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## Hypoglycemic and Hypolipidemic Effects of *Tithonia diversifolia* Aqueous Root Extract in Western Diet-Fed Wistar Albino Rats

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### Abstract

This study investigated the hypoglycemic and hypolipidemic effects of *Tithonia diversifolia* aqueous root extract in Wistar albino rats fed a Western diet, comparing its efficacy to standard drugs. Hyperglycemia and dyslipidemia are major contributors to metabolic and cardiovascular diseases, often managed with synthetic drugs that may have adverse effects. While *Tithonia diversifolia* has been traditionally used to manage these conditions, its efficacy and potential as an alternative therapy remain insufficiently explored. Thirty-five male Wistar albino rats (180–200g) were divided into seven groups (n=5). G1 received a normal diet, while G2 was fed a Western diet throughout. G3 and G4 were treated with atorvastatin (10 mg/kg) and glibenclamide (0.5 mg/kg), respectively, after 35 days on a Western diet. G5 and G6 received *Tithonia diversifolia* extract at 200 mg/kg and 400 mg/kg for seven days. G7 was reverted to a normal diet after 28 days on a Western diet. Fasting blood glucose was measured weekly, and lipid profiles were analysed at the study's conclusion. Western diet-fed groups showed a significant increase in fasting blood glucose (p=0.000). Extract-treated groups (G5, G6) exhibited a significant reduction in fasting glucose and cholesterol (p=0.000), with G6 (1.2 mmol/L) achieving results comparable to atorvastatin (2.0 mmol/L). Triglycerides significantly decreased (p=0.036) in G5, G6, and G3, while HDL-C levels remained unchanged. *Tithonia diversifolia* extract demonstrated hypoglycemic and hypolipidemic effects similar to standard drugs. Further studies should focus on isolating its bioactive compounds, optimising dosage, and evaluating long-term safety for therapeutic applications.

**Key words:** Hypoglycemia, hypolipidemia, rats, *Tithonia diversifolia*, Western diet.



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## INTRODUCTION

Chronic diseases remain a major global health burden, largely driven by metabolic disorders such as hyperglycemia and hyperlipidemia. Hyperglycemia refers to elevated blood glucose levels, while hyperlipidemia denotes an increase in blood lipid concentrations. These conditions are strongly associated with serious complications, including cardiovascular diseases, kidney failure, and cancer, making them critical public health concerns. (DeFronzo et al., 2015).

The global rise in type 2 diabetes exemplifies the growing impact of metabolic disorders, driven by a convergence of modern risk factors such as sedentary lifestyles, dietary transitions, rapid urbanisation, and aging populations. As these lifestyle patterns become more prevalent, they lead to unhealthy eating habits, reduced physical activity, and metabolic imbalances that accelerate the incidence of diabetes and its associated complications (Nadhiya et al., 2024).

Despite notable progress in pharmaceutical development, current therapies for managing hyperglycemia and hyperlipidemia face persistent challenges. These include high treatment costs, limited availability in low-resource settings, and adverse side effects (Widiarti et al., 2024). In response, there is increasing interest in alternative and complementary therapies, particularly those derived from medicinal plants traditionally used across cultures for managing metabolic disorders (Jugran et al., 2021).

One such plant is *Tithonia diversifolia*, commonly known as the Mexican sunflower, which has drawn scientific attention for its potential antidiabetic properties. While previous research has reported that the leaves of this plant may exacerbate hyperglycemia and induce insulin resistance (Istikharah et al., 2023), the effects of the root extract remain underexplored.

This study investigates the hypoglycemic effects of *Tithonia diversifolia* aqueous root extract in Wistar albino rats fed a Western diet. The Western diet is characterised by high levels of saturated fats, refined sugars such as fructose, and cholesterol. It mirrors the nutritional composition of typical fast food consumption and is known to induce obesity, insulin resistance, hyperglycemia, and lipid abnormalities, closely resembling type 2 diabetes in humans (Cordain et al.,

2005; Nguyen et al., 2017; Asgharpour et al., 2016; Franco et al., 2022).

