ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of DEVELOPMENT RESEARCH

International Journal of Development Research
Vol. 5, Issue, 01, pp. 3129-3133, January, 2015

Full Length Research Article

ANTIDIABETIC ACTIVITY OF *STROBILANTHES CILIATUS* IN STREPTOZOTOCIN-NICOTINAMIDE INDUCED EXPERIMENTAL DIABETIC RATS

[1]Annie Shirwaikar, [2]Molly Mathew, [3]Sajith Kumar, P. N., [4]Jeril John, [5]Premaletha, K. and [6*]Rajagopal, P. L.

[1]College of Pharmacy, Gulf Medical University, Ajman, UAE
[2]Malik Deenar College of Pharmacy, Kasaragod, Kerala, India,
[3,4,5,6]Academy of Pharmaceutical Sciences, Pariyaram Medical College, Kannur, India

ARTICLE INFO

Article History:
Received 02nd October, 2014
Received in revised form
14th November, 2014
Accepted 22nd December, 2014
Published online 31st January, 2015

Key words:
Strobilanthes ciliates,
Streptozotocin-nicotinamide,
Diabetes

ABSTRACT

The primary objective of this study was to determine the anti-diabetic activity of *Strobilanthes ciliatus* in streptozotocin-nicotinamide induced diabetic rats In the present study the antidiabetic effects produced by the aqueous and alcoholic extract of whole plant of *Strobilanthes ciliatus* were investigated in the Streptozotocin-Nicotinamide induced experimental diabetic model. The alcoholic extract showed significant reduction in blood sugar level when compared with normal rats ($p<0.05$). This investigation demonstrates significant antidiabetic activity of *Strobilanthes ciliates.* The administration of *Strobilanthes ciliatus* have an anti-diabetic effect in streptozotocin-nicotinamide induced diabetic rats and their effect was equivalent to that of reference drug Glibenclamid.

INTRODUCTION

Diabetes mellitus is a group of metabolic disorders that result in hyperglycemia due to decreased insulin production or inefficient insulin utilization (Rajaram, 2013). Diabetes mellitus, a metabolic disorder characterized by hyperglycemia associated with impairment in insulin secretion, insulin action or both and alteration in intermediary metabolism of carbohydrate, fat and protein. In past there have been many medicinal plants which have been used for traditional medicines for their blood sugar lowering properties without any scientific support (WHO, 1980). The whole plant of *Strobilanthes ciliatus* is used by traditional practitioners of Kerala for the control of diabetes mellitus. The plant is commonly known as *Sahacarah,* (Raphel Tharayil, 1996; Sivarajan, 1996) is an important in Ayurveda, widely used against neurological disorders such as paraplegia, sciatica etc. This drug also helps heal ulcers, glandular swellings, poisonous affections, itching, leprosy and other skin diseases, cough, edema etc. Though widely used for diabetes by traditional practitioner in kerala, India; there is however no available data with pharmacological report on the antidiabetic activity. The present study therefore aims to evaluate the antihyperglycemic potential of the whole plant *Strobilanthes ciliates*.

Corresponding author: Rajagopal, P. L.
Academy of Pharmaceutical Sciences, Pariyaram Medical College, Kannur, India

MATERIALS AND METHODS

Plant material

The whole plant *Strobilanthes ciliatus* was collected from Edapal, Malappuram dist, Kerala, India during the month of August 2007. Its botanical identity was confirmed by botanist Dr. Gopalakrishna Bhat, Professor of Botany, Poorna Prajna College, Udupi, Karnataka. The voucher specimen No (PP557) has deposited at the Department of Pharmacognosy, Manipal College of Pharmaceutical Sciences, Manipal

Preparation of Ethanolic extract

The drug powder was kept for cold maceration with 0.25% chloroform water for 7 days. After the extraction was over the

solvent was recovered by distillation and the residue was concentrated *in vacuo*.

Animals

Swiss albino rats were acclimatized to the experimental room having temperature 23 ± 2 °C, controlled humidity conditions, and 12:12 hour light and dark cycle. Animals were caged in polypropylene cages with maximum of two animals in each cage. The rats were fed with standard food pellets and water *ad libitum*. Study was conducted after obtaining ethical committee clearance from the Institutional Animal Ethics Committee of KMC, Manipal. No. IAEC/KMC/06/2006-2007.

