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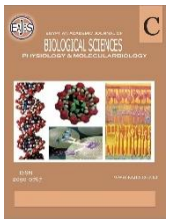

Chronic Effects of Turmeric Root Extract on Hematological, Hepatic, and Renal Parameters in Male Hamsters

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ABSTRACT

This study evaluated the chronic effects of turmeric root extract (*Curcuma longa* L.) at varying doses on hematological, hepatic, and renal parameters in male hamsters over a period of 60 days. A total of 32 hamsters were divided into four groups of 8 hamsters each: a control group and three treatment groups received 750, 1000, & 1500mg/kg of the extract orally, once daily for 60 days. A wide range of parameters was assessed, including red blood cell (RBC) indices, white blood cell (WBC) counts, and immune indicators, as well as platelet indices and liver and kidney function tests. The results showed that low (750) and moderate (1000) doses of turmeric extract led to improvements in certain hematological and immunological parameters. However, high dose (1500mg/kg) was associated with significant alterations in RBC volume and hemoglobin (Hb) content (decreased the mean corpuscular volume (MCV), the mean corpuscular hemoglobin (MCH), and the mean corpuscular hemoglobin concentration (MCHC), indicating a potential adverse effect on RBC quality. Platelet counts (PLT), mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT) were significantly increased in all treated groups. An increase in liver enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) across all treated groups, with a significant elevation in ALT at 1500mg/kg dose, reflected hepatic stress. However, no changes in total bilirubin (T. Bil) or albumin (ALB) were observed, indicating the liver retained much of its synthetic and detoxifying functions. Kidney function tests showed a significant rise in blood urea (BU) levels at 1000 mg/kg dose, but creatinine (Crea) levels were statistically unchanged. These results suggest that turmeric extract provides hematological and immunomodulatory benefits at moderate doses. But chronic exposure to 1500mg/kg doses induced hepatic stress and undesirable hematological alterations, underscoring the need for careful evaluation of optimal dosage and duration of safety.

INTRODUCTION

Curcuma longa L. (turmeric), Zingiberaceae family, was used in ancient times for dyeing, flavoring, coloring, and as a medicine in South Asian cultures, including Ayurveda, Siddha, and Unani, dating back over 4000 years (Tian *et al,* 2025).

Turmeric was documented in the ancient Egyptian Ebers Papyrus (1500 BC) for its use in healing wounds and as a dye (Zucconi, 2007). Its diverse biological activity is attributed to curcumin, the primary polyphenol extracted from the plant's roots. Curcumin has shown remarkable efficacy in modulating various molecular pathways related to oxidative stress, inflammation, and apoptosis. It also possesses antioxidant, anti-inflammatory, antibacterial, and antiviral properties and plays a potential role in the prevention of chronic diseases (Aggarwal & Harikumar, 2009; Zhou *et al,* 2011).

Previous studies have documented that curcumin can improve certain hematological parameters and regulate liver and kidney functions when administered in moderate doses for short periods (Chowdhury *et al,* 2018). It has also been observed that curcumin may enhance immune responses, increase platelet production, and improve the balance of white blood cells and lymphocytes (Jagetia and Aggarwal, 2007). However, most of these studies relied on purified curcumin as an isolated compound. This approach leaves a significant knowledge gap regarding the full effect of unrefined turmeric on critical research challenges.

Moreover, the effect of whole turmeric extract on hematological and biochemical markers in animals has not been adequately studied when administered in escalating doses over a period exceeding four weeks. Most previous experiments lack a systematic correlation between dose and duration, which is essential for assessing the biological safety of widely used herbal extracts. These interconnected research gaps form the rationale for this study, which aims to provide a comprehensive understanding of the physiological effects of whole turmeric extract.

Accordingly, this study aims to assess the long-term effects of Curcuma longa root extract at different doses (750, 1000, & 1500 mg/kg) over 60 days in male hamsters. This will be accomplished by examining a variety of hematological parameters, liver function indices, and kidney function markers. It is anticipated that this study will generate reliable scientific data on the safety and efficacy of turmeric at various doses over time, potentially leading to its use as a safe nutritional or therapeutic supplement in biomedical applications.