Although some studies on the leaves of *Tithonia diversifolia* have reported increased blood glucose and insulin resistance (Istikharah et al., 2023), emerging evidence indicates that the root extract may have different bioactive properties. For example, Adewole et al. (2020) demonstrated that the root extract has antioxidant and liver-protective properties. Phytochemical screening has revealed the presence of several beneficial compounds in the roots, including flavonoids, alkaloids, tannins, saponins, phenols, anthocyanins, and coumarins (Okuna et al., 2024). These findings support the potential of the root extract as a therapeutic agent. By examining whether *Tithonia diversifolia* root extract can mitigate the metabolic disruptions caused by a Western diet, this study aims to build a scientific foundation for the safe and effective use of traditional herbal remedies in managing diabetes and related conditions, thereby integrating ethnobotanical knowledge with biomedical research (Kokwaro, 2009).

## LITERATURE REVIEW

The global prevalence of hyperglycemia and hyperlipidemia continues to rise, posing significant threats to healthcare systems worldwide. It is estimated that by 2045, the number of adults living with diabetes will surpass 700 million, with a significant proportion residing in low- and middle-income countries (Hossain et al., 2024).

In sub-Saharan Africa, including Kenya, these metabolic disorders have become leading causes of mortality among adults over the age of 30. The region faces a unique challenge where urbanisation and lifestyle transitions are accelerating the occurrence of chronic diseases while infectious diseases remain a persistent threat. This dual burden places immense pressure on healthcare systems, necessitating urgent interventions to manage metabolic conditions effectively (Arokiasamy et al., 2021).

One of the major challenges in managing hyperglycemia and hyperlipidemia is the cost of conventional treatments. Many of the available drugs require lifelong administration, making them expensive and inaccessible to many patients, especially in resource-limited settings. Additionally, these medications often have side effects,

such as gastrointestinal disturbances, liver toxicity, and increased risk of cardiovascular events, which deter patient adherence (Shaito et al., 2020). As a result, there has been a growing shift toward traditional herbal remedies, which are perceived as more affordable, natural, and potentially safer alternatives.

In addition to economic barriers, adverse side effects further complicate the management of these conditions. Common side effects of antidiabetic and lipid-lowering drugs include gastrointestinal disturbances, muscle pain, liver toxicity, weight gain, and in some cases, increased risk of cardiovascular events (Shaito et al., 2020; Gerstein et al., 2019). These adverse effects not only reduce patients' quality of life but also contribute to poor medication adherence, ultimately compromising treatment outcomes. Moreover, polypharmacy is often necessary, especially in patients with comorbid conditions such as hypertension, obesity, or cardiovascular disease. This increases the risk of drug-drug interactions and further complicates long-term disease management (Inzucchi et al., 2015). Additionally, the current pharmacological approach largely focuses on symptom control rather than disease reversal or cure, requiring continuous use without addressing underlying pathophysiological mechanisms.

In Kenya, *Tithonia diversifolia* is widely used by the Luo community as a traditional remedy for managing hyperglycemia and hyperlipidemia. Although its therapeutic use is supported by ethnobotanical records (Kokwaro, 2009), comprehensive scientific validation remains limited. Existing studies have primarily investigated crude leaf extracts in vitro or in animal models, often with small sample sizes, short treatment durations, and non-standardised methodologies (Oyewole & Oladejo, 2012; Andrade-Cetto & Heinrich, 2005). Moreover, findings across studies are sometimes contradictory due to variations in the plant part used, extraction techniques, and dosage, making it difficult to establish consistent therapeutic outcomes (Muganga et al., 2010).