Acute toxicity studies

Acute toxicity studies (Ghosh, 1984) were conducted to determine the safe dose as per OECD guidelines.

Oral glucose tolerance test

The oral glucose tolerance test (Bonner-weir, 1985) was performed in overnight fasted (18-h) normal animals. Rats divided into four groups (n=6) were administered 2% gum acacia solution, alcoholic extract (200 mg/kg), alcoholic extract (400 mg/kg) and glibenclamide (0.45 mg/kg), respectively. Glucose (2 g/kg) was fed 30 min after the administration of alcoholic extract. Blood was withdrawn from the retro-orbital sinus at 0, 30, 60, 90 and 120 min of aqueous extract administration. Fasting blood glucose levels ere estimated by glucose oxidase-peroxidase reactive strips (Accu-check, Roche Diagnostics, USA).

Normoglycemic study

For normoglycemic study, rats were divided into four groups (n=6) and were administered 2% gum acacia solution, aqueous extract (200mg/kg), aqueous extract (400mg/kg) and glibenclamide (0.45 mg/kg), respectively. Blood glucose levels were estimated on days 0, 7, 14 and 21.

Induction of Experimental Diabetes

An rat model of type 2 diabetes mellitus (non-insulin dependent diabetes mellitus, NIDDM) was induced (Dulin, 1977; Masiello *et al*., 1998) inovernight-fasted rats by a single intraperitoneal injection of 60 mg kg_1 streptozotocin 15 min after the intraperitoneal administration of 120 mg kg_1 nicotinamide. Hyperglycemia was confirmed by elevated blood glucose levels determined at 72 h and then on day 7 after injection. Only rats confirmed to have permanent NIDDM were used for the antidiabetic study (15, 30).

Experimental Design

Rats were divided into four groups (*n* _ 6): normal rats administered with 2% gum acacia solution, diabetic rats administered with 2% gum acacia solution, diabetic rats administered with *Strobilanthes ciliatus* aqueous extract 200 mg kg_1 and diabetic rats administered with *Strobilanthes ciliatus* aqueous extract 400 mg kg_1, respectively, for 21days orally.

Sample collection

Blood sampling

At the end of day 21, blood samples were collected retro-orbitally from the inner canthus of the eye underlight ether anesthesia using capillary tubes (MicroHemocrit Capillaries, Mucaps). Blood was collected into fresh vials containing anticoagulant and serum was separated in a centrifuge at 2000 rpm for 2 min.

Collection of organs

The animals were euthanized by an overdose of intra peritoneal anesthesia and tissue samples were collected for the assessment of biochemical parameters. serum lipid profiles, liver glycogen levels (Nicholas, 1956), glycosylated hemoglobin levels, thiobarbituric acid reactive substance levels (TBARS) (Ohkawa *et al*. 1979) and changes in body weight assessed in the diabetic animals treated with aqueous extract were compared with diabetic control and normal animals.

Statistical analysis

Data were statistically evaluated by one way ANOVA, followed by post hoc scheffe, s test using 7.5 version of SPSS computer software. The values were considered significant when $p<0.05$.

RESULTS

Acute toxicity studies

No toxic effect was reported upto 2000mg/kg body weight of the aqueous extract and there were no death in any of these groups

Effect on oral glucose tolerance test

Results of oral glucose tolerance test conducted on normal rats fed with aqueous extract of whole plant of *strobilanthes ciliatus* (200 and 400 mg/kg) are shown in table 1. the aqueous extract showed a significant reduction in blood glucose levels from 30 min onwards in oral glucose tolerance test. In normal animals significant reduction in blood glucose level was observed as compared to control.

Normoglycemic study

The effect of two doses of aqueous crude extract of *Strobilanthes ciliatus* on serum glucose level in normal fasted rats shown in table 2. The extract did not show significant blood glucose lowering effect in fasted normal rats as compared to control.

