

Immunomodulatory Effects of Ethanolic Root Extract of *Gmelina arborea* in Wistar Rats

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Abstract

➤ Background:

Gmelina arborea is traditionally used for managing inflammatory and immune-related disorders, yet scientific validation of its immunomodulatory activity remains limited. This study evaluated the immunomodulatory effects of ethanolic root extract of *Gmelina arborea* in Wistar rats.

➤ Methods:

A controlled experimental design was used involving five groups of Wistar rats. Group 1 served as the negative control. Group 2 received 20 mg/kg levamisole as the positive control. Groups 3–5 received 20 mg/kg levamisole followed by 50, 100, and 150 mg/kg of *Gmelina arborea* extract for 28 days, with levamisole administered 12 hours before the extract. Inflammatory markers, leukocyte indices, platelet parameters, and spleen histology were assessed.

➤ Results:

Levamisole significantly increased IL-6 and ESR, confirming immunosuppression, while co-administration of *Gmelina arborea* produced dose-dependent amelioration. The 150 mg/kg group showed IL-6 and CRP levels comparable to the negative control and restored leukocyte and granulocyte balance. Platelet indices revealed improved hematopoietic stability and white pulp architecture.

➤ Conclusion:

Gmelina arborea demonstrated notable immunomodulatory potential by regulating cytokine expression and supporting leukocyte function. These findings provide scientific support for its traditional use and highlight its promise as a natural immunomodulatory agent.

Keywords: *Gmelina arborea*, Immunomodulatory, Wistar Rats

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I. INTRODUCTION

Gmelina arborea Roxb (commonly known as Gambhari or white teak) is a fast-growing deciduous tree belonging to the Lamiaceae (or Verbenaceae) family. It has a long history in traditional medicine, especially in Ayurveda and folk practices, where its roots, bark, leaves, and fruit are used to treat a wide range of ailments such as fever, ulcers, anemia, piles, and urinary disorders^{1,2}. Phytochemical investigations have revealed that *Gmelina arborea* contains bioactive compounds including flavonoids, lignans, coumarins, iridoid glycosides, terpenes, and Pharmacologically, the plant has shown antioxidant, anti-microbial, diuretic, anti-ulcer, cardioprotective, anti-diabetic, and immunomodulatory activities in various in vitro and in vivo studies^{2,3}.

Despite its widespread ethnomedicinal use, especially for conditions where immune function may be compromised or dysregulated, there remains a need for rigorous experimental evaluation of *G. arborea*'s immunomodulatory potential. Previous studies (e.g., using methanolic extracts) have indicated that the root extract can enhance humoral and cell-mediated immunity in immunosuppressed animals. Understanding how *G. arborea* modulates key immune parameters, such as leukocyte populations, cytokine production, and inflammatory markers, could validate its traditional applications and support its development as a natural immune-support agent^{4,5,6}.

However, current knowledge has several gaps. For one, many earlier immunology studies used non-ethanolic extracts

(e.g., methanolic), leaving uncertainties about the effects of the ethanolic root extract⁷. Moreover, data on how *G. arborea* affects specific immune biomarkers (e.g., IL-6, CRP, ESR) and platelet indices in controlled animal models are limited. Without such information, the mechanistic basis of its immunomodulatory effects remains poorly understood, limiting its clinical translation. The aim of this research is to investigate the immunomodulatory effects of ethanolic root extract of *Gmelina arborea* in Wistar rats.

II. MATERIALS AND METHODS

A. Drugs and Chemicals

Ethanol, Levamisole, Formalin, Paraffin, Hemotoxylin and Eosin.

All drugs and chemicals used for this research was of analytical grade was obtained from Zayo Sigma Chemical Limited Jos.

➤ Plant:

Fresh roots of *Gmelina arborea* was collected from Melina tree in Kodape, Karu Local government Area, Nasarawa State, Nigeria. The specimen was identified and authenticated by Dr. Tayo Famojuro, Department of Pharmacognosy, Bingham University. A voucher specimen (DPHBHU 0068) has been deposited in the department’s herbarium.



Fig 1 *Gmelina arborea*

➤ Animals:

25 young adult Wistar rats (150-170g) was purchased grouped in to five groups of five in each and housed in the Animal Care Unit Bingham University, Karu and left to acclimatized for seven days.

• Animal Grouping

- ✓ Group 1: served as an experimental negative control, the rats in this groups was fed with animal feed and distilled water only.
- ✓ Group 2: served as an experimental positive control, the rats was fed with animal feed, water; 20mg/kg body weight Levamisole (a standard immunologic drug) administered.
- ✓ Group 3: served as test group; 50 mg/kg body weight ethanol-root extract *Gmelina arborea* was administered.
- ✓ Group 4: served as test group; 100 mg/kg body weight ethanol-root extract *Gmelina arborea* was administered.
- ✓ Group 5: served as test group; 150 mg/kg body weight ethanol-root extract *Gmelina arborea* was administered.

All treatment was via the oral route and last for a period of 28 days.

B. Statistical Analysis

The data are expressed as mean ± SEM (standard error of mean). One-way Analysis of Variance (ANOVA) were used for the analysis using SPSS was used to compare the mean difference between and within groups and a P-value (P<0.05) was considered statistically significant.

➤ Sample collection:

Sample collection was done by Cardiac puncture post-anesthesia. Automated Hematology analyzer was used for Full Blood count.

Erythrocyte Sedementation Rate: Westergren method uses 3.8% sodium citrate as an anticoagulant. ESR measured at 1 hour because maximum settling occurs in the first hour, making it the standard reference time. ELISA kits were used for rat CRP and IL-6inflammatory markers (Dean *et al.* (2019).