Additionally, few studies have explored the safety profile of *T. diversifolia* root extracts, which may possess a different phytochemical composition and potentially higher toxicity. This raises concerns about the risk of adverse effects on vital organs such as the liver and kidneys when used without proper clinical oversight

(Passoni et al., 2013; Jimoh et al., 2011). These limitations underscore the need for rigorous, controlled in vivo investigations to evaluate both efficacy and safety. This study, therefore, addressed these knowledge gaps by assessing the hypoglycemic and hypolipidemic effects of aqueous root extracts of *Tithonia diversifolia* using standardised experimental procedures.

With hyperglycemia and hyperlipidemia contributing significantly to the burden of non-communicable diseases in low- and middle-income countries, especially in sub-Saharan Africa, there is an urgent need for affordable and accessible treatment options. The World Health Organization (2021) notes a sharp rise in diabetes and related disorders in these regions, driven by lifestyle changes, urbanisation, and limited healthcare access. Conventional treatments are often costly and place financial strain on low-income households (Atun et al., 2017).

In this context, scientifically validated herbal remedies like *Tithonia diversifolia* offer promising complementary or alternative therapies. Traditionally used by the Luo community in Kenya to manage blood sugar and lipid levels, *T. diversifolia* leaf extract has shown hypoglycemic, hypolipidemic, antioxidant, and anti-inflammatory effects in preliminary studies (Suherman et al., 2022; Jimoh et al., 2011; Oyewole & Oladejo, 2012). However, most studies have focused on leaf extracts, with limited data on root preparations and long-term safety. This study therefore seeks to investigate the efficacy and safety of *T. diversifolia* root extracts, integrating traditional knowledge with scientific research to support cost-effective interventions for managing metabolic disorders.

### METHODOLOGY

A laboratory experimental design was employed using thirty-five healthy male Wistar albino rats (*Rattus norvegicus*), aged two months and weighing 180–200 g. The rats were randomly assigned into seven groups of five and housed under standard conditions ( $25 \pm 2^\circ\text{C}$ , 12-hour light/dark cycle) with free access to water and standard chow. After one week of acclimatisation, the animals were fed a Western diet formulated to induce hyperglycemia and hyperlipidemia, characterised by high levels of fat, fructose, and cholesterol (Table 2), in line with protocols by Nguyen et al. (2017) and Franco et al. (2022).

Fresh roots of *Tithonia diversifolia* were collected from Kamagambo sub-location, Migori County, and authenticated by a taxonomist. A voucher specimen (M.U.H/MD/0020/21) was deposited at the university herbarium. The roots were shade-dried, powdered, and 100 g of the powder was extracted in 1000 ml distilled water for 12 hours with continuous agitation. The extract was filtered and concentrated using a rotary evaporator at 50°C, then air-dried to yield a final extract with 19.4% w/w yield.

The rats were administered orally with daily doses of 200 mg/kg or 400 mg/kg of the extract, 10 mg/kg atorvastatin, or 0.5 mg/kg glibenclamide. Dosages were calculated based on group average weights using Olukunle's (2014) formula (Table 1). Fasting blood glucose was measured weekly. At day 35, blood was collected via cardiac puncture under anaesthesia, and serum analysed for lipid profiles using a Biobase BK-200 analyser. Data were analysed using SPSS v20. One-way ANOVA, LSD, and Duncan's tests were used, with significance at  $p \leq 0.05$ . Ethical approval was granted by the University of Eastern Africa, Baraton (UEAB/REC/16/03/2020).

**Table 1: Daily Mass of Plant Extract and Drugs Given To Rats in each Group**

| Groups | Average Mass | Dosage                        | Daily Mass of plant extract/drugs administered |
|--------|--------------|-------------------------------|------------------------------------------------|
| G3     | 191.86 g     | 10mg/kg bw of Atorvastatin    | 29.56 mg                                       |
| G4     | 191.76 g     | 0.5 mg/kg bw of Glibenclamide | 14.88 mg                                       |
| G5     | 192.06 g     | 200mg/kg bw of extract        | 38.4mg                                         |
| G6     | 191.34 g     | 400mg/kg bw of extract        | 76.54 mg                                       |

