Advances in Bioresearch
Adv. Biores., Vol 12 (3) May 2021: 181-187

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.12.3.181187

Advances in Bioresearch

ORIGINAL ARTICLE

Insulin mimetic and Pancreas Protective Effect of *Leptadenia pyrotechnica* (forssk) decne. Stem Extract In Type-2 Diabetic Albino Rats

Manisha Solanki[1], Ashok Purohit[2]
Department of Zoology, J.N.V. University, Jodhpur (Rajasthan), India. 342001
e-mail: manusolanki999@gmail.com, purohitashok14@gmail.com

ABSTRACT
Diabetes is a group of metabolic disorders disease which characterized by elevated blood glucose which ultimately leads to many health complications. There many synthetic drugs are available in market for the treatment of diabetes but these drugs cause a number of side effects on health like diabetic neuropathy, retinopathy, liver injury, headache, organ damage and stomach problems. So there need to work on some alternative mode of treatment such explain in Ayurveda, sidha and traditional therapies for the treatment of diabetes. The aim of present study is to show the anti-hyperglycemic effects of plant. Adult white albino rats weighing from 150-200 gm were used for diabetic animal model and divided into four groups including treatment vehicle, diabetic, metformin and treatment groups. The diabetes was induced by giving dexamethasone IP (1mg/kg body weight) for seven days. The dose of stem extract of Leptadenia pyrotechnica was administrated orally at 250 mg/kg and 500 mg/kg for 28 days. Reduced glucose level is monitored at 7days, 14 days, 21 days and 28 days. Non-significant changes were observed in heart, liver and kidney weight and a significant change is observed in the weight of pancreas. Significant reduction ($P \leq 0.001$) was observed in total blood glucose and also significant decrease in cholesterol and LDL-cholesterol in stem extract treated hyperglycemic rats. Reformation was show histoarchitecture of pancreas with normal cellular status of islet cells by treatment of stem extract of Leptadenia pyrotechnica so through this experiment it is concluded that stem extract of Leptadenia pyrotechnica is having potential to control hyperglycemia.
KEY WORDS: *Hyperglycemic, Traditional, Histo-architecture, Dysfunction, Synthetic, Intraperitonial*

Received 22.04.2021 Revised 29.04.2021 Accepted 15.05.2021

How to cite this article:
M Solanki, A Purohit. Insulin mimetic and Pancreas Protective Effect of *Leptadenia pyrotechnica* (forssk) decne. Stem Extract In Type-2 Diabetic Albino Rats. Adv. Biores. Vol 12 [3] May 2021. 181-187

INTRODUCTION

Diabetes Mellitus (DM) is group of disease which results to metabolic dysfunction and characterized by enhanced blood glucose level [1] which is due to no or very less production of insulin or acquiring resistance by cells towards insulin [2]. There are two major forms of DM- Type 1 Diabetes mellitus (T1DM) and Type 2 Diabetes mellitus (T2DM). Both are mainly a result of dysfunction in β-cell of pancreas [2]. Among these two forms T2DM is more common (about 90-95% of all diabetes) and dangerous [3, 4] because children, adolescent and youngsters are getting more exposure towards T2DM [2].

There are many synthetic drugs and oral hypoglycemic agents are available for the treatment of DM [5] including Biguamides, Sulfonylurease, Meglitinide, Thiazolidinedione (TZD), Dipeptidase 4 (DPP4) inhibitors, Sodium-glucose co-transporter (SGLT2) inhibitors and α-Glucosidase inhibitors [6]. But long term use of these drugs act adversely on human health for example metformin cause diarrhea, nausea, vomiting, and stomach problems [7], so there is need to search some other alternative treatment [5].

In comparison of synthetic drugs natural medicinal plants are very affordable and have very less side effects on health [8], also there are many plants which are used to cure a number of diseases and in advancement in medical science [9,10]. Research shows that dry and deciduous vegetations have more number of medicinal plants in compare of evergreen areas [11]. The Great Indian Thar Desert is a

marvelous place having a number of medicinal floras which grows in draught condition but still contains rich source of medicinal bioactive compounds [12].