III. RESULTS

Table 1 Effects of Ethanolic Root Extract of *Gmelina arborea* on Wister Rats Inflammatory Marker

Groups	CRP (mg/L)	IL-6 (pg/mL)	ESR (mm)
Control	0.60 ± 0.07	1.48 ± 0.01 ^b	4.00 ± 0.00 ^a
LM 20mg/kg	0.54 ± 0.02 ^b	6.13 ± 0.84 ^a	5.00 ± 0.06 ^b
LM 20mg/kg + GM 50 mg/kg	0.61 ± 0.08	3.40 ± 0.65 ^{ab}	4.70 ± 0.06 ^{ab}
LM 20mg/kg + GM 100 mg/kg	0.50 ± 0.01 ^b	4.78 ± 0.85 ^a	4.47 ± 0.03 ^{ab}
LM 20mg/kg + GM 150 mg/kg	0.59 ± 0.02	1.60 ± 0.11 ^b	4.20 ± 0.06 ^a

LM = levamisole, GM = ethanolic extract of Gmalena arborea, CRP = c-reactive protein, IL-6 = interleukin 6, ESR = erythrocyte sedimentation rate, P < 0.05 = statistical

significant, the superscript alphabets represent statistical significance where a = significant compared to group 2 while b = significant compared to group 1

Table 2 Effects of Ethanolic Root Extract of *Gmelina arborea* on Total White Blood Cells Count in Wister Rats

Groups	WBC (10 ⁹ /L)	Lymph %	Gran %	Lymph#	Gran#
Control	5.13 ± 0.73	68.43 ± 4.97	10.97 ± 1.51 ^a	3.70 ± 0.76	0.63±0.07
LM 20mg/kg	3.47 ± 0.26	84.30 ± 3.25	4.40 ± 1.21 ^b	2.93 ± 0.29	0.17 ± 0.07
LM 20mg/kg + GM 50 mg/kg	4.67 ± 0.97	79.80 ± 0.87	5.97 ± 0.27 ^b	3.67 ± 0.78	0.33 ± 0.09
LM 20mg/kg + GM 100 mg/kg	5.30 ± 2.26	75.30 ± 3.30	8.77 ± 2.02 ^a	3.97 ± 1.64	0.47 ± 0.18
LM 20mg/kg + GM 150 mg/kg	5.67 ± 1.14	68.10 ± 13.48	6.47 ± 1.26 ^b	3.63 ± 0.78	1.37 ± 1.02

P < 0.05 = statistical significant, the superscript alphabets represent statistical significance where a = significant compared to group 2 while b = significant compared to group 1, WBC= white blood cell count, Lymph%

= percentage lymphocyte, Gran% = percentage granulocyte, Lymph# = absolute lymphocyte number, Gran# = absolute granulocyte number.

Table 3 Effects of Ethanolic Root Extract of *Gmelina arborea* on Platelet Indices in Wister Rats

Groups	RDW (%)	MPV (fL)	PDW (%)	PLT (10 ⁹ /L)
Control	11.50 ± 0.59	5.63 ± 0.07	15.57 ± 0.43	195.00 ± 37.00 ^a
LM 20mg/kg	10.93 ± 0.61	5.70 ± 0.25	16.77 ± 0.18	534.33 ± 69.29 ^b
LM 20mg/kg + GM 50 mg/kg	10.73 ± 0.81	5.67 ± 0.15	17.00 ± 0.50	473.33 ± 209.77
LM 20mg/kg + GM 100 mg/kg	9.50 ± 0.10 ^b	5.90 ± 0.40	16.77 ± 0.23	738.33 ± 46.28 ^b
LM 20mg/kg + GM 150 mg/kg	10.63 ± 0.67	5.37 ± 0.23	16.17 ± 0.15	953.67 ± 106.41 ^{ab}

50mg/kg body weight of ethanolic extract of *Gmelina arborea* root, Levamisole (a standard immunosuppressive drug) 20 mg/kg body weight, RDW = red cell distribution width, MPV = mean platelet volume, PDW = platelet distribution width; PLT = platelet count.

➤ Effects of Ethanolic Root Extract of *Gmelina arborea* on Wister Rats Inflammatory Marker