Antidiabetic activity

Diabetic rats treated with crude aqueous extract at oral dose of 200 mg /kg and 400mg/kg for 21 days showed 44.02% and53.64% reduction in blood glucose levels respectively in comparison to untreated diabetic rats. Fasting blood glucose levels of control diabetic and treated animals are shown in

Table 1. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on glucose tolerance test

Group	Treated(n=6)	Dose (mg/ kg)	O min (mg/dl)	30 min (mg/dl)	60 min (mg/dl)	120 min (mg/dl)	180 min (mg/dl)
1	Normal	-	84.17±13.34	128.66±7.97	122.5±8.6	118.17±8.47	101.16±8.52
2	Glibenclamide	0.45	90.6±4.04	90±11.37	87.6±9.99	64.2±7.46	55.6±9.07
3	Aq. Ext A	200	89±8.44	106.5±10.07	112±3.35	91.67±2.73	82.17±7.81
4	Aq. Ext B	400	83.83±6.79	116.5±10.29	102.83±6.65	92.83±15.70	78.83±14.61

Table 2. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on fasting blood sugar in normal rats

Group	Treated(n=6)	Dose (mg/kg)	O th day	7 th day	14 th day	21st day
1	Normal	-	72.83±3.0	75.5±2.40	72.5±1.3	70.83±1.7
2	Glibenclamide	0.45	70.5±2.95	46.5±3.03	47.17±1.68	53.17±2.22
3	Aq. Ext A	200	74.5±3.84	79.33±3.65	71.17±3.13	68.5±1.78
4	Aq. Ext B	400	71±2.63	75.83±2.23	69.17±2.57	71.833±1.38

Table 3. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on fasting blood sugar in diabetic rats

Group	Treated(n=6)	Dose (mg/kg)	O th day	7 th day	14 th day	21st day
1.	Normal	-	72.83±3	75.5±3.40	72.5±1.31	70.83±1.74
2.	Control	-	223.17±11.98	224.33±9.61	222.33±9.50	228.67±9.19
3.	Glibenclamide	0.45	216.83±7.49	160.83±8.70	94.5±2.72	83.83±3.32
4.	Aq. Ext A	200	247.83±22.77^{a}	207.83±21.32^{a}	170.5±16.11^{a,b}	125±14.39^{a,b}
5.	Aq. Ext B	400	221.67±7.63^{a}	185.33±4.81^{a}	132.33±6.19^{a,b}	106±4.52^{b}

Table 4. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on the changes in body weight in normal rats

Group	Treated(n=6)	Dose (mg/kg)	O th day	7 th day	14 th day	21st day
1	Normal	-	190.67±7.077	190.67±7.2	192±7.22	192±7.23
2	Glibenclamide	0.45	204.67±9.02	207.33±9.16	205.17±8.34	204±8.36
3	Aq. Ext A	200	210.5±6.52	202.67±6.26	201.17±6.28	203.17±4.57
4	Aq. Ext B	400	214±8.8	206.83±8.25	201.5±201.5	202.67±6.95

Table 5. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on changes in body weight in diabetic rats

Group	Treated(n=6)	Dose (mg/kg)	O th day	7 th day	14 th day	21st day
1	Normal	-	274.83±8.12	274.0±7.95	271.83±7.98	270.33±7.63
2	Control	-	235.83±6.13	223.5±5.50	215.67±6.21	206.5±6.94
3	Glibenclamide	0.45	230.67±3.60	228.33±3.77	224.17±3.10	222.5±2.53
4	Aq. Ext A	200	228±3.47	222±3.51	226.5±3.61	226±3.39
5	Aq. Ext B	400	215.5±2.99	215±3.49	214±3.02	212.83±3.22

Table 6. Effect of aqueous extract of the whole plant of *Strobilanthes ciliatus* on lipid levels in Normal rats

Group	Treated (n=6)	Dose (mg/kg)	Triglyceride level (mg/dl)	Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)
1	Control	-	144±0.8	65±6.0	58.41±4.45
2	Glibenclamide	0.45	60±1.0	65.5±3.5	69.5±6.52
3	Aqueous ext A	200	116±1.0	87±17	67±5.0
4	Aqueous ext B	400	76.5±2.5	88±3.0	67.5±1.5

