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Antidiabetic and hepatoprotective effects of *Cymbopogon citratus* (lemongrass) oil in streptozotocin-nicotinamide-induced diabetic male rats: Biochemical and histopathological evaluation

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Abstract. *Nurudeen QO, Abdulkadir S, Jamiu SM, Abah MA, Ugwah EJ. 2025. Antidiabetic and hepatoprotective effects of* Cymbopogon citratus *(lemongrass) oil in streptozotocin-nicotinamide-induced diabetic male rats: Biochemical and histopathological evaluation. Cell Biol Dev 9: 64-70.* This study investigated the antidiabetic and hepatoprotective effects of *Cymbopogon citratus* (lemongrass) essential oil in male rats with streptozotocin–nicotinamide-induced diabetes. Forty-two rats were randomly assigned to seven groups (n=6): non-diabetic control, diabetic control, diabetic + metformin (150 mg/kg), and diabetic + lemongrass oil at doses of 50, 100, and 200 mg/kg. Diabetes was induced by a single intraperitoneal injection of streptozotocin (60 mg/kg) 15 minutes after nicotinamide (120 mg/kg), followed by 28 days of oral treatment. Parameters assessed included fasting blood glucose, body weight, and key biochemical markers—superoxide dismutase (SOD), catalase (CAT), glutathione (GSH), and alanine aminotransferase (ALT)—along with histological evaluation of liver tissue. Treatment with lemongrass oil significantly lowered fasting blood glucose and enhanced antioxidant enzyme activity in diabetic rats, with the 100 mg/kg dose showing effects comparable to metformin. Histopathological analysis confirmed improvements in hepatic structure and reduced degenerative changes. These findings indicate that *C. citratus* essential oil exhibits notable antidiabetic and hepatoprotective effects, likely mediated through its antioxidant properties, and may serve as a promising adjunct in diabetes therapy.

Keywords: Antioxidant enzymes, *Cymbopogon citratus*, diabetes mellitus, liver histology, streptozotocin-nicotinamide

INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from both impaired insulin action and defects in insulin secretion (American Diabetes Association 2021). The prevalence of diabetes worldwide has increased substantially, with an estimated 537 million people affected in 2021, and this number is predicted to reach 643 million by 2030 (Sun et al. 2022). The most common form, type 2 diabetes mellitus (T2DM), is often associated with insulin resistance, oxidative stress, and progressive β-cell dysfunction (Szkudelski 2012; Rena et al. 2017). Despite the availability of several pharmacological agents such as metformin, sulfonylureas, and insulin analogues, the long-term management of diabetes remains challenging due to adverse side effects, economic burden, and inconsistent patient responsiveness (Patel et al. 2012). This has prompted the exploration of alternative therapeutic options, particularly plant-derived treatments with antioxidant and antihyperglycemic properties.

At the same time, oxidative stress has been increasingly recognized as a key contributor to the complications and pathogenesis of diabetes mellitus (Evans et al. 2002; Maritim et al. 2003). Hyperglycemia-induced overproduction of reactive oxygen species (ROS) contributes to the impairment of cellular functions, lipid peroxidation, and organ damage, particularly in the pancreas and liver (Matsui et al. 2006). The liver, as a central organ in glucose metabolism, is frequently affected in diabetic conditions, as evidenced by elevated liver enzymes, oxidative injury, and structural abnormalities (Hamdy and Taha 2009). Therefore, agents that can mitigate oxidative stress and preserve hepatic architecture are of great interest in diabetes research, especially those that also address glucose regulation.

In recent years, essential oils from medicinal plants have gained attention for their bioactive properties, including antioxidant, anti-inflammatory, and antidiabetic effects (Bakkali et al. 2008; Eidi and Eidi 2009). Among these, *Cymbopogon citratus* (commonly known as lemongrass) is an aromatic plant widely used across Asia, Africa, and South America in traditional medicine. The essential oil of *C. citratus* contains major constituents such as citral, geraniol, myrcene, and limonene, which have been reported to possess significant pharmacological effects, including free radical scavenging and enzyme-modulating activity (Adeneye et al. 2006; Shah et al. 2011).

