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Dose-Dependent Hematological Changes Induced by Cymbopogon flexuosus Aqueous Extract in Wistar Rats

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ABSTRACT

This study used male Wistar rats to evaluate the effects of subchronic oral administration of Cymbopogon flexuosus aqueous extract on hematological parameters, including packed cell volume (PCV), hemoglobin concentration (Hb), white blood cell count (WBC), and platelet count (PLT). A total of 25 healthy male rats (150–180 g) were randomly divided into five groups (n = 5): a control group (distilled water, 5 mL/kg), a Dulaglutide group (1.5 mg/kg), and three groups receiving C. flexuosus extract at 50, 100, and 200 mg/kg. All treatments were given orally for 28 days. Blood samples were collected at the end of the study and analyzed using an automated hematology analyzer. Data were expressed as mean ± SE and analyzed using the Student's t-test (SPSS v24, $p < 0.05$).Results showed that Dulaglutide significantly increased WBC (10.20 ± 0.68 vs. 7.54 ± 0.67 × 10^3/µL, $p = 0.036$) and PLT (771.0 ± 26.49 vs. 607.4 ± 43.76 × 10^3/µL, $p = 0.013$), while it decreased PCV (38.92 ± 1.48 vs. 42.66 ± 0.59%, $p = 0.047$) and Hb (13.90 ± 0.69 vs. 16.14 ± 0.15 g/dL, $p = 0.013$). Administration of C. flexuosus extract at 50 and 100 mg/kg did not cause significant hematological changes. However, at 200 mg/kg, the extract significantly reduced WBC (5.70 ± 0.31 vs. 7.54 ± 0.67 × 10^3/µL, $p = 0.038$) and Hb (13.94 ± 0.77 vs. 16.14 ± 0.15 g/dL, $p = 0.022$), while PCV and PLT remained unaffected. These findings indicate that the aqueous extract of C. flexuosus is hematologically safe at doses below 100 mg/kg, but higher doses (200 mg/kg) may induce mild adverse effects, including behavioral changes. This suggests a narrow safety margin at elevated exposure levels.

KEYWORDS: Cymbopogon flexuosus, Dulaglutide, Platelet, Wistar rat, Oral administration.

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INTRODUCTION

Diabetes remains a major health issue. In 2018, about **34.2 million Americans** had diabetes, and **88 million** had prediabetes. The **CDC** estimated **$237 billion** in healthcare costs. Around **25%** of diabetics develop **foot ulcers or lesions**, which take up about **one-third of total diabetes care costs** due to complications. Chronic **high blood sugar** causes poor circulation, **vascular damage**, and **neuropathy**, leading to delayed wound healing. Diabetic wounds often show **swelling**, **poor blood vessel growth**, **slow fibroblast activity**, and **reduced keratinocyte migration**, resulting in **infections** and **chronic wounds** [1] **Lemongrass (Cymbopogon flexus)** is widely grown for its **essential oil (LEO)**, rich in **bioactive compounds** such as **citral, geraniol, citronellal, citronellol, germacrene-D, and elemol**. These give LEO **antibacterial, antifungal, antiviral, antioxidant, and anticancer** properties. LEO is used in **pharmaceuticals, cosmetics, and food preservation**. Some LEO components show **anticancer potential in vitro**, but human studies are limited—more research is needed.Cymbopogon species (lemongrass, citronella, palmarosa, etc.) are known for producing **essential oils** used in **medicines and repellents**. Lemongrass oil mainly contains **monoterpenoids**, especially **citral**, which is valuable for making **vitamin A** and **ionone**. These plants also show **anthelmintic, anti-inflammatory, analgesic, antibacterial, and mosquito-repellent** effects, and have potential in **Alzheimer's treatment** and **other health uses [2-4]**. Blood indicators such as **packed cell volume (PCV)**, **hemoglobin (Hb)**, **white blood cell count (WBC)**, and **platelet count (PLT)** are important signs of normal or abnormal body function. Changes in these values can signal problems like **anemia, infection, inflammation, or bone marrow damage**. Because **aqueous plant extracts** contain concentrated active compounds, they may influence blood formation or cause blood toxicity if taken in high doses. In this study, **Dulaglutide** was used as a reference drug to compare the effects of different doses of **Cymbopogon flexuosus (lemongrass) aqueous extract** on blood parameters in **male Wistar rats**. The goal was to better understand how lemongrass extract affects blood health, determine its **safe dosage levels**, and provide **scientific data** to support its traditional and clinical use [5].