Specific objectives aimed to include: (1) effect of turmeric root extract on red blood cell indices (RBC, Hb, HCT, MCV, MCH, MCHC) in male hamsters, (2) changes in white blood cell indices (WBCs, Lymph, MID, GRAN) resulting from chronic turmeric treatment, (3) effect of extract on platelets and their indices (PLT, MPV, PDW, PCT) at different doses, (4) impact of different doses of turmeric extract on liver enzymes and functions (AST, ALT, ALB, T.Bil), (5) effect on kidney function (BU, Crea) due to chronic extract administration, and (6) compare the effects among doses 750, 1000, & 1500mg/kg to determine the relationship between doses, duration, and positive or negative physiological effects.

MATERIALS AND METHODS

Study Design:

Turmeric roots (*Curcuma longa*) were obtained from the local market in Zliten city, Zliten province, Libya. The plant material was authenticated and prepared following standard botanical procedures, including washing, drying, grinding, and storage under controlled conditions. The roots were thoroughly cleaned to remove dirt, then washed several times with distilled water and dried in the shade at room temperature. After drying, the roots were ground using an electric grinder to obtain a fine powder of turmeric root.

Preparation of Turmeric Root Water Extraction:

To prepare the extract, 200g of turmeric powder was mixed with 1000mL of a 50:50 mixture of ethanol and distilled water, and the mixture was stirred intermittently for 48 hours at room temperature. The mixture was allowed to settle at 4°C in conical glass containers and subjected to multiple centrifugation cycles at 1000×*g* for two hours.

The extract was filtered using a 0.2µm pore-size filter and concentrated using a rotary evaporator at 45°C until complete dryness. Finally, the dried extract was re-dissolved in distilled water at a concentration of 1 gram per 100 mL (Nazdar *et al.,* 2024).

Experimental Design:

This study used 32 male Syrian hamsters (*Mesocricetus auratus*) weighing between 85 & 150g housed in specialized cages in a controlled environment (temperature: 21-25°C, humidity and ventilation controlled, with a 12-hour light/dark cycle). They were randomly divided into four groups of 8 hamsters each: Control group: Didn't receive turmeric extract. Low-dose group: Received 750mg/kg body weight of turmeric extract daily. Medium-dose group: Received 1000mg/kg of turmeric extract daily, High-dose group: Received 1500mg/kg body weight of turmeric extract daily. The extract was administered orally using an oral gavage once daily for 60 days. After treatment, hamsters were sacrificed 24 hours later. Blood samples were collected in heparin-free tubes and centrifuged to separate plasma for biochemical analysis.

Hematological and Biochemical Tests:

Hematological and biochemical analyses were conducted based on the methods described by Chowdhury *et al.* (2018) and Samarghandian *et al.* (2014), with minor modifications. Hematological parameters were measured using an automated hematology analyzer (Sysmex XP-300) at the laboratory of the Medical Technology College, Misurata University, while biochemical parameters such as ALT, AST, urea, and creatinine were evaluated using a semi-automated chemistry analyzer (Mindray BA-88A) in the same laboratory. The methods and calculation procedures followed the protocols described by Chowdhury *et al.* (2018) and Samarghandian *et al.* (2014).

1.The RBC count, hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC).

2.Total WBCs count, lymphocytes (Lymph), monocytes (MID), and granulocytes (GRAN).

3.The PLT count, mean platelet volume (MPV), platelet distribution width (PDW), and plateletcrit (PCT).

4. Liver function tests: AST, ALT, total bilirubin (T.BIL), and albumin (ALB) levels.

5. Kidney function tests: Blood urea (BU) and creatinine (Crea) concentrations.

Statistical Analysis:

Data were expressed as Mean ± SE and analyzed using one-way analysis of variance (ANOVA). Homogeneity of variances was tested by Levene's test. In cases where variances were not homogeneous, Tukey's multiple comparison test determined significant differences at a confidence level of $p < 0.05$. Lowercase letters (a, b, & c) indicated significant differences between groups, with different letters denoting significant differences and identical letters indicating non-significant differences. An asterisk (*) next to a letter indicated a validated significance level.

