Research Article

Hypoglycaemic Activity of Bark Extracts of *Albizia lebbeck* Benth. in Streptozotocin induced Diabetic Rats

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ABSTRACT

In the present study, the chloroform, methanol and aqueous extracts of the barks of *Albizia lebbeck* Benth. (Family: Mimosaceae) were evaluated for hypoglycaemic activity in adult Wistar albino rats at 100, 200 and 400 mg/kg p. o. respectively using normoglycemic, glucose loaded and streptozotocin induced hyperglycaemic rat models. Metformin (250 mg/kg, p.o.) was used as reference standard for the activity comparison. Among the tested extracts, the methanol and aqueous extracts showed significant reduction in blood glucose levels in normal, glucose loaded and streptozotocin induced diabetic rats that is comparable to metformin, with more promising decrease in glucose concentration observed in methanol extract than the aqueous extract. The chloroform extract on the other hand, did not elicit significant reduction of blood glucose concentration. The preliminary phytochemical screening of *A. leeback* bark extracts revealed presence of steroids and sterols, triterpenoids, tannins and phenolic compounds, saponins, flavonoids, carbohydrates, gums and mucilages, proteins and amino acids. In acute oral toxicity study, no mortality and sign of toxicity were observed at the dose of 2000 mg/kg. The study established the scientific validation for the utility of this plant in the treatment of diabetes mellitus and justifies the use of the bark for treating diabetes as suggested in folklore remedies.

Keywords: *Albizia lebbeck,* Streptozotocin, Hyperglycaemic, Normoglycemic, OGTT.

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder resulting from insulin deficiency characterized by hyperglycaemia, altered metabolism of carbohydrates, protein and lipids and an increased risk of vascular complications. It is projected to become one of the world's main disablers and killers within the next 25 years[1,2]. Although different types of oral hypoglycaemic agents along with insulin for the treatment of diabetes mellitus are available, still these drugs have their own disadvantages and limitations[3]. Drug resistance to these medicines is also reported after prolonged treatment. Apart from currently available therapeutic options, many herbal medicines have been recommended for treatment of diabetes. Traditional herbal medicines have been used throughout the world for treatment of diabetes mellitus since time immemorial and search for antidiabetic factor from the plants always remained a potential area of investigation[4].

Albizia lebbeck Benth (Family: Mimosaceae) is deciduous, unarmed tree found throughout India, tropical and subtropical regions of Asia and Africa[5]. Traditionally, the plant is reported to be used for the treatment of a variety of ailments. The juice from the fresh leaves is credited for its effectiveness in treating conjunctivitis[6]. The use of aqueous extract of the bark (2 teaspoonfuls daily for one week before menses) by the females has been reported to be a good candidate to prevent conception[7]. The flowers are applied externally to boils, eruptions and swellings for quick healing[8]. During our field survey, we came across the tribes of Bangriposi in Simlipal Wild Life Century in Mayurbhanj district of Odisha who use the dried bark powder (two teaspoonfuls) with water orally for treating diabetes mellitus since ancient times and claim for its promising activity.

A good number of phytoconstituents including acyclic ester heneicos – 7 (z) enyl 24-hydroxy tetracos – 10 (z) enoate, lupeol, oleanolic acid, docosanoic acid, β-sitosterol, albigenic acid, 3',5 dihydroxy 4', 7 dimethoxy flavone and N-benzoyl L phenyl alaninol have been reported from the pods[9,10]. Three main saponins named albiziasaponins A, B and C in addition to catechin, lebbecacidin, fridelin and β-sitosterol were reported from the barks [11,12].

Reports on pharmacological activities on this plant are scarce. *A. lebbeck* bark extract posses antispermatogenic, antiandrogenic activities of in male albino rats [13] and antioxidant potential[14]. Scientific studies substantiating the use of bark powder in treatment of diabetes are lacking. Therefore, in the present study we report the antidiabetic activity of the barks using recommended laboratory animal models.

