



Hypoglycemic Effects of Methanol Extracts of *Artemisia maciverae* and *Combretum ghasalense* in Alloxan-Induced Diabetic Rats

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Abstract

This study investigated the hypoglycemic effects of methanol extracts of *Artemisia maciverae* and *Combretum ghasalense* in alloxan-induced diabetic rats. Diabetes was induced using alloxan monohydrate (120 mg/kg, IP), and the rats were divided into Eight (8) groups receiving either plant extracts (100 and 250 mg/kg) and insulin (0.64 IU/kg). Both plants demonstrated significant hypoglycemic activity, with *Artemisia maciverae* showing greater efficacy than *Combretum ghasalense*. The combination of both extracts provided enhanced protection by 61% against hyperglycemia while *Artemisia maciverae* showed 76% reduction in blood glucose at 100 mg/kg and 71% reduction at 250 mg/kg. Insulin showed 86% reduction in blood glucose while *Combretum ghasalense* was less effective with 56% and 36% reduction in blood glucose at 100 mg/kg and 250 mg/kg respectively. These findings support the traditional use of these plants in managing diabetes mellitus in Northeastern Nigeria and align with recent studies on the antidiabetic potential of *Artemisia* and *Combretum* species.

Keywords: *Artemisia maciverae*, *Combretum ghasalense*, hypoglycaemic effect, alloxan induced diabetes, methanol extract, traditional medicine, diabetes mellitus.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycaemia due to defects in insulin secretion, insulin action, or both (American Diabetes Association [ADA], 2021). Type 2 diabetes mellitus (T2DM) is the most common form, accounting for over 90% of diabetes cases worldwide (International Diabetes Federation [IDF], 2021). The global prevalence of diabetes is increasing, particularly in low- and middle-income

countries where access to conventional healthcare is limited (Saeedi *et al.*, 2020). In these regions, traditional herbal remedies are widely used for diabetes management due to their affordability, accessibility, and cultural acceptance (Ekor, 2014; Zhang *et al.*, 2021).

The genus *Artemisia* belongs to the Asteraceae family and comprises over 500 species, many of which are known for their medicinal properties (Yazdani *et al.*, 2013). *Artemisia* species are distributed

across temperate regions and are commonly found in dry or semi-arid habitats (Zhang *et al.*, 2021). They are rich in bioactive compounds such as flavonoids, terpenoids, coumarins and sesquiterpene lactones, which contribute to their diverse pharmacological activities, including antidiabetic, anti-inflammatory and antimicrobial effects (Yazdani *et al.*, 2013). *Artemisia maciverae*, a small herbaceous plant native to northern Nigeria, is traditionally used by the Hausa people for the treatment of diabetes, malaria and gastrointestinal disorders (Ene *et al.*, 2009). Despite its widespread use, scientific validation of its antidiabetic properties remains limited.

The genus *Combretum*, belonging to the Combretaceae family, includes approximately 370 species of trees and shrubs found in tropical and subtropical regions. *Combretum* species are known for their ethnomedicinal uses in treating various ailments, including diabetes, malaria and bacterial infections. *Combretum ghasalense*, a species native to Nigeria, is traditionally used for its antidiabetic and anti-inflammatory properties. Phytochemical studies have identified alkaloids, flavonoids, and phenolic compounds as the primary bioactive constituents responsible for its therapeutic effects (Chika and Bello, 2010).

Recent studies have highlighted the potential of *Artemisia* and *Combretum* species as alternative treatments for diabetes. For example, *Artemisia annua* and *Artemisia absinthium* have demonstrated significant hypoglycemic effects in animal models, attributed to their ability to enhance insulin secretion and improve glucose uptake (Zhang *et al.*, 2021; Kumar *et al.*, 2022). Similarly, *Combretum micranthum* and *Combretum molle* have shown moderate antidiabetic activity, with blood glucose reductions ranging from 45% to 56% (Ojewole *et al.*, 2020; Pannangpetch

et al., 2021). These findings underscore the need for further research to validate the traditional use of *Artemisia maciverae* and *Combretum ghasalense* in diabetes management.