Leptadenia pyrotechnica is a plant of family Asclepiadaceae known as "khimp", "kheep" or "khip" in Thar desert of Rajasthan [13] of which every part having medicinal properties [14]. Traditionally this plant is used to treat inflammation, rheumatism, asthma, and tumors [15]. Plant sap is used to cure eczema, small pox and skin disease [16]. Juice of aerial parts has properties to treat renal dysfunction, kidney stone and cough [17]. Plant also contains antibacterial, antioxidant, antifungal, hepatoprotective [14], hypolipidemic and anti cancerous properties [18] but there is no systematic study was performed in relation to anti-diabetic properties of this plant.

Present experiment is performed to study the anti-diabetic properties of ethanolic extract of stem of *Leptadenia pyrotechnica*

MATERIAL AND METHODS

PREPARATION OF PLANT EXTRACT:- The stem of *Letadenia pyrotechnca* was collected from semi arid areas near by Jodhpur area. Material was shade dried than grind in powder form than soxhalation in 70% ethanol (ratio 1:3) for 18 hours. The solution was filtered and keep in beaker to remove suspended particle. Remaining alcohol was evaporated and the dry extract was used for treatment as per protocol [12].

CHEMICAL AND REAGENTS

All the reagents and chemicals were brought from Loba chemical distributers and other standard grade biochemistry test kits are (Erba) used for biochemical assays.

EXPERIMENTAL ANIMALS

Healthy white albino rats (*Rattus norvegicus*) weighing from 150-250gm were purchased from Lala Lajpat Rai University of veterinary and animal sciences, Hisar (Haryana, India). Animals were kept in clean cages under standard environment conditions i.e. 12 hours light and optimum temperature between 24-28^{o} C. Animals were fed with pellets diet and water *ad libitum*.

All the experimental work was confirmed by the Institutional Animal Committee **(IAEC NO. 1646/GO/Ere/S/19/CPCSEA).**

INDUCTION OF HYPERGLYCEMIA

Diabetes type-2 was induced by intraperitoneal injection of dexamethasone (1 mg/kg) [19] and high sugar contained diet for 7 days.

DOSE AND TREATMENT DESIGN

Animals are divided into five treatment groups having 4 animals each for 28 days.

Group I- vehicle control receiving distilled water

Group II- Diabetic control: Dexamethasone IP induced hyperglyemic group

Group III- Diabetic + *L. pyrotechnica* 70% ethanolic stem extract (low dose 250 mg/kg B.W.) 28 days

Group IV- Diabetic+ *L. pyrotechnica* 70% ethanolic stem extract (high dose 500mg/kg B.W.) 28 days

Group V- Diabetic + Metformin (150 mg/kg B.W.) 28 days

SERUM BIOCHEMISTRY

Weekly glucose fluctuations and lipid profile (Total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol) and other parameters were determined using standard methods.

HISTOLOGICAL STUDY

After the completion of experiment, overnight fasted animals were sacrificed by giving mild anesthesia. Blood was collected and separated serum was used for biochemical testing. Body organs like Pancreas, Liver, Heart and Kidney were removed, weighed and fixed in 10% formalin for histopathological study. Histoarchitecture of pancreas of control, diabetic and treatment group was observed under light microscope.

STATISTICAL ANALYSIS

Results of the biochemical assessments and organ weight are expressed as a mean ± standard error of the mean (SEM) and statistical differences were determined by ANOVA and post hoc mean separation test.

RESULT

The treated animals with stem extract (250 mg/kg and 500mg/kg of body weight) of *Leptadenia pyrotechnica* shows significant changes as shown in following results

BODY AND ORGAN WEIGHT-

Leptadenia pyrotechnica stem extracts treated animals shows a significant increase in body weight, pancreas and liver. Treated animals also shows more activeness in comparison to diabetic animal group (Table 1).

SERUM BIOCHEMISTRY

Animals were shown significant gradual lowering in blood glucose level by treatment of low dose (250 mg/kg) and high dose (500 mg/kg) (7day, 14day, 21day and 28day) in comparison to diabetic group which was 300-400mg/dl (fig. 1).

The lipid profile shows that total cholesterol, LDL- cholesterol, HDL-cholesterol, triglyceride, total lipid and VLDL- cholesterol were also significantly decrease to normal level in comparison to diabetic animal group (fig. 2).

