Anti-diabetic Activity of the Petroleum Ether Extract of *Guar Gum* in Streptozotocin-Induced Diabetic Rats: A Comparative Study

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Abstract

Diabetes mellitus is one of the major causes of morbidity and mortality worldwide. Despite lack of scientific evidences to support its therapeutic efficacy, the use of herbal supplements has significantly increased. *Guar gum* has a wide variety of non-food and food uses as a stiffener in ice cream, yogurt, bakery, and soups; as a stabilizer for cheeses, puddings, and cream; and as a meat binder. Therefore being safe, it was tried in model type II diabetes induced by streptozotocin (STZ) in rats, compared to gliclazide. Healthy Sprague Dawley male adult rats were randomly divided into 5 equal groups namely A, B, C, D, and E. (group A and B) were kept as normal control and diabetic control. The other diabetic groups from group C to group E were treated as follow Gliclazide 4.5mg/kg, *Guar gum* 200 mg/kg and *Guar gum* 200 mg/kg plus gliclazide 4.5mg/kg respectively for 14 consecutive days. Blood glucose, insulin, glycosylated hemoglobin (HbA1c), superoxide dismutase (SOD), malondialdehyde (MDA), reduced glutathione (GSH), lactate dehydrogenase (LDH), urea, insulin resistance, insulin sensitivity and β-cell function were measured. *Guar gum* exerted antidiabetic activity nearly similar to that of gliclazide as indicated by significant reduction of glucose, HBA1c, and insulin resistance. Elevation of insulin and β-cell function was also observed. *Guar gum* and gliclazide showed antioxidant activity as seen by significant reduction of MDA and LDH. This was associated with marked elevation of GSH and SOD. Urea was also reduced after *guar gum* and gliclazide. Similar effects were also seen after combination of gliclazide with *guar gum*. It could be concluded that *guar gum* could be used safely as an adjunct therapy to gliclazide in treatment of type 2 diabetes. In addition, *guar gum* ameliorated its associated complications by reducing the oxidative stress and urea level. Further clinical studies are needed.

Keywords:
Diabetes mellitus; rats; gliclazide; *guar gum*.

Introduction

Diabetes mellitus is a complex, chronic disorder that results from partial, complete or relative lack of insulin secretion by pancreatic β-cells and/or impairment of insulin action (Anderson *et al*., 1994). The crude prevalence rate of known diabetes in Egypt in 2008 was 4.07%. It increased with age, to reach 19.8% among female aged 50-59 (Nagla and Ghada, 2010). It is estimated that by the year 2030, Egypt will have at least 8.6 million adults with diabetes (Shaw *et al*., 2010).

Diabetes mellitus is classified into Type I diabetes mellitus, Type 2 diabetes mellitus, gestational diabetes mellitus (Anderson *et al*., 1994; Sherwin 2006), and other types of diabetes mellitus. Other types of diabetes mellitus include genetic

defects of beta-cell function or defects of insulin action. diseases of the exocrine pancreas, such as pancreatitis or cystic fibrosis; dysfunction associated with other endocrinopathies (e.g., acromegaly); and pancreatic dysfunction caused by drugs-chemicals such as glucocorticoids, phenytoin and thiazides. (Bennett 1994; Vuksan *et al*., 2001).

Hyperglycemia promotes oxidative stress and hence generation of reactive oxygen species (ROS), which is known to play a crucial role in the pathogenesis of diabetic nephropathy (DN) (Pan *et al*., 2010) in which increased ROS production and oxidative stress cause cell membrane damage, enzymes inactivation, apoptosis, and endogenous antioxidant altered gene expression (Swaminathan and Shah, 2008).

Management of hyperglycemia in most patients with Type II DM should begin with lifestyle modification (diet and activity) (Nathan *et al*., 2009). However, diets and exercise fail to achieve glycemic control in most patients thus pharmacologic intervention with oral hypoglycemic agents is necessary. Gliclazide is an effective oral hypoglycemic agent which reduces blood glucose levels in animal models of diabetes, healthy volunteers as well as Type 2 diabetic patients (Holmes *et al*., 1984; Matthews *et al*., 2007). Gliclazide is a second generation sulfonylurea which, like other oral hypoglycemic, is indicated as an adjunct to diet and exercise in Type 2 diabetic patients whose hyperglycemia cannot be controlled by diet and exercise alone.

Herbal drugs are prescribed widely because of their effectiveness, less side effects and relatively low cost **(**Venkatesh *et al*., 2003). *Guar gum* is simple, non-ionic and best-characterized branched polysaccharide extracted from *Cyamopsis tetragonoloba* seeds (Frias & Sgarbier 1998). Numerous studies supported that *Guar gum* lowers the postprandial glucose response when mixed into a variety of test meals (Jenkins *et al*., 1977 ; Collier *et al*., 1986; Leclere *et al*. 1994). The supplementation of high carbohydrate diets with *Guar gum* has been demonstrated to effectively enhance insulin sensitivity in individuals with either NIDDM or IDDM (Tagliaferro *et al*., 1985 ; Ebeling *et al*., 1988; Lalor *et al*., 1990).

