



## Evaluation of Antidiabetic Activity of Mangifera Indica Extracts in Streptozotocin Induced Diabetic Rats

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### Abstract

**Background:** Mangoes (*Mangifera indica*) is a tropical fruiting tree and is widely cultivated in the South Asian region. Ayurvedic studies have shown different medicinal properties of many parts of the tree. Extracts of various parts of the tree have shown antidiabetic, antibacterial, antifungal, and anticancer properties. **Aim:** We in the current study tried to evaluate the antidiabetic property of ethanolic extracts of *Mangifera indica* on streptozotocin-induced diabetic rats and compare it with standard drug Glibenclamide. **Methods:** Soxhlet apparatus was used to obtain an ethanolic extract of *Mangifera indica* dried leaves. Wistar rats of either sex weighing between 150 to 250 gms divided into 6 groups each consisting of 6 rats. Oral feeding tubes were used to administer *Mangifera indica* leaf extract, Glibenclamide, and distilled water orally to the rats. Tuberculin syringes Tuberculin syringe were used for intraperitoneal administration of Streptozotocin to the rats. **Results:** In group IV the percentage reduction in blood glucose levels was about 11.08% on the 5<sup>th</sup> day, 22.71% on the 10<sup>th</sup> day, and 34.54% on the 15<sup>th</sup> day. In group V the percentage reduction in blood glucose levels was about 16.92% on the 5<sup>th</sup> day, 29.18% on the 10<sup>th</sup> day, and 50.10% on the 15<sup>th</sup> day. In group VI percentage reduction in blood glucose levels was about 28.24% on the 5<sup>th</sup> day, 51.02% on the 10<sup>th</sup> day, and 66.57% on the 15<sup>th</sup> day. **Conclusion:** The present study showed *Mangifera indica* has significant antidiabetic activity in streptozotocin-induced diabetic rats. The effective dose at which it had a significant anti-diabetic effect was 300 mg/kg, below which the glucose-lowering effect was not significant and further increments in dose showed no significant increase in its anti-diabetic activity.

**Keywords:** Antidiabetic Activity, *Mangifera Indica*, Diabetic rats

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### Introduction

Diabetes mellitus is the world's largest endocrine disease resulting in disordered metabolism, usually due to combined effects of hereditary predisposition and environmental causes. It often results in abnormally high blood sugar levels due to defects in insulin secretion or insulin action in the body singly or combined. [1] There is an increasing trend of prevalence of diabetes across the world especially in the past two decades. It has been estimated that 30 million diabetes cases were present in 1985 to 366 million in 2011. Based

on the current trends it has been proposed that approximately 522 million people across the world will be diabetic by the year 2030. [2] The most dramatic increases have been recorded in developing countries such as India, and diabetes accounts for a major portion of healthcare expenditure, further emphasizing the need for newer and cheaper modalities of treatment. Even though many drugs and interventions are available to manage diabetes, they are expensive for the large diabetic population in developing countries due to very low per capita income, apart from their inherent adverse effects. Therefore, it is important to look for new cheap

alternatives for the management of this major health problem. [3] Different indigenous drugs had been used in the Indian subcontinent for several centuries for the treatment of Diabetes mellitus. However, there are conflicting reports of their efficacy because of the lack of scientific investigation in a laboratory setting. One such plant, *Mangifera indica* (mango) whose dried leaves have long been used traditionally in the treatment of Diabetes mellitus in South Asian countries is selected for the study. [4] In this study, the anti-diabetic potential of the ethanolic extract of dried leaves of *Mangifera indica* will be screened on a laboratory animal model and compare its effects with the standard drug Glibenclamide.

## Materials and Methods

The study was carried out in the Post Graduate research laboratory of the Department of Pharmacology, Chalmeda Anand Rao Institute of Medical Sciences, Karimnagar, after obtaining permission from the Institutional Animal Ethics Committee (IAEC). Laboratory bred Wistar rats of either sex weighing between 150 to 250 gms were obtained from M/S Sainath Agencies, Hyderabad, and placed in individual cages in the central animal house of the institute.