TABLE-1. BODY AND ORGAN WEIGHT COMPARISION OF 28 DAYS TREATMENT ETHANOLIC EXTRACT OF *L. pyrotechnica* STEM IN DIABETIC ALBINO RATS

Treatment group	Mean Body Weight		Pancreas	Heart	Kidney	Liver
	Initial	Final	-------mg/100gm body weight-------			Gm/100gm body weight
Group-I (Intact control)	210.23 ±13.16	210.23 ±21.23	444.79 ±16.93	476.12 ±12.76	790.12 ±18.12	5.36 ±0.40
Group-II (Diabetic control)	175 ±14.01	179 ±10.02	236.23^{c} ±17.93	469.23^{d} ±10.78	810.76^{d} ±17.12	4.93^{d} ±0.36
Group-III (Stem-250mg/kg)	141 ±2.88	160 ±10	$787.78^{c,g}$ ±48.96	$429.24^{a,e}$ ±4	$894.57^{d,h}$ ±129.06	$3.85^{a,e}$ ±0.27
Group-IV (Stem-500mg/kg)	186.66 ±5.77	203 ±5.77	$591.34^{d,g}$ ±29.28	$373.95^{b,e}$ ±14.86	$834.04^{d,h}$ ±14.42	$3.14^{a,e}$ ±0.19
Group-V (Metformin-150mg/kg)	162 ±10.60	167 ±10.60	$793.83^{c,g}$ ±88.26	$393.03^{a,e}$ ±62.88	$1091^{b,e}$ ±31.99	$2.41^{b,f}$ ±0.82

Gr. I compared with Gr. II to V Gr. II compared with Gr. III to V

P≤0.05 =a P≤0.01 =b P≤0.05 = e P≤0.01=f P≤0.001 = c Non-significant =d P≤0.001 =g Non-significant =h

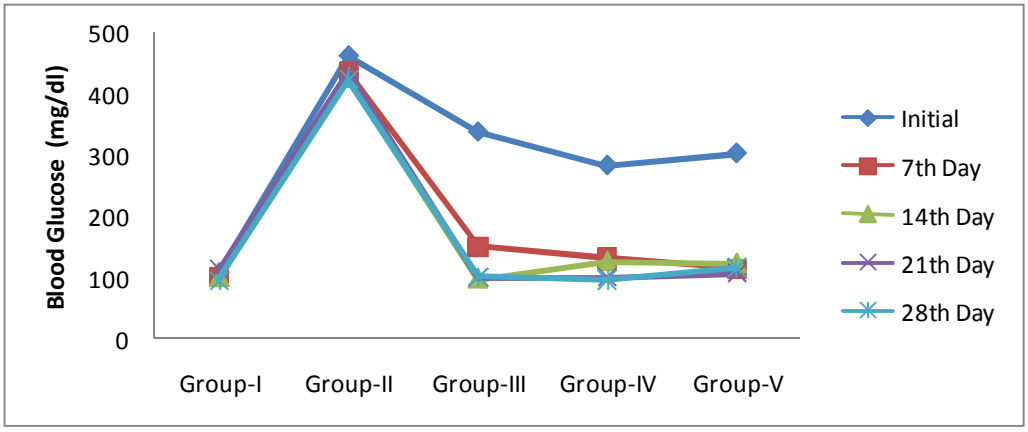

Fig.1- Blood glucose level changes in (7, 14, 21 and 28 days) treatment of 70% ethanolic extract of *L. pyrotechnica* stem in diabetic albino rats

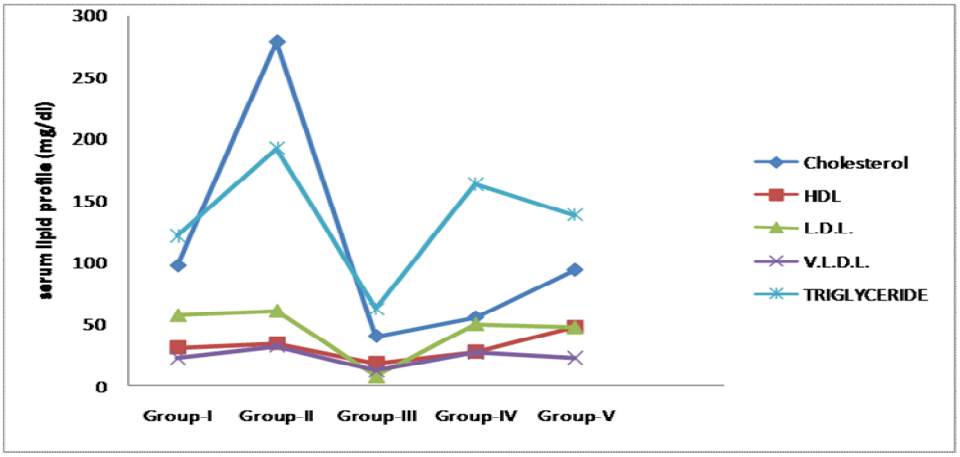

Fig.2- Lipid profile of 28 days treatment of 70% ethanolic extract of *L. pyrotechnica* stem in diabetic albino rats

