Journal of Medicinal Herbs and Ethnomedicine 2020, 6: 11-16
doi: 10.25081/jmhe.2020.v6.5682
https://updatepublishing.com/journal/index.php/jmhe/

Research Article

ISSN: 2455-0485

Evaluation of anti-diabetic and anti-hyperlipidemic activity of *Rhododendron arboreum* bark extract against streptozocin induced diabetes in rats

Suman Gautam[1]*, Kabiraj Chaudhary[2,3]

[2]Mallige College of Pharmacy, Bangalore, Karnataka, India, [3]Curex Pharmaceutical Pvt Ltd, Nepal, [1]Central Department of Biotechnology, Tribhuvan University, Nepal

ABSTRACT

The anti-diabetic and anti-hyperlipidemic activity of *R. arboreum* in bark extract against streptozocin-induced diabetic rats. *R. arboreum* bark extract in ethanolic solution was prepared by soxhlatation method and stored in refrigerator for further use. The plant extract was tested for its hypoglycaemic property in glucose overloaded albino rats. The effect of extract was evaluated for its anti-diabetic action in STZ induced diabetic rats on 7, 14, 21 and 28 days respectively. Treatment with the ethanolic extract of *Rhododendron arboreum* significantly decreased blood glucose in diabetic rats and glucose overloaded rats, where as the extract also improved the others biochemical parameters associated with diabetes like total cholesterol, triglycerides and LDL were reduced and HDL level was increased.The cardioprotective and nephroprotective qualities of the extract was determined by measuring biomarker LDH in diabetic rats. The histopathology of pancreas was studied to support the experimental results. The histology of pancreatic islet cells was normal in non-diabetic animals, whereas in diabetic treated rats. The significant percentage reduction of glucose level was found to be 44.78% at the dose of 200 mg/kg of aqueous extract of *Rhododendron arboreum* at 28th day of the treatment.

Received: June 26, 2019
Accepted: January 17, 2020
Published: January 25, 2020

***Corresponding Author:**
Suman Gautam
Email: gautamsuman94@gmail.com

KEYWORDS: *Rhododendron arboreum*, anti- diabetic, anti-hyperlipidemic, bark, ethanol, Streptozocin

INTRODUCTION

Rhododendron arboreum Sm. (*R. arboreum*) also known as "Laligurans" or simply "Gurans" national flower of Nepal, is a small evergreen tree with a bright red flower. It has habitat in the lap of Himalayas. The plant has the medicinal value and various parts are used for the treatment of the ailments. Flower of the plant is traditionally used in the treatment of diabetes by rural Nepalese people [1]. A flower is also used in the acute inflammation treatment [2] and also has the properties of anti-nociceptive and anti-inflammatory [3]. Hypolipidemic activities in induced hypercholesteremia rabbits [4] and hepatoprotective activity [5] has also been noted. The plant contains many flavonoids and triterpenoids/sterols which are known for their bioactive principles for anti-diabetic potential [6]. Flavinoids also is known for the regeneration of the damaged β-cells in diabetic mice [7,8].

Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by complete or partial insufficiency of insulin action [9,10]. Diabetes mellitus (DM) is a chronic disorder caused by insufficient production of insulin and decreases in the absorption of glucose by the cells in the human system which leads to an increase in the concentration of glucose blood. It is also produced due to the hereditary Characters. Increase glucose level in blood leads to various deficiencies and alters the normal physiological effects of the human system like blood vessels and nerves system etc. It is projected that the Diabetic is the main disease which can increase the deaths retain next coming 25 years in Asian countries and Africans [11].

According to the World Health Organization (WHO), there are approximately 422 million diabetic's people world-wide; the global prevalence of diabetes has risen from 4.7% in 1980 to 8.5% in 2014. In 2016, an estimated 1.6 million deaths were directly caused by diabetics so it was listed as the 7th leading cause of death in 2016 [12]. Diabetes is considered a major medical concern due to its high prevalence and potential deleterious effect on a patient physical and psychological state. The disease remains incurable and can only control with drugs [13].

