International Journal of Phytomedicine 2 (2010) 299-303

http://www.arjournals.org/ijop.html

Research article

ISSN: 0975-0185

Antidiabetic potential of *Lantana aculeata* root extract in alloxan-induced diabetic rats

K. Vinoth Kumar [1], S. Dawood Sharief [2], R. Rajkumar [2], B. Ilango [3], E. Sukumar [4]

***Corresponding author:**

K. Vinoth Kumar

1. Department of Biosciences, Pondicherry University Community College, Pondicherry University, Puducherry – 605 008, India.
2. School of Environmental Sciences, Postgraduate and Research Department of Zoology, The New College, Chennai – 600 14, India.
3. Division of Medical Oncology, University of Colorado, Aurora CO 80045, USA.
4. Department of Applied Sciences, Higher College of Technology, P.B.74, P.C.133, Muscat, Sultanate of Oman.

Abstract

The present study investigates the antidiabetic potential of dried mature roots of *Lantana aculeata*, a weed belonging to *verbenaceae* family on biochemical profile in alloxan-induced diabetic rats. The effects of an ethanolic extract of the dried mature roots of *Lantana aculeata* on serum glucose, total cholesterol, triglycerides, plasma insulin and liver glycogen were examined in control and experimental groups. *Lantana aculeata* root extract reduced the serum glucose concentration at 24, 48 and 72 hours. To verify the activity sub-chronically, the extract administered orally in the doses of 25, 50 and 100 mg/kg to diabetic rats for 30 days, that significantly reduced the level of glucose, total cholesterol and triglycerides with an increase in insulin and glycogen concentration to near normal levels in a dose-dependent manner. The results indicate that roots of *Lantana aculeata* possess antidiabetic potential in alloxan-induced diabetic rats. The activity might be due to high concentration of oleanolic acid present in the roots.

Keywords: Antidiabetic activity, *Lantana aculeata* roots, Oleanolic acid

Introduction

Plants are utilized in native medicines to treat several diseases and are one of the main sources for active molecules in the discovery of new drugs in the modern era. Considered to be of no use, plants such as the common weeds that grow abundantly in large terrains hold promise in the drug discovery which might be very easily accessible and economical. Traditional medicines have used these weeds as remedies for host of diseases according to the literature [1]. *Lantana aculeata* Linn. (family: Verbenaceae) is a sprawling weed which grows in plenty in many parts of the world [2]. Various parts of this taxon are attributed with medicinal properties [3], especially the roots which are used in the treatment of malaria, rheumatism and skin rashes [4]. While screening the roots for toxicity studies, we observed that they were non-toxic and possessed excellent hypoglycemic activity [5], which is the main characteristic of non-insulin dependent diabetes mellitus (NIDDM), a multifactorial disease [6]. Despite numerous preventive strategies and treatments, more than 300 million people worldwide are expected to

doi:10.5138/ijpm.2010.0975.0185.02042
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develop diabetes by 2025 [7,8]. Hence researches are on full swing to develop effective medicines from economical sources, so the mature roots of *Lantana aculeata* were subjected to antidiabetic screening in experimentally induced hyperglycemic rats.

Materials and Methods

Alloxan monohydrate was purchased from Sigma Chemical Company, St Louis, MO, USA. Gliclazide was procured from Dr. Reddy's Lab, Hyderabad, India. All the other chemicals used were of analytical grade and were purchased from commercial sources. The mature roots of *L. aculeata* were collected during the month of October - November 2005 from Puducherry, India. The plant material was identified and authenticated by Dr. P. Jayaraman, Director, Plant Anatomy Research Centre, Medicinal Plant Research Unit, Chennai, India. A voucher specimen has been deposited there for future reference (No. PARC/2006/8). About 1 kg of mature *L. aculeata* roots were chopped into small pieces, shade dried, coarsely powdered and exhaustively extracted with ethanol by cold percolation method. After 72 hours, the solvent was decanted and distilled-off over boiling waterbath. Further concentrations were done under reduced pressure using rotary flash evaporator and finally dried in a dessicator. The yield of the root extract was found to be 0.32% (w/w). Preliminary phytochemical screening of *L. aculeata* root extract revealed the presence of triterpenoids, phenols, flavonoids, glycosides and tannins [9]. A major triterpenoid identified as oleanolic acid (3β-hydroxy-olean-12-en-28-oic acid) isolated from the root extract, compared with an authentic sample, 1H and 13C-NMR spectroscopic data [10,11], which has been reported to be the major phytoconstituent of the genus *Lantana* [12]. Adult male albino rats of Wistar strain weighing 150 - 200 g used for the study were obtained from Tamil Nadu University of Veterinary and Animal Sciences, Chennai, India and maintained according to the guidelines of Committee for the Purpose of Control and Supervision of Experiments on Animals, Chennai, India (Reg. No. 324). The permission of the Departmental Ethical Committee was obtained for the study and the experiments were conducted as per the principles prescribed for laboratory animal use. Animals were fed on commercial pelleted chow obtained from Poultry Research Station, Chennai, India and water was provided *ad libitum*. In the present study, thirty six rats were used. Group I: contained six animals that served as control. The remaining 30 animals were given alloxan intra-peritoneally (120 mg/kg body weight) to induce hyperglycemia. After 72 hours, the hyperglycemic conditions in these animals were ensured from their blood glucose values which were above 250 mg/dl. Further they were segregated into five groups containing six animals each and were treated as follows.

