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RESEARCH ARTICLE

Evaluation of Antidiabetic Activity of *Indigofera prostrate* on Normal and Streptozotocin Induced Diabetic Albino Wistar Rats

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Abstract

Background: Diabetes mellitus is an ailment that affects majority of individuals in the world. The objective of the current study is to estimate the antidiabetic effect of methanol extract of *Indigofera prostrata* whole plant, which is cultivated extensively in India's arid and also desert regions. **Aim:** The aim of the current investigation is to estimate the efficacy of methanol extract of *I. prostrata* (MEIP) to prevent streptozotocin-induced diabetes mellitus in albino wistar strain rats. **Methods:** In current examination, methanol extracts of the whole plant of *I. prostrata* with the doses of 250 and 500mg/kg/b.wt (body weight) are administered through oral route to the streptozotocin made diabetic animals where n=6. We evaluated the differences in water intake, intake of food, glucose in fasting, weight of body and also the oral glucose tolerance test. When extract of *I. prostrata* was used for evaluating the (OGTT) Oral Glucose Tolerance Test for diabetic animals, levels of glucose were found to be pointedly lower when administered with 500 mg/kg b.wt as associated to the control group. *I. prostrata* had specifically reduced the elevated levels of glucose in diabetic rats. *I. prostrata* is a vital alternative source for managing blood glucose levels in diabetes mellitus that have increased during the condition and need to be further reduced by oral medications that cause hypoglycemia. Biochemical parameters were estimated as a part of the investigation. **Results:** The results demonstrated that the dried methanol extract of *I. prostrata* (250 mg/kg/bwt and 500 mg/kg/bwt) considerably declined the levels of blood glucose during the treatment period when compared to glibenclamide (10mg/kg), enhanced the metabolism, improved the health of animals and also enhanced the oral glucose tolerance test. **Conclusion:** As a result, we can conclude that the whole plant of *I. prostrata* methanol extract contains antidiabetic activity.

Keywords: Control Group, Diabetes Mellitus, Hypoglycemic Action, *Indigofera prostrate,* Streptozotocin, Wistar Rats

1. Introduction

According to Chaudhary, diabetes mellitus a continuing metabolic illness prompted through an insufficient supply of the hormone insulin. It is characterized by hyperglycemia, altered protein, carbohydrate and lipid metabolism and also an increased risk of vascular problems[1]. In many parts of the world, diabetes affects around 5% of the population worldwide and now it is a serious health issue. According to estimates, there will be more than 300 million diabetics worldwide by 2025, the expenses of treating the condition and complications might reach US$1 trillion annually[2]. Typically affecting young adults and teenagers, the illness reveals quickly. Low insulin levels result in higher blood glucose levels[3].Consequently, HbA1C is associated to glucose concentration of blood directly and it is also considered a very complex index for glycemic control[4]. Unrestrained diabetes may cause heart problems, blindness and also renal failure[5].

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The genus *Indigofera* has established distinctive properties that make it an interesting choice as a potential perennial crop. The contemporary study reveals that, the preliminary phytochemical analysis of extract of methanol of *I. prostrata* discovered the occurrence of flavonoids, glycosides, steroids, tannins, alkaloids, saponins and carbohydrates. The extract of *I. prostrata* possess significant hepatoprotective activity against paracetamol and alcohol induced hepatotoxicity[6]. Numerous investigations had evaluated the phytochemistry as well as pharmacology of species of *Indigofera*. Almost 199 compounds had been recognized, comprising alkaloids, compounds of phenol, terpenoids and esters of glucose of nitropropanoic acid[7]. Pharmacological investigations have revealed that extracts from crude material and cleaned fractions of species of *Indigofera* possess innumerable properties comprising anti-arthritic and anthelmintic activities[8].

Studies have shown that obesity increases adults risk of cardiovascular illnesses and significantly correlates with insulin resistance in both those with and without type 2 diabetes[9]. Diabetes mellitus has been treated with allopathic drugs; however, these drugs have side effects, including hypoglycemia, flatulence, weight gain, dyspepsia, confusion and joint problems. Herbal medicines are a very popular alternative to allopathic treatments because they practically have no side effects or bad effects[10]. Numerous medicinal herbs have antidiabetic effects. The leaves of *Azima tetracant* have an antidiabetic effect on diabetic rats instigated by streptozotocin[11]. The objective of current investigation was to determine the antidiabetic action of extract of methanol of *I. prostrata* whole plant on normal and STZ induced diabetic rats.

2. Materials

Glibenclamide, streptozotocin bought from the Sigma Aldrich firm. The Taidoc Technology Corporation in San-Chung, Taipei, Taiwan, provided the glucose meter kit. From E. Merck in Mumbai, chemicals and other solvents were obtained. Albino rats were bought from VAB Biosciences, located in Hyderabad, Telangana, India.

2.1 Authentication

In the month of July, the whole plant of *I. prostrata* was acquired and validated in the Andhra Pradesh province's Chittoor district, India. It belongs to *Fabaceae* family. The selected whole plant material of *I. prostrata* has been authenticated by Dr. K. Madhava Chetty, Department of Botany, Retired Assistant Professor, Sri Venkateshwara University, Tirupathi, India. Then, a sample was preserved in herbarium with voucher number1129 for future use.

2.2 Extraction by Maceration

I. prostrata whole plant material was ground into a coarse powder after being shade-dried. The substance was passed through a sieve and then collected on a plate. By macerating the *I. prostrata* plant material using methanol, ethyl acetate and chloroform as solvents, the plant material was extracted. The residual extracts were concentrated and dried, and then placed in a desiccator for future research after the solvents were removed using a rotating vacuum evaporator. The plant's starting amount taken for extraction is 500grams and the extract plant's yield are10%.

2.3 Chemicals and Reagent

Analytical grade chemicals were used in the study.

2.4 Test Drug

Streptozotocin used for current study.

2.5 Standard Drug

Standard drug Glibenclamide was used for current study.

2.6 Procurement of Animals and Maintenance

Albino wistar strain rats 180-200 grams were bought from VAB Biosciences, Bapuji Nagar, Musheerabad, Hyderabad, India. Animals got acclimatized to their surroundings by allowing them to stay in the experimental conditions for around 10 days prior to the animal studies. Each cage had a different number written on it with a marker to help identify the animals. The cages housing the animals were made of polypropylene, and the bedding was rice. Animals were well-supervised, given a regular diet and unrestricted access to the water. The temperature range for the animals enclosure was 20 to 25°C, in consistent 12:12 hours cycle of light as well as dark.

2.7 CPCSEA Approval

Institutional Animal Ethical Committee had accepted the proposed experimental study on December 9, 2022 with number for registration CPCSEA/1657/IAEC/CMRCP/COL-22/105. In accordance with the recommendations made by the committee for the purpose of control and supervision of experiments on animals (CPCSEA), the animals were housed in a traditional manner in an animal house at the CMR College of Pharmacy in Medchal, Hyderabad, India.

