Nallani Venkata Rama Rao. *et al*. / *International Journal of Phytopharmacology.* 4(5), 2013, 311-314.

e- ISSN 0975 – 9328
Print ISSN 2229 – 7472

International Journal of Phytopharmacology

Journal homepage: www.onlineijp.com

IJP

ANTI-DIABETIC ACTIVITY OF *GLOCHIDION VELUTINUM* L. EXTRACT IN ALLOXAN - INDUCED TYPE-II DIABETIC RATS

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ABSTRACT

The current study was done to investigate the anti-diabetic activity of the leaves of *Glochidion velutinum in vivo* by using alloxan induced diabetes model in rats. We want to know its safety and efficacy by local herbalists for the treatment of diabetes mellitus. Active principle is responsible for the therapeutic effect, preliminary phytochemical analysis of the aqueous and methanolic extracts of the plant has been investigated. Crude aqueous (AQ) and methanol (i.e., MEOH) extracts of the leaves of *Glochidion velutinum* were administered to both normal and alloxan induced diabetic male albino rats (Wistar strain). The blood glucose levels were measured at 0, 2, 4, 6 and 8 h each day up to 15 days after oral administration of AQ and MEOH extracts. We observed that significant reduction in blood glucose levels in treated and standard Glibenclamide (0.28 mg/kg) group without causing any hypoglycemic effect compared to normal rats. The statistical significance was evaluated by using dunnet multiple comparison test ($p<0.05$ is significant). Both polar and methanolic extracts of the leaves of *Glochidion velutinum* exhibited significant anti-hyperglycemic activity. Observable parameters in ethanolic extract and aqueous extract of *G. velutinum* (400mg/kg) shows a significant decrease of blood glucose levels i.e., 169±3.05, 165.83±2.98 compared with the positive control 314±05 at various time intervals. This study provides scientific evidence that the leaves of *Glochidion velutinum* have anti-diabetic efficacy and further investigation is need to be conducted for the structural elucidation and isolation of active principle responsible for antidiabetic activity.

Key words: *Golchidion velutinum*, Diabetic, Glibenclamide.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder, enhancing blood sugar levels (hyperglycemia, excessive hepatic glycogenolysis & gluconeogenesis) by this insulin production will be abnormal by the pancreas or its action. Diabetes is a condition in which the body either does not produce enough insulin or cannot use insulin properly. Insulin is a naturally occurring hormone in the blood that is necessary for providing our cells with energy to function. Insulin provides sugar (glucose) which moves from the blood stream into the cells. If glucose is not absorbed in to cells, it will enhance the sugar in the blood which is called as (hyperglycemia). It will be affect on organs like the eyes and kidneys, or damage of blood vessels and nerves (Bethesda *et al*, 1990).

The treating diabetes and associated complications exceeds costs of $100 billion per year. The complications and other health problems are minimized in those one who are using proper pharmacotherapy to control blood sugar levels and frequently checking blood sugar levels will help to develop health standards. Due to the multiplication of diabetics worldwide, a great consideration is given to the disease by health care managements both at national and international levels, last ten years, diabetes cases have raised up-to 5% per annum (p.a.) to approximately 250 million and has been projected to become one of the world's major killers within next 25 years (Zimmet *et al*., 2001).

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The disease affects all regions of the world but the share of diabetics in the overall population is particularly high in the eastern Mediterranean countries and the Middle East (9%), in North America (8%) and in Europe (7%). Up until 2025 the WDF (World Diabetes Foundation) expects the number of diabetics to increase by 2.5% per year to about 380 million (Wild *et al*., 2004).

Herbal products and their derivatives have historically been precious as a source of therapeutic agents. There is now a greater interest in the scientific community to evaluate both crude and isolated active constituents in experimental studies furthermore folklore medicines have proved to be a fruitful source of future drugs to counteract any disease including insulin resistance, consistent with a resurgence of interest in drug discovery from natural products (Frode TS and Medeiros YS, 2008).

***Glochidion velutinum* Plant Leaves & Fruits**

Geographical distribution

Glochidion velutinum is distributed in India, Burma, Nepal and Pakistan. Occasional along the streams in moist deciduous Forests streams near Akkagarla guide in Tirumala, near water fall streams in Talakona, Kambakam (Chaitanya RSNAKK, 2011).

MATERIALS AND METHODS

Collection of plant material: *Glochidion velutinum* plants were collected from the forest area of Tirupathi the plant was identified and authenticated by Dr. Madhava Chetty. Dept. of botany Sri Venkateswra University, Tirupati, The leaves were collected in the month of September 2011, its specimen has been deposited at the museum of Chalapathi Institute of Pharmaceutical Sciences, Guntur. The institutional animal ethics committee (IAEC) (Reg.no.1048/a/07/CPCSEA) Chalapathi institute of pharmaceutical sciences, Guntur, Andhra Pradesh.

