

**ANTIDIABETIC ACTIVITY OF METHANOLIC EXTRACT OF *MEMECYLON MALABARICUM COGN* (MELASTOMATACEAE) LEAVES****M. RAMAIAH^{*1}, B. GANGA RAO² AND G. CHAKRAVARTHI³**^{*1,2}*Department of Phytochemistry & Pharmacognosy, AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam-530003, A.P., India*³*Department of Pharmacognosy, Mother Teresa Pharmacy college, Kothuru, Sathupally, Khammam Dist-507303, A.P, India.***ABSTRACT**

Memecylon malabaricum cogn (Melastomataceae) is an indigenous medicinal plant used in ethno medicine for the treatment of bacterial infections, inflammation and skin diseases including herpes, chickenpox. It's also a root ecboic. The methanolic extract of *Memecylon malabaricum* leaves is subjected to antidiabetic activity using experimental model of alloxan induced diabetes. The results showed that the methanolic extract at the dose of 400 mg/kg body weight showed significantly decreased ($P < 0.01$) of the raised blood glucose level, comparable to reference standard, gliclazide. The preliminary phytochemical analysis reveals that the plant possessing steroids, saponins, flavonoids, tannins, and alkaloids. The antidiabetic activity of the plant may be due to the presence of the above said category of compounds. It is therefore worth study further to isolate the pure molecules responsible for antidiabetic activity. In conclusion, the results of this study explicate justification of the use of this plant in the treatment of diabetes.

KEY WORDS: Antidiabetic activity, *Memecylon malabaricum*, leaves extract.**M. RAMAIAH**

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INTRODUCTION

Diabetes mellitus (DM), often referred to simply as diabetes is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels (hyperglycemia)¹. Diabetes develops due to a diminished production of insulin (in type 1) or resistance to its effects (in type 2 and gestational). Both lead to hyperglycemia, which largely causes the acute signs of diabetes: excessive urine production, resulting compensatory thirst and increased fluid intake, blurred vision, unexplained weight loss, lethargy, and changes in energy metabolism². Diabetes and its treatments can cause many complications. Acute complications (hypoglycemia, ketoacidosis, or nonketotic hyperosmolar coma) may occur if the disease is not adequately controlled. Serious long-term complications include cardiovascular disease (doubled risk), chronic renal failure, retinal damage (which can lead to blindness), nerve damage (of several kinds), and micro vascular damage, which may cause erectile dysfunction and poor wound healing. Poor healing of wounds, particularly of the feet, can lead to gangrene, and possibly to amputation³. It is a major public health problem in the developed as well as developing countries. It is ranked seventh among the leading causes of death, and the third when it's fatal complications are taken into account⁴. Regions with greatest potential are Asia and Africa, where DM rates could rise to two to three-folds than the present rates. As per WHO report, approximately 150 million people have diabetes mellitus worldwide, and this number may well double by the year 2025⁵. Several synthetic drugs such as biguanides and sulfonylureas are presently available to reduce hyperglycaemia in diabetes mellitus. These drugs have side effects and thus searching for a new class of compounds is essential to overcome these problems⁶. Many herbal medicines have been recommended for the treatment of diabetes. Traditional plant medicines are used

throughout the world for a range of diabetic presentations. Thus the present investigation was carried out to evaluate the antidiabetic potential of *Memecylon malabaricum*, cogn.

Memecylon malabaricum, cogn is a tree up to 5 m tall⁷, widely distributed in Western Ghats (Dakshina kannada and Udupi districts of Karnataka, Kerala, and Tamilnadu) of India, China, Srilanka, Asia, Africa, Australia, Madagascar, Pacific Islands, belongs to the family Melastomataceae^{8, 9, 10, 11}. *Memecylon* is genus of shrubs or small tree distributed throughout the world. Up to this 300 species were identified^{12,13}. The Melastomataceae family is a vast source of pharmacologically active tannins, flavonoids, alkaloids, resins, waiting for experimentation and observed for anti-microbial, anti-inflammatory, anti-HIV, anti-hypertensive, for treatment of skin disorders, diarrheal, bleeding, and scavenging of free radicals, inhibition of monoamine oxidase inhibitors (MAO-B), post partum invigoration and astringent activities^{8,9,10,11}. *Memecylon malabaricum* has considerable reputation for its traditional use in the treatment of diabetes, various bacterial infections, inflammatory and skin disorders including herpes, chicken pox. It is also used as a root ecboic like ergot^{14, 15}. Although this herb has many useful claims, no specific scientific study has been carried out to examine the antidiabetic activity of the plant, that's why the current study was designed.

