National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

Effect of *Aloe vera* leaf extract on blood glucose levels in alloxan induced diabetic rats

Manjunath K[1], Bhanu Prakash G[1], Subash KR[1], Tadvi NA[2], Manikanta M[3], Umamaheswara Rao K[1]

[1]Department of Pharmacology, SVIMS-Sri Padmavathi Medical College for Women, SVIMS University, Tirupati, Andhra Pradesh, India, [2]Department of Basic Medical Sciences, College of Medicine, Majmaah University, Al Majmaah, Kingdom of Saudi Arabia,[3]Department of Pharmacology, E. S. I. Medical College, Hyderabad, Telangana, India

Correspondence to: K. Manjunath, E-mail: manjunathsanju@gmail.com

Received: July 04, 2016; **Accepted:** July 13, 2016

ABSTRACT

Background: The prevalence of diabetes is rapidly rising worldwide at an alarming rate. Over the last 30 years, the status of diabetes has changed from being considered as a mild disorder of the elderly to one of the major causes of morbidity and mortality affecting the youth and middle aged people. *Aloe vera* has been used in folk medicine as a remedy for various diseases. It is extensively studied in treating diabetes mellitus. **Aims and Objectives:** This study evaluates the hypoglycemic effect of *A. vera* leaf dried powder and compares it with standard Metformin in alloxan-induced diabetic rats. **Materials and Methods:** Diabetes mellitus was experimentally induced in rats by intraperitoneal injection of alloxan monohydrate at a dose of 150 mg/kg. A pure extract of *A. vera* leaf was given orally once daily for 5 weeks in three graded doses of 100, 200, 400 mg/kg and compared with control (2 ml distilled water) and standard (metformin 50 mg/kg) **Results:** The elevated blood glucose levels in diabetic rats were reduced by the treatment with *A. vera* leaf extract at doses of 200 mg/kg and 400 mg/kg which was comparable to 50 mg/kg of metformin with no statistically significant difference ($P < 0.0001$). **Conclusion:** Our study concludes that *A. vera* leaf extract has a favorable effect in reversing alloxan induced hyperglycemia in rats.

KEY WORDS: Antidiabetic; Hypoglycemia; *Aloe vera*; Alloxan; Metformin; Rats

INTRODUCTION

With the largest number of diabetic subjects in the world, India becomes the "diabetes capital of the world."[1] This epidemic, chiefly of Type 2 diabetes, is brought on by environmental and behavioral factors like overly rich nutrition, obesity and sedentary lifestyle with at least a part due to genetic factors.[2] Although the prevalence of microvascular complications of diabetes like retinopathy and nephropathy are comparatively lower in Indians, the prevalence of premature coronary artery disease is much higher when compared to other ethnic groups. The shift in the age of onset of diabetes to a younger age in the recent years has been the most devastating trend with a major impact on nation's health and economy.[3] According to an estimation of International Diabetes Federation, the total number of diabetic subjects in India would rise to 69.9 million by 2025.[4]

Access this article online	
Website: www.njppp.com	Quick Response code
DOI: 10.5455/njppp.2016.6.0718613072016	

Conventionally, the management protocol of diabetes involves non-pharmacological (diet, exercise, and surgery) and/or pharmacological means (insulin and oral hypoglycemic agents). This approach of simply using insulin and oral drugs to control diabetes mellitus is not only costly but also inadequate and associated with a lot of

health risks and complications, ultimately leading to a lack of compliance.[5,6] For the last few decades, the WHO has been supporting traditional medicine program by realizing the fact that medicinal plants are of great importance to the health of individuals and communities.[7] Among traditional systems of medicine, the unique pro-nature vision of Ayurveda is gaining global relevance.[8]

