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Research Article

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EVALUATION OF HYPOGLYCEMIC AND ANTI ATHEROGENIC EFFECT OF *Aloe vera* IN DIABETES MELLITUS

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ABSTRACT

Diabetes is a metabolic syndrome characterized by hyperglycemia, hyper cholesterolemia and hyper triglyceridemia. Hence, there is a need to search the anti diabetic drugs which apart from lowering the blood glucose levels can also modify the atherogenic lipid profile without producing many side effects. Oral administration of *Aloe vera* leaf extract for 21 days in alloxan induced diabetic rabbits produced a significant reduction in fasting blood glucose levels and HbA1c in our study. Also there was significant decrease in serum levels of triglycerides(TG), total cholesterol (TC) , low density lipoprotein cholesterol (LDL-C) and a concomitant increase in high density lipoprotein cholesterol(HDL-C) in *Aloe vera* treated diabetic rabbit indicates the potential of *Aloe vera* as anti diabetic drug. The significant decrease in 'Atherogenic index' in *Aloe vera* treated group shows its protection against cardio vascular diseases.

Keywords: Alloxan, Atherogenic index, *Aloe vera*, Hyperglycemia, Lipid profile.

INTRODUCTION

Diabetes is a complex and multifarious group of disorders characterized by hyperglycemia, that has reached epidemic proportions in the present century.[1] Several drugs such as biguanides and sulfonylureas are presently available to reduce hyperglycemia in Diabetes Mellitus. These drugs have side effects and thus search for a new class of compounds is essential to overcome these problems.[2] Management of diabetes without any side effect is still a challenge to the medical community. There is continuous search for alternative drugs; therefore it is prudent to look for options in herbal medicine for diabetes as well. Traditional anti diabetic plants might provide new oral hypoglycemic compounds which can counter the high cost and poor availability of the present day drugs for the rural population especially in developing countries. India is well known for its herbal wealth; medicinal plants like Trigoenella foenium graecium, Allium sativum, Gymnema slyvestre and Syzigium cumini have been studied for the treatment of Diabetes Mellitus.[3] However, detailed studies on the efficacy ,mechanism of action and safety of plant extracts are needed. The use of *Aloe vera* has been promoted for a large variety of medical disorders.[4] It is believed to be effective in treating skin diseases[5], as anti-inflammatory[6], an antiulcer[7], and in burns[6] and diabetes[8].

Aloe vera (syn.: Aloebarbadensis Miller) belongs to Lilaceal family, of which there are about 360 species. *Aloe vera* is a cactus like plant that grows readily in hot, dry climate and currently, because of increasing demand, is being cultivated in large quantities. The name was derived from Arabic word alloeh meaning bitter, because of bitter liquid found in the leaves. It is also known as "Lily of the desert", the plant of immortality;" the medicinal plant" with qualities to serve as alternative medicine.[3]

The present study was planned to evaluate the hypoglycemic and anti atherogenic effects of *Aloe vera* leaf extract and to compare the effects with glibenclamide, a known hypoglycemic agent.

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MATERIALS AND METHODS

Animals

Albino rabbits of either sex weighing around 1.5-2.5 Kg were used. Animals were procured from disease free animal house of CCS Haryana Agriculture University, Hissar (Haryana, India). They had free access to food and water ad libitum and were maintained under 12:12 Hour light and dark cycles. Institutional Animal Ethical Committee (IAEC) approved the experimental protocol (vide Number/Phy/09/413 dated13.5.09.) and care of animals was taken as per guidelines of CPCSEA, Dept. of Animal Welfare, Govt. of India.

Plant Material

Specimens of *Aloe vera* were collected from Arjun Park, Kurukshetra. Specimens were planted and cultivated in the greenhouse of the faculty of herbal garden of college of Pharmacy, PGIMS, Rohtak. Fresh leaves of this cultivated plant were used in the study.

Preparation of the Extract

Mature, healthy and fresh leaves of *Aloe vera* having a

length of about 75 to 90 cm were washed with fresh water. They were cut transversely into pieces. The thick epidermis was selectively removed. The semi solid gel in the centre of leaf was homogenized. The resulting mucilaginous, thick and straw colored homogenate was lyophilized using 95% ethanol. The filtrate was collected and evaporated to dryness under reduced pressure in rotary evaporator. The residue was stored in dry sterilized small containers at 4° C until further used. An aqueous suspension, which is the form customarily used in folk medicine, was prepared by dissolving suitable amount of ethanol free extract of *Aloe vera* leaf gel to get the desired concentration. The drug solutions were prepared fresh each time and administered by intra gastric route. The dosing schedule was once per day.[9]

Induction of Experimental Diabetes

Experimental Diabetes was induced in rabbits with alloxan(80mg/Kg body weight) dissolved in 0.1M citrate buffer (pH-4.0) and injected intravenously to overnight fasted animals through their marginal ear vein.[10] The animals were monitored for plasma glucose levels at weekly intervals for a month. Animals showing fasting blood glucose levels more than 250mg/dl were considered as diabetics and included in the study.

