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Research Article

Effects of the Crude Methanolic Extract of Merremia tridentata (Convolvulaceae) Leaves on Blood Glucose Regulation In Vivo

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ABSTRACT

Previous studies have highlighted the relevance of Merremia tridentata, a plant traditionally used in Senegal for diabetes management, in the regulation of blood glucose levels. The present study aimed to evaluate the antihyperglycemic and antidiabetic effects of the crude methanolic extract (CME) of M. tridentata leaves. Powdered leaves were subjected to methanolic maceration to obtain the CME, which was characterized by qualitative phytochemical screening. The extract was evaluated in normoglycemic rats, using an oral glucose tolerance test (OGTT), and in experimentally induced diabetic rats. Oral administration of CME (50 mg/kg) did not significantly affect basal glycemia in normoglycemic rats (0.97 ± 0.05 vs. 0.77 ± 0.06 g/L). However, CME exerted a dose dependent antihyperglycemic effect during OGTT. At doses of 50 and 100 mg/kg, the post glucose hyperglycemic peak was significantly reduced to 0.63 ± 0.04 and 0.73 ± 0.13 g/L, respectively, compared with 1.32 ± 0.26 g/L in control rats. In diabetic rats, repeated administration of CME (50 mg/kg/day) produced a marked reduction in blood glucose levels over 8 days. These effects may be attributed to the presence of phenolic compounds, particularly flavonoids. The results support the traditional use of M. tridentata in diabetes management and warrant further mechanistic studies.

Keywords

Merremia tridentata, Antidiabetic activity, Antihyperglycemic effect, Phytochemicals, Flavonoids.

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Introduction

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin action, or both [1]. It represents a major public health challenge, affecting more than 430 million individuals worldwide. In 2019, diabetes was directly responsible for approximately 1.5 million deaths and is projected to become the seventh leading cause of mortality by 2030 [2]. The burden of diabetes is increasing particularly rapidly in low- and middle-income countries, with Africa expected to reach nearly 15 million cases by 2025 [3].

Type 1 diabetes is an autoimmune disease characterized by absolute insulin deficiency and usually manifests during childhood or adolescence, requiring lifelong insulin therapy. Type 2 diabetes, accounting for nearly 90% of cases, typically occurs in adults and is

associated with insulin resistance and/or relative insulin deficiency. Current pharmacological treatments include biguanides, sulfonylureas, α-glucosidase inhibitors, thiazolidinediones, glinides, and incretin-based therapies, used alone or in combination [4]. However, the high cost and adverse effects of some antidiabetic drugs limit their accessibility and long-term use in developing countries.

Consequently, traditional medicine remains an important alternative therapeutic approach. According to the World Health Organization, nearly 80% of populations in developing countries rely on traditional medicine for primary health care [5]. In Senegal, numerous medicinal plants are traditionally used for diabetes management [6].

Merremia tridentata (L.) Hallier f. (Convolvulaceae) is widely distributed in southern and central Senegal and is commonly used in traditional medicine. Previous phytochemical investigations have reported the presence of sterols, polyphenols, tannins, proanthocyanidins, and flavonoids in its leaves [7-9]. These compounds are known to exert antioxidant and antidiabetic effects. The present study aimed to evaluate the antidiabetic potential of the crude methanolic extract of *M. tridentata* leaves using *in vivo* experimental models.

Materials and Methods

Plant Material

Leaves of *Merremia tridentata* were collected near the commune of Ndoffane (Kaolack region, Senegal; 14°00'00" N, 16°00'00"W). The plant material was authenticated, washed with distilled water, shade-dried, and ground into a fine powder using an electric grinder. The powder was stored in airtight containers until extraction.

Animal Material

Adult normoglycemic Wistar Kyoto rats were obtained from the animal facility of the Laboratory of Pharmacology. Animals were housed under standard laboratory conditions with free access to water and a standard diet (SENTENAC®, Dakar). All experimental procedures were conducted in accordance with institutional guidelines for the care and use of laboratory animals.

Preparation of the Crude Methanolic Extract

Powdered leaves were macerated in methanol at room temperature for 24 h. The mixture was filtered, and the filtrate was concentrated under reduced pressure using a rotary evaporator to obtain the crude methanolic extract (CME).

