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Evaluation and comparison of hypoglycemic activity of bark and leaf of Ficus bengalensis linn. in alloxan induced diabetes in albino rats

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Abstract

Objectives: Evaluation of Hypoglycemic activity of Extract of bark and leaf of Ficus bengalensis Linn.in alloxan induced diabetic albino rats and comparison with standard antihyperglycemic drug Glibenclamide.

Materials and Method: Aqueous extracts of bark and leaf of Ficus bengalensis were evaluated for hypoglycemic activity. Albino rats were divided into six groups of six-animals each. Diabetes was induced by using Alloxan monohydrate (160mg kg.b.wi.p).Control group was treated with normal saline 0.5ml; second group was treated with Glibenclamide 5mg kg as a standard antidiabetic drug. Remaining groups were treated with different doses (150 & 300mg kg.b.w) of bark and leaves of F.bengalensis for a period of 28 days. Fasting glucose level estimated by using Glucometer on days 3, 7, 14, 21 and 28.

Results: An Aqueous Extract of F.Benglensis Linn. produced significant reduction in the fasting blood glucose in diabetic rats. At the dose of 300mg/ kg of bark showed significant fall in blood. glucose level as compared to other doses of extract. Post-prandial reduction in the blood glucose levels on day 3 after 3hrs of drug administration was significant ($p = 0.007$) with bark 300mg as compared to other doses. This is however, highly significant ($p = 0.0001$) when compared with standard drug Glibenclamide.

Conclusions: The current small sample size study shows relevant antidiabetic potential for Ficus bengalensis. Further studies are required to elaborate the antidiabetic activity and mode of hypoglycemic action of Ficus bengalensis.

Keywords: Diabetes, Ficus bengalensis, Aqueous extract, Hypoglycemia

Introduction

Diabetes mellitus (DM) is a group of metabolic disorder characterized by mainly hyperglycemia over a prolonged period of time. As a consequence of this metabolic dysregulation, secondary pathophysiological changes occur in multiple organ system resulting in diabetic keto-acidosis, non-ketotic hyperosmolar coma as acute complications and serious long term complications like heart disease, stroke, renal failure, diabetic foot ulcer, retinal damage.(1)

Globally, as of 2013 an estimated 382 million people are diabetic worldwide, with type 2 constituting 90% of cases. This is equals to 8.3% of adult population. In 2011 and 2013diabetes resulted in 1.5 to 5.1 million death making it the 8th leading cause of death.(2,3)

The number of people with diabetes is expected to rise 592 million by 2035. So it is considered as one of the major public health problem.(3)

Appropriate care should be taken to reduce morbidity and mortality caused by DM. The goals of therapy are to ameliorate the symptoms, to reduce the risk of micro and macro vascular complications and to improve the quality of life as much as possible. Early treatment will reduce the micro vascular complications. Along with this cardiovascular risk factors need to be managed to reduce the macro vascular complications.(4) To attain these goals, the currently available therapy is mainly by oral anti diabetic drugs and insulin. But the use of these drugs is not so cost effective and has side effects like hypoglycemia, hypoglycemic-coma, gastro-intestinal disturbances. This keeps the diabetic individuals under constant medical supervision and impression of being sick.(5) And these drugs are not safe in pregnant woman.(5,6) Hence mortality and morbidity associated with diabetic complications are still a major concern. The substantial effort has been made in recent years to identify the new natural and synthetic anti diabetic agents causing less adverse effects.(7) Considering these points, in this study of *Ficus Bengalensis* has been selected for evaluation of hypoglycemic activity as one of the natural plant source.

Ficus Bengalensis regarded as symbol of peace and harmony. Modern pharmacopeias of Indian medicine contain valuable information about the pharmacological properties of various parts of the plant *Ficus bengalensis.*(8) It possesses anti inflammatory activity, anthelmintic, anti-diabetic and anti-cancer property. In this, the study has been undertaken to know and to compare the hypoglycemic activity and potency of aqueous extract of bark and leaf of Ficusbengalensis in diabetes induced in albino rats.

Materials and Method

Chemicals like alloxan monohydrate obtained from Shri Venkatesh enterprises Dharwad., oral antidiabetic drug- pure form of glibenclamide was obtained from Blue Cross laboratories Limited., A 12, Ambad Industrial area, Ambad, Nasik. Study extract materials from the plant *Ficusbengalensis* (Banayan Tree).