Preliminary studies have shown that *C. citratus* extracts may reduce blood glucose levels and improve lipid profiles in diabetic animal models (Oyedeji et al. 2009; Falode et al. 2023). However, the majority of these studies have focused on aqueous or ethanolic extracts, while the therapeutic efficacy of the volatile-rich essential oil remains underexplored. Moreover, studies that integrate both biochemical and histopathological evaluations to assess the hepatoprotective role of *C. citratus* oil in diabetic models are still lacking. Given the central role of the liver in glucose regulation and its sensitivity to oxidative damage, it is crucial to assess the dual-function effects—antidiabetic and hepatoprotective—of such natural agents.

To establish a reliable model for studying diabetes and evaluating therapeutic agents, the combination of streptozotocin (STZ) and nicotinamide (NA) has been widely adopted (Srinivasan et al. 2005). STZ selectively destroys pancreatic β-cells, while NA partially protects these cells, mimicking the pathophysiology of type 2 diabetes. This model is considered effective for evaluating both insulin sensitivity and β-cell preservation under therapeutic intervention. The use of this model, in conjunction with biochemical and histological analyses, provides a robust platform for testing the potential of botanical-based antidiabetic agents.

The present study aimed to evaluate the synergistic antidiabetic and hepatoprotective properties of *C. citratus* essential oil in male Wistar rats with STZ-NA-induced diabetes. Specifically, this research assessed fasting blood glucose levels, antioxidant enzyme activities (SOD, CAT, GSH), liver enzyme levels (ALT), and histological changes in hepatic tissue following oral administration of lemongrass oil. By examining both biochemical and histological parameters, this study provides a comprehensive assessment of the therapeutic potential of *C. citratus* oil, and supports its consideration as a complementary and functional treatment in the management of diabetes mellitus.

MATERIALS AND METHODS

Experimental animals

Forty-two healthy adult male Wistar rats (150-200 g) were collected from the Animal House of the Faculty of Basic Medical Sciences, University of Ilorin, Ilorin, Kwara State, Nigeria. The animals were sheltered in polypropylene cages under standard laboratory conditions (temperature 22-25°C, 12 h light/dark cycle) with unrestricted access to standard rat chow and clean water. All procedures were conducted in conformity with the National Institutes of Health (NIH) Guide for the Care and Use of Laboratory Animals (2011) and in conformity with institutional guidelines for the care and use of laboratory animals.

Induction of diabetes

Type 2 diabetes mellitus was induced by a single intraperitoneal injection of streptozotocin (STZ, 60 mg/kg body weight), freshly dissolved in 0.1 M cold citrate buffer (pH 4.5), 15 minutes after an intraperitoneal injection of nicotinamide (NA, 120 mg/kg) in normal saline. After 72 hours, blood glucose levels were measured using a glucometer (Accu-Chek®, Roche, Germany). Then, rats with fasting blood glucose levels greater than 200 mg/dL (>200 mg/dL) were considered diabetic and included in the experiment.

Experimental design

The diabetic rats were randomly assigned into seven groups (n = 6 per group), as outlined below: (i) Group 1: Non-diabetic control (received distilled water only), (ii) Group 2: Diabetic control (STZ–NA-induced, no treatment), (iii) Group 3: Diabetic + metformin (150 mg/kg/day), (iv) Group 4: Diabetic + *C. citratus* oil (50 mg/kg/day), (v) Group 5: Diabetic + *C. citratus* oil (100 mg/kg/day), (vi) Group 6: Diabetic + *C. citratus* oil (200 mg/kg/day), (vii) Group 7: Non-diabetic + *C. citratus* oil (100 mg/kg/day). All treatments were administered orally by gavage once daily for 28 consecutive days.

Group 7 was included to assess the tolerability and baseline physiological effects of *C. citratus* essential oil in normoglycemic (non-diabetic) animals. A higher dose (200 mg/kg) was not applied to this group to reduce animal usage and to avoid the potential confounding effects of supraphysiological exposure in healthy subjects. The 100 mg/kg dose was selected for this purpose based on prior reports demonstrating both its pharmacological effectiveness and safety in rodent models (Falode et al. 2023). This dose thus served as a suitable reference for evaluating safety outcomes in non-diabetic conditions.