MATERIALS AND METHODS

Plant Material and Preparation of Extracts

Fresh barks of *A. lebbeck* were collected from the Simlipal forest of Mayurbhanj districts of Odisha during Aug 2011 and authenticated. After authentication, the plant material was collected in bulk, shade dried and pulverized

in a mechanical grinder to obtain coarse powder. The dried powdered plant material (1.5 kg) was defatted with petroleum ether (40º–60ºC) and extracted successively with chloroform, methanol and water using a soxhlet extractor. Following extraction, the liquid extracts were separately concentrated under vacuum and extractive value calculated (yield: Chloroform extract- 1.4%, methanol extract-8.7% and aqueous extract-10.9% w/w with respect to the dried plant material). Qualitative phytochemical studies were performed on the extracts to study the nature of phytoconstituents they contain[15, 16].

Animals

Healthy adult Wistar rats (150-200 g) of either sex were used. The animals were kept in standard polypropylene cages at room temperature (30 ± 2°C, 66-65% RH). The experiments on animals were conducted in accordance with the internationally accepted principles for laboratory animal use and the experimental protocols were duly approved by the Institutional Animal Ethics Committee.

Acute Oral Toxicity Study [17,18]

Toxicity studies of the test extracts were evaluated as per OECD guideline 423. The test extracts were suspended in 0.5% w/v sodium carboxymethyl cellulose in distilled water. The animals were fasted overnight, provided only water, after which the test extracts were separately administered to the respective groups orally at the dose level of 5 mg/kg and the groups of animals were observed carefully and continuously for any behavioural changes for 72 h and for mortality if any up to a period of 14 days. Since no mortality was observed in any of the groups of animals, the procedure was repeated for further higher doses such as 50, 300, and 2000 mg/ kg. The animals were observed for toxic symptoms such as behavioural changes, locomotion, convulsion, and mortality for 72 h.

Screening for Antidiabetic Activity

Screening for antidiabetic activity of the test extracts was assessed using normoglycemic, glucose loaded and streptozotocin induced hyperglycaemic rats. Metformin (250 mg/kg p.o.) was used as reference standard for activity comparison. All the test samples were suspended in 0.5% w/v sodium carboxymethyl cellulose in distilled water. The test samples were fed to the animals through oral route. The selected animals were divided into different groups comprising of six rats in each group in different models adopted.

Using normoglycemic rats

For the normoglycemic study, rats were divided into eleven groups. The animals were allowed free access to food and water before and throughout the duration of experiment. At the beginning of the experiment, taken as zero time (0 h), blood was withdrawn from the tip of the tail of each rat and the blood glucose was estimated with a prestandardized Acu-Chek Active glucometer, Roche Diagnostics, Germany using standard strips. Control was designated as Group I and received vehicle (2 ml/kg) through oral route. Group-II animals received metformin (250 mg/kg p.o.). Group-III, IV and V received 100, 200 and 400 mg/kg of chloroform extract, Group-VI, VII and VIII received 100, 200 and 400 mg/kg of methanol extract, Group-IX, X and XI received 100, 200 and 400 mg/kg aqueous extract of *A. lebbeck* in a similar manner. After 1, 2, 4 and 8 h of administration of single dose of test samples, a drop of blood was collected from tip of the tail of each animal and blood glucose concentrations were measured[19]. The results are presented in Table 1.

Oral glucose tolerance test (OGTT)

Healthy overnight fasted rats were divided into eleven groups. Thirty minute following the various treatment schedules, each rat was given an oral glucose load of 2 g/kg. Group I served as a control and received only vehicle (2 ml/kg) through oral route. Group-II received metformin (250 mg/kg p.o.). The other groups received 100, 200 or 400 mg/kg of chloroform, methanol and aqueous extracts of *A. lebbeck* in a similar manner. Blood samples were collected before and at 30, 60, 150 and 180 min after glucose loading and blood glucose levels were estimated [20]. The results are depicted in Table 2.