MATERIALS AND METHODS

Plant Material

Fresh leaves of *Memecylon malabaricum* were collected from Western Ghats of India in November 2008 and were authenticated from Prof. M. Venkaiah, Taxonomist, Department of Botany, Andhra University, Visakhapatnam, India. A voucher specimen (AU/PCOG/09/09) has been deposited at the herbarium of AU College of Pharmaceutical Sciences, Andhra University, Visakhapatnam, for ready reference.

Preparation of the Extract

The leaves were shade dried at a temperature between 21-30°C for 15-30 days, after which these leaves were chopped and ground. Finally extraction was carried out by the following procedure

The powdered crude drug (700 g) was extracted with methanol in Soxhlet apparatus for 24 hours. The extract thus obtained was concentrated under vacuum (50°C) dried completely and weighed. The yield was found to be approximately 16% w/w.

Toxicity studies

The acute toxicity study¹⁶ is aimed to establish the therapeutic index. The test extracts were administered once orally at 3 dose levels (250, 500, 1000 mg/kg) to a group of 10 rats of both sexes about equal in number which have been fasting over night (about 18hours). The treated rats were observed continuously for 2 hours and then occasionally for further 4 hours and finally over night. The animals were weighed before and 72 h after administration of the drug. The animals were observed for toxic symptoms and mortality was recorded.

Experimental Animals

Wistar albino rats of either sex (200-250 g) procured from National Institute of Nutrition,

Hyderabad, Andhra Pradesh, India, and were used to study the antidiabetic activity. The rats were randomly distributed into groups and housed in cages (5 per cage). The animals were maintained under standard laboratory conditions (light period of 12h/day and temperature 22°C±2°C), with free access to standard rodent pellet diet (Amrut, India) and water ad libitum. The experiment was cleared by Institutional Animal Ethical Committee (registration no. 516/01/A/CPCSEA).

Chemicals and Drugs

All the drugs used in this study were of Pharmaceutical grade. Alloxan monohydrate (Sigma chemicals, St. Louis, USA), Gliclazide (Wockhardt, Aurangabad, India), gum accacia (Sparchem, Maharashtra, India), Blood Glucose kit (Dr.Reddy's Laboratories Ltd. Hyderabad, India) and methanol were supplied by Desai chemicals, Visakhapatnam, India.

Preliminary Phytochemical Analysis

Preliminary phytochemical analysis of *Memecylon malabaricum* was performed for alkaloids, tannins, saponins, terpenes, steroids, flavonoids and glycosides according to the Kokate et al., Table 1.

Table 1
Phytochemical Screening of Methanolic Extract of *Memecylon malabaricum* leaves

Name of the test	<i>Memecylon malabaricum</i> leaves	
	Methanolic extract	Ethylacetate fraction
Phytosterols	+	+
Triterpenes	-	-
Glycosides	-	+
Saponins	+	-
Flavonoids	+	+
Tannins	+	-
Carbohydrates	-	+
Alkaloids	-	+

'+' Present '-' Absent

Antidiabetic Activity Alloxan Induced diabetes¹⁷

Albino rats of either sex were fasted for 18h before injection with alloxan. Alloxan monohydrate was dissolved in saline. A dose of 100 mg/kg body weight injected immediately after preparation through intraperitoneal route. Since alloxan is capable of producing fatal hypoglycaemia as a result of massive insulin release from the pancreas, animals were treated with 10% dextrose orally to combat the immediate hypoglycaemia. Blood sugar was measured after 24-48 h of alloxan treatment to evaluate induction of diabetes.

