JGTPS, 2015, Vol. 6(3): 2765 - 2769

ISSN- 2230-7346

Journal of Global Trends in Pharmaceutical Sciences

Journal home page: www.jgtps.com

EVALUATION OF BLOOD SUGAR LOWERING PROPERTY OF AQUEOUS EXTRACT OF *XIMENIA AMERICANA* IN ALLAXON INDUCED DIABETIC RATS

P. Vasanth Kumar*[1], K.Vijaya[1] M.Siddaiah[2]

[1]*Pacific University, Udaipur, Rajasthan, India.*

[2]*P. Rami Reddy Memorial College of Pharmacy Kadapa, Andhra Pradesh, India.*

ABSTRACT

Now a day there is many allopathic drugs are available to treat this disease. But all these agents causing serious side effects after prolong use. Alloxan is the most commonly employed agent for the induction of experimental diabetic animal models of human insulin-dependent diabetes mellitus. The hypoglycemic effect of aqueous extract of leaves *Ximenia Americana* (AEXA) was evaluated in normal glucose fed and Allaxon induced diabetic rats. Oral administration of extract (250 and 500mg/kg body wt) for 7 days resulted in a significant reduction in blood glucose level. The effect was compared with 10mg/kg (i.p) glibenclamide.

Keywords: Aqueous extract of *Ximenia Americana*, Alloxon , Blood sugar lowering activity, Glucose.

INTRODUCTION:

Diabetes mellitus (DM) is a chronic disease caused by insufficient production of insulin by pancreatic gland and decrease in absorption glucose by the muscles in the systems and caused increase the concentration of glucose in blood [1]. It is also produced due to the hereditary characters. Due to increase glucose level in blood causes various deficiencies and hampers the normal Physiological effects of the human system like blood vessels and nerves system etc [2]. It is projected that the diabetic is the main disease which can increase the deaths retain next coming 25 years in Asian committee and Africans [3]. Now days there are many allopathic drugs are available to treat this disease. But all these agents causing serious side effects after prolong use.

Address for correspondence

P. Vasanth Kumar*
Pacific University, Udaipur, Rajasthan, India.
E-mail: pvasanthtpt@gmail.com

Hence to overcome these adverse effects such as Hematological effects, coma, disturbance of liver and kidney etc [4]. Hence many traditional plants medicines are using throughout the world to treat the diabetic diseases [5]. When compared with synthetic drugs, the plant drugs have less toxic effects with fewer side effects [6]. *Ximenia Americana* is commonly known as Mogi. In Indian system of Medicine, the various plants parts like leaves, fruits etc are using treat the diabetes, mouth ulcers etc [7]. Hence the present investigation was under taken to evaluate the anti-diabetic activity of aqueous extract of leaves of *Ximenia Americana* in a Alloxan induced diabetic rates to confirm the pharmacological evidence in support of Folklore claim [8].

MATERIALS AND METHODS

Plant Materials

Fresh leaves were collected from Tirumala hills, Chittoor district, Andhra Pradesh, India and authentified by Dr. K. Madhava Chetty, Assistant Professor, Department of Botany S.V. University, Tirupati, and Andhra Pradesh, India. Voucher Specimen No. 1295 is kept for further future reference at S.V. University, Andhra Pradesh, India.

Extraction of Plant Materials

The collected fresh leaves were shade dried and powdered in a mechanical grinder to get coarse powder and then passed through sieve 60 mesh to get uniform powder granules. The Powdered leaves (100g) were defatted with hexane and later extracted with water by using Soxhlet extractor at 100^0c 18 hours. The solution was subjected to evaporation by using rotary evaporator until becomes reddish residue. The extract was evaporated to dryness, gave a residue 18% W/W and it was kept in desiccator for further studies and to remove moisture content completely [9]. Phytochemical screening of preliminary phytochemicals of AEXA was carried by using standard procedures [10].

Animals

Wistar albino rats (200-250g) of both sexes were purchased from Sri Venkateswara Enterprises, Bangalore. Before and during the experiment rats were fed with standard diet (Gold Mohr, Lipton India Ltd). After randomization in to various groups and before initiation of experiment, the rats were acclimatized for a period of 14 days under standard environmental conditions of temperature, relative humidity, and dark/light cycle. Animals described as fasting were deprived off food and water for 16 hours ad *libitum*. Ethical clearance for animal study was obtained from the institutional animal ethics committee. (IAEC/ACP/1220/a/08/CPCSE 08).

Chemicals:

Allaxon was procured from Himedia chemical company Hyderabad. Glucose strips procure from M/S Boechringer Mannherim India private limited. The solvents and reagents were analytical grade and purchased from local supplier.

