ORIGINAL ARTICLE

Ameliorative potential of *Vigna mungo* seeds on hyperglycemia mediated oxidative stress and hyperlipidemia in STZ diabetic rats

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Ethnomedicinally the seeds of *Vigna mungo* are used as cooling astringent, diet during fever, poultice for abscesses, soap alternative. The increased oxidative stress plays an important role in the etiology and pathogenesis of diabetes mellitus and its various complications. This study was designed to examine the effect of hydroalcoholic extract (VME) of *V. mungo* seeds on STZ-diabetic rats by measuring glycemia, lipid profile, and lipid peroxidation parameters (MDA, PCO, and GSH) and antioxidant enzymes activities (SOD, CAT, and GPx). The levels of glucose, TG, TC, MDA, and PCO were increased significantly whereas the levels of serum insulin, reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT) and Glutathione peroxidise (GPx) were decreased in STZ induced diabetic rats. Administration of VME (200 mg/kg bw and 400 mg/kg bw p.o.) to diabetic rats for 28 days showed a significant decrease in serum glucose, TG, TC, MDA, and PCO. In addition, we also summarize here that the levels of serum insulin, superoxide dismutase, catalase, GPx, and reduced glutathione (GSH) were increased in VME treated diabetic rats. The antioxidant and antihyperglycemic effect of VME was compared with glibenclamide, a well-known antioxidant and antihyperglycemic drug. The findings in this study suggest that the VME possesses a significant favourable effect on antioxidant defense system in addition to its antidiabetic effect. Nonetheless, this study provides evidence that could help explain how the traditional use of *V. mungo* has been successful in the treatment of various disorders in humans.

Key words: Antihyperglycemic, oxidative stress, *Vigna mungo*

INTRODUCTION

Diabetes is defined as a state in which the homeostasis of carbohydrate and lipid metabolism is improperly regulated by the pancreatic hormone, insulin, ultimately resulting in the increased blood glucose level. It is the world's largest endocrine disorder and is one of the major killers in recent times.[1] According to World Health Organization (WHO), the world-wide global population is in the midst of a diabetes epidemic with people in Southeast Asia and Western Pacific being mostly at risk. The number of cases for diabetes which is currently at 171 million is predicted to reach 366 million by the end of 2030 (World Health Organization.[2] Therefore, it is necessary to search for new drugs and interventions that can be used to manage this metabolic disorder. *Vigna mungo* is a leguminous seed that belongs to the family leguminosae. Ethnomedicinally the seeds of *V. mungo* are used as cooling astringent, diet during fever, poultice for abscesses, soap alternative[3] It is very rich in carbohydrate, fat, protein and fiber and flavonoids such as kaemferol-3-0-rutinoside, kaemferol-3-0-glucoside, robininin etc.[4,5] In many regions of the world, legume seeds are the unique protein supply in the diet. These food proteins are not only a source of constructive and energetic compounds as the amino acids, but also they may play bio-active roles by themselves and/or can be the precursors of biologically active peptides with various physiological functions, for example, casein-derived peptides that have been proved to possess immuno-modulating, antihypertensive, antithrombotic and opioid activities. Grain legumes can hardly be found in the old books of traditional medicine as specific therapeutic agents. Other indications of phytotherapeutic use of legumes comes from the Mediterranean regions, where grain legumes have traditionally been consumed for centuries and constitute an element of the Mediterranean diet. Regular intake of pulses are recommended to human to reduce risk of cardiovascular disease,[6] digestive tract disease, obesity etc.

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MATERIALS AND METHODS

Animals

Adult Wistar rats weighing (150–200 g) were procured from Disease-Free Small Animal House, Chaudhary Charan Singh Haryana Agriculture University, Hisar (Haryana). All the animals were housed in the animal house of Guru Jambheshwar University of Science and Technology (GJUSandT), Hisar, Haryana and were maintained at a standard room temperature of 25±1°C; relative humidity of 45–55% and a 12:12 h light/dark cycle for 7 days with free access to standard rat pellet (Pranav Agro Industries Ltd., Bangalore, India) and water *ad libitum* under hygienic conditions. The animals were selected based on the model criteria and care was taken in such a way that all the animals were used only once. Animals were accustomed to laboratory conditions for 48 h before the initiation of experiment. The approval of the Institutional Animal Ethical Committee (IAEC) of GJUSandT, Hisar (Haryana) was taken before the initiation of the experiments. All the protocols and experiments were conducted in compliance with the ethical principles and guidelines provided by the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA), Chennai, India

Preparation of Extract

V. mungo seeds were obtained as a gift sample from CCSHAU Hisar and authenticated by Dr. H. B. Singh, Head, Raw Materials Herbarium and Museum, National Institute of Science Communication and Information Resources, India. The dried powdered seeds of *V. mungo* were defatted with petroleum ether and then extracted with 70% v/v methanol. The hydroalcoholic (70% methanol) extract was then concentrated using rotary vacuum evaporator.

