IJPSR (2022), Volume 13, Issue 10 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 16 February 2022; received in revised form, 31 March 2022; accepted, 24 April 2022; published 01 October 2022

ANTIDIABETIC POTENTIAL OF HYDROALCOHOLIC EXTRACT OF LEAVES OF *NYCTANTHES ARBORTRISTIS* IN ADRENALINE AND ALLOXAN-INDUCED DIABETIC RATS

Mona Motallebi *, Bipin Bihari Panda, Surya Narayan Das and Soumya Kanta Mishra

Department of Pharmacology, Gayatri College of Pharmacy, Sambalpur - 768200, Odisha, India.

Keywords:

Nyctanthes arbortristis, Alloxan, adrenaline, Gucose tolerance test, Antidiabetic activity

Correspondence to Author:
Ms. Mona Motallebi

Assistant Professor,
Department of Pharmacology, Gayatri College of Pharmacy, Sambalpur - 768200, Odisha, India.

E-mail: monamotallebi18@gmail.com

ABSTRACT: Diabetes mellitus, a metabolic disorder, is a serious universal health problem. The incidence of the disease is increasing in the world in all ethnic groups. Various medicinal plants are conventionally used in the treatment or management of the disease. In this investigation, an attempt was taken to evaluate the antidiabetic property of hydroalcoholic extract of leaves of *Nyctanthes arbortristis* in various rat models such as normoglycemic rats and glucose-loaded rats, adrenaline-induced hyperglycemic rat models as well as alloxan-induced diabetic rats. The extract exerted a significant (P<0.05) hypoglycemic effect at a dose of 200mg/kg on normoglycemic rats for 5 hours. The extract improved glucose tolerance significantly (P<0.05) in comparison to the control (2 gm/kg p.o. glucose) group. The extract significantly (P<0.05) decreased blood glucose concentration in adrenaline (0.8 mg/kg, i.p) treated rats. The extract also significantly (P<0.05) lowered blood glucose levels in alloxan-induced rats. The antidiabetic property of leave extract was comparable to Glibenclamide (standard drug) 0.5 mg/kg p.o. dose. Therefore, this study, "Antidiabetic Potential of Hydroalcoholic Extract of Leaves of *Nyctanthes arbortristis* in adrenaline and alloxan-induced diabetes rats" confirms significant antidiabetic nature of leaves of Nyctanthes arbortristis.

INTRODUCTION: Diabetes mellitus is a chronic metabolic disorder characterized by chronic hyperglycemia, with disturbed protein, carbohydrate, and lipid metabolism. It results from defects in insulin action or insulin secretion or both, causing long-term complications in many organs [1]. Globally, the prevalence of the disease is increasing day by day.

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.13(10).3977-82

This article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.13(10).3977-82

By the year 2025, India shall have the maximum number of diabetics in the world, making it the 'Diabetic Capital of the world'. In 2000, India had the highest number of diabetes patients, followed by China, with the USA in second and third place, respectively. Globally, the prevalence of the disease is predicted to double in 2030 as compared to the year 2000, with a maximum rise in India.

It is predicted that by 2030 diabetes mellitus may badly affect up to 79.4 million individuals in India, while China (42.3 million) and the United States (30.3 million) will also see significant increases in those affected by the disease [2]. In modern system of medicine, treatment of diabetes is performed with sulfonylureas, biguanides and insulin those have

undesirable side effects [3]. So, diabetes management without side effects is a challenge to the medical system. There is an increasing demand to use natural products with antidiabetic activity. However, few traditional antidiabetic plants have received proper scientific validation. Nowadays, it is necessary to provide scientific proof about the justification of the use of plant products as antidiabetic agents that are also claimed to have low toxicity. In India, *Nyctanthes arbortristis* is a useful traditional medicinal plant. It is widely distributed in sub-Himalayan regions along with Southwards to Godavari. Every part of the plant has medicinal value and is therefore commercially utilizable. It is now considered a valuable source of many unique products for medicines against various diseases and the development of some industrial products [4].