EXPERIMENTAL

An acute toxicity study was carried out to determination of LD_{50} values by using different doses 5, 50,300 and 5000mg/kg body weight of the extract in healthy adult female Swiss albino mice weighing between 250-25 body weights were selected for oral acute toxicity study. This study was carried out as per the OECD guidelines Number 401 [11]. From the toxicity study, it was indicated that the extract is safe up to dose 2.0g/kg body weight. It is very safe for further studies at different doses.

Hypoglycemic effect of AEXA on blood glucose levels in Normoglycemic rats

In this study the entire groups of animals were fasted over Night and administered with respective drugs as per the mentioned dosage schedule. Animals were divided in to three groups of six rats in each group. Group – I, II and II receives 1% Tween80 (3ml/kg) 150,300 and 600 mg/kg orally of aqueous extract of XA respectively. Blood glucose levels were determined at O hour (before drug administration) 60, 180 min, after drug administration [12].

Oral Glucose Tolerance Test

Effect of aqueous extract of XA on blood glucose level on glucose fed hyperglycemic rats was carried out in animal models**.** In this study, the entire groups of animals were fasted overnight and administered with respective drugs as per the mentioned dosage schedule. Animals were divided into five groups of six rats in each group. Group-I, II, III and IV. Group I receives glucose 5g/kg only, Group II receive glibenclamide 5mg/kg i.;p. Group III ,IV and group V received 150,300 and 600mg/kg. Glucose 1500gm/kg body weight administered orally, half an hour before administration of standard and test extract respectively. Blood glucose levels were determined at (before glucose challenge) 0, 60,180,300 minutes after glucose administration [12].

Anti-diabetic study

Effect of aqueous extract of XA on blood glucose level in Alloxan induced diabetic rats**.** Different groups of rats were used to study the effects of AEXA. The rats were divided into five groups each consisting of six rats.

Group-I Normal control animals received 1% sodium Tween803ml /kg body wt. per orally

Group-II Alloxan (150 mg/kg body wt) induced diabetic animals received in 1% Tween80 3ml/kg body wt. per orally.

Group-III diabetic animals received glibenclamide 5mg/kg body wt. per orally and served as standard.
Group-IV diabetic animals received 150mg/kg body wt of AEXA and

G**roup-V** diabetic animals received 300mg/kg, body wt. of AEXA per orally.

G**roup-VI** diabetic animals received 600mg/kg, body wt. of AEXA per orally. Significant hyperglycemia was achieved within 48 hours after Alloxan (150mg/kgb.w. i.v.) injection induced diabetic rats with more than 150mg/dl of blood glucose were identified as 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 form the fasted animals prior to the treatment with above scheduled and after administration, at each day up to 7 days . For glucose determination, blood was obtained shipping tail with sharp razor. Then the blood glucose levels were determined by using Haemo - Glukotest (20-800R) glucose strips supplied by M/S Boechringer Mannherim India

Limited. These methods which permit the measurement of blood glucose levels with minimum injury to rat, was previously validated by comparison with glucose oxidase method [13, 14].

Statistical Analysis

The data were analyzed as mean ± SEM and statistical significance between extract treated and diabetic control groups analyzed by using one way analysis of variance followed by Turkey-Kramer multiple comparison test. $P < 0.05$ was considered statistically significant.

RESULTS

Aqueous extract of plant material gave residue of 18%w/w. Preliminary phytochemical studies of AXSA revealed that the presence of alkaloids, tannins flavanoids, proteins, carbohydrates saponins, steroidal, glycosides [15].

Acute oral toxicity study

The results of the acute oral toxicity indicated that the aqueous extract of *Ximenia Americana* leaves were not lethal up to a dose of 5000mg/kg body weight. From the toxicity study it was observed and concluded to select $1/8^{th}$ and $1/4^{th}$ of 625mg/kg dose ie.1250 and 2500mg/kg orally was selected for anti-diabetic. The results presented in Table 1.

Normoglycemic rats

Effect of aqueous AEXA on blood glucose in normoglycemic rats at dose 150mg/kg and 600mg/kg of AEXA on fasting blood sugars level were determined in normal rats at various time interval is shown in table-2.The mean blood glucose level decrease from 77.83 to 77.60 mg/dl to 78. 0mg/dl at dose of 300mg/kg body weight of aqueous extract of XA and 77.67 to 76.60, mg/dl to 75.80mg/dl at dose of600mg/kg body weight.

Oral Glucose Tolerance Test

Effect of AESA on blood glucose level in glucose fed hyperglycemic rats at dose 300mg/kg and 500mg/kg level were assessed and they were presented table3 at various time intervals. The blood glucose levels decreased from 80.50±0.99mg/dl to 78.50 ± 0.62mg/dl at 300mg/kg body weight and 81.00mg/dl to 78.16 ± 0.96* mg/dl at 500mg/kg body Weight.