Streptozotocin Induced hyperglycaemic rats

Experimental diabetes was induced in overnight fasted rats (18 h) by single intraperitoneal injection (65 mg/kg) of streptozotocin in citrate buffer (pH 4.4, 0.1M). After one hour, the animals were provided feed *ad libitum*. The blood glucose level was checked before streptozotocin administration and 72 h after streptozotocin induction by withdrawing blood from the tip of the tail of each rat. Animals were considered diabetic when the blood glucose level was raised beyond 200 mg/100ml of blood. This condition was observed at the end of 72 h after streptozotocin induction. The diabetic animals were then placed in different groups consisting of six animals in each. Group-I which served as diabetic control received vehicle (2 ml/kg) orally. Metformin (250 mg/kg p.o.), was received by Group-II. Chloroform, methanol or aqueous extracts of *A. lebbeck* at doses of 100, 200 or 400 mg/kg were received by the other groups of animals in a similar manner. After 1, 2, 4 and 8 h of administration of single dose of test samples, blood glucose levels were measured[21]. The results are tabulated in Table 3.

Statistical analysis

All values are expressed as mean ± SEM. Statistical analysis was performed by One-way Analysis of Variance (ANOVA) followed by Dunnet's t-test. A 'p' value less than 0.05 was considered significant.

RESULTS AND DISCUSSION

The bark of *A. lebbeck* has been used by the local tribes of Mayurbhanj district of Odisha for the treatment of diabetes mellitus since time immemorial and they claim for its promising activity. The preliminary phytochemical screening of *A. leeback* bark extracts revealed presence of steroids and sterols, triterpenoids, tannins and phenolic

compounds, saponins, flavonoids, carbohydrates, gums and mucilages, proteins and amino acids. In acute oral toxicity study, no mortality and sign of toxicity were observed at the dose of 2000 mg/kg. Results of antidiabetic activity of *A. lebbeck* bark extract established the scientific basis for the utility of this plant in the treatment of diabetes. Among the tested extracts, the methanol and aqueous extracts showed significant reduction in blood glucose levels in normal, glucose loaded and streptozotocin induced diabetic's rats at the tested dose levels with more promising decrease in glucose concentration with the methanol extract in a dose dependant manner. The chloroform extract on the other hand, did not elicit significant reduction of blood glucose concentration (Table 1 to 3).

Table 1: Effect of different extracts of the barks of *A. lebbeck* on the blood glucose level in normal rats

Groups	Treatment	Dose	Blood glucose concentration (mg / dl) Time (h) after treatment				
			Fasting	1 h	2 h	4 h	8 h
I	Control	2 ml/kg	79.43 ± 2.35	77.45 ± 2.17	77.25 ± 2.25	76.46 ± 2.28	74.23 ± 2.11
II	Metformin	250 mg/kg	80.45 ± 2.45	67.33 ± 3.48* (16.30%)	62.5 ± 3.52** (22.31%)	55. 4 ± 3.20** (31.13%)	41.64 ± 3.12** (48.24%)
III	Chloroform extract	100 mg/kg	78 ± 2.60	75.5 ± 2.56 (3.20%)	74.16 ± 2.68 (4.92%)	71.88 ± 2.38 (7.84%)	70.66 ± 2.48 (9.41%)
IV		200 mg/kg	78.25 ± 3.72	73 ± 3.17 (6.71%)	71.53 ± 3.22 (8.58%)	70.1 ± 2.45 (10.41%)	68.43 ± 2.52 (12.55%)
V		400 mg/kg	78.25 ± 2.43	73.53 ± 3.52 (6.03%)	71.63 ± 2.86 (9.26%)	69.56 ± 2.57 (11.10%)	68.16 ± 2.44 (12.89%)
VI	Methanol extract	100 mg/kg	79.66 ± 2.53	74.83 ± 2.42 (4.81%)	72.3 ± 2.7 (9.24%)	68.73 ± 2.25 (13.72%)	63.4 ± 2.33* (20.41%)
VII		200 mg/kg	77.53 ± 3.45	71.5 ± 2.47 (7.78%)	69.16 ± 3.25 (10.79%)	63.83 ± 3.23* (17.67%)	57.5 ± 3.54** (25.83%)
VII		400 mg/kg	74.26 ± 2.85	63.26 ± 2.41 (14.81%)	60.73 ± 2.48* (18.22%)	54.1 ± 2.57** (27.15%)	46.5 ± 3.15**) (37.38%)
IX	Aqueous extract	100 mg/kg	77.53 ± 2.58	75.3 ± 3.82 (2.87%)	73.4 ± 3.56 (5.23%)	68.7 ± 3.41 (11.39%)	67.42 ± 3.11 (13.04%)
X		200 mg/kg	78.23 ± 2.13	74.22 ± 2.53 (5.12%)	72.12 ± 2.52 (7.81%)	67.13 ± 2.25 (14.18%)	64.23 ± 2.27* (17.89%)
XI		400 mg/kg	79.65 ± 2.5	73.426 ± 3.74 (7.81%)	71.36 ± 3.78 (10.41%)	65.25 ± 2.36* (18.08%)	55.25 ± 2.84** (30.63%)

