RESEARCH TYPE

The Effect of Oral Administration of Green Tea and Ginger Extracts on Blood Glucose in Diabetic Rats

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ABSTRACT

In recent years, green tea and ginger have become a subject of interest because of their beneficial effects on human health. The present study aimed to compare the effect of long term administration of green tea and ginger, each alone to the impact of their combination on blood glucose level in streptozotocin-induced diabetic rats.

Method: A group of 50 male albino rats was divided into five groups (10 rats each group). The normal control group (NC) administered tap water, other animals were injected by streptozotocin 45mg/Kg body weight intraperitoneally to induce diabetes mellitus (DM) and then divided into four groups ,diabetic control (DC) without treatment, diabetic group administered green tea extract for four weeks (DGT), diabetic group administered ginger extract for four weeks (DGI), and diabetic group administered mixture of green tea and ginger for four weeks (DGG), then we compare the blood glucose level at 1st,2nd,3rd, and 4th week of experiment.

Results: We observed that in groups whose water drink was substituted by green tea and ginger extract, the blood glucose level was significantly ($p < 0.05$) reduced as compared to diabetic animals. Importantly, we observed that blood glucose level was near the control level when green tea was administered simultaneously with ginger extract.

Conclusion: A combination of green tea and ginger may be of great value as a hypoglycemic agents in diabetic patients, the synergism of their effect on glucose regulation process is underlying this results.

Keywords: Blood glucose, Diabetes mellitus, Ginger, Green tea, Streptozotocin.

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INTRODUCTION

Diabetes mellitus (DM) is a condition in which the pancreas no longer produces enough insulin or cells stop responding to the insulin that is produced, so that glucose in the blood cannot be absorbed into the cells of the body. The incidence of DM disease in 2010 was about 285 million people worldwide and is projected to increase to 438 million in 2030.[1]

Traditional plant remedies or herbal formulations exist from ancient times and are still widely used for the treatment of hyperglycemia all over the world. In some plants like (ginger, green tea, cinnamon, cloves, garlic, and curcumin), active hypoglycemic principles have been isolated, and their mechanism of action studied.[2-4]

Recently, green tea and ginger have been widely studied to assess their beneficial effects in the treatment and prevention of diabetes mellitus.

Green tea GT (*Camellia sinesis*), which is a member of the Theaceae family, its leaves are used to produce the popular beverage tea. Green tea has been widely studied to assess its beneficial effects and medicinal properties in the treatment and prevention of many diseases such as diabetes mellitus.[1,5] The health benefits are related to the polyphenols, which are known as flavonols or catechins. The main catechins are epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC). One cup (200 m) of green tea supplies 140, 65, 28, and 17 mg of these polyphenols, respectively.[6]

Several studies suggested that the administration of green tea or its main constituents by different routes, in various doses, and in different lengths of time lowered the blood glucose level in type 1 and type 2 induced diabetic animals.[7-9] Drinking green tea by Japanese might be a factor in preventing the onset of type 2 DM[10].

Ginger (*Zingiber officinale)* is an underground rhizome of plant belonging to the family Zingiberaceae. It has been used for cooking and to treat a host of ailments throughout Asia, especially in India and China. It can be consumed as a fresh or dried root and is often prepared in teas, soft drinks, and loaves

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of bread. The principal use is to treat nausea due to motion sickness, general anesthesia and chemotherapy.[11] The pungent principles are gingerols (8-gingerol and 10- gingerol), during drying and storage, gingerols are partly dehydrated to the corresponding shogaols which may undergo further reduction to form paradols.[12] In several animal-based types of research, ginger extract and its components were used in various doses, for different periods, and in diverse routes of administration in both types of DM. They exerted a hypoglycemic effect in both types of DM[13-16]. Also, clinical trials revealed that ginger supplementation lowered blood glucose in patients with type 2 DM when administered for an extended period.[17] It was proved that ginger exerted a hypoglycemic effect in normal rats[18,19] and mice.[20]

AIM OF RESEARCH

Our study aimed to evaluate the hypoglycemic effects of green tea and ginger each one alone and to compare these effects to the effect of their combination on blood glucose of diabetic rats. We chose these medicinal plants because they are widely used, cheap, available, and easy to prepare the beverage.