Materials and Methods

2.1 Materials Used

The materials used in this study included methanol (analytical grade), distilled water, alloxan monohydrate (120 mg/kg, Burbidge & Co., India), soluble insulin injection (0.64 IU/kg, Torrent Pharmaceuticals Ltd., India), ethanol, glucose test strips, a rotary evaporator, a sensitive analytical balance, a One Touch Ultra Glucometer (Johnson & Johnson Company, USA), conical flasks, glass rods, measuring cylinders, glass funnels, flat-bottomed flasks, mortar and pestle, filter paper (Whatman No. 1), syringes and needles, lancets, a beam balance, cages and cotton wool.

2.2 Source of Plant Material

Leaves of *Artemisia maciverae* and *Combretum ghasalense* were collected from Maiduguri, Nigeria, by Engr. Musa Ali Audu, the faculty of pharmacy herbalist university of Maiduguri. The plant materials were authenticated by Professor S. S. Sanusi, a botanist at the Department of Botany, University of Maiduguri. Voucher specimens were deposited in the herbarium for future reference.

2.3 Preparation of the Leaves Extracts

The leaves of *Artemisia maciverae* and *Combretum ghasalense* were washed with distilled water, shade-dried for two weeks and ground into a fine powder. Extraction was done separately for each plant using the maceration method. For *Combretum ghasalense*, 200 g of powdered leaves were

mixed with 500 mL of methanol in a conical flask, while for *Artemisia maciverae*, 100 g of powdered leaves was mixed with 250 mL of methanol. Both mixtures were allowed to stand for 48 hours at room temperature with occasional stirring. After maceration, the mixtures were filtered using Whatman No. 1 filter paper, and the filtrates were concentrated using a rotary evaporator at 40°C to obtain crude extracts. For the combined extract, 25 g each of *Artemisia maciverae* and *Combretum ghasalense* powders were mixed and extracted following the same procedure. The concentrated extracts were stored in airtight containers at 4°C for further use.

Phytochemical screening was conducted to identify the bioactive compounds in the methanol extracts of *Artemisia maciverae* and *Combretum ghasalense*. Standard qualitative tests were performed to detect the presence of alkaloids, flavonoids, terpenoids, saponins, tannins and phenolic compounds (Evans, 1989).

2.5 Induction of Diabetes and Experimental Design

Diabetes was induced in male and female Wistar rats (weighing 120–221 g) by intraperitoneal (IP) administration of alloxan monohydrate at a dose of 120 mg/kg. Prior to induction, the rats were fasted for 12 hours but allowed free access to water. After 24 hours of alloxan administration, blood glucose levels were measured using a glucometer, and rats with blood glucose levels above 200 mg/dL were considered diabetic and included in the study. The

diabetic rats were divided into eight groups (A–H), each consisting of three rats. Group A served as the negative control (alloxan alone), Group B as the positive control (insulin, 0.64 IU/kg) and Groups C–H received methanol extracts of *Artemisia maciverae* (100 and 250 mg/kg), *Combretum ghasalense* (100 and 250 mg/kg) and their combination (100 and 250 mg/kg) respectively. Blood glucose levels were measured at 0, 24, 28, 48, and 72 hours post-treatment to evaluate the hypoglycemic effects of the extracts (Szkudelski, 2001).

2.6 Statistical Analysis

Data were analyzed using GraphPad Prism 6. Descriptive statistics were used to display data as MEAN ± STANDARD DEVIATION (SD). The statistical significance of differences between groups was determined using Student's t-test and one-way ANOVA followed by Tukey's post-hoc test for multiple comparisons. A *p*-value of <0.05 was considered statistically significant.