3. Methods

3.1 Acute Toxicity Study

The investigation in experimental rats was carried out following OECD-423 guidelines. Diverse doses (10, 50, 300, 2000 mg/kg b.wt) of *I. prostrata* methanol extract were administered to groups comprising 3 animals of the identical age group and weight by oral route. The experimental animals were frequently monitored for every hour uninterruptedly and then for 4hr and lastly after every 24hr up to 15 days to detect any of toxicity symptoms and also mortality[12].

3.1.1 Consequence of Methanol Extract of I. prostrata on Levels of Blood Glucose of Normoglycemic Rats

Albino rats of both sex of wistar strain (180-200 grams) were employed for the contemporary investigation and had access to a standard food and also water. The dose of the extract was selected based on intense literature survey and by performing acute toxicity studies (OECD-423 guidelines). Rats were made to fast for 18 hours with only water available before to the test. The rats were separated into four groups comprising six rats each. Group-I rats were treated as control. Group II rats were given drug glibenclamide as standard at 10 mg/kg b.wt (dose) orally. Rats of Group-III were managed with 250 mg/kg b.wt of methanol extract of *I. prostrata* whole plant. Whereas, Group-IV rats were administered with *I. prostrata* entire plant extract by 500 mg/kg b.wt.

Samples of blood were withdrawn through tail vein directly prior to dosing and also at 2nd, 4th, 6th, and 8th hour after dosing. The content of blood glucose was determined using a commercially available glucometer kit and the glucose oxidase technique. Comparing the glucose levels at the first and second hours was necessary to calculate the hypoglycemic response. All data were statistically analyzed using ANOVA and reported as mean S.D. The glucose oxidase method was used to measure the amount of blood glucose by using a commonly available glucometer kit.

3.1.2 Oral Glucose Tolerance Test

Albino wistar strain rats (180-200 grams) were employed in current investigation. Animals are given with a consistent diet and unrestricted access to water. Entire rats were kept fasting for about 18 hours before experimental procedure through just water intake. The animals parted into 4 groups, comprising 6 animals each. Group-I marked as controls. Group II rats were received oral administration of standard Glibenclamide10 mg/kg b.wt. While, rats in Group III received *I. prostrata* at 250 mg/kg b.wt. Group IV have received an oral dose of whole plant extract of *I. prostrata* at a dose of 500 mg/kg b.wt. All the rats received 2 gm/kg of p.o. solution of glucose following 30 minutes of medication management. Immediately prior to treatment by plant extract, as well as after treatment with plant extract for 30, 60, 90, and also 120 minutes, the samples of blood obtained from tail vein. The glucose oxidase method was used to measure the blood glucose levels using a commonly used glucometer kit. The hypoglycemia was evaluated by analyzing the change in levels of blood glucose between the 0th and subsequent hours. Data was statistically analyzed using ANOVA and reported as mean S.D.

3.1.3 Induction of Diabetes with Streptozotocin in Albino Wistar Strain Rats

Following acclimatization, the rats are subjected to expedite fast. Diabetes was induced with streptozotocin injection through intraperitoneal route by quantity 35 mg/kg body weight[13]. Injection made set up to contain a volume of 1.0 ml/kg. The selected animals permitted to consume solution of glucose (6%) whole night to get better of medication triggered hypoglycemia. Following 3 days, the levels of blood glucose were evaluated and the concentration of glucose in animals with excess of 250 mg/dL were confirmed diabetic and blood sample was collected for the investigation. Administration of *I. prostrata* methanol extract was commenced on day four after injecting STZ and it was considered as the day one of treatment that was progressed for 28 days.

3.1.4 Evaluation of In Vivo Antidiabetic Effect of Methanol Extract of I. prostrata Whole Plant Using a Streptozotocin-induced Model

Albino wistar strain rats (180-200 grams) of either of sex were used in the current study. Animals were fed normally and had unrestricted access to water. For four weeks, the rats were fed a high-energy diet before going without food all night. At a dose of 35 mg/kg body weight, rats were administered diabetes by administering a single intraperitoneal injection of streptozotocin, dissolved freshly in cold (ice) citrate buffer (pH 4.5). Then, it was preceded by the management of a 5% solution of glucose throughout course of the next 24 hours. For the remainder of the experiment, rats were fed the high-energy diet. Samples of blood were obtained from tail vein, while the rats were gently sedated with ketamine before starting the streptozotocin medication. Centrifugation was used to separate the serum and a glucometer was used to evaluate the levels of blood glucose of each animal. Animals with blood glucose levels at fasting greater than 200 mg/dl were considered as diabetic and subjected to glucometer evaluation. Animals were considered to have diabetes and included in the study if rats fasting glucose levels were more than 200mg/dL.

All rats were subjected to fast for 18 hours before the experimental procedure by providing water. The total number of rats (n=6) were separated into groups of five, each consisting of six rats, using group-I as the standard. Group-II standard rats received glibenclamide orally at a dose of 10 mg/kg body weight. Animals in Group-III received an oral dose of 250 (low dose) mg/kg b.wt. of the whole plant of *I. prostrata*. Animals in Group-IV received a dose of 500 mg/kg b.wt. of the extract of methanol from the whole *I. prostrata* plant. Blood samples were obtained from the tail vein both before and four hours after treatment. Glucose levels were tested using a glucometer kit and glucose oxidase assay kits that are readily available in the market place. The anti-hyper glycemic responses were calculated using the differences in glucose levels between the first and second hours. Overall, the data remained statistically analyzed by means of ANOVA and reported as mean S.D[14].

3.2 Biochemical Analysis

After the completion of entire study for 28 days the serum was separated from the samples of blood collected through tail vein method for various biochemical parameters like lipid profiles of serum (high density lipoprotein cholesterol, very low density lipoprotein cholesterol total cholesterol, low density lipoprotein, plasma glucose) markers of different hepatic enzymes like albumin, total proteins, globulins, alkaline phosphatase, serum glutamic oxaloacetic transaminase, alanine amino transaminase, serum glutamic pyruvic transaminase, markers of kidney (creatinine and uric acid) and serum insulin and also glycosylated hemoglobin.

3.2.1 Evaluation of Concentration of Glucose of Blood

Trinder method was followed for evaluation of levels of blood glucose. By utilizing the reagents in reagent pack, the absorbance of standard as well as test in comparison to blank (reagent) were evaluated. Outcomes were indicated as mg/dL.

3.2.2 Evaluation of Concentration of Serum Triglycerides

By applying GPO-POD model through the proper dilution of diverse reagents comprising in reagent unit, levels of serum triglycerides were evaluated. The absorbance of standard as well as test in contrast to reagent blank at 546 nm were also evaluated. The valuations are indicated in mg/dL.

3.2.3 Evaluation of Concentration of Serum Cholesterol and HDL Cholesterol

Levels of HDL cholesterol as well as serum were evaluated by employing CHOD-POD model. The absorbance of standard and also test contrary to reagent blank are assessed at 504 nm. Outcomes were mentioned in mg/dL.

3.2.4 Estimation of Concentration of Very Low-density Lipoprotein Cholesterol

It was evaluated by Friedewald's equation.