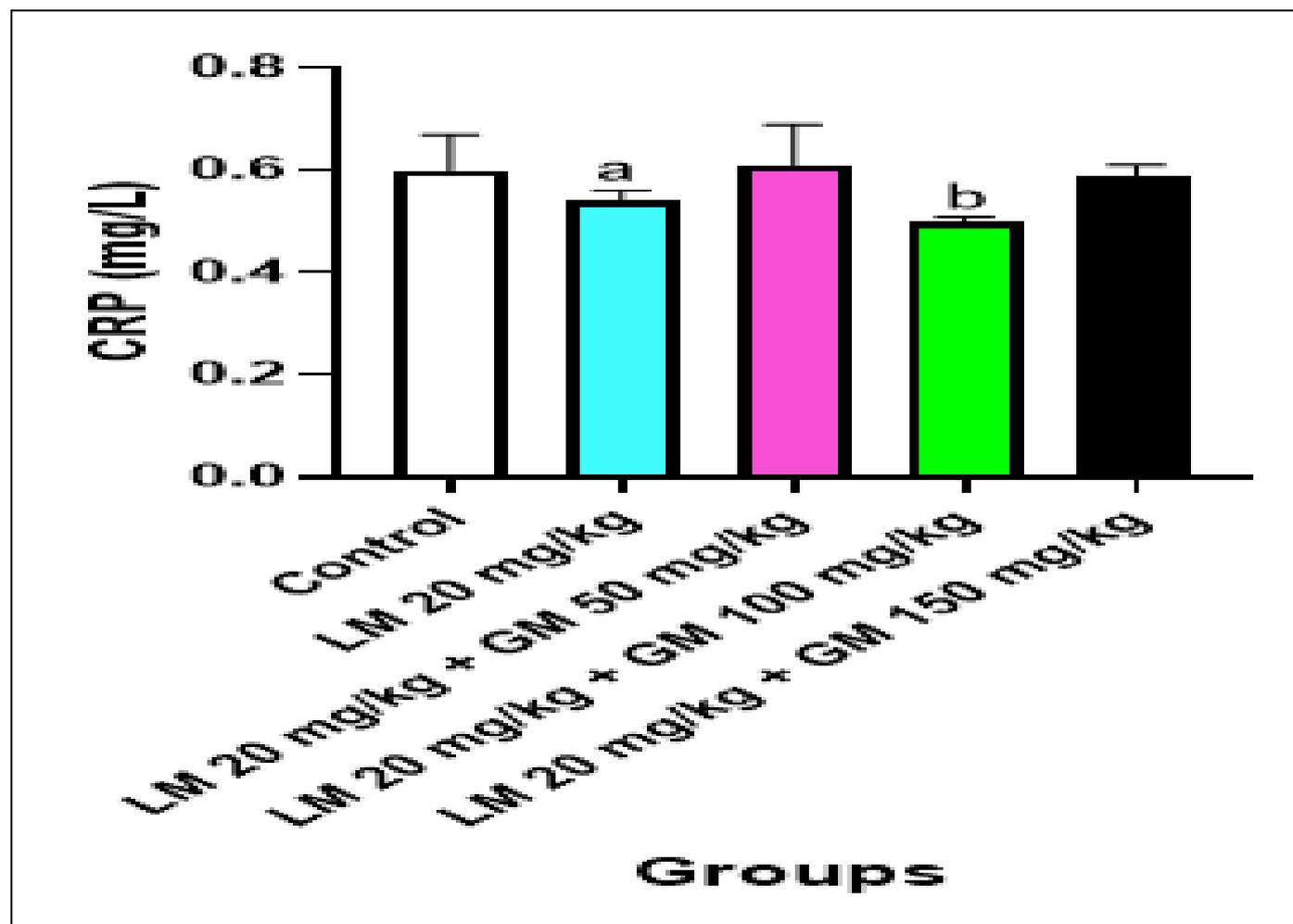


Fig 1 Effects of Ethanolic Root Extract of *Gmelina arborea* on C-Reactive Protein