### Extraction Preparation

Mango leaves were collected from local plantations and they were identified by the Department of Botany, Govt. Junior College of Sciences, Karimnagar. The leaves were dried in shade and were ground to coarse particles and extraction was carried out with Soxhlet apparatus using 50% ethanol. Soxhlet apparatus was used to obtain the ethanolic extract of *Mangifera indica* leaves. Machine Animals were weighed by using the Goldtech weighing machine. It has a range from 1 gm to 5 kg. A rat restraining cage was used to hold the animal while blood was withdrawn for measuring glucose levels. To measure the blood glucose level in the animals, One Touch Horizon glucometer was used. It is manufactured by Life Scan Scotland Ltd., UK. The test strip is inserted into the glucometer and the sample is directly placed on the test strip. The result i.e., blood glucose level will appear on the screen within five seconds in mg/dl. Oral feeding tubes were used to administer *Mangifera indica* leaf extract, Glibenclamide, and distilled water

orally to the rats. Tuberculin syringes Tuberculin syringe were used for intraperitoneal administration of Streptozotocin to the rats. 50% of ethanol was used as a solvent for Soxhlet extraction. Sterile Normal saline was used to dissolve Streptozotocin, Glibenclamide, and *Mangifera indica* leaf extract.

### 1. Streptozotocin (STZ)

STZ was obtained from Himedia Labs, Mumbai, India. It is a naturally occurring chemical that is particularly toxic to the insulin-producing beta cells of the pancreas in mammals. It is the preferred drug to induce type 2 diabetes mellitus in rodent models.

### 2. Glibenclamide

Daonil (Aventis Pharma, India) was used for the study. Glibenclamide is an oral hypoglycemic agent belonging to the sulfonylurea class. It causes hypoglycemia by stimulating insulin release from pancreatic  $\beta$  cells. Glibenclamide was used as the standard drug.

The rats were divided into 6 groups.

#### Group I

Consisted of 6 rats which served as a **normal control group** and were given distilled water orally every day. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

#### Group II

Consisted of 6 STZ induced diabetic rats which served as **the diabetic control group** and were given distilled water orally daily. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

#### Group III

Consisted of 6 STZ induced diabetic rats which served as a **standard group** and were given Glibenclamide at a dose of 0.5 mg/kg body weight orally daily. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

#### Group IV

Consisted of 6 STZ induced diabetic rats which served as **test group-1** and were given *Mangifera indica* leaf extract at a dose of 150 mg/kg dose orally daily. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

#### Group V

Consisted of 6 STZ induced diabetic rats which served as **test group-2** and were given

*Mangifera indica* leaf extract at a dose of 300 mg/kg dose orally daily. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

**Group VI**

Consisted of 6 STZ induced diabetic rats which served as **test group-3** and were given *Mangifera indica* leaf extract at a dose of 450 mg/kg dose orally daily. Blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

**Standard drug administration**

Glibenclamide was administered orally through an oral feeding tube in diabetic rats for 15 consecutive days at a dose of 0.5 mg/kg body weight. The blood glucose concentrations were monitored on 0, 5, 10, and 15 days.

**Test drug administration**

The ethanolic extract of *Mangifera indica* dried leaves was administered orally at a dose of 150 mg/kg, 300 mg/kg, and 450 mg/kg body weight to groups IV, V, and VI respectively through an oral feeding tube for 15 consecutive days. The blood glucose concentrations were monitored on 0,5,10 and 15 days. All the values were expressed as Mean ± S.D., standard error of mean and percentage reduction were calculated. The test of significance was done by using the student t-test.

**Results**

The present study was carried out to evaluate the anti-diabetic effect of *Mangifera indica* dried leaf extract in streptozotocin-induced diabetic rats. The rats were divided into six groups.