MATERIAL AND METHODS

Plant materials

The fresh green tea leaves (*Camellia sinensis*) and rhizomes of ginger (*Zingiber officianal)* were obtained from the local market of herbs in Amman-Jordan.

Extracts preparation and route of administration

Plant extracts were prepared similarly as is typically done by humans. 15 gm of ginger (GI) rhizome slides were soaked in 500ml of boiling water for 30 min and were then filtered. Dried green tea (GT) leaves (1.75 gm) were added to 200 ml of boiled water cooled to 80C. The solution kept to stand for 2.5 minutes of infusion before filtered; these conditions aimed to prepare a tea with a rich and adequate concentration, but also to obtain a pleasant beverage. The extracts of GI and GT cooled to room temperature and dispensed to the animals in clean drinking bottles. The extracts freshly prepared daily for the period of the experiment.

Animals

Fifty healthy adult male Wistar Albino rats weighing between 150-200 gm were bred in the animal house of Applied Sciences University in Amman. Animals were housed in cages at controlled temperature (22C) with 12:12h light: dark cycle and had free access to tap water andstandard pellet diet for one week adaptation period before the experiment. Rats were housed (10 animals per cage) in standard plastic cages with wood chip bedding.

Induction of diabetes

Diabetes mellitus (DM) was induced by using streptozotocin (STZ). It was freshly dissolved in 0.05 M 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 diabetes was induced by IP injection of 45mg/kg body weight STZ. The animals were allowed to drink a 5% glucose solution overnight to overcome the drug-induced hypoglycemia. The animals were considered as diabetic if their blood glucose values were above 150 mg/dl on the third day of STZ injection. The treatment of green tea and ginger was started on the 7th day after STZ injection, and this was considered as the first day of treatment. The treatment was continued for 4 weeks. The control group was injected IP with an equivalent amount of buffer.

Experimental protocol

The experimental animals (50 rats) were divided into 5 groups; each group contained 10 animals.

Group NC: Normal control rats.

Group DC: Diabetic control without treatment.

Group DGT: Diabetic rats administered GT extract.

Group DGI: Diabetic rats administered GI extract.

Group DGG: Diabetic rats administered a mixture of GI andGT extracts.

NCandDC groups (control and diabetic without treatment) were supplied with water and fresh food daily for a period of the experiment.

DGT, DGI, and DGG were supplied by green tea, ginger, and their mixture, respectively, 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,2nd,3rd, and 4th week of the experiment for determination of blood glucose.

Statistical analysis

All values are expressed as mean± SD. Statistical comparisons were performed by one–way analysis of variance (ANOVA) followed by DUN can,s multiple range test (DMRT). A p-value < 0.05 was considered statistically significant.

RESULTS

The present study showed that STZ induced a highly significant increase in serum glucose. Glucose level was increased from 69±11.5 mg/dl (control) to 200.5 ± 25.5 mg/dl after induction of diabetes by using 45 mg/kg of STZ which persisted in a high level during the time of experiment without treatment. The results are shown in Table 1 and plotted in Figure 1.

In diabetic rats, supplementation of GT extract for 4 weeks decreased the blood glucose level from 200.5 ± 25.5 to 80 ± 5.5 mg/dl (Table 1, Figure 2). The administration of GI for four weeks also decreased the glucose level significantly. It reaches82 ± 14.7 at the end of the experiment (Table 1, Figure 3).

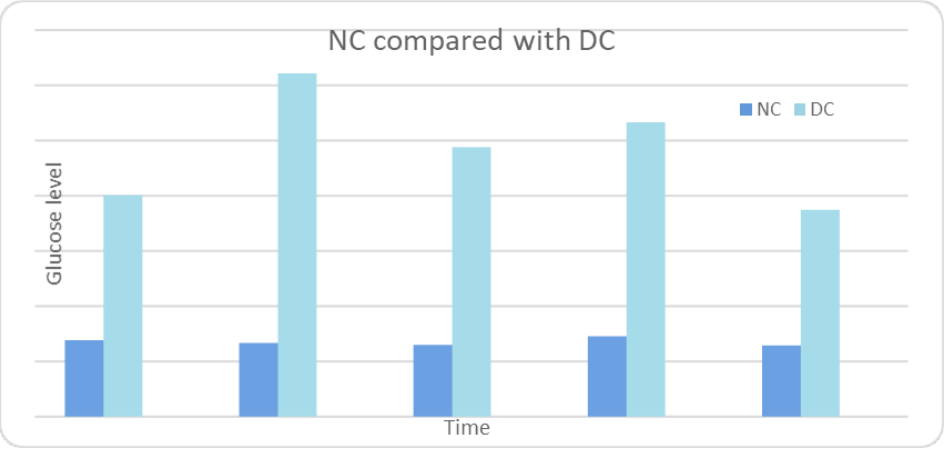

Figure 1: Blood glucose level in the diabetic control group (untreated) compared with normal control during the time of the experiment.