Materials and Methods

Twenty-five (25) both sex Wistar rats in good health, weighing between 150 and 180 grams, were used. They were housed in clean wood shavings that were changed every 48 hours in plastic cages with stainless-steel wire tops and adequate ventilation for two weeks after their arrival. The rats were fed a typical commercial pellet diet and given unlimited access to clean water.

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Experimental Procedure

A total of **twenty-five (n = 25) male Wistar rats** were randomly assigned into **five experimental groups** (n = 5 per group). The sample size was determined according to established animal research guidelines to ensure adequate **statistical power** for detecting biologically meaningful differences among treatment groups [6-8].

The treatment groups were organized as follows:

- **Group 1 (Control):** Received **distilled water (5 mL/kg)**.
- **Group 2 (Dulaglutide):** Received **1.5 milligram/kilogram body weight of Dulaglutide**.
- **Group 3:** Received **50 milligram/kilogram of *Cymbopogon flexuosus* aqueous extract**.
- **Group 4:** Received **100 milligram/kilogram of *Cymbopogon flexuosus* aqueous extract**.
- **Group 5:** Received **200 milligram/kilogram of *Cymbopogon flexuosus* aqueous extract**.

All treatments were **administered orally once daily for 28 consecutive days** using an **intragastric cannula**.

Serum Analysis

At the end of the 28-day treatment period, the animals were fasted overnight and subsequently anesthetized using chloroform vapor in a desiccator. Blood samples were collected via cardiac puncture using sterile syringes. Approximately 4 mL of blood was obtained from each rat: 2 mL was transferred into EDTA tubes for hematological analysis, and the remaining 2 mL was placed into plain tubes for serum separation. The hematological parameters assessed included packed cell volume (PCV), hemoglobin concentration (Hb), white blood cell count (WBC), and platelet count (PLT).

Statistical Analysis

Data were analyzed using GraphPad Prism version 0.5 and expressed as mean ± standard error (SE). Statistical differences between the treatment and control groups were evaluated using the independent Student's t-test, with significance set at $p < 0.05$.

RESULTS

Throughout the 28-day experimental period, all animals tolerated the oral administration of Dulaglutide and Cymbopogon flexuosus extract without any mortality or observable behavioral abnormalities. There were no significant differences in food or water intake between treated and control groups. Physical examinations revealed normal activity levels, grooming behavior, and general appearance in all groups, indicating stable systemic health during the study.

Hematological Results

The effects of *Cymbopogon flexuosus* extract on key hematological parameters—packed cell volume (PCV), hemoglobin concentration (Hb), white blood cell count (WBC), and platelet count (PLT)—are summarized in Tables 1–4. Statistical comparisons between each treatment group and the control group were performed using the independent Student's t-test.

Table 1: Evaluation of Hematological Changes Induced by Dulaglutide (1.5 milligram/kilogram) in Male Wistar Rats

Hematic Parameter	Control Group	Dulaglutide	T-Score	*p*-Score
PCV (%)	42.66 ± 0.59	38.92 ± 1.48	2.39	0.047
Hb (g/dL)	16.14 ± 0.15	13.90 ± 0.69	2.97	0.013
WBC (×10³/µL)	7.54 ± 0.67	10.20 ± 0.68	2.57	0.036
PLT (×10³/µL)	607.40 ± 43.76	771.00 ± 26.49	3.22	0.013

Table 2: Impact of *Cymbopogon flexuosus* (50 milligram/kilogram) on Hematological Parameters Relative to Control