HISTOPATHOLOGY

Histoarchitecture of heart, liver, kidney and pancreas shows a significant normalization in structure. Cells of liver and kidney shows normal histoarchitecture in *L. pyrotechnica* stem extract (250 mg/kg and 500 mg/kg) treatment group as compare to diabetic group. There is no significant changes were shown in heart tissue cell.

Pancreatic tissue cells of islets are showing regeneration as compare to diabetic animal where islets of langerhans and necrotic are present. (Fig 3-7)

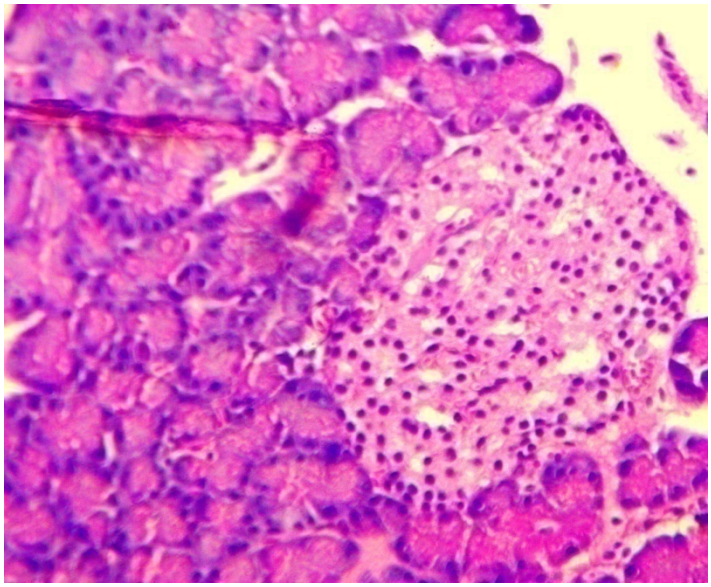

Fig 3- Pancreatic histoarchitecture of vehicle control rats (H & E 200X)- The histoarchitecture shows islets of Langerhans with group of cells arranged.

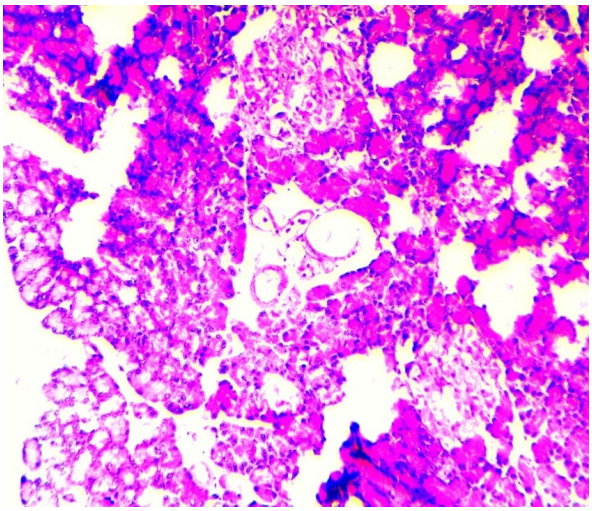

Fig 4- Pancreatic histoarchitecture of diabetic control rats (H & E 200X)- Diabetic pancreatic histoarchitecture consisting of vacuolated islets of Langerhans and necrotic nuclei of islet cells with congested blood vessels.

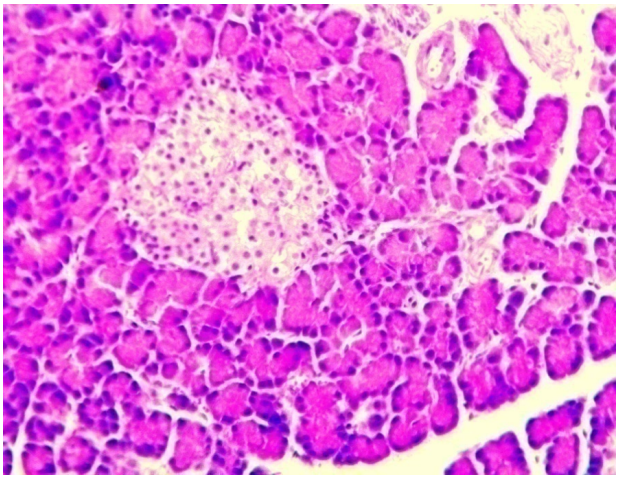

Fig 5- Pancreatic histoarchitecture of *L. pyrotechnica* stem extract (250 mg/kg) treatment (H & E 200 X)- the Pancreatic histoarchitecture consisting of acini and round regenerated part of islets of langerhans with proper arrangement of blood vessels.