Experimental Design

The rabbits were divided into four groups of six animals (n=6) in each group as follows:

Group I: Normal control rabbits

Group II: Alloxan induced diabetic rabbits

Group III: Diabetic rabbits received *Aloe vera* leaf gel extract (300 mg/Kg) in aqueous solution for 21 days.

Group IV: Diabetic rabbits given glibenclamide (600ug/kg) in aqueous solution

All the drugs were administered orally (using an intra gastric tube) in a single dose in the morning for 21 days.

Sample collection

Blood samples were collected from the marginal vein of pinna of overnight fasted rabbits. Fasting blood glucose (FBG) was estimated before the treatment (day-1) and after treatment (day-21). Glycosylated Hemoglobin HbA1c and Lipid profile parameters were determined at the end of the study. Initial and final body weight of all rabbits was recorded. The serum was separated immediately and assayed for the following parameters.

1) Blood Glucose: By Glucose oxidase peroxidase method.[11]
2) HbA1c assay was done on auto analyzer using kits by Randox.[12]
3) Total Cholesterol (TC) and HDL-C and Triglycerides (TG) were estimated on auto analyzer (Kone Lab 30i, Trivitron) by enzymatic methods using kits by Randox.[13] The concentrations of low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C) were calculated as described by the formula of Friedewald.[14] The atherogenic index was calculated using the following formula:

$$Atherogenic\ Index = \frac{Total\ serum\ cholesterol}{Total\ HDL - Cholesterol}$$

Statistical analysis

The results were expressed as mean± SEM and were analysed using student t test (SPSS-14) and p value <0.05 was considered significant.

RESULTS AND DISCUSSION

The diabetic control rabbits (Group II) maintained the marked hyperglycemia throughout the experimental period. A significant increase in HbA1c levels was observed in diabetic rabbits as compared to normal rabbits. A significant decrease (28%) was observed in blood sugar levels (fasting) in *Aloe vera* treated group (Group III). Glibenclamide produced significant reduction in fasting blood glucose levels (37%) which was higher as compared to Group III (Table **1**). Alloxan induced diabetic rabbits showed significant reduction in body weight compared with normal (p<0.01). However treatment with *Aloe vera* extract and Glibenclamide significantly recovered the body weight loss in diabetic rabbits (Table **2**).

Table 1. Effect of *Aloe vera* on fasting blood glucose levels (mg/dl) in control and experimental rabbits.

Group& treatment	Day 1	Day 21	% reduction
Gp-I (N. control)	158±17.86	148.80±19.02	---
Gp-II (Diab. control)	265.17±12.42[a]	258±13.01[a]	---
Gp-III (Diab.+ *Aloe vera*)	260±13.62[a]	185.25±12.86[b]	28%
Gp-IV (Diab.+Glibenclamide)	258±14.8[a]	162.98±13.26[b]	37%

Statistical Comparison values are expressed as Mean ± SD. (n=6)
a; p<0.01 as compared to their corr. Levels in Group I.
b; P<0.01 as compare to their corr. Levels on Day 1

Table 2. Showing values of HbA1c and change in body weights (kg) in various groups.

Group& treatment	HbA1c%	Initial weight	Final weight
Gp-I (N. control)	3.10± 0.1	1.89±0.04	1.95±0.05
Gp-II (Diab. control)	6,5± 0.15	1.68±0.03[+]	1.52±0.04[+]
Gp-III (Diab. + AV)	5.25± 0.18	1.63±0.05[+]	1.75±0.05[++]
Gp-IV (Diab. + Glibenclamide)	5.9± 0.21	1.64±0.07[+]	1.86±0.06[++]

+ p<0.01 as compared to normal control (Group-I).
++ p<0.01 as compared to diabetes (Group-II).

The levels of TG, TC and LDL-C were significantly increased, where as HDL-C was significantly decreased in diabetic rabbits (Group II), compared with the normal (Group I) (Table **3**). Supplementation with *Aloe vera* extract led to significant reversal of these changes in diabetic animals. In Glibenclamide treated rabbits the effect was comparable to *Aloe vera* treated animals but HDL-C was not significantly increased by Glibenclamide.

Table 3. Effect of *Aloe vera* on lipid profile of diabetic rabbits.

