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ANTIHYPERGLYCEMIC ACTIVITY OF *DIPTERACANTHUS PROSTRATUS* NEES. AND ITS PROBABLE MECHNISM OF ACTION IN STREPTOZOTOCIN INDUCED DIABETIC RATS

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Antihyperglycemic activity, diabetes, Streptozotocin, *Dipteracanthus prostratus* Nees.

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ABSTRACT: The present study was aimed to investigate the antihyperglycemic effect of the *Dipteracanthus prostratus* nees. And it's probable mechanism of action in Streptozotocin induced diabetes. Wistar albino rats were used to evaluate the antihyperglycemic effect of toluene (TEDP, 100 mg/kg and 200 mg/kg, body weight) and methanolic (MEDP, 100 mg/kg and 200 mg/kg, body weight) extract of *D. prostratus*. Changes in body weight and blood glucose level were evaluated at the beginning of the experiment and on day 7, 14, and 21 subsequently. Lipid profile and histopathological examination were also performed. TEDP at 200 mg/kg produced a significant stimulating body weight and reduced blood glucose level in treated diabetic rats from day 7, apart that MEDP also showed similar activity from day 14. Furthermore, significant differences in lipid profiles by TEDP treated rats at 200 mg/kg, as compared to diabetic control and normal rats were also observed. Histopathological studies showed comparable regeneration of islet cells necrosed by Streptozotocin, by both the extracts. In conclusion results revealed that the TEDP exhibited dose dependent significant and consistent hypoglycemic action. Probable mechanism of antihyperglycemic action of *D. prostrates*, in Streptozotocin induced diabetic rats were may be due to the presence of flavonoids and phenolic compounds in the extract.

INTRODUCTION: Diabetes mellitus is a group of metabolic disorders of multiple etiologies and it is the fifth most common cause of death worldwide. It is characterized by the elevated blood glucose level with the turbulence of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion (type-1) or reduced sensitivity of the receptors to insulin action (type-2) or both and thus leading to severe complications, more than 90% of the population with diabetes have type 2 diabetes; the leftovers have type 1 diabetes [1, 2].

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Major complications in a diabetic patient are polyuria, polyphagia, polydypsia, ketosis, neuropathy, retinopathy and cardiovascular disorders [3]. In recent years diabetes becomes a global problem in developing countries, currently its prevalence is increasing over 366 million worldwide and this is projected to increase to 552 million by the year 2030, while in India more than 62 million individuals currently diagnosed with the disease [4, 5].

Various treatment options (sulfonylureas, biguanides, thiazolidinediones, α-glucosidase inhibitors and insulin therapy,) are available for the treatment of diabetes. There are several side effects of existing therapies (abdominal pain, anorexia, transient leucopenia, insulin resistance, brain atrophy and fatty liver) [6].

Since long time, diabetes has been treated by medicinal plants based on their traditional use in Indian system of medicine [7, 8]. Ethnopharmacological studies signify that more than 1200 natural herbs and their biologically active phytoconstituents are used worldwide in traditional medicine for their potent hypoglycemic activity [9, 10]. Herbal medication is promising as an alternative treatment to available synthetic drugs for the treatment of different diseases probably due to availability, affordability, lesser adverse effects and proved effectiveness [11].

Dipteracanthus prostratus Nees (Family: Acanthaceae) is an erect hoary pubescent, up to 50 cm tall, basally woody and much branched shrub locally known as Haadjud by tribal peoples. It is widely distributed plant in Africa, Arab, Srilanka, Pakistan and India. In India it is generally found in Tamil Nadu, Western Ghat and Andhra Pradesh [12, 13]. The stem of the plant is greenish and rounded, becoming angular with age. Leaves are 4-10 mm long, lamella elliptic, ovate, and densely pubescent on both sides. Flowering period is July- November. Flowers are sessile, 3-4 cm long, pale white in color, usually solitary, axillary, and 2-3 in cymes. Fruit capsule is elliptic clavate, glabrous, 1.4-1.8 cm in length, 8-10 seeded. Seeds are flat and orbicular [14].

