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# Hypoglycemic Effects of Ethanolic Extract of *Curcuma longa* Rhizome in Alloxan-Induced Diabetic Wistar Rats

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***Abstract:*** *The present study evaluated the antidiabetic activity of the ethanolic extract of Curcuma longa rhizome in alloxan-induced diabetic Wistar rats, using both acute (4 h) and sub-acute (14 days) experimental models. Five groups of rats (n = 5 per group) were treated as follows: normal control, diabetic control, glibenclamide (3 mg/kg), extract (400 mg/kg), and extract (800 mg/kg). In the acute study, the diabetic control group showed a progressive rise in blood glucose from 457.5 ± 23.7 mg/dl post-induction to 518.8 ± 34.4 mg/dl at 4 h, confirming persistent hyperglycemia. Glibenclamide significantly reduced glucose levels from 367.3 ± 20.4 mg/dl to 174.8 ± 6.6 mg/dl, corresponding to a 52.4% fall ($p < 0.001$). The extract produced a dose-dependent reduction, with the 400 mg/kg group showing a 25.1% fall (478.0 ± 53.6 → 357.8 ± 36.9 mg/dl) and the 800 mg/kg group a 29.2% fall (366.8 ± 22.1 to 259.8 ± 10.7 mg/dl) within 4 h. In the sub-acute study, after 14 days, the diabetic control group continued to worsen, reaching 558.3 ± 19.8 mg/dl. In contrast, glibenclamide-treated rats recorded a 66.6% reduction (367.3 ± 20.4 to 122.5 ± 3.4 mg/dl, $p < 0.001$). The extract at 400 mg/kg and 800 mg/kg produced sustained glucose-lowering effects of 60.0% (478.0 ± 53.6 → 191.3 ± 6.6 mg/dl) and 60.5% (366.8 ± 22.1 to 144.8 ± 5.8 mg/dl), respectively, both highly significant compared to the diabetic control ($p < 0.001$). Two-way ANOVA revealed significant main effects of treatment ($F(4,75) = 241.56$, $p < 0.000001$), time ($F(4,75) = 28.04$, $p < 0.000001$), and treatment × time interaction ($F(16,75) = 10.53$, $p < 0.000001$), confirming time- and dose-dependent responses. The extract demonstrated both rapid and sustained antihyperglycemic activity, comparable to glibenclamide in sub-acute treatment. Its effects are likely mediated by preservation of pancreatic β-cell function, enhancement of insulin sensitivity, and attenuation of oxidative stress. These findings support the potential of Curcuma longa as a natural adjunct in diabetes management and justify further mechanistic and clinical investigations.*

***Keywords****: Curcuma longa, Diabetes, Antihyperglycemic, Glibenclamide, Alloxan*

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## 1.0 Introduction

The blood sugar level, also known as glycemia, refers to the concentration of glucose in the blood, which is tightly regulated as part of metabolic homeostasis (Wasserman, 2009). Hyperglycemia occurs when there is excessive glucose in the bloodstream, often due to the body's inability to produce or effectively use insulin (Begum, 2023a,b). Diabetes mellitus is a major cause of persistent hyperglycemia, resulting from either insufficient insulin production in the pancreas or resistance to insulin action in peripheral tissues (Weatherspoon, 2019). If uncontrolled, hyperglycemia can lead to severe and life-threatening complications such as neuropathy, nephropathy, cardiovascular disease, stroke, and heart attack.

Globally, the burden of diabetes is on the rise. The Global Burden of Disease Collaboration Network (2019) reported that 8.5% of adults aged 18 years and older had diabetes in 2019, with 1.5 million deaths attributed to the disease. Notably, 48% of these deaths occurred before the age of 70 years, while raised blood glucose levels accounted for approximately 20% of cardiovascular deaths and 46,000 kidney disease-related deaths. Chronic hyperglycemia also contributes to glucose toxicity, which impairs cellular function and accelerates the development of diabetic complications (Wasserman, 2009).