Phytochemical Screening

Qualitative phytochemical screening was performed to detect major classes of secondary metabolites using standard colorimetric and precipitation reactions. Tests were conducted for alkaloids (Mayer's test), polyphenols and tannins ($FeCl_3$ and Stiasny tests), flavonoids and catechols (cyanidin reaction), sterols and polyterpenes (Liebermann–Burchard test), and coumarins (ammonium hydroxide test), following established protocols [10-12].

Pharmacological Evaluation

Effect on Normoglycemic Rats

Rats were fasted for 12 h and divided into groups (n = 5). At time T0, basal blood glucose was measured. Animals received either physiological saline (10 mL/kg) or CME (50 or 100 mg/kg) orally. Blood glucose levels were measured hourly for 4 h.

Oral Glucose Tolerance Test (OGTT)

After 12 h fasting, rats were divided into three groups (n = 5). Animals were pretreated with saline or CME (50 or 100 mg/kg). Ninety minutes later, basal glycemia (T0) was measured, followed by oral glucose administration (4 g/kg). Blood glucose was measured every 30 min for 120 min.

Induction of Experimental Diabetes and Treatment

Experimental diabetes was induced by intraperitoneal injection of alloxan (120 mg/kg). After 72 h, rats exhibiting stable hyperglycemia (2–4 g/L) were selected. Animals were divided into three groups (n = 3): saline control, glibenclamide (0.3 mg/kg/day), and CME (50 mg/kg/day). Treatments were administered orally for 8 days, with blood glucose measured every two days.

Table 1: Results of Phytochemical Tests on the Leaves of M. tridentata.

		Polyphenols	Flavonoids	Alcaloids	Sterols & polyterpenes	Catechols	Coumarins	T.Catechic	T. Gallic
Leaves	Hexane*	-	-	+	-	-	-	-	-
	Methanol*	+++	+++	++	+	+	+++	-	+
	Ethanol*	+++	+++	-	-	++	+	+++	+++
	Methanol**	+++	+++	-	-	++	-	-	-
	Ethanol**	+++	+++	-	++	+	-	+	+

*: crude extract **: defatted extract +: present ++: moderate +++: abundant –: absent

Determination of Blood Glucose

Blood samples were collected from the retro-orbital sinus, and glucose levels were measured using an Accu-Chek® glucometer.

Results and Discussion

Phytochemical Composition of *Merremia tridentata* Leaf Extracts

Table 1 summarizes the complete phytochemical screening of the leaf extracts of *M. tridentata*. Qualitative phytochemical screening revealed that the leaves of *Merremia tridentata* are rich in several classes of secondary metabolites, including polyphenols, flavonoids, tannins, sterols, polyterpenes, catechols, and coumarins, supporting their traditional medicinal use. The crude methanolic extract exhibited particularly high levels of polyphenols and flavonoids, whereas alkaloids and terpenes were detected at moderate levels. These phytochemical groups are widely reported to possess antioxidant, antihyperglycemic, and insulin-sensitizing properties, which may contribute to the biological activities observed in the present study. The abundance of phenolic compounds is particularly relevant given their documented antioxidant and glucose-lowering properties.

Effect of the Crude Methanolic Extract on Basal Glycemia in Normoglycemic Rats

Oral administration of physiological saline did not significantly modify basal blood glucose levels throughout the 4 h observation period, confirming the stability of glycemia under the experimental conditions. Administration of the crude methanolic extract (CME) at doses of 50 and 100 mg/kg did not induce marked hypoglycemia in normoglycemic rats. A slight reduction in blood glucose was observed at the higher dose after 4 h, but values remained within the normal physiological range. These results suggest that CME does not exert an excessive hypoglycemic effect in normoglycemic animals, indicating a favorable safety profile with respect to glucose homeostasis (Figure1).

The hypoglycemic activity was assessed by measuring blood glucose every 60 minutes in treated rats over a 4-hour period. The results obtained, illustrated in Figure 1, show that after 4 hours of treatment with CME at doses of 50 and 100 mg/kg orally, there were significant variations in normal blood glucose levels compared with the control group.