Nyctanthes arbortristis Linn plant, also called Parajiatham or Harsinghar or Night Jasmine, belongs to the Oleaceae family. It is a large shrub or a small perennial tree widely cultivated in tropical as well as subtropical regions all over the world [5]. The plant grows on rocky ground in dry hill shades of dry deciduous forests [6]. It is often cultivated in gardens for its most pleasant and peculiar fragrance distributed in the Indo-Pak subcontinent and South East Asia, having remarkable folk medicinal use. The different parts of the plant are used as carminative, purgative, anti-oxidant, immune-stimulant, anti-bacterial and significant anticancer activity [7].

Earlier studies have revealed the root extract of the plant to possess acute hypoglycaemic effect at 250 mg/kg and 500mg/kg [8]. Traditional medicine practitioners have used various plant parts as anti-hyperglycemic agents [9]. In the present study, an attempt was taken to evaluate the effect of *Nyctanthes arbortristis* leaf extract (Hydro-alcoholic extraction) on blood glucose in various rat models and to compare its efficacy with the standard drug Glibenclamide.

MATERIALS AND METHODS:

Preparation of *Nyctanthes arbortristis* Leaf Extracts: The mature leaves of *N. arbortristis* were collected from the trees during the months of March from the plants available in Sambalpur, Odisha, locally. It is a well-known medicinal plant in Odisha and has also been identified by matching with Herbarium of the Indian Institute of Integrative Medicine. The leaves were then dried in the shade and powdered using a mixer grinder. The powdered material was taken and 'Hydro-alcoholic' extraction (ethanol: water (6:4)) at room temperature. Then the extract was filtered using Whitman filter paper. The filtrate was evaporated to dryness to get the solid extract. The freshly prepared solution was used for each experiment [10].

Animals: The study was conducted on 24 healthy albino Wistar male rats weighing between 150-200 gm. The animals were housed and maintained in separate cages under controlled conditions of temperature (22±20C), humidity (50—60%), and 12-hour light/ dark cycles at Gayatri College of Pharmacy's animal house, Sambalpur. The experiment was conducted with the approval of the Institutional Animal Ethical Committee (IAEC) of Gayatri College of Pharmacy, Sambalpur bearing registration number 1339/PO/Re/S/10/CPCSEA, according to prescribed guidelines of CPCSEA, Government of India.

Hypoglycemic Activity Screening in Normal Rats: Albino rats weighing 150-200g, fasted overnight, were divided into 3 groups of six animals each. The groups included the control group, which received 5% gum acacia in water as solvent, 2ml/kg rat. Test drug group received 200mg/kg, p.o. N. arbor leaf extract and the Standard drug received Glibenclamide (0.5 mg/kg p.o.). Blood sample was collected from the tail of each rat for analysis. Blood samples were collected again at 0 hr (before treatment) and 1, 3, 5, 7 h after administration of drugs from the treated animals. The blood glucose concentration was estimated by Glucometer (one-touch select) [11].

Glucose Tolerance Test in Normal Rats: In Oral Glucose Tolerance Test (OGTT), glucose (2 gm/kg bw) was given orally to the fasted rats 2 hr of drug administration and blood samples were collected from the tail vein after 30 min, 60 min, 90 min and 120 min of glucose treatment [12].

Group 1: Normal group, receive solvent (5% gum acacia).

Group 2: Glucose-loaded group, receive Glucose+ Solvent.

Group 3: Test group, receive Glucose +test drug (200 mg/kg).

Group 4: Standard drug group, receive glucose + standard drug (Glibenclamide (0.5 mg/kg p.o)).

Adrenaline Induced Hyperglycemic Rats: Animals are divided into four groups of six rats per group. Control groups are administered solvent at a dose of 2ml/kg body wt.

