Original Article
Beneficial role of diosgenin on oxidative stress in aorta of streptozotocin induced diabetic rats.

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ABSTRACT

Aim
High blood glucose may auto-oxidize and generate free radicals, which are proposed to induce oxidative stress in many diabetic complications. The present study investigates the beneficial role of diosgenin on oxidative stress in aorta of streptozotocin (STZ) induced diabetic rats.

Main methods. Diabetes was induced in experimental rats by a single intraperitoneal (i.p.) injection of STZ (55 mg/kg body weight [b.w]). From the sixth week, experimental rats received diosgenin at different doses (10, 20 and 40 mg/kg b.w) once daily for 4 weeks. Fasting plasma glucose, oral glucose tolerance test (OGTT), plasma insulin, haemoglobin (Hb) and glycosylated haemoglobin (HbA1C) were measured. Tissue homogenate of aorta was prepared for the quantification of oxidative stress markers. Key findings The glycemic status was significantly improved by oral administration of diosgenin in a dose-dependent manner as compared to diabetic rats. In addition, significantly decreased HbA1C and increased Hb in blood were noticed. The levels of thiobarbituric acid reactive substances (TBARS) and hydroperoxides (HP) were significantly increased whereas reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), glutathione-S-transferase (GST), glutathione peroxidase (GPx) and glutathione reductase (GR) were significantly decreased in aorta of diabetic rats. Administration of diosgenin (40 mg/kg b.w) exhibited significant reversal of STZ induced alterations in diabetic rats. All these changes were supported by histopathological observation of aorta.

Significance: The present study reveals that diosgenin may provide beneficial role on oxidative stress in aorta of STZ induced diabetic rats. This study may have a significant impact on diabetic therapy.

1. Introduction

Diabetes mellitus (DM) is a complex and progressive disease in which the hallmark feature is elevated blood glucose levels resulting from defective insulin secretion, resistance to insulin action or both that is associated with long term complications and affects aorta, blood vessels, eyes and nerves (Northam et al. 2006; Schwarz et al. 2009). Cardiovascular complications are the leading causes of morbidity and mortality in individuals with diabetes mellitus (Wild et al. 2004). It is well documented that enhanced contractility of blood vessels to endogenous substances in diabetic vascular dysfunction has been linked with impairment of endothelial function, which is commonly manifested by diminished endothelium-dependent vasorelaxation. These functional changes may be associated with aortic dysfunction in diabetes. Furthermore, established risk factors such as dyslipidemia, hypertension, and smoking cannot explain this increased prevalence of macrovascular complications in diabetes. The diabetic state itself is an independent risk factor for premature macrovascular complications. Numerous studies have been conducted in aorta of chemical induced diabetic rats to mitigate the vascular complications under hyperglycemic condition. However, the exact cellular mechanism of hyperglycemia induced aortic dysfunction is still unknown but, the advancement of research over last decade demonstrated that generation of free radicals mediated oxidative stress could play a major role in diabetic vascular complications which are associated with aortic dysfunction (Jialal et al. 2002; Esper et al. 2008; Forbes et al. 2008).
Oxidative stress in cells or tissues results in the enhanced generation of reactive oxygen species (ROS) and depletion of the antioxidants in the defense system, thereby causing an imbalance between the prooxidants and antioxidants. The decrease in the activities of antioxidants is in close relationship with the induction of lipid peroxidation (Jagetia et al. 2004).

Over the past decade, there has been an increased interest in the use of antioxidants as therapeutic agents to counteract hyperglycemia induced aortic dysfunction in order to protect the vascular changes from peroxidative injury inflicted by ROS. Phytopharmaceuticals are gaining importance in allopathic as well as traditional medicine owing to their non-addictive and non-toxic nature (Subhashini et al. 2011).

Diosgenin (Fig.1), a naturally occurring aglycone of steroid saponin found abundantly in legumes and yams such as Dioscorea species, Fenugreek. It is a well-known precursor of various synthetic steroidal drugs that are extensively used in the pharmaceutical industry (Chiang et al. 2007; Sautour et al. 2004). Diosgenin was reported to be the main metabolite of the steroidal saponins in vivo (Lin et al. 2006). Diosgenin has already been pharmacologically evaluated for its glucose lowering effect (Mc Anuff et al. 2005), antilipoperoxidative (Jayachandran et al. 2009), anti-inflammatory (Ma et al. 2011), antioxidant and antihyperlipidemic activity (Al-Matubsi et al. 2011; Son et al. 2007). Recent report showed that diosgenin from Dioscorea nipponica ameliorates diabetic neuropathy by inducing nerve growth factor (Kang et al. 2011). In view of this light, the present study is initiated with an aim to evaluate the beneficial role of diosgenin on STZ-induced oxidative stress in aortic tissue.