Effect of the Crude Methanolic Extract in the Oral Glucose Tolerance Test

In the glucose tolerance test, pretreatment of rats with the crude methanolic extract (CME) (50 and 100 mg/kg, orally) prevented the appearance of the hyperglycemic peak in a dose-dependent manner. At 100 mg/kg orally, blood glucose varied from 0.73 ± 0.13 at T_0 to 1.42 ± 0.14 g/L. Compared to the control group, this variation was highly significant (2.03 ± 0.23 vs 1.42 ± 0.04 g/L) (n = 5). Similar results were also observed with CME at 50 mg/kg orally under the same conditions (2.03 ± 0.23 vs 1.05 ± 0.21 g/L) (n = 5).

In the oral glucose tolerance test, control rats exhibited a rapid and marked increase in blood glucose concentration, with a peak observed 30 min after glucose administration, followed by a gradual decline. Pretreatment with CME significantly attenuated this postprandial hyperglycemic response in a dose-dependent manner. At doses of 50 and 100 mg/kg, CME reduced the magnitude of the hyperglycemic peak and accelerated the return toward baseline glycemia.

The study demonstrated a significant decrease in blood glucose with CME during the 2 hours of treatment. This reduction was more pronounced with the dose of 50 mg/kg orally, particularly at the 30th minute of induced hyperglycemia, where a progressive decrease in blood glucose was observed (see Figure 2). Indeed, in normoglycemic rats, CME containing these secondary metabolites showed a significant effect on baseline blood glucose. Under the same conditions, CME induced an antihyperglycemic effect in the glucose tolerance test. CME also exhibited a highly significant activity in type 2 diabetic rats. These results are consistent with previous studies conducted on the aqueous root extract of ***Merremia tridentata*** [14].

The observed improvement in glucose tolerance suggests that CME may enhance peripheral glucose utilization and/or delay intestinal glucose absorption. Although the precise mechanism was not investigated in the present study, the effect may be partly attributed to the high content of flavonoids and other phenolic compounds, which have been reported to inhibit carbohydrate-digesting enzymes and improve insulin sensitivity. Importantly, CME reduced hyperglycemia without inducing fasting hypoglycemia, highlighting a selective antihyperglycemic effect. Figure 2.

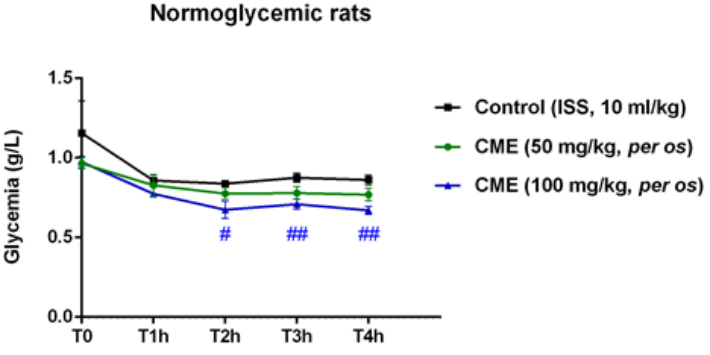

Figure 1: Variation of Blood Glucose Over Time.

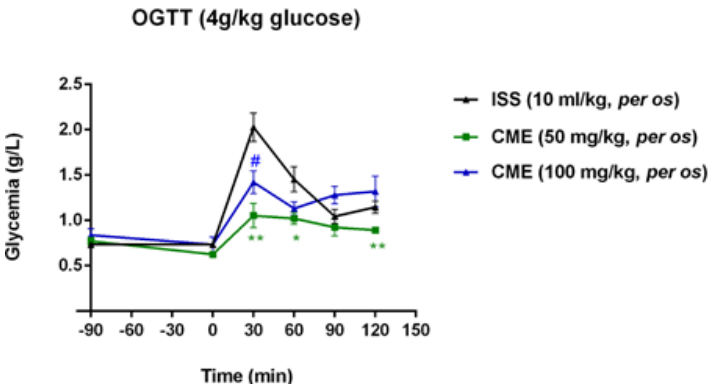

Figure 2: Variation of Blood Glucose (g/L) Over Time.