All groups except the control group were administered adrenaline in the dose of 0.8mg/kg body weight after 1hr of drug treatment [13]. Standard groups were administered Glibenclamide orally at a dose of 0.5mg/kg body wt.

The experimental designs were as follows:

Group I: Normal Control (saline).

Group II: Hyperglycaemic control (Adrenaline 0.8 mg/kg body wt).

Group III: Test drug group (Adrenaline 0.8 mg/kg + extracts of *Nyctanthes arbortristis* leaves (200 mg/kg body wt)).

Group IV: Standard drug group (Adrenaline 0.8 mg/kg + Glibenclamide (0.5 mg/kg p.o)).

Blood glucose levels were estimated at 1, 3, 5 and 7 h after administration of drugs.

Antidiabetic Activity Screening in Experimentally Induced Rats: Animals were divided into four groups, each group consisting of six animals.

Group 1 was treated as normal control. On remaining animals, diabetes was induced by injecting alloxan monohydrate intraperitoneally at a dose of 150 mg/kg body wt.

Diabetes was confirmed by measuring the fasting blood glucose level 72 h after the alloxan injection. The rats with blood glucose levels 250mg/dl were considered to be diabetic and were used in study [14].

After confirmation of induction of diabetes, animals were divided equally into groups. Group II served as diabetic control (alloxan treated only). Group III was the Test drug group (alloxan + Hydroalcoholic extract of *N. arbortristis* (200mg/kg body wt)) and group IV received the standard drug group (alloxan + Glibenclamide (0.5mg/kg). Drugs were administered orally consecutively for 15 days on a once daily basis, with the help of a gastric catheter.

RESULTS:

TABLE 1: EFFECT OF HYDROALCOHOLIC EXTRACTS OF LEAVES OF *NYCTANTHES ARBORTRISTIS* ON NORMOGLYCEMIC RATS

Group	Treatment (Dose mg/kg)	Initial glucose (mg/dl)	Final Glucose Level (mg/dl)			
			1 h	3 h	5 h	7 h
I	Control (solvent 5ml/kg)	90.17 ±4.54	86.50 ±4.25	88.13 ±4.56	85.73 ±4.71	86.67 ±4.45
II	Extract of *N. arbortristis* (200 mg/kg)	92.33 ±4.31	82.24 ±4.00	79.50 ±3.77	73.62 ±4.06*	74.12 ±4.10*
III	Glibenclamide (0.5 mg/kg)	91.15 ±4.29	70.40 ±4.37*	67.52 ±4.76*	60.57 ±4.18*	67.67 ±4.31*

Values are mean± SEM (Standard error of mean); Statistical analysis by Students t-test. p value <0. 01. *Group II, III compared with Group I.

TABLE 2: EFFECT OF HYDROALCOHOLIC EXTRACTS OF LEAVES OF *NYCTANTHES ARBOR-TRISTIS* ON GLUCOSE LOADED RATS

Group	Treatment (mg/kg)	Initial glucose level (mg/dl)	Final glucose level (mg/dl)			
			30 min	60 min	90 min	120 min
Group 1	Solvent	88.6±5.62	85.0±5.4	80.3±4.3	82.0±4.5	81.4±4.3
Group 2	Glucose (2 gm/kg)	87.5±5.75	202.0±8.4*	160.3±7.3*	142.0±7.5*	108.4±6.5*
Group 3	Glucose +Extract (200)	84.5±5.53	192.4±8.5	154.4±7.4	126.6±6.5*	95.4±5.3*
Group 4	Glucose+ Glibenclamide(0.5)	85.7±4.74	126.0±6.9 *	98.3±7.3*	102.2±6.5*	80.4 ±5.4*

Values are mean± SEM (Standard error of the mean); Statistical analysis by Students t-test. p-value <0. 01. *Group II compared with group I, Group III, IV compared to Group II.

