Asian Journal of Pharmaceutical and Clinical Research
Vol. 4, Issue 1, 2011 ISSN - 0974-2441

Research Article

HYPOGLYCEMIC AND ANTIDIABETIC ACTIVITY OF ALANGIUM SALVIFOLIUM WANG IN ALLOXAN INDUCED DIABETIC RATS

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ABSTRACT

The present study is aimed to investigate the effect of aqueous extract of stem and leaves of Alangium Salvifolium (AEAS) on blood glucose level in normal and alloxan induced diabetic rats. Oral administration of AEAS (200,400 and 800mg/kg body weight) resulted in a significant reduction in blood glucose level. The effect was compared with 0.5mg/kg (I.P.) glibenclamide. The results support the traditional usage of the plant of Alangium Salvifolium by ayurvedic physicians for the control of diabetes.

Key words: Alangium Salvifolium, Alloxan, Glibenclamide.

INTRODUCTION

Diabetes is one of the major crippling diseases in the world leading to huge economic losses. The persons suffering from this metabolic disease is considered to 'die-a-bit' and hence 'die-a-bit-is' (diabetes). The global prevalence of diabetes is estimated to increase, from 4 percent in 1995 to 5.4 percent by the year 2025. The World Health Organization has predicted that the major burden will occur in developing countries. Studies conducted in India in the last decade have highlighted that not only is the prevalence of diabetes high but also that it is increasing rapidly in urban population[1]. Today more people around the world have diabetes than ever before. The prevalence of Type II diabetes at present is one out of ten in the population. The incidence is about 3 per 1000 population. The Japanese, European and Eskimo populations have a low prevalence of Type II diabetes, while more modernized African and Chinese populations have a higher prevalence. At the end of the scale are the Pima Indians and Polynesian populations who have very high prevalence[2].

In the recent past many hypoglycemic agents are introduced. still the diabetes and the related complications continue to be a major medical problem not only in developed countries but also in developing countries. Many Indian medicinal plants are reported to be useful in diabetes[3,4]. However, search for new antidiabetic drugs continue.

Alangium Salvifolium Wang belongs to the family Alangiaceae. It is commonly known as sage leaved Alangium. The names of Alngium Salvifolium in various languages are: Tamil: Azhinjil, Telugu: Aankolam, Hindi: Ankol. Sage leaved Alangium is a tall thorny tree native to India. It grows to a height of about 3 to 10 meters.

The bark is ash colored, rough and faintly fissured. The leaves are elliptic oblong, elliptic lanceolate or oblong lanceolate. The flowering season is February to July. In ayurveda the roots and the fruits are used for the treatment of rheumatism and hemorrhoid. Externally it is used for the treatment of bites of rabbit.

Whereas the leaves are used for the treatment of diabetes, fruits as an astringent[5, 6]. Anti-Arthritic activity of Bark extracts of Alangium Salvifolium Wang[7] and Anti-Fertility activity of the stem Bark of Alangium Salvifolium (Linn.F) Wang in Wistar Female Rats[8] has been reported. However the plant is not scientifically explored for its hypoglycemic and antidiabetic activity. Hence an effort has been made here to screen the plant for its antidiabetic activity.

MATERIALS AND METHODS

Collection of Plant Material

The proposed plant material of fresh Alangium Salvifolium stem and leaves were collected from Tirupati, Chittoor district of Andhra Pradesh-India. The species for the proposed study was identified and authentified by Dr.K.Madhave Chetty, Asst.Professor of Dept. of Botany, Sri Venkateswara University, Tirupati, Andhra Pradesh-India. Voucher specimen was deposited at Dept. of Pharmacognosy for further reference.

Preparation of Extracts

Preparetion of the extract of Alangium Salvifolium Wang stem and leaves was done using distilled water. The shade dried powder of the stem and leaves was packed well in Soxhlet apparatus and was subjected to continuous hot extraction with distilled water until the completion of the extraction. The extract was filtered while hot and the resultant extract was distilled in vacuum under reduced pressure in order to remove the solvent completely. It was dried and kept in a desiccator till experimentation. Obtained extract was weighed, practical and percentage yield were calculated in terms of air dried powdered crude material[9-11].

Preliminary Phytochemical Investigation

The extract was subjected to qualitative chemical investigation for the identification of different phytoconstituents like sterols, glycosides, saponins, carbohydrates, alkaloids, flavonoids, tannins, proteins and tri-terpenoids[12, 13].