While synthetic hypoglycemic drugs such as glibenclamide are widely used and effective in controlling blood glucose, they can be costly and are sometimes associated with adverse side effects. This has fueled interest in natural phytochemicals as potential alternatives or complementary therapies for diabetes management. Natural products are often more accessible, affordable, and may present fewer side effects compared to synthetic drugs.

*Curcuma longa* (turmeric) is a rhizomatous herbaceous perennial plant belonging to the Zingiberaceae family (Chan et al., 2009). It is widely cultivated in tropical regions such as India, Southeast Asia, and Indonesia, where it thrives under favorable climatic conditions (Permatananda et al., 2021). Turmeric has a wide range of applications, including as a spice, dye, cosmetic ingredient, ornamental plant, and medicinal herb (Goel et al., 2008). Its medicinal use dates back more than 2000 years (Santana, 2022), with various plant parts—particularly the rhizome—being employed in traditional medicine for diverse therapeutic purposes (Subositi & Wahyono, 2019).

Phytochemical studies have revealed that turmeric is rich in bioactive constituents, notably curcuminoids such as curcumin, demethoxycurcumin, and bisdemethoxycurcumin, with curcumin being the most abundant (Keith, 2020). Curcumin constitutes 60–70% of crude turmeric extracts and is primarily responsible for its health-promoting effects (Fuloria et al., 2022). In addition, turmeric contains sugars, proteins, resins, volatile oils (including turmerone, atlantone, and zingiberene), alkaloids, saponins, tannins, phytic acid, and flavonoids (Fuloria et al., 2022; Nwozo & Effiong, 2019), many of which have potential bioactivity. The pharmacological effects of turmeric are largely attributed to its ethanol extracts, which contain the three principal curcuminoids (Jayaprakasha et al., 2002).

Although studies have documented the antioxidant, anti-inflammatory, and antidiabetic activities of curcumin, there remains a gap in in vivo evidence regarding the dose-dependent hypoglycemic effects of *C. longa* extracts in standardized experimental models of diabetes, especially in comparison with conventional drugs such as glibenclamide under similar conditions.

**Therefore, the aim of this study** was to evaluate the hypoglycemic effect of ethanol extracts of *C. longa* rhizome on alloxan-induced diabetic male Wistar rats and to compare its efficacy with glibenclamide. **The significance of this research** lies in its potential to contribute to the development of affordable, plant-based therapeutic options for diabetes management. This is particularly relevant for populations with limited access to synthetic medications, thus offering a natural and accessible approach to controlling blood glucose levels and preventing diabetes-related complications.

## 2.0 Materials and Methods

### *2.1 Preparation of Plant Material*

Fresh rhizomes of *Curcuma longa* (turmeric) were obtained from Orie-Ugba local market, Umuahia, Abia State, Nigeria. The plant material was authenticated at the Department of Plant Science and Biotechnology, Michael Okpara University of Agriculture, Umudike, and a voucher specimen was deposited in the departmental herbarium for reference. The rhizomes were thoroughly washed under running water to remove adhering soil and debris, sorted, and peeled to remove the outer covering. The cleaned rhizomes were sliced into thin flakes and air-dried at room temperature (28 ± 2 °C) for nine days until a constant weight was achieved. The dried material was milled into fine powder using an electric grinder, stored in an airtight container, and kept in a refrigerator (4 °C) until extraction.

### *2.2 Extraction of the Sample*

The ethanol extract of *C. longa* rhizomes was obtained using the cold maceration technique. A total of 500 g of the powdered rhizome was soaked in 3,000 mL of absolute ethanol and left to stand for three days with intermittent stirring. The mixture was first filtered through a clean muslin cloth and then through Whatman No. 1 filter paper. The filtrate was concentrated to dryness under reduced pressure using a rotary evaporator at 40 °C. The crude extract was transferred into a pre-weighed beaker, and the percentage yield was calculated. The extract was stored in an airtight container at 4 °C until use.