TABLE 3: EFFECT OF HYDROALCOHOLIC EXTRACTS OF LEAVES OF *NYCTANTHES ARBORTRISTIS* ON ADRENALINE-INDUCED HYPERGLYCAEMIC RATS

Groups	Treatment (Dose mg/kg)	Initial glucose (mg/dl)	Final glucose (mg/dl)			
			1h	3h	5 h	7 h
I	Normal control (Solvent 5ml/kg)	86.12 ±5.12	85.62 ±5.51	87.11 ±5.82	84.62 ±5.61	86.15 ±5.22
II	Hyperglycaemic control (Adrenaline)	87.33 ±6.91	191.01 ±8.12*	212.52 ±8.34*	193.31 ±8.43*	142.43 ±7.11*
III	Adrenaline + Extract (200)	85.41 ±5.83	177.43 ±8.43	194.24 ±7.21	155.60 ±6.45*	124.62 ±6.23*
IV	Adrenaline + Glibenclamide(0.5mg/kg)	88.64 ±5.24	162.33 ±8.42	166.52 ±8.34*	148.31 ±6.64*	121.43 ±5.02*

Values are Mean ± SEM (Standard error of mean); Statistical analysis by Students t-test. p-value <0. 01. *Group II compared with group I, Group III, IV compared to Group II.

TABLE 4: EFFECT OF HYDROALCOHOLIC EXTRACTS OF LEAVES OF *NYCTANTHES ARBORTRISTIS* ON BLOOD GLUCOSE CONCENTRATION ON ALLOXAN-INDUCED ACUTE HYPERGLYCAEMIC ALBINO RATS

Group (n)	Dose (mg/kg body wt)	Blood glucose level (mg/dl) (mean ± SEM)				
		Initial	1h	3h	5h	7h
Normal Control (saline)	2 ml saline/kg body weight	91.46 ± 3.39	87.35 ± 3.68	85.25 ± 3.09	82.62 ± 3.26	78.34 ± 3.12
Hyperglycemic control	Alloxan 150mg/kg body weight	93.52 ± 3.27	274.11 ± 6.29	270.01 ± 5.59	266.81 ± 5.82	273.19 ± 6.04
Hydro alcoholic extract	200 mg/kg b. wt.	92.32 ± 3.11	248.32 ± 5.34	249.41 ± 5.51	232.24 ± 5.19*	211.81 ± 5.57*
Standard drug (Glibenclamide)	0.5 mg/kg b. wt.	90.43 ± 3.30	190.57 ± 3.31	183.81 ± 3.41	169.50 ± 4.41*	156.62 ± 4.27*

*P < 0.05–Significant; SEM–Standard Error of Mean, n–Number of animals in each group (6).

TABLE 5: EFFECT OF HYDROALCOHOLIC EXTRACTS OF LEAVES OF *NYCTANTHES ARBORTRISTIS* ON BLOOD GLUCOSE LEVEL ON ALLOXAN-INDUCED CHRONIC HYPERGLYCAEMIC ALBINO RATS

Group (n)	Dose (mg/kg body wt)	Serum Glucose Level (mg/dl) on different Days of treatment			
		Initial	5th Day	10th Day	15th Day
Normal Control (saline)	2 ml saline/kg body weight	91.46 ± 3.39	90.51 ± 3.11	91.25 ± 3.19	90.01 ± 3.31
Hyperglycemic control	Alloxan 150mg/kg body weight	93.52± 3.27	271.20 ± 5.12	275.23 ± 5.31	269.2 ± 5.01
Hydro alcoholic extract	200 mg/kg b. wt.	92.32 ± 3.11	264.2 ± 5.38	224.8 ± 5.12*	192.5 ± 5.67*
Standard drug (Glibenclamide)	0.5 mg/kg b. wt.	90.43 ± 3.30	233.01 ± 5.64	147.71 ± 4.54*	113.81 ± 4.39*

*P < 0.05–Significant; SEM–Standard Error of Mean, n–Number of animals in each group (6).