RESULTS

Male hamsters were orally treated with doses (750, 1000, and 1500 mg/kg) of *Curcuma longa* root extract daily for 60 days. Blood samples were collected at the end of the treatment period to assess various hematological and biochemical parameters.

1. Effect of *C. longa* L. root extract on red blood cell (RBC) parameters

Table 1 and Figures 1, 2, 3, 4, 5 & 6 show the effect of *Curcuma longa* root extract on red blood cell parameters in male hamsters treated for 60 days.

Table 1: Effect of aqueous turmeric root extract (*Curcuma longa* L.) on red blood cell parameters in male hamsters treated for 60 days.

Parameter	Unit / Type	Control (n=8)	Turmeric extract (n=8)		
			750 mg/kg	1000 mg/kg	1500 mg/kg
RBC	Mean ± SE	4.83 ± 0.06[a]	5.93 ± 0.33[ab]	5.42 ± 0.65[ab]	5.80 ± 0.28[ab]
	% change	–	↑ 22.8%	↑ 12.2%	↑ 0.0%
Hb	Mean ± SE	13.6 ± 0.31[a]	12.1 ± 0.62[a]	13.1 ± 0.51[a]	11.2 ± 0.28[a]
	% change	–	↓ 11.0%	↓ 3.7%	↓ 17.6%
HCT	Mean ± SE	43.3 ± 0.61[ab]	38.5 ± 1.66[a]	40.9 ± 2.02[ab]	50.3 ± 1.37[b]*
	% change	–	↓ 11.1%	↓ 5.5%	↑ 16.2%
MCV	Mean ± SE	89.7 ± 1.26[a]	83.5 ± 1.55[ab]	81.2 ± 1.44[ab]	77.4 ± 1.38[b]*
	% change	–	↓ 6.9%	↓ 9.5%	↓ 13.7%
MCH	Mean ± SE	29.1 ± 0.22[a]	25.3 ± 0.25[ab]	24.8 ± 0.32[ab]	22.7 ± 0.40[b]*
	% change	–	↓ 13.1%	↓ 14.8%	↓ 22.0%
MCHC	Mean ± SE	32.5 ± 0.16[b]	29.1 ± 0.21[a]	28.5 ± 0.43[a]	28.7 ± 0.65[a]
	% change	–	↓ 10.5%	↓ 12.3%	↓ 11.7%

Values are expressed as Mean ± Standard Error (Mean ± SE).
Different letters (a, b) indicate significant differences between groups at $p < 0.05$.
Similar letters indicate no significant difference between those groups.
An asterisk (*) next to a letter indicates a statistically significant difference compared to other groups.
Arrows (↑, ↓) indicate the percentage change relative to the control group.

1.1. Effect of Turmeric Root Extract (*C. longa* L.) on Red Blood Cell (RBC) Count:

The results related to the RBC count, as shown in Figure 1, indicated that the group treated with turmeric extract at a dose of 750 mg/kg showed a noticeable increase of 22.8% on average (5.93 ± 0.33ab) compared to the control group (4.83 ± 0.06a). The letter "ab" indicates no clear significant difference compared to the control, as some groups share similar letters, suggesting that the increase is not statistically significant. The doses of 1000 and 1500 mg/kg showed relatively smaller increases, with 5.42 0.65ab and 5.80 ± 0.28ab, respectively. However, the overall statistical analysis (ANOVA) ($F(3,28) = 1.571$, $p = 0.218$) and Tukey's test showed no statistically significant differences between any of the treated groups and the control group or among themselves, confirming the absence of substantial differences.