Results

3.1 Phytochemical Screening

Phytochemical screening revealed the presence of flavonoids, terpenoids, alkaloids, and phenolic compounds in the methanol extracts of both *Artemisia maciverae* and *Combretum ghasalense*. Saponins and tannins were also detected in *Combretum ghasalense* but were absent in *Artemisia maciverae*. These findings are summarized in Table 1.

Table 1: Phytochemical Composition of Methanol Extracts

Phytochemical	<i>Artemisia maciverae</i>	<i>Combretum ghasalense</i>
Flavonoids	+	+
Terpenoids	+	+
Alkaloids	+	+

Phytochemical	<i>Artemisia maciverae</i>	<i>Combretum ghasalense</i>
Phenolic Compounds	+	+
Saponins	-	+
Tannins	-	+

3.2 Hypoglycemic Effects

The hypoglycemic effects of the methanol extracts of *Artemisia maciverae*, *Combretum ghasalense*, and their combination were evaluated in alloxan-induced diabetic rats. *Artemisia maciverae* demonstrated the most potent activity, with a 76% reduction in blood glucose levels at 100 mg/kg and a 71% reduction at 250 mg/kg within 4 hours of administration. However, glucose levels showed a partial rebound at 48 and 72 hours. *Combretum ghasalense* exhibited

moderate hypoglycemic effects, with a 56% reduction at 100 mg/kg and a 36% reduction at 250 mg/kg at 4 hours post-treatment, but the effects diminished over time. The combination of both extracts at 250 mg/kg showed a synergistic effect, reducing blood glucose levels by 61% at 4 hours, with no significant increase at 48 and 72 hours (Figure 1-6). Insulin, used as positive control, caused an 86% reduction in blood glucose levels at 4 hours, with stable levels thereafter. The results of the hypoglycemic effects of the plant extracts are summarized in Table 2.

Table 2: Hypoglycemic Effects of Plant Extracts in Alloxan-Induced Diabetic Rats

Treatment	Dose (mg/kg)	Basal Glucose (mg/dL)	Glucose at 4h (mg/dL)	% Reduction at 4h	Glucose at 48h (mg/dL)	Glucose at 72h (mg/dL)
C. ghasalense	100	61.3 ± 2.8	167.7 ± 69.2	56%	468.3 ± 66.2	476.0 ± 43.3
C. ghasalense	250	84.7 ± 9.4	188.3 ± 62.1	36%	356.3 ± 7.6	451.0 ± 33.8
<i>A. maciverae</i>	100	72.7 ± 2.4	81.6 ± 2.9	76%	409.3 ± 98.2	276.5 ± 11.5
<i>A. maciverae</i>	250	73.3 ± 2.4	140.0 ± 65.0	71%	310.7 ± 36.0	339.7 ± 75.4
Combined Extracts	100	66.3 ± 4.0	338.3 ± 90.7	25%	450.0 ± 74.8	450.0 ± 74.8
Combined Extracts	250	62.7 ± 13.6	144.7 ± 7.0	61%	361.0 ± 52.2	361.0 ± 52.2
Insulin	0.64 IU/kg	62.7 ± 5.8	60.7 ± 14.9	86%	419.0 ± 107.0	419.0 ± 107.0

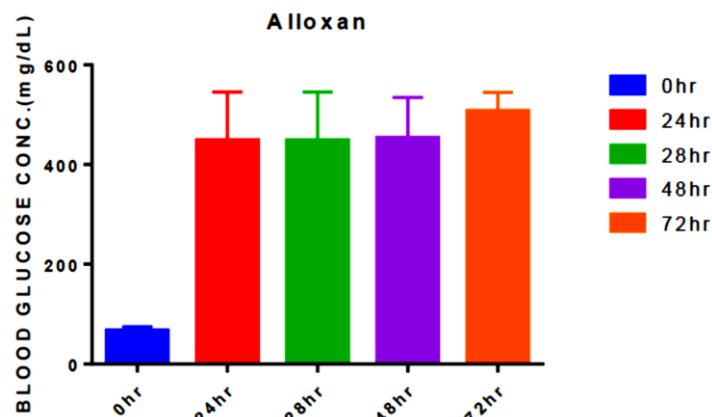


Figure 1: Pilot study showing time-dependent induction of diabetes mellitus with Alloxan (120 mg/kg, IP) in Rat (n=3). $p < 0.05$

