 23.09±5.16) to the normal value in comparison with both positive and negative controls (G2: 24.31±6.38 and G1:22.36±4.52), respectively.

Table 3: shows GOT, GPT) and ALP levels in all the studied groups.

Groups	GOT level (mean ± SD) U/L	GPT level (mean ± SD) U/L	ALP level (mean ± SD) U/L
Group 1 negative control	33.62±4.51[a]	51.33±8.05[a]	210.43±18.47[a]
Group 2 positive control treated with alloxan	67.08±8.04[b]	72.06±7.85[b]	277.90±22.18[b]
Group 3 treated with alloxan + 50 mg/kg ginger extract	44.38±5.37[c]	58.33±7.27[c]	223.75±18.96[c]
Group 4 treated with alloxan + 100 mg/kg ginger extract	42.65±4.91[c]	57.09±6.33[c]	221.85±20.48[c]

a, b, c, d are significant differences for each parameter in the same column

Table 4: shows creatinine , urea and uric acid levels in all the studied groups.

Groups	Creatinine level (mean ± SD) mg/dl	Urea level (mean ± SD)mg/ml	Uric acid level (mean ± SD) mg/ml
Group 1 negative control	128.66±14.83[a]	22.36±4.52[a]	4.06±0.97[a]
Group 2 positive control treated with alloxan	165.47±17.04[b]	24.31±6.38[b]	7.33±1.74[b]
Group 3 treated with alloxan + 50 mg/kg ginger extract	161.85±16.88[b]	23.65±4.08[a]	6.88±0.96[b]
Group 4 treated with alloxan + 100 mg/kg ginger extract	159.22±16.37[b]	23.09±5.16[a]	6.59±0.89[b]

a,b are significant differences for each parameter in the same column

Alloxan and streptozotocin are considered as the most used diabetogenic compounds to induce diabetes in experimental animal models [24, 25]. It was reported that the daily dose of ginger extract of 2000 mg/kg BW of rats for 35 days was not associated with any disorders that could be occurred due to its toxicity [26].

Our findings in present study indicated that treatment by ginger extract at doses of 50 and 100 mg/kg body weight of diabetic mice for 30 days decreased the levels of glucose, TC, TGs and increased both insulin and HDL levels toward the normal values, these findings were in agreement with previous studies [27, 28]. This study was showed that treatment of diabetic mice by ginger extract exhibited significant improvement in biological evaluation including glucose, insulin, lipid profile, liver function and kidney function in different values toward their normal levels in comparison with non treated group (positive control). These results correspond with other literature [29].

Generally, medicinal plants have different mechanisms of hypoglycemic and hypolipidimic action to reduce of glucose and lipid levels in the treated diabetic mice related to non treated ones. In ginger extract, this can be occurred due to the good antioxidants properties of ginger that it can protect the pancreas tissues

from lipid peroxidation in the case of diabetic animals [30,31]. Other mechanisms are including the inhibition of dietary lipid absorption or of its production in liver or by activation of bilary secretion of cholesterol beside to its secretion in feces [32-33]. Our results are in agreement with earlier studies [34-37].

The results in this study were revealed a high antioxidant activity of ginger extract, this result consistent with the more recent study that studied the antioxidant property of ginger extract in patients with cancer [38]. Also, liver function and kidney function parameters were improved after treatment with ginger extract at 50 and 100 mg/kg body weight, this result is in agreement with the recent studies [39, 40].

CONCLUSION

The levels of fasting blood glucose, insulin, total antioxidants, lipid profile, liver function enzymes and kidney function parameters in alloxan induced diabetic mice can be changed toward its normal values related to diabetic condition (positive control) and the normal case (negative control). Accordingly, it can be concluded that ginger extract possesses a potential hypoglycemic and hypolipidemic activities in alloxan induced diabetic mice, in addition to its excellent antioxidants properties that can observed in this type of experimental model in biological system. On the basis of our findings, it can be recommended that ginger rhizome possesses an excellent antioxidants property and consequently it represents a good supplement.

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