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Protective Effect of Zingiber Officinale Extract on Streptozotocin Induced Diabetes Mellitus in Mice

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Abstract:
Spices, the predominant flavoring, coloring, and aromatic agents in food and beverages are now gaining importance for their diversified uses. Ginger (Zingiber Officinale) is a medicinal plant that has been widely used in Chinese, and Tibb Unani herbal medicines all over the world, since antiquity, for a wide array of unrelated ailments that include muscular aches, sore throat, constipation, arthritis, indigestion, vomiting and infectious diseases. Currently, there is a renewed interest in ginger, and several scientific investigations aimed at isolation and identification of active constituents of ginger, scientific verification of its pharmacological actions and of its constituents, and verification of the basis of the use of ginger in several diseases and conditions most common is use of ginger as complementary therapy in diabetes patients is now increasing due to less side effect comparing with antidiabetic drugs. Streptozotocin enter the B cell via glucose transporter (GLUT2) and cause alkylation of DNA. DNA damage induced by activation of poly ADP-ribosylation; a process is more important for diabetogenicity of streptpzotocin than DNA damage itself.

INTRODUCTION

Ginger grows best in tropical and subtropical areas, which have good rainfall with hot and humid conditions during the summer season. It is a member of Zingiberaceae family originated in Southeast Asia and has been introduced to many parts of the globe where it proliferates in suitable environment. Belief in the medicinal properties of ginger existed in ancient Indian and oriental cultures where ginger has been used alone or as a component in herbal remedies [1].

This practice continues today in many areas of the world including Africa, Brazil, China and, Mexico. Ginger has introduced to Europe and other areas by Dutch, Portuguese Arab and Spanish explorers or traders from around the 13th to 16th centuries [2]. Carbohydrates Starch is the major constituent up to 50%. Oleoresin Gingerol homologues (major, about 33%) include derivatives with methyl side chain, shogaol homologues (dehydration products of gingerols), zingerone (degradation product of gingerols) ,1- dehydrogingerdione and 6- ginger sulfonic acid. Lipids 6-8% They include free fatty acids e.g. palmitic acid, oleic acid, linoleic acid, caprylic acid, capric acid, lauric acid, myristic acid, pentadecanoic acid, heptadecanoic acid, stearic acid, linolenic acid, arachidonic acid, triglycerides, phosphatidic acid, lecithin and ginger glycolipids A, B and C. Ulcer are caused due to imbalance between aggressive factors (hydrochloric acid, pepsin, gastrin, steroidal anti-inflammatory drugs, and ethanol) and defensive factor of gastric mucosa (prostaglandin, mucus, bicarbonate) [3].

Figure (1): Zingiber officinale leaves

There are several herbal ayuvedic preparation which have a protective effect against gastric mucosal injury [4]. Herbal medicine is now used by up to 50% of the Western population in a number of instances 10% for treatment or prevention of digestive disorders [5]. Today, pharmacopoeias of a number of different countries list ginger extract for various digestive disease [6]. Aromatic, spasmolytic and carminative properties of ginger are probably responsible for the therapeutic application in digestive tract ailments [.7,8].

Figure (2): Fresh ginger rhizome

Streptozotocin (STZ) was initially isolated from Streptomyces achromogenes in 1960, with its diabetogenic properties not described until 1963 [9] This action was characterized by Junod, [10.11]. showing that the diabetogenic effects are due to selective destruction of pancreatic islet β-cells. As a result of this action, the animals experience insulin deficiency, hyperglycemia, polydipsia, and polyuria, all of which are characteristic of human type 1 diabetes mellitus [12]

Streptozotocin enter the B cell via a glucose transporter (GLUCT2) and cause alkylation of DNA. DNA damage induced activation of poly ADP- ribosylation, a process that is important for diabetogenicity of streptzotocin than DNA damage itself

Poly ADP ribosylation leads to depletion of cellular NAD+ and ATP.

Enhanced ATP dephosphorylation after streptozotocin treatment supplies substrate for xanthine oxidase resulting in formation of superoxide radicals, consequently hydrogen peroxide and hydroxyl radicals are also generated.