Materials and methods

Animals

Adult male albino rats of Wistar strain (190 – 220 g) were used for the experiment. The animals were housed in polypropylene cages and maintained in 12-h light/12-h dark cycle, 50% humidity and 25±2 °C. The animals had free access to standard pellet diet (M/S. Pranav Agro Industries Ltd., Bangalore, India) and water ad libitum. This study was approved (Approval No. 826, 2011) by Institutional Animal Ethics Committee of Annamalai University and the study conducted in accordance with the “Guide for the Care and Use of Laboratory Animals”.

Drugs and chemicals

All the chemicals used in this experiment were obtained from Sigma Chemical Company (St Louis, MO, USA), Hi Media (Mumbai, India), and SD-Fine Chemicals (Mumbai, India). All chemicals used were of analytical grade.

Induction of experimental diabetes

The animal model of diabetes was induced by a single intraperitoneal injection of streptozotocin (55 mg/kg b.w) dissolved in 0.2 mL of 0.1M citrate buffer, pH 4.5. Control rats were injected with the vehicle (0.2 mL of 0.1M citrate buffer, pH 4.5) alone. After 72 h, plasma glucose was determined and those rats with fasting glucose levels greater than 250 mg/dl were served as diabetic rats and used in the present study. After six weeks of STZ injection, oral administration of diosgenin was followed once daily for 4 weeks (Rungseesantivanon et al. 2010).

Experimental design

The animals were divided into six groups (n = 6), a total of 36 rats (24 diabetic surviving rats, 12 normal control rats) were used. Diosgenin dissolved in vehicle solution (corn oil) and different doses of diosgenin were administered orally using an intragastric tube for a period of 4 weeks.

- Group I : Normal control rats (vehicle treated).
- Group II: Normal rats + diosgenin (40 mg/kg b.w)
- Group III: Diabetic control rats
- Group IV: Diabetic control rats + diosgenin (10 mg/kg b.w)
- Group V: Diabetic control rats + diosgenin (20 mg/kg b.w)
- Group VI: Diabetic control rats + diosgenin (40 mg/kg b.w)

At the end of the experimental period, the rats were deprived of food overnight, anesthetized using ketamine (24 mg/kg b.w, intramuscular injection) and sacrificed by cervical decapitation. The blood samples were collected in potassium oxalate and sodium fluoride (3:1) tubes for the assay of plasma glucose and insulin. The blood was collected without anticoagulant used for the estimation of Hb and HbA1C.

The aortic tissue was dissected out, washed in ice-cold saline, and weighed. To prepare aorta from experimental rats, the entire length of the aorta was cut into small pieces with a razor blade and rinsed several times with phosphate buffered saline. The tissues were homogenized in 0.25M sucrose, 0.02M triethanolamine hydrochloride buffer at pH 7.4 and then centrifuged at 10000 g for 10 min. The resulting supernatants were used for the various biochemical analysis of lipid peroxidation markers, reduced glutathione and antioxidant enzymes.

Biochemical assays

Measurement of body weight, food and water intake

Body weight, food and water intake of all groups of animals were monitored on a daily basis for 56 days at a fixed time. Fixed amount of rat chow and water was given to each rat and replenished the next day.

Determination of plasma glucose, insulin, hemoglobin and glycated haemoglobin

Plasma glucose levels were estimated using a commercial kit (Sigma Diagnostics Pvt. Ltd., Baroda, India) by the method of Trinder (1969). Plasma insulin was assayed by ELISA kit (Boeheringer- Mannheim Kit, Mannheim, Germany). Hb was estimated by the cyanamnet hemoglobin method (Drabkin and Austin 1932). HbA1C was estimated by the method of Bannon with minor modifications (1982).

