

Assessment of oral hypoglycaemic activity of water soluble extract of aloe vera and its interaction with glipizide in alloxan induced diabetic Wistar Rats

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ABSTRACT

Background: Assessment of oral hypoglycaemic activity of water soluble extract of Aloe vera and its interaction with Glipizide in Alloxan induced diabetic Wistar rats.

Methods: Under standard condition of testing, alloxan induced diabetic rats were kept in fasting state of 8 hours and then glucose in dose of 1gm/kg was given PO by feeding tube. There after water soluble extract of aloe vera in dose of 200mg/kg BW dissolves in 1ml of Distilled water (DW) to test group 1, Glipizide in dose of 2.5mg/kg BW dissolved in 1ml DW was given to standard group. Test group 2 received combination of Aloe vera 200mg/kg BW and Glipizide in dose of 2.5mg/kg BW dissolved in 1ml Dw. Control group received 1ml of Distilled water. Blood sugars levels of all Rats in each group were checked with Glucometer.

Results: Clinically and statistically significant glucose lowering effect was observed in groups administered with Aloe vera and better results were observed in group receiving Aloe vera and Glipizide combination.

Conclusions: Water soluble extract of aloe vera has significant hypoglycaemic activity and the results showed that co-administration of Aloe vera and Glipizide has superior hypoglycaemic activity compared to Aloe vera and Glipizide given Individually.

Keywords: Alloxan, Aloe vera, Glipizide, Hypoglycaemia

INTRODUCTION

According to the World Health Organization, India had 69.2 million people living with diabetes (8.7%) as per the 2015 data, of these, it remained undiagnosed in more than 36 million people.¹ India is witnessing a silent epidemic of this non communicable life style menace. It is worth noted that there has been a plethora of therapeutic options for Diabetes mellitus. India being the land of Ayurveda, has ancient history of use of medicinal plants for treatment of various diseases like constipation, Osteoarthritis, cancer, wound healing, burns, skin diseases etc.² Patients have the growing tendency to self-treat themselves with herbal drugs along with prescribed allopathic medicines. For

Diabetes in particular, market is studded with many herbal products.

One of the popular herbal drugs considered medicinal plant in Ayurveda is Aloe Vera. There have been scientific evidences of the use of Aloe Vera as an anti-diabetic agent.³

Considering the low cost, ease of availability and literature support in favour of Aloe Vera, the present study was conducted to assess the effect of water soluble extract of aloe vera and effect of aloe vera and Glipizide given concomitantly on glucose metabolism in Alloxan induced diabetic Rats.

METHODS

Albino Wistar rats of up to 230 -250grams were taken and injected 150mg/kg of Alloxan ip and kept in standard experimental conditions for 3 days.⁴ The rats were free to move in their cages. Food, water was available ad-libitum. 12hours light and dark cycle was ensured with temperature maintained at 25 degree centigrade. OECD guidelines were considered for testing of animals with drugs and LD-50 was determined.⁵ The rats were kept in fasting state for 3hours prior to study and were given single dose of Water soluble extract of Aloe vera and were observed for its mortality up to 48 hours. From the LD50 dose 1/5th and 1/10th doses were selected as safe doses and used in acute short term study.

Aloe vera barbedesis was collected from garden of MGM Medical college Indore and was identified by botanist. Wistar Rats of 230 to 250grams were taken and induced diabetes Rats with a cut of value of fasting blood sugar level of more than 200mg/dl in rats were considered diabetic and used during experiment.

Preparation of water soluble extract of Aloe vera

Aloe vera leaves were processed by removing the outer coat and the pulp obtained was kept in shade for drying. The dried pulp was powdered and dissolved in chloroform and filtered through filter paper. The supernatant left in the filter paper was dried and later dissolved in water and separated by filter paper. The water-soluble extract so obtained was dried and stored in air tight bottles for experimental use.