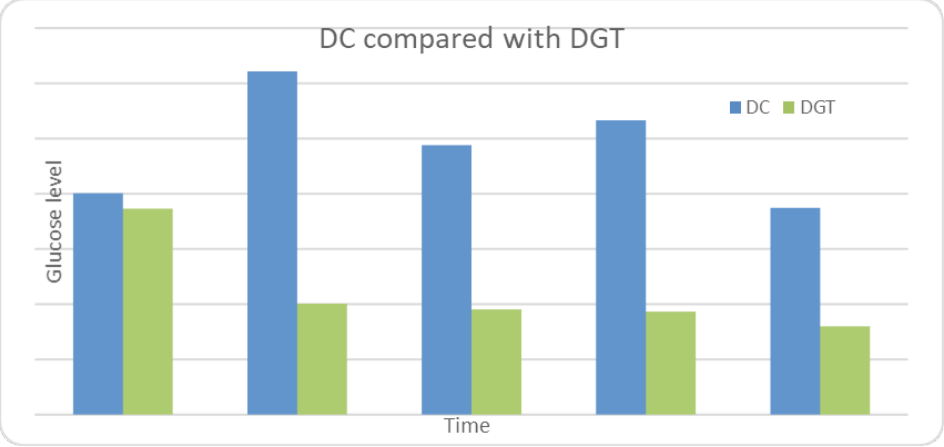

Figure 2: Blood glucose level in the diabetic control group compared with green tea administered group during the time of the experiment

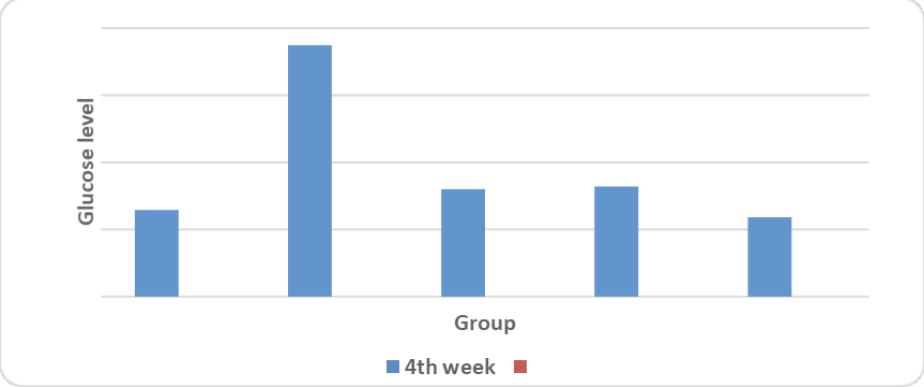

Figure 5: Blood glucose level in treated and untreated groups compared with the control group at the end of the experiment.

Table 1: Blood glucose levels of all groups during the experiment period.

Groups/time	*0 time*	*1week*	*2nd week*	*3rd week*	*4th week*
NC	69.2 ± 11.5	66.8	± 13.8 65 ± 6.3	72.8 ± 9.9	64.5 ± 9.7
DC	200.5 ± 25.5*	310.8 ± 22.2*	244 ± 23.7*	266.6 ± 20*	187.3 ± 37.6*
DGT	186.5 ± 20	100.5 ± 30.56	95.3 ± 18.	93.3 ± 30.5	80 ± 5.5**
DGI	210 ± 18.1	120.4 ± 23.9	100. ± 20.7	95.7	± 10 82 ± 14.7**
DGG	220 ± 8.5	90.6 ± 14.7	67.2 ± 21.4	68.3 ± 16.8	59.1 ± 11.7 **

Values are expressed as the mean ± S.D. of 10 animals.
*Diabetic control Vs control.
**Treated groups are compared with diabetic control.