VLDL cholesterol = Triglycerides / 5

Estimates are displayed as mg/dL.

3.2.5 Evaluation of Concentration of Serum Low Density Lipoprotein Cholesterol

It was estimated by Friedewald's equation[15]

LDL-Cholesterol = Total Cholesterol -VLDL cholesterol- HDL cholesterol

Outcomes are displayed in mg/dL.

3.2.6 Evaluation of Concentration of Serum Total Protein

End point assay model was utilized for evaluation of levels of serum total protein. The absorbance of standard as well as test compared to reagent that is blank were assessed at 578 nm. The assessments obtained from serum were exhibited as g/dL.

3.2.7 Evaluation of Concentration of Albumin from Serum

The outcome was obtained by following end point technique assay employing bromocresol green. Outcomes of both standard and also test in contrast to reagent blank were also projected at 630 nm. The valuations exhibited as g/dL.

3.2.8 Evaluation of Concentration of Serum Globulin

The levels of serum globulin were evaluated by formula:

Globulins = Total proteins - Albumin

Outcomes indicated as g/dL.

3.2.9 Evaluation of Concentration of Serum Uric Acid

It was evaluated by applying Uricase-Pap Trinder's model. The absorbance of test and standard contrary to blank were assessed at 505 nm. The approximations were mentioned as mg/dL.

3.3 Evaluation of Serum Creatinine

The levels of serum creatinine were determined by AGD biomedicals reagents. The absorbance of standard in addition to test contrary to blank were appraised at 520 nm[16]. The assessments were displayed as mg/dL.

3.3.1 Evaluation of Serum Urea

It was obtained by utilizing GLDH/UV-Kinetic model[17]. The absorbance projected on nm at 541. Outcomes exhibited as mg/dL.

3.3.2 Assessment of Serum Transaminases

Reitman and Frankel model was followed for the estimation of serum transaminases. The absorbance assessed at nm 504. Data was indicated as IUL^{-1}.

3.3.3 Assessment of Serum Alkaline Phosphatase

Kind and King model was followed for the assessment of serum alkaline phosphatase[18]. The absorbance of standard as well as test compared to blank were valued at 641 nm. Data displayed as UL^{-1}.

3.3.4 Assessment of Serum Alanine Amino Transaminase

It was assessed through IFCC model by applying commercial pack (Coral/clinical System, India). The absorbance was projected at 541 nm. Evidence indicated as UL^{-1}.

3.3.5 Assessment of Serum Insulin

It was evaluated by ELISA kit. The data was communicated in µU/ml.

3.3.6 Assessment of Glycosylated Hemoglobin

It was determined by whole blood through units available commercially. Evidence was indicated as % Hb.

3.3.7 Analysis of Statistics

Entire data regarding investigations was specified as mean ± standard error mean. The study of statistics was performed through one-way ANOVA model and then employing Dunnet-t test along through the SPSS statistical program design to correlate by that of the control group. $p \leq 0.001$ were evaluated.

3.3.8 Histopathology Study

After 28 days, one animal from every group was sacrificed by mild ether sedation. The pancreas was placed in formalin 10% solution, followed by cleaning with normal saline and the remaining part of pancreas is subjected to valuations of histology.

4. Results

4.1 Yield of Extract

The yields of dissimilar extracts of *I. prostrata* were 8.9% 9.1% and 10% intended for ethyl acetate, chloroform and methanol correspondingly.

4.1.1 Acute Toxicity Study

In the investigation, any signs of behavioral changes or mortality were not detected during the 15 days study with *I. prostrata* up to 2000 mg /kg dose levels.

4.1.2 Effect of Methanol Extract of I. prostrata on Blood Glucose Level in Normoglycemic Rats

Significant variations in levels of glucose of rat's blood were seen in all experimental groups after the administering of methanol extract from the entire *I. prostrata* plant. High dosage of methanol extract of *I. prostrata* was superior than low dose treatment, and exhibited a further drop in the glucose levels. The outcome obtained by treatment with *I. prostrata* were compared with those of glibenclamide standard. The results exhibited a reduction of glucose in a dose-related manner by Streptozotocin induced diabetic animals that were managed with the extract of methanol of *I. prostrata*. *I. prostrata* methanol extract was tested for its antidiabetic effect.

Following administration by *I. prostrata* extract, AUC of diabetic control rats considerably decreased. These findings showed that the extract from *I. prostrata* improved the bodily tissues ability to absorb and tolerate glucose in diabetic rats. It is widely accepted that dyslipidemia and uncontrolled diabetes mellitus are related. It is common knowledge that administering insulin to diabetics raises plasma levels and activity of lipoprotein lipase[19]. The potential of the extract may be brought on by a escalation for the levels of insulin, according to the reported improvement in plasma lipid profiles in diabetic rats fed *I. prostrata*. Levels of blood glucose in group IV rats significantly decreased following a large dosage of extract of plant. The effects of antidiabetic action had shown in Figure 1.

4.1.3 Consequence of Methanol Extract of I. prostrata (Oral Glucose Tolerance Test)

After 2 hours (from 0 to 30, 60, 90, and 120 minutes, respectively), the extract of methanol significantly diminished the elevated levels of blood glucose, severe hypoglycemia condition continued for an additional 2 hours. The blood glucose levels were decreased, with methanol extract and reached a peak after five hours, and were then sustained for an additional two hours. The glucose levels of blood in control rats spiked at 60 minutes following the glucose loads and then recovered to normal levels at 2 hours. In control diabetic animals, the extent of blood glucose increased most rapidly after 60 minutes. The standard glibenclamide and methanol extract both effectively lowered blood sugar levels after 60 minutes. Group II and Group IV rats had a higher drop in levels of blood glucose than the other groups. The control group, rats exhibited no variation. A slight decline in levels of blood glucose was seen with rats in groups III and IV. The outcomes were displayed in Figure 2.

