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Hypoglycemic Effect of 6-Gingerol, an Active Principle of Ginger in Streptozotocin Induced Diabetic Rats.

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Research Article

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ABSTRACT

6-gingerol is an aromatic polyphenol, active ingredients of ginger used for various pharmacological activities. The present study was investigated to evaluate the hypoglycemic effect of 6-gingerol (25, 50mg/kg bw) in streptozotocin (STZ) induced diabetic rats. The study was carried out by oral administration of 6-gingerol in a dose dependent manner (25, 50mg/kg bw) once a day for 42 days. Diabetes was induced in rats with STZ (60mg/kg bw/i.p). Albino rats (n=30) each weighing 160-180g were divided in to 5 groups in 6 animals each. Group A served as normal control, group B served as diabetic and was not given 6-gingerol. Group C and D rats were diabetic and oral administration of 6-gingerol (25, 50mg/kg bw). Group E rats were diabetic and given oral administration of glibenclamide (600µg/kg bw) as standard reference standard. Blood samples of each group were collected and analyzed blood glucose on 1st day (after making them diabetic), 21st and 42nd day. Blood glucose level remained unaltered in group A and B over time. However, group C, D and E given 6-gingerol (25, 50mg/kg bw) and glibenclamide (0.05mg/kg bw) showed significant ($P<0.05$) reduction in blood glucose level after day1, 21 and 42 post treatment. It may be concluded that 6-gingerol has hypoglycemic effect on diabetic rats.

INTRODUCTION

Diabetes mellitus is a serious metabolic disorder that characterized by hyperglycemia resulting from malfunction in insulin secretion and /or insulin action both causing by impaired metabolism of carbohydrate, protein and lipids [1]. It is well known that the incidence of diabetes mellitus is high all over the world, especially in Asia. The WHO has expected that the worldwide number of patients with diabetes will double by the year 2025, from the current number of approximately 150 million to 300 million [2].

Different types of oral hypoglycemic agents such as biguanides and sulphonylurea are available along with insulin for the treatment of diabetes mellitus [3], but have side effects associated with their uses [4, 5]. There is a growing interest in herbal remedies because of their effectiveness, minimal side effects in clinical experience and relatively low costs. Herbal drugs or their extracts are prescribed widely, even when their biological active compounds are unknown. Even the World Health Organization (WHO) approves the use of plant drugs for different diseases, including diabetes mellitus. Therefore, studies with plant extracts are useful to know their efficacy and mechanism of action and safety [6].

6- gingerol ((S)-5-hydroxy-1-(4-hydroxy-3methoxyphenol)-3-decanone) is an aromatic polyphenol main constituents of ginger. It has different pharmacological activities including antioxidant, anti-inflammatory [7, 8]; antitumor [9]; anti-atherosclerotic [10]; hematopoietic [11]; anticancer [12]; analgesic [13]; antipyretic [14] and prevents adipogenesis [15, 16]; Alzheimer's disease [18] and cardiovascular disorders [19]. It also has an inhibitory effect on xanthine oxidase responsible for generation of ROS like superoxide anion [20] and inhibit the expressions of

cyclooxygenase-2, lipoxygenases and nuclear factor kB which play a key roles in progression of inflammation and cancer [21].

There are several allopathic hypoglycemic drugs available in human beings; however, they have long term side effects. There is dire need to explore hypoglycemic drugs that have less or no side effects at all. The 6-gingerol is an alternative. Rats are genomically resembling humans, more than 90% and the rat model experiment may prove beneficial for diabetic human population. The present study was planned to see the hypoglycemic effects of 6-gingerol (25, 50mg/kg bw) on serum glucose level in STZ induced diabetic rats, which is compared with the standard drug glibenclamide (0.05mg/kg bw)

MATERIALS AND METHODS

Experimental animals

Either sex of Wistar albino rats (weighing 160–180g) were procured from the Animal house, Management and Science University, Shah Alam under standard environmental conditions (12 h light/dark cycles at 25–28 °C, relative humidity 60–80 %). The rats were acclimatized under standard rat house conditions for 21 days before the trial was initiated. These rats were housed in steel wire cages and maintained in controlled temperature at 27^{0}C with light cycle of 12h light and 12h dark. Isonitrogenous and isocaloric chick feed and tap water was available to all rats round the clock [21]. All studies were conducted in accordance with the National Institute of Health Guide [22].