Results expressed as Mean ± SEM from six observations (n = 6). *P<0.05, **P<0.01 as compared with control group (One way, ANOVA followed by Dunnet's t-test). Figures in parenthesis denote percentage reduction of blood glucose.

The normoglycaemic study (Table 1) indicated that the methanol extract of *A. lebbeck* produced more promising activity over the aqueous extract. The standard drug metformin showed 48.24% reduction of blood glucose at 8 h whereas the methanol extract showed 20.41%, 25.83% and 37.38% reduction in the glucose concentration at 100, 200 and 400 mg/kg respectively.

A significant reduction in blood glucose level (compared with initial level) was also observed with the methanol and aqueous extracts at all tested doses, with the maximum fall of 16.65, 23.79 and 31.29 percentage reduction in blood glucose concentration at the end of 180 min with the methanol extract (Table 2). The aqueous extract on the other hand, showed percentage reduction of 16.16 and 22.02 at the dose of 200 mg/kg and 400 mg/kg respectively at the end of 180 min after glucose administration. The standard drug metformin showed maximum lowering glucose concentration of 38.98% at the end of 180 min. The oral glucose tolerance test is the only form of glucose tolerance testing recommended for diagnosis of diabetes[22]. The changes in blood glucose concentration, which results from oral carbohydrate load is theoretically dependent on the rate at which carbohydrate enter the small intestine, the rate of digestion and intestinal absorption of glucose and the rate of insulin driven metabolism.

The result streptozotocin induced hyperglycemic rats is presented in Table 3. Single dose of administration of test samples indicated that metformin showed its significant action from 1 h onwards of its administration, whereas methanol extract at 200 and 400mg/kg produced significant and consistent antihyperglycemic effect from 2 h onwards. Metformin reduced the blood glucose concentration by 61.86% at 8 h of its administration. Methanol extract at 100, 200 and 400 mg/kg reduced blood glucose concentration to 17.54%, 31.19% and 54.85% respectively at the end of 8 h. The aqueous extract treated group also revealed significant reduction (15.24% and 29.48%) in blood glucose concentration at the dose of 200 mg/kg and 400mg/kg respectively at different time. Streptozotocin is widely used to induce experimental diabetes in animals.

Table 2: Effect of different extracts of the bark of *A. lebbeck* in Oral Glucose Tolerance Test