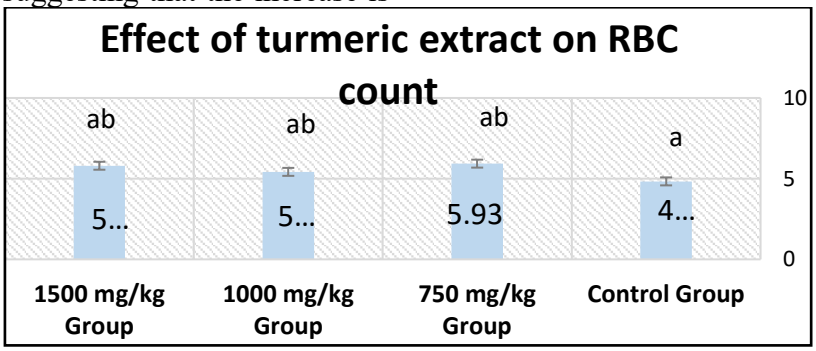

Fig. 1: Effect of turmeric root extract (*Curcuma longa* L.) on red blood cell (RBC) count in male hamsters treated for 60 days. No statistically significant differences were observed.

1.2. Effect of Turmeric Root Extract (*C. longa* L.) on hemoglobin (Hb) Concentration:

Figure 2 shows that a numerical decrease in hemoglobin concentration was observed in all treated groups compared to the control group (13.6 ± 0.31). The mean values were 12.1 ± 0.62 in the group treated with 750

mg/kg, 13.1 ± 0.51 in the 1000 mg/kg group, and 11.2 ± 0.28 in the 1500 mg/kg group. Despite these numerical decreases, one-way ANOVA analysis ($F(3,28) = 1.681$, $p = 0.194$) and post hoc Tukey tests, along with the identical letter "a" annotation, indicated no statistically significant differences between groups. This suggests that the decreases were not important.

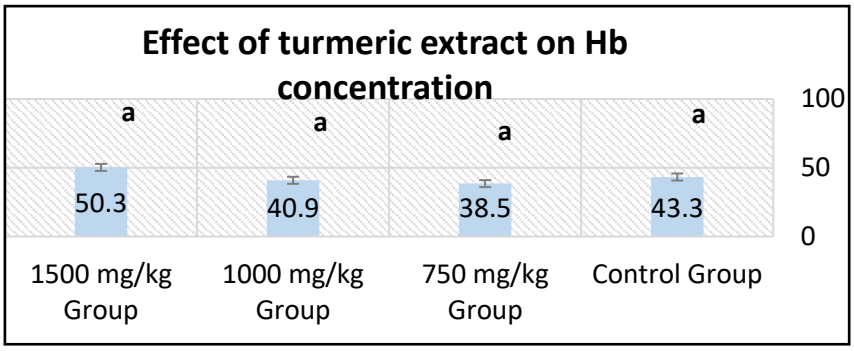

Fig. 2: Effect of turmeric root extract (*Curcuma longa* L.) on hemoglobin (Hb) concentration in male hamsters treated for 60 days. No significant differences were observed between any of the treated groups and the control group or among the treated groups.

1.3 Effect of Turmeric Root Extract (*C. longa* L.) on hematocrit (HCT) Percentage:

A numerical decrease in hematocrit percentage was observed in the groups treated with 750 and 1000 mg/kg, recording 38.5 ± 1.66 and 40.9 ± 2.02, respectively. Meanwhile, the group treated with 1500 mg/kg showed a numerical increase of 16.2% (50.3 ± 1.37) compared to the control group (43.3 ± 0.61). The letter "b" and the asterisk "*" indicate a significant difference in the highest dose group. One-way ANOVA analysis revealed a significant overall difference between groups ($F(3,28) = 4.910$, $p = 0.007$). However, post hoc Tukey's test showed that the only significant difference was between the 1000 mg/kg and 1500 mg/kg groups (mean difference = -10.58750, $p = 0.006$). No significant difference was observed between the 1500 mg/kg group and the control group ($p = 0.418$), which contradicts the indication of statistical significance (Fig. 3).

