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Original Article

# Hypoglycemic, hypolipidemic properties of *aloevera* in streptozotocin induced diabetic rats

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ABSTRACT

Lipids play a vital role in the pathogenesis of diabetes mellitus. The elevated serum lipids represent the risk factor for coronary heart disease in diabetes mellitus patients. Aim& objective: To evaluate the hypoglycemic, hypolipidemic properties of Aloe vera. Methods: Normal euglycemic rats were treated with distilled water, *Aloe vera* 150 and 300mg/kg body weight. Diabetic rats (streptozotocin 50 mg/kg intraperitoneum) in groups were treated with distilled water (control), Aloe vera extract (150mg and 300mg/kg) and standard drugs. Blood samples were collected and analysed for blood glucose, lipid profile on day 0, 8, 15, and 22. Results: *Aloe vera* (300mg/kg) produced significant reduction ($p < 0.001$) in blood glucose as well as on lipid profile only in diabetic rats at the end of treatment. Conclusion: Aloe vera has significant lipid lowering effect and could be useful in diabetes.



## 1. Introduction

Diabetes mellitus is a complex and multifunctional group of disorder. At present it affects more than 100 million people worldwide and considered as one of the leading cause of morbidity and mortality in human population[1].The World Health Organization (WHO) has reported that about 300 million people would suffer from diabetes mellitus by the year 2025[2]. In diabetes patients hyperglycemia is associated with the development of micro and macrovascular complications. Lipids play a vital role in the pathogenesis of diabetes mellitus[3]. The level of serum lipids is usually elevated which increases the risk for coronary heart disease in patients with diabetes mellitus[4]. Hyperlipidemia coexists with hyperglycemia and is characterized by increased levels of cholesterol, triglycerides and phospholipids, and also changes in lipoproteins.[5] An ideal oral treatment for diabetes mellitus would be a drug which not only controls the glycemic level, but also prevents the development of different cardiovascular consequences associated with diabetes mellitus.Various plants like *Allium cepa, Allium sativum, Azadirachtaindica, Eugenia jambolona, Momordicacharantia, Ocimum sanctum etc.* are well known for their hypoglycemic activities [6].But studies of the plants with added beneficial effects on the lipid profile are needed.

*Aloe vera* (L.)Burm is as old as civilization and has been used as a popular folk medicine.Several studies have been done to know the hypoglycemic activity of *Aloe vera* in diabetes mellitus. But research of its possible effect on lipid profile with the hypoglycemic effect are lacking. So the present study was undertaken to evaluate the hypoglycemic, hypolipidemic properties of *Aloe vera* in streptozotocin induced diabetic rats.

## 2. Materials and Methods

Aqueous extract of *Aloe vera* was collected from the Indian Herbs Research and Supply Co Ltd. Sharda Nagar, Saharanpur, India (R&D/2008-09/247). Adult wistar albino rats of either sex were kept under standard condition of temperature ($22^0$ C + $20^0$ C), humidity (50-70%) and 12 hr light and dark cycle. The animals were given standard pellet diet and water ad libitum. The study protocol was approved by the Institutional Animal Ethics Committee (03/CPCSEA). MKCG Medical College, Berhampur.

Streptozotocin was procured from Himedia Laboratories Pvt. Ltd., India. The kits for estimation of lipid profile were obtained from Crest Biosystem. The standard drugs like metformin and atorvastatin was obtained from Franco-India Pharmaceutical Ltd, India and Macleod Pharmaceutical Ltd, India respectively. All ingredients used were of analytical grades.

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An acute oral toxicity study was done as per OECD guidelines. Adult wistar albino rats were administered 5, 50, 300 and 2000mg/kg b.w of aqueous extract of *Aloe vera*. The control group was treated with distilled water only. The animals were observed for 14 days. There was no mortality observed during this toxicity study.

The experimental work was done in two phase. In first phase, eighteen animals (120-150 gm) were divided into three groups (n=6).

Group 1: Normal control (distilled water 1ml)

Group 2: Aloe vera (150 mg/kg bw)

Group 3: Aloe vera (300 mg/kg bw)

All the animals were treated for 21 days. The blood samples were collected by retro orbital puncture from overnight fasted animals. The biochemical parameters were estimated on day 0,8,15 and day 22.

The second phase of the study was done after inducing diabetes in animals.

***Induction of diabetes:*** The animals were given single intraperitoneal injection of streptozotocin (50mg/kg) dissolved in freshly prepared 0.1M of citrate buffer (pH 4.5) after overnight fasting for 12 hrs. The animals showing blood glucose level above 250mg/dl were selected for the study.[7,8]

Group 4: Disease control (normal saline)

Group 5: Aloe vera (150 mg/kg bw)

Group 6: Aloe vera (300 mg/kg bw)

Group 7: Metformin (500mg/kg)

Group 8: Atorvastatin (1mg/kg)

All the animals were treated for 21 days and biochemical estimations of the blood samples were done on day 0, day8, day15, and day22.The animals were fasted overnight. Blood samples were collected in test tubes containing EDTA by retro orbital puncture of venous plexus under light ether anaesthesia. The samples were centrifused at 5000 rpm for 5 minutes. The plasma were separated and the parameters like plasma glucose, Cholesterol, Triglyceride, and LDL, HDL were measured according to procedure described in the manufacture's kit.