Hematic Parameter	Control Group	*Cymbopogon flexuosus* 50 milligram/killogram	T-Score	*p*-Score
PCV (%)	42.66 ± 0.59	41.90 ± 1.76	0.41	0.693
Hb (g/dL)	16.14 ± 0.15	15.82 ± 0.69	0.45	0.661
WBC (×10³/µL)	7.54 ± 0.67	7.32 ± 0.69	0.19	0.855
PLT (×10³/µL)	607.40 ± 43.76	614.60 ± 30.69	0.13	0.896

Table 3: Comparative Analysis of Hematological Indices in Control and *Cymbopogon flexuosus* (100 milligram/kilogram)–Treated Rats

Hematic Parameter	Control Group	*Cymbopogon flexuosus* 100 miligram/kilogram	T-Score	*p*-Score
PCV (%)	42.66 ± 0.59	42.46 ± 0.36	0.29	0.778
Hb (g/dL)	16.14 ± 0.15	15.32 ± 0.44	1.65	0.116
WBC (×10³/µL)	7.54 ± 0.67	7.16 ± 1.19	0.28	0.788
PLT (×10³/µL)	607.40 ± 43.76	509.40 ± 38.01	1.68	0.129

Table 4: Effect of *Cymbopogon flexuosus* (200 milligram/kilogram) on Hematological Parameters in Comparison with Control Rats

Hematic Parameter	Control Group	*Cymbopogon flexuosus* 200 miligram/killogram	T-Score	*p*-Score
PCV (%)	42.66 ± 0.59	39.10 ± 1.59	0.45	0.669
Hb (g/dL)	16.14 ± 0.15	13.94 ± 0.77	2.82	0.022
WBC (×10³/µL)	7.54 ± 0.67	5.70 ± 0.31	2.50	0.038
PLT (×10³/µL)	607.40 ± 43.76	633.80 ± 39.65	0.44	0.667

DISCUSSION

Independent t-tests showed that *Cymbopogon flexuosus* at 50 and 100 **milligram/kilogram** did not significantly alter any hematological parameters ($p > 0.05$). However, the 200 **milligram/kilogram** dose caused significant decreases in Hb ($p = 0.022$) and WBC ($p = 0.038$). Dulaglutide (1.5 **milligram/kilogram**) significantly affected all indices ($p < 0.05$), indicating pharmacological modulation of hematological function.

A dose-related decline was observed in PCV and Hb, reaching significance only at 200 **milligram/kilogram**. WBC showed a biphasic trend—minor changes at lower doses and a marked reduction at the highest dose. PLT values remained stable, with a slight, non-significant rise at 200 **milligram/kilogram**.After 28 days of oral administration, *Cymbopogon flexuosus* aqueous extract produced dose-dependent hematological responses in male Wistar rats. Lower doses (50–100 **milligram/kilogram**) caused no significant changes in PCV, Hb, WBC, or PLT, suggesting no adverse effects on erythropoiesis, leukopoiesis, or thrombopoiesis and confirming a good hematological safety profile. At a higher dose (200 **milligram/kilogram**), however, reductions in Hb and WBC suggest mild anemia and leukopenia, likely due to oxidative stress or bone marrow suppression. High concentrations of bioactive compounds in *C. flexuosus* may promote lipid peroxidation or membrane damage, impairing red and white blood cell integrity.The stable platelet and PCV levels across all doses indicate minimal effects on thrombopoiesis and overall hematological homeostasis. These findings align with previous studies showing that low phytochemical doses support antioxidant adaptation, while higher doses may induce toxicity.Overall, *C. flexuosus* extract demonstrates a narrow safety margin, being safe at low to moderate levels but potentially harmful at high concentrations [9-12].

CONCLUSION

Subchronic oral exposure to *Cymbopogon flexuosus* aqueous extract produced dose-dependent hematological changes in male Wistar rats. Doses of ≤100 **milligram/kilogram** were hematologically safe, while 200 **milligram/kilogram** caused significant decreases in Hb and WBC, suggesting possible anemia and immunosuppression. These results establish a preliminary safety threshold for *C. flexuosus* and caution against high-dose orprolonged use. Further studies involving cytokine assays, oxidative stress markers, and histopathology are recommended to clarify the mechanisms underlying these hematological effects.

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