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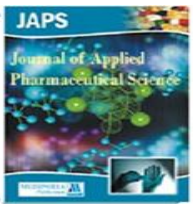

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Invivo Antidiabetic evaluation of Neem leaf extract in alloxan induced rats

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ABSTRACT

Azadirachta indica has been used medicinally throughout history by many different cultures. Many compounds have been found in the exudates of the, *Azadirachta indica* plant that have been used medically by humans. We have examined the pharmacological hypoglycemic action of *Azadirachta indica* in diabetic rats. After treatment for 24 hrs, *Azadirachta indica* 250mg/kg (single dose study) reduced glucose (18%), cholesterol (15%), triglycerides (32%), urea (13%), creatinine (23%), and lipids (15%). Multiple dose study for 15days also reduced creatinine, urea, lipids, triglycerides and glucose. In a glucose tolerance test in diabetic rats with neem extract 250 mg/kg demonstrated glucose levels were significantly less compared to the control group. , *Azadirachta indica* significantly reduce glucose levels at 15th day in diabetic rats. *Azadirachta indica* serves as an important alternative source in the management of diabetes mellitus involved in reducing increased blood glucose during diabetes which should be examined further by oral hypoglycemic therapy.

Key words: Diabetes, glucose, Azadirachta indica, Cholesterol, Urea, Creatinine, Triglycerides.

INTRODUCTION

Azadirachta indica can grow into a big tree to a height of about 20 to 35 m. Its canopy of leaves makes it a useful shade tree. It is planted along roads and avenues in the towns and villages of India. It is a tall evergreen tree with the small bright green leaves. It is up to 100 feet tall. It blossoms in spring with the small white flowers. It has a straight trunk. Its bark is hard rough and scaly, fissured even in small trees. The colour of the bark is brown grayish. The leaves are alternate and consist of several leaflets with serrated edges. Its flowers are small and white in color. The edible fruit is oval, round and thin skinned. Several pharmacological activities and medicinal applications of various parts of neem are well known (Jacob et al., 2006). Biological activity of neem is reported with the crude extracts and their different fractions from leaf, bark, root, seed and oil (Serrano et al., 2009). However, crude extract of different parts of neem have been used as traditional medicine for the treatment of various diseases. Various parts of the neem tree have been used as traditional ayurvedic medicine in India from time immemorial. The medicinal utilities have been described, especially for leaf, fruit and bark. Neem oil and the bark and leaf extracts have been therapeutically used as folk medicine to control leprosy, intestinal helminthiasis, respiratory disorders, and constipation and also as a general health promoter. Its use for the treatment of rheumatism, chronic syphilitic sores and indolent ulcer has also been evident. Neem oil finds use to control various skin infections1. Bark, leaf, root, flower and fruit together cure blood morbidity, biliary afflictions, itching, skin ulcers, burning sensations and pthysis. However, apart from these uses, there are several reports on the biological activities and pharmacological actions of neem based on modern scientific investigations. (Ramchandran et al.,2001). Diabetic rats have been widely used as model for diabetic studies. Diabetic rats are

Table 1. Effect of ethanolic neem leaf extract on serum glucose levels in alloxan induced diabetic rats after single dose administration

GROUPS	DRUG	DOSE	0 Hr	1 Hr	2 Hr	4 Hr	6 Hr	8 Hr	12 Hr	24 Hr
I	Normal control	Distilled water	113.2 ± 7.43	113.2 ± 7.43	114.4 ± 8.84	111± 9.97	111.4± 7.73	111.6± 6.30	110.6± 6.42	111± 5.7
II	Diabetic Control	5% w/v Tween 80	179.4 ± 17.3	351.8± 91.259	437.6± 88.71	485± 43.92	474.6± 37.44	463.2± 42.5	428.8± 38.7	408.4± 35.36
III	Diabetic Control+ NLE	100 mg/Kg	229 ± 16.7	199± 17.46	178± 11.51	136.5± 14.96	122.24± 59.61	122.2± 13.71	130.16± 45.16	95.94± 21.41
IV	Diabetic Control+ NLE	250 mg/Kg	888.1 ± 136.9	879.2± 140.18	677.7± 68.79	587.6± 94	412.2± 59.61	359.4± 133.76	317.6± 119.03	296± 123.46
V	Diabetic Control+ Glibenclamide	2.5 mg/kg suspended in 2% v/v Tween 80	298.2 ± 7.66	282.8± 4.91	272± 6.51	240.2± 3.96	191.8± 5.40	132± 4.89	104.94± 5.59	98.66± 7.24