Plant extract: The bark and leaves of *Ficusbengalensis* were collected from Ayurvedic Medical College, Bagalkot. Plant was authenticated by ayurvedic professionals and botanist. The tender bark and leaves were collected and washed with 30% of alcohol, made it

to dry in a shade for about 10 days. After drying both bark and leaves were powdered using 26 size mesh and stored in a dessicator, a air tight container. With the help of Soxhlet apparatus aqueous extract of bark and leaf were obtained and was weighed and kept it in the refrigerator for further use.

Animals procured from the Animal House of Department of Pharmacology, S N Medical College, Bagalkot after approval obtained from IEAS clearance (IAES/SNMC, Reg. No.829/AC/04/CPCSEA).

Wistar Albino rats of either sex weighing 150-250gms were taken. The rats showing some signs of infection, injuries, cuts and pregnant rats were excluded from the study. Animals were acclimatized to the laboratory atmospheric condition for a week at a temp of 23±2 degree Celsius, 50-60% humidity with regular 12 hour light cycle.

Induction of Diabetes: Induction of diabetes was done by using chemical method with alloxan monohydrate. After 8 hours of fasting, freshly prepared 2% alloxan monohydrate in normal saline was given in the dose of 160mg/kg body wt. intraperitoneally.[9,10] The rats showing hyperglycemia after three days of induction of diabetes were considered for the study.

The selection of dose of extract was taken from previous study done by Gayatri M et al., showed that aqueous extract of *Ficus bengalensis*upto 2gm/kg body wt. did not show any toxic reactions and mortality.[11]

Experimental design:

The rats were divided into following groups with six animals in each group.

Group 1: Controlled Diabetic rats; fed with 0.5 ml of normal saline.

Group 2: Treated with standard drug glibenclamide with 5mg/kg body wt.

Group 3: Treated with aqueous extract of bark 150mg/kg body wt.

Group 4: Treated with aqueous extract of bark 300mg/kg body wt

Group 5: Treated with aqueous extract of leaf 150 mg/kg body wt.

Group 6: Treated with aqueous extract of leaf 300mg/kg body wt.

Animals were fed with artificial standard pellet diet and water libitum throughout the experiment. The standard drug and the extracts were given through the oral route using oral feeding tube. Before starting the experiment, the fasting blood glucose readings were taken as zero reading. And further fasting blood glucose readings were taken on day 3, 7, 14, 21 and on 28th day by using an instrument Glucometer (After standardization). It works on the principle of God-pod. On 30th day 3 animals in each group sacrificed and diffuse pancrease was taken for histipathological study. Finally the data was presented statistically in terms of Mean ±SD, statistical differences in the groups were evaluated by Annova followed by post hoc and Dunnets multiple comparison test to know the significance between the groups and un-paired t test to know the significance in between the groups.

Results

Herbal medicine is gaining importance because of least adverse effects with slow sustained action *Ficusbengalensis* is one of the indigenous medicinal plant. It is A large evergreen tree found throughout India. It comes under Kingdom Plantae, Moraceae family and genus- ficus. The tree has spreading branches with aerial roots. The phytochemical study showed that the stem bark contains anthocynidin derivatives (methyl esters of leucodelphinidin-3-O-L-rhamnoside, leucopelargonidin-3-O-L-rhamnoside and lecocynidin-3-O-D gala ctosylcellobioside) and aliphatic long chain ketones, beta sitosterolglucoside and meso inositol. The leaves contain 9.63% crude protein, 26.84% crude fiber, 2.53% calcium oxalate and 45 of phosphorius. Ethanolic and aqueous extract of leaves contain strerols, flavanoids, phenol, tannins and saponins.[12,13] It has a property of anti-inflammatory, anthelmintic, analgesic, antipyretic, anti diabetic, antibacterial activity. In olden days leaves were used to obstinate vomiting, as cooling agent and as tonic agent.[8] This study *F.bengalensis* has shown antidiabetic activity.

Table 1: Shows the blood glucose levels (Mean ±SD) in all group of rats on various days i.e. Day 3, 7, 14, 21 and 28. It showed that, oral administration of aqueous extract of bark and leaves produced a hypoglycemic activity at all the doses. But bark 300mg/kg and 150mg/kg has produced decrease in the blood glucose levels (p value<0.0001) (description for levels of significance should land up in discussion} and also with leaf extract 150mg/kg from day 14 (p<0.0001). Bark has produced a dose dependent increase in the hypoglycemic activity. However decreased hypoglycemic activity was observed with leaf 300mg/kg as the days progressed, when compared to leaf extract 150mg/kg.