Streptzotocin liberates toxic amount of nitric oxide that inhibits aconitase activity and participates in DNA damage

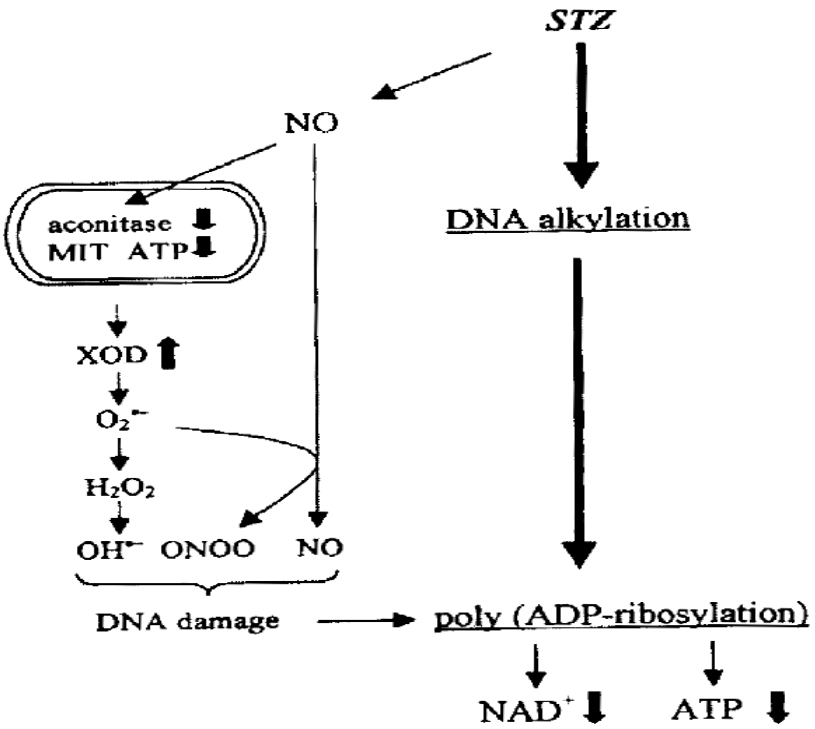


Figure (3): Mechanism of action of streptozoticin

MATERIAL AND METHOD

Experimental an Albino mouse of either sex weighing 20-30 g, and male Wistar strain rats Weighing 200-250 g were maintained in the animal house of Faculty of Medicine – Al Arab Medical University, Benghazi, Libya. The mice and Rats were bred in the faculty animal house. All animals were housed in Standard polypropylene cages (48×35×22 cm) and kept under controlled Room temperature (20±5 ◦C; relative humidity 60-70%) in a 12 h light-dark Cycle. The animals were given a standard laboratory diet and free water Food was withdrawn 12 h before and during the experimental hours. e Maceration method: In this method fresh ginger rhizome was cut into small pieces, dried, and then pulverized into coarse powder and weighing about 400 g of powder. It was macerated in 1000 ml hydroalcoholic solution (70% Ethanol, 30% distilled water) for seventy-two hours. The extract was then shaked, filtered by using filter paper and the solution was evaporated in a rotatory evaporator under reduced pressure until dryness. Evaporation and removal of the solvent give hydroalcoholic extract of ginger out of 400 g of crude plant, 8 g of hydroalcoholic extract of ginger were obtained and kept for use in pharmacological experiments (Iranian Herbal Pharmacopea).

The mice were divided into five groups each contain six mice

1. Control group: given normal saline is a dose of 0.1 ml each mouse
2. The streptozotocin in a dose of 180mg/ kg was used with sodium citrate pH 4.5, 0.1 ml is given intraperitoneal to each mouse
3. Extract of ginger given in a dose of 300mg/kg (orally p.o) and then after three hours blood glucose was assessed.
4. Extract of ginger given in a dose of 300mg/kg (intraperitonealy i.p) and then after three hours blood glucose was assessed.
5. Glibecclamide was given in a dose of 0.5mg/kg by dissolving 5mg of glibenclamide tablets in 50ml of distilled water and each mouse given 0.3 ml orally. Then after three hours, blood glucose was assessed.