Table 2. Effect of ethanolic neem leaf extract on serum creatinine levels in alloxan induced diabetic rats after single dose administration

GROUPS	DRUG	DOSE	0 Hr	1 Hr	2 Hr	4 Hr	6 Hr	8 Hr	12 Hr	24 Hr
I	Normal control	5% w/v Tween 80	0.38± 0.02	0.38± 0.02	0.37± 0.02	0.37± 0.09	0.37± 0.02	0.38± 0.02	0.38± 0.02	0.37± 0.02
II	Diabetic Control	5% w/v Tween 80	7.22± 0.31	6.98± 0.32	6.86± 0.30	6.72± 0.33	6.52 ± 0.30	6.3± 0.3	6.46± 0.23	6.62± 0.19
III	Diabetic Control+ NLE	100 mg/Kg	6.46± 0.27	6.5± 0.21	6.2± 0.20	5.86± 0.24	5.24± 0.23	4.58± 0.24	3.68± 0.19	2.82± 0.83
IV	Diabetic Control+ NLE	250 mg/Kg	6.66± 0.18	6.54± 0.11	5.92± 0.23	5.36± 0.28	4.78± 0.20	4.1± 0.27	3.32± 0.29	2.28± 0.25
V	Diabetic Control+ Glibenclamide	500 mg/kg	6.7± 0.15	6.48± 0.17	6.24± 0.20	5.94± 0.20	5.68± 0.21	5.12± 0.19	3.9± 0.29	3.1± 0.31

characterized by hyper glycemia, glucose intolerance, and hyper secretion of insulin after glucose feeding, low glucagons secretion, hyper-triglyceridemia and hypercholesterolemia. In particular, very low density lipoproteins (VLDL) and high density lipoproteins (HDL) are increased. (Huber et al., 2005). In the present study, the diabetic model was used to investigate the characteristics of anti-hyperglycemic effect of *Azadirachta indica* in this model. Possible mechanisms of Azadirachta *indica* Anti-diabetic action are described using these models.

METHODS AND MATERIALS

Animals

Wistar rats of weight between 150 to 200 gms obtained from NIN, Hyderabad, India, were used in the study. The animals were maintained under standard conditions in animal house of Vaageswari Institute of Pharmaceutical Sciences.

The rats were males 8-10 weeks old with average weight of 150-200g.Animals were housed 3-4 per cage in a temperature-controlled (22+/-1) c room, with a light/dark cycle of 12hr.For a week following their arrival, the animals were allowed free access to the standard rat chow diet and tap water they were acclimating to the environment. Rats were also monitored daily and cages cleaned thrice weekly. At the start of the experiment animals were randomly distributed so that body weights, initial triglycerides (TG), total cholesterol (TC), other parameters in all the experimental groups were similar.(Chandra et al.,2007)

Materials

Azadirachta indica leaves are collected from Local areas of Karimnagar (dist), Andhra Pradesh, India. The collected plant leaves was sun dried, pulverized by a mechanical grinder, sieved through 40mesh. About 120g of powdered materials were extracted using ethanol (50°C) using soxhlet apparatus (Grover et al.,2002). The extraction was carried out until the extractive becomes colorless. The extracts is then concentrated by distillation process and dried under reduced pressure. The solvent free semisolid mass thus obtained is used for the experiment. This semisolid mass contains the active compound Nimbidin.(Johann et al., 1998-2002)

DATA ANALYSIS

All data are expressed as the standard error of the mean. Comparisons among the control and treatment groups were made using analysis of variance followed by a Student- Newman-Keuls t-test using the Graph pad instat statistical program. With all analyses, an associated probability (p value)of less than 5%($P<0.05$) was considered significant.