Chemical and Reagents

Glibenclamide was obtained as a gift sample from Torrent Pharmaceutical, Ahemdabad. Streptozotocin (STZ) and heparin were procured from SRL, India. All the solvents and chemicals used for extraction and phytochemical investigation were of analytical grade purchased from S.D. Fine Chemicals Pvt. Ltd., Mumbai, India.

Induction of Experimental Diabetes

Diabetes was induced by a single i.p. injection of STZ in fasted rats at dose of 60 mg/kg. STZ was freshly dissolved in 0.1 M cold sodium citrate buffer, pH. 4.5. Development of diabetes was confirmed 72 h after injection of STZ by measuring fasted blood glucose levels. Only rats with fasting blood glucose levels greater than 250 mg/dl were considered diabetic and then included in the experiment. Treatment with plant extract was started on the third day after STZ injection and continued for 28 days.

Preliminary Phytochemical Screening

Preliminary phytochemical screening of hydroalcoholic extract of *V. mungo* seeds was carried out for the detection of phytoconstituents using standard conventional protocols.[7]

Acute Toxicity Study

Acute toxicity study of extracts was studied in Wistar rats by up and down method.[8] Animals were treated with Vigna mungo methanolic extract (VME) extract (1 g/kg, 2 g/kg, 3 g/kg, and 4 g/kg) and observed continuously for the first 4 h for general behavioral, neurological, autonomic profiles and mortality within 24 h. One fifth and one tenth of safe dose were selected as the experimental doses.

Experimental Design

Group I: **N**ormal control rats, received vehicle solution (1 ml/kg, p.o.) for 28 days**.**
Group II: Diabetic rats received vehicle solution (1 ml/kg, p.o.) for 28 days**.**
Group III and IV: Diabetic animals were treated with 200 mg/kg p. o. and 400 mg/kg p. o. methanolic extract of *V. mungo* seeds respectively**.**
Group V: Diabetic rats were administered Glibenclamide (600 µg/kg; p.o.).

On the last day of experiment, animals were sacrificed and blood samples were collected without heparin for biochemical estimations. Some pancreas were removed, cleaned, and washed in ice-cold normal saline solution for biochemical analysis. Other portions of pancreas were taken out, washed in ice-cold saline solution and immediately fixed in the 10% neutral buffered formalin solution.

Biochemical Assays

Estimation of glucose levels, lipid profile, and insulin level

Serum glucose, total cholesterol (TC), triglycerides (TG) was assayed by enzymatic methods, using commercial reagent kits (Sigma Diagnostics Pvt. Ltd., Baroda, India). Serum insulin was determined using rat Insulin enzyme-linked immunosorbent assay (ELISA, Boerhriger Mannheim, Germany) kit.

Lipid peroxidation assay

Lipid peroxidation in the pancreas tissue was estimated colorimetrically by measuring thiobarbituric acid reactive substances (TBARS) which were expressed in terms of the malondialdehyde content.[9] Briefly, aliquots of pancreas homogenates were mixed with 1 ml of 5% TCA and centrifuged at 4000×*g* for 10 min. One milliliter of thiobarbituric acid reagent (TBA, 0.67%) was added to 500 ml of supernatant and heated at 95°C for 15 min. The mixture was then cooled and was measured for absorbance at 532 nm. The malondialdehyde (MDA) values were calculated using 1,1,3,3-tetraethoxypropane as the standard and expressed as nmoles of MDA/g of tissue.

Protein carbonyl assays

Protein oxidation was determined based on the reaction of the carbonyl groups with 2,4-dinitrophenylhydrazine (DNPH) to form 2,4-dinitrophenylhydrazone by method.[10] Samples were read at 370 nm and carbonyl content was calculated using the molar absorption coefficient for aliphatic hydrazones (22,000 $M^{-1}cm^{-1}$) and expressed as nmol carbonyl/mg protein.