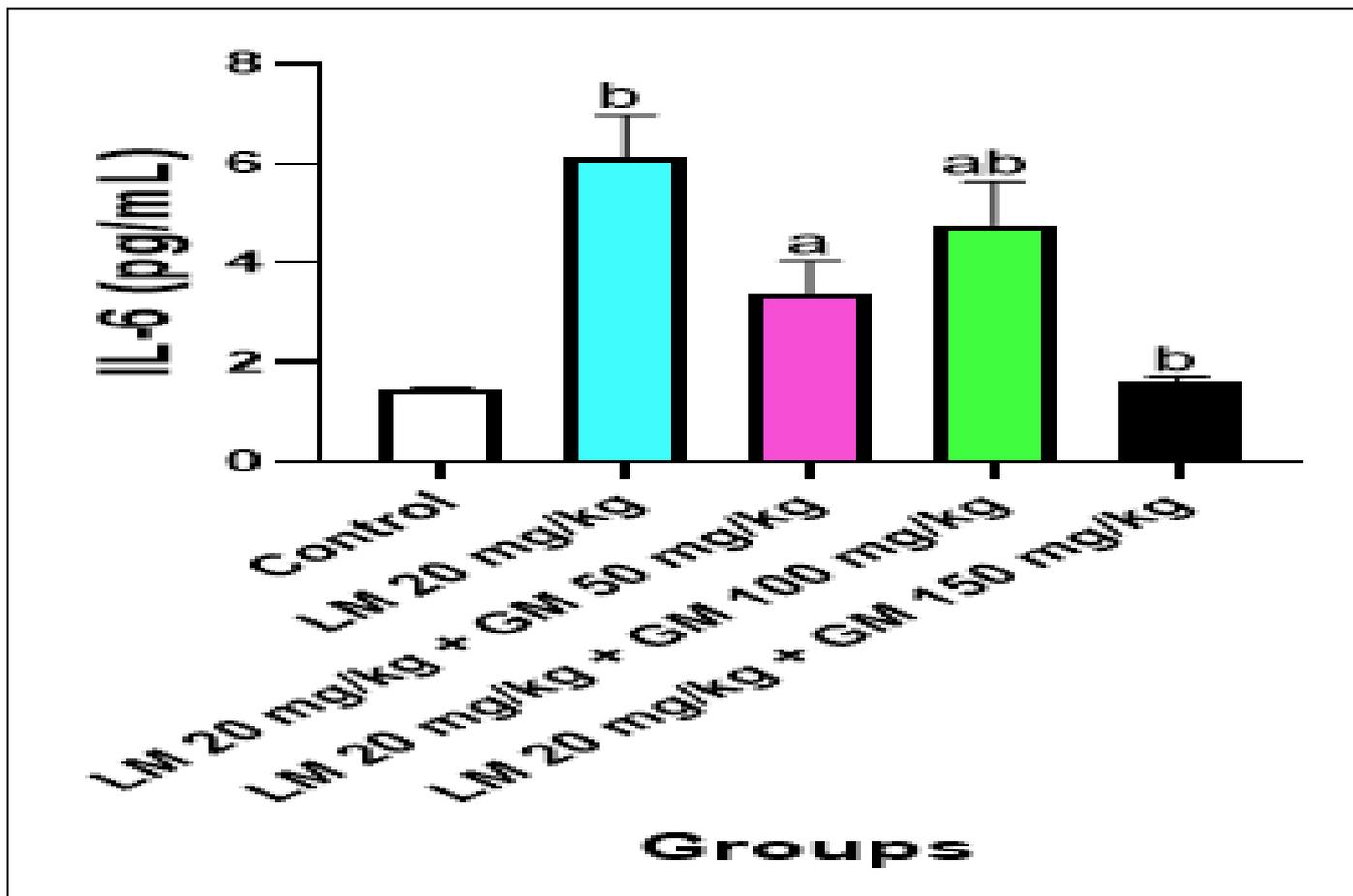


Fig 2 Effects of Ethanolic Root Extract of *Gmelina arborea* on Interleukin-6

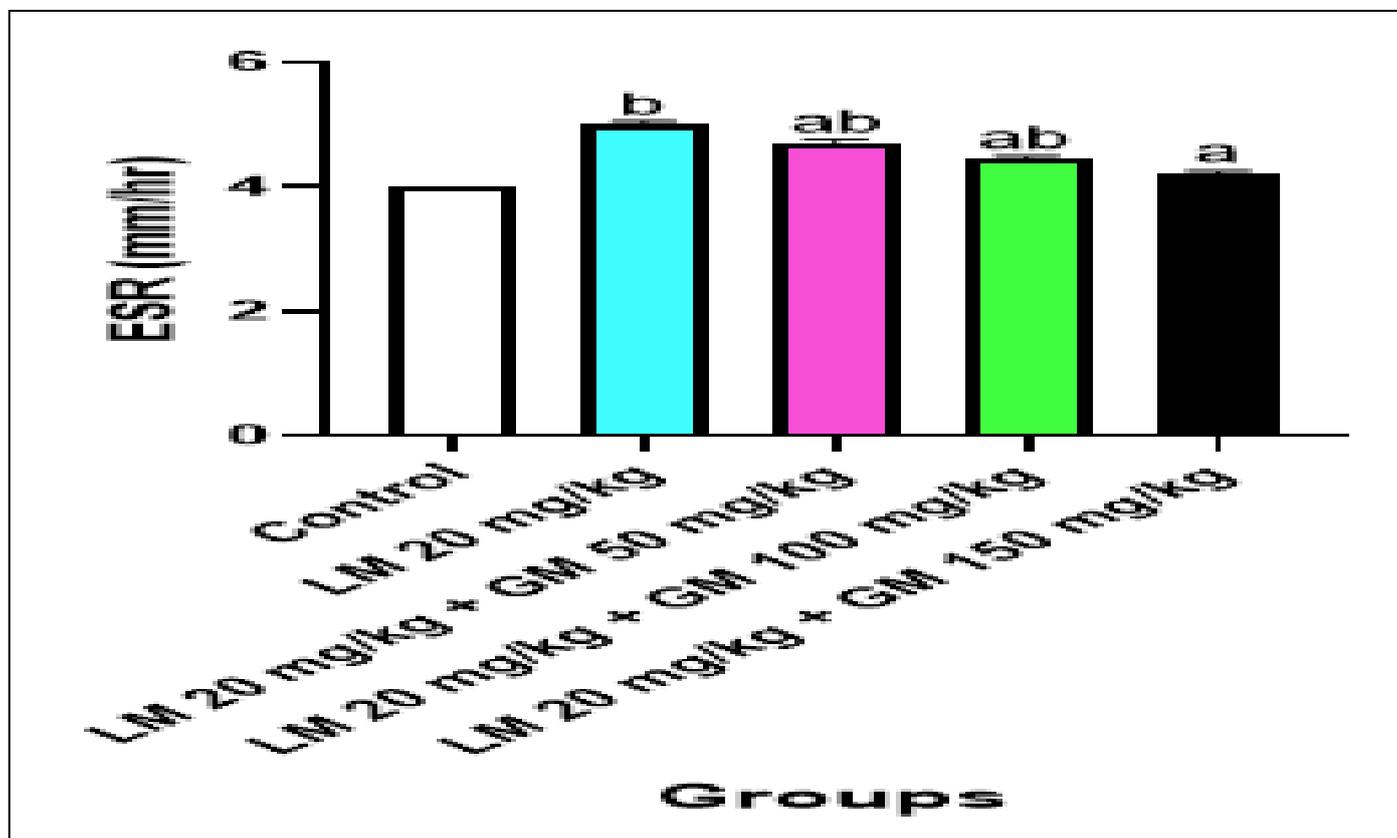


Fig 3 Effects of Ethanolic Root Extract of *Gmelina arborea* on Erythrocyte Sedimentation Rate

