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Anti-Diabetic and Safety Properties of Aqueous Stem Bark Extract of *Vitelleria paradoxa* in Streptozotocin-Induced Diabetic Rats

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Abstract
Background: *Diabetes is considered the third leading cause of death around the globe with a projection increase of its prevalence by 2030.*
Aim: *The study was aimed at investigating the anti-diabetic and safety properties of aqueous extract of Vitellaria paradoxa (VPX) stem bark in streptozotocin-induced diabetic rats.*
Materials and methods: *A total of thirty (30) albino rats weighing 150 ± 40.5 g were randomized into six groups (A-F). Group A (Control) are non-diabetic while group(s) B-F were made diabetic following administration of streptozotocin (90mg/kg body weight, i.p.) after which animals in groups C-F were administered 2.5 mg/kg b.w glibenclamide (reference drug), 80, 400 and 800mg/kg body weight of the extract respectively once daily for 21 days whereas animals in group(s) A and B received 0.5ml of distilled water orally. Blood sugar level, antioxidant enzyme status (catalase and superoxide dismutase), anti-dyslipidemic and kidney function parameters were determined in the experimental rats.*
Results: *The results showed that aqueous extract of V. paradoxa stem bark produced a significant reduction ($p<0.05$) in fasting blood glucose level and serum lipid profile (T-chol, TAG and LDL-c) of diabetic rats in a dose dependent manner. The extract also improved the antioxidant status in diabetic rats and as well induced the synthesis of protein by significantly ($p<0.05$) elevating the activities of aspartate transaminase (EC. 2.6.1.1), alanine transaminase (EC. 2.6.1.2) and alkaline phosphatase (EC 3.1.3.1) in the liver of rats at all the doses investigated. However, 800mg/kg body weight of the extract showed better comparison with glibenclamide.*
Conclusion: *Overall results showed that Vitellaria paradoxa possess anti-diabetic as well as antioxidant properties by facilitating pancreatic insulin secretion, glucose uptake and mopping up generated free radicals respectively. It may therefore be considered safe for use in the management of diabetes.*
Key words: *Vitellaria paradoxa, Sapotaceae, Streptozotocin, Diabetes, Glibenclamide.*

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I. Introduction

Diabetes mellitus, often referred to as diabetes, is a metabolic condition characterized by chronic hyperglycemia (abnormal high blood sugar level) due to the body either not producing enough insulin, or the body cells developing resistance to the insulin produced [i]. Polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger) are the most common symptoms associated with diabetes mellitus. Diabetes is one of the commonest diseases around the globe [ii] whose prevalence is becoming worrisome particularly in Nigeria. International Diabetes Federation [iii] proposed that the number of people living with diabetes worldwide will increase to 552 million by 2030 from 366 million in 2012 unless a proactive action is taken. The reports also predicted that one in 10 adults will have diabetes by 2030, posing a huge challenge to health care delivery systems around the world. In Nigeria, World Health Organisation (WHO) puts the incidence of diabetes as at 2010 to be 576,000 while it is projected to increase above 685,000 for another decade [iv]. The complications associated with diabetes are retinopathy, nephropathy, neuropathy, loss of body mass and weight, cardiovascular disorders and failure of organs. Wild *et al.* [v] reported that people with diabetes may likely develop coronary diseases. Type I diabetes also known as Insulin Dependent Diabetes Mellitus (IDDM) and

Type II diabetes also known as Non-Insulin Dependent Diabetes Mellitus (NIDDM) are the two most common types of diabetes. In Type I diabetes, the pancreas that produce insulin hormone which regulates blood sugar is impaired resulting to insufficient amount of insulin while in Type II diabetes, the body cells developed resistance to the insulin produced. The World Health Organization has also identified gestational diabetes mellitus which occur during pregnancy and malnutrition-diabetes mellitus as types of diabetes. However, malnutrition-related diabetes was omitted from the new classification because its main etiology is not yet known, and it is unclear whether it is a separate type of diabetes [vi-viii]. Currently available synthetic drugs used in the treatment of diabetes have many side effects among which are liver problem, lactic acidosis and diarrhea [ix] thus making the efficacy of these drugs arguable. The search for alternative drug from natural source that will not only provide better treatment for diabetes but that will also be safe, readily available, and with little or no side effects is therefore necessary. Plants are considered to be the new lead for alternative source of anti-hyperglycemic agents. V*itellaria paradoxa* which belongs to the *Sapotaceae* family is locally abundant in the derived savannah and Guinea zones of Africa like Mali, Cameroon, Congo, Cote d'Ivoire, Ghana, Guinea, Togo, Nigeria, Senegal, Sudan, Burkina Faso and Uganda. V*itellaria paradoxa* have very long leaf stalks, more widely spaced nerves and abundant white latex when slashed [x]. The vegetable fat extracted from the fermented fruit stone (shea butter) of this plant species has been considered as an economic function [xi]. The shea butter is frequently used to make ointments and poultices for emollients and healing. Ethnobotanical studies revealed that the leaf and bark of this plant are used for the treatment of Burili ulcer [xii], treatment of malaria, dental pain and neuralgia [xiii]. In addition, scientific reports on the antibacterial activity of various extracts of *Vitellaria paradoxa* has also been documented [xiv]. The traditional efficacy of *Vitellaria paradoxa* in treating diabetes has also been established [xv] however; there is paucity of scientific information on their anti-diabetic and safety properties. *Vitellaria paradoxa* are among the locally used medicinal plants by the south-western people of Nigeria to treat diabetes. This study aims to investigate the anti-diabetic potential and safety evaluation of aqueous extract of *Vitelleria paradoxa* stem barks in streptozotocin-induced diabetes which could serve as an alternative source for the development of new anti-diabetic therapy.