Effect of the Crude Methanolic Extract in Alloxan-Induced Diabetic Rats

This study was undertaken to evaluate the antidiabetic activity of the crude methanolic extract (CME) of ***Merremia tridentata*** leaves, which contains several secondary metabolites such as polyphenols (flavonoids), tannins, sterols, etc.

In alloxan-induced diabetic rats, sustained hyperglycemia was observed in the untreated control group throughout the experimental period. Daily oral administration of CME at 50 mg/kg produced a progressive and statistically significant decrease in baseline blood glucose (3.17 ± 0.74 vs 1.09 ± 0.03 g/L) after 8 days of observation (Figure 3). By the end of the experiment, glycemia in CME-treated rats was markedly lower than in the control group and approached near-normal values.

Treatment with the reference drug glibenclamide also reduced blood glucose levels, confirming the validity of the experimental model. The antihyperglycemic effect of CME was comparable to that of glibenclamide, although differences in mechanisms of action cannot be excluded. The glucose-lowering effect observed in diabetic rats suggests that CME may preserve residual pancreatic function and/or enhance peripheral glucose utilization. However, further studies involving insulin measurement and histological analysis of pancreatic tissue are required to clarify these mechanisms.

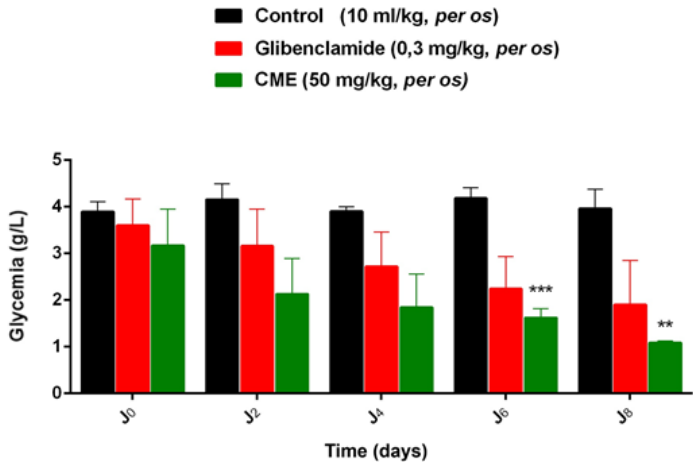

Figure 3: Evolution of Blood Glucose (g/L) in Type 2 Diabetic Rats Treated Daily.

Alloxan-induced type 2 diabetes is a characteristic model of insulin secretion disorders, in contrast, for example, to the db/db mouse model of type 2 diabetes, which is a model of insulin resistance characterized by obesity, persistent hyperglycemia, and hyperinsulinemia [15]. The results obtained, illustrated in Figure 1, show that in alloxan-induced type 2 diabetic rats, the crude methanolic extract (CME) significantly prevents the persistent hyperglycemia previously observed in the control group.

Moreover, the prevention of hyperglycemia with CME in type 2 diabetic rats is more pronounced than that typically observed with insulin secretagogues such as glibenclamide. Indeed, glibenclamide is an antidiabetic drug that acts on peripheral tissues without stimulating insulin secretion. Its hyperglycemia-preventing effect is more pronounced in an insulin resistance model, such as the db/db mouse, than in alloxan-induced type 2 diabetic rats [16].

The antidiabetic activity observed may be attributed to the synergistic effects of flavonoids and other polyphenols, which are known to enhance insulin sensitivity, modulate carbohydrate-digesting enzymes, and reduce oxidative stress. These findings are consistent with previous reports on *M. tridentata* extracts [14].

Conclusion

The crude methanolic extract of *Merremia tridentata* leaves exhibits significant antihyperglycemic and antidiabetic activities in experimental rat models. The extract effectively improves glucose tolerance and reduces hyperglycemia, likely due to its high content of flavonoids and other phenolic compounds. These results provide scientific support for the traditional use of *M. tridentata* in diabetes management. Further studies are required to elucidate the precise mechanisms of action and to evaluate long-term efficacy and safety.

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