Experimental protocol

The test samples were suspended in distilled water. Glibenclamide (2.5 mg/kg) was used as reference control during the study. All the test samples were administered through oral route.(Bhat et al., 2009)

Single dose study

In normoglycemic rats

The rats were fasted for 18 h, but were allowed free access to water before and throughout the duration of experiment. At the end of the fasting period, taken as zero time (0 h), blood was withdrawn (0.1 ml) from the retro orbital route of each rat under mild ether anesthesia. Plasma was separated following centrifugation the glucose was estimated by using Glucose

Table 3. Effect of ethanolic neem leaf extract on urea levels in serum in alloxan induced diabetic rats after single dose administration

GROUPS	DRUG	DOSE	0 Hr	1 Hr	2 Hr	4 Hr	6 Hr	8 Hr	12 Hr	24 Hr
I	Normal control	5% w/v Tween 80	29± 1	28.4± 1.6	28.6± 0.89	28.9± 1.4	29.4± 1.4	30.2± 1.2	29.2± 1.3	29.6± 1.5
II	Diabetic Control	5% w/v Tween 80	147.16± 4.52	144.6± 3.2	145.06± 1.9	144.48± 2.6	143.66± 2.2	144.56± 2.6	144.38± 2.7	145.36± 2.8
III	Diabetic Control+ NLE	100 mg/Kg	1.55± 4.1	153.14± 5.4	149.4± 6.2	133.08± 5.38	130± 5.7	127.4± 5.8	120.24± 1.5	94. 76± 1.7
IV	Diabetic Control+ NLE	250 mg/Kg	160± 1.6	157.64± 1.8	154.66± 1.77	153.3± 1.6	150.26± 1.8	124.46± 1.6	123.66± 2.4	92.78± 1.9
V	Diabetic Control+ Glibenclamide	500 mg/kg	148± 8.6	144.4± 9.8	133.5± 12.9	127.38± 12.6	120.14± 12.45	112.48± 9.4	106.12± 10.2	99.4± 9.9

Table 4. Effect of ethanolic neem leaf extract on cholesterol serum in alloxan induced diabetic rats

GROUPS	DRUG	DOSE	0 Hr	1 Hr	2 Hr	4 Hr	6 Hr	8 Hr	12 Hr	24 Hr
I	Normal control	5% w/v Tween 80	71.18± 1.39	70.88± 1.0	70.76± 1.4	70.92± 0.8	70.78± 1.25	69.84± 1.3	70.84± 0.89	70± 0.9
II	Diabetic Control	5% w/v Tween 80	293.28± 3.9	293.08± 3.2	292.9± 3.5	292.48± 3.2	289.68± 2.7	291.5± 3.02	291.8± 1.8	291.32± 1.76
III	Diabetic Control+ NLE	100 mg/Kg	301.54± 4	300.76± 4	297.88± 4.5	293± 3.3	292.72± 2	290.02± 1.99	285.74± 2.1	275.74± 4.3
IV	Diabetic Control+ NLE	250 mg/Kg	310.4± 3.3	310.02± 3	300.7± 1.8	294.14± 1.7	285.44± 2.2	277.02± 2.43	268.9± 2.9	257.22± 4.6
V	Diabetic Control+ Glibenclamide	500 mg/kg	289.76± 3.2	289.04± 3	286.16± 3	282.42± 3.4	277.89± 2.5	270.2± 2.73	260.18± 1.8	250.68± 1.7

estimation kit from 'One touch ultra', U.S.A. The normal rats were then divided into four groups of five rats each. Groups III and IV received the test extract at a dose of 100 and 250 mg/kg, respectively, through oral route. Group V received glibenclamide (2.5 mg/kg) and served as reference control. All the test samples were administered in a similar manner. Blood glucose levels were examined after 1,2, 4, 6, 8,12 and 24 hrs of administration of single dose of test samples.