II. Materials And Methods

Plant Material and Authentication

Fresh stem barks of *Vitellaria paradoxa* were obtained from a farmland at Temidire area in Ogbomoso area of Oyo State, Nigeria. Authentication was done at the Department of Plant Biology, University of Ilorin, Ilorin, Kwara State, Nigeria where a voucher number UILH 001/952 was deposited.

Preparation of Extract

The Fresh stem barks of *V. paradoxa* were washed with distilled water to remove dirt particles and air-dried in the laboratory for 14 days. They were cut into smaller pieces and pulverized using a mechanical blender and later sieved to obtain a more homogenous powdered sample. A known weight (100 g) of the powdered sample was macerated in 500 ml of distilled water which was shaken at regular interval to achieve maximum extraction for 48 hours. The extract was filtered using Whatman No.1 filter paper and later lyophilized. The dried extract was then reconstituted in distilled water to obtain the required doses (80, 400 and 800 mg/kg body weight) for administration.

Qualitative Phytochemical Screening

The stem bark extract of *V. paradoxa* was screened for phytochemical properties using standard methods described by Sofowora [xvi].

Experimental Animals

30 albino rats (*Rattus norvegicus*) weighing 150 g ± 2.50 were selected for the study and were obtained from the Animal Holding Unit of the Department of Biochemistry, University of Ilorin, Ilorin, Kwara State, Nigeria. Ethical approval was issued by the University Ethical Committee, University of Ilorin, Kwara State, Nigeria. The rats were acclimatized for 7 days and were maintained under standard laboratory conditions (12-h light/dark cycle, 25 ± 2^{o}C). They were fed with standard pelleted diet and water *ad libitum*. Animals were fasted 24 hours before commencement of the experiment.

Glucometer and Assay Kits

Fine Test Glucometer and strips used were products of Roche Diagnostic, Mannheim, Germany. Assay kits for alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine, albumin, bilirubin, cholesterol, triglycerides and high density lipoprotein were products of Randox Laboratories Ltd. Co- Antrim, UK.

Drugs and Chemicals

Streptozotocin was procured from Sigma Chemical Company, St Loius, MO, USA. Glibenclamide was a product of HOVID Bhd., Ipoh, Malaysia. All other chemicals used were of analytical grade and were prepared in all-glass using distilled water.

Animal Grouping and Extract Administration

Thirty (30) albino rats of both sexes were randomized into six groups (A-F) of five rats each.
Group A: (Control) received 0.5 ml of distilled water orally
Group B: Diabetic untreated received 0.5 ml of distilled water orally on daily basis repeatedly for 21 days.
Group C: Diabetic and treated with 0.5 ml of glibenclamide (2.5 mg/kg body weight) as reference drug once daily.
Groups D-F: Diabetic and treated with 0.5ml doses of 80, 400 and 800 mg/kg body weight of aqueous extract of *V. paradoxa* bark respectively once daily.
Vehicle, extract and reference drug administration lasted for 21 days. The blood samples were collected from the tail three days each of the 21 days to determine the blood glucose.

Induction of Diabetes and Determination of Blood Glucose

Diabetes was induced by a single intra-peritoneal injection of 90 mg/kg body weight of Streptozotocin (STZ) prepared in cold citrate buffer (pH 4.5). Control group were injected with citrate buffer alone. Blood samples were taken from the tail vein and glucose levels were determined to confirm the induction of diabetes using the Fine Test strips and glucometer. Animals were considered diabetic, if the fasting blood sugar were above 12mmol/L at the end of the third day after STZ injection. The treatment started on the fourth day after STZ injection and this was considered the first day of treatment.