The detailed survey of literature revealed that *Rhododendron arboreum* is an important plant of a hilly region with extensive medical and commercial uses. The plant exhibited anti-inflammatory, hepato-protective, anti-diarrhoeal, anti-diabetic,

antioxidant properties due to the presence of flavonoids, saponins, tannins, and other phytochemicals [1].

So, the present study was conducted to find out the antidiabetic activity of the *Rhododendron arboreum* bark extract in streptozotocin-induced diabetic rats.

The plant is taxonomically classified as.
Kingdom: Plantae
Phylum: Magnoliophyta
Class: Angiospermae
Order: Ericales
Family: Ericaceae
Genus: *Rhododendron*
Species: *R. arboreum*.

MATERIALS AND METHOD

Collection and Authentication of Plant Material

The bark of *Rhododendron arboreum* was collected from the hilly region of Nepal. The plant was identified and authenticated by Dr. K. Ravi kumar, senior botanist at FRLHT (Foundation for Revitalisation of Local Health Traditions) Jarakabande Kaval, Post Attur, Yehalanka, Bengaluru (560106). The barks were shade dried at room temperature for 15 days and pulverized.

Preparation of Extract

The bark of *Rhododendron arboreum* was shade dried and then powdered with a mechanical grinder. The powder was stored in an airtight container and stored at 5°C. Powdered bark (500 g) was defatted with 1L petroleum ether (40–60°C) to remove lipid constituents by soxhlation for 24 hours not exceeding the boiling point of the solvent. It is then filtered with filter paper, and the residue was air-dried at 30°C and extracted with 95% ethanol (1L) by soxhlation for 48 h, not exceeding the boiling point of the solvent. Ethanol is evaporated in a rotary evaporator at 40–50°C under reduced pressure [14].

Experimental animal

Albino Wistar male rats (180–220 gm) were selected for experimental study. The animals were kept and maintained under laboratory conditions of temperature (24 ± 2°C), humidity (60 ± 1%), and 12-hour light/dark cycle. They were allowed free access to food (standard pellets) and water ad libitum. Experimental protocols and procedures used in the following ways:

Acclimatization

One week in the experimental room.

Selection of animals

After acclimatization, the animals were subjected to a gross observation to ensure that the selected rats were in good state of health. Rats were randomly selected for final allotment to the study.

Acute toxicity studies

Acute toxicity studies were performed according to OECD (Organization for Economic Co-operation and Development) guidelines 423. Rats are selected for the study and are fasted for 3-4 h with free access to water. Extracts of above plant parts at a dose of 5, 50, 300, 2000 mg/kg are given p.o. at 48 h intervals simultaneously to the respective groups. Animals are observed individually after dosing for signs of toxicity and mortality rates [15].

Induction of Diabetes

Rats were fasted overnight before inducing diabetes with streptozotocin. The rats were given an intraperitoneal injection of streptozotocin (60 mg/kg) freshly prepared in 0.1M sodium citrate buffer. The diabetic state was confirmed 48 h after streptozotocin injection. A threshold value of fasting blood glucose was taken as >200mg\dl.

Blood Sugar and Biochemical Estimation

Blood samples were obtained through puncture tail vein and collected blood samples were analyzed by Accu-Check Glucometer. Blood glucose levels were expressed in terms of mg/dl and TC, TG, HDL, and LDH were also estimated.

Qualitative Phytochemical Analysis

The ethanolic extract was tested to know the different constituents present in it by the standard procedures. The extracts were tested for the alkaloids, carbohydrates, saponins, flavonoids, triterpenoids, sterols and protein.

Experimental Design

4 Groups of animals having six animals in each group were used.

Groups	Treatment	Number of animals
Group I	Control	6
GroupII	Standard Glibenclamide (0.25mg/kg. p.o)	6
Group III	*Rhododendron arboreum* bark extract (100 mg/kg)	6
Group IV	*Rhododendron arboreum* bark extract (200 mg/kg)	6

RESULTS

Phytochemical Analysis

The ethanolic extract of *Rhododendron arboreum* was subjected to a qualitative test to identify the presence of phytoconstituents. The result of phytochemical analysis summarized in Table 1 confirmed the presence of alkaloids, flavonoids, saponins, carbohydrates, steroids, phenol, proteins, tannins and triterpenoids compounds.