Table 2: Shows blood glucose levels before and after 3hrs of administration of extract of bark and leaf with the doses of 150 and 300 mg. Feeding of extract and standard drugs were started on day 3. So to know the immediate effect of plant extract on day 3 pre prandial and post prandial blood glucose levels were taken and evaluated. It was observed that there is decrease in the blood glucose with all the doses after 3 hours of administration but significant decrease in the blood glucose (p value 0.007) seen with test dose of bark 300mg/kg. Day 3, before and after or pre and post prandial observations indicate that the bark 300 mg/kg has got a potent hypoglycemic activity with value less than 0.05. Extract of leaf 300mg/kg has shown potent decrease in the glucose level but statistically not significant. This indicates bark has a more potent hypoglycemic activity than leaf with highly significant statistical value.

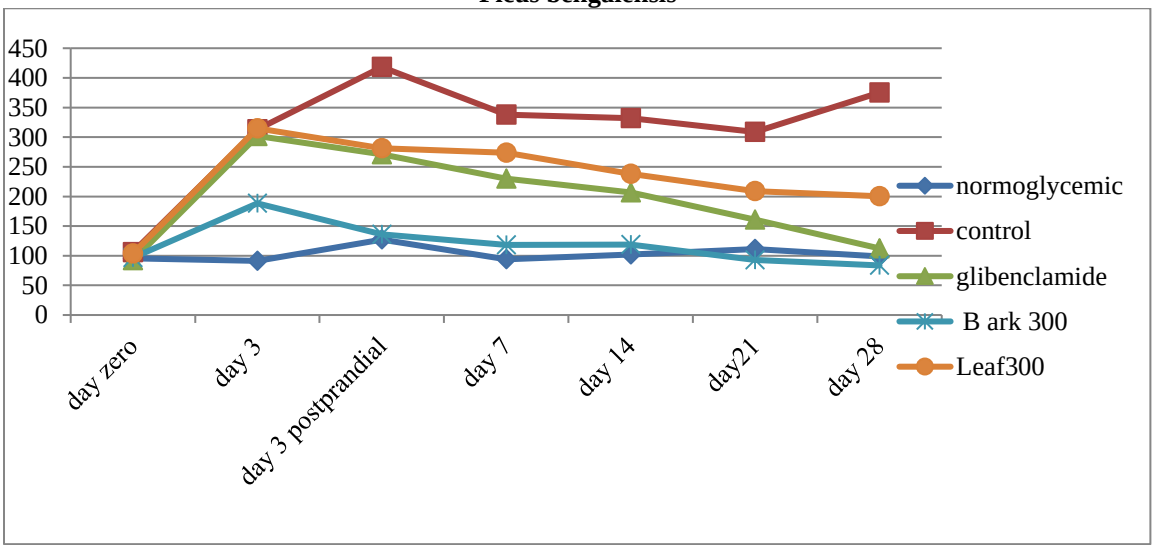
Table 1: Blood glucose levels expressed in Mean±SD

Days	Normoglycemic	Diab. Control	Std. Glibenclamide	AEBFB 150mg	AEBFB 300mg	AELFB 150mg	AELFB 300mg
On Day zero	95.6±15.9	106± 10.7	92.3±13.5	99.6±9.5	96.5±4.9	96.81±11.9	103.±67.7
Day 3	91.3±17.1	313±37.3	302±37.1	222.6±104.8	188.3±30.9	467.8±64.9	314.8±58.5
Day 7	94.1±17.3	337.6±50.4	230.1±53.9	198.6±84.2	118±43.5	424.3±93.3	273.5±57.2
Day 14	101.8±17.4	332±54.3	207±61.3	162.8±60.4	118.8±27.7	395.680.6	238.1±41
Day 21	111.3±10.4	309±76.8	161±21.1	128.6±47.1	93±10.9	351.6±99.4	209.1±29.7
Day 28	99±18.0	375.3±91.3	112.5±6.6	93.1±15.6	83.6±5.8	292± 98	200.5±29.5

Table 2: Bl.glucose level on day 3 before and after administration of extract of both Bark and Leaf

Extract dose in mg/kg.	Day 3	Mean	Std. Deviation	P
Bark150	Before	222.67	104.854	0.075
	After	183.00	72.44	
Bark300	Before	188.33	30.995	0.007
	After	136.17	44.593	
Leaf 150	Before	467.83	64.9	0.095
	After	445.8	89.2	
Leaf300	Before	314.3	58.5	0.070
	After	281.3	54.1	

Diagram showing blood glucose levels (mean) from day 0-28 days treated with Glibenclamide & extracts of Ficus bengalensis