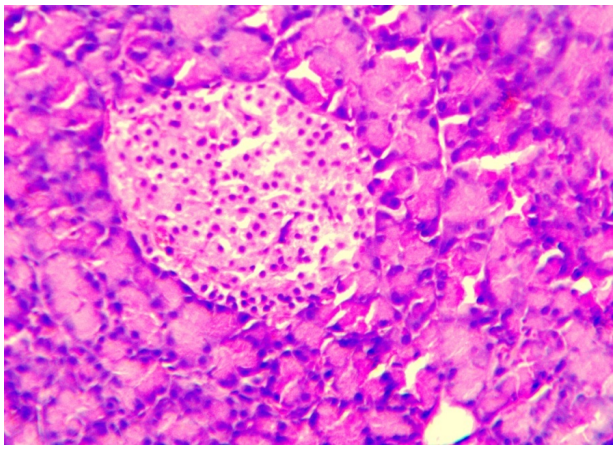

Fig 6- Pancreatic histoarchitecture of *L. pyrotechnica* stem extract (500 mg/kg) treatment (H & E 200 X)- the Pancreatic histoarchitecture consisting of acini and regenerated cellular part of islets of langerhans with proper arrangement of blood vessels.

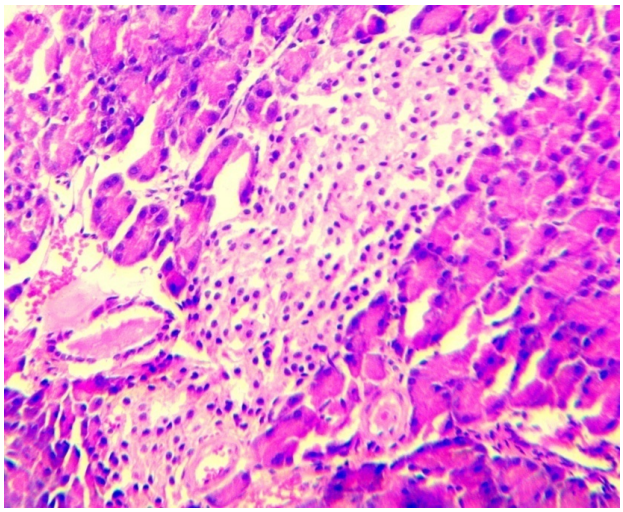

Fig 7- Pancreatic histoarchitecture of Metformin (150 mg/kg) treatment (H & E 200 X)- The Pancreatic histoarchitecture consisting of acini and regenerated part of islets of langerhans with proper arrangement of blood vessels.

DISCUSSION

T2DM is a major form of chronic diabetes mellitus which occurs due to destruction in β-cells of pancreas (produce insulin hormone) or insulin resistance [20]. This life taking disease accounts approximately 87-91% of all diabetes types [1]. India is now known as diabetic capital of the world due to a horrific increase in the number of diabetic patients in last decade [21].

Popularly used oral hypoglycemic agents which used to treat T2DM are Sulfonylureas, Biguanides, Glucosidase inhibitors, Glinides [22], Thiazolidinediones etc. which reduces blood glucose level [23], but the major disadvantage of these drugs is that the patient have to take these drug throughout their life [22]. These drugs are also cause savior health complications such as renal dysfunction, fatigue, stomach problems and diarrhea [21].

Plants are most promising, effective and safe source of medication [24]. Most of plants contains a number of compounds (glycosides, alkaloids, terpenoids, flavonoids, curtenoids etc.) which having hypoglycemic properties [25].