STATISTICAL ANALYSIS

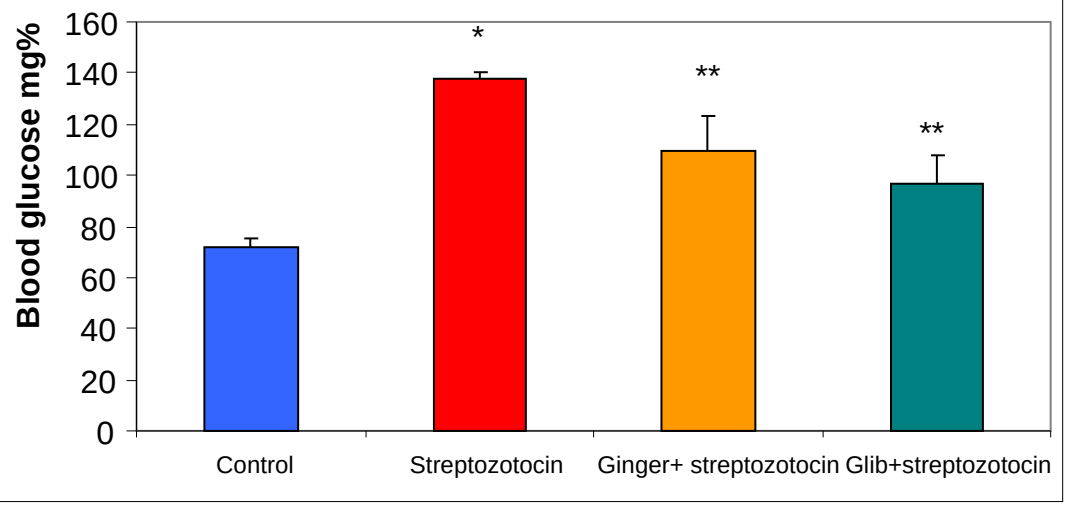
The experimental results were expressed as the mean± S.E.M and are accompanied by the number of observations. Data were assessed by the method of one-way analysis of variance (ANOVA), if this analysis indicated significant difference among the group means, then each group was compared by rather LSD or paried sample test. A.P value less than 0.05 was considered statistically significant. P value less than 0.001 was considered statistically highly significant.

As shown in the figure (4) highly significant ($p<0.001$) increase in the blood glucose level in the streptozotocin treated compared with control group.

The data also reveals significant reduction in the blood glucose level in the ginger treated (p.o) c ($p<0.05$) compared with streptozotocin treated group.

The data also shows highly significant ($p<0.001$) reduction in the blood glucose level in glibenclamide treated group compared with streptozotocin treated group

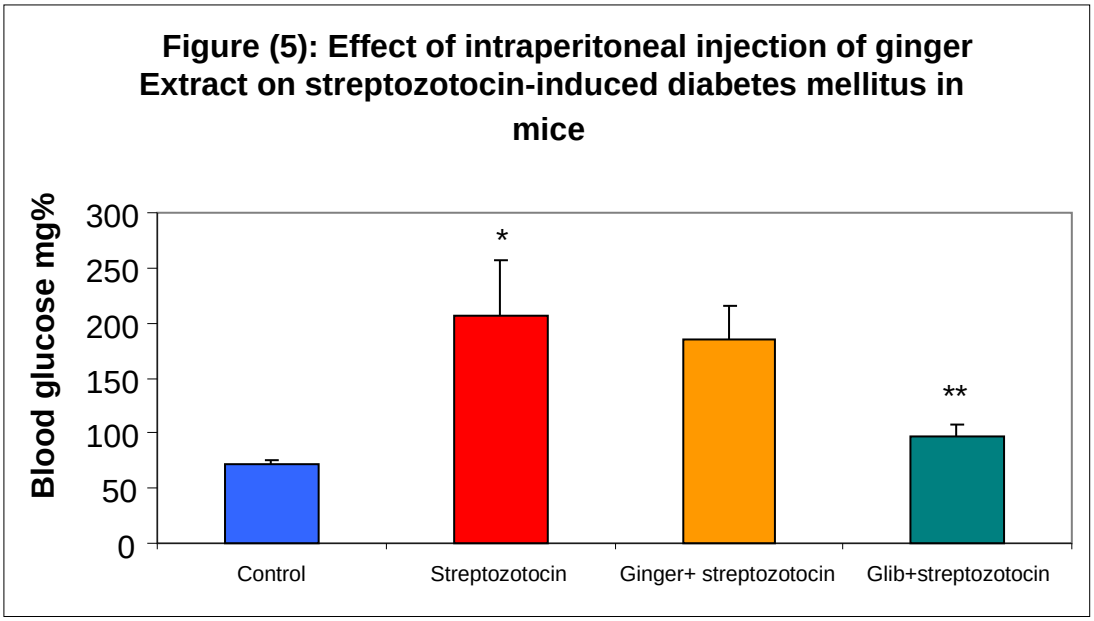
Figure (4): Effect of oral administration of ginger extract on streptozotocin-induced diabetes mellitus in mice