Preparation of Serum and Tissue Homogenate

At the end of the experimental period (21days), animals were anaesthetized with diethyl ether. Blood samples were collected into plain sample tubes for serum analysis. Serum was centrifuged at 3000 rev/mins for 10 minutes [xvii]. The supernatant was aspirated with Pasteur's pipette and stored until required for further analysis. The liver and pancreas were isolated and homogenized in ice cold 0.25 M sucrose solution and the homogenates were kept frozen to ensure maximum release of enzymes.

Determination of Liver and Kidney Function Indices

The procedure used for the determination of serum albumin and bilirubin were the methods described by Doumas *et al.* [xviii], Sherlork [xix] respectively. The method of Tietz [xx] was employed for creatinine and urea determination in the serum.

Lipid Profile Analysis

Lipid profile analysis was carried in the serum for total cholesterol, low-density lipoprotein, high-density lipoprotein and triglycerides using the method described by [xxi- xxiv] respectively.

Determination of Liver Enzyme Activities

The activity of alanine aminotransferase and aspartate aminotransferase in the liver and serum were assayed using the method described by [xxv].

Determination of Superoxide Dismutase, Catalase Activity and Malondialdehyde Concentration

Misra and Fridovich [26] method was employed in the determination of superoxide dismutase activity. The activity of catalase and malondialdehyde concentration in the pancreas was determined by the method described by [xxvii, xxviii] respectively.

Data Analysis

Data were expressed as mean of five replicates ± standard error of mean (SEM). Statistical evaluation of data the was performed by SPSS version 16 using one-way analysis of variance followed by Duncan's Multiple Range Test for multiple comparisons. Values were considered statistically significant at ($P < 0.05$).

III. Results

The photochemical screening of the aqueous extract of *Vitellaria paradoxa* stem bark revealed the presence of alkaloids, tannins, saponins, phenols, steroids, anthraquinones, glycosides and phlobatannins (Table I). The glycemic effect of aqueous extract of *Vitellaria paradoxa* (VPX) stem bark in streptozotocin-induced

diabetic rats is shown in Table II. The intraperitoneal injection of streptozotocin significantly ($p < 0.05$) elevated the blood glucose level in all diabetic rats after 72 hours when compared with non-diabetic control. The oral administration of 2.5 mg/kg body weight of glibenclamide and aqueous extract of VPX stem bark at doses of 80, 400 and 800 mg/kg body weight significantly ($p < 0.05$) lowered the blood glucose level from the fourth day of treatment to the last day of treatment i.e day 21. Group treated with 800 mg/kg body weight of VPX exhibited a remarkable anti-hyperglycemic effect comparable to glibenclamide group as it lowered the blood glucose level progressively.

The intraperitoneal injection of STZ resulted in a significant loss ($p<0.05$) of body weight in diabetic untreated rats when compared with the control. However, improvement was observed in the body weight of rats upon the administration of 800 mg/kg body weight of the extract when compared to the diabetic group that received no medical intervention and was comparable with the reference drug (Table III). The effects of oral administration of aqueous extract of *Vitellaria paradoxa* bark on serum parameters of the experimental rats is presented in Table IV. Urea and creatinine levels were significantly elevated ($p < 0.05$) in the serum of diabetic untreated rats when compared to the control. Upon the gavaging of the extract at the three doses investigated, the urea and creatinine levels significantly ($p < 0.05$) reduced in dose dependent manner, but the extract at 800 mg/kg body weight was more efficacious in reducing the urea and creatinine and as well was comparable with the reference drug.

There was an alteration in albumin and globulin levels of STZ-induced untreated diabetic rats when compared with the control. However, this alteration was attenuated in all the extract treated groups in a dose dependent pattern and also compared favorably with the glibenclamide treated group (Table IV). Figure 1 shows the effect of aqueous extract of *Vitellaria paradoxa* stem bark on serum total cholesterol (TC), High density lipoprotein (HDL-c), low density lipoprotein (LDL-c) and triglyceride. The total cholesterol, low density lipoprotein and triglyceride significantly ($p < 0.05$) reduced upon the administration of the aqueous extract of *Vitellaria paradoxa* bark and glibenclamide when compared to the STZ-induced group. The high density lipoprotein (HDL-c) was significantly ($p < 0.05$) increased in the glibenclamide and the extract treated group when compared with the diabetic group. In addition, 400 and 800 mg/kg body weight of aqueous extract of *Vitellaria paradoxa* bark compared favorably with the reference drug in lowering the triglyceride and low density lipoprotein concentrations.