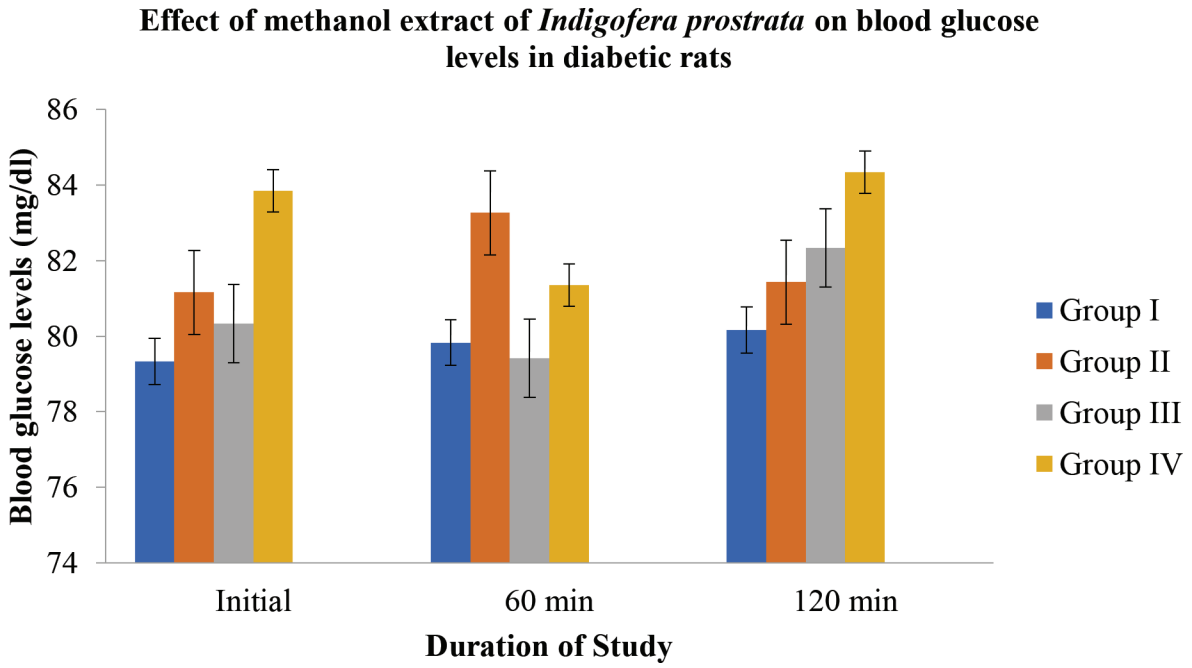


Figure 1. Effect of *I. prostrata* methanol extract on diabetic rats (hypoglycemic activity).

4.1.4 Consequence of Methanol Extract of I. prostrata on Diverse Biochemical Levels in Streptozotocin Induced Model

After 5 hours, the blood glucose level significantly decreased (from 0 hours to 2, 4, 6, and 8 hours, respectively), and the methanol extract continued to cause severe hypoglycemia for an additional 2 hours. At the eighth hour, the greatest decline in blood sugar was noted, and it remained for a further 2 hours with the extract of methanol. The extent of blood glucose of the Group II (glibenclamide) and Group IV (high dose) of rats decreased more than those of the other rat groups. Rats in Group I, the control group exhibited no change. The glucose of blood in rats for Groups III and IV (low dose and high dose) were moderately reduced. The results are depicted in Figure 3.

Diabetes is still difficult for the medical system to manage without causing side effects, which drives up demand for natural solutions with tolerable side effects. Traditional botanicals are utilized to treat diabetes mellitus all around the world. *I. prostrata* employed in the preparation of medicine (traditional), offers antidiabetic qualities, according to our past research. Together normal and also Streptozotocin induced diabetic rats were resistant to the activity of the whole plant extract from *I. prostrata*. At four hours, the short trial of antidiabetic activity showed the greatest decline in glucose levels. The binding of hemoglobin and augmented levels of blood glucose inside the body may result in production of reactive oxygen species. The outcomes were displayed in Figure 3.

Figure 4 exhibit methanol concentrates of *I. prostrata* repercussion for levels of lipid in serum. The observed outcomes revealed that the rats of diabetic Group (II) displayed the elevated levels of LDL cholesterol, triglycerides of serum, total cholesterol and VLDL cholesterol and also declined levels of HDL cholesterol on comparison to Group-I normal animals. Oral treatment of *I. prostrata* methanol extract at 250 and also 500 mg/kg b.wt (dose) pointedly declined elevated levels of serum triglycerides, LDL, total and also VLDL cholesterols and elevated levels of cholesterol (HDL) on contrast to animals of control with diabetes. These influences are displaying an imprint of being

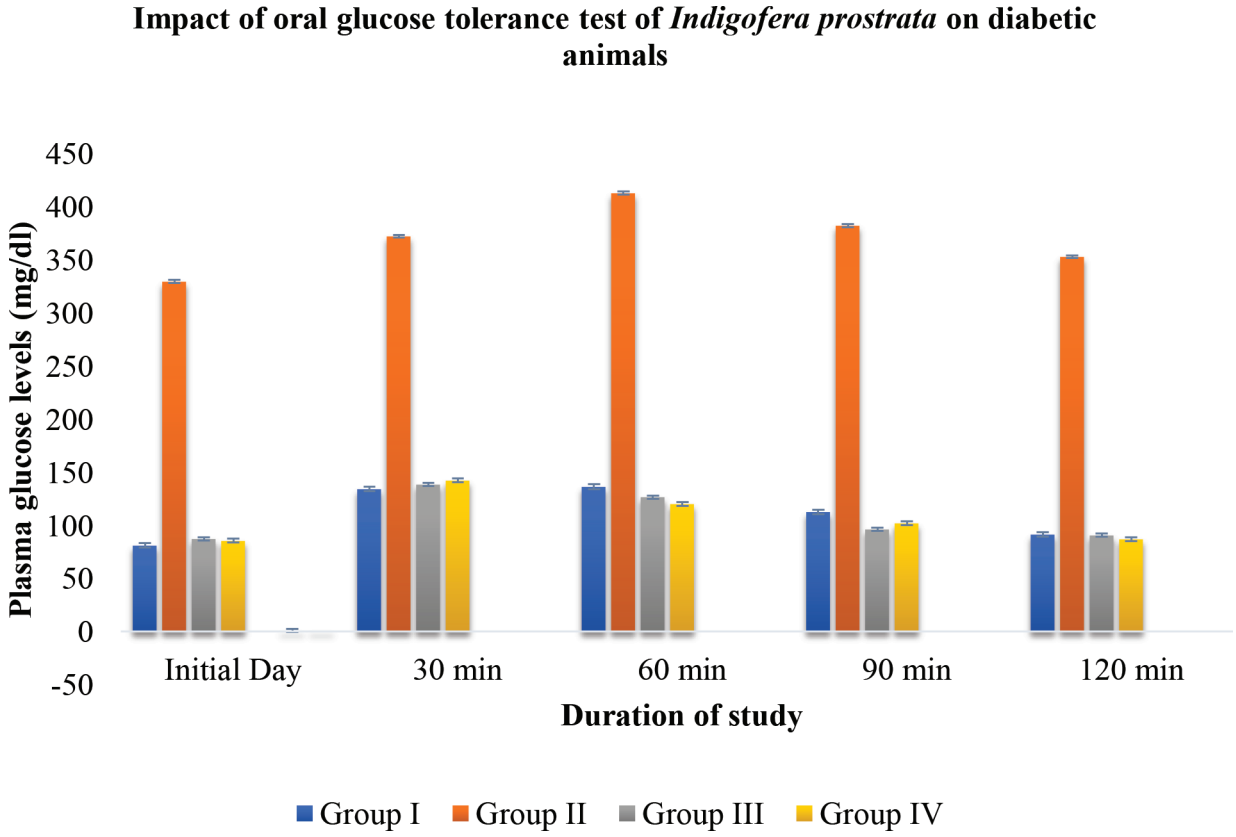


Figure 2. Diabetic rats responses to an oral glucose tolerance test with *I. prostrata.*

comparable to that of glibenclamide standard at 10 mg/kg quantity. In this way, impact of concentrates of methanol of *I. prostrata* consequences for levels of serum lipid reports in a decline in the cardiovascular damage that is associated to diabetes.