**Table 2. Comparison between the Composition of Rodent Chow and the Western Diet**

| Component       | % composition in the Western diet (Nguyen et al., 2017) |
|-----------------|---------------------------------------------------------|
| Polysaccharides | 43                                                      |
| Animal fat      | 21                                                      |
| Protein         | 19                                                      |
| Kcal energy     | 40                                                      |
| Cholesterol     | 0.15                                                    |

## RESULTS AND DISCUSSION

### Findings

#### Body Weights

Weekly weight measurements showed a steady increase for all groups until week four. At week five, results indicated a significant weight reduction in groups treated with 10 mg/kg atorvastatin (G3), 0.5 mg/kg glibenclamide (G4), 200 mg/kg (G5), and 400 mg/kg

*Tithonia diversifolia* extract (G6), as well as the group that switched to normal chow (G7), compared to the normal (G1) and negative control (G2) groups. Post hoc LSD analysis confirmed significant weight differences, establishing that treatment groups experienced notable weight reductions ( $p=0.000$ ) against the negative control ( $p=0.00$ ).

**Table 3: Effects of Treatments on Mean Weights of Western Diet-Fed Wistar Albino Rats within the Five Weeks**

| Week | Normal Control (G1) | negative Control (G2) | 10mg/kg b.w Atorvastatin (G3) | 0.5mg/kg b.w Glibenclamide (G4) | 200mg/kg b.w extract (G5) | 400mg/kg b.w extract (G6) |
|------|---------------------|-----------------------|-------------------------------|---------------------------------|---------------------------|---------------------------|
| 1    | 187.52±0.1          | 186.34±0.3            | 187.74±0.5                    | 187.74±0.4                      | 188.14±0.5                | 187.14±0.6                |
| 2    | 189.46±0.5          | 188.72±0.2            | 188.94±0.1                    | 189.25±0.3                      | 189.20±0.1                | 189.18±0.5                |
| 3    | 190.22±0.2          | 191.38±0.3            | 190.12±0.4                    | 190.46±0.7                      | 190.38±0.6                | 190.64±0.3                |
| 4    | 191.20±0.4          | 194.84±0.3            | 191.86±0.3                    | 191.76±0.5                      | 192.06±0.3                | 191.34±0.3                |
| 5    | 192.46±0.6          | 197.12±0.5            | 189.52±0.2                    | 191.38±0.3                      | 191.94±0.1                | 190.7±0.03                |

**Fasting Blood Glucose**

Fasting blood glucose levels were measured weekly for five weeks. Groups treated with 10 mg/kg atorvastatin (G3), 0.5 mg/kg glibenclamide (G4), and both 200 mg/kg (G5) and 400 mg/kg (G6) *Tithonia diversifolia* root extract showed a decrease in blood glucose levels by week five, contrasting with the normal control (G1), negative control (G2), and the group that switched back to rodent chow (G7), which exhibited an increase.

Post hoc LSD analysis revealed a significant decrease in fasting blood glucose levels for rats given 400 mg/kg *Tithonia diversifolia* extract (G6) (p=0.029) compared to the normal control (G1). Using the negative control (G2) as the baseline, significant reductions were observed in groups treated with atorvastatin, glibenclamide, and both doses of *Tithonia diversifolia* extract (p=0.000), while the diet-reverted group (G7) showed an insignificant decrease (p=0.849). This highlights the potential efficacy of *Tithonia diversifolia* extract in lowering blood glucose levels in diet-induced hyperglycemic rats.