Figures 2-4 depict aspartate aminotransferase, alanine aminotransferase and alkaline phosphate activities in the serum and liver of STZ-induced diabetic rats. There was a significant increase ($p < 0.05$) in the activity of alanine aminotransferase, aspartate aminotransferase and alkaline phosphatase in the serum of STZ-induced group when compared with the control which also resulted to a corresponding decrease in the activity of the enzymes in the liver. The continued administration of glibenclamide and the extract at the doses investigated in the present study significantly ($p<0.05$) enhanced the activity of ALT, AST and ALP in the liver with also a corresponding decrease in the activity of these enzymes in the serum when compared with the diabetic group that received no medical attention. However, no alteration was observed in the activity of ALP in the serum of glibenclamide treated group and the control whereas only 800 mg/kg body weight of VPX showed a robust serum AST and ALT activities similar to the reference drug. The extract showed a significant ($p<0.05$) higher activity of catalase and superoxide dismutase at dose of 400 mg/kg body weight when compared with diabetic untreated group and as well compete favorably ($p>0.05$) with the glibenclamide treated group and their respective distilled water group. However, all the diabetic treated groups expressed a significant ($p < 0.05$) up regulation in the activity of catalase when compared with the diabetic untreated group. Moreso, dose of 800 mg/kg body weight of the extract did not show any significant difference ($p < 0.05$) in catalase level when compared to the group treated with the reference drug (Figure 5).

Figure 6 depict the level of lipid peroxidation in the pancreas of STZ-induced diabetic rats. A significant elevation ($p < 0.05$) was observed in malondialdehyde concentration in the pancreas of diabetic rats when compared with non-diabetic control. The concentration of thiobarbituric acid (TBA) reacting substances in the pancreas of rats administered 800 mg/kg body weight of VPX extract and 2.5 mg/kg body weight of glibenclamide was lowered to the values comparable with the control. Also the extract at 80 mg/kg and 400 mg/kg body weight were able to significantly ($p < 0.05$) reduce malondialdehyde in the pancreas of diabetic rats upon administration when compared with the diabetic untreated rats.

IV. Discussion

In this present study, the phytochemical screening of the aqueous bark extract of *Vitellaria paradoxa* revealed saponins, alkaloids, phenolics, steroids, cardiac glycosides to be present. These phytoconstituents are of medicinal values particularly in the treatment of diabetes mellitus as phenolics, saponins and alkaloids have been reported to show efficacy against diabetes [xxix, xxx]. The result obtained on blood glucose level is in accordance with the investigation carried out by [xv] on the hypoglycemic and antihyperglycemic activity of aqueous and hydro-ethanolic extracts of *Vitellaria paradoxa* bark in rabbit at the same doses (80, 400 and 800

mg/kg body weight) investigated in this study. The blood glucose level that was elevated in the diabetic untreated group was reduced in the diabetic treated group with the extract. Although, the mechanism of action by which the extract exhibit its hypoglycemic is not clearly known. It may be that the extract stimulates the production of insulin from the islet cells as well enhance the utilization of glucose [xxxi] due to the presence of the phytoconstituents of the extract which have been reported to exhibit hypoglycemic activity. Like the plant extract, glibenclamide also produced significant reduction in the elevated blood glucose levels. Glibenclamide is a standard anti-diabetic drug used to compare the efficacy of hypoglycemic compounds and has been reported to enhance the activity of β-cells of the pancreas resulting in production of huge amount of insulin thus, reducing glucose level [xxxii]. It was observed that the weight of STZ-induced rats was significantly reduced when compared with the control. This may be a direct consequence of insulin resulting to increased muscle wasting and loss of tissue proteins [xxxiii]. The oral administration of the extract at doses of 400 mg/kg and 800mg/kg body weight showed robust improvement in the body weight of experimental rats. The increased body weight may be attributed to the anti-diabetic property of the extract. The kidney plays a vital role in the removal of metabolic wastes from the blood stream. However, its functionality can be assessed by determining the serum concentrations of certain biomolecules [xxxiv] among which is urea and creatinine. The elevated levels in urea and creatinine observed in the diabetic untreated rats suggest disturbance in the metabolism of these biomolecules. The levels of urea and creatinine in the serum were attenuated in the VPX treated groups which is likely an indication that the extract aid in the recovery of animals from metabolic disorders associated with diabetes mellitus [xxxv]. The increased levels of total cholesterol, triacyglycerols and LDL-c of STZ-induced diabetic rats correlate with previous report that diabetes is associated with increase in serum total cholesterol and triacyglycerols which is related to significant changes in lipid metabolism and structure in the disease state [xxxvi-xxxvii]. These increased levels of total cholesterol, triacyglycerols and LDL-c may increase the risk of developing coronary disease. Ingestion of aqueous bark extract of *Vitellaria paradoxa* to rats produced a significant lowering effect of cholesterol, triacyglycerols, LDL-c and increase HDL-c level. The increase in HDL-c level maybe beneficial owing to the correlation between HDL-c level and the low risk of developing cardiovascular diseases. High density lipoprotein (HDL) is also called good cholesterol because it transport excess cholesterol from the tissues to the liver where it is metabolized to bile acids and then excreted, this make HDL beneficial to health. The serum lowering activity of the extract maybe attributed to the plant components like saponins, phenols, alkaloids, steroids, cardiac glycosides. These compounds have been reported to have anti-hyperlipidemic and anti-atherosclerotic properties [xxxviii]. Aspartate and alanine aminotransferases are biomarker enzymes used in clinical diagnosis. The increase in the activities of AST and ALT in the serum of STZ-induced rats which resulted to a corresponding decrease in their activities in the liver suggests that the integrity of the plasma membrane of the liver is compromised causing a spillage of these enzymes (AST and ALT) out of the membrane into the serum. Administration of the extract at the doses investigated in this study caused a reduction in the serum activity of AST and ALT, this suggests the hepatoprotective ability of the extract. Also increase in alkaline phosphatase activity in the liver of the extract treated group suggests that the extract induce the synthesis of the protein. Several studies have implicated oxidative stress in diabetes, as this process results in the damage of cells. An increase in oxidative stress may occur due to generation of increased free oxygen species. These reactive oxygen species (ROS) are capable of altering the levels of biomolecules including the levels of antioxidant enzymes (catalase and superoxide dismutase). In the diabetic untreated group, the activity of catalase reduced in the pancreas of experimental rats which suggests increased oxidative stress that resulted to the decrease in the activity of this enzyme. In our study, we observed that the aqueous stem bark extract of *Vitellaria paradoxa* at 400 mg/kg and 800 mg/kg body weight improved the antioxidant status of catalase and superoxide dismutase. This improved antioxidant status in the extract treated group may be due to the free radical scavenging ability of the phytoconstituents present in the aqueous stem bark extract of the plant. The result obtained on lipid peroxidation in this study is similar to that of [xxxix] who reported the lipid profile, antidiabetic and antioxidant activity of *Acacia ataxacantha* bark extract in streptozotocin-induced diabetic rats. Malondialdehyde is a biomarker of lipid peroxidation generated by oxidative stress in living cells by participating in a variety of biochemical reactions. The significant increase ($p<0.05$) in pancreatic malondialdehyde concentration in the diabetic but treated groups which reduced upon oral administration of the aqueous stem bark extract of *Vitellaria paradoxa* may be due to the extract antioxidant phytoconstituents which reduced the oxidative stress that caused lipid peroxidation thereby reducing the generation of free radicals and thus may have prevented the damage of cellular organelles either by decreasing localized oxygen concentration, presenting first chain initiation by scavenging initial radicals and binding metals or by decomposing peroxide [xxxix].