Plants extracts have been used for a long time as a traditional remedy for diabetes in many parts of the world. For instance, *Aloe vera* (*Aloe barbadensis* Miller), a perennial succulent xerophyte, with elongated pointed fleshy leaves consisting of two parts, an outer skin (green rind) and an inner pulp (colorless mucilaginous gel), has been widely used as a healing plant in the history of mankind.[9] Leaf exudate and mucilaginous gel of *A. vera* possess anti-inflammatory, antifungal, antibacterial, anticancer, antioxidant, cytoprotective, cardiac stimulatory, and immunomodulatory activities. It has also been extensively studied in treating diabetes mellitus in developing countries.[10] The dried sap of *A. vera* is a traditional remedy for diabetes in the Arabian peninsula.[11] Conversely, the plasma glucose levels were reported to rise in alloxan-induced diabetic rats by *A. vera* gel.[12] This type of controversial report on the action of *A. vera* in diabetes was probably due to differences in the part of the plant used or due to the model of diabetes chosen.[13,14] This study is done to evaluate and compare the antidiabetic activity of leaf extract of *A. vera* with the standard antidiabetic drug, Metformin in albino rats.

MATERIALS AND METHODS

A. vera Leaf Extract

A. vera spray dried powder was obtained from Bhaskara Biotech, Hyderabad.

Drugs and Chemicals

Metformin pure powder (Franco-Indian Pharmaceuticals Pvt. Ltd., Mumbai) was used as the standard drug. Alloxan for inducing diabetes in rats was obtained from Rolex Chemical Limited, Mumbai.

Animals

Adult healthy albino rats of either sex weighing between 150 g and 200 g were procured from the National Institute of Nutrition, Hyderabad and housed in the air-cooled central animal house of Kamineni Institute of Medical Sciences, Narketpally, Nalgonda where this study was conducted. They were allowed to get acclimatized to laboratory conditions (12:12 h dark/light, 25-2°C) for a period of 7 days. They had free access to food and water *ad libitum*. This study was done during August 2012 to February 2013 after obtaining prior approval from the Institutional Animal Ethics Committee. All animals were handled according to the guidelines of CPCSEA, Government of India.

Induction of Diabetes

Diabetes was induced in rats with normal blood glucose levels by intraperitoneal (i.p.) injection of alloxan monohydrate - 150 mg/kg body weight. After 2 h of alloxan injection, dextrose 10% was fed to all rats *ad libitum* to prevent hypoglycemia. After 7 days, fasting blood glucose of all rats was estimated and those with blood glucose levels of >250 mg/dl were considered as diabetic and selected for further study. Their blood glucose levels were estimated daily for 6 days and then weekly for 5 weeks.

Treatment Schedule

All the rats successfully induced with alloxan were randomly allocated into five groups of 6 animals each and treated once daily for 5 weeks as follows:

- Group I received control (1 ml distilled water orally)
- Group II received standard antidiabetic (metformin 50 mg/kg orally)
- Groups III, IV, and V received *A. vera* leaf extract in three graded doses of 100, 200 and 400 mg/kg, respectively.

Determination of Blood Glucose

All the diabetic rats after giving control, standard and three graded doses of *A. vera* leaf extract were kept fasting overnight, and their fasting blood glucose levels were determined by pre-standardized glucometer with reagent strips by glucose oxidase method daily in the 1st week after induction of diabetes and then once a week for 5 weeks.

Statistical Analysis

The data were presented as mean ± standard error of the mean (SEM). One-way analysis of variance followed by *post-hoc* least significant difference analysis at $P < 0.05$ was performed using the Statistical Package for Social Science (SPSS) version 19 to compare all treated groups. $P < 0.05$ was considered statistically significant.

RESULTS

Administration of alloxan monohydrate (50 mg/kg i.p.) produced hyperglycemia that was maintained almost up to 5 weeks in Group I (control) fed with distilled water. At the end of 5 weeks, *A. vera* leaf extract reduced the hyperglycemic effect of alloxan in Groups IV and V (at 200 mg/kg and 400 mg/kg doses, respectively) which was statistically highly significant ($P < 0.0001$) when compared to the control (Group I), but in Group III (at 100 mg/kg) it did not show significant reduction in the blood glucose levels

which was comparable to the control (Group I) as shown in Table 1.