Collection of Blood Samples

The animal was restrained (un anaesthetized) in such a way that loose skin of the neck was tightened while handling the head with the left hand. With the help of the index finger the eye was pressed just behind the angle of the jaw resulting in the engorgement of the retro orbital plexus. Then tip of the capillary was inserted at the medial canthus into the retro-orbital plexus with gentle rotation by the other hand. As the vessels are ruptured, blood wells up in

the peri-orbital space. The tip of the capillary was then slightly withdrawn, so that the blood flows into the capillary, which was collected in micro centrifuge tube containing small quantity of potassium oxalate and sodium fluoride as anticoagulant. Blood samples were collected from retro-orbital plexus at 0, 1, 2, 4, 6, 8, 10, and 12 hour. Blood glucose levels were estimated by GOD-POD method.

Experimental set up

The rats (with blood sugar levels between (250-350 mg/dl) were used for the experiment. Each group consisted of 6 animals (n=6).

Group-I: Received vehicle (5% gum acacia) and served as control,

Group II: Received methanolic extract of *Memecylon malabaricum* 100 mg/k g, p.o

Group III: Received methanolic extract of *Memecylon malabaricum* 200 mg/k g, p.o

Group IV: Received methanolic extract of *Memecylon malabaricum* 400 mg/k g, p.o

Group V: Received a standard drug gliclazide 7.2 mg/kg (the human dose of gliclazide was converted into the animal dose using the standard dose-converting table¹⁸).

Table 2
Effect of methanolic extract of leaves of *Memecylon malabaricum* on percentage blood glucose Reduction in Diabetic rats

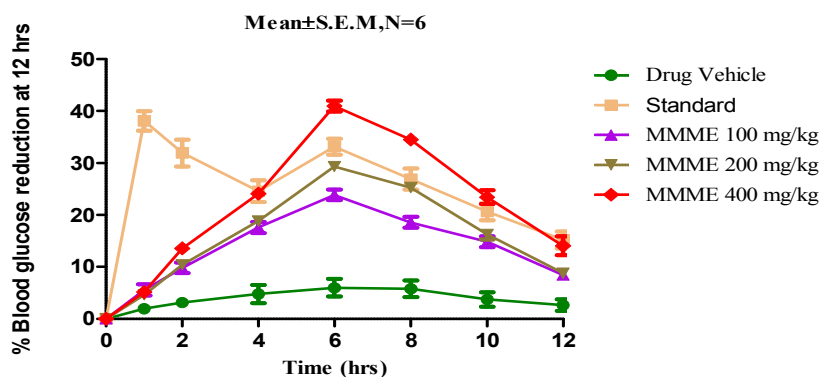
Time (hrs)	Control	Standard 7.2 mg/kg	MMME 100 mg/kg	MMME 200 mg/kg	MMME 400 mg/kg
0	0	0	0	0	0
1	1.95±0.84	38.09±1.9***	5.55±1.08**	4.63±0.20*	5.16±0.4**
2	3.16±0.96	31.92±2.6***	9.82±1.03**	10.37±0.47*	13.55±0.3**
4	4.78±1.75	24.58±2.1***	17.59±1.11**	18.80±0.62*	24.11±0.8**
6	5.98±1.68	33.16±1.5***	23.85±0.98**	29.29±0.32*	40.97±1.1**
8	5.77±1.60	26.89±2.0***	18.56±1.06**	25.26±0.64*	34.54±0.3**
10	3.72±1.39	20.63±1.7***	14.85±1.05**	16.25±0.97*	23.41±1.3**
12	2.62±1.08	15.18±1.6***	8.43±0.89**	8.81±0.70*	14.05±1.8**