4.1.5 Histopathological Studies

Figure 9 displays the outcomes of histopathology of streptozotocin prompted pancreas of diabetic rat of diverse clusters treated with methanol extract of *I. prostrata* for about 28 days. The structural variations

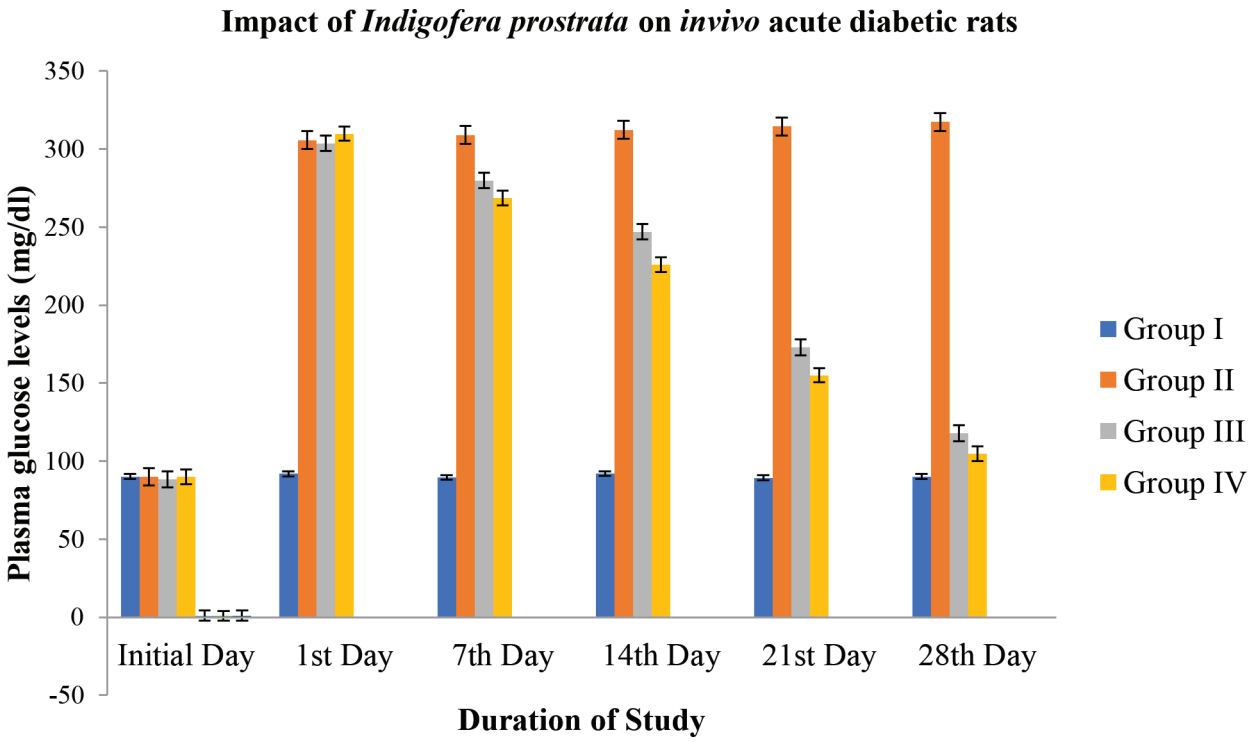


Figure 3. Effect of methanol extract of *I. prostrata* on *invivo* acute diabetic rats.

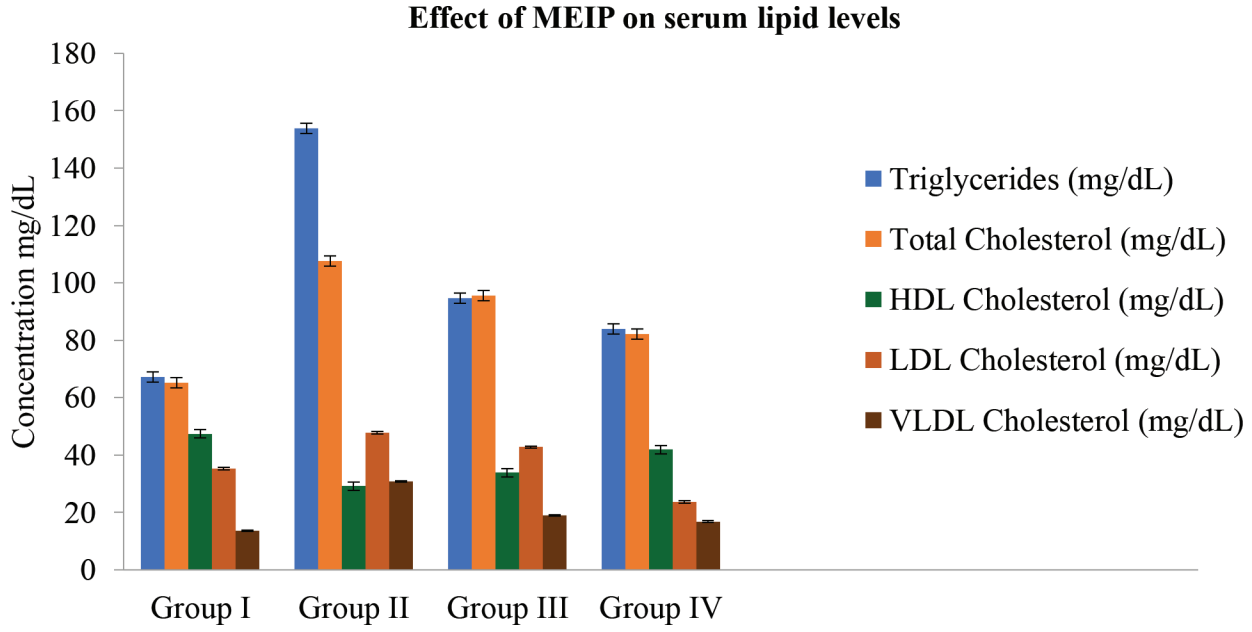


Figure 4. Effect of methanol extract of *I. prostrata* on serum lipid levels.