Groups	Treatment	Dose	Blood glucose concentration (mg / dl) Time (min) after treatment				
			Fasting	30 min	60 min	150 min	180 min
I	Control	2 ml/kg	79.4 ± 2.15	118 ± 2.53	126.5 ± 7.25	133 ± 6.85	129.83 ± 7.53
II	Metformin	250 mg/kg	80.43 ± 2.29	118.73 ± 2.46	100.14 ± 4.54* (15.25%)	86.42 ± 6.52** (27.11%)	72.144 ± 6.57** (38.98%)
III	Chloroform extract	100 mg/kg	81.12 ± 2.23	122.85 ± 2.53	119.7 ± 6.81 (2.56%)	115.42± 4.46 (6.05%)	111.4 ± 5.45 (9.32%)
IV		200 mg/kg	80.72 ± 2.25	118.28 ± 2.49	114.6 ± 4.72 (3.11%)	110.74 ± 6.78 (6.37%)	107.14 ± 6.26 (9.42%)
V		400 mg/kg	80.56 ± 2.18	118.23 ± 2.75	112.53 ± 5.12 (4.82%)	109.42 ± 6.17 (7.45%)	103.3 ± 5.13 (12.63%)
VI	Methanol extract	100 mg/kg	82.23 ± 2.42	123 ± 2.29	115.4 ± 5.23 (6.18%)	114.25 ± 5.13 (7.11%)	102.52 ± 4.61* (16.65%)
VII		200 mg/kg	82.5 ± 2.57	122.3 ± 2.16	112.5 ± 5.25 (8.1%)	105.26 ± 6.25* (13.93%)	93.2 ± 6.18** (23.79%)
VIII		400 mg/kg	80.4 ± 2.25	121.24 ± 2.15	103.25 ± 4.23* (14.8%)	89.23 ± 5.54** (26.40%)	83.3 ± 6.29** (31.29%)
IX	Aqueous extract	100 mg/kg	81.45 ± 2.4	119.23 ± 2.23	113.56 ± 5.25 (4.75%)	111.52 ± 4.24 (6.46%)	107.27 ± 8.59 (10.03%)
X		200 mg/kg	83.25 ± 2.45	124.35± 2.46	113.73 ± 4.31 (8.54%)	107.4 ± 6.50* (13.63%)	104.26 ± 5.52* (16.16%)
XI		400 mg/kg	82.7± 2.6	122.15± 2.64	107.22 ± 6.18 (12.22%)	102.56 ± 7.6* (16.04%)	95.25 ± 7.15* (22.02%)

Results expressed as Mean ± SEM from six observations (n = 6). *P<0.05, **P<0.01 as compared with control group (One way, ANOVA followed by Dunnet's t-test). Figures in parenthesis denote percentage reduction of blood glucose.

Table 3: Effect of different extracts of the barks of *A. lebbeck* on the blood glucose level in streptozotocin induced diabetic rats

Groups	Treatment	Dose	Blood glucose concentration (mg / dl) Time (h) after treatment				
			Fasting	1 h	2 h	4 h	8 h
I	Control	2 ml/kg	228.43 ± 7.25	236.54 ± 7.14	237.46 ± 6.24	242.52 ± 7.25	246.78 ± 6.32
II	Metformin	250 mg/kg	229.25 ± 8.26	191.60 ± 9.14* (16.57%)	157.25 ± 8.81** (31.37%)	106.32 ± 10.23** (53.70%)	87.28 ± 11.52** (61.86%)
III	Chloroform extract	100 mg/kg	227.75 ± 11.15	224.45 ± 9.48 (1.45%)	215.32 ± 11.23 (5.44%)	214.25 ± 9.25 (5.92%)	208.4 ± 13.23 (8.47%)
IV		200 mg/kg	225.4 ± 11.2	219.42 ± 10.95 (2.66%)	209.75 ± 11.65 (6.96%)	208 ± 13.42 (7.71%)	202.53 ± 14.14 (10.15%)
V		400 mg/kg	224.5 ± 11.25	211.4 ± 10.54 (5.83%)	202.58 ± 09.74 (9.79%)	191.44 ± 14.56 (14.74%)	186.52 ± 14.62 (16.92%)
VI	Methanol extract	100 mg/kg	228.52 ± 8.37	211.12 ± 9.4 (7.61%)	209.35 ± 11.22 (8.40%)	197.75 ± 15.43 (13.47%)	188.4 ± 11.52* (17.54%)
VII		200 mg/kg	230.25 ± 09.15	208.55 ± 10.36 (9.44%)	194.72 ± 11.47* (15.42%)	177.23 ± 16.23* (23.02%)	158.43 ± 11.45** (31.19%)
VIII		400 mg/kg	222.75 ± 11.8	197.42 ± 12.12 (11.36%)	180.72 ± 10.52* (18.85%)	131.13 ± 13.35** (41.12%)	100.56 ± 12.75** (54.85%)
IX	Aqueous extract	100 mg/kg	226.36 ± 11.56	218.23 ± 11.87 (3.57%)	213.52 ± 8.75 (5.65%)	204.52 ± 12.23 (9.63%)	199.2 ± 15.42 (11.97%)
X		200 mg/kg	221.12 ± 11.32	209.42 ± 13.45 (5.29%)	203.43 ± 12.41 (8.05%)	192.5 ± 12.57 (12.93%)	187.45 ± 14.19* (15.24%)
XI		400 mg/kg	223.25± 10.86	206.42 ± 10.74 (7.54%)	200.2 ± 13.74 (10.30%)	189.41 ± 14.4* (15.14%)	157.4 ± 14.75** (29.48%)