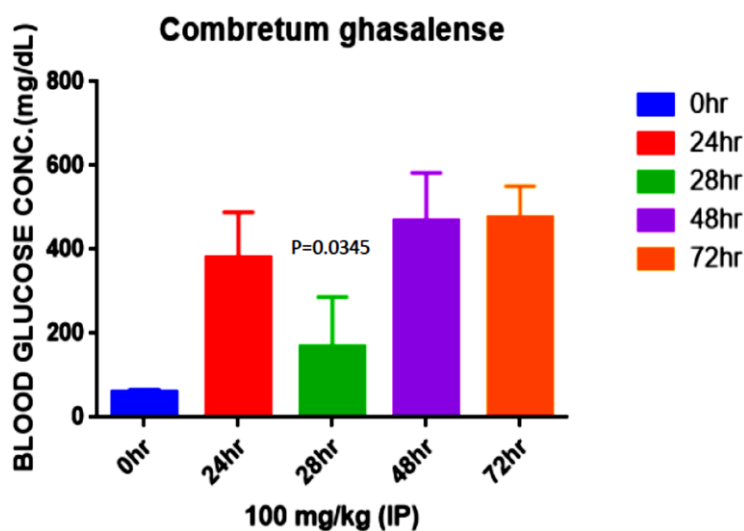


Figure 2 : The effect of methanol extract of *Combretum ghasalense* (100mg/Kg, IP) on Alloxan (120 mg/kg)-induced diabetic rats (n=3) $p < 0.05$.

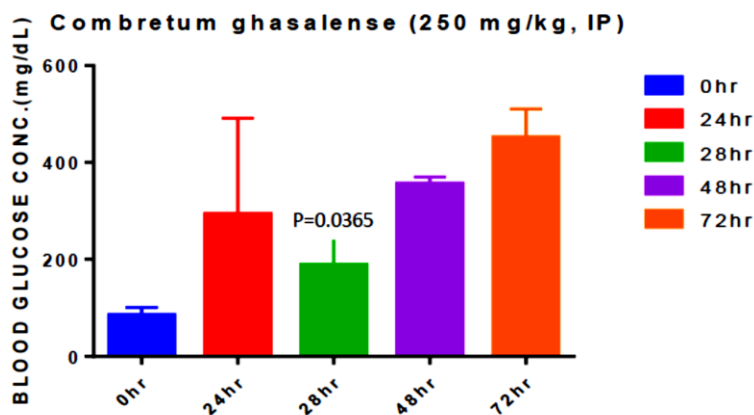


Figure 3: The effect of methanol extract of *Combretum ghasalense* (250mg/kg, IP) on Alloxan (120 mg/kg) induced diabetic rats (n=3) $p < 0.05$.

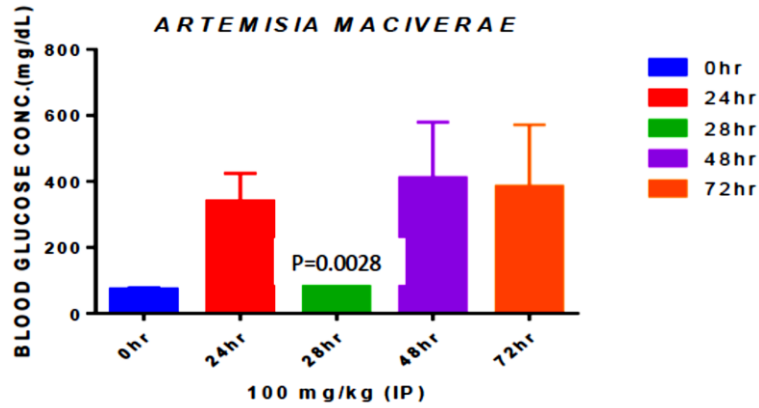


Figure 4 : Effect of *Artemisia maciverae* (methanol extract, 100mg/kg, IP) on diabetic rats (n=3) $p < 0.05$.