Previous phytochemical studies confirmed that *Dipteracanthus prostratus* contains a rich amount of bioactive compounds, including flavonoids, saponins, steroids, phenols, tannins, and lignin [15]. In traditional medicinal system of India different parts of the plant have been used in the treatment of a variety of diseases. It is used as cardiotonic, antiulcer, antioxidant, paranychia, venereal diseases, rheumatic complaints, eye diseases, insect bite and healing of wounds [16, 17].

In the light of above mentioned fact about the plant, present study was designed to investigate the antihyperglycemic activity of the methanolic and toluene extract of the whole plant of *Dipteracanthus prostratus* Nees.

MATERIALS AND METHODS:

Plant material collection: *Dipteracanthus prostratus* (whole plant) was collected in the month of December from the ABS Botanical Conservation, Research & Training Centre, Kaaripati, Salem, Tamil Nadu, India. The herbarium of the plant was prepared and authenticated by Dr. A. Balasubramanian (Executive Director) Former Siddha Research Consultant (Ayush), Ministry of Health & Family Welfare, New Delhi, India. The specimen voucher number (AUT/JNU/029) was deposited with the herbarium in the Department of Pharmacognosy, ABS Botanical Conservation, Research and Training Centre, Kaaripati, Salem, Tamil Nadu, India for future reference.

Extraction:

Whole plant of *Dipteracanthus prostratus* was shade dried for four weeks, pulverized to the coarse powder, passed through sieve no. 20 to maintain uniformity and coarsely dried powder was first defatted with petroleum ether (60-80ºC) to remove fatty materials and then successively extracted with toluene and then finally extracted with methanol using soxhlet apparatus. After complete extraction extracts were collected, and concentrated in vacuum under reduced pressure using a rotary flash evaporator and the dried crude extracts were stored in air tight glass containers at 4ºC for further study. The percentage yield of toluene and methanolic extract of whole plant of *Dipteracanthus prostratus* was 9.65% and 11.41% respectively.

Phytochemical screening:

Both the crude extracts (toluene and methanolic) of whole plant of *Dipteracanthus prostratus* were subjected to qualitative phytochemical investigation for the identification of the different phytoconstituents using standard tests and procedures [18].

Preparation of test formulations of extracts:

Suspension formulations of both the crude extracts (toluene and methanolic) were prepared separately in 0.5% carboxy methyl cellulose (CMC) solution in distilled water stored at 2-8ºC for further studies.

Chemicals and reagents:

Streptozotocin was purchased from Aldrich Sigma (St. Louis, USA, CAS no. 18883-66-4). Glibenclamide was obtained as a gift sample from Sapience Bio-analytical Research Lab, Bhopal,

Madhya Pradesh, India. All the other reagents, solvents and chemicals used in the study were of analytical grade and procured from S.D. Fine Chemicals (Mumbai, India) Diagnostic kits for various biochemical studies were obtained from Span diagnostics, India.

Animal care and handling:

The experiment was carried out on healthy Wistar albino rats, weighing between 150-200 g. Animals were provided by the authorized animal house of Sapience Bio-analytical Research Lab, Bhopal, Madhya Pradesh, India. The animals were acclimatized to the standard laboratory conditions of temperature 25±2°C relative humidity 44-56% and 12:12 hours light and dark cycles, fed with standard pellet diet and water *ad libitum* during experiment. The experiment was approved by the Institutional Animal Ethics Committee (IAEC) as per the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA) guidelines (Approval no. 1413/PO/a/11/CPCSEA)

Acute oral toxicity study:

The acute oral toxicity study was evaluated as per Organization for Economic Cooperation and Development (OECD) guidelines no. 425 on Wistar albino rats, weighing between 140-200g. Before experiment rats were fasted overnight with water *ad libitum*. Six animals were selected for the assessment of maximum tolerable dose of toluene and methanolic extract of *Dipteracanthus prostratus*. First three animals received 2000 mg/kg body weight dose of toluene extract of *Dipteracanthus prostratus* and other three animals received 2000 mg/kg body weight dose of methanolic extract of of *Dipteracanthus prostratus*. Both extracts were given in suspension form by gavage using oral canula. Animals were observed individually for any toxicity sign of gross changes like convulsion, tremor, circling, depression, and mortality after dosing for 24 hours, with special attention given during the first 4 hours and daily thereafter, for a total of 14 days. All observations were systematically recorded with individual records being maintained for each animal [19].