Rats were made to remain in fasting state 8 hours prior to experiment. Then Rats were divided in four groups. Each group had 8 rats. Each rat was fed with glucose in dose of 1gm/kg of body weight. Then experiment was conducted in which Group 1 (control) was fed with 1ml Distilled water (DW) via feeding tube. Group 2 (standard) received Glipizide in the dose of 2.5mg/kg BWpo. Group 3 (test 1) received Aloe vera in dose of 200mg/kg BW po.⁶ Group 4 (test 2) received both Aloe vera 200mg/kg BW PO and 2.5mg/kg BW PO of Glipizide.

Blood samples were collected from tail vein of rats and glucose estimation was done using Glucotrend II Glucometer made by Nicholas USA at the interval of 1hour, 2hours and 3hours.⁷

RESULTS

In all the groups the blood glucose levels were measured 4 times in the Alloxan induced diabetic Wistar Rats.

- Pre-test glucose levels
- 1 hour after administration of the group specific agent
- 2 hours after administration of the group specific agent
- 3 hours after administration of the group specific agent

Since there were four groups, in the first group (Control) the effect was recorded after administration of 1 ml. of Distilled water (DW) (Table 1).

Table 1: Group 1 control - effect on administration of 1ml of DW*.

Pre test blood glucose levels	Blood glucose level at 1 hour	Blood glucose level at 2 hours	Blood glucose level at 3 hours
388 mg/dl	374 mg/dl	350 mg/dl	343 mg/dl
442 mg/dl	422 mg/dl	390 mg/dl	375 mg/dl
390 mg/dl	364 mg/dl	347 mg/dl	336 mg/dl
392 mg/dl	367 mg/dl	351 mg/dl	340 mg/dl
426 mg/dl	402 mg/dl	381 mg/dl	368 mg/dl
371 mg/dl	359 mg/dl	326 mg/dl	316 mg/dl
370 mg/dl	368 mg/dl	350 mg/dl	328mg/dl
404 mg/dl	396 mg/dl	382 mg/dl	361 mg/dl

* Rats were made to remain in fasting state 8 hours prior to experiment; Blood glucose levels were monitored at 1 hours, 2 hours and 3 hours

In Group 2 the effect was observed after administration of Glipizide 2.5 mg/kg Body Weight (BW).

The blood glucose levels were measured in similar fashion as mentioned above (Table 2).

Table 2: Group 2 - effect on administration of glipizide 2.5mg/kg BW*.

Pre test blood glucose levels	Blood glucose level at 1hour	Blood glucose level at 2 hours	Blood glucose level at 3 hours
447 mg/dl	363 mg/dl	202 mg/dl	107 mg/dl
398 mg/dl	288 mg/dl	165 mg/dl	101 mg/dl
387 mg/dl	269 mg/dl	154 mg/dl	87 mg/dl
380 mg/dl	270 mg/dl	210 mg/dl	128 mg/dl
357 mg/dl	270 mg/dl	166 mg/dl	100 mg/dl
374 mg/dl	289 mg/dl	199 mg/dl	123 mg/dl
393 mg/dl	317 mg/dl	227 mg/dl	158 mg/dl
402 mg/dl	312 mg/dl	216 mg/dl	155 mg/dl

* Rats were made to remain in fasting state 8 hours prior to experiment; Blood glucose levels were monitored at 1 hours, 2 hours and 3 hours

In Group 3 the effect was observed after administration of test 1- Aloe vera 200mg/kg BW.

The blood glucose levels were measured in similar fashion as mentioned above (Table 3).

In Group 4 the effect was observed after administration of test 2- Aloe vera 200mg/kg BW+ Glipizide 2.5mg/kg BW.

The blood glucose levels were measured in similar fashion as mentioned above (Table 4).

Table 3: Group 3 - effect on administration of test 1- Aloe vera 200mg/kg BW.