Table 7. Effect of aqueous and alcoholic extract of the whole plant of *Strobilanthes ciliatus* on lipid levels in Diabetic rats

Group	Treated (n=6)	Dose(mg/kg)	Triglyceride level (mg/dl)	Cholesterol (mg/dl)	HDL Cholesterol (mg/dl)
1	Normal	-	144±0.8	65±6.0	58.41±4.41
2	Control	-	160.83±10.19	111.833±9.11	74.33±2.7
3	Glibenclamide	0.45	82.83±3.36^{b}	48.5±6.8^{a,c}	64.6±6.63
4	Aqueous ext A	200	74±4.0^{a,b}	113±3.0^{a,c}	55.5±4.5
5	Aqueous ext B	400	61±2.0^{a,b}	70.5±2.5^{a}	49±1.0

Table 8. Effect of aqueous and alcoholic extract of the whole plant of *Strobilanthes ciliatus* on Glycated Hemoglobin level in Normal rats

Group	Treated (n=6)	Dose (mg/kg)	Glycated Hemoglobin Whole blood (%)
1	Control		3.64±0.14
2	Glibenclamide	0.45	3.3
3	Aqueous ext A	200	4.21±0.3
4	Aqueous ext B	400	4.21

Table 9. Effect of aqueous and alcoholic extract of whole plant of *Strobilanthes ciliatus* on Glycated Hemoglobin level in Diabetic rats

Group	Treated (n=6)	Dose(mg/kg)	Glycated Hemoglobin Whole blood (%)
1	Normal	-	3.64±0.14
2	Control	-	7.5±0.25
3	Glibenclamide	0.45	4.97± 1.0[b]
4	Aqueous ext A	200	4.45±0.15[b]
5	Aqueous ext B	400	3.85±0.15[b]

Table 10. Effect of aqueous and alcoholic extract of whole plant of *Strobilanthes ciliatus* on Liver Glycogen level in Diabetic rats

Group	Treated (n=6)	Dose (mg/kg)	Liver Glycogen level (mg/g)
1.	Normal	-	4.11±0.23
2.	Control	-	1.05±.07
3.	Glibenclamide	0.45	3.45±0.24
4.	Aqueous ext A	200	1.12±0.07
5.	Aqueous ext B	400	1.21±0.08

Table 11. Thiobarbituric acid reactive substances

Sl. No	Groups	Liver(nM/mg)	Kidney(nM/mg)
1.	Normal	0.113±0.0078	0.0858±0.0078
2.	Control	0.0.248±0.0436	0.201±0.0010
3.	Glibenclamide	0.1705±0.0120	0.1705±0.0040
4.	Aqueous Extract 200mg/Kg bw	0.0258±0.0110	0.156±0.0050
5.	Aqueous Extract 400mg/Kg bw	0.2258±0.0060	0.143±0.0065

Table 3. The body weight in the treated diabetic groups not decreased significantly after 21 days compared with vehicle treated. The various parameters of blood lipid profile of diabetic rats were estimated after 21 days of treatment. The enhanced level of triglycerides and total cholesterol were brought down significantly ($p<0.05$) after 21 days treatment period. A fall of 53.98% and 62.07% in TG were observed in diabetic rats treated with crude aqueous extract at oral dose of 200 mg /kg and 400mg/kg respectively. A fall of 36.95% in TC were observed in diabetic rats treated with crude aqueous extract at oral dose of 400mg/kg but not with 200mg/kg. The triglycerides and total cholesterol levels of control diabetic and treated animals are shown in table 7. A fall of 40.66% and 48.66% in glycated hemoglobin also was observed after 21 days treatment. The glycated hemoglobin levels of control diabetic and treated animals are shown in table 9. After 21 day's treatment period 6.25% and 13.22%increase in liver glycogen level also observed in diabetic treated animals as compared with vehicle treated group.