### *2.3 Experimental Animals*

Twenty-five (25) adult male Wistar rats (150–200 g) were obtained from the Animal House of the Department of Zoology and Environmental Biology, Michael Okpara University of Agriculture, Umudike. The animals were housed in well-ventilated metal cages under standard laboratory conditions (12 h light/12 h dark cycle, temperature 25 ± 2 °C, relative humidity 50–60%). They were fed standard pellet diet (Vita Finisher's Mash, Vital Feeds, Nigeria) and had free access to clean drinking water. Animals were allowed to acclimatize for two weeks before the experiment and were fasted for 12 h prior to induction of diabetes. All experimental procedures were conducted in accordance with international guidelines for the care and use of laboratory animals and were approved by the Institutional Animal Ethics Committee (Approval No: [Insert approval number here]).

### *2.4 Induction of Diabetes Mellitus*

Diabetes was induced in overnight-fasted rats by a single intraperitoneal injection of alloxan monohydrate (120 mg/kg body weight) dissolved in freshly prepared normal saline. Blood glucose levels were measured 5–8 days after induction using a single-touch glucometer (Accu-Chek Active, Roche Diagnostics, Germany) from blood samples obtained by tail prick. Rats with fasting blood glucose levels ≥180 mg/dL were considered diabetic and included in the study.

### *2.5 Experimental Design*

The animals were randomly assigned into five groups (n = 5 per group) as follows:

**Group 1 (Normal Control):** Non-diabetic rats administered 0.2 mL of normal saline daily.

**Group 2 (Diabetic Control):** Diabetic rats administered 0.2 mL of normal saline daily.
**Group 3 (Standard Drug):** Diabetic rats treated with glibenclamide (3 mg/kg body weight).
**Group 4 (Low-Dose Extract):** Diabetic rats treated with ethanol extract of *C. longa* (400 mg/kg body weight).
**Group 5 (High-Dose Extract):** Diabetic rats treated with ethanol extract of *C. longa* (800 mg/kg body weight).
All treatments were administered orally once daily for 14 days. At the end of the treatment period, blood glucose levels were measured using the Accu-Chek glucometer from tail-prick blood samples. Body weights of all animals were recorded at baseline and at the end of the experimental period using an electronic balance.

## 3.0 Results and Discussion

### *3.1 Acute Effect of Extract on Blood Glucose Levels of Diabetic Rats*

The acute hypoglycemic effect of the ethanolic extract of *Curcuma longa* rhizome was assessed within four hours of administration in diabetic rats and compared with glibenclamide and control groups. Table 1 presents the mean blood glucose levels across groups at different time intervals.

**Table 1: Acute effect of extract on blood glucose levels of diabetic rats (mg/dl, Mean ± SEM, n=5)**

| Group | Treatment | Pre-induction | Post-induction | 2 h | 4 h | % Fall in Blood Glucose |
|---|---|---|---|---|---|---|
| **1** | Normal control | 83.0 ± 2.5 | 82.3 ± 1.9 | 81.0 ± 2.1 | 79.8 ± 1.8 | – |
| **2** | Diabetic control | 79.8 ± 1.4 | 457.5 ± 23.7 | 468.5 ± 20.9 | 518.8 ± 34.4 | –13.4 |
| **3** | Glibenclamide (3 mg/kg) | 80.3 ± 1.5 | 367.3 ± 20.4 | 248.5 ± 20.8 | 174.8 ± 6.6 | 52.4 |
| **4** | Extract (400 mg/kg) | 80.8 ± 2.1 | 478.0 ± 53.6 | 408.0 ± 50.5 | 357.8 ± 36.9 | 25.1 |
| **5** | Extract (800 mg/kg) | 87.0 ± 3.0 | 366.8 ± 22.1 | 310.0 ± 9.7 | 259.8 ± 10.7 | 29.2 |

**Values are mean ± SEM of 5 rats per group. % fall in blood glucose = [(Post-induction – 4 h) / Post-induction] × 100.**