DISCUSSION: *Nyctanthes arbortristis* Linn extract exhibits significant radical scavenging activity and thus antioxidant activity. The plant is a widely available species in western Odisha. Leaves of the plant can be used in the treatment of many diseases. The extract of *Nyctanthes arbortristis* root confirms the possibility that major function on protection protects tissues including, thereby pancreas, diabetes in animals. In the present study, an attempt was made to establish the effect of plant Nyctanthes arbortristis on normoglycemic rats, adrenaline-induced hyperglycemia, glucose-loaded rats as well, and diabetic rats. The oral dose of 200 mg/kg body weight was selected for studies. In normoglycemic rats, the drug reduces blood glucose level significantly after 5 h of administration. So, it shows significant glucose-lowering activity in single dose in 5 h and 7 h time points **Table 1**. In normoglycemic glucose-loaded rats, also it reduces blood glucose level significantly when administered 2 h before administration glucose **Table 2.** In adrenaline-induced hyperglycaemic rats, the extract in the dose of 200 mg/kg also reduces blood glucose levels significantly in comparison to solvent (control) groups after 5 h of administration. The adrenaline induces hyperglycemia by releasing glucocorticoids, which alter glucose metabolism in the liver. It also inhibits insulin release from the pancreas resulting increase in blood glucose level **Table 3**. The effect of a single dose of hydroalcoholic extracts of leaves on blood glucose

levels of alloxan-induced acute hyperglycaemic rats is shown in **Table 4**. The blood glucose level was reduced significantly (P<0.05) by the hydroalcoholic extract at 5th and 7th h after treatment. The effect of continuous treatment (15 days) of extract on blood glucose levels of alloxan-induced hyperglycaemic rats is shown in **Table 5**. The blood glucose level was reduced at 10th and 15th day after treatment. After treatment, blood glucose level reduced (P < 0.05) in alloxan-induced diabetic rats. Alloxan exerts two different pathological effects. It inhibits glucose-induced insulin secretion selectively through the inhibition of the enzyme glucokinase, the glucose sensor of the beta cell. It also causes a state of insulin-dependent diabetes through its ability to induce ROS formation. These two effects are responsible to the specific chemical properties of alloxan.

The leaves contain D-mannitol, β-sitosterole, Flavanol glycosides-Astragaline, Nicotiflorin, Oleanolic acid, Nyctanthic acid, tannic acid, ascorbic acid, methyl salicylate, carotene, friedeline, lupeol, mannitol, glucose and fructose, benzoic acid [15]. The leaves possess antioxidant [16], anti-inflammatory [17], hepatoprotective [18] actions.

Plants have antidiabetic property act on blood glucose levels through different pathways. Some of them are insulin-like substances. Some stimulate β-cells to produce and release insulin. Others increase β-cells in the pancreas by activating pancreatic cells regeneration. The hypoglycemic activity of the extract in both normal and diabetes rats in single and multiple doses may be due to release of insulin and activation of existing pancreatic cells in animals with diabetes.

CONCLUSION: According to the results of this study, *N. arbortristis* leaves extracts show interesting possibilities as a source of oral hypoglycemic agents. The plant may be considered as an excellent candidate for future studies in finding mechanisms of its hypoglycemic activity. In summary, the present investigation demonstrated that the administration of hydroalcoholic extract of leaves of *N. arbortristis* significantly improved systemic insulin sensitivity and glucose homeostasis in normoglycemic rats. The results support overall anti-hyperglycemic activity and activity on impaired glucose tolerance of the extract. It proved its clinical importance in diabetes management. In the light of our pharmacological studies, we can assume that further experiments should be performed to isolate the possible hypoglycemic compounds and then explain the actual mechanism of actions of the plant fractions. The present study has given some preliminary idea of the hypoglycemic compounds present in reported plant fractions.

ACKNOWLEDGEMENT: The author would like to thank Dr. Surya Narayan Das, Principal, Gayatri College of Pharmacy, Sambalpur, India, for their keen interest and valuable guidance in carrying out the work.