The standard drug (metformin 50 mg/kg) showed statistically highly significant reduction ($P < 0.0001$) in blood glucose levels in Group II at the end of 5 weeks in comparison to control (Group I). The hypoglycemic effect of *A. vera* at 200 mg/kg and 400 mg/kg was comparable to metformin (50 mg/kg) with no statistically significant difference between Groups II, IV and V after 5 weeks (Table 1).

The reduction in blood glucose level was evident from day 3 with Metformin and *A. vera* leaf extract at doses 200 mg/kg and 400 mg/kg in Groups II, IV and V, respectively, which sustained till the end of 5 weeks (Figure 1).

DISCUSSION

The existing antidiabetic drugs address one of the key symptoms of Type 2 diabetes, i.e. hyperglycemia but most of them, on the other hand, promote weight gain. Further, due to various reported adverse effects of currently used antidiabetic drugs, there exists a need for their substitution with natural products which have a better hypoglycemic effect and fewer side effects. Large numbers of plants and herbs have been known for their antidiabetic effects through traditional medicine but in this era of evidence-based medicine; their introduction into modern therapy can only be done after thorough pharmacological testing by preclinical and clinical trials.

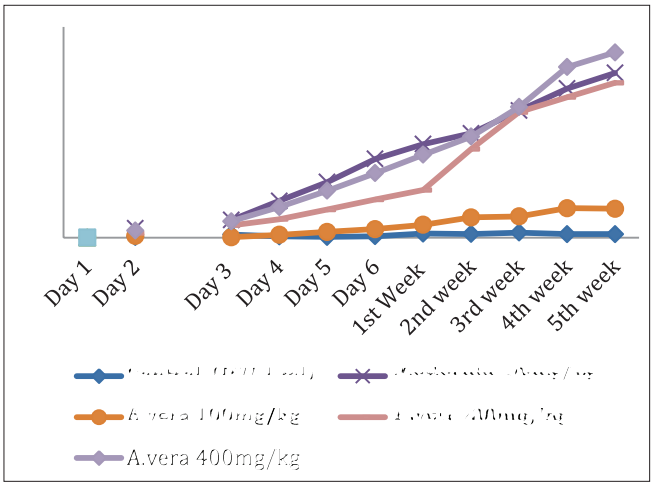

Figure 1: Percentage change in blood glucose levels at different intervals in between groups

Among several plants, *A. vera* with hypoglycemic trace elements such as Cr, Zn, and Mn which potentiate insulin action was a strong candidate, as it has been used for treating diabetes in Arab and other developing countries.[15] It has been reported to produce antidiabetic effect by multiple mechanisms, but there were some controversies on its antihyperglycemic effect. Hence, this study aimed to evaluate and compare the hypoglycemic effect of *A. vera* leaf extract with metformin in alloxan induced diabetic rats. Alloxan acts as a cytotoxic agent on the insulin secreting β cells of pancreas and effectively induces diabetes mellitus in a wide variety of animal models which share many features with that of human type.

In our present study, three graded doses of *A. vera* (100 mg/kg, 200 mg/kg and 400 mg/kg orally) were compared with metformin (50 mg/kg orally) and control (distilled water 1 ml orally). The antidiabetic effect of *A. vera* at 200 mg/kg (Group IV) and 400 mg/kg (Group V) was comparable to metformin, 50 mg/kg (Group II) with no statistically significant difference between these groups (Table 1). Oral administration of *A. vera* leaf extract reduced the blood glucose levels in rats (mean ± SEM) from 257 ± 9.9 (day 1) to 106 ± 3.8 (5th week) at the dose of 200 mg/kg (Group IV) while at the dose of 400 mg/kg (Group V) it reduced from 258 ± 9.6 (day 1) to 76.6 ± 1.8 (5th week) in comparison to control (Group I) which caused a decrease from 255 ± 10.41 (day 1) to 251.5 ± 7.69 (5th week). Moreover, 50 mg/kg of metformin (Group II) reduced the blood glucose levels from 251 ± 8.9 (day 1) to 94 ± 6.8 (5th week) as shown in Table 1.