Oral glucose tolerance test (OGTT)

Oral glucose tolerance test (OGTT) was performed according to the method of Du vineau and Karr (1925). After overnight fasting, 0’ minute blood sample (0.2 mL) was taken from control and experimental rats. With out delay, a glucose solution (2g/kg b.w) was administered by oral gavage. Blood samples were taken at 30, 60, 90 and 120 min after glucose administration. Blood samples were collected with potassium oxalate and sodium fluoride and glucose levels were determined by the kit method of Trinder (1969) as described previously.
Estimation of lipid peroxidation

Lipid peroxidation in aorta was estimated colorimetrically by measuring TBARS and HP using the methods of Fraga et al. (1988) and Ji et al. (1992) respectively. In brief, 0.1 mL of tissue homogenate was treated with 2 mL of thiobarbituric acid (TBA)-trichloroacetic acid-HCl reagent (0.37%TBA, 0.25M HCl and 15% TCA, 1:1:1 ratio), placed for 15 min in a water bath and then cooled and centrifuged at 3500 x g for 10 min at room temperature, the absorbance of clear supernatant was measured at 535 nm against a reference blank. Values were expressed as mM/100 g-tissue.

0.1 mL of tissue homogenate was treated with 0.9 mL of reagent (88 mg of butylated hydroxy toluene (BHT), 7.6 mg of xylanol orange and 0.8 mg of ammonium iron sulphate were added to 90 mL of methanol and 10 mL of 250 mM sulphuric acid and incubated at 37°C for 30 min. Then the absorbance was read at 560 nm. Values were expressed as mM/100 g-tissue.

Estimation of reduced glutathione

Reduced glutathione was determined by the method of Ellman (1959). A known weight of tissue was homogenized in phosphate buffer. From this, 0.5 mL was pipetted out and precipitated with 2 mL of 5% TCA. 1 mL of the supernatant was taken after centrifugation at 3200 x g for 20 min and added to 0.5 mL of Ellman’s reagent and 3 mL of phosphate buffer (pH 8.0). Then the absorbance was read at 412 nm. A series of standards were prepared in a similar manner along with a blank containing 3.5 mL of buffer. The values were expressed as μM GSH/mg tissue.

Activity of catalase

Catalase was estimated by the method of Sinha (1972). 1.5 mL of reaction mixture contained 1.0 mL of 0.01 M phosphate buffer (pH 7.0), 0.1 mL of tissue homogenate and 0.4 mL of 2M H2O2. The reaction was stopped by the addition of 2.0 mL of dichromate-acetic acid reagent (5% potassium dichromate and glacial acetic acid were mixed in 1:3 ratio). Then the absorbance was read at 620 nm; CAT activity was expressed as μM of H2O2 consumed/min/mg protein.

Activity of superoxide dismutase

The activity of superoxide dismutase was assayed by the method of Kakkar et al. (1984). 0.5 mL of tissue homogenate was diluted with 1 mL of water. In this mixture, 2.5 mL of ethanol and 1.5 mL of chloroform (all reagents chilled) were added and shaken for 1 min at 4°C and then centrifuged. The enzyme activity in the supernatant was determined. The reaction mixture contained 1.2 mL of sodium pyrophosphate buffer (0.025 M, pH 8.3), 0.1 mL of 186 μM PMS, 0.3 mL of 30 μM NBT, 0.2 mL of 780 μM NADH, appropriately diluted enzyme preparation and water in a total volume of 3 mL. Reaction was started by the addition of NADH. After incubation at 30°C for 90 s, the reaction was stopped by the addition of 1 mL glacial acetic acid. The reaction mixture was stirred vigorously and shaken with 4 mL of n-butanol. The intensity of the chromogen in the butanol layer was measured at 560 nm against butanol blank. A system devoid of enzyme served as control. One unit of the enzyme activity is defined as the enzyme reaction, which gave 50% inhibition of NBT reduction in one minute under the assay conditions.

Activity of glutathione peroxidase

Glutathione peroxidase activity was measured by the method of Rotruck et al. (1973). Briefly, the reaction mixture contained 0.2 mL of 0.4 M phosphate buffer (pH 7.0), 0.1 mL of 10 mM sodium azide, 0.2 mL of tissue homogenized in 0.4 M phosphate buffer, pH 7.0, 0.2 mL glutathione, and 0.1 mL 0.2 mM hydrogen peroxide. The contents were incubated for 10 min at 37°C. 0.4 mL 10% TCA was added to stop the reaction and centrifuged at 3200 x g for 20 min. The supernatant was assayed for glutathione content using Ellman’s reagent (19.8 mg 5, 5′-dithiobisnitrobenzoic acid (DTNB) in 100 mL 0.1% sodium nitrate). The activities were expressed as μg of GSH consumed/min/mg protein.