The main goal of the present study is to use *guar gum* alone or in combination with gliclazide to increase its antidiabetic, antioxidant activity and decrease its adverse effects in the treatment of diabetes mellitus induced experimentally in rats by STZ .

Materials and Methods

Materials

Animals

Sprague Dawley male adult rats weighing 150-200 g obtained from National Research Center, Cairo, Egypt. Animals were housed in plastic cages (28 cm x 43 cm x 18 cm) and were maintained under conventional laboratory conditions of temperature (20 ± 5°C), with a regular 12-h light/12-h dark cycle throughout the study. They were fed standard pellet chow (El-Nasr chemical Co., Cairo, Egypt.) and were allowed water *ad libitum*.

All experimental procedures were conducted in accordance with ethical procedures and policies approved by the Ethics Committee of Faculty of Pharmacy, Beni Suef University.

Drugs

a-Gliclazide

Gliclazide was provided as a gift from Amoun, Co. (EGYPT). Gliclazide was suspended in 2% Tween 80, gum acacia 2% and orally administered in a dose of 4.5 mg/kg (Habib *et al*., 2005).

b-*Guar gum*

Guar gum seeds available in powder form, were purchased from local market. *Guar gum* was extracted with petroleum ether (60-80°C) in a soxhlet apparatus for

72 hrs. After removal of the solvent in under vaccum at 40°C, the residual extract was collected. The petroleum ether extract obtained was suspended in 2% tween 80, 2% gum acacia and given orally (p.o) in a dose of 200 mg/kg (Bhandari and Sharma 1999).

Methods

Induction of experimental diabetes

After fasting for 18 h, diabetes was induced by intraperitoneal injection of streptozotocin (Sigma, St. Louis, MO, USA) dissolved in 0.1 M cold sodium citrate buffer, pH 4.5, at a dose of 50 mg/kg (Hounsom *et al*., 1998).The animals were allowed to drink 5% glucose solution overnight to overcome the drug induced hypoglycemia (Hajduch *et al*., 1998). Diabetes was confirmed by the presence of glucosuria using gluckotest strips at 24, 48, and 96 hours after STZ injection in order to ensure persistent hyperglycemia.

Experimental Design

Group 1: Normal rats received citrate buffer and served as the normal control.

Group 2: Diabetic control rats received STZ (50 mg/kg, i.p.) and served as the diabetic control.

Group 3: Diabetic rats received gliclazide (4.5 mg/kg, p.o.).

Group 4: Diabetic rats received *Guar gum* (200 mg/kg, p.o.).

Group 5: Diabetic rats received gliclazide (4.5 mg/kg, p.o.) and *Guar gum* (200 mg/kg, p.o.).

At the end of the experiment rats were subjected to light ether anaesthesia then blood were collected from the retro - orbital venous plexus following the technique described by Coccheto and Bjornsson (1983), using heparinized microhematocrit capillary tubes into Wassermann tubes. Serum was separated by centrifugation at 3000 rpm for 10 - 15 minutes at room temperature for the determination of serum glucose, insulin, MDA, LDH and urea levels. For the ,assessment of blood SOD and GSH level blood samples were hemolyzed by addition of cold distilled water. On the 35th day of the experiment, blood samples of each rat were collected after decapitation, using EDTA for the determination of glycosylated hemoglobin.

Determination of serum glucose and insulin levels

Fasting serum glucose was estimated by glucose oxidase method Trinder (1969).Insulin in samples were estimated using Enzyme Linked Immunosorbent Assay (ELISA) (King *et al*., 2002).

Determination of insulin resistance, insulin sensitivity and β-cell function

Insulin resistance and β-cell function were done using homeostasis model assessment (HOMA) (Mattewes *et al*., 1985). Insulin sensitivity was calculated using quantitative insulin sensitivity check index (QISCKI) (Katz *et al*., 2000).

Determination of glycosylated hemoglobin in blood

Glycosylated hemoglobin level was determined according to the method described by Trivelli *et al*. (1971), using glycohemoglobin kit (TECO DIAGNOSTICS, U.S.A.).

Determination of serum malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione (GSH)

Serum MDA was estimated by the method of Mihara and Uchiyama (1978). SOD activity was measured based on the ability of the enzyme to inhibit the autoxidation process of pyrogallol method of Marklund and Marklund (1974). Glutathione was estimated by the method of Beutler *et al*. (1963).

Determination of serum lactate dehydrogenase (LDH) and blood urea nitrogen (BUN)

Serum LDH level was determined according to the method of Weisshaar *et al*., (1975) using LDH kit purchased from Randox Laboratories Ltd, Crumlin, U.K. Serum urea was determined according to the method of Tobacco *et al*., (1979) using

the kit purchased from Stanbio Laboratory, Texas, U.S.A.

Statistical Analysis

Data were expressed as the mean ± standard error of the mean (S.E.M); and comparison between the different treatments was carried out using analysis of variance (ANOVA) followed by Tukey - Kramer multiple comparisons test.

Results

Effect of two week daily dose administration of gliclazide and Guar gum alone or in combination on serum glucose and insulin levels in streptozotocin-induced diabetic male rats.