Group II - Disease-control (alloxan 120 mg/kg i.p)
Group III - Diabetic + Glidazide (25 mg/kg of Body wt)
Group IV - Diabetic + *L. aculeata* root (25 mg/kg of Body wt)
Group V - Diabetic + *L. aculeata* root (50 mg/kg of Body wt)
Group VI - Diabetic + *L. aculeata* root (100 mg/kg of Body wt)

The doses of *Lantana aculeata* root extract were chosen based on earlier preliminary toxicity studies [5]. Serum glucose concentration was measured at 24, 48 and 72 hours from the blood samples drawn by reto-orbital puncture [13]. The doses was continued for 30 days and on day 31, the animals were sacrificed by cervical decapitation under mild anesthesia and the blood were collected in tubes with clot activators and heparin to get serum and plasma while the liver was removed immediately, washed with ice-cold saline and stored in deep freezer at -20ºC for glycogen estimation. Plasma insulin was estimated by ELISA method using Biotech-ELX-50, (U.S.) [14], liver glycogen using UV visible spectrophotometer [15], Serum glucose [13], total cholesterol and triglycerides [16,17] were estimated using Randox-*daytona* fully automated random axis analyzer (U.K.). Statistical evaluation of analytical data was done by Student's *t*-test using SPSS package. The values are expressed as the mean ± standard Deviation (S.D) and values with $P<0.01$, $P<0.001$, $P<0.05$ were considered significant.

Results

Table 1 shows the effect of *Lantana aculeata* root extract on serum glucose level in hyperglycemic animals. The level of glucose in animals treated with gliclazide and *Lantana aculeata* root extract (25 mg/kg) for 24, 48 and 72 hours showed a decrease in the level of glucose. In 50 and 100 mg/kg dose, the level of glucose further decreased with 24, 48 and 72 hours, the decrease was drastic in 72 hours. On observing the response with 100 mg/kg dose for 72 hours, the level of glucose was found near to the control value, thereby indicating the ntidiabetic potential of *Lantana aculeata* root. Table 2 illustrates the effect of *Lantana aculeata* root extract for a sub-chronic period of 30 days. The diabetic control rats (Group II) showed a significant increase in glucose, total cholesterol and Triglycerides levels, while plasma insulin and liver glycogen were reduced drastically when compared to the control animals. On treatment with standard drug gliclazide, all the parameters found to attain near normal values. The animals treated with *Lantana aculeata* root extract in different doses (25, 50 and 100 mg/kg) showed dose-dependent decrease in levels of glucose, total cholesterol and triglycerides while increase in plasma insulin and liver glycogen were obtained when compared to the disease-control group.

Table 1 Effect of *Lantana aculeata* root extract (LAR) on serum glucose (mg/dl) levels in hyperglycemic rats for 24, 48 and 72 hours

Treatment (mg/kg)	24 hours	48 hours	72 hours
Group I Control	113.00 ± 5.10	114.00 ± 6.09	114.00 ± 6.07
Group II Diabetic control Alloxan 120 mg/kg	602.66 ± 13.80a***	630.83 ± 10.68a***	613.33 ± 11.40a***
Group III Standard drug Gliclazide 25 mg/kg	585.50 ± 10.05b**	453.83 ± 9.45b***	322.50 ± 12.40b***
Group IV *LAR* 25 mg/kg	590.00 ± 11.83bNS	405.50 ± 9.64b***	367.50 ± 10.83b***
Group IV *LAR* 50 mg/kg	444.17 ± 9.81b***	287.17 ± 12.42b***	201.67 ± 10.80b***
Group IV *LAR* 100 mg/kg	430.00 ± 10.27b***	285.50 ± 8.35b***	125.83 ± 10.57b***