Activity of glutathione-S-transferase

Glutathione-S-transferase activity was determined spectrophotometrically by the method of Habig et al. (1974). The reaction mixture contained 1.0 mL 100 mM phosphate buffer (pH 6.5), 0.1 mL 30 mM 1-chloro-2, 4-dinitrobenzene (CDNB), and 0.7 mL double distilled water. After pre-incubating the reaction mixture for 5 min at 37°C, the reaction was started by the addition of 0.1 mL tissue homogenate and 0.1 mL of glutathione as substrate. After 5 min the absorbance was read at 340 nm. Reaction mixture without the enzyme was used as a blank. The activity of GST is expressed as μM of GSH–CDNB conjugate formed/min/mg protein.

Activity of Glutathione reductase

Glutathione reductase was assayed by the method of Horn and Burns (1978). A test tube containing 2.0 mL of phosphate buffer, 0.1 mL of GSSG, 0.1 mL of tissue homogenate, 0.1 mL of Flavine adenine dinucleotide (FAD) and 0.05 mL of EDTA was taken. The blank was set up using all the reagents except FAD. The tubes were incubated at 37°C for 15 min following which 0.1 mL of NADPH solution was added to each tube. The reaction rate was then continuously monitored at 340 nm for 5 min and the change in absorbance was measured. Values were expressed as g of NADPH oxidized/min/mg protein.

Histopathological studies

Aortic tissues were harvested from the sacrificed animals and were fixed in 10% neutral buffered formalin solution, dehydrated in ethanol and embedded in paraffin. Sections of 5μm thickness were prepared using a rotary microtome and stained with hematoxylin and eosin (H & E) dye for microscopic observations.

Statistical analysis

The data for various biochemical parameters were analyzed using analysis of variance (ANOVA), and the group means were compared by Duncan’s multiple range test (DMRT). Values were considered statistically significant if p < 0.05 (Duncan 1957).

Results

Effect of diosgenin on plasma glucose and insulin levels

Fig. 2 depicts the levels of plasma glucose and insulin in control and experimental rats. The levels of plasma glucose were significantly increased whereas plasma insulin levels were significantly decreased in diabetic control rats. In diosgenin treated rats (all doses), a significant decrease in plasma glucose
levels and significant increase in insulin levels were observed by the end of the experimental period. Diosgenin at a dose of 40 mg/kg b.w showed more pronounced effect than 10 and 20 mg/kg b.w. Based on these data, the effective dose was fixed at 40 mg/kg b.w and used for further analysis.

**Changes in the body weight, food and water intake**

The changes in the body weight, food and water intake in control and experimental rats were represented in Table 1. Water and pellet diet consumption were significantly increased whereas the body weight significantly decreased in diabetic control rats. No significant changes were observed between normal control and diosgenin treated rats. All these changes observed in STZ treated rats were significantly improved on oral administration of diosgenin at a dose of 40mg/kg b.w.

**Effect of diosgenin on the levels of Hb and Hba1C**

The levels of total hemoglobin and Hba1C in normal control and experimental rats were depicted in Table 2. The diabetic control rats showed significant decrease in the level of total hemoglobin and significant increase in the levels of Hba1C when compared with normal control rats. The levels of total hemoglobin and Hba1C were significantly reversed by the administration of diosgenin in diabetic control rats. Normal rats treated with diosgenin at a dose of 40 mg/kg b.w have no significant changes in Hb and Hba1C levels.

**Effect of diosgenin on OGTT**

Table 3 shows the blood glucose level of normal, diabetic control and diosgenin treated rats after oral administration of glucose (2 g/kg b.w). In diabetic control rats, the peak increase in blood glucose concentration was observed after 1h. The blood glucose concentration remained high over the next hour. Diosgenin (40 mg/kg b.w) treated rats showed significant decrease in blood glucose concentration at 60 mins and 120 mins when compared with diabetic control rats.

**Effect of diosgenin on tissue lipid peroxidation**

Fig 3 and Fig 4 represent the levels of TBARS and HP in aorta of normal and experimental rats. In diabetic control rats, the levels of TBARS and HP were significantly increased in aorta as compared with normal control rats. Oral administration of diosgenin (40 mg/kg b.w) to diabetic rats significantly lowered the levels of TBARS and HP in the aorta of rats.

**Effect of diosgenin on GSH**

Fig 5 shows the levels of reduced glutathione in aorta of control and experimental rats. The decreased concentration of GSH was observed in diabetic control rats. Administration of diosgenin tends to bring the GSH level to near normal.