Effect of *Rhododendron arboreum* Bark Extract on Blood Glucose Level of Glucose Overloaded Healthy Albino Rats

The result of the OGTT is summarized in Table 2 as well as in Figure 1. The standard drug glibenclamide 0.25 mg/kg, p.o. reduced blood glucose level 36.39 % at 1.5th hr and 37.3% at 2nd hr. The ethanolic extract of *Rhododendron arboreum*100 mg/kg, p.o. also reduced the blood glucose from 0.5th to the 2nd hour of treatment the highest being 22.05% at the 2nd hour. The ethanolic extract of *Rhododendron arboreum* at 200 mg/kg reduced the blood glucose from 0.5th hour to 2nd hour and 28.34% was the highest reduction observed at the 2nd hour.

Effect of *Rhododendron Arboreum* Bark Extract on Streptozocin Induced Diabetic Albino Rats

The *Rhododendron arboreum* ethanolic extract at 200 mg/kg exhibited a significant reduction of blood glucose level from 7th day to 28th day of the treatment 42.37 % of the reduction was found to be the highest and was shown on the 28th day with 200 mg/kg of ethanolic extract. The ethanolic extract at a dose of 100 mg/kg also significantly reduced the blood glucose level in diabetic rats. The percentage of reduction was highest at 32.71% on the 28th day. As compared to 200 mg/kg of ethanolic extract 100 mg/kg of ethanolic extract of *Rhododendron arboreum* showed nearly 9.66% less. And the results are presented in Table 3 and Figure 2.

Table 1: Phytoconstituents screening

Sl.No	Phytoconstituents	Ethanolic extract of *R. Arboreum*
1	Alkaloids	+
2	Carbohydrates	+
3	Flavonoids	+
4	Proteins	+
5	Saponins	+
6	Steroids	+
7	Tannins	+
8	Triterpenoids	+

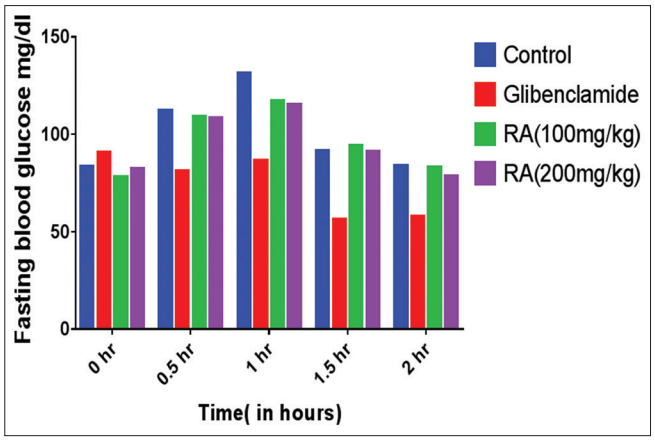

Figure 1: Effect of *R. arboreum* bark extract on glucose overloaded albino rats

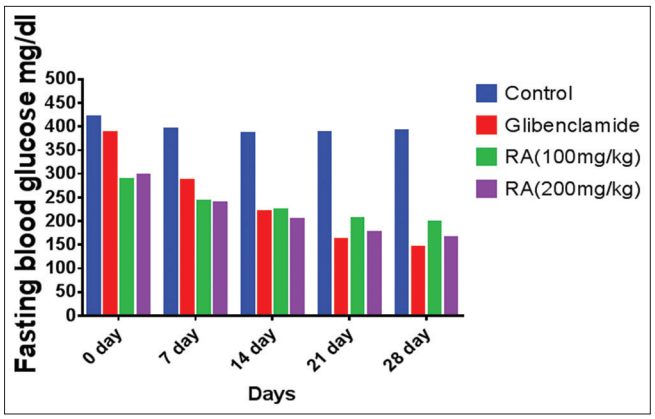

Figure 2: Effect of *R. arboreum* plant bark on STZ induced diabetic albino rat

Table 2: Effect of extract of *Rhododendron arboreum* bark on blood glucose overloaded albino rats

