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Original Article

Hypoglycemic and Hypotriglyceridemic Effects of Aloe Vera Whole Leaf and Sitagliptin in Diabetic Rats

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ABSTRACT

Background:. *Aloe Vera* with excellent metabolic properties is playing wonders in diabetes treatment.

Objective: "To compare the hypoglycemic and hypotriglyeridemic effects of *Aloe Vera* whole leaf and Sitagliptin on Streptozotocin induced diabetic rats"

Methodology: Randomized Control Trial, conducted at Department of Pharmacology, Riphah University, in collaboration with NIH, Islamabad, Pakistan, from September 2019 to August 2020. Healthy, 40, albino rats were randomly divided into Groups A and B. Group B was further subdivided into: GroupB1 (Diabetic Control), Group B2 (*Aloe Vera* whole Leaf treated), GROUP B3 (Sitagliptin treated), n=10 each, (after diabetes induction). At Day 60, FBS and serum triglycerides were measured in all rats. SPSS version 25 was applied for statistical analysis. One-way ANOVA test was used for assessing any difference in the mean values. Post-hoc Turkey analysis was done to compare inter-group mean differences. P value of <0.05 was considered significant.

Results: On terminal sampling, mean FBS of Rats in Group A was 82.40 mg/dl, Group B1 498.40mg/dl, Group B2 89.30mg/dl and Group B3 93.00mg/dl; Serum Triglycerides for Group A 125.40mg/dl, B1 221.00mg/dl, B2 112.50mg/dl, B3 125.00mg/dl respectively. In Group B2 and Group B3 significant reduction in fasting blood glucose and triglycerides is observed, compared to Group B1, with no statistically significant intergroup differences in results of Group B2 and B3.

Conclusion: *Aloe Vera* whole leaf extract significantly decreased fasting blood glucose and triglyceride levels with nearly similar efficacy to Sitagliptin in diabetic rats.

Keywords: Aloe Vera, Hypoglycemic Agents, Sitagliptin, Blood Glucose, Triglycerides.

Introduction

Approximately 1 in 11 adults currently suffer from diabetes mellitus, 90% of whom have type 2 diabetes mellitus.[1,2] Financial impacts of such a prevalent, devastating disease presently appeal substantial consideration as the global diabetes epidemic proceeds hold and the healthcare arrangements of nations come under great stress to accomplish further within constrained means.[2]

Abnormalities in lipid metabolism prevalent in type 2 diabetes are amongst the key factors contributing to an augmented cardiovascular risk. The primary quantifiable lipoprotein irregularities are amplified triglyceride levels and diminished HDL-cholesterol levels.[3]

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The underlying abnormalities are hepatic overproduction and hindered clearance of triglycerides.[4] The raised circulating triglyceride level has strong association with reduced skeletal muscle and entire body insulin action, the root cause behind the development and progression of type 2 diabetes mellitus.[5]

Sitagliptin is new among antidiabetic drugs available for treating diabetes mellitus type 2.It inhibits dipeptidyl peptidase-IV and leads to increase in the life span of the two incretin hormones, glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP). Both these hormones stimulate insulin secretion from the pancreatic beta cells and inhibit glucagon secretion from the alpha-cells. Dose-dependent inhibition of DPP-4 enzyme, with a low risk of hypoglycemia, is its primary mechanism and is known to raise the concentrations of incretins , GLP-1 and GIP by about two to three- times in patients with type 2 diabetes mellitus.[6-7]

Aloe Vera and its medicinal usage dates back to 4th century B.C.[8] Cleopatra stated that her beauty was

owed to the use of *Aloe Vera* plant.[9] *Aloe Vera* causes significant reduction in serum levels of glucose, total cholesterol, triglycerides, low density lipoprotein cholesterol and very low-density lipoproteins. Hypoglycemic property of *Aloe Vera,* is thought to be related to insulin synthesis and release. Normalization of plasma lipid status by *Aloe Vera* is supposed to be brought about by changes in lipid metabolism, along with increased clearance and decreased synthesis of major transporters of endogenous cholesterol and triglycerides.[10] In present study, comparative hypoglycemic and hypotriglyeridemic effects of *Aloe Vera* whole leaf with oral DPP4-inhibitor, Sitagliptin are compared, as previously no study was done for such comparative effects..

Methods

The present study was randomized control trial (RCT) performed at Pharmacology Department of Riphah international university Almeezan campus, Rawalpindi in collaboration with National Institute of Health (NIH) Islamabad for one year (September 2019 -August 2020). 2 months old, healthy adult Sprague Dawley rats were procured from animal house of NIH and housed in standard cages under standard laboratory conditions. The care and handling of subjects was done according to internationally accepted standard guidelines for animal care. Rats had free access to food and water and randomly divided in 2 groups; 10 rats in group A and 30 rats in Group B. Group A was Normal Control group and received normal standard diet while the Group B received high fat standard diet for two weeks.