Antihyperglycemic activity:

Induction of diabetes in rats using Streptozotocin: Streptozotocin induced diabetes has been commonly used as an experimental model to study the activity of hypoglycaemic agents. Diabetes was induced by a single intraperitoenal (i.p.) injection of a freshly prepared Streptozotocin solution (Sigma, CAS no. 18883-66-4) (50 mg/kg, body weight, in ice-cold citrate buffer 0.1 M, pH 4.5) to overnight fasted Wistar albino rats (150-200 g). After the injection, animals have free access to food and water *ad libitum*. The development of diabetes was confirmed after 72 h of the Streptozotocin injection. The animals having blood glucose levels above 150 mg/dl were considered as diabetic rats and used for experimentation [20, 21].

Experimental Protocol:

After the induction of diabetes, 42 rats (6 normal and 36 diabetic rats) were randomly divided into seven groups consisting of six animals in each group.

Group I: Normal control (vehicle only, 1ml/100gm)

Group II: Diabetic control, Streptozotocin induced diabetic rats.

Group III: Glibenclamide (5 mg/kg, b.w., p.o.) once daily for 21 days.

Group IV: Toluene extract of *Dipteracanthus prostratus* (TEDP, 100 mg/kg, b.w., p.o.) once daily for 21 days.

Group V: Toluene extract of *Dipteracanthus prostratus* (TEDP, 200 mg/kg, b.w., p.o.) once daily for 21 days.

Group VI: Methanolic extract of *Dipteracanthus prostratus* (MEDP, 100 mg/kg, b.w., p.o.) once daily for 21 days.

Group VII: Methanolic extract of *Dipteracanthus prostratus* (MEDP, 200 mg/kg, b.w., p.o.) once daily for 21 days. All the group of animals received the treatment for 21 days.

Evaluation of antihyperglycemic activity:

Change in body weight:

Body weight of each animal from all the groups was observed every 7th day to assess the percentage

change in body weight during overall study period of 21 days.

Determination of Blood Glucose level:
Blood samples were collected from the tail vein of rats and blood glucose estimation was done on the 3rd day of induction of diabetes using an electronic glucometer (Glucocheck, Biotest Medical Corp.) and thereafter treatment was continued for 21 consecutive days. The post induction blood glucose levels were estimated on days 3, 7, 14 and 21.

Determination of lipid profile:
On day 21, blood was collected from retro-orbital plexus of the overnight fasted rats under light ether anesthesia. Serum was separated by centrifuging the sample at 3000 rpm for 15 min. The serum was analyzed for cholesterol (CHL), high-density lipoprotein (HDL), triglycerides (TG), low-density lipoprotein (LDL) and Very low-density lipoprotein (VLDL) using the Span diagnostic kit and employing standard methods and protocols.

Histopathological Study:
At the end of the study, all rats were anesthetized and whole pancreas was removed from each animal. Pancreatic tissues were fixed in 10% formalin solution. Histological sections of about 5 µm thickness were prepared by microtomy and stained with hematoxylin and eosin (H & E) dye for histological examination. Histological slides were examined under a light microscope at 40X magnification.

Statistical analysis:
The results are expressed as mean ± Standard error of mean (SEM). The statistical significance was analyzed using One-way Analysis of Variance (ANOVA) followed by Tukey-Kramer Multiple Comparisons Test by employing statistical software, GraphPad, InStat 3. Differences between groups were considered significant at $P<0.05$ levels.

RESULTS:

Phytochemical screening: The phytochemical screening revealed that toluene and methanolic extract of *Dipteracanthus prostratus* whole plant contain a rich amount of flavonoids, alkaloids, glycosides, tannins, carbohydrates and phenolic compounds.

Acute toxicity study:
There was no change in the behavioral pattern and not any sign of toxicity and mortality observed with administration of TEDP and MEDP at the dose level of 2000 mg/kg, body weight, during the overall toxicity studies (OECD 425). Both the extracts were found nontoxic and safe as no death occurs. Thus, the final doses for further studies selected were 100 mg/kg and 200 mg/ kg.