The results are graphically illustrated in Fig. 1 & 2. Streptozotocin significantly increased serum glucose level and significantly decreased serum insulin level as compared to normal control value. Gliclazide and *Guar Gum* significantly decreased serum glucose level by 51.58 % and 36.82 respectively of the diabetic control value. Concurrent administration of gliclazide and *Guar gum* significantly reduced serum glucose level and significantly increased serum insulin level as compared to the diabetic control value.

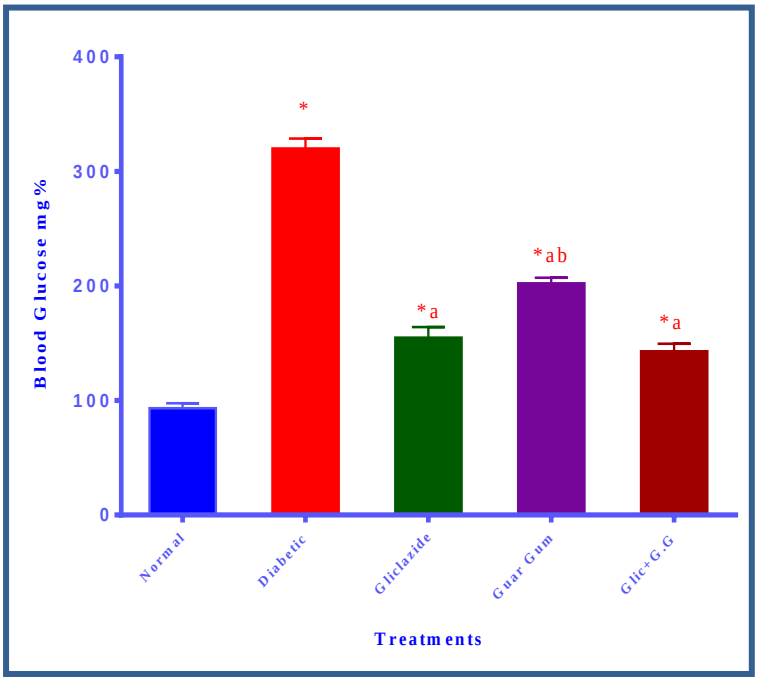

Fig. 1. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on serum glucose level in streptozotocin-induced diabetic male rats.

∗: Significantly different from the normal control group at P <0.05.
a: Significantly different from the diabetic control group at P < 0.05.
b: Significantly different from gliclazide treated group at P <0.05.
Glic = Gliclazide
G.G= *Guar gum*

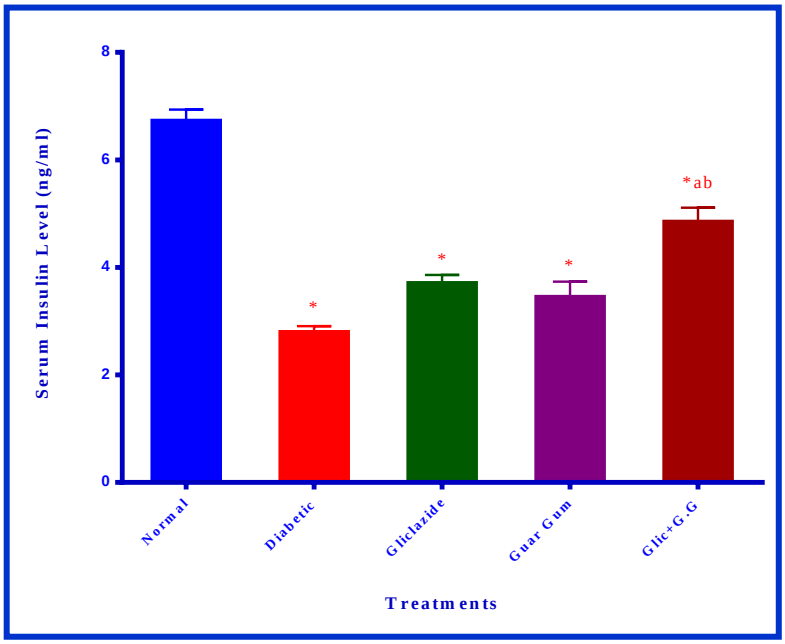

Fig. 2. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on serum insulin level in streptozotocin-induced diabetic male rats.

Effect of two week daily dose administration of gliclazide and Guar gum alone or in combination on insulin resistance insulin sensitivity and β-cell function in streptozotocin-induced diabetic male rats.

The results are graphically illustrated in Fig. 3-5. There was a significant increase in insulin resistance and significant decrease in insulin sensitivity and β-cell function as compared to the corresponding normal control value. Administration of glicalzide significantly decreased insulin resistance level and significantly increased insulin sensitivity. Similarly, *Guar gum* reduced insulin resistance. Concurrent administration of gliclazide and *Guar gum* significantly decreased insulin resistance .