Treatment	FBS (mg/dl±SEM)					% Reduction in blood sugar			
	Hours					Hours			
	0	0.5	1	1.5	2	0.5	1	1.5	2
Control	86±2.27	133±3.59	104±2.62	90.7±1.71	88.3±1.84	_	_	_	_
Glibenclamide (0.25 mg/kg, p.o)	77±2.31	112±2.24*	89.3±3.22**	80.3±2.91**	80±3.45**	45.45	15.97	4.28	3.89
R.arboreum 100 mg/kg	77.8±2.43	117±4.62	94±2.41*	84±1.71*	86.3±2.23*	50.38	21.03	8.05	10.92
R.arboreum 200 mg/kg	82±2.13	115±6.98*	90.8±1.54**	78.3±2.08**	81±1.39**	40.24	10.73	4.5	1.21

N=6 animals in each group. Values are expressed as Mean±SEM. *p<0.05, **p<0.01, ***p<0.001

Table 3: Effect of extract of *Rhododendron arboreum* on streptozocin induced diabetic albino rats

Treatment	FBS (mg/dl±SEM)					% Reduction in blood sugar			
	Days					Days			
	0	7	14	21	28	7	14	21	28
Control	420±0.643	394.2±00.381	385.5±0.581	387.2±0.361	390.0±0.525	_	_	_	_
Glibenclamide (0.25 mg/kg, p.o)	387±0.348	286.8±0.323***	219.5±0.545***	161.3±0.322***	145.4±0.609***	25.89	43.28	58.32	62.42
R.arboreum 100 mg/kg	288±3.82	241±11***	223±4.4***	206±2.93***	198±5.12***	16.31	22.56	28.47	31.25
R.arboreum 200 mg/kg	297±3.24	239±4.83**	204±3.96***	176±4.29***	164±8***	19.52	31.31	40.74	44.78

N=6 animals in each group. Values are expressed as Mean ± SEM. *p<0.05, **p<0.01, ***p<0.001

Table 4: Effect of *R. arboreum* bark extract on biochemical parameters in STZ induced diabetic rat

	TC (mg/dl)	TG (mg/dl)	HDL (mg/dl)	LDH (IU/I)
Healthy control	83.2±0.824	109.2±0.742	35.7±0.636	115±0.817
Glibenclamide	63.9±0.419	51.9±0.879***	67.0±1.05***	67.4±0.772***
R. arboreum 100 mg/kg	61.3±3.18	83.3±1.5***	42.8±2.39***	83.5±1.88***
R. arboreum 200 mg/kg	51.2±1.91	50.±1.41***	54.2±1.45***	82±0.894***

Effect of *Rhododendron arboreum* Bark Extract on Biochemical Parameters in STZ Induced Diabetic Rats

The results of *R. arboreum* ethanolic bark extract on biochemical parameters in STZ induced diabetic rats are shown in Table 4 and Figure 3. The STZ induced diabetic rats showed significant hypercholesterolemia, hyper-triglyceridemia and an increase in levels of LDH and a decrease in the level of HDL when it is compared with the normal control rats.

Treatment with *R. arboreum* bark extract at the dose of 200 mg/kg *p.o.* showed a significant decrease in total cholesterol levels nearly to the normal. The cholesterol reduction property of *R. arboreum* bark extract (200 mg/kg) was found to be almost equal to the Glibenclamide which was used as a standard drug. *R. arboreum* bark extract at the dose of 100mg/kg *p.o.* significantly reduces the cholesterol as compared to diabetic control.

Hyper-triglyceridemia was also significantly prevented by treatment with ethanolic extract of *R. arboreum* compared with Glibenclamide (0.25 mg/kg) treated groups. The *R. arboreum* extracts at the dose of 100 and 200 mg/kg *p.o.* reduced triglycerides significantly nearly to the normal value. Glibenclamide was also found to reduce triglycerides level significantly almost near to normal group values.

The HDL level in diabetic rats was decreased when compared to normal animals. The alcoholic extract at 200 mg/kg significantly increased the HDL level. The *R. arboreum* at 100 mg/kg also increased the HDL level significantly. Standard drug Glibenclamide increased the HDL level almost equal to normal.