**Table 4. Effects of Aqueous Root Extract of *T. diversifolia* on Blood Sugar in Western Diet-Fed Wistar Albino Rats**

| Treatments                     | Fasting Blood glucose in mmol/l |           |           |           |           |
|--------------------------------|---------------------------------|-----------|-----------|-----------|-----------|
|                                | Week 1                          | Week 2    | Week 3    | Week 4    | Week 5    |
| Normal Control (G1)            | 4.06±0.01                       | 4.14±0.01 | 4.18±0.02 | 4.20±0.02 | 4.32±0.04 |
| Negative Control (G2)          | 4.00±0.02                       | 4.22±0.01 | 4.36±0.03 | 4.52±0.02 | 4.82±0.03 |
| 10mg/kg bw Atorvastatin (G3)   | 3.90±0.01                       | 4.26±0.01 | 4.27±0.02 | 4.28±0.01 | 4.18±0.01 |
| 0.5mg/kg bw Glibenclamide (G4) | 3.94±0.03                       | 4.04±0.02 | 4.12±0.02 | 4.22±0.05 | 4.12±0.02 |
| 200mg/kg bw extract (G5)       | 3.94±0.01                       | 4.00±0.03 | 4.12±0.02 | 4.24±0.02 | 4.18±0.02 |
| 400mg/kg bw extract (G6)       | 3.94±0.01                       | 4.18±0.02 | 4.24±0.01 | 4.25±0.04 | 4.08±0.01 |
| Rodent chow (G7)               | 4.02±0.02                       | 4.04±0.04 | 4.16±0.02 | 4.62±0.01 | 4.84±0.01 |

**Lipid Profile**

**Serum Cholesterol**

The post hoc LSD analysis revealed that, compared to the normal control group (G1), the rats treated with 10 mg/kg atorvastatin (G3) and 200 mg/kg *Tithonia diversifolia* root aqueous extract (G5) showed an insignificant decrease in serum cholesterol levels (p=0.538), whereas the rats given 400 mg/kg *Tithonia diversifolia* root aqueous extract (G6) had a significant decrease (p=0.004). Conversely, the rats fed a Western diet for

four weeks and switched to a normal diet in the fifth week (G7) exhibited a significant increase in cholesterol levels (p=0.000). When the negative control (G2) was used as a baseline, significant cholesterol level decreases were noted in the groups receiving 10 mg/kg atorvastatin (G3), 200 mg/kg (G5), and 400 mg/kg (G6) *Tithonia diversifolia* extracts (p=0.000), while the G7 group's cholesterol levels matched the control. Duncan's test for homogeneity showed consistent mean cholesterol levels among groups G3, G4, G5, and G1, as well as G2 and

G7, but distinguished these from the G6 group and the rest. The treatment groups formed three distinct subsets, with no significant differences within the subsets but clear distinctions between them.

## High-Density Lipoprotein (HDL-C)

Rats administered 0.5 mg/kg glibenclamide (G4) and 400 mg/kg *Tithonia diversifolia* root aqueous extract (G6) showed a reduction in mean HDL-C levels, while those given 200 mg/kg of the extract (G5) and those switched from a Western diet to rodent chow (G7) exhibited an increase. When compared to the negative control (G2), rats receiving 10 mg/kg atorvastatin (G3), 0.5 mg/kg glibenclamide (G4), and 400 mg/kg extract (G6) displayed decreased HDL-C levels, but those receiving 200 mg/kg extract (G5) and the diet-switched rats (G7) showed no significant change. Post hoc LSD analysis, using both normal (G1) and negative controls (G2) as baselines, indicated no significant differences in HDL-C levels among the treatment groups. Duncan's test further confirmed uniformity in HDL-C mean values across all groups.

## Serum Triglycerides (TG)

Rats administered 10 mg/kg atorvastatin (G3), 0.5 mg/kg glibenclamide (G4), 200 mg/kg *Tithonia diversifolia* aqueous root extract (G5), and those subjected to a Western diet for four weeks followed by rodent chow (G7) showed increased serum triglyceride levels compared to the normal control (G1). Conversely, rats given 400 mg/kg *Tithonia diversifolia* extract (G6) had decreased triglyceride levels. Compared to the negative control (G2), all treatment groups except G7 exhibited decreased triglyceride levels. Post hoc LSD analysis, using G1 as the reference, revealed a significant decrease in triglyceride levels for the group given 0.5 mg/kg glibenclamide ( $p=0.034$ ) and a significant increase for G7 ( $p=0.001$ ), while other groups showed no significant differences. Using G2 as the reference, significant decreases were noted in the groups administered 10 mg/kg atorvastatin ( $p=0.036$ ), 200 mg/kg extract ( $p=0.036$ ), and 400 mg/kg extract ( $p=0.000$ ).