Effect of toluene and methanolic extract of *Dipteracanthus prostratus* on body weight of Streptozotocin induced diabetic rats:
Administration of TEDP at dose levels of 100 mg/kg and 200 mg/kg, body weight, respectively inhibit the change in body weight of the diabetic animals (group IV and V) dose dependently at all week. The effect of TEDP at 200 mg/kg, body weight was more prominent and significant as there was more improvement in the body weight of treated animals (group IV) in comparison to TEDP at a dose level of 100 mg/kg, body weight (group V). Treatment of animals (group VI and VII) with MEDP at dose levels of 100 mg/kg and 200 mg/kg, body weight exhibits the similar effect only in the third week. The body weight of the diabetic control rats (group II) was consistently reduced weekly till day 21. As a standard drug Glibenclamide (5 mg/kg, body weight) was more efficient during the three weeks of treatment and efficiently prevent the percentage change in body weight in diabetic animals (group III) **(Tab 1)**.

TABLE 1: EFFECT OF TOLUENE AND METHANOLIC EXTRACT OF *DIPTERACANTHUS PROSTRATUS* ON BODY WEIGHT OF STREPTOZOTOCIN INDUCED DIABETIC RATS

Group	Treatment	Body weight (g)				% change in body weight
		Initial	Day 7	Day 14	Day 21	
I	Normal control	176.66±7.03	175.16±10.94	177.0±10.84	177.16±10.98	-
II	Diabetic control	180.66±3.88	174.66±3.61	171.83±3.69	168.0±3.38	7.0
III	Standard (Glibenclamide, 5 mg/kg)	169.16±3.0	165.83±2.94	165.5±2.87	165.83±3.06	1.96
IV	TEDP 100 mg/kg	168.33±8.62	164.83±8.45	164.5±8.7	164.0±8.49	2.57
V	TEDP 200 mg/kg	170.0±7.3	166.66±7.35	165.83±7.35	166.16±7.14	2.25

VI	MEDP 100 mg/kg	165.83±5.06	162.5±5.05	160.5±5.42	160.5±5.4	3.21
VII	MEDP 200 mg/kg	157.5±6.29	153.5±6.78	152.16±6.84	152.66±6.7	3.08

All values are represented as mean ± SEM, n = 6 animals in each group.

Effect of toluene and methanolic extract of *Dipteracanthus prostratus* on blood glucose level of Streptozotocin induced diabetic rats:

The antihyperglycemic effects of different extracts of *Dipteracanthus prostratus* on the blood glucose level of normal and diabetic rats are shown in **Tab 2**. Blood glucose level of normal control animals (group I) remains unchanged throughout the overall study period of 21 days. Diabetic control animals (group II) showed a significant (P<0.001) increased level of blood glucose after the intraperitoneal injection of Streptozotocin and this was tending to increase consistently from day 3 to day 21. After 14 days, animals treated with Glibenclamide (5 mg/kg, body weight) (group III) showed significant decrease in the blood glucose level in comparison to diabetic control rats (group II).

Treatment of diabetic animals with TEDP (group IV and V) at dose levels of 100 mg/kg and 200 mg/kg body weight showed significant antihyperglycemic activity from day 7 and MEDP (group VI and VII) at dose level 200 mg/kg body weight from day 14. Antihyperglycemic effect of TEDP was significant (P<0.001) at both dose level and the effect of MEDP was more statically significant (P<0.05) at the dose level of 200 mg/kg **(Tab 2)**.

TABLE 2: EFFECT OF TOLUENE AND METHANOLIC EXTRACT OF *DIPTERACANTHUS PROSTRATUS* ON BLOOD GLUCOSE LEVEL OF STREPTOZOTOCIN INDUCED DIABETIC RATS