It was found that the LDH level significantly reduced by ethanolic bark extract of *R. arboreum* when compared to diabetic control. It was observed that the alcoholic extract of *R. arboreum* at a dose of 200 mg/kg *p.o.* showed better activity than at the dose of 100 mg/kg *p.o.*

Histopathological Investigation

Histopathology of the pancreas is present in Figure 4-7. The pancreas of albino rats of the control group showed normal histology, the normal appearance of the islet of Langerhans containing α, ß and δ cells. The ß-cells are the most abundant cells.

Diabetic rat pancreas showed a reduction in the pancreatic ß-cell numbers and necrosis along with few surviving ß-cells. Severe infiltration of inflammatory cells was also observed. It

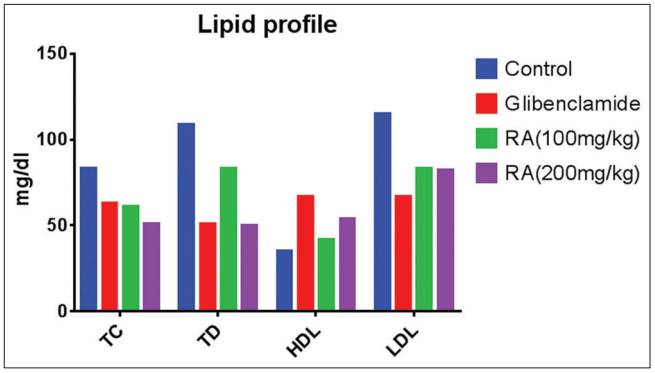

Figure 3: Effect of *R. arboreum* bark extract on biochemical parameters in diabetic albino rats

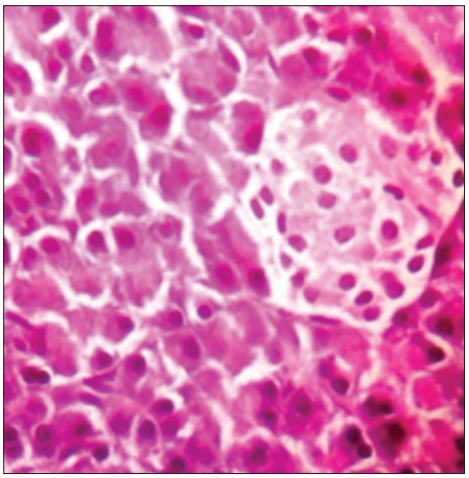

Figure 4: Normal

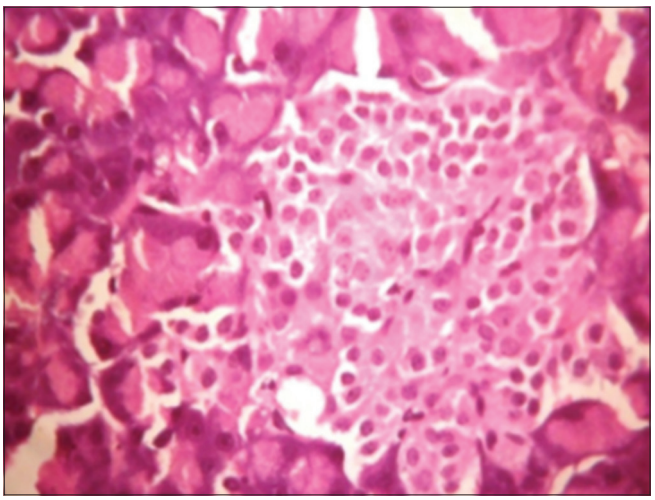

Figure 5: Glibenclamide

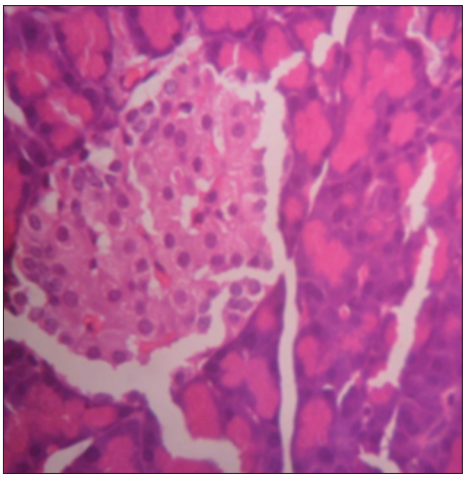

Figure 6: *R. arboreum* (100mg/kg)