Chemicals

All the drugs and chemicals used in this experiment were purchased from Sigma Chemical Company Inc., St. Louis, USA. The chemicals were of analytical grade.

Induction of experimental diabetes

Rats were made diabetic by a single intraperitoneal administration of streptozotocin (65 mg/kg) dissolved in 0.1M citrate buffer, pH 4.5 [23]. Forty-eight hours later, blood samples were collected and glucose levels were determined to confirm the development of diabetes. Only those animals which showed hyperglycemia (blood glucose levels > 240mg/dl) were used in the experiment [24, 25].

Experimental design

In the experiment, a total of 30 rats (24 diabetic surviving rats, 6 normal rats) were used. The rats were divided into 5 groups of 6 rats each.

Group 1: Normal rats.
Group 2: Diabetic control rats
Group 3: Diabetic rats given 6-gingerol (25 mg/kg b.w.) in an aqueous solution daily for 42 days using an intragastric tube.
Group 4: Diabetic rats given 6-gingerol (50 mg/kg b.w.) in an aqueous solution daily for 42 days using an intragastric tube.
Group 5: Diabetic rats given glibenclamide (0.05mg/kg b.w.) in an aqueous solution daily for 42 days using an intragastric tube.

Estimation of Food, fluid intake, body weight and blood glucose

Food, fluid intake amount and changes in body weights and blood glucose levels were measured at the beginning of the experiment and at 5-day intervals. Blood samples were obtained by tail-vein puncture of the normal and STZ-induced diabetic rats on day one (1), day 21, day 42. Blood glucose levels were determined by the O-toluidine method [26].

Statistical analysis

All data were expressed as Mean ± SD of number of experiments (n=6). The statistical significance was evaluated by one-way analysis of variance (ANOVA) using SPSS version 7.5 (SPSS, Cary, NC, USA) and the individual comparisons were obtained by Duncan's Multiple Range Test (DMRT). A value of $p<0.05$ was considered to indicate a significant difference between groups[27].

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RESULTS

Effect of 6-gingerol on blood glucose levels

The results of blood glucose levels were measured in normal and STZ-induced diabetic rats on day 1, 21, and 42 days shown in Fig. 1. There was a significant increase in blood glucose levels in STZ-induced diabetic rats (Group 2). Administration of 6- gingerol at a dose of 25 mg and 50 mg/kg bw and glibenclamide (600µg/kg bw) significantly decreased blood glucose levels in STZ-induced rats (Group 3, 4 and 5). The results were found to be dose dependent .

Effect of 6-gingerol on body weight, food and liquid intake

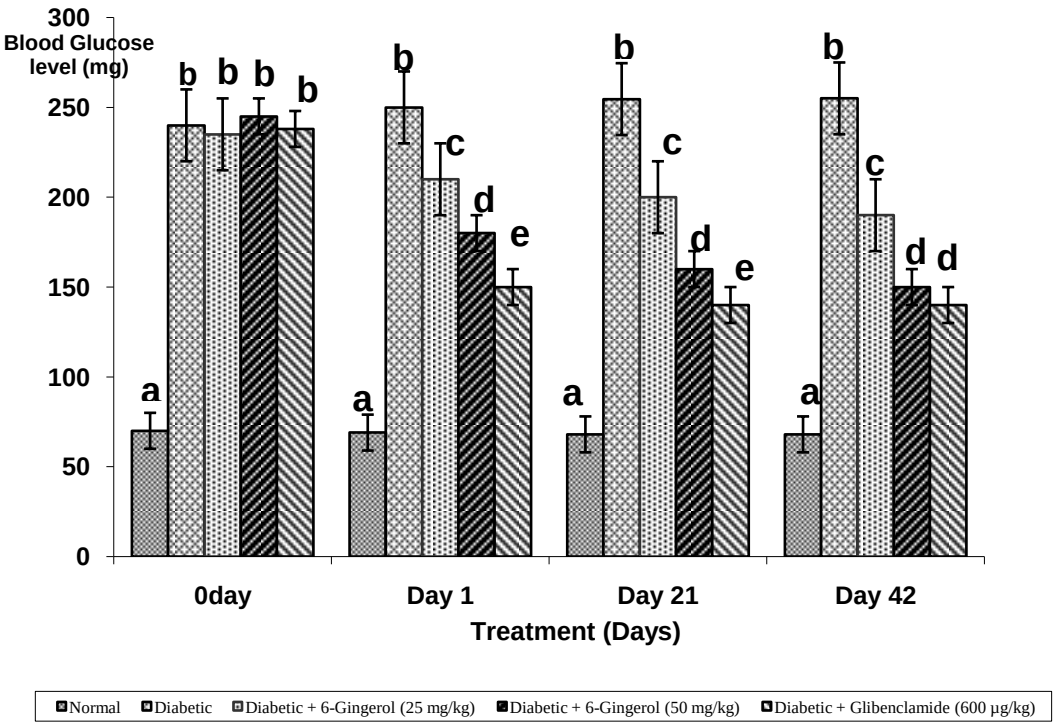
The results of body weight, food and liquid intake were measured and were summarized in Table 1. The initial body weights were similar in normal and diabetic groups, whereas the final body weights were significantly decreased in the diabetic control (Group 2) when compared with the normal control (Group 1). At the same time, there was no significant difference in the body weights in 6- gingerol and glibenclamide treated diabetic rats (Group 3, 4 and 5). Food and fluid intake amount were significantly higher in the diabetic group than the normal (Table 1).