This reduction due to GT or GI administration separately was not enough to reach normal levels but it is significantly lower than diabetic rats.

It is clear from the data in the table 1 that the serum glucose levels of the DC animals (leave untreated) continued to increase during the 4 weeks of the experiment compared with other groups. In contrast, the ginger and green tea treated diabetic rats exhibited significantly reduced glucose levels during the treatment period when compared with the diabetic control rats.

The administration of GI and GT simultaneously to the diabetic rats significantly reduced plasma glucose levels to reach 59.1 ± 11.7 mg/dl when compared with the diabetic group without treatment (Table 1, Figure 4 and 6). This reduction is also less than the blood glucose level in DGT and DGI with $p < 0.05$. At the end of the experiment, the BGL in rats receiving GGT and GGI is nonsignificant when compared with the control level (Table 2 and Figure 5).

DISCUSSION

Several investigators reported that treatment with STZ produces DM, evident by the increase in blood glucose levels[21]. In the present study, we used 45 mg/kg of STZ IP. The results confirmed that STZ at this dose produces DM, and this evidenced by an increase in blood glucose level.

Our work demonstrated that oral administration of GT extract for 4 weeks lowered blood glucose level in diabetic rats, this finding is consistent with other studies using the extract orally showed a decrease in glucose level in comparison with diabetic rats.[22,23]

In vitro and *in vivo* studies suggested different mechanisms by which tea and its components may normalize glucose level in diabetes mellitus, EGCG was observed to protect pancreas cells by ameliorating cytokine-induced beta cells damage *in vitro*[24] and by preventing the decrease in islets mass induced by treatment with multiple doses of STZ *in vivo*.[25] Another study

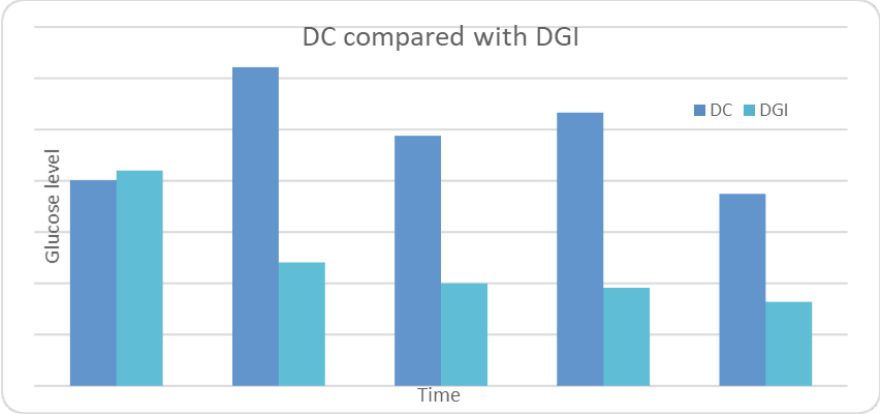

Figure 3: Blood glucose level in the diabetic control group compared with ginger administered group during the time of the experiment

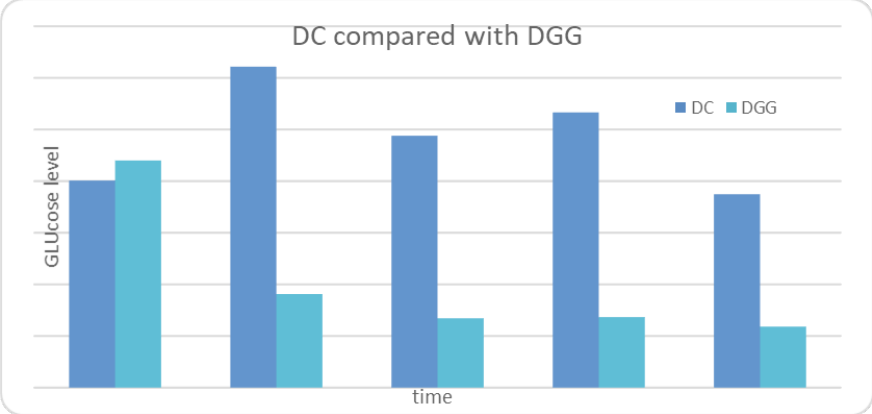

Figure 4: Blood glucose level in the diabetic control group compared with green tea and ginger administered group during the time of the experiment.