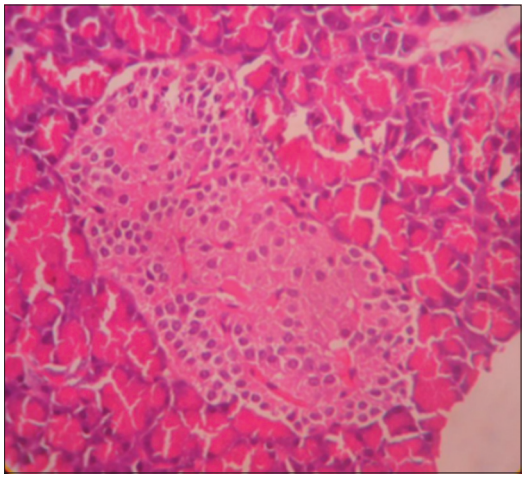

Figure 7: *R. arboreum* (200mg/kg)

showed marked degeneration of the Islet of Langerhans and it also showed the fat deposition.

In the reference group, i.e., diabetic rats treated with Glibenclamide, pancreas architecture was similar to that observed in the control rat and it also showed slight regeneration of the beta cell, less damage to beta cells as compared with the diabetic rat.

Histopathological study of the pancreas of diabetic rats treated with alcoholic extract of *R. arboreum* at the dose of 100 mg/kg *p.o.* showed a significant improvement in the number of β-cells. It was observed that it exhibited less damage to beta cells, improved beta cell regeneration and showed slight necrosis as compared to diabetic rats.

The pancreas of the rats treated with the alcoholic extract of *R. arboreum* at the dose of 200 mg/kg *p.o.* showed a reduction in the extent of necrosis and inflammation where as increased in the number of islet cells of the pancreas and less deposition of the fatty material as compared with diabetic control.

DISCUSSION

In this study, the anti-diabetic action of ethanolic extract of *Rhododendron arboreum* bark extract has been evaluated and its efficacy has been compared with that of standard oral hypoglycemic drug Glibenclamide owing to its traditional uses and proved its claimed uses. The ethanolic extract of *Rhododendron arboreum* found to contain wide varieties of chemical constituents such as carbohydrate, saponins, flavonoids, triterpenoid, and sterols.

The ethanolic extract of *Rhododendron arboreum* was evaluated for its hypoglycemic effect in healthy rats and STZ induced diabetes in albino rats. The ethanolic extract of *Rhododendron arboreum* significantly reduced blood glucose in normal healthy rats. The ethanolic extract of *Rhododendron arboreum* also reduced the blood glucose in glucose overloaded healthy albino rats. This effect may be due to the reduction of glucose absorption or due to increased insulin secretion and alteration in carbohydrate and lipid metabolism.

The number of β-cell improved significantly by extract may be the mechanism of anti-diabetic action of *R. arboreum* extract. The leaves extract of *R. arboreum* also reported for its potent antioxidant activity. Treatment with both extracts elevated enzymatic and non-enzymatic antioxidant levels. This property may also play a role in the reduction of inflammation, and necrosis leading to the regeneration of damaged beta cells in the pancreas.

The subsequent increase in uptake of blood glucose and its utilization may be another mechanism of action of the extract. Other possible mechanism includes the stimulation of β-cells and subsequent release of insulin and activation of the insulin receptors. Estimation of insulin level and insulin receptor may give more insight into the mechanism of the anti-diabetic activity exhibited by the extract.

A plant may act on blood glucose through different mechanisms, some of them may have insulin-like substances and some may inhibit insulinase activity. The extract might possess an insulin-like effect on peripheral tissues either by promoting glucose uptake and metabolism or inhibiting hepatic gluconeogenesis. The phytochemical studies on ethanolic extract of *R. arboreum* revealed the presence of tannins and flavonoids. Flavonoid and tannins isolated from other anti-diabetic medicinal plants has been found to stimulate the secretion or possess an insulin-like effect.