Preparation of *Cymbopogon citratus* oil

The essential oil of *C. citratus* was obtained through steam distillation of fresh leaves collected from a local farm and authenticated at the Faculty of Natural and Life Sciences, University of Ilorin. The oil was then stored in amber glass bottles at 4°C until use. Doses of 50, 100, and 200 mg/kg body weight were prepared in 1% Tween-80 as the vehicle and administered by oral gavage. Although the GC-MS profiling of the oil used in this study was not conducted, previous studies have reported that lemongrass essential oil from West Africa typically contains citral (as a mixture of neral and geranial), geraniol, and limonene as dominant constituents (Oyedeji et al. 2009; Shah et al. 2011). These components are believed to contribute to the observed bioactivities.

Measurement of blood glucose and body weight

Fasting blood glucose levels were analyzed on days 0, 7, 14, 21, and 28 using tail vein blood and a digital glucometer. Body weights were also recorded weekly. Glucose measurements were taken after an of 12 hours overnight fasting.

Biochemical analysis

At the end of the treatment period, rats were fasted again overnight and euthanized under light anesthesia. Then, the blood samples were collected via cardiac puncture into plain tubes. To obtain the serum, the samples were allowed to clot and centrifuged for 10 minutes at 3,000 rpm. The following biochemical parameters were assayed

using commercial diagnostic kits (Randox Laboratories, UK): Alanine aminotransferase (ALT) - liver function marker, Superoxide dismutase (SOD) - antioxidant enzyme, Catalase (CAT) - an antioxidant enzyme, Reduced glutathione (GSH) - an oxidative stress indicator. All assays were performed following the manufacturers' protocols, and an UV-visible spectrophotometer read absorbance.

Histological analysis

Liver tissues were excised, washed with normal saline, and fixed in 10% neutral-buffered formalin. The tissues were processed, embedded in paraffin wax, and sectioned at 5 µm thickness. Next, those sections were stained with hematoxylin and eosin (H&E) and analyzed using a light microscope for structural changes. Photomicrographs were captured to document histopathological findings.

Statistical analysis

Data were expressed analysis as the mean ± standard deviation (SD), and the statistical comparisons among groups were performed by a one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for multiple comparisons. Effect sizes (η^2) and F-values were calculated for each test, and exact p-values were reported where relevant. Confidence intervals (95% CI) were computed for key outcome variables. Then, a p-value of less than 0.05 ($p<0.05$) was regarded statistically significant. Next, all analyses were conducted using SPSS version 25.0 (IBM Corp., USA).

RESULTS AND DISCUSSION

Induction of diabetes and baseline glucose levels

Diabetes mellitus was successfully induced in experimental rats using the streptozotocin–nicotinamide (STZ–NA) protocol, as confirmed by significant elevations in fasting blood glucose (FBG) levels within 72 hours post-injection. Rats with FBG values exceeding 200 mg/dL were regarded as diabetic and included in the study. Baseline FBG levels before treatment (Day 0) are shown in Table 1. Diabetic groups (Groups 2 to 6) exhibited hyper-glycemia compared to the non-diabetic control (Group 1), confirming successful induction of diabetes. The initial blood glucose levels ranged from 210 to 267 mg/dL across diabetic groups, with no statistically significant differences among them, indicating uniform baseline hyperglycemia.

Effect of treatments on fasting blood glucose and body weight

Oral administration of *C. citratus* oil resulted in reduced fasting blood glucose (FBG) levels significantly over the 28-day treatment period in diabetic rats. As shown in Figure 1, all treatment groups (Groups 3-6) demonstrated progressive decreases in FBG compared to the diabetic control (Group 2), which maintained elevated glucose levels throughout the study. The group receiving 100 mg/kg of lemongrass oil (Group 5) exhibited the greatest glycemic reduction by Day 28, with efficacy comparable to that of the metformin-treated group (Group 3). The analyses, using one-way ANOVA followed by Tukey's post hoc test, showed statistically significant differences ($p<0.05$) in fasting blood glucose levels between the treated diabetic groups and the untreated diabetic control group from Day 14 onward.