V. Conclusion

The results of this study clearly demonstrated that the plant possesses anti-diabetic property by stimulating glucose utilization by peripheral tissues or increasing insulin production by the pancreas from regenerated *β*-cells. This further affirms the ethnobotanical claims of the plant in the treatment of diabetes mellitus. Aqueous stem bark extract of *Vitellaria paradoxa* at 800 mg/kg body weight exhibited the most remarkable anti-diabetic activity. A further study will therefore be necessary to isolate and characterize the bioactive principle(s) responsible for the anti-diabetic property.

Table I: Secondary metabolites present in aqueous extract of *V*PX stem bark

Secondary Metabolites	Inference
Alkaloids	+
Tannins	+
Saponins	+
Flavonoids	-
Anthraquinones	+
Steroids	+
Phenols	+
Glycosides	+
Cardenolides	-
Terpenoids	+

Keys: + (present), - (absent)

Table II: Effect of administration of aqueous extract of VPX stem bark on blood glucose level of STZ-induced diabetic rats

Days	Control	Diabetic group	Glibenclamide (mmol/L)	80 mg/kg b.wt VPX	400 mg/kg b.wt VPX	800 mg/kg b.wt VPX
0	5.80±0.96^{a}	5.84±1.00^{a}	5.87±1.50^{a}	5.60±1.40^{a}	6.04±1.18^{a}	5.90±1.00^{a}
3	4.97±0.60^{a}	32.63±0.90^{b}	22.83±0.32^{c}	35.00±0.00^{b}	34.83±0.40^{b}	21.80±0.11^{c}
6	3.73±0.51^{a}	33.07±0.91^{b}	14.33±0.60^{c}	18.73±1.90^{d}	21.57±1.30^{d}	13.03±0.90^{c}
9	4.00±0.31^{a}	32.77±0.20^{b}	9.87±0.25^{c}	17.17±0.22^{d}	16.03±0.53^{d}	10.10±0.60^{c}
12	4.27±0.60^{a}	33.13±0.70^{b}	5.17±0.60^{a}	16.10±0.80^{c}	15.30±0.73^{c}	7.10±0.81^{a}
15	5.80±0.46^{a}	32.67±0.90^{b}	4.60±0.28^{a}	21.43±1.80^{c}	14.67±1.1^{d}	6.87±1.01^{a}
18	5.00±0.42^{a}	34.00±1.22^{b}	4.30±0.35^{a}	20.77±1.50^{c}	15.77±1.40^{d}	5.63±0.52^{a}
21	4.40±0.10^{a}	31.33±0.91^{b}	4.10±0.11^{a}	20.93±1.10^{c}	12.87±1.04^{d}	4.53±0.20^{a}

Values are means of five replicates ± SEM. (Values with different superscript are statistically different at $p < 0.05$).