Table 1: Effect of 6-gingerol on body weight, food and liquid intake in normal and STZ induced diabetic rats

Treatment	Treatment		Food intake	Liquid intake
	Initial	Final	(g/rat/day)	(ml/rat/day)
Normal rats	179.2 ± 1.2^{a}	190.6 ± 3.5^{a}	11.12 ± 5.3^{a}	16.33 ± 0.21^{a}
Diabetic control	180.4 ± 4.3^{a}	159.1 ± 2.1^{b}	16.88 ± 2.2^{b}	32.14 ± 0.55^{b}
Diabetic + *6-gingerol* (25mg/kg bw)	164.3 ± 5.8^{c}	191.6 ± 4.3^{c}	14.24 ± 1.6^{c}	27.67 ± 0.11^{c}
Diabetic +6- *gingerol* (50mg/kg bw)	177.3 ± 4.1^{d}	194.1 ± 3.2^{c}	12.14 ± 1.8^{d}	22.81 ± 0.12^{d}
Diabetic + glibenclamide (600µg/kg bw)	178.5 ± 4.1^{d}	192.2 ± 3.2^{c}	12.32 ± 4.4^{d}	21.10 ± 0.18^{d}

Values are given as means ± SD of six animals in each group. Values not sharing a common superscript (a, b, c and d) differ significantly (Duncan's Multiple Range Test)

Figure1: Effect of 6- Gingerol on blood glucose levels in STZ induced diabetic rats



Values are given as means ± SD of six animals in each group. Values not sharing a common superscript (a, b, c and d) differ significantly at $p < 0.05$, Duncan's Multiple Range Test (DMRT)

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DISCUSSION

The aim of the present study was to prove the hypoglycemic potential of 6-gingerol in STZ induced diabetes rats. At the present juncture, it is not possible to pinpoint the mechanism of hypoglycemic action of 6- gingerol. However, based on an previous report, some suggestions can be made for its possible mechanism. It has been reported that an infusion of 6-gingerol in a dose dependent inhibits blood glucose absorption from the gut [28] that maintain cell function related to receptors and membrane transport [13]. Thus, a possibility that retardation of intestinal glucose absorption may also be partially responsible for inhibition of hyperglycemia in glucose-fed rats.

In STZ-induced diabetic rats, increased food consumption and decreased body weight were observed. This indicates polyphagic condition and loss of weight due to excessive break-down of tissue proteins [29]. Hakim et al. [30] have stated that decreased body weight in diabetic rats could be due to dehydration and catabolism of fats and proteins. Increased catabolic reactions leading to muscle wasting might also be the cause for the reduced weight gain by diabetic rats [31] . Administration of 6-gingerol to diabetic rats decreased food consumption and improved body weight and this could be due to a better control of the hyperglycemic state in the diabetic rats. Decreased levels of blood glucose could improve body weight in streptozotocin-diabetic rats [32].

Pharmacokinetic and bioavailability studies provide further information for understanding the metabolism of 6-gingerol, especially its hypoglycemic actions. Sufficient acute and chronic toxicity studies have demonstrated the broad safety of 6-gingerol as a complementary hyperglycaemic control agent.

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