Table 2 summarizes body weight changes. Diabetic control rats (Group 2) showed a gradual decrease in body weight over 28 days, a common feature of uncontrolled diabetes. In contrast, treatment with metformin or lemongrass oil (Groups 3-6) helped preserve or slightly increase body weight, suggesting improved metabolic stability. Notably, the 100 mg/kg dose of *C. citratus* oil (Group 5) was most effective in maintaining body weight close to baseline levels.

Effect on antioxidant enzyme activities (SOD, CAT, GSH)

Oxidative stress markers were significantly altered in diabetic rats, as shown in Table 3. In the diabetic control group (Group 2), levels of superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) were significantly decreased compared to the non-diabetic control (Group 1), indicating increased oxidative stress due to hyperglycemia.

Figure 2 illustrates the observed changes in serum antioxidant enzyme activities across all groups. Group 5 (100 mg/kg) showed a near-complete restoration of SOD and GSH levels, while Group 3 (metformin) exhibited the highest CAT activity among treated groups. Treatment with *C. citratus* oil led to dose-dependent improvements in antioxidant enzyme activities. Among the treated groups, Group 5 (100 mg/kg lemongrass oil) showed the most significant restoration of SOD, CAT, and GSH levels, closely approximating the effects of metformin (Group 3). Group 6 (200 mg/kg) also improved antioxidant markers, though less effectively than the 100 mg/kg dose. These findings support the hypothesis that lemongrass oil exerts its antidiabetic effects, at least in part, by enhancing endogenous antioxidant defenses.

Table 1. Fasting blood glucose levels before treatment (Day 0)

Group	Description	FBG (mg/dL)
1	Non-diabetic control	93.6±4.8a
2	Diabetic control	235.4±11.2b
3	Diabetic + Metformin	232.1±12.5b
4	Diabetic + lemongrass (50 mg/kg)	243.6±9.3b
5	Diabetic + lemongrass (100 mg/kg)	267.2±14.0b
6	Diabetic + lemongrass (200 mg/kg)	252.3±13.4b
7	Non-diabetic + Lemongrass	91.5±5.1a

Note: Values are expressed as mean ± SD (n=6 per group). Superscripts indicate no significant difference among diabetic groups (Groups 2–6), but a significant difference exists between diabetic and non-diabetic ($p<0.05$; ANOVA+Tukey post hoc)

Table 2. Body weight changes over the 28-day treatment period

Group	Description	Day 0 (g)	Day 28 (g)	% Change
1	Non-diabetic control	185.2±5.3	204.8±4.7	+10.6%
2	Diabetic control	182.4±6.0	162.7±5.9	−10.8%
3	Diabetic + Metformin	183.3±4.2	192.6±4.1	+5.1%
4	Diabetic + Lemongrass oil (50 mg/kg)	184.0±5.6	187.2±5.3	+1.7%
5	Diabetic + Lemongrass oil (100 mg/kg)	181.5±6.2	191.3±5.7	+5.4%
6	Diabetic + Lemongrass oil (200 mg/kg)	183.7±4.8	189.4±5.0	+3.1%
7	Non-diabetic + Lemongrass oil	184.9±5.5	203.5±5.2	+10.0%

Note: Those values are expressed as mean ± SD (n=6)

Table 3. Effect of treatments on antioxidant enzyme activities in serum (day 28)

Group	Description	SOD (U/mL)	CAT (U/mL)	GSH (µmol/mL)
1	Non-diabetic control	9.45±0.36a	8.23±0.29a	7.31±0.32a
2	Diabetic control	4.27±0.28b	3.89±0.21b	3.12±0.18b
3	Diabetic + Metformin	8.32±0.34a	7.44±0.30a	6.87±0.25a
4	Diabetic + lemongrass (50 mg/kg)	6.78±0.31c	5.65±0.26c	5.03±0.19c
5	Diabetic + lemongrass (100 mg/kg)	8.16±0.29a	7.21±0.22a	6.75±0.24a
6	Diabetic + lemongrass (200 mg/kg)	7.36±0.35ac	6.49±0.24ac	5.98±0.27ac
7	Non-diabetic + Lemongrass	9.28±0.33a	8.11±0.26a	7.20±0.28a