VPX = *Vitellaria paradoxa*

Table III: Effect of administration of aqueous extract of VPX stem bark on body weight of STZ-induced diabetic rats

Days	Control	Diabetic group	Glibenclamide	80 mg/kg b.wt VPX	400 mg/kg b.wt VPX	800 mg/kg b.wt VPX
0	197.33±1.23^{a}	176.33±1.01^{a}	179.67±1.26^{a}	165.00±1.11^{b}	156.67±1.28^{b}	166.33±1.13^{b}
3	197.67±1.39^{a}	169.00±1.23^{b}	172.33±1.16^{b}	158.33±1.18^{c}	153.67±1.20^{c}	161.33±1.35^{c}
6	202.67±1.49^{a}	165.33±1.81^{b}	171.67±1.67^{b}	153.67±1.10^{c}	148.67±1.88^{d}	167.33±1.49^{b}
9	202.00±1.44^{a}	162.00±0.93^{b}	176.33±1.17^{c}	150.00±1.16^{d}	147.00±1.73^{d}	168.00±1.10^{b}
12	205.67±1.50^{a}	158.33±1.41^{b}	180.33±1.17^{c}	148.00±1.73^{d}	150.67±1.24^{d}	174.33±1.04^{c}
15	212.00±1.56^{a}	154.00±4.16^{b}	183.33±1.22^{c}	144.00±4.58^{d}	155.33±6.36^{b}	179.00±1.15^{c}
18	212.33±1.76^{a}	151.67±0.84^{b}	187.67±1.22^{c}	141.67±0.92^{d}	154.00±1.21^{b}	177.00±1.28^{e}
21	208.33±1.08^{a}	147.00±1.51^{b}	192.00±1.12^{a}	138.00±1.04^{b}	151.00±1.07^{b}	169.11±1.10^{c}

Values are means of five replicates ± S.E.M. (Values with different superscript are statistically different at $p < 0.05$).

VPX = *Vitellaria paradoxa*

Table IV: Effect of administration of aqueous extract of VPX stem bark on some serum biomolecules of STZ-induced diabetic rats

VPX = *Vitellaria paradoxa*

Parameters	Control	Diabetic control	Glibenclamide	80mg/kg b.wt VPX	400 mg/kg b.wt VPX	800 mg/kg b.wt VPX
Urea (U/L)	0.14±0.01[a]	1.17±0.12[b]	0.18±0.53[a]	0.85±0.12[d]	0.69±0.16[e]	0.16±0.08[a]
Creatinine (U/L)	0.58±0.39[a]	1.40±0.45[b]	0.60±0.44[a]	0.75±0.22[a]	0.65±0.24[a]	0.62±0.35[a]
Albumin (U/L)	10.25±0.42[a]	7.22±0.75[b]	10.14±0.25[a]	11.21±0.14[a]	11.02±0.11[a]	10.75±0.64[a]
Globulin (U/L)	10.50±0.14[a]	34.75±0.05[b]	16.28±0.06[c]	28.90±1.20[d]	19.75±1.74[e]	14.34±0.20[f]
Total Protein	205.67±1.50[a]	140.33±1.41[b]	180.33±1.17[c]	148.00±1.73[a]	158.67±1.24[ab]	179.33±1.04[c]

Values are means of five replicates ± S.E.M. (Values with different superscript are statistically different at $p < 0.05$).

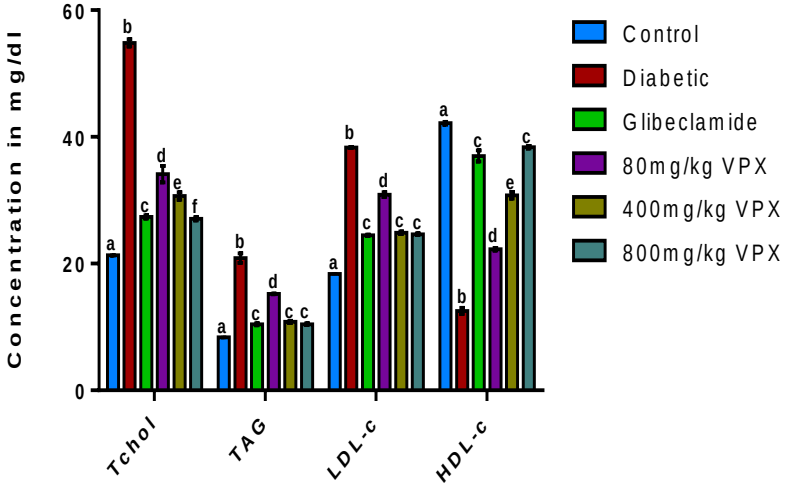

Figure 1: Effect of Administration of Aqueous Extract of *Vitellaria paradoxa* bark on Serum Lipid Profile of STZ-induced Diabetic Rats

VPX = *Vitellaria paradoxa*

Each bar is a mean of five replicates ± S.E.M. Error bars with different superscripts are statistically different ($p < 0.05$).

