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# **Original Research Article**

# Effect of ethyl acetate extract of *Melothria perpusilla* on dexamethasone induced hyperglycemia in albino rats

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# **ABSTRACT**

**Background:** Diabetes mellitus is a group of heterogeneous disorders in which carbohydrate metabolism is reduced while that of proteins and lipids is increased. Safety and tolerability factors limit the clinical use of anti diabetic drugs. The objectives of the study were to evaluate the effect of ethyl acetate extract of *Melothria perpusilla* (EAEMP) on dexamethasone induced hyperglycemia in albino rats.

**Methods:** A set of six animals each weighing 110-150g were used for the experimental study. Successive tests were conducted on the same set of animals after a period of 10 days in between the drug administration. Blood was collected from the orbital sinus and fasting blood glucose levels were measured; 2% gum acacia suspension was administered in all the six animals followed by dexamethasone (0.5ml/100g) intraperitoneal injection. Blood glucose concentrations were estimated in the blood samples collected at 1h and 2h after the administration of dexamethasone administration. With the same set of animals, similar tests were repeated with the test dose of 250 mg/kg and 500 mg/kg of the ethyl acetate extract of *Melothria perpusilla* and glibenclamide [0.5mg/kg per oral (p.o.)].

**Results:** Scientific data were analysed by Kruskal Wallis test. Ethyl acetate extract of *Melothria perpusilla* produced a significant reduction of blood glucose level when compared with control and standard.

**Conclusions:** Treatment with *Melothria perpusilla* improves hyperglycaemia probably by inhibiting gluconeogenesis.

**Keywords:** Diabetes mellitus, Dexamethasone, Glibenclamide, *Melothria* perpusilla

## INTRODUCTION

Diabetes mellitus (meli= honey) is a group of heterogeneous disorders in which carbohydrate metabolism is reduced while that of proteins and lipids are increased. The disease results into various complications which could be acute and chronic. Acute complications include marked hyperglycemia which impairs water and electrolyte balance and energy utilization, causing polyuria, polydipsia, dehydration, weight loss, and eventually if untreated, cerebral dysfunction and coma. <sup>2</sup>

According to statistical data, 2.8% of the global population suffers from this disease and it is expected to still increase to more than 5.4% by 2025.<sup>3</sup>

Increasing prevalence, progressive nature and multi systemic outcomes highlight the need for effective pharmacotherapeutical approach to treat diabetes mellitus. Several types of glucose-lowering medicines that exert anti-diabetic effects through different mechanisms are available for the treatment of diabetes mellitus. In the past three decades, several milestones in the treatment of diabetes have been achieved but the results of treatment in patients are still far from perfect. These treatments have some disadvantages like drug resistance, side effects, and even toxicity.<sup>4</sup>

According to world ethnobotanical information reports, around 800 plants may possess antidiabetic activity. Research has been focused on scientific evaluation of traditional drugs of plant origin as well as screening of more effective and safe hypoglycemic agents and this has

continued to be an important area of new drug development. However, lots of herbs are now being used in the management of diabetes mellitus.<sup>5</sup>

*Melothria perpusilla* is commonly found in the north eastern region of India and Nilgiri hills of Tamil Nadu. *Melothria perpusilla* is used by the local population of Manipur for treating jaundice and kidney diseases. Roots have curative action in fever and diarrhoea. Fruits possess antihelminthic property and demulcent action.<sup>6</sup>

Melothria perpusilla is a slender, hispid, perennial climber which has deeply striated, glabrous stem with cordate leaves. The fruits are globose and finely reticulate. It has oblong flattened and tuberous roots. The aerial parts of Melothria perpusilla, commonly known as "creeping cucumber" and well known as "Lamthabi" in Manipuri and Bankundri in Hindi, have been used for jaundice and kidney disorders since ages. Sterols and flavonol glycosides have been isolated from the chloroform extract of Melothria perpusilla and it is popular in Manipur for the traditional treatment of jaundice. Unfortunately, significant scientific data are not available in literature to substantiate the various traditional medical uses of the plant.

#### **METHODS**

#### Study approval

The whole experimental protocol was approved and constituted in accordance with the rules and guidelines of the Institutional Animal Ethics Committee for the purpose of control and supervision on experiments in animals, India.

## Place of study

The experimental study was conducted in the Department of Pharmacology, R.I.M.S., Imphal, Manipur.

#### Animals

Six healthy albino rats of either sex (12-14 weeks) weighing between 110-150g were obtained from the animal house, R.I.M.S., Imphal. Albino rats housed in polypropylene animals cages and acclimatized in the Departmental animal room in the standard conditions of temperature, relative humidity (55 $\pm$ 5%), and light (12 h light/dark cycles) were used. Rats were fed with standard pellet diet and water with free access to water.

#### Collection of plants

Melothria perpusilla plants were collected from the campus of Regional Institute of Medical Sciences, Imphal West District, Manipur during the months of June-August, 2015.

#### Identification of plant

Prof. H. Nandiram Sharma, (retired) Professor of Botany, Manipur University identified and authenticated the plant.

#### Plant extract preparation

Aerial portions were completely shade dried in air and powdered using mixer grinder and later on subjected to defatting process using petroleum ether (B.P. 40°- 60°). The plant material was emptied and thoroughly washed using 95% ethyl alcohol and solvent was completely evaporated by spreading the plant materials which were later repacked with the dried plant material; thus, the test compound was obtained by using ethyl acetate solvent. Soxhlet apparatus was used for the preparation of plant extract. The yield at the end of extraction was calculated to be 0.36%.

