

# Antidiabetic Activity of Alcoholic Extract of Neem (Azadirachta Indica) Root Bark

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## ABSTRACT

**Background:** Most of the parts of neem tree were studied in details by many researchers but neem root bark was not screened for antidiabetic effect. To evaluate antidiabetic effect of neem root bark this study was conducted.

**Aims & Objective:** The present study was undertaken to evaluate the 70% alcoholic neem root bark extract (NRE) in diabetes.

**Materials and Methods:** Basal blood sugar levels were estimated in overnight fasted wistar albino rats of either sex. To evaluate antihyperglycemic action of Neem root bark extract (NRE) OGTT was done by giving glucose orally 60 minutes after giving standard drug (Glibenclamide), Test drug (NRE) in the dose of 200,400 and 800 mg/kg and blood sugar levels were estimated every half hourly up to 4 hours. To evaluate hypoglycemic activity in alloxan induced diabetic rats similar doses once daily for 15 days. Blood sugar levels were estimated by using glucometer.

**Results:** For glucose tolerance test Glibenclamide significant ( $p < 0.01$ ) reduction in blood sugar levels. The NRE showed statistically significant results in only 800 mg/kg dose. In comparison to glibenclamide it did not show. In alloxan induced diabetes Glibenclamide showed significant ( $p < 0.01$ ) reduction in blood sugar levels. The NRE showed statistically significant results in only 800 mg/kg dose.

**Conclusion:** Neem root has antihyperglycemic and hypoglycemic activity. It is not as significant as glibenclamide.

**KEY WORDS:** Alloxan; Antihyperglycemic; Hypoglycemic; Neem Root Bark

## INTRODUCTION

Neem plant was tested for different activities. Isolation of active gradient from neem was started by Siddiqui in 1942. After that more than 135 compounds were isolated from different parts of neem.<sup>[1]</sup> Different types of extracts from different part of plant were used for different activities e.g. aqueous extract leaf-immunostimulant activity, ethanolic extract of the flowers- hypolipidemic activity, methanolic leaf extract - antipyretic activity, chloroform extract of stem bark - anti-inflammatory activity, acetone leaf extract- CNS depressant activity, Hexane extract of neem seed- antifertility effect.<sup>[2-7]</sup> But antidiabetic activity of neem root bark was not evaluated. Considering these things in our study we evaluated whether 70% of alcoholic neem root bark extract has antidiabetic activity?

## MATERIALS AND METHODS

**Plant Material:** Neem roots were collected from neem tree in Navodaya Medical College campus. The root bark was shade dried in department of pharmacology. Shade dried root bark was powdered. Alcoholic extract of bark was obtained by continuous extraction in percolator using 70% ethyl alcohol. Fresh solution was prepared by dissolving extracts in distilled water before each experiment.

**Animals:** Wistar albino rats of either sex weighing 200-250 grams were used in present study. The rats were provided standard laboratory feed and tap water. They were exposed to an alternate light and dark cycle of 12 hours and had free access to food and water. The experimental protocol was approved by institutional animal ethics committee. The whole project was carried out as per guidelines of the Committee for the Purpose of Control and Supervision of Experiments on Animals (CPCSEA).

**Reagents and Drugs:** Alloxan s.d. fine -chem Ltd. Boisar, Tab. Glibenclamide:-5 mg in each tablet (Daonil- Aventis)

**Instruments:** Blood glucose levels were measured with the help of Glucometer [Prestige smart system (Andheri, Mumbai)]. Percolator was purchased from Maharashtra Emporium, Wardha, Maharashtra.

### Methods for Evaluating Antidiabetic Activity

**1. Glucose Tolerance Test<sup>[8]</sup>:** Animals were overnight fasted. Fasting blood sugar levels were detected by taking blood samples. Then the test drugs were administered orally 60 minutes prior to administration of glucose to the 5 groups of animals each containing 6 animals.

**Group I (Control):** Received 2 ml of distilled water

**Group II (Standard):** Received Glibenclamide (0.5 mg/kg)<sup>[9]</sup>

**Group III:** Received NRE (200 mg/kg) single dose

**Group IV:** Received NRE (400 mg/kg) single dose

**Group V:** Received NRE (800mg/kg) single dose

After 60 minutes glucose (in the dose of 1.25 grams/kg) was administered orally to each rat. Blood samples were drawn every half hourly up to 4 hours and blood sugar levels were detected by glucometer. The blood was taken by chopping tail of rat.<sup>[10,11]</sup>

**2. Alloxan Induced Diabetes:** Overnight fasted animals were given 100 mg/kg alloxan monohydrate.<sup>[12]</sup> After 48 hours blood sugar levels were estimated by glucometer. Then the animals were divided into 5 groups. In each group 6 rats were kept. All rats received drugs orally for 15 days. In pilot study NRE in single daily dose reduced blood sugar levels but they were not significant. So we gave NRE twice daily.

