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Research Article

ANTIDIABETIC EFFECTS OF [10]-GINGEROL IN STREPTOZOTOCIN- AND HIGH-FAT DIET-INDUCED DIABETIC RATS

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ABSTRACT

Objective: India is the "diabetes capital of the world" with 62.4 million Indians having type 2 diabetes as 2011. A major risk factor for insulin resistance is obesity, which is generally caused by regular physical inactivity and high-fat diet (HFD). Obesity and diabetes are closely related to each other as about 80% of diabetics are obese. Obesity is a common finding in type 2 diabetes. The objective of the study was to investigate the antidiabetic effects of [10]-gingerol in streptozotocin (STZ)- and HFD-induced diabetic rats.

Methods: Wistar rats were used for the study. Animals were divided into six groups. The six groups in this study were, Group I (normal control), Group II (diabetic control), Group III (glibenclamide at 5 mg/kg p.o.), Group IV (orlistat at 60 mg/kg p.o.), Group V ([10] gingerol at 15 mg/kg p.o.), and Group VI ([10]-gingerol (30 mg/kg p.o.), respectively. The antidiabetic activity was assessed using blood glucose level, body weight, and various biochemical parameters such as serum total cholesterol (TC) level, triglyceride (TG) level, high density lipoproteins (HDL-C), total protein (TP), serum alanine transaminase, and aspartate aminotransferase (serum glutamic oxaloacetic transaminase) respectively.

Results: [10]-gingerol exhibited an antidiabetic effect by significantly decreased the level of blood glucose, body weight, TG, TC, TP, and increase HDL. The results of the study demonstrated that the treatment with [10]-gingerol significantly ($p<0.05$) and dose dependently prevented STZ- and HFD-induced diabetic rats.

Conclusions: The findings of the study suggest that [10]-gingerol possesses potential antidiabetic activity as it lowers serum glucose level.

Keywords: [10]-gingerol, Diabetes, High-fat diet, Streptozotocin.

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INTRODUCTION

The occurrence of type 2 diabetes mellitus is rapidly rising around the world's population. India is the "diabetes capital of the world" with 62.4 million Indians having type 2 diabetes in 2011 [1]. Blood glucose level was increased in type 2 diabetes mellitus due to a progressive decline in insulin action (insulin resistance) and pancreatic β cell dysfunction [2]. A major risk factor for insulin resistance is obesity, which is generally caused by regular physical inactivity and high-fat diet (HFD) [3]. Obesity and diabetes are closely related to each other as about 80% of diabetics are obese. Obesity is a common finding in type 2 diabetes. There is impaired insulin sensitivity of peripheral tissues such as muscle and fat cells to the action of insulin in obese individuals (insulin resistance). The reduction of weight in obese patients produces an enhancement in diabetic state [4]. Obesity increases the risk of type II diabetes, cardiovascular disease, cancer, and premature death [5]. A pharmacological factor involved in obesity and diabetes includes lipoprotein lipase (LL) having a central role in the metabolism of both triglyceride (TG)-rich particles and high-density lipoproteins (HDLs). LL is determinant of serum TG and HDL concentrations [6]. The influence of obesity on type 2 diabetes risk is determined not only by the amount of obesity but also by fat deposition [7].

The current treatment for type 2 diabetes includes insulin and oral hypoglycemic drugs i.e. sulfonylurea derivatives, thiazolidinediones, biguanides, and α glucosidase inhibitors, but these medications have most of the side effects. Many traditional plant remedies for obesity and diabetes are used throughout the world. Ginger, the rhizome of the *Zingiber officinale* is commonly consumed dietary condiments. Ginger and its constituents show antioxidant activity and prevent the damage of macromolecules, caused by the free radicals/oxidative stress [8]. The components derived from natural sources, which are considered to be safe and cost effective, are needed. Ginger is one of the most widely used natural products consumed as a spice and medicine for treating nausea, dysentery, diabetes, heartburn, flatulence, diarrhea, loss of appetite, infections, cough, and bronchitis. Experimental studies showed that its active components [10]-gingerol exert antidiabetic effects against streptozotocin (STZ)- and HFD-induced diabetic rats.

METHODS

Animals

Wistar rats (150–200 g) were group housed (n=6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2°C, 55–65%). Rats received standard rodent chow and water *ad libitum*. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All the experiments were carried in a room-five events between 08:00 and 15:00 h. A separate group (n=6) of rats was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee, constituted for the Purpose of Control and Supervision of Experimental Animals by the Ministry of Environment And Forests, Government of India, New Delhi, India.

Drugs and chemicals

[10] gingerol (Sigma-Aldrich) and STZ (Sigma-Aldrich) were used in the present study. All other chemicals and other biochemicals used in the experiments were of analytical grade from different firms.

Experimental design and treatment protocol

After 28 days of administration of HFD, the rats were injected intraperitoneally by a single dose of a prepared solution of STZ (30 mg/kg suspended in 0.1 mol/L citrate buffer at pH 4.5). If the fasting blood glucose was more than 300 mg/100 ml after 72 h of STZ injection,

Diabetes mellitus is also associated with hyperlipidemia with a profound alteration in the concentration and composition of lipid [18]. Changes in the concentrations of the lipid with diabetes mellitus contribute to the development of vascular disease [19,20]. Fatty acids, an important component of cell membranes, are eicosanoid precursors and are therefore required for both the structure and function of every cell in the body [21]. STZ was significantly increased TL, TC, TG, FFA, phospholipids, LDL, and VLDL levels. The abnormally high concentration of serum lipids in diabetes mellitus is mainly due to an increase in the mobilization of free fatty acids from the periphery fat depots since insulin inhibits the hormone-sensitive lipase. The marked hyperlipidemia that characterizes the diabetic state may, therefore, be regarded as a consequence of the uninhibited actions of lipolytic hormones on the fat depots [22]. Excess of fatty acids in the plasma produced by STZ promotes the liver conversion of some fatty acids to phospholipids and cholesterol.

Administration of [10]-gingerol to STZ- and HFD-induced diabetic rats produced a significant reduction in serum lipid profile, suggesting its potential in the prevention of hyperlipidemia and obesity. During the experimentation, Wistar rats did not show any mortality or any other adverse effects when the rats fed orally with [10]-gingerol at the doses of 15 and 30 mg/kg. Thus, the [10]-gingerol has a good periphery of safety. Furthermore, all diabetic-treated groups showed histopathological changes of varying degree of alveolar histiocytosis due to phospholipidosis.

Diabetes is the second most common cause of death and different types of oral hypoglycemic agents are available for its treatment but none offers complete glycemic control. The side effect of taking insulin and oral hypoglycemic agents has brought about a growing interest for alternative traditional herbal medicine [23]. Herbal medicine is prepared from various plant parts to contain many bioactive compounds used primarily for treating [24]. The present study showed that [10]-gingerol exhibits significant insulin secretion and β cells regeneration as well as antioxidant activity in experimental rats. Thus, a sufficient supply of antioxidants may prevent or delay β cells dysfunction in diabetes by protecting against glucose toxicity. Moreover, antioxidant activity regulates glucose homeostasis through a multitude of actions. Further studies are in progress to isolate the active principle and elucidate the exact mechanism of the action of [10]-gingerol.

CONCLUSIONS

The findings indicated that the usefulness of the [10]-gingerol STZ and HDF-induced diabetic rats. Our study suggested that [10]-gingerol dose dependently produced antidiabetic activity. This study might be helpful to understand the role of [10]-gingerol in the clinical treatment of diabetes mellitus.

AUTHORS' CONTRIBUTIONS

The authors declare that this work was done by the author named in this article.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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