At the end of 5th week, the percentage of hypoglycemic effect in Group IV (*A. vera* 200 mg/kg) was 58.75, Group V (*A. vera* 400 mg/kg) was 70.31 and in Group II (Metformin 50 mg/kg) was 62.54. These results suggest that *A. vera* leaf extract at 200 mg/kg and 400 mg/kg produced hypoglycemic effect comparable to that of metformin 50 mg/kg in alloxan induced diabetic rats (Figure 1).

The results of this study are in accordance with the results of earlier studies which indicated that *A. vera* gel extract was

Table 1: Mean blood glucose levels between different groups

Group	Day 1	1st week	2nd week	3rd week	4th week	5th week
I	255±10.41	251±9.80	251.3±8.89	250.1±7.71	251.5±7.73	251.5±7.69
II	251±8.9	161.8±10.1*	151.6±11.1**	130±8.7***	109±7.7***	94±6.8***
III	250±6.83	237.8±6.34	230.8±7.04	229.8±6.55	222±8.14	222.5±9.17
IV	257±9.9	210.5±7.05	170.5±4.8*	143.6±2.8**	120±4.2***	106±3.8***
V	258±9.6	176.8±2.3*	159±2.8**	130±2.9***	91±2.5***	76.6±1.8***

Data presented as mean±SEM, *P<0.05 as compared to control, **P<0.01 (significant), ***P<0.0001 (highly significant). SEM: Standard error of the mean

also effective in lowering hyperglycemia in streptozotocin-induced rats.[16,17] In another study, it was concluded that *A. vera* gel extracts not only normalized the fasting blood glucose and plasma insulin levels but also reduced the concentrations of cholesterol, triglycerides, and free fatty acids in the plasma, liver, and kidney of streptozotocin-induced diabetic rats.[18]

Another study reported that *A. vera* extract prevented hyperglycemia in rabbits treated with alloxan.[19] It was also confirmed that treatment with *A. vera* juice filtrate resulted in a significant improvement in serum glucose in diabetic rats as compared to non-diabetic control.[20]

The hypoglycemic effect of *A. vera* leaf extract was by enhancing glucose metabolism. It was further proposed that the glucose lowering effect of *A. vera* could be explained by an antioxidant mechanism because it attenuated oxidative damage in the brains of streptozotocin-induced mice and reduced peroxidation levels in the kidneys of streptozotocin-induced diabetic rats.[21]

CONCLUSION

From our study, it may be concluded that *A. vera* leaf extract has antidiabetic action thereby validating the rationale of its use in indigenous medicine. Further studies are required to identify the probable mechanism of action to establish its hypoglycemic effect.