Preparation of methanolic extract of *Glochidion velutinum* (Kunga Mohan Ramkumar et.al., 2011) *Glochidion velutinum* leaves dried under shadow environment and to male coarse powdered in electrical grinder, than passed through sieve no 60# .total 500 gm of sieved powder was weighed accurately packed into soxhlet column (borosil, Mumbai, India). The extraction was carried out by continuous hot percolation process with the help of Soxhlet apparatus using methanol and water as solvents. The two extracts were concentrated in rotary flash evaporator (Roteva Equitron, Mumbai) and dried in a desiccator. The yield was 5%w/w of methanolic extract and 50% w/w for aqueous extract. The dried extracts were stored in air tight containers and subjected to preliminary screening for the identification of active chemical constituents.

Preliminary phytochemical studies

Phytochemical test like preliminary phytochemical analysis and thin layer chromatography were performed .Through chemical tests presence of flavonoids, saponins, tannins, steroids was revealed. From the TLC analysis presence of gallic acid was identified (*Sandhya S, 2011).

Drugs and Chemicals: Alloxan, Glibenclamide were procured from Sigma Aldrich Labs, Glucometer ACCU CHECK, were procured from National Scientific Products**,** 4th Line, Sambasivapet . Guntur - 522001.

Experimental Animals

Male Albino Wistar rats of male (Kunga Mohan Ramkumar *et al*., 2011) (120–300 g body weight) purchased from (Mahaveer Enterprises, Hyderabad) used for study. All animals were acclimatized under laboratory conditions for two weeks prior to experiments. All the experiments with animals were carried out according to the guidelines of the institutional animal ethical committee (IAEC) laboratory conditions [temperature (22 ± 2°C) and humidity 50 ± 15%] with 12 hours day: 12 hours night cycle. The animals were fed with normal laboratory diet and allowed to drink water *ad libitum*. The experimental protocol has been approved by the Institutional Animal Ethics committee (CIPS/IAEC/27/2012) and by the regulatory body of government of India.

Grouping of Animals

The experiment was carried out in the healthy male wistar strain rats weighing about 120-300g and divided into 5 groups as the following each group consist 5 animals. All the groups were administered with the alloxan 140mg/kg (B.S. Ashok Kumar *et al*., 2012) to induce diabetes except control group.

Group I: - Control group consists of normal rats administered with 2ml of saline orally by using oral gavage for 15 days daily.

Group II: - Negative control group contains Diabetes mellitus induced by single intra peritoneal injection of 140 mg/kg B.W of freshly prepared alloxan monohydrate in normal saline. In order to prevent fatal hypoglycemia due to massive pancreatic insulin release, rats were treated with 20% glucose solution intra peritoneal after 6 h followed by 5% glucose solution bottles in their cages for a period of 24 h. The glucose levels will be elevated after one week measured by using glucometer strips. (Xiao-Shun Shua *et al*., 2009)

Group III: - Diabetic rats treated with Methanolic extract solution of *Glochidion velutinum* 400g/kg body weight administered orally by using oral gavage for 15 days.

Group IV: - Diabetic rats treated with aqueous extract solution of *Glochidion velutinum* 400g/kg body wt administered orally by using oral gavage for 15 days.

Group V: - Diabetic rats are treated with the standard drug Glibenclamide 0.28mg/kg in aqueous solution administered using oral gavage for 15 days (Sagar Naskar, 2011).

Statistical Analysis

The statistical analysis by using analysis variance as mean ±SD followed by Dunnet's multiple comparison tests were used for comparison between control and treated groups. P-values < 0.05 were considered as significant.

Treatment of Diabetic Rats with Methanolic and Aqueous Extracts

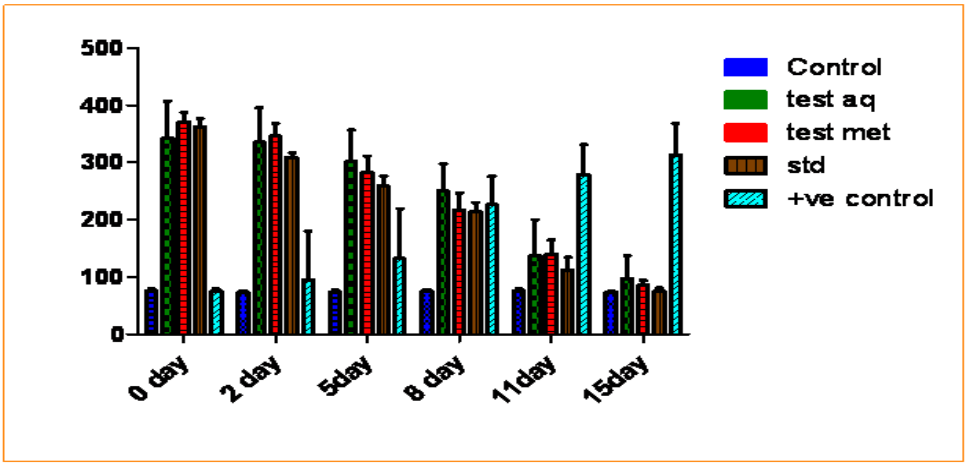
The effect of different doses of methanolic extract 400 mg was decreased blood sugar levels from day 1 to day 15 is 314±5 to 155±4 mg/DL and aqueous extract of *G. velutinum* (400mg/kg) decreased blood sugar level from 314±5 to 160±4 mg/DL . Comparison with the control rats at various time intervals (Table-1). It predeceased significant ($p<0.05$) maximum reduction in blood glucose level from respectively methanolic and aqueous extract of *Glochidion velutinum*, similarly when compared with Methanolic and aqueous extract of *Glochidion velutinum* with standard drug (Glibenclamide) reaches blood glucose levels near to the standard (Figure 1). Whereas control and +ve control observed in inter related bars, they are more than to control.