Leptadenia pyrotechnica is an important plant of The Indian Thar Desert [12] which widely used to treat a number of diseases. According to previous researches *L. pyrotechnica* shows the presence of various bioactive compounds like steriodal glycoside, cardiac glycosides, cardenolides, alkaloids, flavonoids, triterpenes, tennins, saponins [24] and polyphenolic compounds (gallic acid, vanilli acid, caffeic acid, epicutechin and quercetin-3-β-D—glucoside) [22]. These compounds are found in highest amount in ethanolic extract and shows effective dose dependent reduction in blood glucose level [24,14]. In present experiment with stem ethanolic extract treatment (250 mg/kg and 500 mg/kg) also shows similar effects by reduced glucose level, also there is a significant reduction is shown in the level of glycogen in liver, cholesterol and triglycerides in serum as compare to diabetic group [26].

In same research there is a significant improvement observed in the body and organ weight in treatment groups [27] which is also proven by this experiment where *L. pyrotechnica* stem extract treated group shows a marked improvement in body weight [14] also *L. pyrotechnica* stem extract treated group showed normalized liver cells. Deterioration in pancreatic β-cells by dexamethasone induction is also shows regeneration [12].

Other renal and hepatic parameters are also come to under normal level in extract treatment animal. So we can say that *L. pyrotechnica* stem extract contains phytochemicals which play an active role to reduce blood glucose level. So it can be concluded that 70% Ethanolic extract of *L. pyrotechnica* stem, possessing bioactive compounds which have pancreas-protective properties and it lowers the blood glucose level by regenerating β-cells or by increasing the capacity of animal tissues to absorb more glucose. So it can be said that hypoglycemic properties of *L. pyrotechnica* can further more explore to treat diabetes mellitus.

ACKNOWLEDGEMENT

The study is financially supported by Council of Scientific and Industrial Research (CSIR), New Delhi. (09/098(0139)/2019-EMR-I).

CONFLICT OF INTEREST

Authors have declared no conflicts of interest for this study.

REFERENCES

1. Okur, M.E., Karantas, I.D. and Siafaka, P.I. (2017). Diabetes Mellitus: A Review On Pathophysiology, Current Status of Oral Medication and Future Perspectives. Acta Pharma. Sci., 55 No:1. 1307-2080.
2. Eizirik, D.L., Pasquali, L. and Cnop, M. (2020). Pancreatic β-cells in type 1 and type 2 diabetes mellitus: different pathways to failure. Nature Reviews Endocrionology., 16: 349-362.
3. Sharma, A. (2018). Assessment of type-2 antidiabetic profile of slcoholic extract from Chenopodium album plant., International Journal of Medical and Biomedical Studies.
4. Alberti, K.G.M.M. and Zimmet, P.Z. (2014). Diabetes: a 21st century challenge: The Lancet Diabetes & Endocrinology., 2(1):56-64.
5. Peter, E.L., Mthewa, A.G., Nagendrappa, P.B., Kaligirwa, A. and Sesaazi, C.D. (2020). Systematic review and meta-analysis protocol for efficiency and safety of *Momordica charantia L.* on animal models of type 2 diabetes mellitus. Systematic Reviews., 9:7.
6. Chaudhary, A., Duvoor, C., Dendi, V.S.R., Kraleti, S., Chanda, A., Ravilla, R., Marco, A., Shekhawat, N.S., Montales, M.T., Kuriakose, K., Sasapu, A., Beebe, A., Patil, N., Musham, C.K., Lohani, G.P. and Mirza, W. (2017). Clinical Review of Antidiabetic Drugs: Implications for Type 2 Diabetes Mellitus Management. Frontier in Endocrinology., 8.
7. Tiwari, P. (2015). Recent Trends in Therapeutic Approaches for Diabetes Management: A Comprehensive Update. Journal of Diabetes Research., Vol. 2015: 1-11.