**Group I:** The animals in this group received distilled water orally. The blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

**Group II:** Diabetes induced animals in this group were given distilled water and they served as the diabetic control group. The blood glucose levels were measured on 0, 5, 10, and 15th day and body weight was measured on 0 and 15th day.

**Group III:** Diabetes induced animals in this group were given Glibenclamide (0.5 mg/kg body weight) and they served as diabetic standard group. The percentage reduction in blood glucose levels of these animals when compared with the diabetic control group was about 35.15% on the 5th day, 62.93% on the 10th day, and on day 15, it was 73.64% as shown in the

**Group IV:** The diabetic animals in this group were treated with *Mangifera indica* leaf extract at a dose of 150mg/kg body weight. The percentage reduction in blood glucose levels was about 11.08% on the 5th day, 22.71% on the 10th day, and 34.54% on the 15th day.

**Group V:** The diabetic animals in this group were treated with *Mangifera indica* leaf extract at a dose of 300mg/kg body weight. The percentage reduction in blood glucose levels was about 16.92% on the 5th day, 29.18% on the 10th day, and 50.10% on the 15th day.

**Group VI:** The diabetic animals in this group were treated with *Mangifera indica* leaf extract at a dose of 450mg/kg body weight. The percentage reduction in blood glucose levels was about 28.24% on the 5th day, 51.02% on the 10th day, and 66.57% on the 15th day.

**Table 1:** Mean blood glucose levels mg/dl

Group	Parameters	Day – 0	Day – 5	Day – 10	Day – 15
Normal Control	Mean ±SD	101.00±10.95	105.66±10.70	100.16±7.19	99.50±9.99
	SEM	4.47	4.37	4.08	
Diabetic Control	Mean ± SD	360.83±35.12	371.16±54.11	380.83±51.66	384.50±29.51
	SEM	14.33	22.09	12.04	
Diabetic Standard	Mean ± SD	337.16±42.99	240.66±21.83	141.16±16.37	101.33±10.23
	SEM	17.55	8.91	4.17	
% reduction	-	35.15*	62.93**	73.64**	
Diabetic Test-1	Mean ± SD	356.16±28.98	330.00±31.79	294.33±35.33	251.66±30.29
	SEM	11.83	12.98	12.36	
% reduction	-	11.08	22.71	34.54**	
Diabetic Test-2	Mean ± SD	324.83±20.68	308.33±18.65	269.66±24.58	191.83±24.21
	SEM	8.44	7.61	9.88	
% reduction	-	16.92	29.18	50.10**	
Diabetic Test-3	Mean ± SD	311.16±15.75	266.33±28.48	186.50±19.21	128.50±08.28
	SEM	6.43	11.62	3.38	
% reduction	-	28.24*	51.02**	66.57**	

\* Significant

**Table 2:** Mean body weight in Kgs of all the groups

Group				Parameters	Day – 0	Day - 15
Normal Control				MEAN ± SD	200.33±17.50	207.00±20.38
SEM				7.14	8.32	
Diabetic Control				MEAN ± SD	106.33±13.35	91.00±11.91
SEM				5.45	4.86	
Diabetic mg/kg)	Standard	(Glibenclamide	0.5	MEAN ± SD	111.00±17.33	186.00±14.31
SEM				7.07	5.84	
Diabetic 150mg/kg)	Test-1	(Mangifera	indica	MEAN ± SD	114.00±15.12	129.33±14.62
SEM				6.17	5.97	
Diabetic 300mg/kg)	Test-2	(Mangifera	indica	MEAN ± SD	108.66±13.36	153.33±8.64
SEM				5.45	3.52	
Diabetic 450mg/kg)	Test-3	(Mangifera	indica	MEAN ± SD	109.00±10.09	180.00±11.93
SEM				4.12	4.87	