DISCUSSION

The present study indicates that the aqueous extract of whole plant of the *Strobilanthes ciliatus* reduces the blood glucose level in diabetic rats. The perusals of tables1 and 3 reveals that the aqueous extract produced significant decrease in the blood glucose level when compared with controls in glucose loaded and STZ induced hyperglycemic rats at tested dose levels. In the study the test extract constantly maintained significant reduction of the glucose level in the diabetic rats throughout the 21 days experimental period suggesting the hypoglycemic property of the extract. Similar action was not observed in the normoglycemic rats. The levels of serum lipids usually elevated in diabetes mellitus which will be the risk factor for coronary heart diseases. The most common lipid abnormalities in diabetes are hypertriglyceridemia and hypercholesterolemia (Khan *et al*., 1995; Mitra *et al*., 1995).

Hypertriglyceridemia is also associated with metabolic consequences of hypercoagulability, hyperinsulinemia, insulin resistance and insulin intolerance. Significant lowering of total cholesterol is a very desirable biochemical state for prevention of atherosclerosis and ischaemic conditions (Gingsberg, 1994). Lowering of serum lipids concentration with the aqueous extract of *Strobilanthes ciliatus* seems to be associated with a decrease in risk of vascular diseases. The glycogen content of the skeletal muscle and liver, which markedly decrease in diabetes (Prasannan and Subramanian, 1965; Grover *et al*., 2000) increased marginally in the treated animals as compared to the diabetic control. This may be because of the activation of glycogen synthase system by the extract (Whitton *et al*., 1975). Significant fall in glycosylated hemoglobin indicated the efficiency of the extract in glycemic control. A marked increase in the concentration of TBARS has been observed in STZ diabetic rats (Venkateswaran and Pari, 2003). The increased susceptibility of the tissues of diabetic animals may be due to the activation of lipid peroxidation system (Suresh Kumar and Menon, 1993). Treatment with the extract caused a significant decrease in the TBARS level in kidney and liver may be which may be due to the in activation of the lipid peroxidation system. The present study reveals the antidiabetic potential of the whole plant of *Strobilanthes ciliatus*. There is a need to explore the plant for possible isolation of the active constituents responsible for the said activity.

REFERENCES

Bonner-weir, S., 1988. Morphological evidence of pancreatic polarity of beta cells within islets of Langerhans, Diabetes, 37:616-621

Dulin, W.E., Soret M.G., 1977. Chemically and hormonally induced The Diabetic pancreas, 1st Edition, Pleunum press, New York, 425.

Fr. Raphel Tharayil, 1996. "oushadha sasyangal, "II nd edition, 139

Gandhidasan, R., Thamaraichelvan, A. and Baburaj, S. 1991. Anti inflammatory action of Lannea coromandelica by HRBC membrane stabilization. Fitoterapia.; 12(1):81-83.

Ghosh, M.N., 1984. Toxicity studies. In: Fundamentals of Experimental Pharmacology. Scientific Book Agency, Culcutta, 153-158

Gindsberg, H.N., 1994. Lipoprotein metabolism and its relationship to atherosclerosis. Medicinal and clinical North America, 78,1-20

Grover, J.K., Vats, V. and Rathi, S.S., 2000. Antihyperglycemic effect of Eugenia jumbolana and Tinospora cordifolia in experimental diabetes and their effects on key metabolic enzymes involved in carbohydrate metabolism. Journal of Ethnopharmacology, 73, 461-470

Harborne, J. B. 1973. Phytochemical Methods: A Guide to Modern Technique of Plant Analysis, Cambridge University Press Cambridge, UK.

Karl., J., 1993. Development And Standardization Of A New Immunoturbidimetric Hb1Ac Assay. Klin lab: 39:991-996

Khan, B.A., Abraham, A., Leelamma, S., Hypoglycemic action of Murraya koenigii (curry leaf), Brassica juncea, (Mustard), Mechanism of action. *Indian Journal of Biochemistry and Biophysics*, 1995; 32:106-108

Masiello, P., Broca, C., Gross, R., Michele Roye, *et al*. 1998. Development of new model of type 2 diabetes in adult rats administered with STZ and nicotinamide. Diabetes; 47: 224-229.