Group	Treatment	Blood Glucose (mg/dl)			
		Day 3	Day 7	Day 14	Day 21
I	Control	86.16±1.27	83.66±1.49	83.66±1.38	86.33±3.0
II	Diabetic control	160.66±1.99	183.83±3.46 a***	226.66±6.91 a***	235.83±7.7 a***
III	Standard (Glibenclamide, 5 mg/kg)	154.83±4.59	163.33±2.24 a***, b**	165.5±2.59 a***, b***	171.16±1.85 a***, b***
IV	TEDP 100 mg/kg	159.5±4.69	176.16±4.5a***	182.33±4.68 a***, b***	188.83±3.67 a***, b***
V	TEDP 200 mg/kg	167.5±5.34	172.0±3.73a***	175.83±3.35 a***, b***	181.33±3.41 a***, b***
VI	MEDP 100 mg/kg	154.16±3.75	176.0±5.42a***	199.33±7.26 a***,b**,c***	207.16±5.26 a***, b**, c***
VII	MEDP 200 mg/kg	160.5±3.91	172.16±3.07a***	189.33±6.35 a***, b***, c*	194.83±5.62 a***, b***, c*

All values are represented as mean ± SEM, n = 6 animals in each group, Data were analyzed by one-way ANOVA, followed by Tukey-Kramer Multiple Comparisons Test, Where a-Significance difference as compared to control group, b-Significance difference as compared to the diabetic control group, c-Significance difference as compare to standard group and *P<0.05, **P<0.01 and ***P<0.001

Effect of toluene and methanolic extract of *Dipteracanthus prostratus* on the lipid profile of Streptozotocin induced diabetic rats: Different lipid parameters were studied in the assessment of the effect of different extracts of *Dipteracanthus prostratus* in normal and diabetic rats. **Tab 3** showed the effect of different extracts of *Dipteracanthus prostratus* on the lipid profile of the animals.

TABLE 3: EFFECT OF TOLUENE AND METHANOLIC EXTRACT OF *DIPTERACANTHUS PROSTRATUS* ON THE LIPID PROFILE OF STREPTOZOTOCIN INDUCED DIABETIC RATS

Group	Treatment	Lipid profile				
		CHL (mg/dl)	HDL (mg/dl)	TG (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Control	149.83±2.83	67.66±2.04	134.16±2.71	54.83±3.86	26.86±0.52
II	Diabetic control	218.16±3.0 a***	42.0±1.71 a***	195.5±1.8 a***	136.95±2.58a***	39.1±0.36 a***

III	Standard (Glibenclamide, 5 mg/kg)	169.83±4.1 a**, b***	58.0±1.23 a*, b***	156.83±1.0 a***, b***	80.46±4.74 a**, b***	31.4±0.21 a***, b***
IV	TEDP 100 mg/kg	184.16±3.79a***, b***, c***	45.16±2.21 a***, c**	171.33±1.47a***, b***, c**	105.03±3.64a***, b***, c**	34.03±0.23 a***, b***, c**
V	TEDP 200 mg/kg	174.33±3.25 a***, b***	55.16±3.18 a**, b**	163.5±4.05 a***, b***	90.3±4.35 a***, b***	32.7±0.81 a***, b***
VI	MEDP 100 mg/kg	193.5±4.58 a***, b***, c**	47.66±2.12 a***, c*	174.66±1.8 a***, b***, c***	109.56±6.41 a***, b**, c**	34.93±0.36 a***, b***, c***
VII	MEDP 200 mg/kg	188.66±3.57a***, b***, c*	52.5±1.78a***, b*	169.33±1.7 a***, b***, c**	102.2±4.92 a***, b***, c*	33.86±0.34a***, b***, c**

All values are represented as mean ± SEM, n = 6 animals in each group, Data were analyzed by one-way ANOVA, followed by Tukey-Kramer Multiple Comparisons Test, Where a-Significance difference as compared to control group, b-Significance difference as compared to the diabetic control group, c-Significance difference as compare to standard group and *P<0.05, **P<0.01 and***P<0.001

Overall the treatment with TEDP (200 mg/kg) (group IV and V) showed dose dependent significant (p<0.01) activity of various lipids as compared to diabetic control animals (group II) and glibenclamide (5 mg/kg) (group III) found to be significant changes in cholesterol, high-density lipoprotein, triglycerides, low-density lipoprotein and Very low-density lipoprotein levels. In normal control animals (group I), no significant changes in various lipid parameters were noted **(Tab 3)**.