MMME = *Memecylon malabaricum* methanolic extract

Significance: *P<0.05, **P<0.01, ***P<0.001

Figure 1

Dose dependent effect of methanolic extract of leaves of *Memecylon malabaricum* and gliclazide on percentage blood glucose reduction in alloxan induced diabetic rats



MMME = *Memecylon malabaricum* Methanolic extract

Statistical analysis

Results of the study were expressed as Mean \pm S.E.M. ANOVA followed by Dennett's test were used to determine significant differences between groups. P- Values less than 0.05 and 0.01 were considered as indicative of significance

RESULTS AND DISCUSSION

The mean percent decrease in blood glucose levels of control and extract treated animals after oral administration of different doses of methanolic extract of *Memecylon malabaricum* at various time intervals are shown in table 2 and figure 1. The mean percent reduction in blood glucose levels were statistically evaluated in comparison to control group at identical time intervals. The mean percent decrease in blood glucose levels produced by all doses were significant ($P < 0.001$, $P < 0.05$) up to 12th hour. The mean percent decrease in blood glucose produced by 100 mg/kg b.w of methanolic extract of *Memecylon malabaricum* were 0, 5.55 \pm 1.08, 9.82 \pm 1.03, 17.59 \pm 1.11, 23.85 \pm 0.98, 18.56 \pm 1.06, 14.85 \pm 1.05, and 8.43 \pm 0.89 at 0, 1, 2, 4, 6, 8, 10 and 12 hours respectively. The mean percent decrease in blood glucose level after oral administration of 200 and 400 mg/kg b.w of methanolic extract of *Memecylon malabaricum* were 0, 4.63 \pm 0.20, 10.37 \pm 0.47, 18.80 \pm 0.62, 29.29 \pm 0.32, 25.26 \pm 0.64, 16.25 \pm 0.97, 8.81 \pm 0.70 and 0, 5.16 \pm 0.4, 13.55 \pm 0.3, 24.11 \pm 0.8, 40.97 \pm 1.1,

34.54 \pm 0.3, 23.41 \pm 1.3, 14.05 \pm 1.8 at 0, 1, 2, 4, 6, 8, 10 and 12 hours respectively. The oral administration of the standard drug Gliclazide 7.2 mg/kg b.w showed 0, 38.09 \pm 1.9, 31.92 \pm 2.6, 24.58 \pm 2.1, 33.16 \pm 1.5, 26.89 \pm 2.0, 20.63 \pm 1.7, and 15.18 \pm 1.6 at 0, 1, 2, 4, 6, 8, 10 and 12 hour respectively. The extract at all dose levels showed statistically significant percent decrease in blood glucose. The percent reduction in blood glucose was significant at 4th hour and gradually increased to the maximum level at 6th hour and fallen back at 12th hour. The results suggested that the plant *Memecylon malabaricum* possessing antidiabetic activity and the results are comparable to that of Gliclazide. The extract at 400 mg/kg, p.o, showed a maximum reduction of raised blood glucose level as that of 100 and 200 mg/kg. The results obtained indicates that the extract found to have significant ($P < 0.01$) antidiabetic activity in rats which is a dose dependent. The preliminary phytochemical examination suggested that the plant having steroids, saponins, flavonoids, tannins, and

alkaloids. (Table 1). Literature review revealed that the natural products like steroids eg: 28nor-22(R) witha 2,6,23-trienolide¹⁹, saponins eg: ginsenoside Rb 1²⁰, flavonoids eg: Quercetin²¹, tannins eg: lagerstroemin (ellagitannin)²², alkaloids eg: berberine²³ possessing antidiabetic activity. It is therefore

assuming that since the plant possessing steroids, saponins, flavonoids, tannins, and alkaloids (Table 1). The antidiabetic activity of the plant may be due to the presence of the above said category of compounds. It is therefore worth study further to isolate the pure molecules responsible for antidiabetic activity.

CONCLUSION

Methanolic extract of leaves of *Memecylon malabaricum* possesses an antidiabetic activity. Further studies are required to identify the active fractions that are responsible for antidiabetic activity and to clarify mechanisms of their actions.

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