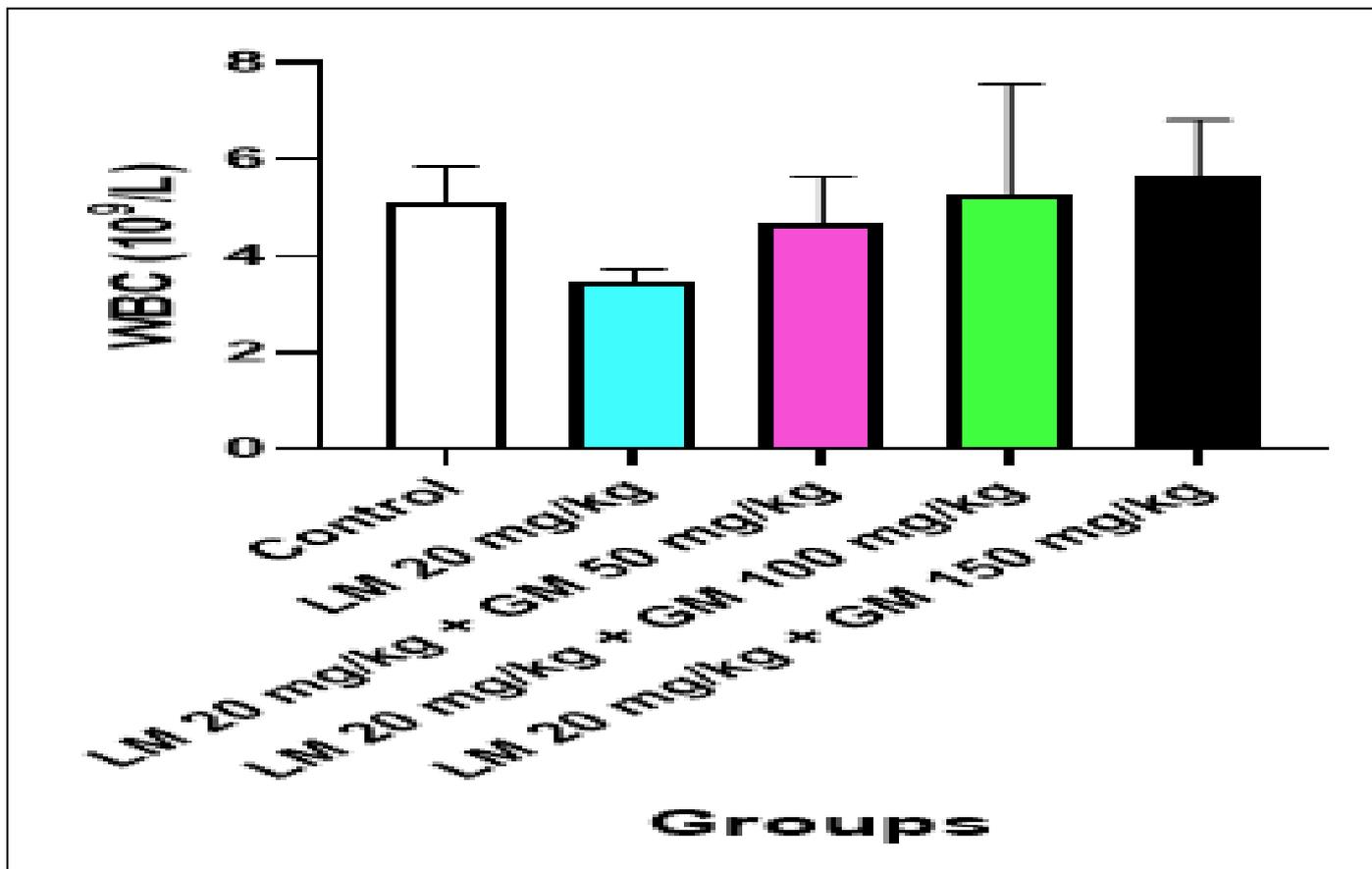


Fig 4 Effects of Ethanolic Root Extract of *Gmelina arborea* on White Blood Cells Count

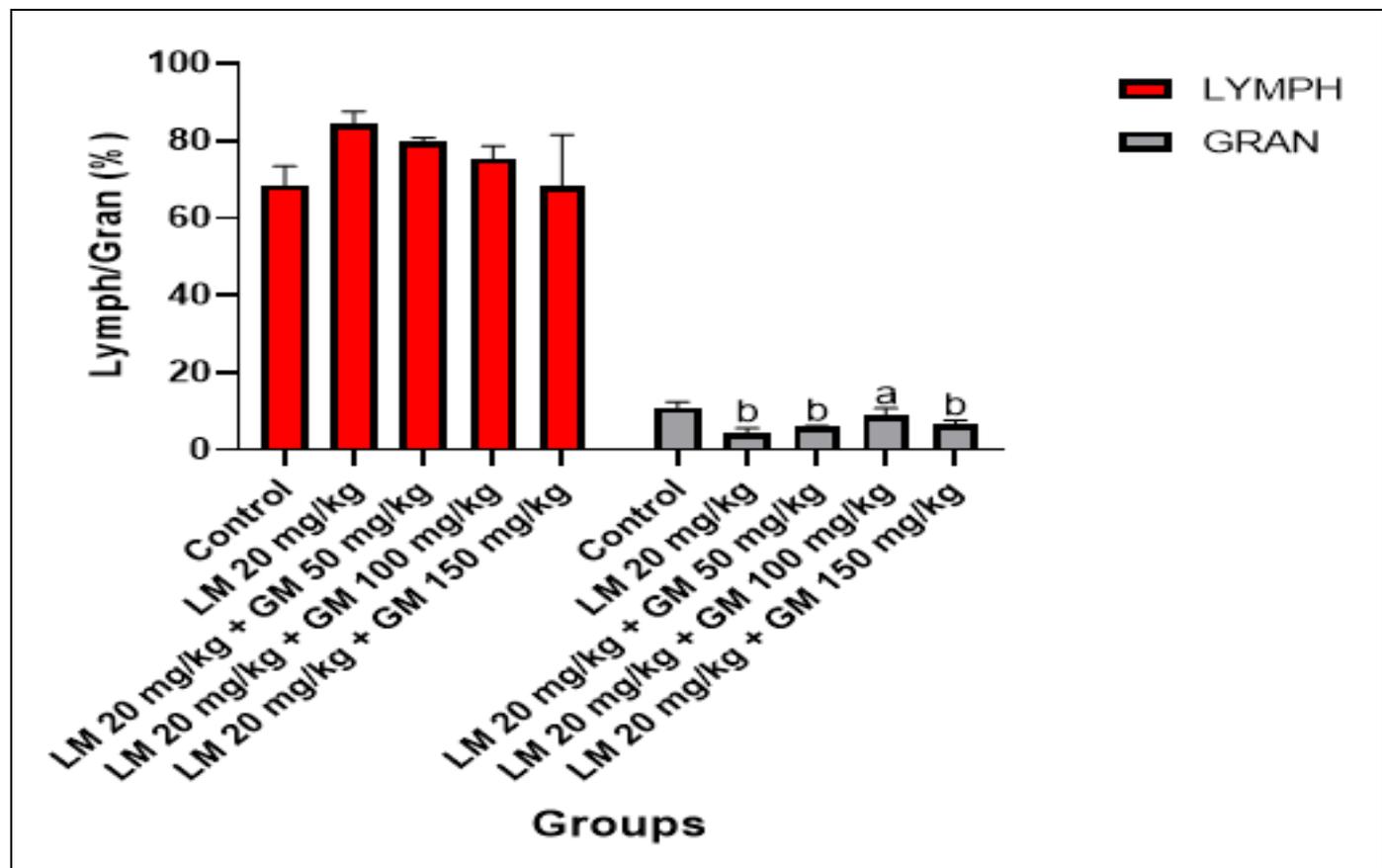


Fig 5 Effects of Ethanolic Root Extract of *Gmelina arborea* on Lymphocyte/Granulocyte Percentage