Animals

Wistar albino rats of either sex weighing between 150-250gm were used. They were maintained under standard laboratory conditions at a temperature of 23±2ºC, with 12 h light- dark cycle. The animals were fed with standard food pellets (Hindustan Lever Ltd, India) and water ad libitum. All animal procedures have been approved and prior permission from the Institutional Animal Ethical Committee was obtained as per the prescribed guidelines (IAEC/PRRMCP/2006/07).

Acute Toxicity Studies

Healthy adult albino rats of either sex, starved overnight, were divided into groups (n=6) and were orally fed with increased dose of AEAS. Total AEAS administered orally in doses of up to 1500 mg/kg did not produce any sign of toxicity and mortality in rats when observed for 14 days after administration[14].

Assessment of Hypoglycemic Activity

The test samples were suspended in 25% Tween 20 in distilled water. Glibenclamide (2.5 mg/kg) was used as reference control during the study. All the samples were administered through oral route. The animal were fasted for 20 h, but were allowed free access to water before and throughout the experiment. At the end of the fasting period, taken as zero time (0 h), blood was withdrawn from the tip of the tail of each rat under mild ether anesthesia. Plasma was estimated by GOD/POD method using Glucose estimation kit.

Table -1: Acute Toxicity Study of AEAS

Group	Dose (mg/kg)	No. of Animals	No. of Survival	No. of Death	Percentage mortality	LD_{50}
1	50	6	6	0	0	-
2	100	6	6	0	0	-
3	500	6	6	0	0	-
4	1000	6	6	0	0	-
5	1500	6	6	0	0	-

Table -2: Statistical Analysis of Hypoglycemic Activity of AEAS

	Blood Glucose Level (mg dL^{-1})					
Group	**0 min**	**30 min**	**1 h**	**2 h**	**4 h**	**8 h**
I (Control)	84.6±0.21	84.3±0.22	83.5±0.15	81.8±0.20	78.6±0.17	75.4±0.34
II (AEAS 200mg/kg)	87.1±0.22**	85.8±0.16**	82.4±0.44	77.8±0.32**	69.6±0.39**	62.6±0.27**
III (AEAS 400mg/kg)	86.5±0.17**	83.9±0.23	79.6±0.40**	74.0±0.26**	65.2±0.20**	58.2±0.23**
IV (AEAS 800mg/kg)	86.1±0.22**	83.8±0.24	75.5±0.23**	64.2±0.32**	57.5±0.23**	54.4±0.24**
IV (Glibenclamide)	87.3±0.19**	83.5±0.23	72.0±0.27**	61.3±0.29**	55.8±0.34**	50.9±0.29**

All values are expressed as Mean±SEM, N=6, analysis by One-way ANOVA followed by Dunnet's test, significant at **p<0.01, in comparison to group I.

Table -3: Statistical Analysis of Antidiabetic Activity of AEAS

	Blood Glucose Level (mg dL^{-1})					
Group	**0 min**	**30 min**	**1 h**	**2 h**	**4 h**	**8 h**
I (Control)	83.2±0.41	76.2±0.28	78.2±0.12	76.4±0.22	69.2±0.41	69.8±0.25
II (Diabetic Control)	140.0±0.43++	131.0±0.27++	127.2±0.30++	127.8±0.24++	126.4±0.20++	125.1±0.26++
III (Glibenclamide)	83.0±0.21**	78.6±0.25**	70.4±0.16**	66.2±0.24**	65.8±0.24**	64.0±0.29**
IV (AEAS 200mg/kg)	105.0±0.10**	91.8±0.25**	84.2±0.33**	80.4±0.27**	76.4±0.36**	75.2±0.27**
V (AEAS 400mg/kg)	94.2±0.20**	80.6±0.25**	79.4±0.28**	79.8±0.23**	75.8±0.25**	69.8±0.18**
VI (AEAS 800mg/kg)	93.4±0.20**	80.4±0.26**	76.8±0.22**	74.4±0.22**	69.0±0.47**	68.6±0.14**

All values are expressed as Mean±SEM, N=6, analysis by One-way ANOVA followed by Dunnet's test. significant at **p<0.01 in comparison to group II, ++p<0.01 in comparison to group I.