Duncan's test categorised the treatment groups into four subsets based on their mean triglyceride (TG) levels, indicating statistical similarities and differences. Subset 1 includes the normal control (G1), 10 mg/kg atorvastatin (G3), 200 mg/kg (G5), and 400 mg/kg (G6) *Tithonia diversifolia* extracts, all showing similar TG levels.

Subset 2, containing G1, G3, G5, and 0.5 mg/kg glibenclamide (G4), also exhibits similar TG levels but differs from Subset 1, highlighting distinct TG levels for G4 compared to G6. Subset 3 comprises the negative control (G2), G3, G5, and G4, with similar TG levels, differing significantly from Subset 1, indicating differences between G2 and G6. Subset 4 includes G4, G2, and the group subjected to a Western diet then switched to rodent chow (G7), showing similar TG levels within the subset but significantly different from Subsets 1, 2, and 3.

## Discussion

The study revealed that a four-week Western diet significantly elevated fasting blood glucose levels in Wistar rats, indicating the diet's ability to induce hyperglycemia. However, a notable reduction in blood glucose levels was observed when the rats were treated with 200 mg/kg *Tithonia diversifolia* aqueous root extract for seven days, an effect comparable to glibenclamide at 0.5 mg/kg. These results align with prior studies by Chunudom et al. (2020) showing the hypoglycemic potential of *Tithonia diversifolia*, suggesting the presence of effective compounds like coumarin, anthocyanins, and carbohydrates, though further research is needed to fully understand their roles.

Further analysis demonstrated that administering 400 mg/kg of the aqueous root extract significantly reduced fasting blood glucose levels, corroborating previous research findings by Olukunle (2014) and Mabou et al. (2018). This dosage achieved substantial hypoglycemic effects within a shorter administration period compared to earlier studies that used leaf extracts for longer durations. The hypoglycemic activity of the root extract could be attributed to specific bioactive compounds, including alkaloids, tannins, and anthocyanins, which enhance insulin sensitivity, inhibit gluconeogenesis, and activate AMPK (Shen et al., 2012), thereby improving glycemic control.

In terms of lipid profiles, the Western diet caused a significant increase in serum triglycerides and cholesterol levels. However, administering 200 mg/kg of the aqueous root extract for seven days significantly reduced these levels, comparable to the effects of atorvastatin. Increasing the dose to 400 mg/kg further decreased serum cholesterol and triglycerides, consistent with previous studies by Nguepi et al. (2021) using different

dosages and durations. The hypolipidemic effects are likely due to phytochemicals in the root extract, such as saponins, terpenoids, and phenolic compounds, which influence lipid absorption and metabolism (Marrelli et al., 2016). These findings suggest that *Tithonia diversifolia*'s aqueous root extract is effective in reducing serum cholesterol and triglyceride levels, although further studies are needed to confirm these results and determine the optimal administration period.

#### CONCLUSION AND RECOMMENDATION

**Conclusion:** This study demonstrates that *Tithonia diversifolia* aqueous root extract significantly reduces fasting blood glucose levels and improves lipid profiles in Wistar albino rats fed a Western diet. These findings

support the traditional use of this plant by the Luo community in Kenya for managing hyperglycemia and hyperlipidemia. The observed hypoglycemic and hypolipidemic effects are likely due to the bioactive compounds present in the extract, which may enhance insulin sensitivity, inhibit gluconeogenesis, and affect lipid metabolism. Therefore, *Tithonia diversifolia* holds promise as a natural therapeutic agent for managing diabetes and associated lipid disorders.

**Recommendations:** Through further research, clinical trials, and thoughtful integration into healthcare, this traditional medicinal plant could significantly impact managing and preventing diabetes and related conditions.

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