Results expressed as Mean ± SEM from six observations (n = 6). *P<0.05, **P<0.01 as compared with control group (One way, ANOVA followed by Dunnet's t-test). Figures in parenthesis denote percentage reduction of blood glucose.

The mechanism of action on β-cells of the pancreas has been intensively investigated and now is quite well understood. The deleterious effect of streptozotocin results from the generation of highly reactive carbonium ions (CH_3^+) that cause DNA breaks by alkylating DNA bases at various positions, resulting in activation of the nuclear enzyme, poly(ADP-ribose) synthetase, thereby depleting the cellular enzyme substrate (NAD^+), leading to cessation of NAD^+ -dependent energy and protein metabolism. This in turn leads to reduced insulin secretion[22]. It has been suggested that free radical stress occurred during β-cell destruction mediated by mononuclear phagocytes and cytokines[24, 25].

In our present study, we have observed that the methanol and aqueous extracts of *A. lebbeck* could reverse the hyperglycemic condition in diabetic rats and brought about hypoglycemic action because blood glucose once lowered by the extracts did not increase again throughout experiment when compared to untreated control. The possible mechanism of action of the test extracts may be due to by promoting the insulin release from the undestroyed β-cells or its action may be insulin like[26]. Further studies are recommended to find out the possible mode of action.

CONCLUSION

The results provided a scientific validation of the folklore use of the *A. lebbeck* and suggested that this plant (bark) has promising therapeutic activity for the maintenance of diabetes mellitus.