8. Salah, H., Shaza, A. and Mohamed, A.M. (2019). Isolation and Characterization of a Dihydrochalocan from Sudaness *Leptadenia pyrotechnica* L. (Asclepiadaceae). Journal of Research in Pharmacy and pharmaceutical Sciences., 4(3): 92-94.
9. Patel, D.K., Kumar, R., Laloo, D. and Hemalatha, S. (2012). Diabetes mellitus: An overview in its pharmacological aspects and reported medicinal plants having antidiabetic activity. Asian Pacific Journal of Tropical Biomedicine., 2(5): 411-420.
10. Purohit, A. and Sharma, A. (2006). Antidiabetic efficacy of *Bougainvillea spectabilis* bark extract in streptozotocin induced diabetic rats. Journal of Cell and Tissue Research., 6(1): 537-540.
11. Sharma, M. and Kumar, A. (2013). Traditional Medicinal Plants of Rajasthan Used in Tribal Medicine: A Review. International Journal of Life Science & Pharma Research., 3(2): 38-42.
12. Lal, K., Purohit, A. and Ram, H. (2017). Insulin Mimetic and Pancreas-Protective Effects of *Tecomella undulata* Leaves Extract in Diabetic Rats. World Journal of Pharmacy and Pharmaceutical Sciences., 6(2): 924-938.
13. Idrees, S., Qureshi, R., Bibi, Y., Ishfaq, A., Iftikhar, A., Shabir, A., Riaz, I., Saboon and Ahmad, N. (2016). Ethnobotanical and Biological Activities of *Leptadenia pyrotechnica* (Forssk.) Decne.: A Review., Afr J Tradit Complement Altern Med., 13(4):88-96.
14. Preet, R. and Gupta, C. (2018). Simultaneous Determination of Phenolic Compounds in *Leptadenia pyrotechnica* (FOSSK.) Decne. by Using High-Performance Liquid Chromatography (HPLC-DAD-UV). Advances in Pharmacological Sciences., Vol. 2018.
15. Khasawneh, M.A., Koch, A., Elwy, H.M., Hamza, A.A. and Stock, R.S. (2015). *Leptadenia pyrotechnica* Induced P^{53}-Dependent Apoptosis in Colon Cancer Cells. Natural Products Chemistry & Research. Vol. 3(3).
16. Ullah, F., Uzair, M., Chaudhry, B.A. and Zafar, Z.U. (2015). Phytochemical and Pharmacological studies of *Leptadenia pyrotechnica*. Pakistan journal of Pharmaceutical Research., 1(2).
17. Ram, B. (2016). Important Uses of *Leptadenia pyrotechnica* of Bikaner. International Journal of Advances in Science and Technology., 4(4).
18. Khasawneh, M.A., Elwy, H.M., Hamza, A.A., Fawazi, N.M. and Hassan, A.H. (2011). Antioxidant, Anti-Lipoxygenase and Cytotoxic Activity of *Leptadenia pyrotechnica* (Forssk.) Decne Polyphenolic Constituents. Molecules., 16: 7510-7521.
19. Wego, M.T., Kamani, S.L.P., Miaffo, D., Nchouwet, M.L., Kamanyi, A. and Ngnokam, L.W. (2019). Positive effects of Aqueous Extract of *Baillonella toxisperma* Stem Bark on Dexamethasone Induced Insulin Resistance in Rats. Advances in Pharmacological Sciences., Vol. 2019.
20. American Diabetes Association: Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes care., 42:S13-S28.
21. Jacob, B. and Narendhirakannan, R.T. (2019). Role of medicinal plants in the management of diabetes mellitus. Biotech., 9:4.
22. Mohammed, S.A., Yaqub, A.G., Sanda, K.A., Nicholas, A.O., Arastus, W., Muhammad, M. and Abdullahi, S. (2013). Review on diabetes, synthetic drug and glycemic effects of medicinal plants. Journal of Medicinal Plants Research., 7(36):2628-2637.
23. Adapa, D. and Sarangi, T.K. (2015). A Review on Diabetes Mellitus: Complications, Management and Treatment Modalities. Journal of Medical and Health Sciences., 4(3).
24. Gupta, G.K., Joshi, T., Madhudiya, K. and Chaudhuri, A. (2017). Therapeutic Properties and Nutritive Values of Some Fruit Bearing Medicinal Plants of Rajasthan State in India. UK Journal of Pharmaceutical and Biosciences., 5(5): 18-26.
25. Malviya, N., Jain, S. and Malviya, S. (2010). Antidibetic Potential of Medicinal Plants. Acta Poloniac Pharmaceutica., 67:113-118.
26. Chaudhary, S. and Khosa, R.L. (2011). Evaluation of antidiabetic activity of whole plant of *Leptadenia pyrotechnica* (Forssk.) decne against streptozotocin induced diabetes in rats., 2:1196- 1204.
27. Chaudhary, S., Khosa, R.L., Jha, K.K. and Kumar, S. (2011). Evaluation of anti-diabetic activity of whole plant of *Leptadenia pyrotchica* (Forssk.) decne against streptozotocin induced diabetes in rats, Pharmacologyonline., 2:1196-1204.