In Alloxan induced diabetic rats

The acclimatized rats were kept fasting for 24 hrs with water *ad libitum* and injected intraperitoneally a dose of 120 mg/kg of Alloxan monohydrate in normal saline. After 1 hr, the rats were provided feed *ad libitum.* The blood glucose level was checked before Alloxanisation and 24 h after Alloxanisation as above.(Nahar et al., 2010)

Experimental Design

Rats were considered diabetic when the blood glucose level was raised beyond 200 mg/100 ml of blood. This condition *was* observed at the end of 48 hrs after
Alloxanisation. The rats were segregated into five groups of five rats in each (Chattopadhyaya et al.,1999)

Group I – Normal Control and rats received only vehicle that is distilled water.

Group II – Diabetic control and rats received only vehicle that is distilled water.

Group III – Rats received Ethanol Extract of *Azadirachta indica* (100 mg/kg/day p.o) suspended in distilled water.

Group IV - Rats received Ethanol Extract of *Azadirachta indica* (250 mg/kg/day p.o) suspended in distilled water.

Group V – Rats received Glibenclamide (2.5 mg/kg p.o) suspended in 2% v/v Tween 80 solution.

Multidose study

In Alloxan induced diabetic rats

The selected rats were treated with similar test samples as above, but the blood glucose level was measured on 1, 3, 5, 7, 9 and 14 days of treatment. Glucose testing kit utilized for the measuring of plasma glucose levels was manufactured by Excel Diagnostic Pvt. Ltd.

Estimation of Lipid Profile

Estimation of Lipid profile such as Total Cholesterol, Triglycerides, HDL, LDL, VLDL and serum glucose level was conducted appropriately as per specifications. Cholesterol- EGD test kit manufactured by Excel Diagnostics Pvt. Ltd. was used for this purpose. The test kit utilizes CHOD/ POD method for cholesterol analysis. Triglycerides testing kit utilized for measuring the triglycerides in the plasma was also manufacture by Excel Diagnostics Pvt. Ltd.

Estimation of Urea and Creatinine

Urea and Creatinine levels were also checked using the respective kits that were both manufactured by Excel Diagnostics Pvt. Ltd.

Statistical Analysis

The data were expressed as mean ± standard error mean (SEM). The Significance of differences among the group was assessed using one way and multiple way analysis of variance

Table 5. Effect of ethanolic neem leaf extract on triglyceride levels in serum in alloxan induced diabetic rats after single dose administration

GROUPS	DRUG	DOSE	0 Hr	1 Hr	2 Hr	4 Hr	6 Hr	8 Hr	12 Hr	24 Hr
I	Normal control	5% w/v Tween 80	91.8± 2.8	91.52± 2.8	91.68± 3.1	92.74± 3.04	91.36± 3.4	91.96± 2.5	93.66± 2.5	92.99± 3
II	Diabetic Control	5% w/v Tween 80	180.2± 4.4	180.24± 4.3	179.4± 4.31	179.53± 4.8	179.02± 4.7	168.76± 4.5	162.94± 6.5	153.2± 4.8
III	Diabetic Control+ NLE	100 mg/Kg	168.24± 5.7	166.8± 4.4	166.42± 2.6	162.18± 1.8	157.52± 1.9	153.12± 1.75	147.78± 1.5	141.18± 2
IV	Diabetic Control+ NLE	250 mg/Kg	168.34± 5.7	167.26± 7.7	162.6± 4.9	157.80± 3.2	151.52± 1.3	148.24± 0.51	144.9± 0.94	141.64± 0.96
V	Diabetic Control+ Glibenclamide	500 mg/kg	170± 3.4	168.66± 3.3	165.26± 3.2	162.5± 3.11	153.82± 3.36	149.2± 2.5	143.4± 3	137.48± 3.01

Table 6. Effect of ethanolic neem leaf extract on serum glucose levels in alloxan induced diabetic rats during prolonged treatment