***Estimation of plasma glucose:***

Blood glucose was estimated by glucose oxidase/peroxidase method. The samples were mixed with reagents and absorbance was measured by spectrophotometer at 505nm.

***Plasma cholesterol***

Measured by the CHOD/PAP method. The reagents were mixed well and incubated at $37^0$C for 5 mins. The absorbances of the standard and test samples were measured against the blank at 505 nm.

***Plasma Triglyceride: (GPO/PAP method)***

The blood samples and reagents were mixed well and incubated at room temperature for 15mins. The absorbances were measured by spectrophotometer.

**Estimation of plasma HDL:**

The plasma HDL was estimated by PEG (Polyethylene glycol) precipitation method. The reagents were mixed with the samples and the absorbance was measured at 505 nm within 60 minutes of preparation.

***Plasma LDL estimation:***

The LDL cholesterol was calculated from the formula of *Friedwald et al* (1972). LDL = Total Cholesterol – [ HDL + VLDL] Where VLDL = Triglyceride/5

***Statistical analysis:***

All the data were measured as mean± standard error of mean (SEM) and analysed by one way ANOVA with post hoc test using SPSS-12 version. p value less than 0.05 was considered statistical significant.

**3. Result**

In the present work, the effects of Aloe vera in different doses (150 mg, 300mg) were studied in both normal and diabetic rats. The mean plasma glucose concentration of control group (gr 1) was 88.5±5.8 mg/dl on day 0 and 84.25±7.02 mg/dl on day 22nd. The mean fasting plasma concentration of the test drug animals (gr 2 and gr3) did not change significantly as compared to the control group on their respective day of treatment. Similarly the lipid profile of the animals like cholesterol, triglyceride, HDL and LDL in Aloe vera treated groups did not show any significant change as compared to the normal control after 21 days of treatment (Table1).

**Table 1. Fasting blood glucose and lipid profile of normal group after 21 days of treatment**

| Groups | Fasting Blood glucose (mg/dl) | Total cholesterol (mg/dl) | Triglyceride (mg/dl) | LDL (mg/dl) | HDL (mg/dl) |
|---|---|---|---|---|---|
| Control | 84.25±7.02 | 61.25±1.49 | 82.75±2.14 | 19.95±1.48 | 24.75±0.48 |
| AV-150 | 89.25±4.75 | 62.75±3.47 | 86.75±4.66 | 22.90±3.71 | 22.5±1.50 |
| AV-300 | 86.5±5.90 | 62.5±3.80 | 85.5±3.93 | 21.65±3.62 | 23.75±1.44 |

AV – Aloe vera, Values expressed as mean ±SEM, n=6 in each group

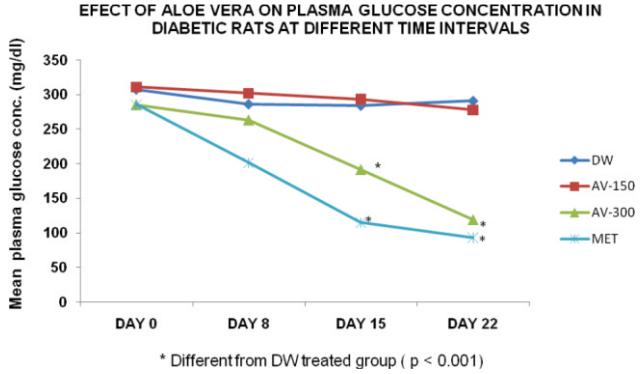
In the second phase of the experiment, the diabetic was induced in animals. Forty eight hours after streptozotocin injection, there was increase in mean fasting plasma glucose (302mg/dl) from it's basal value (88.75 mg/dl). Similarly there was increase in total cholesterol, LDL and triglyceride level and significant decrease in plasma HDL level (Table 2).

**Table 2 . Different biochemical parameters in wistar rats following induction of diabetes**

| Biochemical parameters (mg/dl) | Before induction | After induction |
|---|---|---|
| Fasting blood glucose | 88.75±5.07 | 304±7.75** |
| Total Cholesterol | 67±2.04 | 91.3±3.47* |
| Triglyceride | 84±2.20 | 220.8±7.95** |
| LDL | 21.7±3.53 | 34.1±4.29* |
| HDL | 28.5±2.33 | 13±0.91* |

Values expressed as mean±SEM, * $p < 0.05$, ** $p < 0.001$

Aloe vera (150mg/kg) did not change the mean plasma glucose concentration significantly ($p>0.05$) from that of the control group on different days of observations (day 0, day8, day15 and day 22). Whereas Aloe vera (300 mg/kg) reduced the mean plasma glucose level to 191.5 mg/dl and 100.5 mg/dl on 15th day and 22nd day respectively as compared to the diabetic control group ($p<0.001$) which was comparable to the standard drug metformin (figure 1).