Streptozotocin (STZ) Catalogue number 4191002-1(714986) of Brand bio world USA, bought from commercial supplier, was dissolved in the 50mM sodium citrate buffer (pH 4.5), shortly before injection. Group B rats were fed on high fat diet for 2 weeks to develop insulin resistance and kept overnight fast and then given single intra-peritoneal injection of streptozotocin at the dose of 35 mg/kg [11] body weight. Fasting blood glucose was checked, 3 days [12] after streptozotocin administration to confirm type 2 diabetes. Rats with fasting blood glucose equal and above 250mg/dl were considered diabetic.

CCL Pharmaceuticals Lahore provided the research grade Sitagliptin, Batch No: M-20191010-D05-M06-01, which was orally administered at dose of 10mg/kg body weight/day for 40 days.[13] Fresh, 2-3 years old, healthy *Aloe Vera (Aloe Barbadensis Miller)* brought from local nursery and plant material identification was done at Herbarium of Pakistan- Quaid-e-Azam University Islamabad, by Department of Plant Sciences. Accession Number is 132644 and Voucher Specimen Number 125 is preserved there. *Aloe Vera* leaves were washed under tap water and cut into thin slices and dried in sun.[14] Powder of whole leaf obtained after grinding was mixed in feed for rats as standard food pellets, and given to Group B2 rats at calculated dose (300mg/kg body weight/day)[15], for 40 days. After completion of study, at Day 60, terminal blood samples were taken through cardiac puncture. Estimation of Fasting Blood Sugar was done after enzymatic oxidation by glucose oxidase method and serum triglycerides determination is done after enzymatic splitting with lipoprotein lipase, both parameters measured via semi-automated, clinical chemistry analyzer, Microlab 300.

Statistical analysis was done by applying the statistical package for Social Sciences version 25 (SPSS 25). Results were documented as mean ± SEM. Comparisons of quantitative parameters among the four groups were analyzed by using one way ANNOVA (post hoc turkey test).P value of less than 0.05 was considered as significant.

Results

At the start of study, levels of fasting blood glucose and serum triglycerides were comparable to each other in all groups. On administration of Streptozotocin single I/P injection at a low dose of 35 mg/kg, diabetes was successfully induced in group B rats. Fasting blood glucose was frequently measured via rat tail vein, to see the progress of study. At day 60, on final sampling, mean FBS values for rats in Group A were 82.40 mg/dl, for Group B1 498.40mg/dl, for Group B2 89.30mg/dl and for Group B3 93.00mg/dl; Serum Triglycerides for Group A 125.40mg/dl, B1 221.00mg/dl, B2 112.50mg/dl, B3 125.00mg/dl, respectively. In Group B2 and Group B3 significant reduction in fasting blood glucose and triglycerides is observed, compared to diabetic control Group B1, with no statistically significant intergroup differences in results of Group B2 and B3.

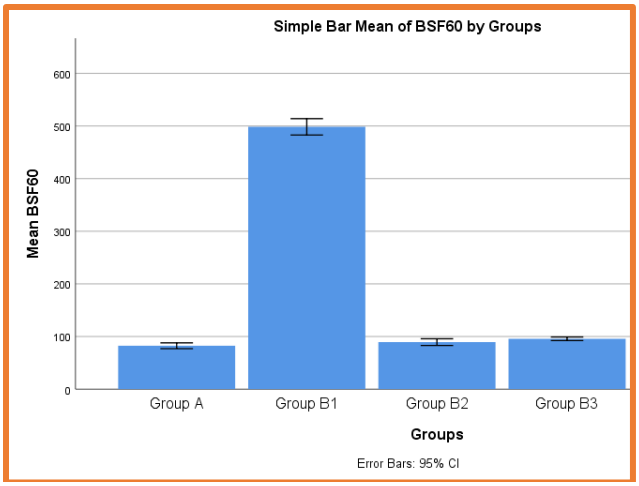

Figure i: Graphical Representation of Mean of Fasting Blood Glucose levels (mg/dl) of all Groups on Day 60 (n = 40)

Key: Group A: Normal control, Group B1: Disease Control, Group B2: Aloe Vera Leaf, Group B3: Sitagliptin

Table i: Comparison of Mean Value ± SEM (Standard Error of Mean) of Serum Triglycerides (mg/dl) in all Groups on Day 60 (n = 40)