RESULTS

Table 1. Treatment of Diabetic Rats with Methanolic and Aqueous Extracts of *Glochidion velutinum*

Time in days	Control			Negative control			Methanolic extract of *Glochidion velutinum* (400mg/kg)			Aqueous extract of *Glochidion velutinum* (400mg/kg)			Standard Glibenclamide (0.28mg/kg)		
	n	$\bar{x}$	σ	n	$\bar{x}$	σ	n	$\bar{x}$	σ	N	$\bar{x}$	σ	n	$\bar{x}$	σ
0	5	75.8	2.55	5	342	64.8	5	371	16.7	5	362	14.4	5	75	4.19
2	5	73.6	2.33	5	335	60.4	5	346	22.4	5	309	7.8	5	95.2	84.9
5	5	74.0	3.16	5	302	54.6	5	282	28.6	5	259	16.6	5	132	87.4
8	5	74.6	3.01	5	249	47.3	5	217	29.9	5	214	16.4	5	226	49.2
11	5	75.2	3.34	5	137	63.3	5	140	24.3	5	112	21.4	5	279	52.3
15	5	73.6	1.62	5	97.4	40.2	5	85.4	8.5	5	74.4	6.3	5	312	55.3

Figure 1. Various blood glucose levels within 15 days



DISCUSSION

The current study was observed in *Glochidion velutinum* leaf extracts act as antidiabetic activity in both aqueous and Methanolic extracts. Alloxan directly affect the β -cells of the islets of langerhans there by reduces in insulin release, inducing hyperglycaemia (Fisher, 1985). The diabetic rats (induced by alloxan) showed a persistent rise in blood glucose level after 7 days with the characteristic features of diabetes mellitus. Traditional plant medicines are used throughout the world for a range of diabetic presentations. The study of such medicines might offer a natural key to unlock a diabetologist's pharmacy for the future. In light of this we made an attempt for the first time to study the effect of *Glochidion velutinum* in normoglycaemic and hyperglycaemic rats. These studies have identified that compounds such as

polysaccharides, flavonoids, terpenoids and tannins and steroids are responsible for antidiabetic effect.

Oral hypoglycemic agents and insulin are currently available for treating DM. However, there is a growing interest in herbal remedies due to the side effects associated with the existing drugs. The present investigation indicates the hypoglycemic. We have observed a significant ($P < 0.05$) decrease in blood glucose in *Glochidion velutinum* treated diabetic rats, when compared with diabetic control rats. The possible mechanism of *Glochidion velutinum* on hypoglycemic action may be through potentiation of pancreatic secretion of insulin from β-cell of islets *Glochidion velutinum* contains flavonoids, saponins and carbohydrate, steroids, tannins, and phenolic compounds. The observed hypoglycemic effects of this plant could have resulted from the combined activity of these compounds present in the extract. However, the possibility of enhanced tissue uptake by cannot be ruled out. In addition, the glucose lowering effect of extracts was more powerful when compared to normal rats suggesting that it could be caused by an increase in peripheral glucose consumption, this reinforces the hypothesis that the hypoglycaemic mechanism involves insulin like effect through peripheral glucose consumption, delay in insulin catabolism or inhibition of glucose reabsorption by the kidney. The fact that some herbal preparations enhance the beta cell regeneration and peripheral glucose utilization in Alloxan and Streptozotocin induced diabetic rats supports the above assumption (Chakravarthy *et al*., 1982; Mitra *et al*., 1996). Plants containing flavonoids, isoflavanoids, triterpenoids have been shown to be effective in diabetes due their antioxidants property (Jafri *et al*., 2000; Syed *et al*., 2005).

CONCLUSION

These observations confirm that Methanolic and Aqueous extract of the *Glochidion velutinum* leaves have anti diabetic activity. From this study, it is concluded that *Glochidion velutinum* may be useful in treating Diabetes mellitus with no visible signs or symptoms of toxicity in normal rats indicating a high margin of safety. The extracts exhibited anti-hyperglycaemic activity comparable to that of a standard drug Glibenclamide. The traditional use of *Glochidion velutinum* to treat diabetes is supported by laboratory results from this study, suggesting a need to isolate and evaluate active constituents responsible for the exhibited biological activity.

Acknowledgement

The authors are thankful to the management and principal of Chalapathi Institute of pharmaceutical sciences, Guntur -India for their constant support and providing facilities to carry out the research work.

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