Group& treatment	TG (mg/dl)	S. Cholesterol (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)
Gp-I (N. control)	91.62±4.7	60.23±5.9	21.22±2.16	20.26±1.66
Gp-II(Diab. control)	110±4.5*	75±4.86*	15.93±1.8*	24.18±1.3*
Gp-III(Diab.+ AV)	104±4.3*	68.16±4.34*	18.54 ±1.38*	19.24±1.6*
Gp-V(Diab.+ glibenclamide)	95±3.8*	63.48±4.64*	16.18±1.26*	18.94±1.6*

** p<0.05 (significant)*

In diabetic control group (Group II) protection was 0% where as in normal healthy animals (Group I); it was 43% (Table **4**). Both Glibenclamide and *Aloe vera* extract produced marked decrease in atherogenic index in diabetic animals. *Aloe vera* extract produced 27% protection where as Glibenclamide produced 38% protection in diabetic rabbits. Graph **1** show the comparison of serum lipid profile in four groups.

Graph 1. comparison of serum lipid profile in four groups

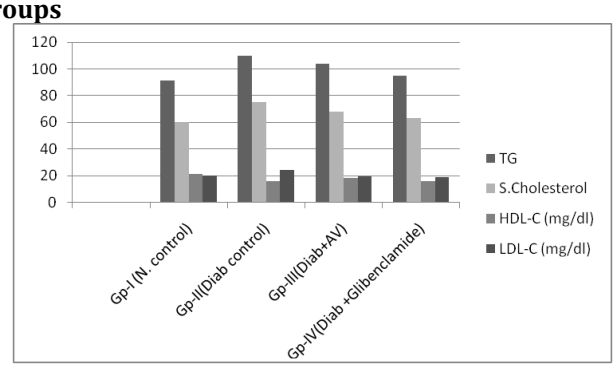

Table 4. Effect of *Aloe vera* on atherogenic index of diabetic rabbits

Groups and treatment	Atherogenic index	Protection rate %
Gp-I (N Control)	2.85	43%
Gp-II(Diabetic control)	5.0	0%
Gp-III (Diabetic on AV)	3.77	26.6%
Gp-IV (Diabetic+ glibenclamide)	3.9	38.2%

n=6 in each group

$$Protection\ \% = \frac{AI\ of diabetic\ control group - AI\ of\ treated\ group}{AI\ of diabetic\ control\ group} \times 100$$

Diabetes mellitus, a group of metabolic disorder with multiple etiology, is characterized by chronic hyperglycemia with disturbances in carbohydrate, fat and protein metabolism due to defect in insulin secretion, insulin action or both.[15] Abnormal increase in blood glucose levels in diabetes is associated with dyslipidemia in both clinical and experimental diabetes.[16] Alloxan, a simple nitrogenous organic compound, can produce diabetes mellitus in laboratory animals by simple intraperitonial injection. Although the precise diabetogenic mechanism of alloxan has not yet been fully understood, several studies indicate that pancreatic β-cell oxidative damage could play a possible role.[17]

Phytochemicals identified from traditional medicinal plants are presenting an exciting opportunity for the development of new types of therapeutics.[18] A number of plants have been reported to exhibit glycemic control by stimulating insulin release.[3] *Aloe vera* leaf extract has been found to be significantly effective in lowering blood glucose in experimental diabetics and in normal controls. It is possible that *Aloe vera* may contain some active insulinogenic ingredients which help in lowering blood glucose levels in diabetic rabbits.[4,5,6,9]

HbA1c is an important parameter used in the management and prognosis of diabetes as it increases proportionately to fasting blood glucose (FBG) levels.[19] The significant decrease in HbA1c levels in *Aloe vera* treated group indicates the glycemic control induced by the plant extract.[20]

Insulin deficiency in diabetics is responsible for the derangement of lipid and lipoprotein metabolism (hypertriglyceridemia i.e. increase LDL-C & hypercholesterolemia which was quite evident in our study).[15,16] The significant improvement in lipid profile in Group III animals, might have been due to improvement in insulin levels upon administration of *Aloe vera*, could be beneficial in preventing diabetic complications. The risk for CHD (coronary heart disease) in diabetes increases many folds. It is the most dangerous complication of DM.[21,22] Reduction in atherogenic index in diabetic rabbits fed with *Aloe vera* extract suggests that its dietary supplement decreases the risk of developing heart diseases.

CONCLUSION

A decrease in FBG levels, improvement in the lipid profile along with decrease in atherogenic index by administration of *Aloe vera* leaf extract suggests that *Aloe vera* could be useful as an anti diabetic agent with cardio protective activity. Further study is required to isolate the active constituents of *Aloe vera* and elucidate the mechanism of action for developing a potent herbal anti diabetic drug which could be used as an adjunct to oral hypoglycemics in the management of diabetes.

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