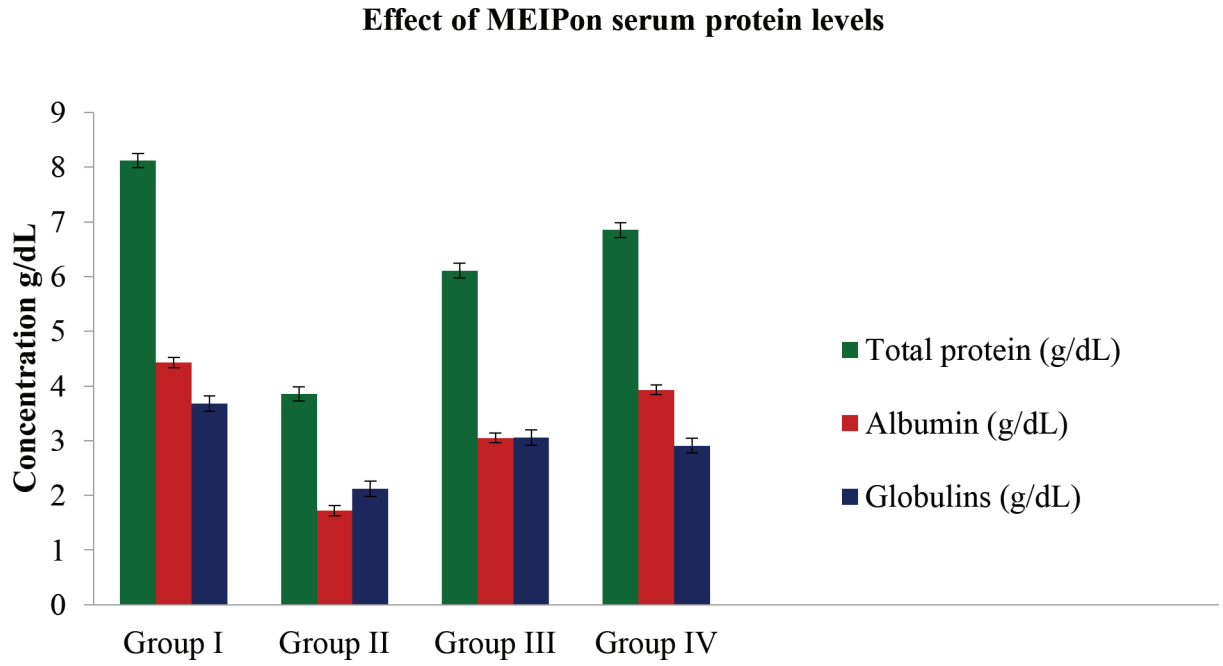


Figure 5. Effect of methanol extract of *I. prostrata* on serum protein levels.

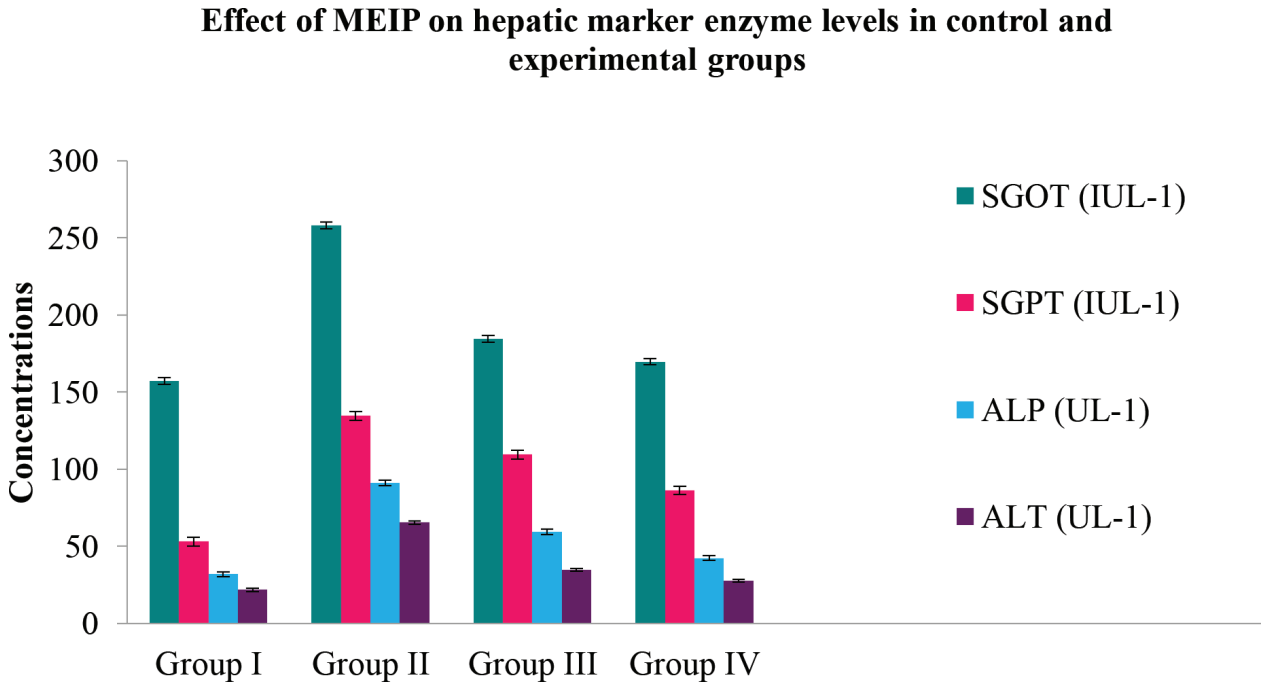


Figure 6. Effect of methanol extract of *I. prostrata* on hepatic marker enzyme levels in control and experimental groups.

in pancreas reproduce fluctuations in metabolic cycles of sensitivity, discharge as well as regulation of insulin. Destruction of pancreas was indicated by deterioration in the beta cells and collapse of cells. Deposition of amyloid tissue and fat accumulation in the islets and also the extent of beta cells is also radically diminished in end stages of diabetes[20]. In the contemporary examination islets of pancreas were visible without any variation in proportions, structure for control rats. While in the streptozotocin