**Group I (Control):** Received 2 ml of distilled water daily.

**Group II (Standard):** Received Glibenclamide 0.5 mg/kg daily<sup>[9]</sup>

**Group III:** Received NRE 200 mg/kg twice daily

**Group IV:** Received NRE 400 mg/kg twice daily

**Group V:** Received NRE 800 mg/kg twice daily

The blood was taken by chopping tail of rat.<sup>[14]</sup> Blood sugar level was measured on 48 hours, 5,10 and 15 days by using glucometer.

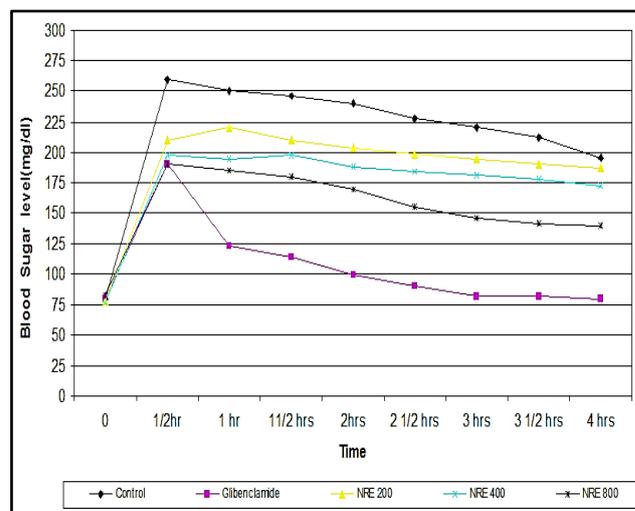
**Statistical Analysis:** Analysis was done with one way ANOVA followed by Dunnet test.

## RESULTS

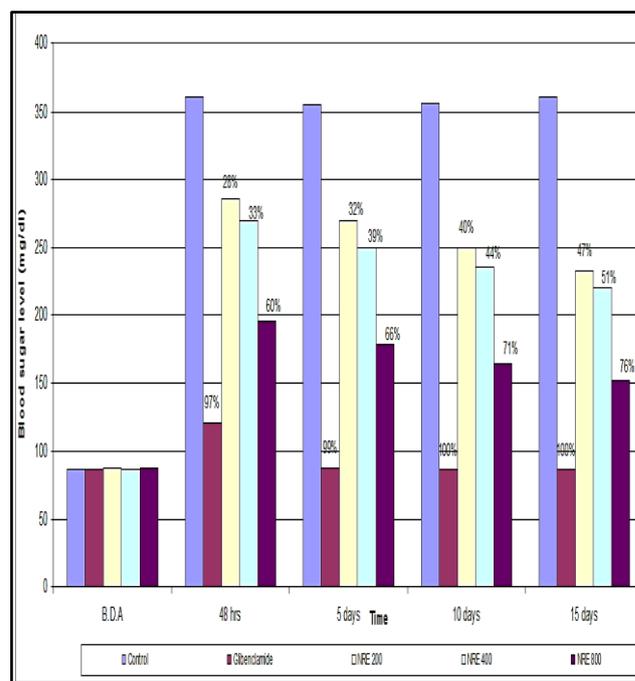
For glucose tolerance test Glibenclamide was given in the dose of 0.5 mg/kg showed significant ( $p < 0.01$ ) reduction in blood sugar levels. It reduced blood sugar level to basal line after 4 hours as comparison to control. The NRE was given in the dose of 200 and 400 mg/kg showed reduction in blood sugar level, but it was not statistically significant. The NRE was given in the dose of 800 mg/kg showed significant ( $p < 0.05$ ) reduction in blood sugar level. It reduced blood sugar level by 54% after 4 hours as comparison to control. But in comparison to glibenclamide it was not showing significant result (Table 1, Fig 1)

In alloxan induced diabetes Glibenclamide was given in the dose of 0.5 mg/kg showed significant ( $p < 0.01$ ) reduction in blood sugar levels. It reduced the blood sugar level to basal line on 10th day. NRE reduced blood sugar levels with dose 200 and 400 mg/kg but it was not significant. In dose 800 mg/kg it showed significant ( $p < 0.05$ ) reduction in blood sugar

levels as comparison to control. Maximum reduction of blood sugar level was 76%. This was seen on 15th day with same dose. (Table.2, Fig.2)