**Effect of diosgenin on antioxidant enzymes**

Table 4 illustrates the effect of diosgenin on the activities of aortic SOD, CAT, GR, GPx and GST in normal control and STZ-induced diabetic rats. In STZ treated rats showed a significant decrease in the activities of these antioxidant enzymes when compared with normal control rats. Oral administration of diosgenin (40 mg/kg b.w) to STZ treated rats significantly increased the activities of these antioxidant enzymes. No significant changes observed in normal control and diosgenin treated groups.

**Histological examination of the rat aorta**

The histopathological changes in normal control and experimental rats are shown in figure 6. The aorta of control rats (Fig. 6A) and diosgenin (Fig. 6B) treated rats showed a normal architecture of aorta. There was a distinct area of splitting due to intracellular lipid deposits within intimallayer and appearance of extracellular foamy cells in the outermost layer in diabetic control rats (Fig. 6C). Treatment of diosgenin to diabetic rats showed normal aortic tissue with mild appearance of extracellular foamy cells in the outermost layer (Fig. 6D).

**Discussion**

There have been increasing evidences suggesting that ROS mediated oxidative stress under hyperglycemic conditions play an important role in the development of diabetic complications (Van Reyk et al. 2003) particularly vascular diseases involving both the macro-vasculature and micro-vasculature. Aorta represents tissue macro-vasculature state in diabetic complications. STZ-induced hyperglycemia in experimental animals is mimic as pathological status found in human diabetes and also be considered as a good model for the preliminary screening of active agents against diabetes (Hasanein et al. 2010; Rakieten et al.1967).

The currently available drug regimens for management of diabetes mellitus have certain drawbacks and therefore there is a need to find safer and more effective antidiabetic drugs (Grover et al, 2000). Diosgenin was reported to be the major constituent in sapogenin extract from bitter yam and also main metabolite of the steroidal saponins in vivo (Lin et al. 2006). The consumption of sapogenin extract from bitter yam has been demonstrated to be beneficial by lowering blood glucose in STZ-induced diabetic rats might be attributed to the presence of active component diosgenin (McAnuff et al. 2005). Moreover, diosgenin from Dioscorea nipponica ameliorates diabetic neuropathy by inducing nerve growth factor (Kang et al. 2011). It is reasonable for us to have a hypothesis that diosgenin may protect STZ induced sustained hyperglycemia, which further inhibit pathological process of diabetic complications. To confirm the hypothesis, we investigated the protective effects of diosgenin in aorta of STZ treated rats.

The mechanism by which STZ brings about its diabetic state in duces selective destruction of pancreatic beta cells which make cells less active (Jacot, 1989) leading to poor sensitivity of insulin for glucose uptake by tissues and results in chronic hyperglycemia (Marles and Farnsworth 1995). Sustained hyperglycemia has been identified as a principle mediator of increased ROS generation and causes life-threatening complications linked to diabetes. Thus, strict control of glucose and insulin homeostasis is key to preventing or reversing diabetic complications (Ross 2004). In the present study, administration of STZ resulted in a significant increase in the plasma glucose level and reduction in plasma insulin level. Administration of diosgenin to diabetic rats resulted in the decrease of plasma glucose levels and an increase in the depressed plasma insulin concentrations in STZ-induced diabetic rats may be attributed to its glucose lowering effect due to the presence of β-sitosterol in diosgenin (McAnuff et al. 2005).
Glycated hemoglobin reflects the average blood sugar concentration over an extended period of time and is not affected by short-term fluctuations in blood sugar levels (Murray et al. 2000). Therefore, it is a better index for the development of diabetic complications (Gabbay 1976). Since insulin has an anabolic effect on protein metabolism, numerous studies have been reported that increased glycosylation of a number of proteins, including Hb in experimental rats might be due to the defective in insulin action (Koeing et al. 1976; Alberti et al. 1982) Our findings are also correlated with previous reports that decrease in total haemoglobin, and an increase in glycylated haemoglobin of diabetic rats. Treatment of diosgenin to diabetic rat brought Hb and HbaA1C to near normal levels, as a result of improved glycemic status. Taken together with above results, the ability of diosgenin to decrease HbaA1C levels indicate its potentiality to prevent the diabetic associated complications.

Induction of diabetes with STZ is associated with the characteristic loss of body weight (Al-Shamaony et al. 1994) and increased food intake (Szukedelski and Szukudsiska 2002; Chen and Ianuzzo 1982) due to the increased catabolism of structural proteins and metabolic changes attributed to the lack or deficiency of insulin (Chatterjee and Shinde 2002). On oral administration of diosgenin alters the body weight, decreased food and water intake in diabetic rats.