Note: Values are expressed as mean ± SD (n=6 per group). Different superscript letters suggest statistically significant differences (p<0.05) based on one-way ANOVA followed by Tukey's post hoc test

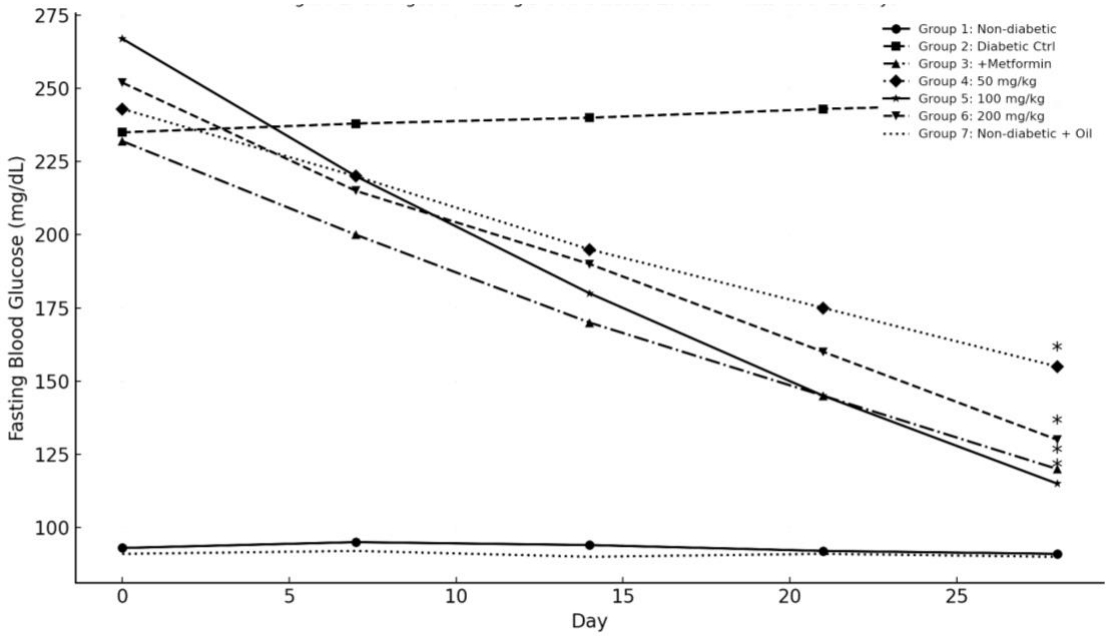

Figure 1. Changes in fasting blood glucose levels in rats over 28 days. Data were analyzed using one-way ANOVA followed by Tukey's post hoc test. Those values are expressed as mean ± SD (n=6 per group). Asterisks (*) indicate significant differences from diabetic control (Group 2), *p<0.05

Effect on liver function marker (ALT)

Serum alanine aminotransferase (ALT) levels, a marker of hepatocellular injury, were markedly elevated in the diabetic control group (Group 2) compared to the non-diabetic control group (Group 1), indicating liver damage associated with hyperglycemia and oxidative stress (Table 4).

Treatment with *C. citratus* oil significantly reduced ALT levels in diabetic rats in a dose-dependent method. The most pronounced reduction was observed in Group 5 (100 mg/kg), which showed ALT values statistically comparable to those of the metformin-treated group (Group 3). Group 4 (50 mg/kg) and Group 6 (200 mg/kg) also showed moderate improvements, suggesting a hepatoprotective effect of lemongrass oil.

Figure 3 presents these group-wise differences in serum ALT levels. Group 5 (100 mg/kg) exhibited ALT values close to those of the non-diabetic control, indicating effective hepatoprotection, whereas the diabetic control group showed the highest elevation. These findings suggest that *C. citratus* oil may confer protection against diabetes-induced hepatic injury, possibly via its antioxidant components.

Histological observations of liver tissue

Histological analysis of liver sections revealed marked differences in tissue architecture among the experimental groups (Figure 4). The non-diabetic control group (Group 1) exhibited normal hepatic histoarchitecture, with well-preserved hepatocytes arranged in radial plates around the central vein, intact sinusoids, and no signs of cellular damage.