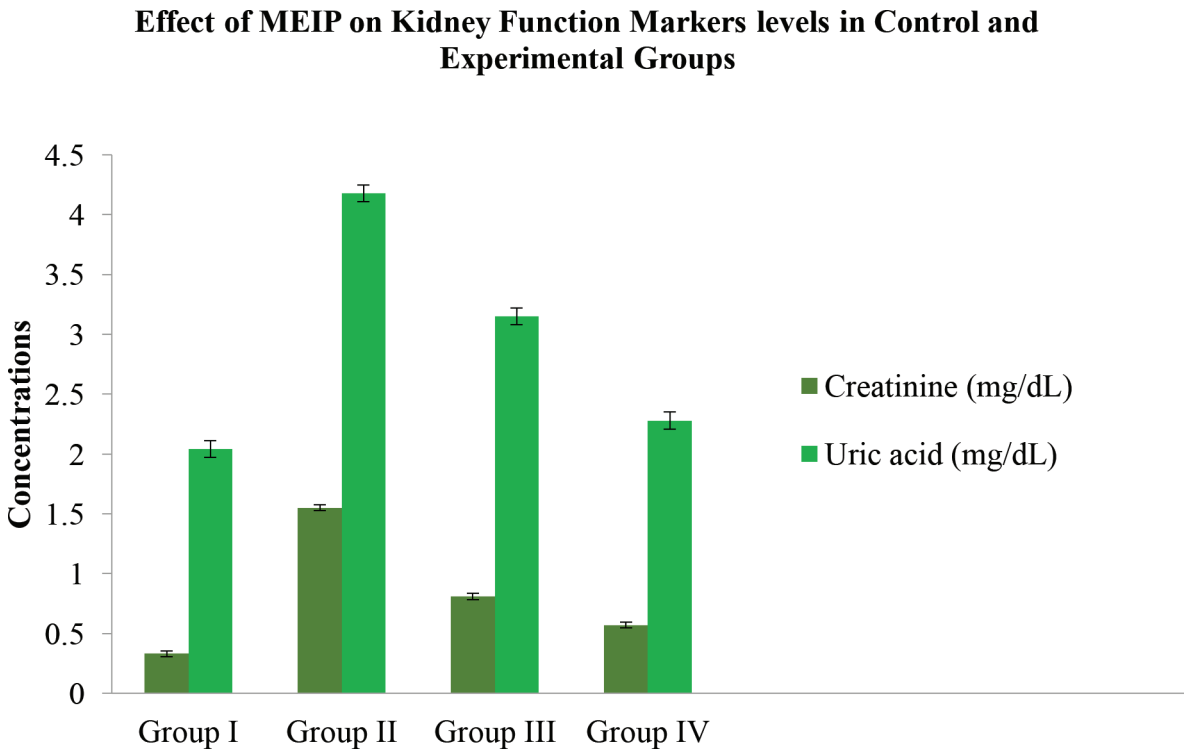


Figure 7. Effect of methanol extract of *I. prostrata* on kidney function marker levels in control and experimental groups.

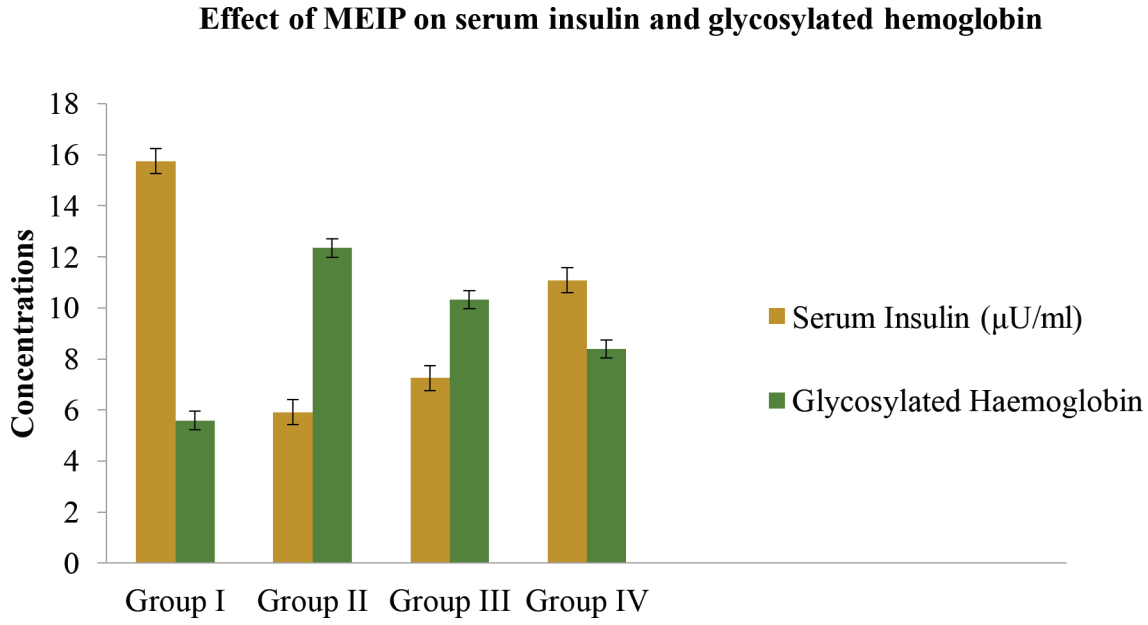


Figure 8. Effect of methanol extract of *I. prostrata* on serum insulin and glycosylated hemoglobin.

prompted animals of diabetes there is destruction of islets and size reduction for pancreas. In streptozotocin mediated diabetic animals managed with *I. prostrata* at 500 mg/kg and glibenclamide standard with dose10 mg/kg independently, pancreatic islet cells are almost indistinguishable with healthy animals and slight variation in their dimensions and also the structure with slight impairment were observed.

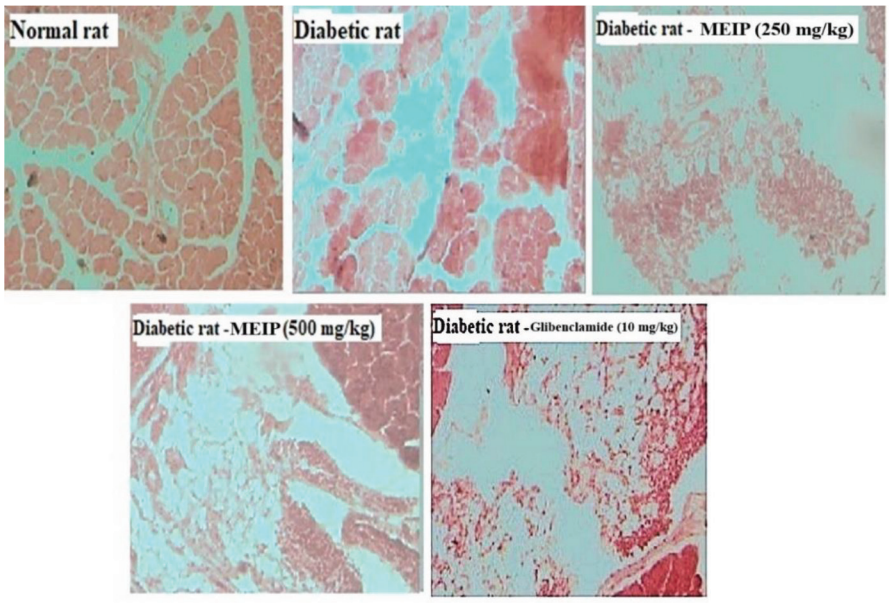


Figure 9. Outcome of methanol extract of *I. prostrata* on histopathological studies of rat pancreas.

5. Discussion

Natural sources of medicinal plants and their phytoconstituents are attaining popularity, due to their capability to scavenge free radicals[21]. While taking drugs of synthetic type, to treat illness, some patients may exhibit adverse effects or interactions with drugs[22]. Inhibitors of the enzyme glucosidase can delay the absorption of dietary carbs and prevent post lunch blood glucose levels, which may be a valuable strategy in development of antidiabetic drugs. Glucosidase catalyses last stage in digestion of carbohydrates[23-25]. *I. prostrata* whole plant extract and its different constituents demonstrated to show-up their hypoglycemic effects through different mechanisms, including the consumption of glucose by skeletal and peripheral muscles, glucose uptake inhibition from intestine, restriction of adipocyte differentiation, stimulation of a crucial enzyme of the HMP shunt pathway, and also protection of the islet cells[26].