## Discussion

Plants have played a major role in the development of new therapeutic agents for the treatment of diabetes mellitus. But there is still an extensive demand for new oral anti-diabetic drugs which are cheaper and have lesser side effects. Different indigenous drugs are used in the traditional systems of medicine for the treatment of diabetes mellitus but they lack scientific investigations for their efficacy in a laboratory setting. [5] One such plant, *Mangifera indica* (family *Anacardiaceae*) dried leaf extract has long been used traditionally for culinary purposes in South Asian and African countries, is selected for the study. *Mangifera indica* dried leaf extract has been shown to possess many beneficial therapeutic properties it is a rich source of organic acids, carbohydrates, amino acids, vitamins and phenolic acids such as caffeic acid and tannic acid. [6, 7] The major pharmacologic properties present in mango are due to the presence of phenolic acids. They possess potent antioxidant activity that can protect tissues against oxidative stress, they have anti-diabetic, anti-inflammatory, antilithiatic, and anticarcinogenic properties. [8, 9] Different parts of the tree-like bark, leaves, and fruit have been used for a variety of diseases diarrhea, cough, dental caries, diabetes, wound treatment, and also as an emetic. The present study was carried out to evaluate the anti-diabetic effect of extract of dried leaves of *Mangifera Indica* in streptozotocin-induced diabetic rats. In the present study, 50% ethanolic extract of dried leaves of *M. Indica* was given to different groups of animals at a dose of 150, 300 and 450 mg/kg body weight (groups IV, V and VI) and the blood-glucose-lowering effect of

these groups were compared with the diabetic control group. Statistical analysis of the test groups with the control group showed a significant reduction in blood glucose levels, especially from the 5th day onwards. JA Badmus et al; found that fasting blood glucose concentration of alloxan-induced diabetic rats was significantly reduced by ethanolic extracts of *M. indica* the decrease in fasting blood glucose levels was significant when compared to untreated diabetic rats. [11] In a similar study A. Aderibigbe et al; [11] found the aqueous extracts of *M. indica* produced a reduction of blood glucose levels in streptozotocin-induced diabetic mice. They also concluded that the hypoglycemic effects of aqueous extracts were comparable to an oral dose of chlorpropamide. M Saleem et al; [12] found a hydro-alcoholic extract of the *M. indica* on Alloxan induced diabetic mice decreased postprandial blood glucose levels in diabetic mice after seven days of therapy. The found the extracts prevented the rise in blood glucose levels and prevented a decrease in body weight and a decline in beta-cell mass associated with alloxan and improved lipid profile. In the current study, we have compared to the diabetic rats to the standard group, the following observations were made. The diabetic test group -1 which was treated with 150 mg/kg extract showed antidiabetic effect but it was not as significant as the diabetic standard group treated with glibenclamide. The diabetic test groups 2 and 3 (300 and 450 mg/kg respectively) both showed statistically comparable anti-diabetic effect as to the diabetic standard group and percentage reduction was also as effective as glibenclamide. There was no significant difference between the glucose-lowering effects of diabetic test group -2 (300



mg/kg) and diabetic test group – 3 (450 mg/kg) which implies 300 mg/kg to be the ideal dose below which the effect is not significant and further increment in dose doesn't increase its effect. These results suggest that *Mangifera indica* has a definite anti-diabetic property. The probable mechanism for the glucose-lowering effect is due to the presence of foliamangiferosides such as mangiferin which has antidiabetic effects through increasing insulin sensitivity and inhibiting alpha-glucosidase activity. [13] Ififlophenone 3-C-β-D-glucoside has also been reported to exhibit anti-diabetic potential. [14]

## Conclusion

The present study showed *Mangifera indica* has significant antidiabetic activity in streptozotocin-induced diabetic rats. The effective dose at which it had a significant anti-diabetic effect was 300 mg/kg, below which the glucose-lowering effect was not significant and further increments in dose showed no significant increase in its anti-diabetic activity.

**Conflict of Interest:** None declared

**Source of Support:** Nil

**Ethical Permission:** Obtained

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