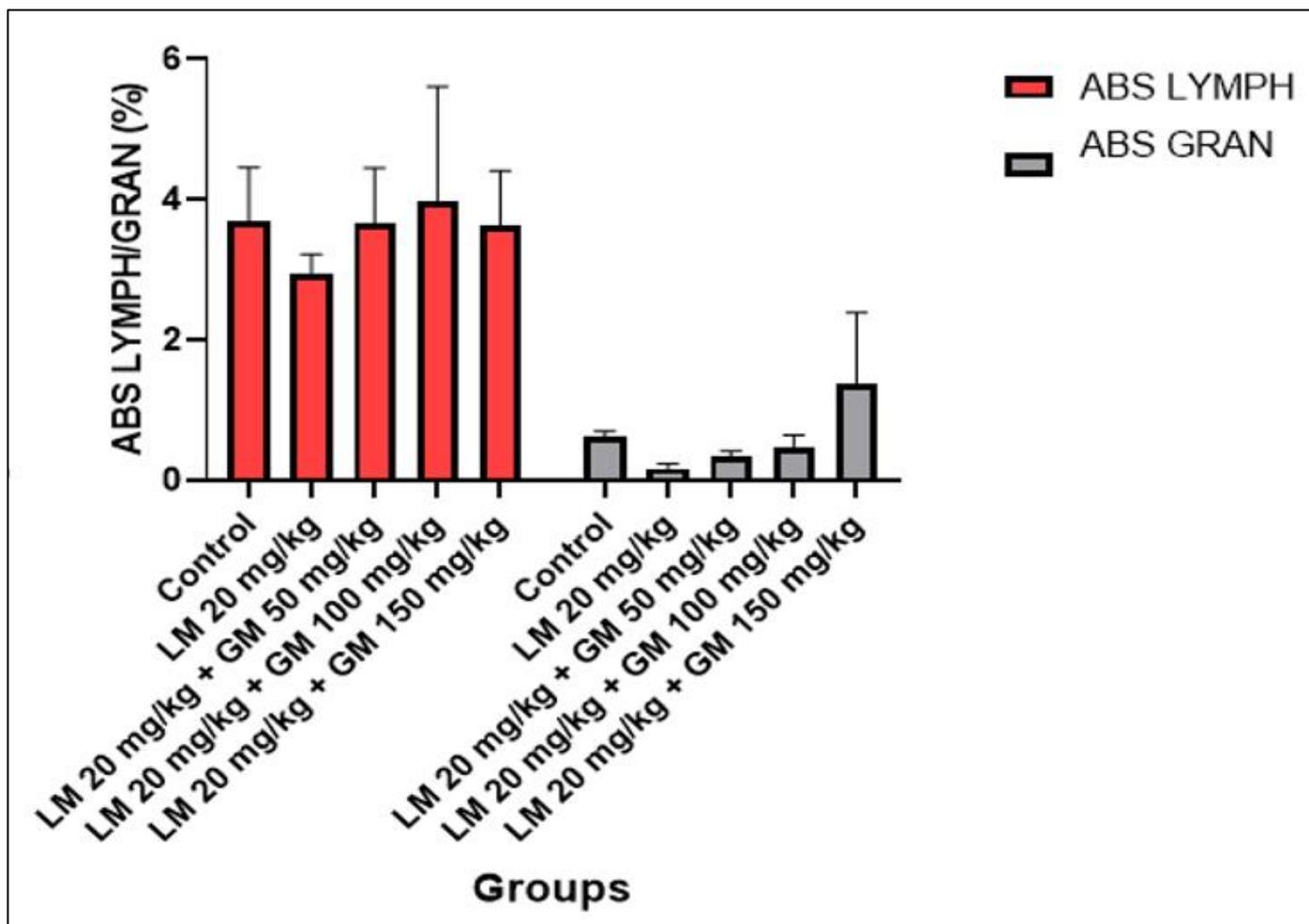


Fig 6 Effects of Ethanolic Root Extract of *Gmelina arborea* on Absolute Lymphocyte/Granulocyte

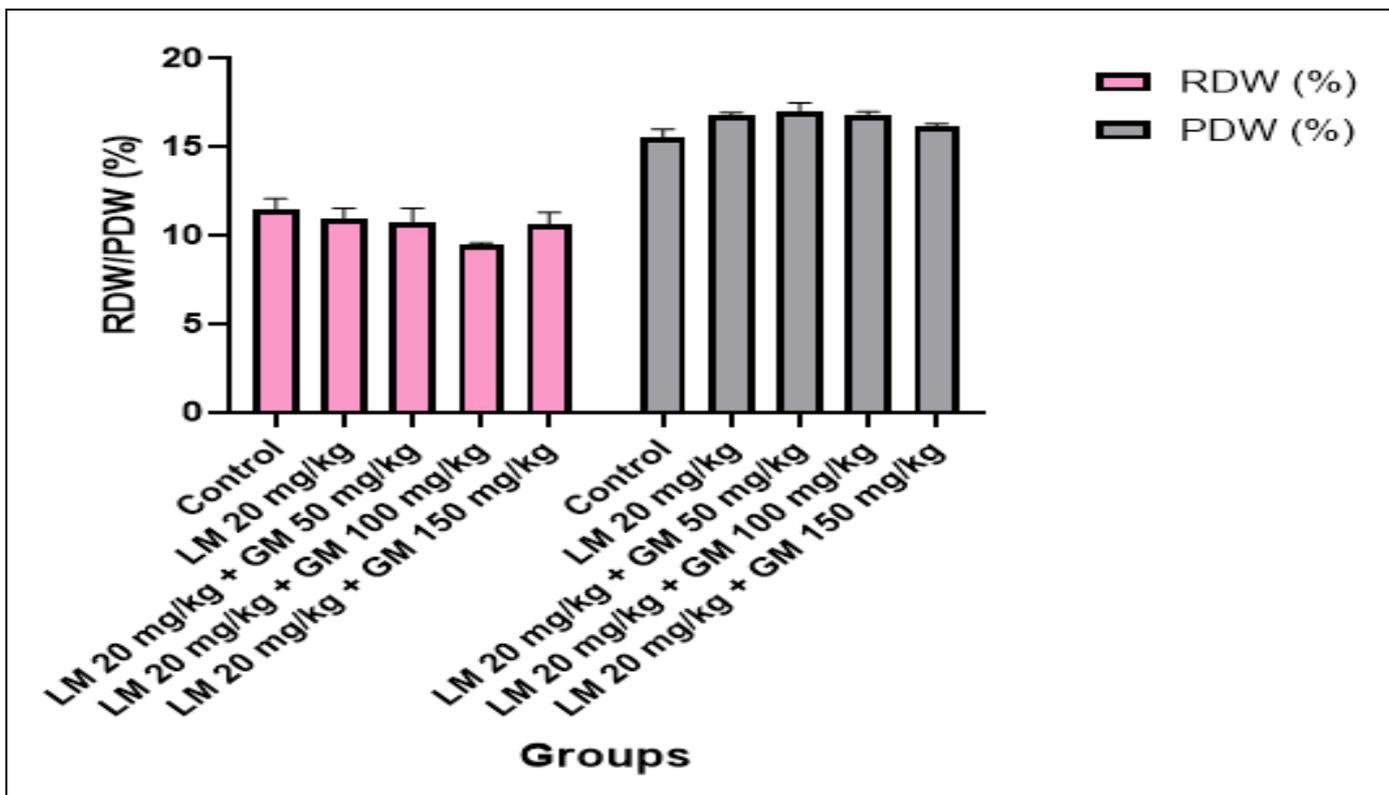


Fig 7 Effects of Ethanolic Root Extract of *Gmelina arborea* on Red Distribution Width/Platelet Distribution Width