People who use STZ develop diabetes that resembles type 2 diabetes because the drug specifically kills pancreatic insulin-secreting cells. The diabetic rats used in the current study showed high blood glucose levels in the extent of 150-350mg/dl, that are comparable to diabetes 150-250 mg/dl, while having a healthy pancreas[27]. This demonstrates that the complete *I. prostrata* methanol extract may be beneficial for those with type-2 diabetes. Flavonoids are potential antidiabetic agents as they employ manifold activities on β-cells. While, In the contemporary aspect, the activities of flavonoids may be separated into defense against damage of β-cells, augmented proliferation for β-cells are amplified insulin secretion[28]. This is another benefit of the extract above the current drug options[29]. The proposed mechanism for *Gmelina asiastica's* hypoglycemic effects was moreover an increase in pancreatic insulin secretion from cells or its release from bound insulin. Similar types of hypoglycemic effects were also seen in normal rats. According to the *in vivo* research, streptozotocin-induced diabetic rats levels of fasting were pointedly inferior in the extract of methanol from the whole plant than in the control group. After injecting streptozotocin to diabetic rats, pretreatment of aqueous root extract from *Ichnocarpus fructescens* and also *Pterocarpus marsupium* reduced the elevated levels of blood glucose. It was anticipated that the process would increase insulin production from the few remaining cells. According to the findings of a study on oral glucose tolerance test, ethanol extracts are more effective at increasing glucose tolerance. Methanol extracts exhibit greater glucose tolerance activity, according to an examination of oral glucose tolerance tests.

Because of diverse metabolic confusions in diabetes mellitus and progression for insulin interference may

also emerges lipid damage in the tissue of fat and also result hyperlipidemia. Henceforth, hyperlipidemia associate with diabetes may arise and that is associated through cardiovascular threat[30]. Figure 4 reveal the methanol extract of *I. prostrata* consequences of levels of lipid in serum. Evidence was that Group II revealed the elevated levels of LDL cholesterol, total cholesterol, serum triglycerides and VLDL cholesterol also declined levels of HDL cholesterol on contrary to Group I animals. 250 and 500 mg/kg body weight treatment with extract of methanol of *I. prostrata* significantly reduced the elevated levels of LDL cholesterol, serum triglycerides, VLDL cholesterol, total cholesterol and elevated the levels of HDL cholesterol on contrast to diabetic control. These impressions produced is being comparable with that of standard glibenclamide at 10 mg/kg. In this way, results of methanol extract of *I. prostrata* for levels of lipid serum reports in reducing in cardiac threat associated through diabetes[31]. Image 5 depicts to the capability of methanol extract of *I. prostrata* on levels of serum protein. Globulin, total protein and albumin pointedly (p<0.001) altered for streptozotocin induced diabetic animals compared to healthy animals. Decline in albumin, total serum protein and also globulin levels are described for diabetic animals, later confirmed via a development in peroxidation of lipids and a weakened protection for antioxidant activity[32]. The current examination revealed diabetic animals managed by *I. prostrata* and standard glibenclamide at body weight 10 mg/kg pointedly enhanced the albumin, levels of serum total protein and levels of globulin on comparison to healthy and control groups with diabetes. In insulin metabolism and homeostasis of glucose, liver has a vital role. The defective liver results into hepatic insulin resistance and also leads to progression in diabetes[33]. Aminotransferases, SGPT, SGOT, ALT and ALP are the communal hepatic markers that reflect in necrosis of hepatic cells as these are transported into blood after impairment of cell membrane[34]. The ALT elevated levels and also SGOT are clinical components in type 2 diabetes for metabolic syndrome. Figure 6 displays the role of enzymes of hepatic markers in experiment. After comparison to those healthy animals, diabetic animals pointedly (p<0.001) elevated the levels of SGPT, SGOT, ALT and ALP. In the contemporary examination *I. prostrata* methanol extract treated rats at 250 and 500 mg/kg body weight and glibenclamide at 10 mg/kg b.wt (p<0.001) declined the elevated levels of SGPT, SGOT, ALT and ALP in contrary to diabetic animals.

Impairment of kidney leads to diabetic nephropathy, the reason for the cause is elevated glucose and blood pressure. Streptozotocin induced animals display the highlights of diabetic nephropathy, like, elevated levels of serum creatinine and uric acid[35]. In the contemporary examination markers of kidney function, like uric acid and creatinine levels were pointedly (p<0.001) elevated in diabetic animals compared to normal animals. The diabetic rats treated by *I. prostrata* methanol extract and glibenclamide standard suggestively (p<0.001) declined the elevated levels of uric acid and serum creatinine and in contrary with diabetic control animals. The outcomes give the impression in Figure 7 of methanol extract of *I. prostrata* consequences that markers of kidney function improve the function of kidney in diabetic rats.

Figure 8 states to the capability of extract of methanol of *I. prostrata* on the stages of serum insulin and also glycosylated hemoglobin. Streptozotocin promote an unbalanced β-cell working by flagging oxidation of glucose and also weakening biosynthesis of glucose[36]. The diabetic rats accomplished with extract of methanol of *I. prostrata* and glibenclamide pointedly (p<0.001) elevated in contrary to treated animals. Upsurge in serum insulin level for *I. prostrata* extract treated animals in streptozotocin diabetic animals perhaps due to the protective action against streptozotocin prompted damage to the **β-cells of** pancreas and moreover believable owing to regaining of injured β-cell or extended insulin release or delivery.

HbA1C is an indicator for increase of continuing glycemic control in patients of diabetes and forecasts threat for the enhancement of and furthermore movement of complications of diabetes[37]. In the contemporary examination, Figure 8 express the elevated value of HbA1c reveals the event of diabetic rats glycosylation for hyperglycemia. *I. prostrata* methanol extract at 250 and 500 mg/kg b.wt and glibenclamide suggestively (p<0.001) declined the levels of HbA1c serum analogized with diabetic animals. Later, the impact of *I. prostrata* extract of methanol influences on HbA1c reveals the capability to avoid the enhancement of complications associated to diabetes. Levels of glucose stimulated by insulin produced by pancreas (β cells), when β cells are destroyed, the insulin production will be declined and content of glucose will escalate in blood[38].

The plants show a considerable increase in glucose tolerance activity when compared to the normal rats. By intensifying the release of insulin from β cells of pancreas or by releasing it from the bound insulin, it is clear from the data above that the methanol extract from the *I. prostrata* whole plant revealed the likely mechanism.

6. Conclusion

The above-mentioned investigation found that the whole plant extract of *I. prostrata* has significant *in vivo* antidiabetic activity. It has been found that the extract of methanol from the whole *I. prostrata* plant is efficient in decreasing the elevated glucose levels in blood in rats. *I. prostrata* whole plant's methanol extract showed noticeable antidiabetic effect in through *in vivo* testing utilizing a Streptozotocin induced diabetes rat model that is comparable to glibenclamide standard. The entire plant shown noticeable action in an oral glucose tolerance test using a methanol extract of *I. prostrata* in normal rats. Histopathological things conformed the activities of *I. prostrata*. The plant was discovered to have significant antidiabetic action in the ongoing research and the reason may be because it stimulates beta cells to produce more insulin and improves peripheral glucose uptake. These results indicate that STZ-induced diabetic rats respond well to the complete *I. prostrata* plant's potent antidiabetic effect.

6.1 Authors Declaration

All the authors have contributed equally

6.2 Acknowledgement

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