Values represent mean ± S.D. of six animals
$^{*}P< 0.05$, $^{**}P<0.01$, $^{***}P<0.001$ when compared to control animals; ^{NS} -Non-significant

Table 2 Anti diabetic effect of *Lantana aculeata* root extract (LAR) treated in alloxan-induced rats for 30 days

Treatment (mg/kg)	Serum glucose (mg/dl)	Plasma insulin (µU/L)	Liver glycogen (mg/gm tissue)	Total cholesterol (mg/dl)	Triglycerides (mg/dl)
Group I - Control	114.00 ± 6.06	13.50 ± 2.81	58.17 ± 3.12	65.17 ± 3.54	68.17 ± 4.02
Group II Diabetic control Alloxan 120mg/kg	494.17 ± 32.00 a***	6.00 ± 2.45 a***	6.00 ± 1.67 a***	138.00 ± 8.60 a***	113.66 ± 5.46 a***
Group III Standard drug Gliclazide 25 mg/kg	103.33 ± 7.63 b***	11.50 ± 2.43 b**	23.50 ± 3.33 b***	65.00 ± 3.69 b***	74.83 ± 4.17 b***
Group IV *LAR* 25 mg/kg	111.00 ± 6.81 b***	11.83 ± 2.48 b**	52.17 ± 3.82 b***	68.17 ± 6.18 b***	83.67 ± 5.46 b***
Group V *LAR* 50 mg/kg	102.67 ± 5.92 b***	12.00 ± 1.89 b***	55.50 ± 5.58 b***	62.50 ± 4.04 b***	62.67 ± 5.92 b***
Group VI *LAR* 100 mg/kg	92.00 ± 5.09 b***	15.57 ± 3.38 b***	58.67 ± 4.72 b***	53.00 ± 5.44 b***	58.17 ± 5.07 b***

Values represent mean ± S.D. of six animals
$^{*}P< 0.05$, $^{**}P<0.01$, $^{***}P<0.001$ when compared to control animals; ^{NS} -Non-significant

Discussion

The results of antidiabetic study clearly showed that *Lantana aculeata* root extract produced a significant hypoglycemic action. At 25 mg/kg dose, the activity of *Lantana aculeata* root extract in lowering the serum glucose and promoting glycogen storage was found to be higher than the standard drug. The possible mechanism for this action might be due to the inhibition of the enzyme glycogen phosphorylase, an enzyme that catalyzes the process of glycogenolysis thereby inhibiting glucagon which on feedback inhibition favours the production of insulin as reported by Liu [18], who also proposed the role of maslinic acid (a pentacyclic tritepene obtained by the semi-synthesis starting from readily available oleanolic acid) in reducing the blood glucose level. Our studies showed a high concentration of oleanolic acid in *L. aculeata* roots [5]. The role of oleanolic acid in reducing blood glucose level was also substantiated by Dawei [19] who isolated the compound from *Ligustrumlucidum*. Oleanolic acid has also been indicated to be the causative factor for the increase of insulin which plays an important role in the glycogenesis (Storage of glycogen in the liver) and lipogenesis (metabolism of lipids) [20]. This might be the cause for drastic depletion of glucose and lipid parameters such as total cholesterol and triglyceride in hyperglycemic condition [19]. Our observations on the antihyperglycemic activity of *L. aculeata* root in diabetic rats as well as the isolation of high yield of oleanolic acid from the root extract go along with these findings. Further studies are necessary to determine the exact nature of the active principles and mechanism of action of *Lantana aculeata* root extract.

Conclusion

From this study we can conclude that *Lantana aculeata* root extract has beneficial effects on blood glucose and lipid abnormalities. It has the potential to impart therapeutic effect in diabetes.

Acknowledgements

The authors wish to thank Dr. K. Balakrishna, Central Research Institute for Siddha, Chennai and Dr. A. R. Nareshraj, Department of Chemistry, SRM College of Engineering and Technology, SRM university, Chennai for their help in phytochemical analysis.

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