Histopathological Study:

Fig 1 (A-G) represented the histological examination of the pancreas of rats in different groups. Histological section of the normal control group **(Fig 1A)** rat pancreas showed normal acini and normal cell arrangement of the islets of Langerhans. However streptpozotocin treated rat pancreas **(Fig 1B)** showed the irregular arrangement of the islets of Langerhans representing the chronic damage of pancreatic cells. Treatment of diabetic rats with Glibenclamide as a standard drug prevents the cellular damage of the pancreas and there was a moderate growth in size and population of islet cells **(Fig 1C)**. Treatment of diabetic rats with TEDP (100 mg/kg and 200 mg/kg, body weight) also prevent the changes in cellular level of islet cells in a dose dependent manner **(Fig 1D** and **1E)**, however histological section of rat pancreas **(Fig 1E)** treated with TEDP at the dose level of 200 mg/kg showed moderate globules of acini with normal islet cells in comparison to TEDP at the dose level of 100 mg/kg. While, MEDP (100 mg/kg and 200 mg/kg, body weight) treated rats showed partial restoration of the population of islet cell growth in size of islets **(Fig 1F** and **1G)**.

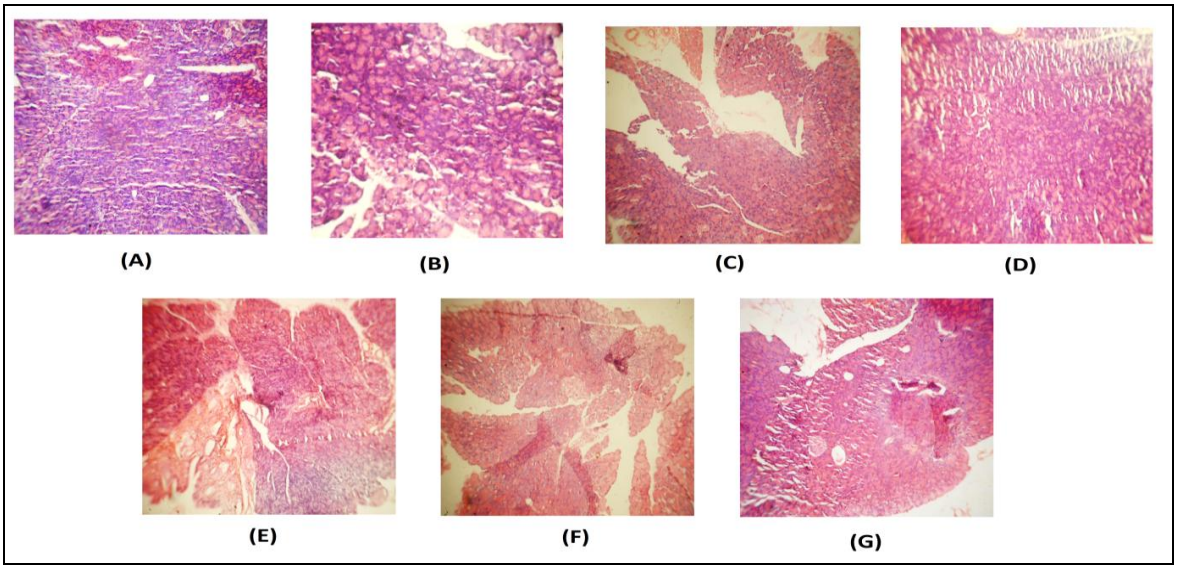

FIG.1: HISTOPATHOLOGICAL EXAMINATION (H & E) OF PANCREAS, SECTIONS OF (A) normal control rat (group-I) stained with H & E, (B) Diabetic control rat (group-II) stained with H & E, (C) Standard, Glibenclamide (5 mg/kg) treated rat (group-III) stained with H & E, (D) TEDP treated rat (group-IV) at the dose of 100 mg/kg stained with H & E, (E) TEDP treated rat (group-V) at the dose of 200 mg/kg stained with H & E, (F) MEDP treated rat (group-VI) at the dose of 100 mg/kg stained with H & E, (G) MEDP treated rat at (group-VII) the dose of 200 mg/kg stained with H & E (40X)

DISCUSSION: Treatment of diabetic animals with toluene extract of *Dipteracanthus prostratus* increase the body weight dose dependently. Toluene extract at the dose level of 200 mg/kg were able to maintain a significant growth of diabetic rats by the second week, while methanolic extract exhibits the similar effect only in the third week. Prevention in the reduction of body weight can be related to its stimulant effect on food intake **(Tab 1)**.