**Figure-1: Effect of Neem Root Bark Extract on OGTT**



**Figure-2: Effect of Neem Root Extract on Alloxan Induced Diabetes**

**Table-1: Oral Glucose Tolerance Test Using Azadirachta Indica (Neem) Root Bark Extract in Albino Rats**

Drugs	Doses mg/kg	Blood Sugar Level (mg/dl) (Mean ± SEM)								
		B.D.A.	A.D.A.							
			0.5 hr	1 hr	1.5 hr	2 hr	2.5hr	3 hr	3.5 hr	4 hr
Distilled Water	2 ml	80 ± 2.1	260 ± 1.3	250 ± 6.8	246 ± 9.8	240 ± 9.8	228 ± 9.2	220 ± 14	212 ± 13	196 ± 13
Glibenclamide	0.5	80 ± 2	190 ± 1.8**	123 ± 2.3**	114 ± 1.6**	99 ± 2.7**	90 ± 1.2**	82 ± 1.5**	82 ± 2**	80 ± 2**
NRE 200	200	78 ± 2.6	210 ± 1.6	220 ± 9.1	210 ± 9	204 ± 8.5	199 ± 7.6	195 ± 7.3	190 ± 8.5	187 ± 8.2
NRE 400	400	77 ± 3	198 ± 1.2	195 ± 7.3	198 ± 7.8	188 ± 7.8	184 ± 7.1	181 ± 7.7	178 ± 7.9	173 ± 7.5
NRE 800	800	83 ± 2.1	180 ± 2.3*	185 ± 4.6*	178 ± 6.2*	167 ± 5*	155 ± 6.3*	130 ± 5.9	130 ± 6.4*	128 ± 5.7*

\*  $p < 0.05$ ; \*\*  $p < 0.01$ ; \*\*\*  $p < 0.001$ ; B.D.A.- Before drug administration; A.D.A.- After drug administration; n - Number of animals

**Table-2: Anti-Diabetic Effect of Azadirachta Indica (Neem) Root Bark in Albino Rats (Alloxan Induced Diabetes)**

Group	Drug and Doses	Blood Sugar Level (mg/dl) (Mean ± S.E.M.)				
		B.D.A.	A.D.A.			
			48hrs	5 days	10days	15 days
I	Distilled Water 2ml orally	86 ± 1.1	360 ± 15	355 ± 12	356 ± 13	360 ± 14
II	Glibenclamide 0.5 mg/kg orally	86 ± 1.6	120 ± 14**	87 ± 1.5**	86 ± 1**	86 ± 1.1**
III	NRE (200 mg/kg orally)	87 ± 1.6	87 ± 7.6	270 ± 7.6	250 ± 7.6	232 ± 8.3
IV	NRE (400 mg/kg orally)	86 ± 3.1	86 ± 10	250 ± 10	236 ± 10	220 ± 7.8
V	NRE 800 mg/kg orally)	87 ± 1.8	86 ± 12*	178 ± 11*	165 ± 12*	152 ± 18*

\* p<0.05; \*\* p< 0.01; \*\*\* p< 0.001; B.D.A.- Before drug administration; A.D.A.- After drug administration; n - Number of animals

## DISCUSSION

Nimbidin is a mixture of tetranortriterpenes and is the major active principle of the seed oil of *Azadirachta indica* A. Juss (Meliaceae). In study carried out by Pillai et al 1981 in oral glucose tolerance test nimbidin was studied in rabbits. In this study nimbidin (200 mg/kg) significantly delayed rise in blood glucose level after oral glucose administration as compared to control. Nimbidin brought down blood sugar level to base line in 4<sup>th</sup> hour.<sup>[8]</sup> In our study alcoholic root bark extract delayed the rise in blood sugar level. It shows that NRE has antihyperglycemic activity.

For anti-diabetic activity evaluation of neem many studies were done. Khosla et al. (2000) showed that when aqueous extract of neem leaf (500 mg/kg orally) when administered for 4 weeks after alloxan induced diabetes in rabbits, it significantly (P< 0.001) reduced blood glucose levels.<sup>[13]</sup> In the study carried out by Kar et al 95% alcoholic extract of neem leaf in the dose of 250 mg/kg twice daily orally for one week reduced blood sugar level by 55% and urine sugar by 100% (p<0.05) in alloxan induced diabetes in rats.<sup>[12]</sup> In our study with NRE given twice daily for 15 days reduced blood sugar levels significantly. This effect was less significant and less potent than glibenclamide. Neem root bark contains terpanoids like nimbin and nimbidin).<sup>[14]</sup> Nimbidin is having antidiabetic activity and it may be responsible for the activities seen in our study. As NRE is delaying onset of diabetes produced by alloxan it may be used as prophylactic agent in diabetes. As it is reducing levels of sugar in alloxan induced diabetes it can be used as adjuvant.

## CONCLUSION

70% alcoholic neem root extract has antidiabetic activity. Further studies are required to know which active ingredients are responsible for this action.

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