Measurement of reduced glutathione

Pancreas glutathione (GSH) content was determined by Ellman's method,[11] modified by Jollow *et al*.[12] based on the development of a yellow color when Ellman's reagent (5,5-Dithiobis-(2-nitrobenzoic acid)) is added to compounds containing sulfhydryl groups. Briefly, 3 ml of sulfosalicylic acid (4%) was added to 500 µl of homogenate tissues for deproteinization. The mixture was centrifuged at ×2500 *g* for 15 min. Then Ellman's reagent was added to 500 µl of supernatant. The absorbance was measured at 412 nm after 10 min. Total GSH content was expressed as mg/g of tissue.

Assay of antioxidant enzymes

1. The catalase (CAT) activity was determined according to the Aebi method.[13] The rate of H_2O_2 decomposition was followed by monitoring absorption at 240 nm. One unit of CAT activity is defined as the amount of enzymes required to decompose 1 µmol of hydrogen peroxide in 1 min. The enzyme activity was expressed as µmol H_2O_2 consumed/min/mg protein
2. Superoxide dismutase (SOD) activity was estimated according to the method of Beauchamp and Fridovich.[14] The developed blue color in the reaction was measured at 560 nm. Units of SOD activity were expressed as the amount of enzyme required to inhibit the reduction of NBT by 50% and the activity was expressed as U/mg protein
3. Glutathione peroxidase (GPx) activity was measured according to the method of Flohe and Gunzler.[15] The enzyme activity was expressed as nmol of GSH oxidized/min/mg protein.

Protein analysis in pancreas

Protein concentrations were measured using the method of Lowry *et al*.[16] Briefly, 200 µl of reaction mixture (Na_2CO_3 2%, Tartrate double of Na and K 2%, and CuSO4 1%) was added to 200 µl of homogenate pancreas. The mixture was treated with 200 µl Folinphenol reagent diluted to 1/2 and then incubated in the dark for 28 min. The absorbance was measured at 500 nm. Bovine serum albumin was used as a standard.

Data Analysis

All the results were expressed as mean±standard error of mean (SEM). The data of all the groups were analyzed using one-way ANOVA followed by Dunnett's t-test using the software Instat. In all the tests, the criterion for statistical significance was $P<0.05$.

RESULTS

Preliminary Phytochemical Screening

The preliminary phytochemical screening of *V. mungo* seeds hydroalcoholic extract showed the presence of proteins, flavonoids, glycosides, saponins, and sterols.

Acute Toxicity Study

In an acute toxicity study, the hydroalcoholic extract did not show any observable toxic effects in behavior and physiology up to 2 g/kg. For further experimental study, the concentration of extract was fixed 200 mg/kg and 400 mg/kg.

Effects of *Vigna mungo* Methanolic Extract on Body Weight, Hyperglycemia, and Hypoinsulinemia Induced by STZ

Table 1 depicts the initial and final body weight, the levels of fasting blood glucose and serum insulin in control and experimental groups of rats. At the end of treatment, a severe loss (-24.73%) of body weight was observed in diabetic rats (STZ). In addition, the levels of blood glucose were increased by (>300%) and those of serum insulin were decreased by (-61%) in the diabetic rats when compared

Table 1: Body weight, serum glucose, and insulin levels in adult rats

Treatment	Body weight		Serum glucose level at corresponding day					Serum insulin level (ng/ml)
	Initial	Final	0	7	14	21	28	28 days
Control	242±2.5	245±2.1	82±1.0	80.5±0.98	86.12±2.4	83.56±2.56	84.5±2.67	1.24±0.2
Diabetes	232±7.5	186±3.6*	330±2.2	356.56±9.85	378.62±5.9	393.45±6.15	367.01±8.9	0.45±0.01
Diabetes + VME 200 mg/kg	235±6.4	208.67± 5.5*	334.83±2.15	219.50± 2.63*[a]	210.33± 3.08*[a]	188.67± 2.44*[a]	211.50± 3.11*	0.78±0.05[a]
Diabetes + VME 400 mg/kg	230±5.6	220±4.5*	324.67±2.59	205.50± 3.93*[a]	189.50± 5.14**[a]	150.33± 3.8**[a]	148±2.25*	0.89±0.05[a]
Diabetes + Gli 600 µg/kg	235±5.4	230±4.5*	356±2.4	246± 11.75**[a]	180.40± 8.72**[a]	147.20± 4.5**[a]	142.80± 3.79**	0.96±0.03[a]