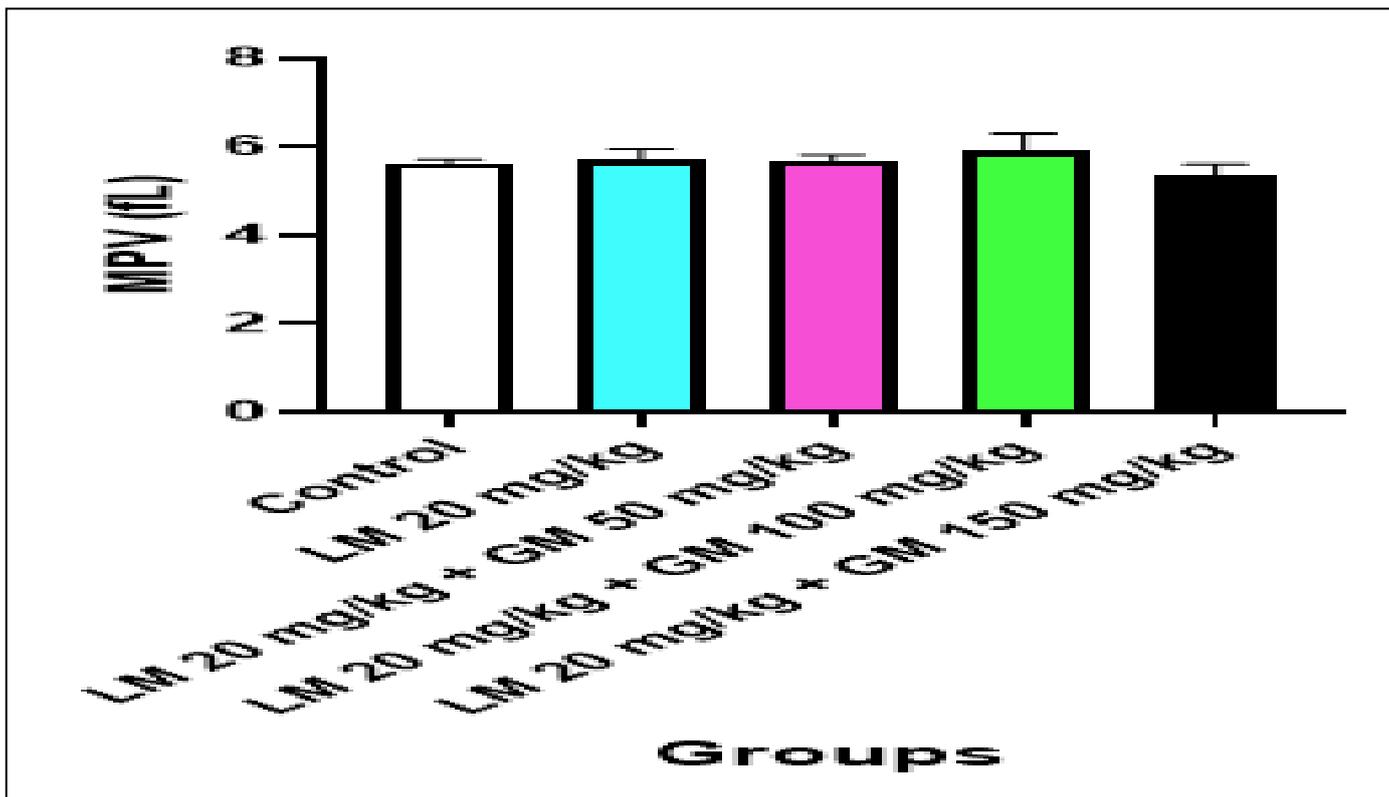


Fig 8 Effects of Ethanolic Root Extract of *Gmelina arborea* on Mean Platelet Volume