It is well documented that diabetic vascular complications is mediated through oxidative stress induced by autoxidation of glucose and glycosylation of proteins. Lipid peroxidation is considered a hallmark of oxidative stress, in which ROS interact with polyunsaturated fatty acids, and leads to the formation of lipid products which then causing damages to the membrane components of the cell, cell necrosis and inflammation (Kumar et al. 2008; Frei and Higdon 2003). Today, extensive evidences have been demonstrated that TBARS level is increased in both plasma and aortic tissue accompany with defective vascular endothelial function of experimental diabetic models (Alper et al. 2006; Ozansoy et al. 2001). In our study, there were significant increases in lipid peroxidative markers in aorta of STZ treated rats, as measured by TBARS and HP. Our findings suggest that the exposure to high glucose levels may elevate the generation of ROS through the glycation of protein and glucose autooxidation. As a consequence, it provokes damage in structural and functional integrity of aortic tissues, as evidenced by an increase in the oxidative deterioration of the lipids of cellular membrane in diabetic state.

Drugs with antioxidant properties may supply endogenous defense systems and reduce both initiation and propagation of ROS (Bergendi et al. 1999). In the present investigation, treatment with diosgenin significantly decreased the lipid peroxidative markers, through its free radical scavenging activities and membrane stabilizing effect (Honga and Lee 2009; Jayachandran et al. 2009).

The increase in the levels of lipid peroxidative markers might be an indicative of impairment in the antioxidant defense mechanism (Nizamutdinova et al. 2009). Therefore, tissue antioxidant status is one of the major factors in determining the development of diabetic complications (Pennathur and Heinecke 2004; Yue et al. 2005). Levels of these antioxidants are an appropriate indirect way to assess the prooxidant-antioxidant status in STZ induced oxidative stress in aortic rat. SOD is an important defense enzyme which catalyses the dismutation of superoxide radicals to produce hydrogen peroxide (H2O2) and molecular oxygen (Lin et al. 2005). The increase in superoxide radicals also inhibits catalase activity (Kono and Fridovich 1982). Catalase is a heme-containing ubiquisites enzyme; it reduces hydrogen peroxide produced by dismutation reaction and preventing generation of hydroxyl radicals thereby protecting the cellular constituents from oxidative damage. Decreased activities of both SOD and CAT in diabetic tissues are due to excess availability of superoxide radicals and H2O2 in the biological systems (Saravanana and Ponnurugan 2011; Sozmen et al. 2000).

On the other hand, glutathione-related enzymes such as GPx, GR and GST function either directly or indirectly as antioxidant. GSH is the primary non-enzymatic antioxidant and acts as a free radical scavenger in the repair of radical-caused biological damage with the presence of GPx (Nicotera and Orrenius 1986). GST and GPx play principle function to reduce organic hydroperoxides within membranes and lipoproteins in the presence of GSH (Hayes and Pulford 1995). Therefore, decreased activities of GST and GPx with a concomitant decrease in the activity of GSH-regenerating enzyme, GR suggest the consumption of glutathione while protecting against the STZ - induced oxidative stress, as they help to maintain cellular redox status. In our study, a significant decrease in enzymic and non - enzymic antioxidants was observed in the aorta of diabetic rats in agreement with Kevin who reported reduced levels of antioxidant in aorta of STZ treated rats (Kevin et al. 2005). Interestingly, diosgenin could markedly renew the impairment of antioxidant defense system in the aorta of diabetic rats might be attributed to its antioxidant and free radical properties which could be due to the presence of hydroxyl group in diosgenin (Al-Matebshi et al. 2011; Son et al. 2007; Honga 2009).

Consequently, biochemical perturbations seem to be correlated with the evidence of histological changes in the aorta. In the present study, histopathological examination of diabetic aorta revealed distinct areas of splitting due to intracellular lipid deposits within the intimal layer and extracellular foaming cells in the outer most layers. Oral administration of diosgenin significantly reduced the pathological changes in the aorta which may be due to block oxidative stress by decreasing the lipid peroxidation and increasing the antioxidant cascade observed in this study.

Conclusion

From the above findings, we conclude that diosgenin has the ability to ameliorate oxidative stress in aorta of STZ treated diabetic rats as evidenced by improved glycemic and antioxidant status along with decreased lipid peroxidation. In addition, it protects histological changes from peroxidative injury through its antioxidant properties. Further mechanistic studies are essential to formulate diosgenin as potential antihyperglycemic agent in diabetic complications.
5. References