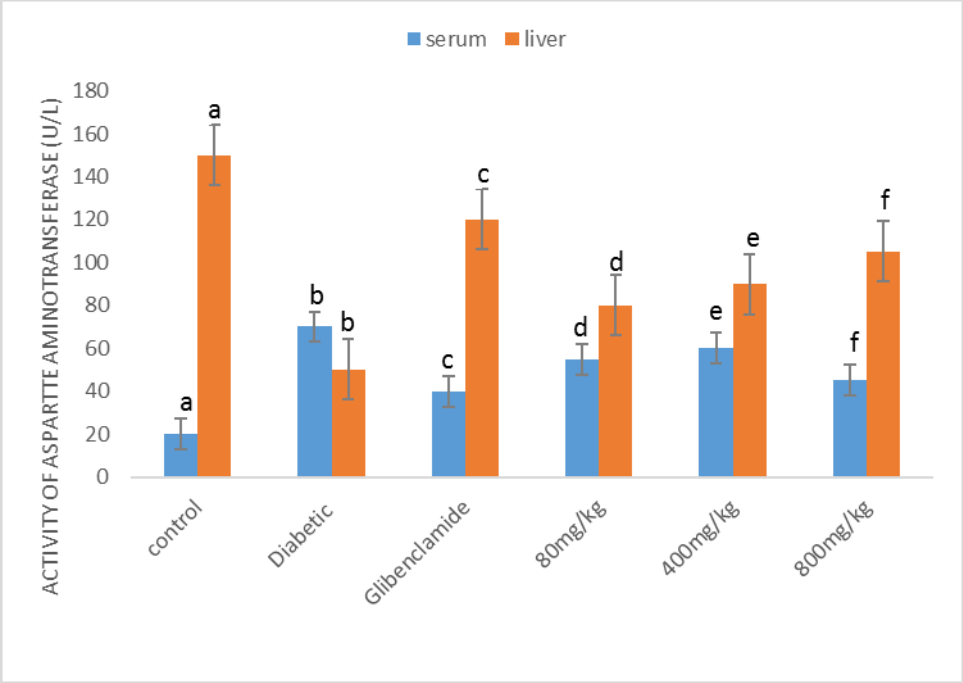

Figure II: Activity of Aspartate aminotransferase in the serum and liver of STZ-induced Rats after *Vitellaria paradoxa* stem bark extract treatment

Each bar is a mean of five replicates ± S.E.M. Bars with different superscripts are statistically different ($p < 0.05$).

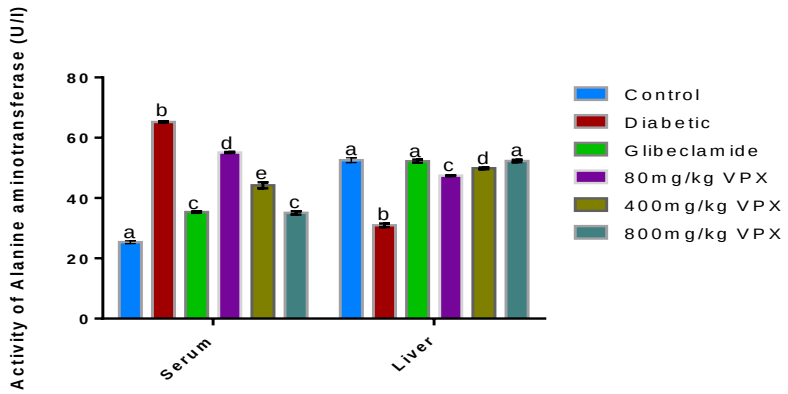

Figure III: Activity of Alanine aminotransferase in the serum and liver of STZ-induced diabetic rats after *Vitellaria paradoxa* stem bark extract treatment

VPX = *Vitellaria paradoxa*

Each bar is a mean of five replicates ± S.E.M. Bars with different superscripts are statistically different ($p < 0.05$).