CONFLICTS OF INTEREST: The authors declare that they have no conflicts of interest.

REFERENCES:

1. American Diabetes Association, Diagnosis and Classification of Diabetes Mellitus, Diabetes Care 2009.
2. Kaveeshwar SA and Cornwall J: The current state of diabetes mellitus in India. Australas Medical Journal 2014.
3. Tripathi KD: Essential of medical Pharmacology, Japee publication. Edition 6th 254-274.
4. Rani C, Chawla S, Mangal M, Mangal AK, Kajla S and Dhawan AK: *Nyctanthes arbortristis* Linn. Night Jasmine: A sacred ornamental plant with immense medicinal potentials. Indian Journal of Traditional Knowledge 2012; 11: 427-35.
5. Verma N and Yadav RK: *Nyctanthes arbortristis* a review, 2020.
6. Sharma R and Raina N: A review article on parijat. World Journal of Pharmaceutical Life Sciences 2018.
7. Rawat H, Verma Y, Ayesha, Saini N, Negi N, Pant HC, Mishra A, Singhal M, Khan A and Gaurav N: *Nyctanthes arbortristis*: A traditional herbal plant with miraculous potential in medicine 2018.
8. Sharma V and Marwaha A: Hypoglycemic activity of methanolic extracts of *Nyctanthes arbortristis* Linn. Root in Alloxan Induced Diabetic Rats 2011; 3(3): 210-12.
9. Chetty M, Sivaji K and Rao KT: Flowering plants of Chittoor district Andhra Pradhesh. Edition 1st Published by Student of Set Printer Tirupati 2008; 193.
10. Sarkar R and Mandal N: Hydroalcoholic extracts of Indian medicinal plants can help in amelioration from oxidative stress through antioxidant properties. Journal of Complementary and Integrative Medicine 2012; 9(1): 1-19.
11. Mandlik RV and Desai SK: Antidiabetic activity of polyherbal formulation (DRF/AY/5001). Indian Journal of Experimental Biology 2008; 46: 599-06.
12. Jain S, Sharma R, Barik R, Kumar P and Bhatt D: Effect of fruit extract of *Artocarpus heterophyllus* in alloxan induced diabetic rats. International Journal of Pharmaceutical Sciences and Research 2010; 1: 59-64.
13. Naik SR and Filho JMB: Probable mechanism of hypoglycemic activity of basic acid. Journal of Ethnopharmacology 1991; 33: 37.

14. Antia BS and Okokon JE: Hypoglycemic activity of aqueous leaf extract of *Persia americana* Mill. Indian Journal of Pharmacology 2005; 37: 325.
15. Gupta P, Bajpai SK, Chandra K, Singh KL and Tandon JS: Antiviral profile of *Nyctanthes arbortristis* against encephalitis causing viruses. Indian Journal of Experimental Biology 2005; 43: 1156-1160.
16. Amarite O, Bhuskat P, Patel N and Gadgoli C: Evaluation of antioxidant activity of carotenoid from *Nyctanthes arbortristis*. International journal of Pharmacology Biology Science 2007; 1(2): 57-59.
17. Omkar A, Jeeja T and Chhaya G: Evaluation of anti-inflammatory activity of *Nyctanthes arbortristis* and *Onosma echiodes*. Pharma Magazine 2006; 2(8): 258-60.
18. Lucas DS and Sekhar RAR: A review of experimental studies on antihepatoprotective activity of certain medicinal plants used in Ayurveda. Phytomedicine Supplement-II 2000; 23.

How to cite this article:
Motallebi M, Panda BB, Das SN and Mishra SK: Antidiabetic potential of hydroalcoholic extract of leaves of *Nyctanthes arbortristis* in adrenaline and alloxan induced diabetic rats. Int J Pharm Sci & Res 2022; 13(10): 3977-82. doi: 10.13040/IJPSR.0975-8232.13(10). 3977-82.