Anti-diabetic study

Effect of AEXA on blood glucose level in Alloxan induced diabetic rats was carried out. The blood sugar lowering effect of the extracts on the blood sugar level on diabetic rats is shown in table – 4. The blood glucose level of diabetic animal significantly ($P<0.05$) reduced from 208.37mg/dl to 130.57 mg/dl at 300mg/kg body wt.of Aq. extract of XA and 206.37 mg/dl to 123.57 mg/dl at 600mg/kg body wt. of aqueous extract of XA. These results are comparable with o., 5mg/kg of glibenclamide.

DISCUSSION AND CONCLUSION

In the recent times many traditionally used medicinally important plants were tested for their anti-diabetic potential by various investigators in experimental animals. These properties were attributed to different formulations, extracts and active principles. Working on the same line, we have undertaken a study on *Ximenia Americana* for its anti-diabetic Property. The values are expressed as mean ± SEM. n = number of animals in each group. Statistical significant test for comparison was done by ANOVA, followed by Turkey-Kramer multiple tests. The blood glucose values of groups are compared with initial value. The AEXA at a dose of 300mg/kg body weight per orally did not significantly suppress blood glucose levels in overnight fasted normoglycemic animals. The same effect was observed at a higher dose level of 600mg/kg body weight per orally normoglycemic animals after 1^{st}, 2^{nd} and 3^{rd} hour of oral administration, when compared with control group of animals[16]. The AEXA showed significant improvement in glucose tolerance in glucose fed hyperglycemic normal rats. Such an effect may be accounted for, in part, by a decrease in the rate of intestinal glucose absorption, achieved by an extra pancreatic action including the stimulation of peripheral glucose utilization or enhancing glycolytic and glycogenic process with concomitant decrease in glycogenolysis and glyconeogenesis [17]. However, the effect was less significant when compared to standard drug glibenclamide. Alloxan is the most commonly employed agent for the induction of experimental diabetic animal models of human insulin-dependent diabetes mellitus. There is increasing evidence that Alloxan caused diabetes by selective destruction of pancreatic insulin secreting beta cells which makes less active and leads to poor glucose utilization by tissues. This indicates that the extract may possess as insulin like effect on peripheral tissues by either promoting glucose uptake or metabolism, by inhibiting hepatic gluconeogenesis or absorption of glucose in to the muscles and adipose tissues by stimulation of regeneration process and revitalization of the remaining beta cells. From the Phytochemical analysis it was found that the major chemical constituents of the extract and some of this active principle including flavanoids are known to be used for the treatments of diabetes [18-20]. On the basis of the above evidences it is possible that the presence of flavanoids and tannins are responsible for the observed anti-diabetic activity

Treatment	Dose (mg/kg body wt)	No. of animals	No. of Survival	No. of death	Percentage of morality	LD_{50} value
Control	1% Tween80	10	10	0	0	-----
AEXA	100	10	10	0	0	-----
	150	10	10	0	0	-----
	300	10	10	0	0	-----
	5000	10	10	0	0	>5.0/kg,bw

Table 2. Effect of AEXA on blood glucose in normoglycemic rats

Group	Dose mg/kg	Blood glucose Levels (mg/dl)		
		Initial	60min	180 min
Group 1	3ml	79.10 ± 0.66	78.03 ± 0.61	79.60 ± 0.43
Group II	150 mg	77.83 ± 0.89	76.83 ± 0.84	77.06 ± 0.44
Group III	300 mg	77.60 ± 1.10	74.15 ± 0.65	76.01 ± 0.85
Group IV	600 mg	78. 0 ± 0.66	76.03 ± 0.61	77.60 ± 0.43

The values are expressed an mean ± SEM. n = number of animals in each group. Statistical significant test for comparison was done by ANOVA, followed by Turkey-Kramer multiple tests. The 3hours and 5hours min values are compared with initial value.

Table 3. Effect of AEXA on blood glucose in rats

Group	Treatment Dose mg/kg	Blood glucose Levels mg/dl				
		O hour	1hour	3hour	5hour	
I	1.5gm/kg	83.34 ± 0.46	116.83 ± 1.64	103.34 ± 1.11	83.50± 0.66	
II	GBM	76.50 ± 0.81	110.50 ± 1.84*	99.34 ± 1.05*	87.50 ± 0.79*	
III	AEXA 150	80.50 ± 0.99	118.34 ± 0.71*	108.60 ± 0.84*	98.50 ± 0.62*	
IV	300	82.50 ± 0.94	117.50 ± 0.63*	107.00 ± 0.34*	88.16 ± 0.96*	

The values are expressed as mean ± SEM. n = number of animals in each group. Statistical significant test for comparison was done by ANOVA, followed by Turkey-Kramer multiple tests. The blood glucose values of groups are compared with initial value.