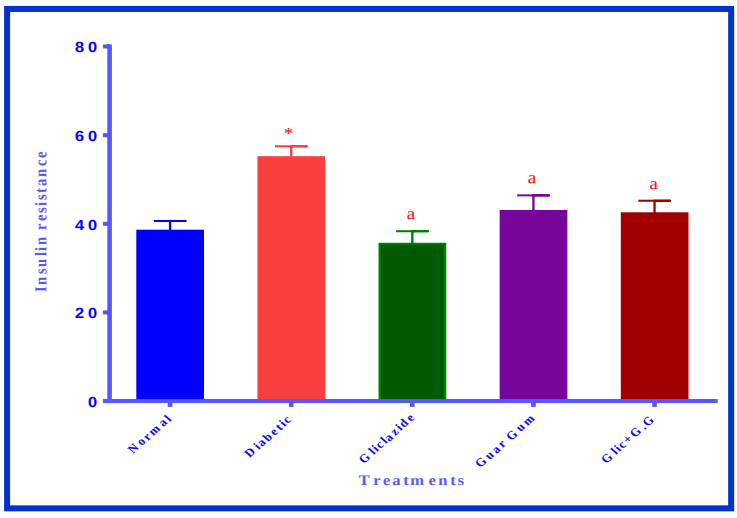

Fig. 3. Effect of two weeks daily dose administration of gliclazide and *Guar gum* alone or in combination on insulin resistance level of streptozotocin-induced diabetic male rats.

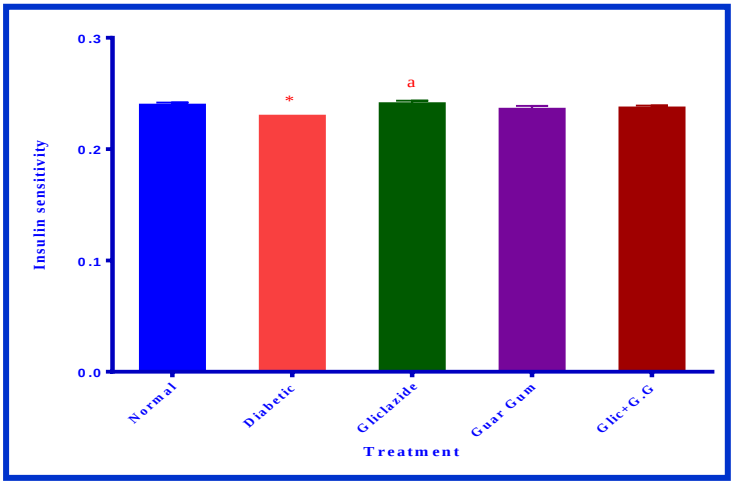

Fig. 4. Effect of two weeks daily dose administration of gliclazide and *Guar gum* alone or in combination on insulin sensitivity level of streptozotocin-induced diabetic male rats.

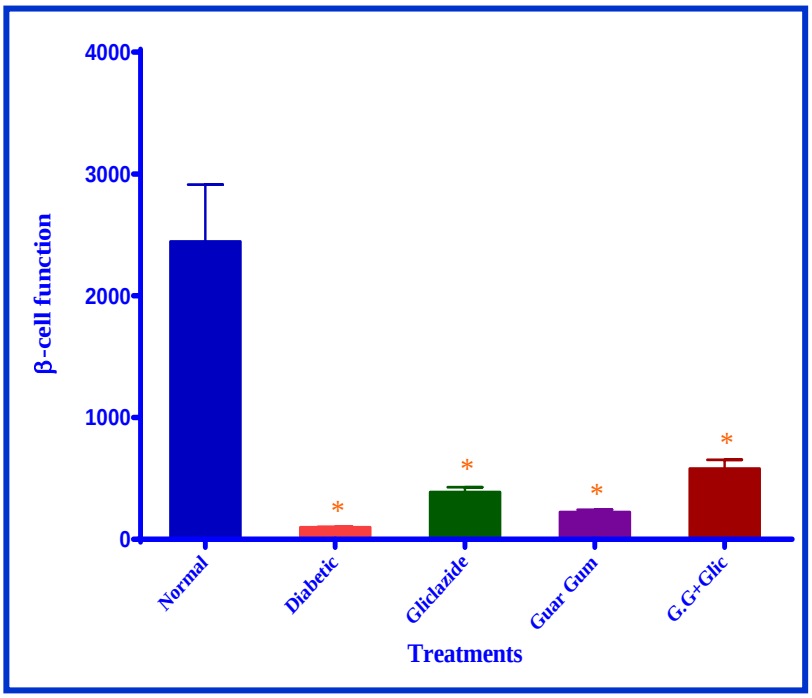

Fig. 5. Effect of two weeks daily dose administration of gliclazide and *Guar gum* alone or in combination on β-cell function level of streptozotocin-induced diabetic male rats.

Effect of two weeks daily dose administration of gliclazide andGuar gum alone or in combination on blood glycosylated haemoglobin(HBA1c) level of streptozotocin-induced diabetic male rats.

The results are graphically illustrated in Fig. 6. Streptozotocin significantly elevated blood HBA1c level as compared to the corresponding normal control value. Gliclazide and *Guar gum* significantly decreased blood HBA1c as compared to the corresponding diabetic control value. Concurrent administration of gliclazide and *Guar gum* nearly normalized blood HBA1c.