Discussion

Diabetes mellitus is an endocrine disorder caused by an absolute lack of insulin or a relative lack of insulin that is insufficient to overcome insulin resistance.[14] Type 2 diabetes is the common form of diabetes, accounting for 85 to 95% of cases in developed nations and an even higher percentage in developing nations, according to the International Diabetes Federation. It usually presents in adult life. The treatment is initially diet management, exercise and weight loss that improves insulin resistance and it can reverse back to normal if patient is in pre-diabetes and requires anti diabetic drugs if patient is diabetic. In this study *F.bengalensis* has shown antidiabetic activity, the oral administration of aqueous extract of bark and leaves produced a hypoglycemic activity at all the doses. But bark 300mg/kg and 150mg/kg has shown reduction in the blood glucose levels (p value<0.0001) and also with leaf extract 150mg/kg from day 14 (highly significant, p<0.0001). Bark has produced a dose dependent increase in the hypoglycemic activity. However decreased hypoglycemic activity was observed with leaf 300mg/kg as the days progressed as compared to leaf extract 150mg/kg. Such phenomenon of less hypoglycemic response at higher doses is not uncommon with indigenous plants and has already been observed in plant Murrayakoenigii (Kesari et al., 2005),[15] Cynodondactylon (Singh et al., 2007), Trichosanthesdioica (Rai et al., 2008)[16] and Aeglemarmelos (Kesari et al., 2006).[17]

To know the immediate hypoglycemic effect of plant extract on day 3 pre prandial and post prandial

blood glucose levels were taken and evaluated. It was observed that there is decrease in the blood glucose with all the doses after 3 hours of administration but significant decrease in the bl.glucose (p value 0.007) seen with test dose of bark 300mg/kg on day 3, before and after or pre and post prandial observations indicate that the bark 300 mg/kg has got a potent hypoglycemic activity with p value less than 0.05 (Table 2). Extract of leaf 300mg/kg has shown potent decrease in the glucose level but statistically not significant. This indicates bark has a more potent hypoglycemic activity than leaf with highly significant statistical value.

This study goes in accordance with Rimishukla et al,[18] which showed that even at the dose of 50mg/kg of aqueous extract of bark of *F.bengalensis* has produced hypoglycemic activity. Vikas V Patil[19] in his study found that, aqueous extract of bark of f.bengalensis in the dose of 500mg/kg has exhibited significant antidiabetic activity which was evidenced by histopathological studies in normal and *F.bengalensis* treated alloxan induced diabetic rats.[20]

In a review article, Saxena A et al, observed the blood glucose lowering activity of dimethoxy derivative of leucocyndin-3-O-beta-d-galactogyl cellobiocide isolated from the bark, in normal and diabetic rats with extract of bark 250 mg/kg.[21,22] Other studies like Achrekar et al[23] and Augusti et al[24] showed the potent hypoglycemic activity of aqueous extract of bark. Its action seems to be probably both pancreatic by releasing insulin and also has extra pancreatic effect of stimulating utilization of glucose in peripheral tissues because it is active even in severely diabetic rabbits with FBG of 500 or even 700 mg/dl in whom beta cell reserve is likely to be destroyed almost completely. So F. bengalensis is known to have a considerably good hypoglycemic activity. A dimethoxy derivative of leucocyanidin 3-O-beta-D-galactosyl cellobioside isolated from the bark of F.bengalensis Linn. Demonstrated antidiabetic action. The leaves contain 9.63% crude protein, 26.84% crude fiber, 2.53% calcium oxalate and 45 of phosphorius. Ethanolic and aqueous extract of leaves contain strerols, flavanoids, phenol, tannins and saponins.[25,26]

The present study suggested that the plant extract can be successfully utilized for the management of diabetes due to their hypoglycemic action. Further studies on the nature of active principles involved would enlighten the exact mechanism involved and thus help to rationalize their use in the treatment of diabetes more effectively. There is a necessity to undertake further research to ascertain its exact mechanism of action and the implicating phytochemical constituents.

Conclusion

Further studies on the nature of active principles involved would enlighten the exact mechanism involved and thus help to rationalize their use in the treatment of diabetes more effectively.