Mitra, S.K., Gopumadhavan, S., Muralidhar, T.S., Anturlikar, S.D. and Sujata, M.B., 1995. Effect of D-400, a herbomineral preparation on lipid profile, glycated hemoglobin and glucose tolerance in STZ induced diabetes in rats. Indian Journal of experimental biology, 33:798-800

Nicholas, V., 1956. The determination of glycogen in liver and muscle by use of anthrone reagent. *Ind. J. Biol. Chem*: (2) 583.

Omale, J. and Okafor, PN. 2008. Comparative antioxidant capacity and cytotoxicity of the leaf and stem of Cissus multistriata. *African Journal of Biotechnology*; 7(17):3129-3133.

Prasannan, K.G. and Subrahmanyam, K., 1965. Effect of insulin on the glycogen synthesis in vivo in the brain and liver of rats under different contitions. *Indian Journal of medical research*; 53:1003

Rajendran Vadivu and Lakshmi, K.S. 2008. In vitro and in vivo anti inflammatory activity of leaves of Symplocos cochinchinensis (Lour) Moore ssp Laurina. *Bangladesh J Pharmacol*.; 3:121-124.

Robert, J., Nijveldt, Elsvan Nood, Danny, EC. and van Hoorn, 2001. "Flavonoids: A Review of Probable Mechanisms of Action and Potential Applications", *Am. J. Clin. Nut*., (74): 418-425.

Shirwaikar, A., Rajendran, K. and Punitha, I.S.R. 2005. Antidiabetic activity of alcoholic stem extract of Coscinium fenestratum in Streptozotocin-nicotinamide induced type 2 diabetes rats. *Journal of ethnopharmacology*, 2005; 97:369-374

Shirwaikar, A., Rajendran, K. and Barik, R. 2006. Effect of aqueous bark extract of Garuga pinnata Roxb. in streptozotocin-nicotinamide induced type-II diabetes mellitus. *Journal of Ethnopharmacology*: 2006; 107(2): 285-290.

Suresh kumar, J.S. and Menon, V.P., 1993. Effect of diabetes on levels of lipid peroxides and glycolipids in rats brain. Metabolism, (42):1435-1439

Tapan Kumar Chatterjee, 1996. Herbal options, Esatern Traders, Calcutta, 157-161.

Tapas, A. R., Sakarkar, D. M. and Kakde, R. B. 2008. "Flavonoids as Nutraceuticals", *A Review, Tropical Journal of Pharmaceutical Research*., (7)3:1089-1099.

Turner, M.A., 1965. Screening methods in Pharmacology. Academic press, Newyork, 26

Umapathy, E., Ndebia, EJ., Meeme, A., Adam, B., Menziura, P., Nkeh-Chungag, BN. and Iputo, JE. 2010. An experimental evaluation of Albuca setosa aqueous extract on membrane stabilization, protein denaturation and white blood cell migration during acute inflammation. Journal *of Medicinal Plant Research*; 4(5):789-795.

Vane, JR. 1971. Inhibition of prostaglandins synthesis as a mechanism of action for aspirin like drugs. *Nature*; 231(2): 232-235.

Vane, JR. and Botting, RM. 1995. New insights into the mode of action of anti-inflammatory drugs. *Inflammation Research*, 1995;44 (1): 1-10.

Venkateswaran, S., Pari, L., Effect of Coccinia indica leaves on antioxidant status in streptozotocin induced diabetic rats. Journal of ethnopharmacology, 2003; (84)163-168

Whitton, P.D, and Hems, D.A., Glycogen synthesis in perfused liver of STZ diabetic rats. *Biochem. J.*1975;150-153.

Rajaram, K. 2013. Antioxidant and antidiabetic activity of tectona grandis linn. in alloxan induced albino rats. *Asian J Pharm Clin Res*, Vol 6 (3):174-177.

Ramjith, U.S., Roopitha, P., Cyril Mathew Jacob, 2013. Isolation anti-diabetic and antioxidant evaluation of aqueous extract of Cansjera rheedii leaves, *Asian J Pharm Clin Res*, (6) 3:228-234 .

****