Results in the figure (5) shows highly significant increase($p<0.001$) in the blood glucose level in the streptozotocin compared with control

The data also reveals non-significant reduction ($p>0.05$) in the blood glucose level in ginger treated (i.p) compared with streptozotocin treated group.

The data shows nonsignificant difference ($p>0.05$) between ginger extract (p.o and i.p) and glibenclamide.



DISCUSSION

In this model of diabetes induction, we use streptozotocin as its commonly used agent and ginger extract showed significant reduction in blood glucose. Our results in accordance with study of hypoglycemic effect of ginger in streptozotocin – induced persistent hyperglycemia in rats by Al-Amin [13]. ginger in a dose of 500mg/kg was significant effective in lowering serum glucose. The ginger treatment also resulted in significant reduction in urine protein levels and decreased both water intake and urine output in the streptozotocin – induced diabetic rats. In addition, raw ginger was effective in reversing the diabetic proteinuria observed in the diabetic rats. Thus, ginger may be of value in managing the effects of diabetic complications in human subjects.

The hypoglycemic effect of plant extract was investigated in rats by using streptozotocin as models of persistent hyperglycemia, ginger extract at a dose of 50- 800 mg/kg caused dose related significant hypoglycemia in normal and diabetic rats. The finding of this animal study indicated that zingiber officinale rhizome extract possess hypoglycemic properties and thus lend pharmacological support to folkoric, ethnomedical uses of ginger in the management and control of type 2 diabetes mellius [14]

Additionally, another study assessed the antihyperglycemic activity of its aqueous Extract given orally (daily) to streptozotocin (STZ)- induced diabetic rats at three different doses (100, 300, and 500 mg/kg body weight) For a duration of 30 days. After the rats were given 500 mg/kg, a dose dependent antihyperglycaemic effect showed a drop in plasma glucose levels by 38 and 68% on the 15th and 30th day, respectively.

ZO dramatically boosted ($P < 0•05$) the activities of phosphofructokinase, pyruvate kinase, and glucokinase in STZ- diabetic rats, whereas the activities of these enzymes dropped in diabetic controls by 94, 53, and 61%, respectively, as compared to normal controls.

Thus, by influencing the activities of glycolytic enzymes, the current study demonstrated that gi nger is a viable phytomedicine for the treatment of diabetes. [15].

Furthermore, the aqueous extract of raw ginger was administered daily (500 mg/kg, intraperitoneally) for a period of 7 weeks to streptozotocin (STZ)-induced diabetic rats. Fasting blood serum was analyzed for blood glucose, cholesterol and triacylglycerol levels. The STZ-injected rats exhibited hyperglycemia accompanied with weight loss, indicating their diabetic condition. At a dose of 500 mg/kg, raw ginger was significantly effective in lowering serum glucose, cholesterol and triacylglycerol levels in the ginger-treated diabetic rats compared with the control diabetic rats. The ginger treatment also resulted in a significant reduction in urine protein levels. In addition, the ginger-treated diabetic rats sustained their initial weights during the treatment period. Moreover, ginger decreased both water intake and urine output in the STZ-induced diabetic rats [16].

6-Shogaol exhibited an antidiabetic effect by significantly decreased the level of blood glucose, body weight and attenuated pathological changes to the normal levels in the diabetic mice, and has effect against pancreas, kidney, liver damage in the diabetic mice. Since, 6-shogaol prevented the damage for STZ induced stress [17].

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