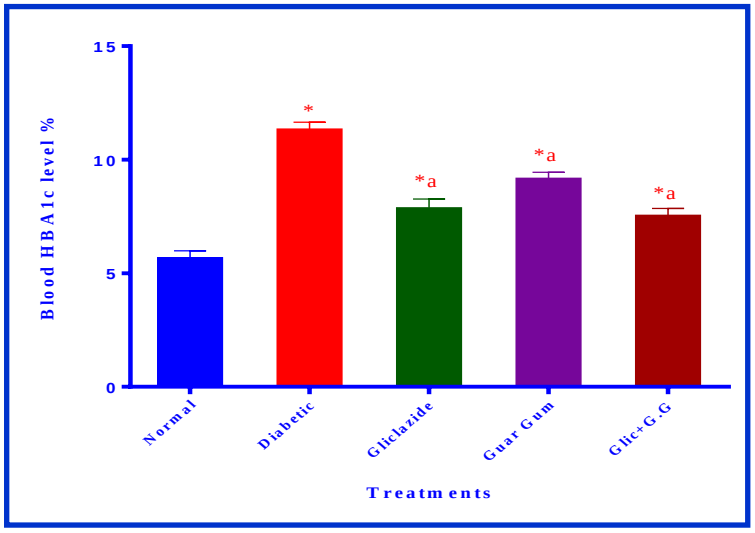

Fig. 6. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on blood HBA1c level in streptozotocin-induced diabetic male rats.

Effect of two weeks daily dose administration of gliclazide andGuar gum alone or in combination on blood SOD, serum MDA and blood GSH levels of streptozotocin-induced diabetic male rats.

The results are graphically illustrated in Fig. 7-9. There was a significant increase in serum MDA and significant decrease blood GSH and SOD during diabetes as compared to corresponding control group. Gliclazide significantly increased blood SOD and GSH levels and significantly decrease serum MDA level as compared to the diabetic control value. *Guar gum* did not show any significance in blood SOD level when compared to the diabetic control. However, it significantly decreased serum MDA level and significantly elevated blood GSH as compared to the diabetic control value. Concurrent administration of gliclazide and *Guar gum* showed significantly decreased blood SOD level and serum MDA level and significantly increased blood GSH level. It is to be noted that administration of this combination gave nearly similar effect to gliclazide alone.

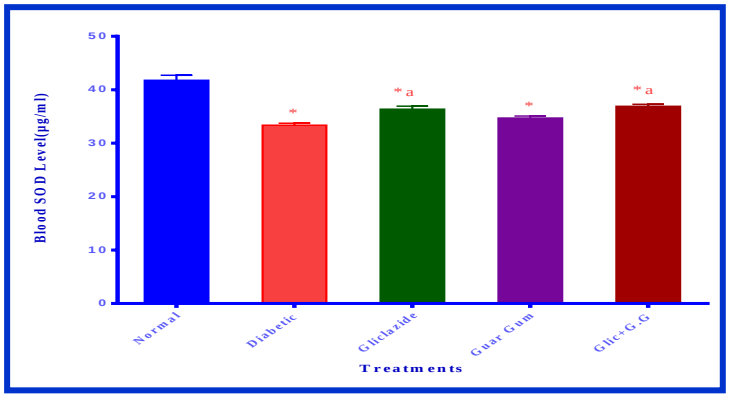

Fig. 7. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on blood SOD level in streptozotocin-induced diabetic male rats.

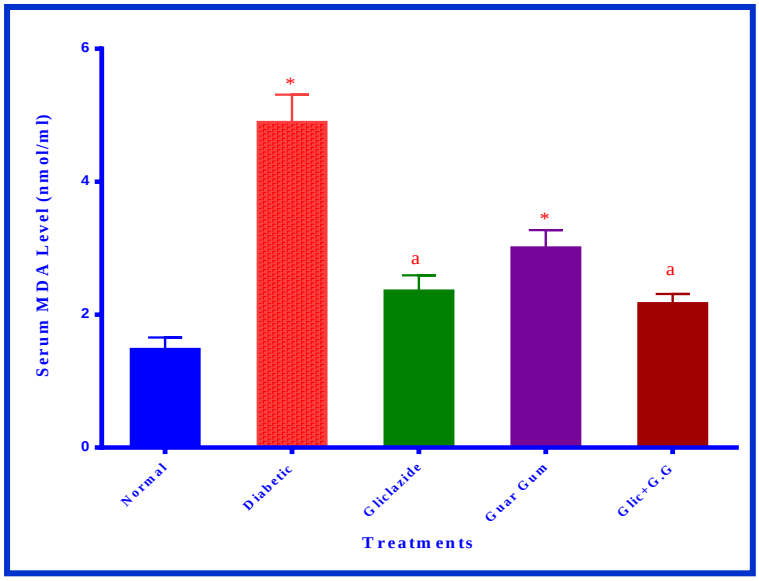

Fig. 8. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on serum MDA level in streptozotocin-induced diabetic male rats.