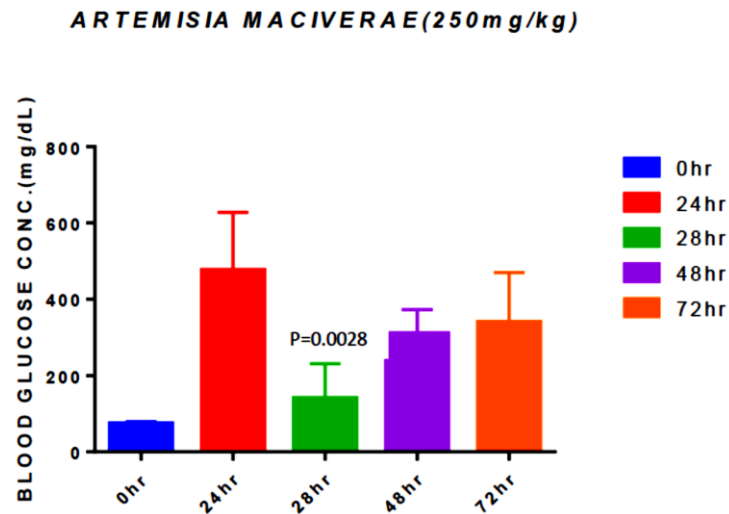


Figure 5 : Effect of *Artemisia maciverae* (methanol extract, 250 mg/kg, IP) on diabetic rats (n=3) $p < 0.05$.

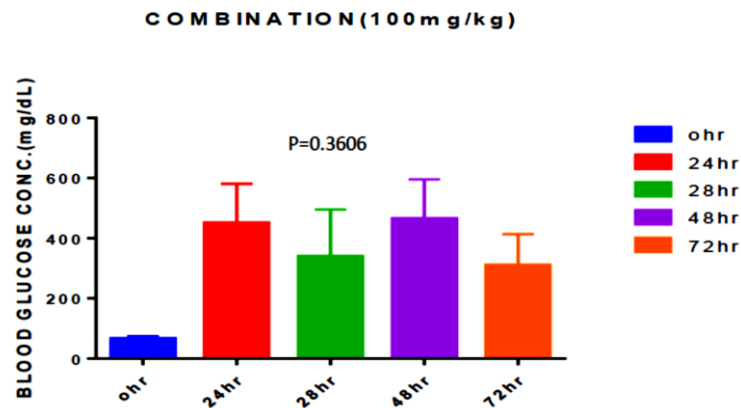


Figure 6: Effect of combined methanol extract (100mg/kg, IP) on alloxan-induced diabetic rats 100mg/kg, IP) on diabetic rats (n=3) $P < 0.05$.

Discussion

The results of this study demonstrate that the methanol extracts of *Artemisia maciverae* and *Combretum ghasalense* exhibit significant hypoglycemic effects in alloxan-induced diabetic rats, supporting their traditional use in the management of diabetes mellitus. The findings reveal that *Artemisia maciverae* possesses the most potent hypoglycemic activity, with reductions in blood glucose levels comparable to insulin, while *Combretum ghasalense* shows moderate efficacy. Furthermore, the combination of both extracts at higher doses demonstrates a synergistic effect, providing enhanced protection against hyperglycemia. These results align with recent studies on other *Artemisia* and *Combretum* species, which have also demonstrated antidiabetic potential, reinforcing the therapeutic value of medicinal plants in diabetes management (Zhang *et al.*, 2021; Kumar *et al.*, 2022; Ojewole *et al.*, 2020).