Pre test blood glucose levels	Blood glucose level at 1hour	Blood glucose level at 2 hours	Blood glucose level at 3 hours
382 mg/dl	260 mg/dl	146 mg/dl	98 mg/dl
390 mg/dl	280 mg/dl	151 mg/dl	104mg/dl
363 mg/dl	256 mg/dl	138 mg/dl	87 mg/dl
400 mg/dl	285 mg/dl	140 mg/dl	106 mg/dl
394 mg/dl	270 mg/dl	146 mg/dl	90 mg/dl
386 mg/dl	251 mg/dl	121mg/dl	74 mg/dl
441 mg/dl	282 mg/dl	159 mg/dl	101 mg/dl
426 mg/dl	257 mg/dl	143 mg/dl	70 mg/dl

* Rats were made to remain in fasting state 8 hours prior to experiment; Blood glucose levels were monitored at 1 hours, 2 hours and 3 hours

Table 4: Group 4 - effect on administration of test 2- Aloe vera 200mg/kgBW+ Glipizide 2.5mg/kg BW.

Pre test blood glucose levels	Blood glucose level at 1 hour	Blood glucose level at 2 hours	Blood glucose level at 3 hours
411	216	118	62
438	200	100	70
395	196	119	58
379	177	106	71
418	198	92	53
390	188	117	75
399	202	116	66
380	165	101	52

* Rats were made to remain in fasting state 8 hours prior to experiment; Blood glucose levels were monitored at 1 hours, 2 hours and 3 hours

The glucose lowering effect of the group 4 (combined Aloe vera 200mg/kg BW+ Glipizide 2.5mg/kg BW) was statistically significant with P value = 0.001 using Anova test with post hoc tukey and scheffé, Bonferroni and Holm multiple comparison using SPSS software thus indicating that Aloe vera has definite glucose lowering effect.

DISCUSSION

Many drugs are prescribed concurrently in diabetes for glycemic control but still patients continue to have glycemic variability and higher blood sugar levels. Many people tend to self treat diabetes with commercially available herbal products and naturally growing plants of medicinal value like aloe vera, which has been studied in past. Many authors have found blood glucose lowering, hypolipidemic effect in Rats and Mice.⁸⁻¹⁰ Other authors found Aloe vera to be having wound healing activity and anti-psoriatic property.¹¹⁻¹³ Using Pubmed and Google scholar as search engines, we found that there are many studies with ethanolic extract of Aloe vera but a few only

with water soluble extract of Aloe vera. In our study, the results suggested that Aloe vera is having significant Blood glucose lowering potential better than Glipizide an insulin secretagogue. Similar results were observed by Naveen et al, but with ethanolic extract of aloe vera.¹⁴ The group receiving combination of Aloe vera and Glipizide has shown further better values of blood sugar lowering effect in rats suggesting the possibility of multiple mechanism of causing hypoglycaemia which was seen by P Naveen et al as well.¹⁴ As Alloxan treated diabetic Rats have low beta cells of Langerhans. In group 4 receiving Aloe vera and Glipizide concurrently, Glipizide administration the maximum beta cells stimulation would have occurred leaving behind little or no chance for aloe vera to stimulate Beta cells of Pancreas. But still the blood sugar lowering effect was better in group 4. This is probably because of additional property of Aloe vera by which aloe vera inhibits Alfa-Amylase in intestine.¹⁵ Also some authors have found increase in Bioavailability of few vitamins when co-administered with aloe vera.¹⁶ This may be one of the reason by which Aloe Vera would have increased the Bioavailability of Glipizide and hence the results in combination group were better. As in many other diseases inflammation is responsible for morbidity, similarly in diabetes as well, Inflammation has its role in pathogenesis of causing Hyperglycaemia. Authors have published many articles with the results suggestive of Anti-Inflammatory action of Aloe Vera.¹⁷ This can be one the effect by which Aloe vera by virtue of its anti inflammatory property reduces glucotoxicity in diabetes.

CONCLUSION

Water soluble extract of Aloe vera has significant hypoglycaemic property suggesting the possibility of Aloe vera to be a cheap alternative in diabetes. Further higher studies like Pharmacokinetic (PK) and Pharmacodynamic (PD) etc are required to postulate the Mechanism of Action of Aloe Vera in diabetes and to test real time effect of Aloe vera in Glucose and other metabolism.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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