In light of the results, our study indicates that toluene extract of *Dipteracanthus prostratus* whole plant exhibited significant antihyperglycemic activity in a dose dependent manner in Streptozotocin induced diabetes. On the other hand methanolic extract of *Dipteracanthus prostratus* also has the potential to reduce the blood glucose level as showed in the results **(Tab 2)**.

Lipids play a key role in the pathogenesis and progression of diabetes. The most frequent lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia. In the present study, increased levels of total cholesterol and triglycerides were observed in diabetic control rats. Increased levels of lipid in diabetic patient represent a major risk factor for coronary heart disease [22]. Under normal conditions, insulin activates lipoprotein lipase and hydrolyzes triglycerides [23]. Insulin increases uptake of fatty acids into adipose tissue and augments triglyceride production and inhibit lipolysis. High density lipoprotein cholesterol is an antiatherogenic lipoprotein. It conveys cholesterol from peripheral tissues in the liver and thus acts as a defensive factor against the coronary heart disease. In the present study, level of HDL-Cholesterol increased following *Dipteracanthus prostratus* treatment. Administration of *Dipteracanthus prostratus* reduced triglycerides level and LDL Cholesterol level, increases the serum HDL-Cholesterol in treated rats **(Tab 3)**.

In the present study, Streptozotocin treated rat pancreas showed an increased population of the irregular arrangement of necrosed islet cells **(Fig 1A)**. Standard group animals showed a curative effect as rejuvenation of pancreatic β-cells **(Fig 1B)**. Comparable effect as exhibited in standard group is also shown by the toluene extract of *Dipteracanthus prostratus* which is evident as shown in histological examination of the pancreas by preventive changes in the globules of acini and less necrosed islets of Langerhans **(Fig 1D** and **1E)**. Methanolic extract of *Dipteracanthus prostratus* also displayed the partial restoration of the population of islet cells growth in size of islets as shown in histological sections **(Fig 1F** and **1G)**.

Previous studies stated that that the flavonoids as biologically active constituents of medicinal plant have the potential as effective hypoglycemic and could be used as an antidiabetic agent in the management of hyperglycemia [24]. Out of many pathogenic factors responsible for the development of diabetes, oxidative stress is one of the most prevalent one in the pathogenesis of diabetes.

Oxidative stress in diabetes subsequently results, stimulation of the polyol pathway, formation of advanced glycation end products (AGE), activation of protein kinase C (PKC) and consequent formation of reactive oxygen radicals [25, 26]. Due to their capability to directly oxidize and damage DNA, lipids and proteins, free radicals are believed to play a key role in the onset and development of late diabetic obstacles [27].

Flavonoids are a group of polyphenols and are well-known for their multiple biological activities as well as antidiabetic effectively. These effects are commonly associated with free radical scavenging activity of flavonoids [28]. The valuable effect of antioxidants has been reported in different studies of diabetes involving animal model and in diabetes patients. Flavonoids may be able to bind the transition metal ions, which play a key role in glycoxidation, thus preventing metal catalyzed development of hydroxyl radicals or related species from H_2O_2 [29, 30].

In present study flavonoids present in extracts could be possibly responsible for significant reduction in blood glucose level and also prevent the cellular changes in pancreatic β cells. Phytochemical studies of extracts confirmed the presence of flavonoids thus on the basis of findings of phytochemical studies and the results of *in-vivo* studies we can conclude that the probable

mechanism produced by *Dipteracanthus prostratus* in Streptozotocin induced diabetes model may be due to the multiple mechanisms provoked by the flavonoids.

CONCLUSION: In conclusion, *Dipteracanthus prostratus* exhibited significant antihyperglycemic activity in Streptozotocin induced diabetic rats. The toluene extract of *Dipteracanthus prostratus* also showed an enhancement in lipid profile as well as rejuvenation of β-cells of the pancreas and so may be of worth in management of diabetes.

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CONFLICT OF INTEREST: The authors declare that there are no conflicts of interest.

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