The results of the present study indicate the *Rhododendron arboreum* bark extract exhibited a dose-dependent reduction in blood glucose levels in healthy and diabetic rats. The results from the present study also indicate that the *Rhododendron arboreum* bark extract can reduce the levels of serum cholesterol, serum triglyceride, lactate dehydrogenase and increase the level of HDL, confirms the possibility that the major function of the leaves extract are on the protection of vital tissues including the pancreas, thereby reducing the causation of diabetes in the experimental animals.

Flavonoids like quercetin and its derivatives were reported to potentiate insulin secretion and protect INS-1 pancreatic β-cells against oxidative damage via phosphorylation pathways. The presence of such active components might be responsible for the anti-diabetic as well as anti-hyperlipidemia activity by the *R. arboreum* bark extract supported by the various research work [1,2,16-21].

The aqueous extract of *Rhododendron arboreum* at 200 mg/kg dose significantly reduced blood glucose levels in diabetic rats. The extract at the dose of 100 and 200 mg/kg reduced 31.25% and 44.78 % of blood glucose respectively on the 28th day of treatment. The results of histopathological studies revealed that the aqueous extract of *Rhododendron arboreum* 100 mg/kg and 200 mg/kg have increased the number of β-cells and also decrease necrosis and inflammation in the pancreas as seen in various work [22,23].

From the above discussion, we have observed that the ethanolic extract of *R. arboreum* bark has anti-diabetic activity as well as major role in the reduction of TG, TC, LDL and increase HDL.

COMPETING INTERESTS

The author declares that we have no competing interests concerning the information reported in this paper.

AUTHURS' CONTRIBUTIONS

Kabiraj has reviewed literature, design, execute, perform the work and analyzed the result. Suman has reviewed literature, supervised the execution of the work, analyzed the result, prepared and finalized the manuscript.

ACKNOWLEDGMENTS

The author is deeply grateful to the subjects participating in this study. The author is very grateful to the D.R Dhananjaya sir and H.S Yogesh sir who always supervise and guide throughout the work, staff of the Mallige College of pharmacy for their kind support in the collection of data and performing the necessary laboratory tests during the study. And finally like to thank and appreciate our family, friends and Mr. Deepak Pathak for their support and help throughout the publication.

FUNDING

The research did not receive any fund and logistic support was from Mallige College of Pharmacy.