GROUPS	DRUG	DOSE	Day 1	Day 3	Day 5	Day 7	Day 9	Day 15
I	Normal control	5% w/v Tween 80	110.2± 5.07	110.2± 4.3	109.6± 2.88	110.2± 3.16	108.3±2.54	106.4±4.23
II	Diabetic Control	5% w/v Tween 80	443.67± 4.04	442± 3	438.33± 4.16	438.33± 5.5	437.2±4.5	430±3.25
III	Diabetic Control+ NLE	100 mg/Kg	83.38± 9.4	78.8± 8.06	70.3± 6.2	68.22± 6.1	66.3±5.6	64.2±4.8
IV	Diabetic Control+ NLE	250 mg/Kg	157± 0	98± 0	95.2±3.1	90.1±2.1	90±2.2	85±1.8
V	Diabetic Control+ Glibenclamide	500 mg/kg	71.4± 7.04	69.8±3.80	68.6± 3.50	63.90± 1.50	60.8±2.1	58.6±2.4

Table 7. Effect of ethanolic neem leaf extract on serum creatinine levels in alloxan induced diabetic rats during prolonged treatment

GROUPS	DRUG	DOSE	Day 1	Day 3	Day 5	Day 7	Day 9	Day 15
I	Normal control	5% w/v Tween 80	0.38± 0.02	0.37± 0.02	0.36±0.01	0.37± 0.02	0.36±0.01	0.37±0.02
II	Diabetic Control	5% w/v Tween 80	7± 0.25	6.93± 0.20	6.8±0.2	6.56± 0.25	6.6±0.2	6.4±0.2
III	Diabetic Control+ NLE	100 mg/Kg	2.37± 0.17	2.02± 0.17	1.8±0.16	1.62± 0.17	1.5±0.12	1.1±0.13
IV	Diabetic Control+ NLE	250 mg/Kg	1.7± 0	1.4± 0	1.1±0	0.9±0	0.8±0	0.5±0
V	Diabetic Control+ Glibenclamide	500 mg/kg	3.2± 0.16	2.3± 0.21	1.57±0.26	1.22± 0.17	0.99±0.12	0.48±0.10

Table 8. Effect of ethanolic neem leaf extract on total cholesterol in alloxan induced diabetic rats during prolonged treatment

GROUPS	DRUG	DOSE	Day 1	Day 3	Day 5	Day 7	Day 9	Day 15
I	Normal control	5% w/v Tween 80	70.38± 1.34	71.38± 0.84	71.34± 1.66	71.5± 0.6	70.5±1.34	71.4±0.84
II	Diabetic Control	5% w/v Tween 80	288.2± 1.31	285.63± 1.81	286.63± 1.49	286.53± 2.06	285.4±2.06	286.4±1.49
III	Diabetic Control+ NLE	100 mg/Kg	271.95± 2	230.2± 1.42	198.87± 0.97	156.8±0.90	111.34±1.3	89.9±0.85
IV	Diabetic Control+ NLE	250 mg/Kg	247.1± 0	204.5± 0	178±0	123±0	99.36±0	81.2±0
V	Diabetic Control+ Glibenclamide	500 mg/kg	242.15± 1.61	210.07± 4.52	1895± 0.41	1545± 4.32	97.6±3.5	76.5±2.8

(ANOVA). The test followed by Dunnet's test p values less than 0.05 were considered as significance.

RESULTS

Upon administration of ethanolic extract of neem leaves, significant changes were recorded in blood glucose levels, triglycerides, total cholesterol levels, urea and creatinine levels both in acute as well as in chronic study groups. It was observed that the higher dosage of NLE exhibited increased reduction in the values of parameters compared to low dosage administration. The values of the blood glucose levels observed by treating diabetes induced rats with ethanolic NLE was comparable to the values obtained by treating with glibenclamide. Recorded values showed a dose dependant reduction of blood glucose levels, total cholesterol, triglycerides and urea levels in the alloxan induced diabetic rats treated with ethanolic extract of *A. Indica.*

Single dose study

Administration of single dose of NLE, 100 mg/Kg and 250 mg/Kg, oral, each to two study groups which are diabetes induced by alloxan, significant reduction (P>0.05) in blood glucose levels was observed. The study period encompassed 24hrs. The results were significantly comparable to the standard drug glibenclamide. NLE at 250 mg/Kg exhibited better blood glucose level reduction compared to NLE administered at 100 mg/Kg and results shown in Table. No. .1,2,3,4,5. Figure.No..1,3,5,7,9.