REFERENCES:

1. Syed Mansoor Ahmed, Anti-Diabetic Activity of *Terminalia catappa* Linn. Leaf Extracts in Alloxan-Induced Diabetic Rats. *Iranian J Pharmacol Therapeutics*, 4, 2005, 36-39.
2. Larmer J. Insulin and oral hypoglycemic drugs, glucogan in, Gilman AG, Goodman LS. Rall TW, Murad F, Editors. The Pharmacological basis of therapeutics. 7th ed. Newyork, Macmillan Publishing, 1985, 1490.
3. Moming A. Role of indigenous medicine in primary health care. Proceeding of first international seminar on Unani Medicine, New Delhi, 1987, 54
4. Kirti K, Joanna MT, Shamim IA, Eva MK, Rakesh C. Introduction to diabetes mellitus. Landes Bioscience and Springer Science Business media, LLC, 2012, 1-11.
5. Madhava Chetty K, SivajiK, Tulasi Rao, Flowering Plants of Chittoor District –Andhra Pradesh, India, 1st Ed. Students offset printers, Tirupathi, 2008, 85.
6. Pulok KM. Quality control Herbal Drugs-An Approach to Evaluation of Botanicals, 1st ed., Business Horizons, New Delhi. 2010, 39-55.
7. Yasodha Krishna, Ravindra Reddy K, Rupesh K, Raghavendra D, Siddaiah M. *J Pharmacy and Chemistry*, 2(3), 2008, 156-160.
8. Khandelwal KR. Practical Pharmacognosy, 10th ed. Nirali Prakashan, 2003, 123.
9. Niren NS, Nayak BS. Experimental Pharmacognosy.1st edn, S.Vikas & Co, Jalandar, 2009, 190- 199.
10. Organization for Economic co-operation and Development. (OECD).OECD guidelines for testing of chemicals for acute oral toxicity, OECD no.401.

11. Lanjhiyana and M Karuppaih. Antidiabetic activity of methanolic extract of stem barks of *Elaeodendron glaucum* Pers in alloxanized rat model. *Advanced in applied Science Research*, 2(1), 2011, 47-62.
12. Santosh Ghule et al. Anti-diabetic activity if *Celosia arhentea* root in Streptozocin induced diabetic rats. *International Journal of Green Pharmacy,* 101, 2010, 206-211.
13. Chakravarthy BK, S Gupta, SS Gambir and KD Gode. Pancreatic β-cell regeneration, novel antidiabetic mechanism of *Pterocarpus marsupium* Roxb. *Indian Journal of Pharmacology*, 12, 1980, 123-127.
14. Siddaiah, M.,Phytochemical screening and anti-diabetic activity of methanolic extract of leaves of *Ximenia americana* in rats. *International Journal of Innovative, Pharmaceutical Research*, 2(1), 2011, 78-83.
15. Murthy BK, Evaluation of hypoglycemic and anti-hyperglycemic effect of *Datura metel* (Linn.) seeds in normal and alloxan induced diabetic rat. *Journal of Ethnopharmacology*, 2004, 91(1), 95-98.
16. BK Choudhary and NG Bandyopadhyay. Comparative evaluation of hypoglycaemic activity of some Indian medicinal plants in Alloxan diabetic rats. *Journal of Ethnopharmacology*, 84(1), 2003, 105-108.
17. Kumar R, Patel DK, Anti-diabetic activity of alcoholic root extract of *Caesalpinia digyna* in streptozotocin-nicotinamide induced diabetic rats. *Afr Health Sci*, 2010, 276-282.
18. Daisy P, Feril G, Jeeva K. Evaluation of anti-diabetic activity of various extracts of *Cassis auriculata* Linn. Bark on Streptozotocin-induced diabetic Wistar Rat. *Int J Pharm Pharm Sci*, 4(4), 2012, 312-318.
19. Akhani SP, Viswakarma SL, Goyal RK. Anti-diabetic activity of *Zingiber officinale* in streptozotocin-induced type I diabetic rats. *J Pharm Pharmacol*, 56(1), 2004, 101-5.
20. Thabrew I, Arambewela L. Antidiabetic activity of *Trichosanthes cucumerina* in normal and streptozotocin-induced diabetic rats. *Int J Biol Chem Sci*, 3(2), 2009, 287-296.

How to cite this article:

P. Vasanth Kumar*, K.Vijaya, M.Siddaiah, Evaluation of blood sugar lowering property of aqueous extract of *ximenia americana* in allaxon induced diabetic rats, 6 (3): 2765 – 2769 (2015)