In contrast, the diabetic control group (Group 2) showed severe hepatocellular degeneration, including cytoplasmic vacuolation, sinusoidal congestion, pyknotic nuclei, and inflammatory infiltration. These changes indicate substantial liver injury resulting from hyperglycemia-induced oxidative stress. Treatment with metformin (Group 3) and *C. citratus* oil (Groups 4-6) alleviated these pathological features to varying degrees. The 100 mg/kg lemongrass oil group (Group 5) showed the most substantial histological improvement, with reduced vacuolation and nearly normal hepatocyte appearance, comparable to metformin-treated rats. Groups 4 (50 mg/kg) and 6 (200 mg/kg) exhibited partial restoration of hepatic structure, though some mild degeneration remained.

The non-diabetic + lemongrass group (Group 7) maintained normal histological features, suggesting the oil is non-toxic at the administered dose. Overall, these findings support the hepatoprotective role of *C. citratus* oil in diabetes-induced hepatic injury.

Discussion

The present study demonstrated that *Cymbopogon citratus* (lemongrass) oral administration of essential oil exerted significant antidiabetic and hepatoprotective effects in streptozotocin-nicotinamide (STZ-NA) induced diabetic rats. These effects were evident from the reduction in fasting blood glucose levels, the improvement in antioxidant enzyme activities, the normalization of liver enzyme ALT, and the restoration of hepatic histoarchitecture. Among the tested doses, 100 mg/kg showed the most consistent and significant improvements, comparable to the standard antidiabetic drug, metformin.

The ability of lemongrass oil to reduce hyperglycemia may be attributed to its phytoconstituents, such as citral, geraniol, and limonene, which have been reported to enhance insulin secretion, improve peripheral glucose uptake, and inhibit gluconeogenesis (Shah et al. 2011; Falode et al. 2023). Citral, in particular, has been shown to upregulate PPAR-γ expression and modulate GLUT4 translocation in insulin-sensitive tissues (Chen et al. 2019), suggesting a plausible mechanism for insulin sensitization.

Table 4. Effect of treatments on serum ALT levels (U/L)

Group	Description	ALT (U/L)
1	Non-diabetic control	42.3±3.1a
2	Diabetic control	86.7±4.5b
3	Diabetic + Metformin	48.2±2.8a
4	Diabetic + Lemongrass oil (50 mg/kg)	61.7±3.6c
5	Diabetic + Lemongrass oil (100 mg/kg)	49.5±2.9a
6	Diabetic + Lemongrass oil (200 mg/kg)	55.3±3.2ac
7	Non-diabetic + Lemongrass oil	43.5±2.6a

Note: Values are expressed as mean ± SD (n=6). Different superscripts suggest statistically significant differences between groups (p<0.05; one-way ANOVA followed by Tukey's post hoc test)

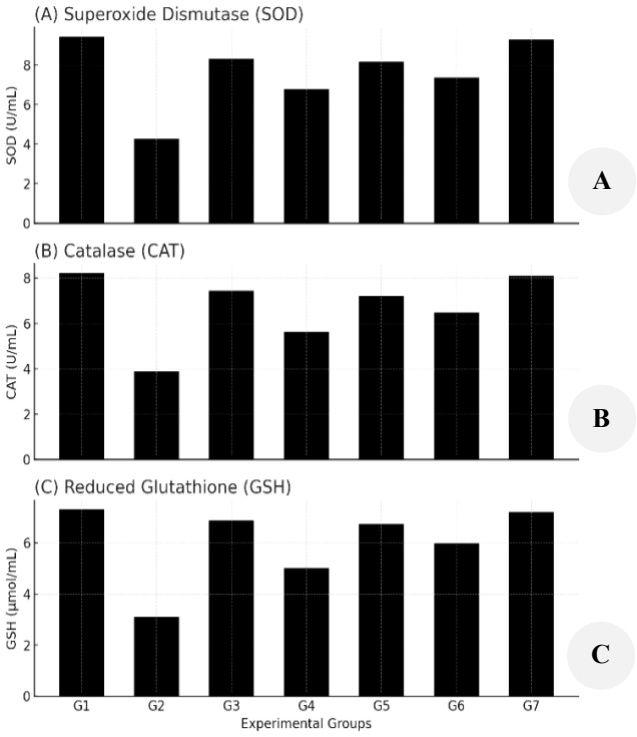

Figure 2. Antioxidant enzyme activities in serum on day 28. A. Superoxide Dismutase (SOD), B. Catalase (CAT), C. Reduced Glutathione (GSH). Note: Bars represent mean ± SD (n=6). A one-way ANOVA followed by Tukey's post hoc test was used to compare the groups. Bars with different letters suggest significant differences (p<0.05)