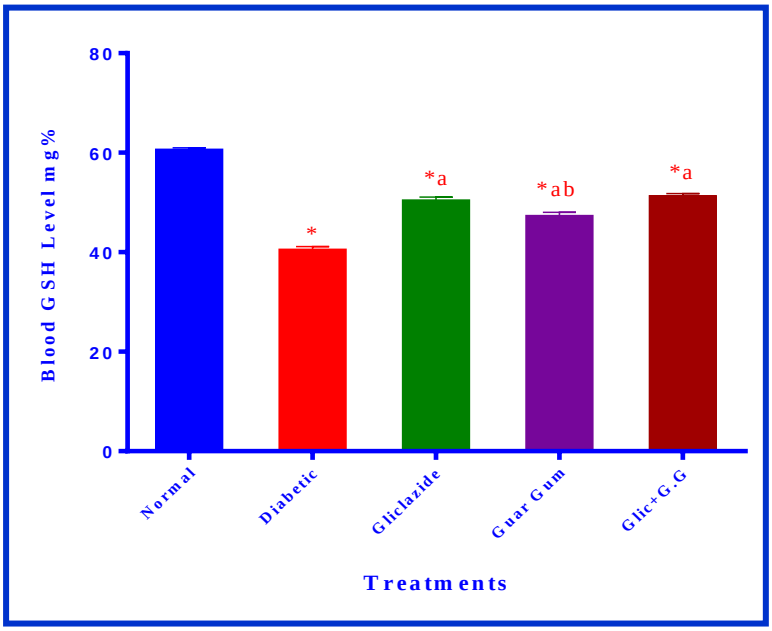

Fig. 9. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on blood GSH level in streptozotocin-induced diabetic male rats.

Effect of two weeks daily dose administration of gliclazide and Guar gum alone or in combination on serum LDH and urea levels of streptozotocin-induced diabetic male rats.

The results are graphically illustrated in Fig. 10 &11. Streptozotocin increased serum LDH level and serum urea level compared to the corresponding normal control value. Gliclazide and *Guar gum* significantly reduced serum LDH and urea levels as compared to the diabetic control value. *Guar gum* showed no significance difference on serum LDH level or serum urea level as compared to gliclazide alone. Concurrent administration of gliclazide and *Guar gum* significantly reduced serum LDH and serum urea level as compared to the diabetic control value. The effect of this combination on serum LDH level was not better than gliclazide alone.

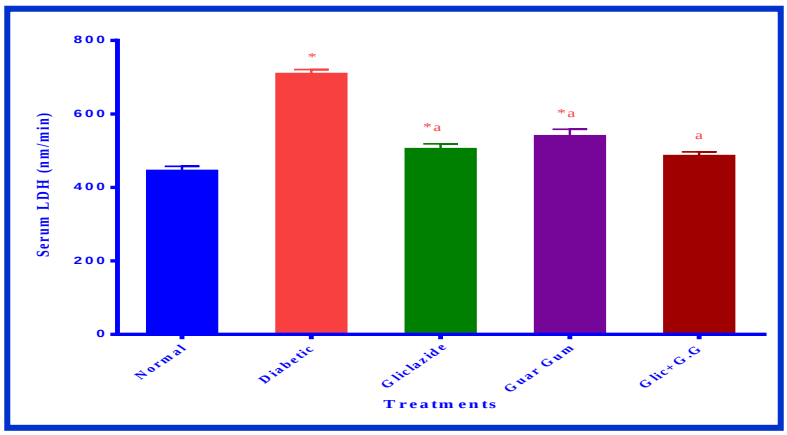

Fig. 10. Effect of two week daily dose administration of gliclazide and*Guar gum* alone or in combination on serum LDH level in streptozotocin–induced diabetic male rats.

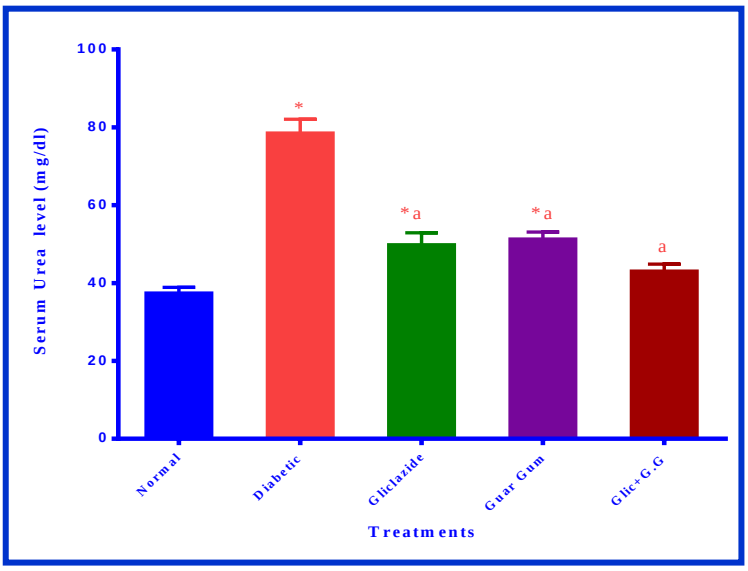

Fig. 11. Effect of two week daily dose administration of gliclazide and *Guar gum* alone or in combination on serum urea level in streptozotocin–induced diabetic male rats.