Assessment of Hypoglycemic Activity

The test samples were suspended in 25% Tween 20 in distilled water. Glibenclamide (2.5 mg/kg) was used as reference control during the study. All the samples were administered through oral route. The animal were fasted for 20 h, but were allowed free access to water before and throughout the experiment. At the end of the fasting period, taken as zero time (0 h), blood was withdrawn from the tip of the tail of each rat under mild ether anesthesia. Plasma was estimated by GOD/POD method using Glucose estimation kit. The normal rats then divided into five groups of six animals each. Group I served as a solvent control, Group II, III and IV received the test extract at a dose of 200, 400 and 800 mg/kg respectively, through oral route. Group V received Glibenclamide (2.5 mg/kg, p.o) and served as reference control. All the test samples were administered in a similar manner. Blood glucose levels were examined after 30 mins, 1, 2, 4 and 8 h of administration of test samples[15].

Assessment of Antidiabetic Activity

Different groups of rats were used to study the effects of AEAS. The rats were divided into six groups each consisting of six rats. **Group I**: Normal control animals received 1% sodium carboxy methyl cellulose 2 ml/kg body wt per. orally. **Group II**: Alloxan (150 mg/kg body wt) induced diabetic animals received 1% sodium carboxy methyl cellulose 2 ml/kg body wt. per orally. **Group III**: Alloxan (150 mg/kg body wt) induced diabetic animals received Glibenclamide 0.5 mg/kg body wt. intraperitonially. **Group IV**: Alloxan (150 mg/kg body wt) induced diabetic animals received AEAS 200 mg/kg body wt. per orally. **Group V**: Alloxan (150 mg/kg body wt) induced diabetic animals received AEAS 400 mg/kg body wt. per orally. **Group VI**: Alloxan (150 mg/kg body wt) induced diabetic animals received AEAS 800 mg/kg body wt. per orally.

Significant hyperglycemia was achieved within 48 hours after Alloxan (150 mg/kg body wt. i.p.) induction. Alloxan induced diabetic rats with more than 200 mg/dl of blood glucose were considered to be diabetic and used for the study. In acute study all the surviving diabetic animals and normal animals were fasted overnight.

Blood samples were collected from the fasted animals prior to the treatment with above schedule and after administration at each day up to 7 days. For glucose determination, blood was obtained by snipping tail with sharp razor. Then the blood glucose levels were determined by using Haemo-Glukotest (20-800R) glucose strips supplied by M/s Boehringer Mannheim India Ltd. These methods, which permit the measurements of blood glucose levels with minimum injury to rats, was previously validated by comparison with glucose oxidase method[16-19].

Statistical Analysis

All values were expressed as Mean±SEM. The data were statistically analyzed by One-Way ANOVA followed by Dunnett's test.

RESULTS AND DISCUSSION

The ayurvedic system of medicine includes a number of plants and minerals which should be investigated to determine the hidden potential using the modern methodology. The plant Alangium Salvifolium is an indigenous herb which was chosen for this study. The attempt was made to study the phytoconstituents present in the stem and leaves of the plant and the pharmacological activities of the

plant. The study can be categorized into two major sections, viz,

- Phytochemical Screening
- Pharmacological Studies

Phytochemical Screening

The phytoconstituents present in the plant were extracted by using different solvents of increasing polarity like n-hexane, chloroform, ethyl acetate, acetone, ethanol and water. The phytoconstituents were identified by various chemical tests which showed the presence of alkaloids, carbohydrates, tannins, phenolic compounds and glycosides in aqueous extract of Alangium Salvifolium.

Pharmacological Studies

Acute Toxicity Studies

The acute toxicity studies mainly aims at establishing the therapeutic index, i.e., the ratio between the pharmacologically effective dose and the lethal dose on the same strain and species. The AEAS did not produce any sign of toxicity and mortality in rats up to 1500mg/kg body wt. The results were shown in table-1.

Hypoglycemic Activity

Hypoglycemic activity of AEAS was performed on Wistar albino rats. The results show the significant hypoglycemic activity at the dose of 800 mg/kg. The results were shown in table-2.

Antidiabetic Activity

After the assessment of antidiabetic activity of AEAS on alloxan induced diabetic rats , it can be confirmed that the extract shows the significant antidibetic activity. The results were shown in table-3.

CONCLUSION

The plant has been selected based on its traditional uses. The phytochemical and pharmacological studies were performed on the stem and leaves of Alangium Salvifolium Wang belonging to the family Alangiaceae.