These findings align with previous reports using the STZ-NA model to evaluate plant-based interventions. For instance, Zamanian et al. (2024) demonstrated that *Curcuma longa* extract significantly lowered fasting glucose and improved liver histology in diabetic rats via suppression of NF-κB-mediated inflammatory pathways. Similarly, Eidi and Eidi (2009) reported that garlic essential oil enhanced antioxidant defense and restored hepatic function through modulation of SOD and GSH levels. The current results confirm and expand on these findings by showing that lemongrass oil can exert comparable hepatoprotective effects, possibly through the synergistic action of its terpenoid components.

The STZ-NA model is considered a mild and reproducible model for type 2 diabetes, characterized by partial β-cell dysfunction and insulin resistance (Srinivasan et al. 2005). In this context, the observed improvement in antioxidant enzyme levels (SOD, CAT, GSH) suggests that *C. citratus* oil may attenuate oxidative stress, a key driver of diabetic complications. Oxidative stress has been implicated in mitochondrial dysfunction, β-cell apoptosis, and hepatic inflammation (Rains and Jain 2011). Therefore, the normalization of these markers may reflect both direct free radical scavenging and indirect effects on redox-sensitive signaling pathways.

At the same time, the exact molecular mechanisms remain to be elucidated; it is plausible that citral and related terpenoids modulate signaling cascades such as the Nrf2/ARE pathway, which regulates the transcription of endogenous antioxidant enzymes (Ma 2013; Rabelo et al. 2015). This regulatory axis has been shown to be activated by several monoterpenes and may underlie the observed restoration of SOD, CAT, and GSH levels in this study.

Furthermore, lemongrass oil may influence AMPK activation, a central energy sensor that promotes glucose uptake and lipid metabolism (Hardie et al. 2012). These proposed mechanisms merit further investigation using transcriptomic or proteomic approaches. One strength of this study lies in its combined evaluation of biochemical and histopathological endpoints, providing a more holistic view of organ-level effects. However, certain limitations should be acknowledged. The study did not measure plasma insulin levels or conduct oral glucose tolerance tests, which could provide deeper insight into β-cell function and systemic glucose handling. Additionally, the absence of GC-MS profiling of the essential oil limits the ability to correlate specific compounds with observed bioactivities. Future studies should aim to isolate individual constituents and validate their actions in vitro and in vivo.

The findings suggest that lemongrass essential oil, particularly at 100 mg/kg, holds promise as a natural therapeutic agent for diabetes management, offering dual benefits on glycemic control and liver protection. These outcomes justify further exploration, including clinical translation and mechanistic studies that target the molecular pathways of insulin action and oxidative stress. Moreover, the observed safety of *C. citratus* oil in non-diabetic rats supports its therapeutic potential. However, further studies are important to assess long-term toxicity, pharmacokinetics, and interactions with standard antidiabetic drugs. Previous findings suggest low acute toxicity, but data on chronic and reproductive effects are lacking. Translational development would also require standardization of active compounds, optimized formulations, and clinical validation.