Discussion

In the present study, streptozotocin was chosen to induce diabetes in rats because of its lower toxicity and higher β-cell specificity relative to other diabetogens (Rakieten *et al*., 2003). Findings of the present investigation revealed that STZ - induced diabetes resulted in a significant increase in serum glucose level and significant decrease in serum insulin level. In addition, STZ caused elevation in glycosylated hemoglobin (HBA1c) level.

The diabetogenic effects of STZ confirmed in this study is in accordance with Bwititi *et al*., (2000) in STZ-diabetic rats and Serradas *et al*., (1993) who reported that STZ in rats is associated with hyperglycemia. This diabetogenic effect could be due to the destructive effect streptozotocin on pancreatic islets.

The mechanism of decreased insulin secretion could be attributed to the resultant hyperglycemia that induced abnormalities in insulin action and secretion (Rossetti *et al*., 1987; Evans *et al*., 2003). Hyperglycemia is also associated with the consequences of hyperinsulinemia, insulin resistance, and glucose intolerance in diabetes (Kaur *et al*., 2002).

The marked increase in HbA1c level noticed in this study in the diabetic group, is in accordance with Vijayaraghavan *et al*., (2012) who reported that streptozotocin induced diabetic rats showed a decrease in the hemoglobin level and a concomitant increase in HbA1c. This could be due to excessive glycosylation of a number of proteins including hemoglobin (Gloria *et al*., 2000; Sampson *et al*., 2002). Furthermore, STZ significantly increased oxidative stress biomarkers as indicated by significant increase in serum MDA level and significant decrease in blood SOD and blood GSH levels. This observed increase in oxidative stress in STZ – induced diabetic rats is in agreement with the findings of many authors, Kinalski *et al*., (2000) who reported a significant elevation in MDA concentration in serum, liver and uterus of STZ diabetic female rats. In addition Zadeh *et al*., (1997), Sundaram *et al*., (1996); Kim *et al*., (2009) showed that thiobarbituric acid reactive substances (TBARS) increased and GSH content decreased in the liver of STZ- induced diabetic rats.

During diabetic state, increased generation of ROS occur and cause an imbalance between the oxidant and antioxidant status (Noda *et al*., 2000). Sustained hyperglycemia has been identified as a principle mediator of increased reactive oxygen species generation in diabetes (Santakumari *et al*., 2003). This might be the result of suppression of β-cell proliferation and inhibition of insulin gene transcription (Kaneto *et al*., 1999; Robertson *et al*., 2003) that caused impairment of insulin release.Moreover,STZ caused elevation in serum lactate dehydrogenase (LDH). The observed activity in LDH in the diabetic rats could be attributed to the excessive accumulation of pyruvate, which is converted to lactate for which LDH is needed (Chang *et al*., 1972), as LDH is a cytosolic enzyme that catalyzes the conversion of pyruvate to lactate in anaerobic glycolysis, which is subsequently converted to glucose in gluconeogenic flux. This explanation is in accordance with Ainscow *et al*., 2000 who observed an increase in LDH activity due to the impairment in glucose-stimulated insulin secretion.

In the present study the elevated serum urea levels in the STZ diabetic rats, is in accordance with Almadal *et al*., (1986) who reported that diabetic rats produce two times as much urea that is produced by normal rats.The mechanism of increased serum urea level in STZ induced diabetes could be attributed to increased protein catabolism and renal dysfunction (Vijayaraghavan *et al*., 2012). This damage to the renal cells is mainly due to glucose mediated osmotic diuresis, reactive oxygen species and glucose overload.

Data of the current study showed that daily dose administration of gliclazide for

14 days reduced hyperglycemia in STZ-induced diabetic rats. This is evidenced by significant reduction in serum glucose level and serum HBA1c level as well as significant rise in serum insulin level. The observed hypoglycemic action of gliclazide in this study is in agreement with Pulido *et al*., (1997) who reported that gliclazide has a glucose lowering effect in STZ – induced diabetic rats and with the work of Zhao *et al*., (2002) who showed that gliclazide increase blood insulin and decreases blood glucose in STZ diabetic rats. Antidiabetic sulfonylureas are thought to stimulate insulin secretion solely by inhibiting their high-affinity ATP-sensitive potassium (K (ATP)) channel receptors at the plasma membrane of beta-cells. This normally occurs during glucose stimulation, where ATP inhibition of plasma membrane K (ATP) channels leads to voltage activation of L-type calcium channels for rapidly switching on and off calcium influx, governing the duration of insulin secretion. (Geng *et al*., 2007).

Data of the present investigation showed that gliclazide reduced insulin resistance and improved insulin sensitivity. This result is in accordance with Bak *et al*., (1989) who reported that gliclazide increased insulin sensitivity in skeletal muscle. Moreover, Tsiani *et al*., (1995) reported an increase in glucose utilization in muscles and adipose tissues and increase in glucose uptake by rat and mouse skeletal muscle cells. Also Ananya *et al*., (2011) reported that gliclazide increases peripheral glucose utilization, decrease hepatic gluconeogenesis and may increase the number and sensitivity of insulin receptors .This may explain the effect of gliclazide in elevated insulin sensitivity and lowered insulin resistance.