Groups	Group A Control	Group B1 Disease Control	Group B2 Aloe Vera Leaf	Group B3 Sitagliptin
Mean	125.40	221.00	112.50	125.00
SEM	2.68	5.73	5.03	5.09
P Value	**< 0.001***			

Table ii: Comparison of Mean ± SEM (Standard Error of Mean) of Serum Triglycerides (mg/dl) in all Groups on Day 60 (n = 40)

Key: Group A: Normal control, Group B1: Disease Control, Group B2: Aloe Vera Leaf, Group B3: Sitagliptin

Groups	Mean Difference	P Value
A vs B1	95.60 ± 6.24	< 0.001*
A vs B2	12.90 ± 6.24	0.252
A vs B3	0.40 ± 6.24	1.000
B1 vs B2	108.50 ± 6.24	< 0.001*
B1 vs B3	96.00 ± 6.24	< 0.001*
B2 vs B3	12.50 ± 6.24	0.281

Discussion

Diabetes Mellitus is a chronic disorder of carbohydrates, fat and protein metabolism with catastrophic impacts on health and economy globally. Acute and chronic hyperglycemia could increase the level of serum triglycerides, LDL, VLDL and decrease levels of HDL cholesterol. *Aloe Vera* with abundant phytochemicals, can bring the distribution of fatty acids in the blood to normal levels. In present RCT, we observed significant reduction in blood glucose and triglyceride levels after 40 days treatment with *Aloe Vera* whole leaf extract at 300mg/kg/day dose in High Fat diet-Low dose Streptozotocin-Type 2 Diabetes(HFD-STZ-Type 2DM) Rat model. The findings of present study are in accordance with useful work by Samaneh Alinejad-Mofrad et all, on *Aloe Vera* extract for improving glucose and lipid profile in pre-diabetic subjects. They concluded that *Aloe Vera* extract in pre–diabetic patients can considerably regulate levels of fasting blood glucose and triglycerides as reflected by significant reduction in fasting blood glucose, total cholesterol, triglyceride, and LDL-cholesterol, in their study.[16]

Another study was conducted on type 2 diabetic Sprague Dawley rats by Meena Gul et all., to measure the synergistic effects of Aloe Vera whole leaf and rosiglitazone on plasma glucose, oxidative stress and lipid profile. They also induced type 2 diabetes in rats by using combination of High Fat diet and low dose streptozotocin (35mg/kg body weight) as we did in our study. They gave combination of *Aloe Vera* whole leaf extract 150mg/kg and rosiglitazone 2.5mg/kg body weight through I/P to diabetic rats for 21 days and found that plasma glucose, serum triglycerides, cholesterol, LDL and VLDL were significantly reduced in those rats as compared to diabetic control group.[17]

Monika Choudhary , Anita Kochhar and Jaswinder Sangha did their study to see the hypoglycemic and hypolipidemic effects of *Aloe Vera* in non-insulin dependent diabetics. They selected ninety non-insulin dependent diabetic subjects from Punjab Agricultural University and Civil hospitals of Ludhiana and divided them into three groups. Group-I did not receive any treatment while group-II and III were supplemented with 100 mg and 200 mg of *Aloe Vera* powder respectively for a period of 3 months, and found that 200mg of *Aloe Vera* extract powder lead to significant reduction in fasting blood glucose, post prandial glucose, total cholesterol and triglyceride levels.[18].

Mediha Sefi1, Mariem Chaâbane1, Moez Rafrafi and Najiba Zeghal conducted research to evaluate hypoglycemic and hypolipidemic activities of *Aloe Vera* Leaf extract in Alloxan-Induced Diabetic Adult male Wistar rats. They found that *Aloe Vera* mucilage administration to diabetic rats for three weeks, significantly corrected hyperglycemia and liver glycogen content and serum insulin level, along with improvement in total cholesterol and triglyceride levels. They postulated this improvement in lipid and glucose levels by *Aloe Vera* to be due to its richness in polysaccharides and glycoproteins. They strongly recommended the use of medicinal herbs, including *Aloe Vera*, to treat hyperglycemia and hyperlipidemia in diabetic patients so as to prevent the adverse effects of modern drugs.[19]

The results of these studies strongly support our effort to highlight the hypoglycemic and hypotriglyeridemic effects of *Aloe Vera* whole leaf extract in treatment of type 2 diabetes as an alternate to synthetic antidiabetic medicines.

Duo to availability and time constraints complete lipid profile and serum insulin levels could not be performed.

Conclusion

Aloe Vera whole leaf extract had significantly reduced fasting blood glucose and serum triglyceride levels in HFD-STZ-Type 2 Diabetic rat model with almost significant efficacy to Sitagliptin with statistically insignificant differences (P value >0.05 to each other. So, *Aloe Vera* may be used safely in place of Sitagliptin in treatment of type 2 diabetes mellitus.