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References

1. Michael JC, James M C, Vinaykumar, Cotran SR, Robbins LS. The pancreas. Robins editor. Basic pathology,7th ed. Newdelhi, Elsevier, 2003; 635-55.
2. International Diabetes Federation. IDF diabetes atlas. In: IDF, eds. A Book. 6th ed. Brussels, Belgium: International Diabetes Federation; 2013.
3. Kaveeshwar S A, Cornwall J. "The current state of diabetes mellitus in India". Australia Med J. 2014:7:45-8.
4. Lupi R, Del Prato S B-cell apoptosis in Type 2 Diabetes: quqntitative and functional consequences. DiabeteMetab.2008:34:556-64.
5. Alvin C, David D'Alessio. Endocrine pancreas and Pharmacotherapy of Diabetes Mellitus and Hypoglycemia. The pharmacological basis of therapeutics. Goodman and Gilman, 12thed.McGraw-Hill, 2011; 237-73.
6. Sicree R, Shaw J, Zimmet P. Prevalence and projections. In: D. Gan ed. Diabetes Atlas, World Diabetes foundation, 3rd ed., Brussels, Belgium International Diabetes Federation, 2006; 16-104.
7. Andalu B, Varadacharyalu "A. Control of hypoglycemia and retardation of cataract by mulberry leaves in streptozotocin diabetic rats". Indian J ExpBiol 2002; 40:791-95.
8. The wealth of India, Raw Material, Vol. IV, 1st edn. New Delhi, CSRI, 2003; 2426.
9. Kodoma T, Iwase M, Nunoi k, et al. "A diabetes model induced by neonatal alloxan treatment in rats". Diab Res Clin Pract 1993;20:183-9.
10. Lenzen S, Panten U. "History and mechanism of action". Diabetologia 1988;31:337-42.
11. The effect of oral administration of Aqueous Extract of Ficusbengalensis stem bark on some hematological and Biochemical parameters in rats with streptozotocin induced Diabetes. Turk J Biol 2009;3:9-13
12. Sankar S, Nair A. G. R. I. srerols and flavunoids of ficusbengalensis. Phytochemistry 2001;9(12):2583-84
13. Manoj A, Urmila A. Anti helimenthic activity of ficusbengalensis. Green pharmacy 2008;1702.
14. Asulander W, HaireJoshu D, Houstan C, Rhee CW, Williums JH.A controlled evaluation of staging dietary pattern to reduce the risk of diabetes in African American women. Diabetes care 2002; 25:809-14.
15. Kesari, AN, Gupta RK, Watal G. Hypoglycemic effect of Murrayakoenigii on normal and alloxan diabetic rabbits. Journal of Ethnopharmacology 2005:97:247–51.
16. Rai PK, Jaiswal D, Diwakar S, Watal G Antihyperglycemic profile of Trichosanthesdioica seeds in experimental models. Pharmaceutical Biology 2008; 46:360–365.
17. Kesari, AN, Gupta RK, Singh, SK, Diwakar S, Watal G. Hypoglycemic and anti-hyperglycemic activity of Aeglemarmelos seed extract in normal and diabetic rats. Journal of Ethanopharmacology 2006;107: 374–379.
18. Rimishukla, Kiran K, Prabhu KM, Suryanarayanamurty. Hypoglycemic effect of the water extract of Ficusbengalensis in alloxan recovered, mildly diabetic and

severely diabetic rabbits. Ind J Diab Dev Countries 1994;14:78-81.
19. VikasPatil, Vijay Patil. Ficusbengalensislinn, an overview. International Journal of Pharma and Biosciences 2010;V1(2):1-11.
20. Vijay SP, Chitra PV, Laxmiprasanna, Krishnaraju K.. Indian journal of Pharmacol 2008;40(4):183-185
21. Singh Ayodhya, Singh Kusum, Saxena Anjali. Review article: Hypoglycemic activity of different extracts of various herbal plants. International Journal of research in Ayurveda and pharmacy. (2010): Vol. 1(1) Sept-Oct 212-24.
22. Saeed Ahmad. Journal of Medicinal Plants Research 2011:Vol. 5(28): 6393-6400.
23. Achrekar S, Kaklij GS, Pote MS, Kelkar SM. Hypoglucemic activity of Eugenia jambolana and Ficusbengalensis: Mechanism of action. In Vivo 1991;5:143-47.
24. Sheeja Cherian, Vinod Kumar R, Augusti K.T. Antidiabetic effect of a glycoside of pelargonidin isolated from the bark of Ficusbengalensis Linn.. Ind. J. Biochem. Biophys. 1992; 29: 380-2.
25. Sankar S, Nair A.G.R.I. srerols and flavunoids of ficus bengalensis, phytochemistry 2001;9(12):2583-84.
26. Manoj A, Urmila A. Anti helimenthic activity of ficus bengalensis. Green pharmacy 2008:1702.