Oral administration of gliclazide to diabetic rats significantly decreased the level of glycosylated hemoglobin, this result is in accordance with Campbell *et al*., (1982). The observed decrease in HbA1c level is probably due to improved glycemic control. Furthermore, gliclazide exerted antioxidant effects where it reduced serum MDA and elevated both SOD and GSH. This result is in accordance with Harun *et al*., (2012) who reported that treatment with gliclazide prevented the increase level of lipid peroxidation markers in plasma and pancreas of diabetic rats. Also Onozato *et al*., 2004 and Alper *et al*., 2005 reported that gliclazide reduced oxidative stress in liver and kidney tissues of diabetic rats This observed antioxidant effects of gliclazide could be attributed to the aminoazabicyclo-octyl ring grafted onto its sulfonylurea core (Ziegler and Drouin, 1994). Also Agnieszka *et al*., (2008) reported that gliclazide may diminish the risk of hyperglycemia driven oxidative stress and diabetic complications, possibly due to its direct action as a free radical scavenger (Jennings, 2000).

The present study showed that gliclazide significantly decreased LDH level. This result supported by Prasath and Subramanian (2011) who reported that oral administration of gliclazide to diabetic groups of rats showed a significant reduction in the LDH activity. This is probably due to the regulation of NAD^+/NADH ratio by the oxidation of glucose. In addition ,there was significant decrease in serum urea level after administration of gliclazide. This could be due to hypoglycemic and antioxidant effect of gliclazide (Vijayaraghavan *et al*., 2012).

Data of the current study revealed that administration of *Guar gum* for 14 consecutive days improved hyperglycemia in STZ-induced diabetic rats as evidenced by significant reduction in serum glucose level and significant rise in serum insulin level. In addition, *Guar gum* lowered insulin resistance and improved insulin sensitivity as well as β-cell function.

The hypoglycemic effect of *Guar gum* in this study is in agreement with Bhandari and Sharma (1999) who reported that the oral administration of petroleum ether extract significantly decreased blood glucose. This antihyperglycemic action of *Guar gum* could be related to the ability of

its fiber to produce high viscosity at low concentration in the gut lumen, (Lecer *et al*., 1994; Edwards, 2003), as these fibers are molecules that hold water and have the property of forming colloidal gels. This decreases the association of food with the intestinal mucosa and the enzymatic digestion rate, consequently decreasing the intestinal absorption of monosaccharides and disaccharides (Wilson *et al*., 1998) by delaying gastric emptying or by interaction with digestive enzymes of the intestine (Nandini *et al*., 2003).

The improvement in insulin action following *Guar gum* supplementation is in agreement with David *et al*., (1997) who showed that elevated insulin mediated by increased peripheral tissue insulin sensitivity. Also Tagliaferro *et al*., (1985); Ebeling *et al*., (1988) and Lalor *et al*. (1990), reported that the supplementation of high carbohydrate diets with *Guar gum* has been demonstrated to effectively enhance insulin sensitivity.A possible mechanism by which the guar diet could improve insulin sensitivity in the STZ diabetic rats is the inhibition of urinary glucose loss resulting in a suppression of the hyperphagia.

As insulin resistance develops when both insulin secretion is reduced and plasma glucose levels are elevated (David *et al*., 1997), so the lowering effect of *Guar gum* on insulin resistance in the present study may be attributed to this concept. Also Lang *et al*., (1991) reported that the detrimental actions of hyperglycemia are likely to be directed towards insulin-sensitive glucose transport and metabolism within skeletal muscle because the majority of the infused glucose load during hyperinsulinemia is cleared from the plasma by skeletal muscle (Beck-Nielsen *et al*., 1992).Moreover *Guar gum* in the present study showed antioxidant properties as it significantly decreased MDA level and increased GSH levels. This is in accordance with Trommer and Neubert (2005) who reported that *Guar gum* has lipid protective effects, also Albertini *et al*., (2000) reported lipid peroxidation reducing effects of polysaccharides such as *Guar gum*. This effect seems to be due to the chelation of transition metal ions. This chelation can lead to antioxidant effects (Sipos *et al*., 2003).

In the present study, there was significant decrease in serum LDH level after treatment with *Guar gum*. As mentioned before that LDH is released into the blood stream following loss of membrane integrity resulting from either apoptosis or necrosis. LDH activity, therefore, can be used as an indicator of cell membrane integrity (Haslam *et al*., 2000; Wolterbeek *et al*., 2005), so the antioxidant effect of *Guar gum* could be the main reason for significant decrease in LDH activity.

Guar gum significantly decreased serum urea level, this result is in accordance with Bhandari and Sharma (1999) who reported that the petroleum extract of *Guar gum* significantly decreased blood urea levels and decreased the serum proteins and albumin levels, which is a significant finding as it indicates reversal in pathological events occurring secondary to diabetes mellitus. Also Nandini *et al*., (2003) reported that *Guar gum* effective in controlling renal enlargement, which occurs during early stages of diabetes.

It could be concluded that *Guar gum* decreased STZ- induced hyperglycemia and ameliorated oxidative stress, similar to gliclazide alone. Its antidiabetic activity may be related to increased insulin secretion and antioxidant activity.

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