REFERENCES

1. Zhang P, Zhang X, Brown J, Global healthcare expenditure on diabetes for 2010 and 2030, Diabetes Research and Clinical Practice, 87(3),2010, 293–301.
2. Shaw JE, Sicree RA, Zimmet PZ, Global estimates of the prevalence of diabetes for 2010 and 2030, Diabetes Research and Clinical Practice, 87(1),2010,4-14.
3. Wadkar KA, Magdum CS, Patil SS, Naikwade NS, Review Article Anti-Diabetic Potential and Indian medicinal Plants, Journal of Herbal Medicine and Toxicology, 2(1), 2008, 45-50.
4. Odhav B, Kandasamy T, Khumalo N, Baijnath H, Screening of African traditional vegetables for their alpha-amylase inhibitory effect, Journal of Medicinal Plants Research, 4(14),2010,1502–1507.
5. Kirtikar KR, Basu BD, Indian Medicinal Plants, 2nd edition , Vol.II, International Book Distributer, Dehradun, 1987, 912-913.
6. Venkata Ratnam K, Reddy, G, Tirupati, Venkata Raju RR, Herbal remedies for eye infections used by the tribals of Nallamala forests, Andhra Pradesh, Indian Journal of Traditional Knowledge, 9(4), 2010,765-767.
7. Shah GM, Khan MA, Ahmad M, Zafar M, Khan AA, Observations on antifertility and abortifacient herbal drugs, African Journal of Biotechnology. 8 (9), 2009, 1959-1964.
8. Panhwar AQ, Abro H, Ethnobotanical studies in Mahal Kohistan, Pak. J. Bot. 39(7), 2007, 2301-2315.
9. Barua AK, Raman SP, The constitution of albigenic acid-A new triterpenoid sapogenin from Albizia lebbeck Benth, Tetrahedron, 7, 1959, 19-23.
10. Rashid RB, Chowdhury R, Jabbar A, Hasan CM, Rashid MA, Constituents of *Albizia lebbeck* and antibacterial activity of an isolated flavone derivative, Saudi Pharma.Journal, 11 (1-2),2003, 52-6.
11. Anonymous, The Wealth of India. Vol. 1, New Delhi Publication & Information Directorate, CSIR, 1985, 126-127.
12. Pal BC, Achari B, Yoshikawa K, Shigenobu A, Saponins from *Albizia lebbeck*,Phytochemistry, 38(5),1995,1287-1291.
13. Gupta RS, Kachhawa JBS, Chaudhary R, Antispermatogenic, antiandrogenic activities of *Albizia lebbeck* (L.) BENTH bark extract in male albino rats, Phytomedicine, 13, 2006, 277-283.
14. Resmi CR, Venukumar MR, Latha MS, Antioxidant activity of *Albizzia Lebbeck* in alloxan diabetic rats, Indian J Physiol Pharmacol, 50(3), 2006, 297–302.
15. Kokate CK, Practical Pharmacognosy. Vallabh Prakashan, Delhi, 4th: Edition, 1994, 107.
16. Harborne JB, Phytochemical Methods, A Guide to Modern techniques of Plant analysis, Chapman and Hall, New York, 1984,37-214.
17. OECD. Guidelines for the Testing of Chemicals /Section 4, Health Effects Test No. 423, Acute Oral toxicity - Acute Toxic Class Method, Organization for Economic Cooperation and Development, Paris, France, 2002.
18. Patel MA, Patel PK, Patel MB, Effect of ethanol extract of Ficus bengalensis (bark) on inflammatory bowel disease, Indian Journal of Pharmacology, 2010, 42(4), 214-218.
19. Mondal S, Dash GK, Hypoglycaemic activity of the bark of *Spondras pinnata* Linn. Kuz, Phatmacognosy Magazine. Supplement. 19 (4), 2009, 42-45.
20. Shirwaikar A, Rajendran K, Barik R, Effect of aqueous bark extract of Garuga pinnata Roxb. in streptozotocin–nicotinamide induced type-II diabetes mellitus, Journal of Ethnopharmacology, 107, 2006, 285–290.
21. Ortiz-Andrade RR, Sanchez-Salgado JC ,Navarrete-Vazquez G, Webster SP, Binnie M, Garcıa-Jimenez S, Leon-Rivera I, Cigarroa-Vazquez P, Villalobos-Molina R, Estrada-Soto S, Antidiabetic and toxicological evaluations of naringenin in normoglycaemic and NIDDM rat models and its implications on extra-pancreatic glucose regulation, Diabetes, Obesity and Metabolism, 10,2008, 1097–1104.
22. Srinivasan S, karundevi B, Comprative evaluation of hypoglycaemic activity of two medicinal Plants in alloxan diabetic rats, Int.J.Pharmacol. vol.1, 2005, 267-276.
23. Yamamoto H, Uchigata Y, Okamoto H, Streptozotocin and alloxan induce DNA strand breaks and poly (ADP-ribose) synthetase in pancreatic islets, Nature, 294, 1981, 284-286.
24. Pitkanen O, Martin J, Hallman M, Akerblom H, Free radical activity during development of insulin-dependent diabetes mellitus in the rat, Life Sci. 50, 1992, 335-339.
25. Nagy MV, Chan EK, Teruya M, Forrest LE, Likhite V, Charles MA, Macrophage-mediated islet cell cytotoxicity in BB rats, Diabetes, 38(10), 1989, 1329-1331.
26. Chandola HM, Tripathi SN, Udupa KN, Effect of *Cinnamomum tamala* on plasma insulin vis-a-vis blood sugar in patients of 269 diabetes mellitus, J. Res. Ayur Sidha. Vol.1, 1980, 345-57.

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