Values are presented as mean±S.E.M; *n*=6 in each group. One way ANOVA followed by Dunnett's test. *$P<0.05$; **$P<0.01$ compared to 0 value; [a]$P<0.01$ compared to the dia value; VME – Vigna mungo methanolic extract

to the control group. The oral administration of VME 200 mg/kg and 400 mg/kg to the diabetic rats for 28 days significantly (P<0.001) reduced glycemia by 36.83% and 54.41%, respectively, and increased serum insulin levels by 56% and 78%, when compared to those of diabetic rats

Effects of VME on Lipid Profile of STZ-induced Diabetic Rats

The effects of Vigna seed extracts on lipid parameters are presented in Table 2 and Figure 1. Our results showed that the administration of STZ increased TG and TC by 162% and levels by 68% (P<0.001), after 28 days of treatment, in comparison to control rats. The administration of Vigna extracts 200 mg/kg and 400 mg/kg reduced the significant rise in the levels of the TG significantly (P<0.001) by 44% and 62%, respectively. The level of TC was also found to be significantly lower in VME-treated animals as compared to diabetic rats.

Effects of VME on STZ-induced Lipid Peroxidation, Protein Oxidation, and GSH Content

Table 3 represents the levels of MDA, Protein carbonyl content (PCO), and GSH in pancreatic tissue of the control and experimental rats. The diabetic rats showed a significant (P<0.01) increase in MDA and PCO levels and a decrease (P<0.05) in GSH levels when compared to those of control group. Increased levels of MDA (P<0.01), and PCO (P<0.001) were significantly declined by (15%) and (51.29%), respectively, in the diabetic rats treated with VME 200 mg/kg associated with an increase (P<0.01) of GSH content by (21%) when compared to diabetic rats (STZ). The animals treated with 400 mg/kg VME showed a significant decrease in MDA and PCO by 41% and 79% and increase in GSH level by 43%.

Effects of VME on STZ-induced Changes in the Antioxidant Enzyme Activities

The activities of enzymatic antioxidants such as, SOD, CAT, and GPx in the control and experimental groups of rats are represented in Table 3. The activities of these enzymatic antioxidants were significantly (P<0.01) decreased in the diabetic rats when compared to those of control group. Oral administration of VME 200 mg/kg and 400 mg/kg to the diabetic rats showed a significant increase in the activities of SOD, CAT and GPx by (+288%, +27%, and +15%), and 414% (P<0.001), +71% and +26%, respectively.

DISCUSSION

The present investigation reports the antihyperglycaemic, antihyperlipidemic, and antioxidant effects of *V. mungo* seed extract (VME) on STZ induced diabetic rats. STZ-induced hyperglycemia has been described as a good experimental model to study diabetes mellitus. Its administration to rats showed an increase in the blood glucose levels and a decrease in the serum insulin levels. Antihyperglycaemic potency of VME in STZ induced diabetic rats has been indicated by improvement of fasting bloodt glucose levels

Table 2: Triglycerides and total cholesterol levels in the serum adult rats

Treatment	Triglyceride (mg/dl)	Total cholesterol (mg/dl)
Control	103.76±4.24	109.34±1.45
Diabetes	271.56±7.56	183.56±2.56
Diabetes + VME 200 mg/kg	153±6.78**	95.45±4.56**
Diabetes + VME 400 mg/kg	103.78±5.7**	85.56±6.8**
Diabetes + Gli 600 µg/kg	89.56±6.7**	76.34±6.3**

Values are presented as mean±S.E.M; n=6 in each group. One way ANOVA followed by Dunnett's test. **P<0.01 compared to the dia value; VME – Vigna mungo methanolic extract

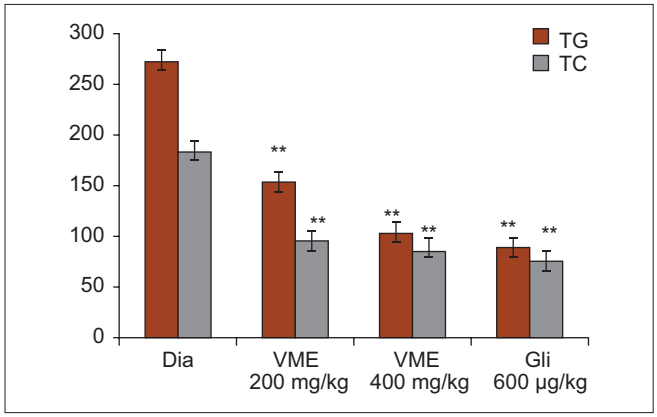

Figure 1: Triglycerides (TG) and total cholesterol (TC) levels in the serum adult rats