Chronic study

During chronic study which encompassed a period of 15 days, the NLE (100 and 250 mg/kg, oral) produced a significant (P>0.05) in BGL of the diabetic rats compared to control. NLE at the dose of 250 mg/kg body weight exhibited better BGL reduction than 100 mg/kg body weight and results shown in Table. No..6,7,8,9,10.Figure.No..2,4,6,8,10.

DISCUSSION

Neem leaves, seeds and bark are already widely used in may ayurvedic and unani medicine systems for cure of wide range of diseases. The usage of neem in controlling blood glucose levels has long been in practice in India. In recent years, tablets and capsules prepared with leaf and seed extracts are widely used by many diabetic patients. Neem leaf extract dilate the blood vessels in diabetic patients and the neem seed oil is found to reduce the amount of insulin required to be administered to a diabetic patient.

Table 9. Effect of ethanolic neem leaf extract on urea levels in serum in alloxan induced diabetic rats during prolonged treatment

GROUPS	DRUG	DOSE	Day 1	Day 3	Day 5	Day 7	Day 9	Day
I	Normal control	5% w/v Tween 80	29± 1.2	28.5± 0.86	28.1± 4	29.7± 1.7	28.6± 4	28.9±± 4.1
II	Diabetic Control	5% w/v Tween 80	147.1± 1.22	146.20± 0.95	145.1± 1.5	144.96± 1.51	145.3± 1.51	111.5± 1.51
III	Diabetic Control+ NLE	100 mg/Kg	92.45± 2	90.3± 2.9	87.42± 3.6	80.57± 2.8	74.37± 2	60.57± 3.2
IV	Diabetic Control+ NLE	250 mg/Kg	90.4± 0	87.7± 0	71.2± 0	63.5±0	58.4± 0	34.2± 0
V	Diabetic Control+ Glibenclamide	500 mg/kg	97.60± 4.9	86.8± 5.7	81.6± 5.5	62.3± 3.9	55.4± 2.9	33.1± 3.5

Table 10. Effect of ethanolic neem leaf extract on triglycerides level in serum in alloxan induced diabetic rats during prolonged treatment

GROUPS	DRUG	DOSE	Day 1	Day 3	Day 5	Day 7	Day 9	Day 15
I	Normal control	5% w/v Tween 80	87.32± 5.4	87.62± 5.2	87.78± 4.9	88.08± 5	87.6± 4.5	88.5± 4.3
II	Diabetic Control	5% w/v Tween 80	170.3± 2.1	170.30± 3.6	170± 2.7	169.6± 2.5	170.1± 2.3	169.8± 2.6
III	Diabetic Control+ NLE	100 mg/Kg	132.15± 2.1	123.97± 1.9	116.6± 2.4	108.65± 2.79	95.6± 3.4	89.6± 2.3
IV	Diabetic Control+ NLE	250 mg/Kg	95.5± 0	97.2± 0	95.4± 0	90.1±0	89.6±0	88.4±0
V	Diabetic Control+ Glibenclamide	500 mg/kg	131.5± 3.2	125.35± 4.2	110.25± 4.05	100.47± 2.3	94.3± 3.4	87.6± 3.9

These actions are supposed to be exhibited due to cumulative effect of glycosides, terpenoids and flavonoides present in the leaf and seed extracts as reported in review of literature.

Models of experimental diabetes that utilizes diabetogenic agent Alloxan induced blood glucose levels higher than 250 mg/dl which has been considered as severe diabetes. Diabetes mellitus is one of the most common chronic disease and is associated with hyperlipidemia and co-morbidities such as obesity, hypertension. Hyperlipidemia is a metabolic complication of both clinical and experimental diabetes.