Table 2: Blood glucose level in all groups at the end of the experiment compared with zero time.

Group	*0 time*	*4th week*
NC	69.2 ± 11.5	64.5 ± 9.7
DC	200.5 ± 25.5	187.3 ± 37.6**
DGT	176.5 ± 20	80± 5.5**
DGI	210 ± 8.5	82 ± 14.7**
DGG	220 ± 8.5	59.1± 11.7*

* nonsignificant vs. control.
** significantly vs. control

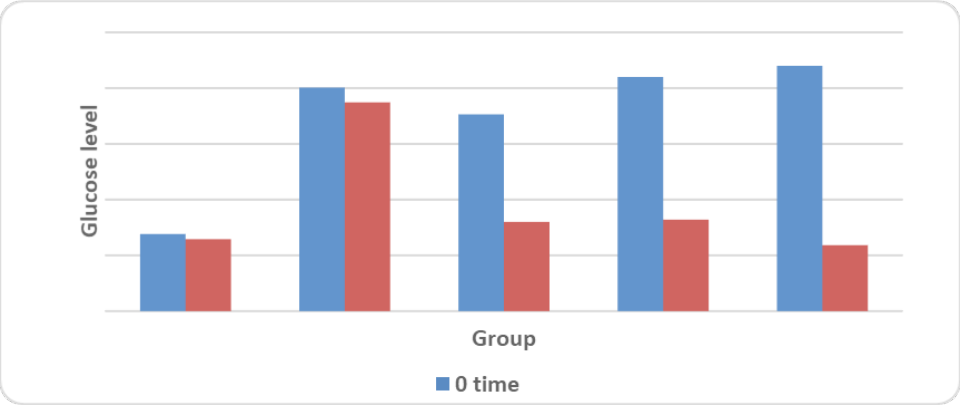

Figure 6: Blood glucose level of treated groups compared with the untreated group at zero time and after 4 weeks of experiment.

suggested that EGCG controls dietary glucose uptake in the intestinal tract by its action as SGLT1 (glucose transporter) an antagonist like molecule.[26] The antihyperglycemic activity of green tea was also ascribed to enhance insulin release[27] and to improve insulin sensitivity and glucose tolerance.[28] Chen *et al*.,2005[29] suggested that there is a direct connection between antioxidant activity and the hypoglycemic activity of green tea.

When ginger was administered for four weeks also showed hypoglycemic effect, and this agreed with other studies that demonstrated that ginger or its components have a hypoglycemic effect and decrease the complications of DM.1 Possible mechanisms related to its hypoglycemic effects were extensively studied. *In vitro*, improved diabetes a result of increased glucose uptake in gingerol treated L6 myotubemic cells[30] and L6 cultured rat skeletal muscle cells.[31] It was also reported that 6-gingerol promoted glucose uptake in the responsive 3T3-LI adipocyte.[32] It was reported that ginger has an effect on digestive enzymes to reduce glucose absorption[31]. Several reports have demonstrated that serotonin receptor (5-HT3) may be involved in the hypoglycemic effect of ginger, serotonin receptors mediated suppression of insulin release, and ginger can antagonize this suppression effect.[33] Several studies demonstrated that ginger improved lipid profiles, and it had a antiobesity impact and subsequently reduced insulin resistance.[34,35] A long term administration of ginger extract to diabetic rats indicated that the antidiabetic effect of ginger is due to inhibition of oxidative stress and its anti-inflammatory activity.[36] Other possible mechanisms are that ginger extract may act by increasing peripheral utilization and inhibition of proximal tubule reabsorption mechanism of glucose in the kidney.[37]

Our results show that administration of green tea and ginger extracts simultaneously have potential hypoglycemic action in diabetic rats and the glucose level at the end of the experiment was near the normal levels, to the best of my knowledge, this is the first experimental study that used this combination, the results may be due to their synergistic and additive effects to reduce glucose level as they share some possible mechanisms to lower glucose level in both types of DM.[38]

CONCLUSION

We conclude that oral administration of a combination of green tea and ginger extract showed more effect as a hypoglycemic agent than green tea and ginger alone; this is maybe due to the synergism of their mechanisms in lowering blood glucose. We expect that this combination may have a benefit in protection against diabetes mellitus.

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