Recommendations

Comparative and combined effects of Aloe Vera leaf extracts with other oral hypoglycemics should be carried out to establish Aloe Vera's potential in treating hyperglycemia and other metabolic changes e.g dyslipidemias, associated with diabetes.

Conflict of entrust/Funding Source: "None to declare".

References

1. Zheng Y, Ley SH, Hu FB. Global aetiology and epidemiology of type 2 diabetes mellitus and its complications. Nat Rev Endocrinol [Internet]. 2018;14(2):88–98. Available from: http://dx.doi.org/10.1038/nrendo.2017.151
2. Piero MN. Diabetes mellitus – a devastating metabolic disorder. Asian J Biomed Pharm Sci. 2015;4(40):1–7.
3. Vergès B. Pathophysiology of diabetic dyslipidaemia: where are we? Diabetologia. 2015;58(5):886–99.
4. Taskinen MR, Borén J. New insights into the pathophysiology of dyslipidemia in type 2 diabetes. Atherosclerosis. 2015;239(2):483–95.
5. Fall T, Xie W, Poon W, Yaghootkar H, Magi R, Knowles JW, et al. Using genetic variants to assess the relationship between circulating lipids and type 2 diabetes. Diabetes. 2015;64(7):2676–84.
6. Scott LJ. Sitagliptin: A Review in Type 2 Diabetes. Drugs [Internet]. 2017;77(2):209–24. Available from: https://doi.org/10.1007/s40265-016-0686-9
7. MIRZA ARSLAN ABID & NAJMA YOUSAF ZAHID. Evaluation of the Sensory Qualities of Ready to Serve Blends of Aloe Vera (Aloe Barbadensis Mill). Int J Bot Res [Internet]. 2016;6(2):1–10. Available from: http://www.tjprc.org/view-archives.php
8. Mehta I. " History OF Aloe Vera " – (A Magical Plant). 2017;22(8):21–4.
9. Verma S. Aloe vera their chemicals composition and applications: A review. Int J Biol Med Res. 2011;2(January 2011):466–71.
10. MQ N, NN N, SA S. Oral aloe vera for treatment of diabetes mellitus and dyslipidemia. Am J Heal Pharm [Internet]. 2010;67(21):1804-1811 8p. Available from: http://search.ebscohost.com/login.aspx?direct=true&db=c8h&AN=105009643&amp%5Cnlang=ja&site=ehost-live
11. Gheibi S, Kashfi K, Ghasemi A. A practical guide for induction of type-2 diabetes in rat: Incorporating a high-fat diet and streptozotocin. Biomed Pharmacother. 2017;95(November):605–13.
12. Christijanti W, Juniarto AZ, Suromo LB. Hypoglycemic effects of Aloe vera peel extract on type 2 diabetic rats. J Phys Conf Ser. 2019;1321(3).
13. Reis F, Ferreira L, Teixeira-De-Lemos E, Pinto F, Parada B, Mega C, et al. Effects of sitagliptin treatment on dysmetabolism, inflammation, and oxidative stress in an animal model of type 2 diabetes (ZDF rat). Mediators Inflamm. 2010;2010.
14. Pattali G, Yenge G, Cheluvadi R, Nidoni U, Hiregoudar S. Mathematical modeling for drying of whole leaf Aloe vera (Aloe barbadensis Miller). Agric Eng. 2015;2(March 2016):41–8.
15. Althwab SA. Anti-diabetic Activity of Aloe vera Supplement REVIEW. 2018;11(1):75–81.
16. Alinejad-mofrad S, Foadoddini M, Saadatjoo SA, Shayesteh M. Improvement of glucose and lipid profile status with Aloe vera in pre-diabetic subjects : a randomized controlled-trial. 2015;1–7.
17. A O, Gul M, Moazzam S, Adil I. Effect of Aloevera Whole Leaf Extract in Combination with Rosiglitazone on Oxidative Stress and Lipid Profile Levels in Type-2 Diabetic Rats. J Islam Med Dent Coll. 2018;7(3):159–64.
18. Choudhary M, Kochhar A, Sangha J. Hypoglycemic and hypolipidemic effect of Aloe vera L. in non-insulin dependent diabetics. J Food Sci Technol. 2014;51(1):90–6.

19. Sefi M, Chaâbane M, Rafrafi M, Zeghal N. Hypoglycemic and Hypolipidemic Activities of Aloe vera Leaf Mucilage in Alloxan-Induced Diabetic Rats. 2019;5(3):29–34

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