Table 3: MDA, PCO, and GSH levels and antioxidant enzymes activities (SOD, CAT, and GPx) in the pancreas tissue of adult rats (controls and experimental groups)

Treatment	MDA nmol/g tissue	GSH mg/g tissue	PCO nmol/mg protein	SOD U/mg protein	CAT µmolH_2O_2/min/mg protein	GPx nmol GSH/min/mg protein
Control	39.23±5.6	114.45±3.45	2.89±0.07	88.67±2.34	54.34±1.23	13.23±0.08
Diabetes	102.25±3.6[b]	91.78±2.3[b]	25.56±5.6[b]	14.45±2.3	22.34±3.56[b]	12.34±0.89
Diabetes + VME 200 mg/kg	87.56± 2.23[b]**	110.56± 2.34**	12.45± 0.78**	56± 1.24**	28.23± 1.2**	14.23± 0.1**
Diabetes + VME 400 mg/kg	60.94± 1.56[b]**	130.72± 1.23**	5.56± 1.23[b]***	74.27± 1.34***	38.27± 0.56[b]**	15.54± 0.24**

Mean±SEM (n=6). [b]P<0.01 compared to control; **P<0.01 compared to Dia, ***P<0.001 compared to the dia value; MDA - malondialdehyde; PCO – Protein carbonyl content; GSH - Glutathione; SOD - Superoxide dismutase; CAT - Catalase; GPx - Glutathione peroxidise; VME - Vigna mungo methanolic extract

which is also an important parameter for monitoring diabetes mellitus. In order to know if VME could stimulate the insulin *in vivo*, serum insulin levels were measured after oral treatment for 28 to diabetic rats with the extract. It was observed that extract treated diabetic rats showed decrease in the levels of blood glucose and increase in the levels of serum insulin.VME by its ability to scavenge free radicals and to inhibit lipid peroxidation, decreases STZ-induced oxidative stress and protects β-cells resulting in increased serum insulin levels and decreased blood glucose levels. Increased insulin level is due to the stimulatory effect of VME, thereby potentiating the existing β-cells of islets of Langerhan's in diabetic rats.

Hakim *et al*.[17] have reported that decreased body weight in diabetic rats is due to dehydration and catabolism of fats and proteins. Increased catabolic reactions leading to muscle wasting might also be the reason for the reduced weight gain by diabetic rats.[18] Extract treated diabetic rats improved body weight and this could be due to a better control of hyperglycaemic state in the diabetic rats. Decreased levels of blood glucose could improve body weight in STZ-induced diabetic rats.

Hyperglycemia, the primary clinical manifestation of diabetes, is the most responsible factor for the development of various chronic diabetic complications and free radical production (ROS).[19] When the generation of ROS and other free radical overwhelms cellular defenses, the unstable radicals react with essential molecules within the cell such as lipids, protein and DNA, leading to histological changes as well as functional abnormalities. According to Yeh *et al*.,[20] the use of phytochemicals compounds on tissues which regulates glucose metabolism, is an interesting area to explore.

Diabetes mellitus is also strictly related to other metabolic abnormalities such as lipid profile, characterized mainly by high triglyceride and cholesterol levels[21,22] which were also observed in our STZ-induced diabetic rats. Our study showed that VME extract lowered not only the level of blood glucose, but also improved lipid metabolism by causing a significant decrease in serum TG and total cholesterol levels. VME extracts could exert its TC lowering activity by decreasing the cholesterol biosynthesis especially by decreasing the 3-hydroxy-3-methyl-glutaryl coenzyme A reductase (HMG CoA reductase) activity, a key enzyme of cholesterol biosynthesis and/or by reducing the NADPH required for fatty acids and cholesterol synthesis. Solanki YB[23] also reported antihyperlipidemic activity of *V. mungo* seeds in poloxamer-407 and diet-induced hyperlipidemia. We suggested also that VME might reverse the catabolic features of insulin deficiency by (1) stimulating peripheral glucose utilization, (2) increasing glucose removal from blood, or (3) reducing glucose absorption from the gastrointestinal tract. In this context, glucose and lipid metabolism might be improved due to an increase in insulin secretion by the remnant cells that were able to synthesize, and secrete more insulin in order to normalize glucose levels and lipid metabolism. In fact, we have obtained a 78% increase of serum insulin levels when compared to those of diabetic rats.