Though work was done on the effect of neem on diabetes in combination with other medicinal plants, so far no work has been done exclusively on the hypoglycemic activity of neem. Present study focuses on the exclusively on the role of neem leaf extract as a hypoglycemic agent and its effect on various other relevant parameters like total cholesterol levels, urea, creatinine and triglyceride levels.

The actual mechanism of action that brings up on the action of hypoglycemia is not understood but it is proved to be brought up on by the presence of terpenoid, flavanoid and glycoside groups in the extracts. The standard drug, glibenclamide, on the other hand works by promoting insulin secretion by closure of potassium-ATP channels, membrane depolarization and stimulation of calcium ion influx, an initial key step in insulin secretion.

The neem leaf extract is found to reduce the serum concentrations of glucose, urea, total cholesterol and creatinine. The reduction in the creatinine and urea levels in the serum samples is attributed to the action of neem leaf extract on blood vessels. The decrease in serum TG level is an important finding because recent studies show that TG is independently related coronary heart disease. Most of the hypolipidemic drugs do not decrease serum TG level, but PFK lowered it significantly since under normal condition, insulin activates the enzyme lipoprotein lipase and hydrolysis TG. Plant extract reduces the serum TG of alloxan induced diabetic rats and may prevent the progression of CHD. Accumulation of TG is one of the risk factor in coronary heart disease (CHD). The preliminary acute toxicity studies have revealed no visible signs or symptoms of toxicity of neem leaf extract in normal rats. Hence, with all data recorded and analyzed, this study concludes that the neem leaf extract can make for an efficient and effective alternate complementary medicine in management of diabetes mellitus.

CONCLUSION

The results obtained from the present study show that the *Azardirachta indica* had beneficial effects on blood glucose levels in glucose- fed hyperglycemic and diabetic rats and it also protects significantly from other metabolic aberrations caused by alloxan, thus scientifically verifying the traditional claim. *Azardirachta indica* appears to be an attractive material for further studies, leading to possible drug development for diabetes. Development of phytomedicines is relatively inexpensive and less time consuming; it is more suited to our economic conditions than allopathic drug development which is more expensive and spread over several years. In conclusion, the results from this study give scientific support to the use of *Azardirachta indica in* folklore medicine for the treatment of diabetes, and show the potential role of anti diabetic activity. It *was* selected for further investigation, involving bioassay guided fractionation, in order to isolate the constituents responsible for the effect of the plant.

REFERENCE

Chattopadhyay R.R. A comparative evaluation of some blood sugar lowering agents of plant origin. J. Ethnopharmacology. 1999; 67: 367–372.

Diane Huber; Disease management, Missouri: Elsevier Saunders. (2005), 81-97

Grover K.S., Yadav V. Medicinal plants of India with anti-diabetic potential; J Ethnopharmacology. 2002; 81: 81-100

Jacob E. Friedman; New transcription factors and their role in diabetes and therapy 1st ed., Oxford: Elsevier. (2006), 1-67

Johann Georg Schnitze; Diabetes causes & cure: including cure of later diabetes consequences, Germany: Privately Printed. 1980- 2002, 127-132

Menakshi Bhat, Sandeepkumar K.K., Tirmale A.R., Bhargava S.Y., Joshi BN. Antidiabetic Properties of Azardiracta indica and Bougainvillea spectabilis: In Vivo Studies in Murine Diabetes Model. Evid Based Complement Alternat Med. 2009; 23:1-8.

Nahar L., Ripa F.A., Hasanat A., Zulfiker Md., Rokonuzzaman Md., Haque M., Islam K.M.S. Comparative study of antidiabetic effect of Abroma augusta and Syzygium cumini on alloxan induced diabetic rat; Agri Bio J North America, 2010; 1267-1272.

Ramchandran A., Snehlata C., Papur A., Vijay V., Mohan V., Das A.K. High prevalence of diabetes and impaired glucose tolerance in India, National Urban Diabetes Survey. Diabetologia 2001; *44* : 1094-101.

Serrano Ríos, M., Gutierrez Fuentes; Type 2. Diabetes Mellitus, Barcelona: Elsevier. 2009, 1-71.