Aloe vera with 150 mg/kg did not change any of the lipid parameters (plasma cholesterol, triglyceride, HDL and LDL ) on different days of observations from the basal values on day 0. But the group 6 animals (Aloe vera 300mg/kg) reduced the plasma cholesterol, TG, LDL and increased the plasma HDL level as compared to the group 4 (diabetic control) from day 8 onwards ($p<0.001$).

As depicted in table 3 , the effect of different doses of Aloe vera on all biochemical parameters after 21 days of treatment. On multiple comparisons it was found that Aloe vera in 300mg/kg reversed all the parameters to normal as compared to the diabetic control group. The effects of these drugs were comparable with the standard drugs (metformin and atorvastatin).

**Table 3. Comparative study of Aloe vera in different doses after 21 days of treatment in diabetic rats**

| Groups | Fasting Blood glucose (mg/dl) | Total cholesterol (mg/dl) | Triglyceride (mg/dl) | LDL | HDL |
|---|---|---|---|---|---|
| Normal control | 84.25±7.02 | 61.25±1.49 | 82.75±2.14 | 19.95±1.48 | 24.75±0.48 |
| Diabetic control | 290.5±3.10 | 87±3.34 | 217.5±4.42 | 33.75±3.56 | 11.75±0.85 |
| AV-150 | 278.75 ±6.04 | 85±2.74 | 206.5±5.72 | 30.2±2.35 | 13.5±0.86 |
| AV-300 | 100.5±3.50$^{*\#}$ | 66.5±1.85$^{*@\#}$ | 92±2.12$^{*@\#}$ | 21.85±2.81$^{*@\#}$ | 26.25±1.11$^{*@\#}$ |
| Metformin | 92.5±4.65$^{*@}$ | | | | |
| Atorvastatin | | 61.25±1.75$^{*@}$ | 81.75±4.55$^{*@}$ | 17.9±3.05$^{*@}$ | 27±1.29$^{*@}$ |

Data expressed as mean±SEM, * p< 0.05 Vs diabetic control, # p > 0.05 Vs reference standard drug, @p> 0.05 Vsnondiabetic control

## 3. Discussion

Diabetes is a complex group of disorder characterized by hyperglycemia, which has reached epidemic proportions in the present century.[9] Several drugs such as biguanides and sulfonylureas are presently available to reduce hyperglycemia in diabetes mellitus. But these drugs are not free from side effects and the search is on for development of a new class of compounds to overcome these problems. Traditional antidiabetic drugs might provide the source of new oral hypoglycemic compounds, which can counter the drawbacks of the presently available oral antidiabetic agents. Also the herbal drugs might show beneficial effects on lipid profile which are abnormal in the patients with diabetes mellitus. So the present study was undertaken to evaluate the beneficial effect of *Aloe vera* in diabetes mellitus.

Streptozotocin induced diabetic wistar rats have shown significantly higher fasting plasma and higher lipid abnormalities in comparison to other strains.[10]

Administration of Aloe vera aqueous extract in doses (150, 300 mg/kg) for a period of 21 days did not change the mean fasting plasma glucose level in normal rats. The mean fasting plasma glucose levels of these groups were comparable to the normal rats fed with distilled water as shown in table 1. This result corroborates with the observations made by Rajasekaran et al (2004)[11]. Similarly the lipid parameters (cholesterol, TG, HDL and LDL) observed in the Aloe vera treated normal rats did not change significantly (Table 1). In the present investigation, Aloe vera (150 mg/kg) produced no significant change in plasma glucose, lipid profile in diabetic animals but Aloe vera extract (300mg/kg) daily to the diabetic rats for a period of 21 days reduced the fasting plasma glucose level.

Aloe vera extract was effective in lowering the plasma glucose level in hyperglycemic rats but not in normoglycemic rats. This is similar to the action of biguanide group of hypoglycemic drug (Metformin) that do not cause hypoglycemia in normal subjects.[12] Their mechanism of action is by inhibition of hepatic glucose production and increase in muscle glucose uptake. Blumenhal et al reported that Aloe vera contain high calcium level[13]. Calcium stimulates the β cells of Langerhans that lead to an increase in insulin and liver glycogen level. Other possible mechanism for hypoglycemic action of Aloe vera might be due to its effect by preventing the death of β cells and recovery of partially destroyed β cells. The hypoglycemic effect of Aloe vera is mediated through the stimulation and release of insulin from β cells of pancreas [14].

Diabetes mellitus is also associated with hyperlipidemia with profound alteration in the concentration and composition of lipid. Administration of aqueous extract of Aloe vera(300mg/kg) for a period of 21 days lowered the plasma total cholesterol, TG, LDL level. In addition, the decreased plasma levels of HDL in diabetic rats were restored to near normal levels following treatment with the extract. Possible mechanism for the beneficial effect of Aloe vera on lipid profile might be due to the improved glycemic status in the diabetic animals.

## 4. Conclusion

This investigation reaffirms the potential of *Aloe vera* for use as a natural oral antidiabetic agent, with hypoglycemic, hypolipidemic effects and show therapeutic promise to protect against the development and progression of cardiovascular complications in diabetes mellitus. Further studies are needed to isolate the active principle and elucidate the exact mechanism of action.

## 5. Acknowledgment

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