The diabetic control rats showed a steady rise in blood glucose levels within four hours, confirming the establishment of hyperglycemia. Glibenclamide produced a rapid and significant fall in glucose levels, with a 52.4% reduction at 4 h, validating the experimental model. The extract also demonstrated marked hypoglycemic effects, with the higher dose (800 mg/kg) achieving a greater fall (29.2%) than the lower dose (25.1%). This dose-dependent response agrees with Attamah et al. (2021), who reported a significant blood glucose reduction with methanolic extracts of turmeric in alloxan-induced diabetic rats. Similarly, Kumar (2021) observed hypoglycemic effects of fresh turmeric root juice in diabetic models.
The progressive decline in blood glucose after extract administration indicates that turmeric possesses acute antihyperglycemic properties, likely attributable to curcuminoids. Butler et al. (2019) noted that curcumin is the principal bioactive constituent responsible for many of *Curcuma longa*'s pharmacological effects, including hypoglycemia.

### *3.2 Sub-Acute Effect of Extract on Blood Glucose Levels of Diabetic Rats*

The sub-acute antidiabetic effects of the extract were evaluated over 14 days of repeated administration, with measurements at 2 h, 4 h, 7 days, and 14 days post-treatment. Table 2 summarizes the results.

**Table 2: Sub-acute effect of extract on blood glucose levels of diabetic rats (mg/dl, Mean ± SEM, n=5)**

| Group | Treatment | Post-induction | 2 h | 4 h | 7 days | 14 days | % Fall in Blood Glucose (Day 14) |
|---|---|---|---|---|---|---|---|
| **1** | Normal control | 82.5 ± 1.9 | 81.0 ± 1.9 | 79.8 ± 1.8 | 83.0 ± 2.2 | 83.5 ± 2.5 | – |
| **2** | Diabetic control | 457.5 ± 23.7 | 468.5 ± 20.9 | 518.8 ± 34.4 | 543.3 ± 22.2 | 558.3 ± 19.8 | –22.0 |
| **3** | Glibenclamide (3 mg/kg) | 367.3 ± 20.4 | 248.5 ± 20.8 | 174.8 ± 6.6 | 136.0 ± 5.2 | 122.5 ± 3.4 | 66.6 |
| **4** | Extract (400 mg/kg) | 478.0 ± 53.6 | 408.0 ± 50.5 | 357.8 ± 36.9 | 211.3 ± 8.2 | 191.3 ± 6.6 | 60.0 |
| **5** | Extract (800 mg/kg) | 366.8 ± 22.1 | 310.0 ± 9.7 | 259.8 ± 10.7 | 172.0 ± 9.6 | 144.8 ± 5.8 | 60.5 |

**Values are mean ± SEM of 5 rats per group. % fall in blood glucose = [(Post-induction – Day 14) / Post-induction] × 100.**

In the sub-acute study, untreated diabetic controls maintained high glucose levels throughout, while Glibenclamide progressively reduced glucose to 122.5 mg/dl by Day 14 (66.6% fall). The extract groups also showed significant reductions, with both doses producing ~60% decreases after 14 days. Notably, the 800 mg/kg dose achieved a slightly greater reduction than 400 mg/kg, though the difference was marginal, suggesting a plateau effect.

These results align with Alsulaim et al. (2024), who demonstrated curcumin's sustained glucose-lowering effect in streptozotocin-induced diabetic rats. Furthermore, Zhang et al. (2013) and Pivari et al. (2019) reported that curcumin improves insulin sensitivity, enhances β-cell function, and reduces inflammation, which could explain the progressive reductions observed in this study. Rashid and Sil (2015) also highlighted curcumin's protective role against oxidative stress in pancreatic β-cells, supporting its long-term antihyperglycemic effect.

### 3.3 Statistical Analysis

A two-way ANOVA was performed to assess the effects of treatment (Group), time, and their interaction on blood glucose levels.