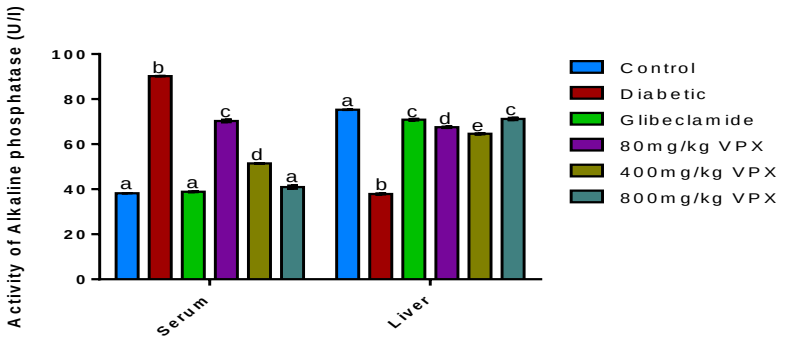

Figure IV: Activity of Alkaline Phosphatase in the serum and liver of STZ-induced diabetic rats after *Vitellaria paradoxa* stem bark extract treatment

VPX = *Vitellaria paradoxa*
Each bar is a mean of five replicates ± S.E.M. Error bars with different superscripts are statistically different ($p < 0.05$).

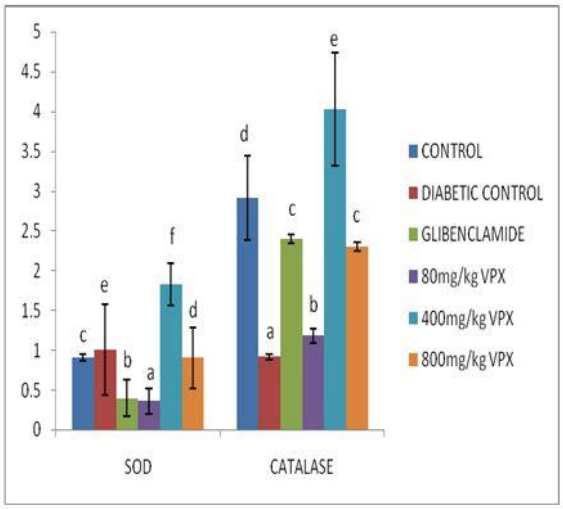

Figure V: Activity of Superoxide dismutase [SOD] (U/mg protein) and Catalase [CAT] (U/mg protein) in the Pancreas of STZ-induced Rats after *Vitellaria paradoxa* stem bark extract treatment
VPX = *Vitellaria paradoxa*
Each bar is a mean of five replicates ± S.E.M. Error bars with different superscripts are statistically different ($p < 0.05$).

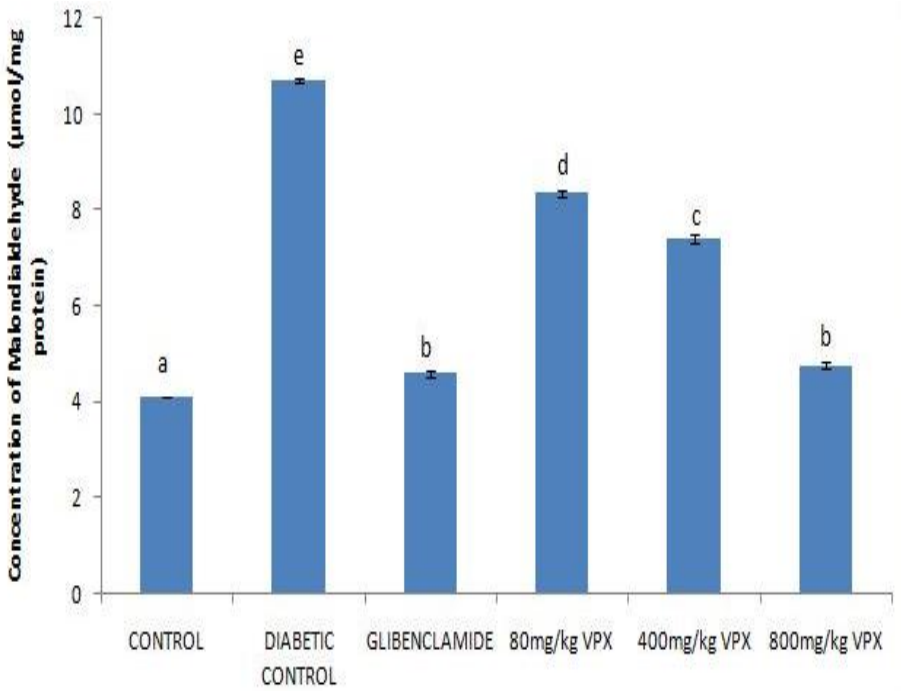

Figure VI: Concentration of malondialdehyde in STZ-induced diabetic rats after *Vitellaria paradoxa* stem bark extract treatment

VPX = *Vitellaria paradoxa*

Each bar is a mean of five replicates ± SEM. Error bars with different superscripts are statistically different ($p < 0.05$).

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