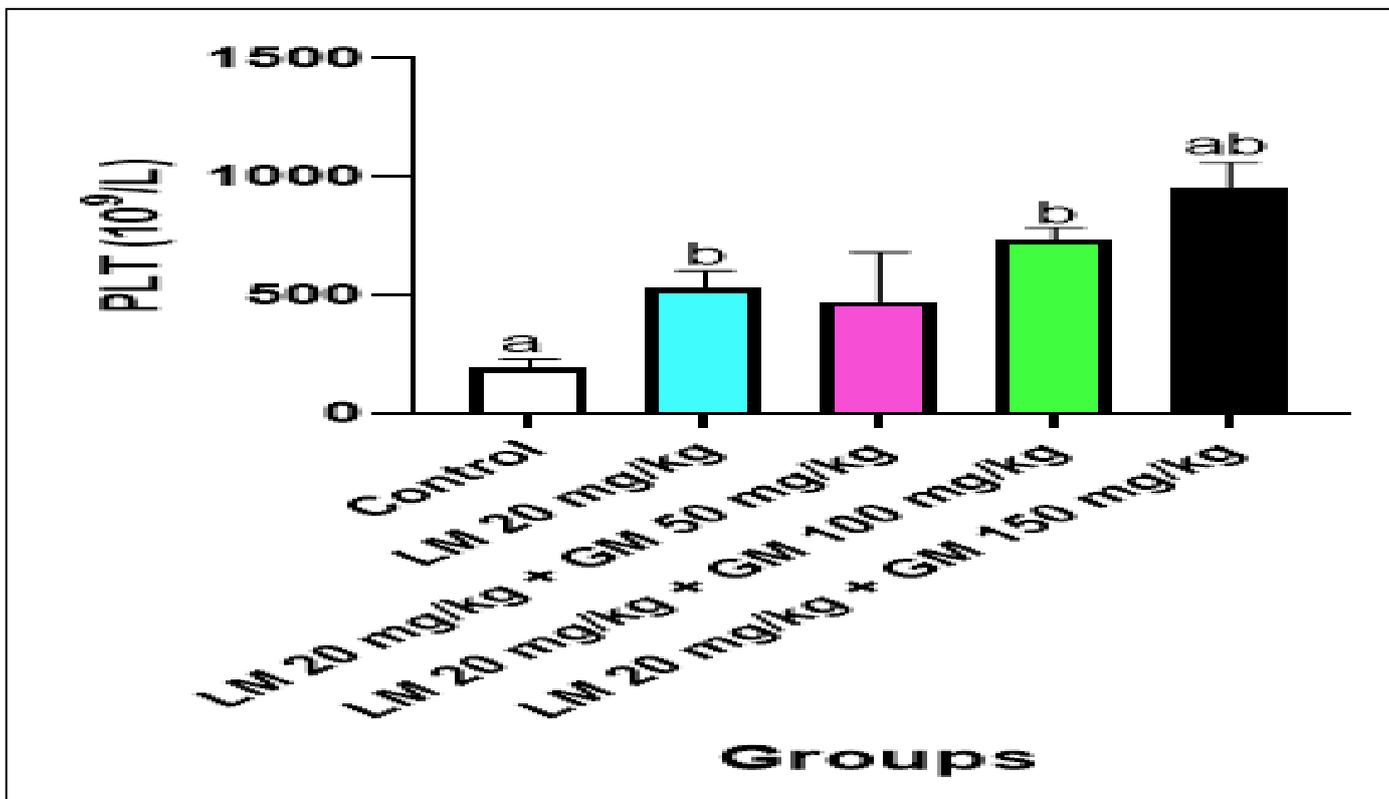


Fig 9 Effects of Ethanolic Root Extract of *Gmelina arborea* on Platelet Count

The results of this study demonstrate that the ethanolic root extract of *Gmelina arborea* exerts significant immunomodulatory effects in Wistar rats, with observable responses across inflammatory markers, leukocyte profiles,

and platelet indices. Effects on Inflammatory Markers: Levamisole (LM 20 mg/kg) significantly increased IL-6 (6.13 ± 0.84 pg/mL) and ESR (5.00 ± 0.06 mm) compared to the control (IL-6: 1.48 ± 0.01 pg/mL; ESR: 4.00 ± 0.00 mm),

confirming its immunosuppressive action. Co-administration of *G. arborea* extract (GM) resulted in dose-dependent modulation of these markers. At 150 mg/kg, IL-6 (1.60 ± 0.11 pg/mL) and ESR (4.20 ± 0.06 mm) values approximated those of the negative control, indicating restoration of normal inflammatory status. CRP levels remained relatively stable across groups, suggesting that the extract does not trigger systemic acute-phase inflammation. Effects on Leukocyte Profiles. Levamisole decreased total WBC counts ($3.47 \pm 0.26 \times 10^9/L$) and absolute granulocyte numbers (0.17 ± 0.07), while increasing lymphocyte percentages ($84.30 \pm 3.25\%$), reflecting immunosuppression. *G. arborea* extract counteracted these effects dose-dependently. Notably, the 150 mg/kg group exhibited normalized WBC counts ($5.67 \pm 1.14 \times 10^9/L$) and granulocyte numbers (1.37 ± 1.02), demonstrating enhancement of innate immune components while maintaining lymphocyte balance, critical for adaptive immunity. Effects on Platelet Indices. Platelet counts (PLT) and mean platelet volume (MPV) increased with levamisole, indicating altered hematopoiesis. GM co-treatment further modulated these parameters, particularly at higher doses (PLT: $953.67 \pm 106.41 \times 10^9/L$ at 150 mg/kg), suggesting a supportive role in hematologic stability and platelet function. This is in agreement with that of Olanrewaju et al⁸ and that of Afolayan et al⁹. Phytochemical Contributions: Bioactive compounds such as flavonoids, saponins, terpenoids, and iridoid glycosides likely mediate these effects by regulating cytokine signaling, enhancing phagocytic activity, and promoting lymphocyte proliferation. Innate and Adaptive Immunity. The extract enhanced innate immunity by normalizing granulocyte counts and improving ESR and IL-6 levels, while adaptive immunity was supported through balanced lymphocyte percentages and restoration of immune organ structure⁹. Ethanolic root extract of *Gmelina arborea* exerts dose-dependent immunomodulatory effects, mitigating levamisole-induced immunosuppression, enhancing both innate and adaptive immune responses, and restoring hematological and inflammatory markers toward normal ranges. These findings support its potential development as a natural immunotherapeutic agent.

IV. CONCLUSION

Ethanolic root extract of *Gmelina arborea* exerts dose-dependent immunomodulatory effects, mitigating levamisole-induced immunosuppression, enhancing both innate and adaptive immune responses, and restoring hematological and inflammatory markers toward normal ranges. These findings support its potential development as a natural immunotherapeutic agent.

RECOMMENDATIONS

➤ The extract demonstrates dose-dependent immunomodulatory activity, suggesting potential for therapeutic use in conditions involving immune suppression or dysregulation, such as chronic infections or autoimmune modulation therapies. The reduction in inflammatory cytokine IL-6 highlights anti-inflammatory potential, which could be explored in inflammatory or

autoimmune diseases following human safety assessments.

- The extract's enhancement of platelet count suggests possible application in thrombocytopenic conditions, though further dose standardization and toxicity studies are required.
- *Gmelina arborea* ethanolic root extract exhibits promising immunomodulatory, anti-inflammatory, and hematopoietic properties in Wistar rats, warranting further controlled clinical research to assess its efficacy and safety in humans.

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