**Table 3: Two-way ANOVA results for the effects of Treatment, Time, and their Interaction on blood glucose levels**

| Source of Variation | Sum of Squares | df | F-value | p-value |
|---|---|---|---|---|
| **Treatment (Group)** | 1,998,817.06 | 4 | 241.56 | $5.13 \times 10^{-42}$ |
| **Time** | 232,045.06 | 4 | 28.04 | $2.99 \times 10^{-14}$ |
| **Group × Time** | 348,647.24 | 16 | 10.53 | $2.27 \times 10^{-13}$ |
| **Residual** | 155,148.75 | 75 | — | — |

The analysis revealed highly significant effects of treatment ($F(4,75) = 241.56$, $p < 0.000001$) and time ($F(4,75) = 28.04$, $p < 0.000001$) on glucose levels. Importantly, the treatment × time interaction was also significant ($F(16,75) = 10.53$, $p < 0.000001$), confirming that treatment effects varied with duration.

This statistical evidence supports the experimental findings: Glibenclamide exerted a rapid hypoglycemic effect within hours, while turmeric extract produced a gradual but sustained effect that became statistically comparable by Day 14. The significant interaction suggests that turmeric may act via progressive restoration of β-cell function, enhancement of insulin sensitivity, or modulation of hepatic glucose metabolism, mechanisms supported by previous reports (Zhang et al., 2013; Rashid & Sil, 2015).

## 4.0 Conclusion

The present study demonstrates that the ethanolic extract of *Curcuma longa* rhizome exhibits both acute and sub-acute antihyperglycemic effects in streptozotocin-induced diabetic rats. The extract significantly reduced blood glucose levels in a dose-dependent manner within 4 hours of administration and produced a sustained glucose-lowering effect over 14 days that was comparable to glibenclamide. These findings provide strong pharmacological evidence supporting the antidiabetic potential of *C. longa*.

Mechanistically, the hypoglycemic effects observed may be attributed to multiple complementary pathways. Curcumin, the principal bioactive compound of turmeric, has been reported to protect pancreatic β-cells from oxidative stress–induced damage, thereby preserving insulin secretory capacity (Rashid & Sil, 2015). It may also enhance insulin sensitivity by improving glucose uptake in peripheral tissues and reducing systemic inflammation (Zhang et al., 2013; Pivari et al., 2019). Furthermore, its potent antioxidant and anti-inflammatory activities (Santana, 2022) likely mitigate hyperglycemia-driven oxidative stress, a major factor in the pathogenesis of diabetes and its complications. These multimodal mechanisms suggest that the extract not only lowers glucose acutely but may also modify disease progression by protecting β-cell integrity and restoring metabolic balance.

Translationally, these results highlight the promise of *Curcuma longa* as a natural, cost-effective adjunct or alternative therapy for diabetes management. The sustained glucose-lowering activity observed with repeated administration indicates that the extract could be valuable for long-term glycemic control, particularly in resource-limited settings where access to conventional drugs may be restricted. Further studies, including phytochemical standardization, mechanistic investigations, and ultimately clinical trials, are warranted to establish its efficacy, safety, and integration into therapeutic protocols for diabetes mellitus.

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**Declaration**

**Consent for publication**

Not applicable

**Availability of data**

Data shall be made available on demand.

**Competing nterests**

The authors declared no conflict of interest

**Ethical Consideration**

All animal experiments were conducted in strict compliance with internationally accepted guidelines for the care and use of laboratory animals. Ethical approval was obtained from the Institutional Animal Ethics Committee of Michael Okpara University of Agriculture, Umudike (Approval No: [insert number]). Efforts were made to minimize animal suffering, and only the minimum number of animals required to achieve statistical validity was used.

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**Authors' Contribution**

FO designed the study, supervised the experiments, and prepared the first draft of the manuscript. GGO contributed to plant authentication, extraction processes, and literature review. PROE assisted with animal handling, data collection, and statistical analysis. CIN contributed to biochemical assay design, interpretation of results, and critical revision of the manuscript. All authors reviewed, edited, and approved the final version of the work.