The phytoconstituents were extracted and the constituents were identified by performing various chemical tests. The results of the pharmacological studies clearly demonstrates that the aqueous extract of stem and leaves of Alangium Salvifolium Wang has significant hypoglycemic activity in normal rats and antidiabetic activity in alloxan induced diabetic rats. Thus the present study supports the traditional folklore and reveals that the stem and leaves of Alangium Salvifolium Wang possess good hypoglycemic and antidiabetic activity.

ACKNOWLEDGEMENT

The authors are very much grateful to P.Rami Reddy Memorial College of Pharmacy, kadapa, Andhra Pradesh- India for providing necessary facilities to carry out this work. Authors are also thankful to Miss.B.Jyothi, Asst.Professor, for her help pertaining to publish this work.

REFERENCES

1. Dixit PP, Londhe JS, Saroj S Ghaskadbi, Devasagayam TPA. Antidiabetic and Related Beneficial Properties of Indian Medicinal Plants. Herbal Drugs: A Twenty First Century Prospective. 1st ed. Jaypee Brothers Medical Publishers (P) Ltd: New Delhi; 2006. P- 377.
2. Lele RD. Clinical Science and Clinical Research. 2nd ed. The National Book Depot: Mumbai; 2008. P-81-82.
3. Kirithikar KR, Basu BD, An ICS. Indian Medicinal Plants, Vol.I. International book distributors: Dehradun, India; 1995. p- 371-372.
4. Nadkarni KM, Nadkarni AK. Indian Materia Medica, Vol.I. Popular Prakashan: Bombay, India; 1976. P-615-616.
5. Sage Leaved Alangium [Internet]. Available from: http://www.flowersofindia.net/catalog/slides/Sage%20Leaved%20Alangium.html
6. Madhava Chetty K, Sivaji K, Tulasi Rao K. Flowering Plants of Chittoor District-Andhra Pradesh, India. 1st ed. Students Offset Printers: Tirupati; 2008. P-150.
7. Jubie S, Jawahar N, Ruby Koshy, Gowramma B, Murugan V, Suresh B. Anti-Arthritic activity of bark extracts of Alangium Salvifolium Wang. Rasayan J.Chem. 2008; 1(3): 433-436.
8. Murugan V, Shareef H, Rama Sarma GVS, Ramanathan M, Suresh B. Anti-Fertility Activity of the Stem Bark of *Alangium Salvifolium* (Linn.F) Wang in Wistar Female Rats. Indian J.Pharmacol. 2000; 32(6): 388-389.
9. Harbone JB. Phytochemical method. 3rd ed. Chapman and Hall: London; 1988. P-117-119.
10. Beckett AH, Stenlake JB. Practical Pharmaceutical Chemistry, Vol.II, 3rd ed, CBS Publication; 2000. P-333-336.
11. Agarwal OP. Advanced Practical Organic chemistry. 17th ed, Goel Publishing House: Meerut; 2000. P-43-59.
12. Yarnalkar S. Practical Pharmacognosy. Nirali Prakashan: Pune. 1991.
13. Khandelwal KR. Practical Pharmacognosy, Techniques and Experiments, 11th ed. Nirali Prakashan: Pune. 2004.
14. OECD Guidelines for the testing of chemicals, revised draft guidelines 423: Acute oral toxicity- Acute toxic class method, revised document, CPCSEA, Ministry of Social Justice and Empowerment, Govt. of India: 2000.
15. Radhika T, Mahendar P, Venkateshan A, Reddy ARN, Narsimha Reddy Y, Sadanandam et al. Hypoglycemic Activity of Red Kino Tree in Normal and Streptozotocin Induced Diabetic Rats. Int. J Pharmacol. 2010; 6(3): 301-305.
16. Jayakar B, Suresh B. J Ethnopharmacol. Antihyperglycemic and hypoglycemic effect of *Aporosa lindleyana* in normal and alloxan induced diabetic rats. 2003; 84(2-3) : 247-9.
17. Teixeira CC, Fuchs FD, Costa AP, Mussnich DG, Ranquetat CG, Gataldo G. Diabetes Care: 1990.13; p-907.
18. Porchezhian E, Ansari SH, Shreedharan NK. Antihyperglycemic activity of *Euphrasia officinale* leaves. Fitoterapia. 2000; 71(5); 522-526.
19. Aydin A, Fahrettin K, Hulusi K, Huseyin U, Yalcin T, Muzaffer U.). Hypoglycemic effect of Zizyphus jujube leaves. J Pharm Pharmacol: 1995; 47; 72-74.