During the diabetic state, increased generation of ROS occur and cause an imbalance between the oxidant and antioxidant status.[24] Sustained hyperglycemia has been identified as a principle mediator of increased reactive oxygen species generation in diabetes. Free radicals may also be formed via the auto-oxidation of unsaturated lipids in serum and membrane lipids. They may react with polyunsaturated fatty acids in cell membrane leading to lipid peroxidation (LPO).[25]

In this study, the increased formation of LPO in pancreas tissue of diabetic rats supported these findings. Oral administration of VME to experimental diabetic rats abrogated the increased MDA levels suggesting that VME might have a high antioxidant capacity to scavenge free radicals generated by reactive oxygen species and prevent radical damage. Furthermore, our results demonstrated that VME exhibited a high antioxidant capacity.

The oxidative stress, a key factor in the progression and development of diabetes and its late-complications, is mediated through the diabetogenic action of STZ as well as chronic hyperglycemia.[26,27] It is reported that STZ can stimulate free radicals generation, which may be one of the most essential causes of cell damage and diabetogenic effect of STZ.[28,26] Free radicals mediated damages were counterbalanced by GSH, a major endogenous antioxidant. It is well known that GSH is involved in the protection of the normal cell structure and function by maintaining the redox homeostasis, quenching of free radicals and participating in detoxification reactions. It is a direct scavenger of free radicals as well as a co-substrate for peroxide detoxification by glutathione peroxidases.[29] In our study, we have found a decrease of GSH levels in pancreas of diabetic rats. This reduction could be explained, according to previous studies[30,29] by a decrease of GSH synthesis or an increase of its degradation induced by STZ oxidative stress. Administration of VME to experimental diabetic rats resulted in a marked increase in the levels of glutathione.

This indicated that the VME extracts could also increase the biosynthesis of GSH or reduce the oxidative stress leading to less degradation of GSH, or could have both effects. Superoxide dismutase, another antioxidative defence enzyme, destroyed the superoxide radical through dismutation and generated hydrogen peroxide, which

is consecutively reduced by the activities of catalase or glutathione peroxidase. Several studies have reported a reduced activity of SOD in experimental diabetes.[31-34] Thus, the reduced activity of SOD could be the result of superoxide anion over accumulation in the cell,[35] and its inactivation by hydrogen peroxide[36] or by glycation of the enzyme.[32] In our study, oral administration of VME to diabetic rats showed a marked increase in the activity of superoxide dismutase by virtue of its antioxidant as well as insulin stimulatory potential. Catalase, another enzymatic antioxidant predominantly present in peroxisomes, ameliorated the deleterious effect of hydrogen peroxide, which was produced by SOD, into water and nonreactive oxygen species. It restrained the generation of hydroxyl radical and protected the cells from oxidative damage. In diabetic conditions, the uncontrolled production of hydrogen peroxide due to the auto-oxidation of glucose, protein glycation, and lipid oxidation led to amarked decline in the catalase activity.[37,38] Recently, the decreased activity of catalase in the protection of pancreatic β-cells from oxidative stress during diabetic conditions has been reported.[37] In our study, oral administration of VME to diabetic rats showed a significant elevation in the activity of catalase, since it stimulated the remnant cells to secrete more insulin for normalizing the streptozotocin-induced hyperglycemia. Another antioxidant enzyme, glutathione peroxidise was a selenium-containing tetrameric glycoprotein involved in the detoxification of hydrogen peroxide into water and molecular oxygen. During diabetic conditions, the activity of glutathione peroxidase is decreased as a result of radical-induced inactivation and glycation of the enzyme.[39] Subsequent to VME administration to diabetic rats for 28 days, the glutathione peroxidase activity was increased in diabetic rats which could be attributed to the insulin stimulatory properties of this extract. Moreover, the results of the present investigation are consistent with other studies[40-42] that reported the correlation between the increased lipid peroxides and the decreased enzymatic antioxidants in experimental diabetes. Thus, it may be concluded that VME possesses significant antidiabetic and antioxidant potential in streptozotocin-induced diabetic rats. The results of the present study suggest that VME protects the pancreatic β -cells from free radical-mediated oxidative stress and thereby stimulates the remnant pancreatic β cells to synthesize and secrete more insulin and thus the status of antioxidant system is fortified. In fact, STZ administration elicited severe injury of pancreas and reduction in the number of β- cells. While, administration of VME showed increase in insulin production, suggesting that β-cells are probably functioning at higher capacity. Further studies are needed to identify the molecular mechanism exhibited by VME extract to protect pancreas tissue in STZ-induced diabetic rats.

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