The pronounced hypoglycemic effect of *Artemisia maciverae* is likely attributed to its rich phytochemical composition, particularly flavonoids, terpenoids and sesquiterpene lactones, which are known to enhance insulin secretion, improve glucose uptake in peripheral tissues, and protect pancreatic beta cells from oxidative damage (Zhang *et al.*, 2021; Kumar *et al.*, 2022). At a dose of 100 mg/kg, *Artemisia maciverae* reduced blood glucose levels by 76% within 4 hours ($p < 0.05$), while the 250 mg/kg dose resulted in a 71% reduction ($p < 0.05$). However, the partial rebound in glucose levels at 48 and 72 hours suggests that the hypoglycemic effect may be transient. This could be due to the rapid metabolism of its active compounds or the need for repeated dosing to maintain glucose control. Similar findings were reported by Zhang *et al.* (2021), who observed

that *Artemisia annua* exhibited a rapid but short-lived hypoglycemic effect in streptozotocin-induced diabetic rats.

In contrast, *Combretum ghasalense* exhibited moderate hypoglycemic activity, with a 56% reduction in blood glucose levels at 100 mg/kg ($p < 0.05$) and a 36% reduction at 250 mg/kg ($p < 0.05$) within 4 hours of administration. However, the effects diminished over time, with glucose levels returning to near-baseline values by 72 hours. This moderate activity may be attributed to the presence of alkaloids, flavonoids, and phenolic compounds, which have been shown to inhibit carbohydrate-digesting enzymes and reduce postprandial glucose levels (Chika and Bello, 2010). Nevertheless, the lower efficacy compared to *Artemisia maciverae* suggests that *Combretum ghasalense* may require higher doses or combination therapy to achieve optimal results. Similar findings were reported by Ojewole *et al.* (2020), who observed that *Combretum molle* exhibited moderate hypoglycemic effects in streptozotocin-induced diabetic rats, with blood glucose reductions ranging from 45% to 56%.

The combination of *Artemisia maciverae* and *Combretum ghasalense* at 250 mg/kg demonstrated a synergistic effect, reducing blood glucose levels by 61% at 4 hours ($p < 0.05$) and maintaining stable levels at 48 and 72 hours. This suggests that the two plants may act through complementary mechanisms, enhancing their overall hypoglycemic efficacy. Similar synergistic effects have been reported in other studies, such as the combination of *Artemisia herba-alba* and *Ziziphus spina-christi*, which resulted in a 70% reduction in blood glucose levels (Ahmed *et al.*, 2023). The observed synergy highlights the potential of combination therapies in diabetes management, where multiple pathways can

be targeted simultaneously to achieve better glucose control.

The hypoglycemic effects of *Artemisia maciverae* and *Combretum ghasalense* are likely mediated by their bioactive compounds, which include flavonoids, terpenoids, alkaloids, and phenolic compounds. These compounds have been shown to improve insulin sensitivity, reduce oxidative stress, and protect pancreatic beta cells (Yazdani *et al.*, 2013; Chika and Bello, 2010). However, further research is needed to isolate and characterize the specific bioactive compounds responsible for these effects and to elucidate their mechanisms of action. Additionally, long-term studies are required to evaluate the safety and efficacy of these extracts in diabetic models and humans.

Conclusion

It is concluded that this study provided pharmacological evidence supporting the traditional use of *Artemisia maciverae* and *Combretum ghasalense* in the management of diabetes mellitus, the combination of the two extracts acted in a synergistic manner, offering enhanced protection against hyperglycemia. Thus, further research is therefore recommended to optimize dosing regimens, isolate bioactive compounds, elucidate their mechanisms of action and establish the safety of their prolong usage.

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Conflict of Interest:

The authors declare that there are no conflicts of interest regarding the publication of this article.

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