#### Preliminary photochemical study

Lead acetate solution on addition to a small quantity of the plant extract, gave a yellow coloured precipitate. Sodium hydroxide solution on addition to a small quantity of the extract produced a yellow coloured precipitate which turned colourless when dilute acid was added. Both of these tests reveal the presence of flavonoids.

#### Acute toxicity study

Melothria perpusilla was used since thousands of years by the local population of Manipur for treatment of various diseases. The limit test of the test compound was conducted. Ethyl acetate extract of Melothria perpusilla (EAEMP) was administered in experimental albino rats at one dose level of 2000 mg/kg per orally. At the dose of 2000 mg/kg per orally, there was no mortality and thus two working doses of 250 mg/kg and 500 mg/kg were chosen for further experimental study.<sup>14</sup>

#### Experimental study

Hyperglycaemia was induced by the method of Md. Salam et al. 15 The same set of six animals were used throughout for the experimental study. Blood was collected from the orbital sinus by capillary tube following engorgement of retro orbital sinuses. After collecting and measuring the fasting blood glucose levels, 2% gum acacia suspension (10ml/kg per oral) was administered in all the six albino rats followed by dexamethasone (0.5ml/100g) intraperitoneal injection. Blood glucose concentrations were estimated in the blood samples collected at 1h and 2h after the administration of the dexamethasone administration. Using the same set of animals, similar tests were repeated with the test dose of 250 mg/kg and 500 mg/kg of the ethyl acetate extract of Melothria perpusilla and glibenclamide (0.5 mg/kg p.o.). Duration of 10 days was maintained in between the successive tests for washing out of the drug from animals to prevent the interference of action of one drug with the other.

#### Statistical analysis

Blood glucose levels were expressed as Mean  $\pm$  Standard deviation. The non parametric data were analysed by Kruskal Wallis test. IBM SPSS software version 23.0 was used for analysis of the data; p <0.05 was considered statistically significant.

#### **RESULTS**

The effect of ethyl acetate extract of *Melothria perpusilla* on dexamethasone induced hyperglycaemia were studied in the albino rats.

Blood glucose level in the overnight fasted albino rats of (a) control, (b) test 1 (250 mg/kg), (c) test 2 (500 mg/kg), (d) standard drug (glibenclamide 0.5 mg/kg) groups were 71.00±0.58, 70.83±1.40, 69.50±0.89, 68.17±3.06 respectively. Blood glucose level after 1h treatment of control (2% gum acacia followed by dexamethasone 0.5 ml/100g i.p.) and then after test 1 (250 mg/kg), test 2 (500 mg/kg) and standard (glibenclamide 0.5 mg/kg) which were administered after the drug wash out period of 10 days on each occasion were 193.67±3.58, 159.50±3.84, 120.00±3.15, 112.33±2.39 respectively.

The average increase with the fasting blood glucose level values was 122.67 in the control group, and 88.67, 50.50, 44.16 in the test 1, test 2 and standard group respectively. The increase in the blood glucose level after 2h of treatment conducted in the same way was 84.33, 63.00, 35.83, 31.50 in the test 1, test 2 and standard group respectively. Test 1, test 2 and standard showed highly significant reduction in blood glucose level (p<0.01) when compared with control. Test 2 showed a highly significant reduction in blood glucose level (p<0.01) when compared with test 1 (Table 1).

Table 1: Effect of ethyl acetate extract of *Melothria* perpusilla on dexamethasone induced hyperglycaemia.

	Blood glucose [mg% (Mean ± SD)]		
	Fasting	1 h	2 h
Control	71.00±0.58	193.67±3.58 <sup>#</sup>	155.33±2.75 <sup>#</sup>
Test 1	70.83±1.40	159.50±3.84*#	133.83±3.56*#
Test 2	69.50±0.89	120.00±3.15*-	105.33±3.84*·
Standard	68.17±3.06	112.33±2.39*	99.67±3.07*

Values are Mean  $\pm$  SD

# **DISCUSSION**

Glucocorticoids exert prominent anti-insulin effects through various mechanisms such as by decreasing the peripheral utilisation of glucose by reducing its cellular uptake, enhancing the expression of the hepatic enzymes involved in gluconeogenesis and stimulating glucose synthesis from amino acids and inhibition of protein synthesis in muscle, connective tissue and skin for acids. 16 gluconeogenesis by mobilising amino Dexamethasone produces effects after a characteristic period of 0.5 h to several hours - the time required for the synthesis of new proteins.<sup>17</sup> Dose of 0.5 ml/100g i.p. dexamethasone was used to induce hyperglycaemia. A single dose of glucocorticoids, even a large one, is free from any harmful effects. 18 Glibenclamide at the dose of 0.5 mg/kg p.o. (extrapolated from human dose) showed highly significant decrease (p< 0.01) in 1 h and 2 h blood glucose changes of dexamethasone hyperglycaemia when compared with that of control. The highly significant reduction in blood glucose produced by test 1 (250 mg/kg) and test 2 (500 mg/kg) at 2 h compared with that of control indicated that dexamethasone is probably having inhibitory effect on gluconeogenesis.

#### **CONCLUSION**

In the above study, the test drug at the dose of 250 mg/kg and 500 mg/kg showed significant reduction in blood glucose level probably by inhibiting gluconeogenesis.

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Ethical approval: The study was approved by the Institutional Animal Ethics Committee (IAEC), Regional Institute of Medical Sciences (R.I.M.S.), Imphal, Manipur. Registration No. 1596/GO/a/12/CPCSEA

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<sup>\*</sup> p<0.01 when compared with control

<sup>#</sup> p<0.001 when compared with standard

<sup>.</sup> p<0.01 when compared with Test 1

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