REFERENCES

1. Srivastava P., "Rhododendron arboreum: an overview," Journal of Applied Pharmaceutical Science 2012; 02 (01); 158-162.
2. Bhandary MR, Kawabata J. Antidiabetic activity of Laligurans (Rhododendron arboreum Sm.) flower. J Food Sci Technol 2008; 4: 61-63.
3. Shyam SA, Kalpana S. Anti-inflammatory activity of flowers of Rhododendron arboreum (SMITH) in rat's hind by various phlogistic agents. Indian J Pharmac opla 1988;20;86-89.
4. Verma N, Singh AP, Amresh G, Sahu PK, Rao ChV. Antiinflammatory and anti nociceptive activity of Rhododendron arboreum. J Pharm Res 2010; 3: 1376-1380.
5. Murty D, Rajesh E, Raghava D, Raghavan TV, Surulivel MK. Hypolipidemic effect of arboreum plus in experimentally induced hypercholestermic rabbits. Yakugaku Zasshi 2010; 130(6): 841-846
6. Verma N, Singh AP, Amresh G, Sahu PK, Rao ChV. Protective effect of ethyl acetate fraction of Rhododendron arboreum flowers against carbon tetrachloride-induced hepatotoxicity in experimental models. Indian J Pharmacol 2011; 43(3): 291-295.
7. M. A. Ebrahimzadeh, S. M. Nabavi, S. F. Nabavi, and B. Eslami, "Antioxidant activity of the bulb and aerial parts of *Ornithogalum sintenisii* L (Liliaceae) at flowering stage," *Tropical Journal of Pharmaceutical Research*, 2010; vol. 9, no. 2, pp. 141–148.
8. D. Ghosh, T. K. Bera, K. Chatterjee, K. M. Ali, and D. De, "Antidiabetic and antioxidative effects of aqueous extract of seed of *Psoralea corylifolia* (somraji) and seed of *Trigonella foenum-graecum* L., (methi) in Separate and composite manner in streptozotocin-induced diabetic male Albino rat," *Tropical Journal of Pharmaceutical Research*, 2009; vol. 1, no. 7, pp. 1–10.
9. Modak M, Dixit P, Londhe J, Ghaskadbi S, Devasagayam TPA. Indian Herbs and Herbal Drugs Used for the Treatment of Diabetes. J Clin Biochem Nutr. 2007;40(3):163-73.
10. American Diabetes Association, "Diagnosis and classification of diabetes mellitus," *Diabetic Care*, 2007; vol. 30, supplement 1, pp.s42–s46.
11. Siddaiah M, Jayaveera K N, Souris K, Yashodha Krishna J P, Vasanth Kumar P. Phytochemical Screening and Anti Diabetic Activity of Methanolic Extract of Leaves of Ximenia Americana in Rats. *International Journal of Innovative Pharmaceutical Research.* 2011; 2(1):78-83.
12. World Health Organization. Diabetes fact sheet. 2018. Available from: http://www.who.int/news-room/fact-sheets/detail/diabetes [cited 2 december 2018].
13. Macedo C.S,Capelletti S.M, Mercadante M.C.S, Padovani CR. Role of metabolic control on diabetic nephropathy. Acta cir Bras 2002; 17(6):37-5.
14. Khan MY, Sagrawat H, Upmanyu N, Siddique S. Anxiolytic Properties of *Myricanagi* Bark Extract; January 2009; 46(10-11):757-761.
15. Swathi D, Prasad K. V. S. R. G. Antioxidant and Antiulcer Potential of Ethanolic Extract Of Bark Of *Myrica Esculenta* In Pyloric Ligation Ulcer Model. Int J Pharm Pharm Sci 2015; 7(10); 195-8.
16. Verma N, Amresh G, Sahu Pk, Rao CV, Singh AP. Antihyperglycemic and antihyperlipidemic activity of ethyl acetate fraction of Rhododendron arboreum Smith flowers in streptozotocin induced diabetic rats and its role in regulating carbohydrate metabolism. Asian Pac J Trop Biomed. 2012; 02(09):696-701.
17. Parveen R., Singh N. A rewiew on Antidiabetic Angiospermic plants from the regions of Uttarakhand, India. IOSR Journal of Pharmacy; 2016; 6 (10); 14-61.
18. Collier E, Watkinson A, Cleland CF, Roth J. Partial purification and characterization of an insulin-like material from spinach and Lemna gibba G3. *The Journal of biological chemistry*. 1987; 262(13):6238-47.
19. Chakravarthy BK, Gupta S, Gambhir SS. Pancreatic beta cell regeneration: A novel antidiabetic mechanism of *Petercarpus marsupium*. *Indian Journal of Pharmacology*. 1980; 12:123-28.
20. Marles JR, Fransworth. Antidiabetic plants and their active constituents. Phytomedicine. 1995; 2(2):123-89.
21. Youl E, Bardy G, Magous R, Cros G, Sejalon F, Virsolvy A, *et al*. Quercetin potentiate insulin secretion and protect INS-1 pancreatic β-cells against oxidative damage via the ERK 1/2 pathways. *British Journal of Pharmacology*. 2010;(161); 799-814.
22. Latha S, Rajaram K, Suresh kumar P. Hepatoprotective And Antidiabetic Effect Of Methanol Extract Of *Caralluma Fimbriata* In Streptatozocin Induced Diabetic Albino Rats. Int J Pharm Pharm Sci, 2014; Vol 6, Issue 1, 665-668.
23. Bhanudas K.S. and Gopal P.K. Histological structure of pancreas in normal control, diabetic control and extract treated *Albino* rats. Int. J. of Life Sciences, 2016, 4 (1): 78-82.