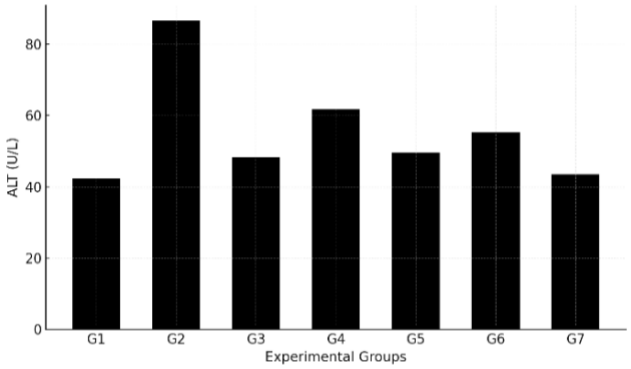

Figure 3. Serum ALT levels in rats on day 28, and the values were expressed as mean ± SD (n=6 per group). Group-wise differences were analyzed using one-way ANOVA followed by Tukey's post hoc test. Bars with different superscript letters suggest statistically significant differences ($p<0.05$)

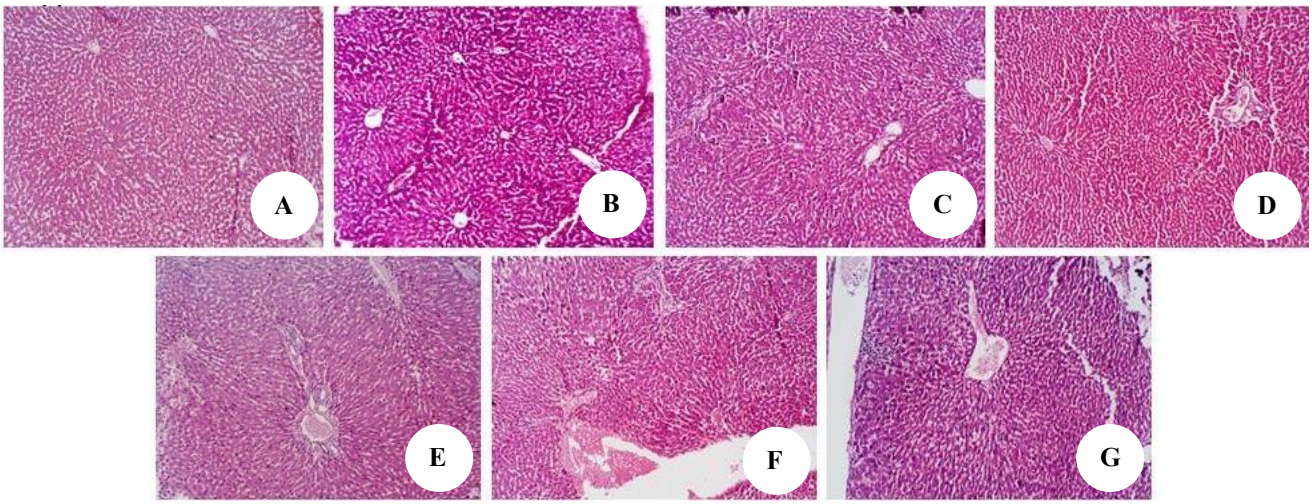

Figure 4. Representative photomicrographs of the liver sections from experimental groups (H&E staining, 400×). A. Group 1: Normal hepatic cords and central vein. B. Group 2: Degeneration, inflammation, congestion. C. Group 3: Near-normal architecture. D. Group 4: Mild cytoplasmic changes. E. Group 5: Well-preserved structure. F. Group 6: Partial recovery. G. Group 7: Normal histology

This study has certain limitations. Only male rats were used, which may overlook sex-specific metabolic responses. The 28-day duration limits insight into long-term efficacy or adverse effects. Important metabolic parameters, such as insulin levels, lipid profiles, and glucose tolerance, were not assessed, which constrains mechanistic interpretation. Additionally, the essential oil was not chemically profiled, which makes it difficult to attribute effects to specific constituents. Lastly, while the STZ-NA model reflects aspects of type 2 diabetes, it does not fully capture the complexity of human disease. Future studies should address these gaps.

In conclusion, this study demonstrated that oral administration of *C. citratus* essential oil, particularly at a dose of 100 mg/kg, significantly improved glycemic control, enhanced antioxidant enzyme activities, and protected liver tissue in streptozotocin-nicotinamide-induced diabetic rats. The comparable efficacy to metformin, along with observed histological improvements and normalization of liver enzyme markers, suggests that *C. citratus* oil possesses both antidiabetic and hepatoprotective properties. These findings support its potential use as a complementary therapeutic agent in the management of type 2 diabetes. However, further studies are needed to validate its clinical relevance and elucidate its molecular mechanisms.

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