REFERENCES

1. Mohan V, Madan Z, Jha R, Deepa R, Pradeepa R. Diabetes-social and economic perspectives in the new millennium. Int J Diabetes Dev Ctries. 2004;24:29-34.
2. Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. Nature. 2001;414(6865):782-7.
3. Mohan V, Sandeep S, Deepa R, Shah B, Varghese C. Epidemiology of type 2 diabetes: Indian scenario. Indian J Med Res. 2007;125(3):217-30.
4. Sicree R, Shaw J, Zimmet P. Diabetes and impaired glucose tolerance. In: Gan D, editor. Diabetes Atlas. International Diabetes Federation. 3rd ed. Belgium: International Diabetes Federation; 2006. p. 15-103.
5. Milton JB. Diabetes: The New Approach. New York: Grosset and Dunlap Publishers; 1976. p. 15-7.
6. Okolie UV, Okeke CE, Oli JM, Ehiemere IO. Hypoglycemic indices of *Vernonia amygdalina* on postprandial blood glucose concentration of healthy humans. Afr J Biotechnol. 2008;7(24):4581-5.
7. Nwanjo HU. Efficacy of aqueous leaf extract of *Vernonia amygdalina* on plasma lipoprotein and oxidative status in diabetic rat models. Niger J Physiol Sci. 2005;20(1-2):39-42.
8. Singh RH. Exploring larger evidence-base for contemporary Ayurveda. Int J Ayurveda Res. 2010;1(2):65-6.
9. Lanjhiyana S, Garabadu D, Ahirwar D, Bigoniya P, Rana AC, Patra KC, et al. Antihyperglycemic potential of *Aloe vera* gel in experimental animal model. Ann Biol Res. 2011;2(1):17-31.
10. Helal EGE, Hasan MHA, Mustafa AM, Al-Kamel A. Effect of *Aloe vera* extract on some physiological parameters in diabetic albino rats. Egy J of Hosp Med. 2003;12:53-61.
11. Yeh GY, Eisenberg DM, Kaptchuk TJ, Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. Diabetes Care. 2003;26(4):1277-94.
12. Koo MW. *Aloe vera*: Antiulcer and antidiabetic effects. Phytother Res. 1994;8:461-4.
13. Okyar A, Can A, Akev N, Baktir G, Sütlüpinar N. Effect of *Aloe vera* leaves on blood glucose level in type I and type II diabetic rat models. Phytother Res. 2001;15(2):157-61.
14. Saghir AJ, Hasan SS, Nadeem A, Kalsoom S, Iqbal J. Hypoglycemic effect of *Aloe vera* extract in alloxan-induced diabetic albino rats. Med J Islamic World Acad Sci. 2011;19(3):127-30.
15. Mohamed EA. Antidiabetic, antihypercholestermic and antioxidative effect of *Aloe vera* gel extract in alloxan induced diabetic rats. Aust J Basic Appl Sci. 2011;5(1):1321-7.
16. Rajasekaran S, Sivagnanam K, Ravi K, Subramanian S. Hypoglycemic effect of *Aloe vera* gel on streptozotocin-induced diabetes in experimental rats. J Med Food. 2004;7(1):61-6.
17. Noor A, Gunasekaran S, Manickam AS, Vijayalakshmi MA. Antidiabetic activity of *Aloe vera* and histology of organs in streptozotocin induced diabetic rats. Curr Sci. 2008;94(8):25.
18. Rajasekaran S, Ravi K, Sivagnanam K, Subramanian S. Beneficial effects of *Aloe vera* leaf gel extract on lipid profile status in rats with streptozotocin diabetes. Clin Exp Pharmacol Physiol. 2006;33(3):232-7.
19. Akinmoladun AC, Akinloye O. Prevention of the onset of hyperglycaemia by extracts of *Aloe barbadensis* in rabbits treated with alloxan. AJB. 2007;6(8):102.
20. Mohamed AE, Abdel-Aziz AF, El-Sherbiny EM, Mors RM. Anti-diabetic effect of *Aloe vera* juice and evaluation of thyroid function in female diabetic rats. Biosci Res. 2009;6(1):28-34.
21. Boudreau MD, Beland FA. An evaluation of the biological and toxicological properties of *Aloe barbadensis* (miller), *Aloe vera*. J Environ Sci Health C Environ Carcinog Ecotoxicol Rev. 2006;24(1):103-54.

How to cite this article: Manjunath K, Prakash GB, Subash KR, Tadvi NA, Manikanta M, Rao KU. Effect of *Aloe vera* leaf extract on blood glucose levels in alloxan induced diabetic rats. Natl J Physiol Pharm Pharmacol 2016;6(5):471-474.

Source of Support: Nil, **Conflict of Interest:** None declared.