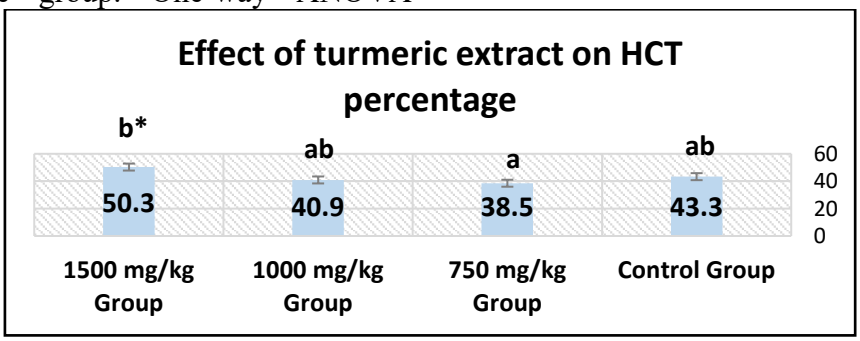

Fig. 3: Effect of turmeric root extract (*Curcuma longa* L.) on hematocrit (HCT) percentage in male hamsters treated for 60 days. Post hoc Tukey's test showed that the only significant difference was between the 1000 mg/kg and 1500 mg/kg groups.

1.4. Effect of Turmeric Root Extract (*C. longa* L.) on Mean Corpuscular Volume (MCV):

As shown in Figure 4, the MCV gradually decreased with increasing dose. The values were 83.5 ± 1.55 (750 mg/kg), 81.2 ± 1.44 (1000 mg/kg), and 77.4 ± 1.38 (1500 mg/kg) compared to the control group (89.7 ± 1.26). The letter "b" and the asterisk "*" indicate a significant difference in the highest dose group. One-way ANOVA revealed highly significant differences between groups

(F(3,28) = 90.062, p = 0.000). Tukey's post hoc tests showed highly significant reductions in MCV between all treated groups and the control ($p < 0.001$ for all comparisons). Furthermore, a significant decrease was observed between the 1500 mg/kg and 750 mg/kg groups ($p = 0.002$).

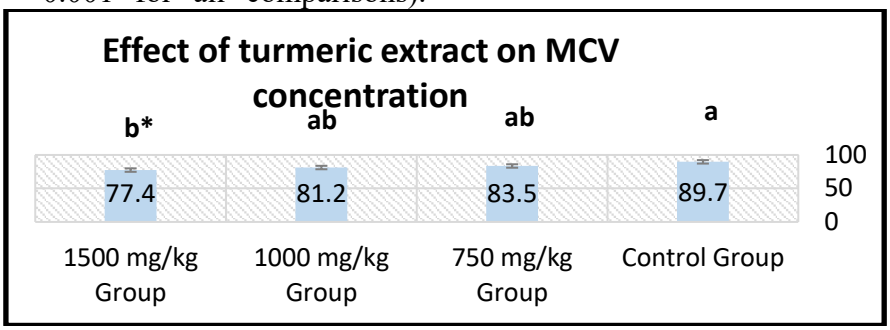

Fig. 4: Effect of turmeric root extract (*Curcuma longa L.*) on mean corpuscular volume (MCV) parameter in male hamsters treated for 60 days. Post hoc Tukey's test showed that the only significant difference was between the 1000 mg/kg and 1500 mg/kg groups.

1.5. Effect of Turmeric Root Extract (*C. longa* L.) on Mean Corpuscular Hemoglobin (MCH):

A gradual decrease in MCH was observed with increasing doses (Fig. 5). The recorded values were 25.3 ± 0.25 (750 mg/kg), 24.8 ± 0.32 (1000 mg/kg), and 22.7 ± 0.40 (1500 mg/kg), compared to the control group (29.1 ± 0.22). One-way ANOVA revealed highly significant differences among the groups. Tukey's post hoc test confirmed highly significant reductions in MCH in all treated groups compared to the control ($p < 0.001$ for all comparisons). Additionally, significant reductions were observed in the 1500 mg/kg group compared to both the 750 mg/kg ($p < 0.001$) and 1000 mg/kg groups.

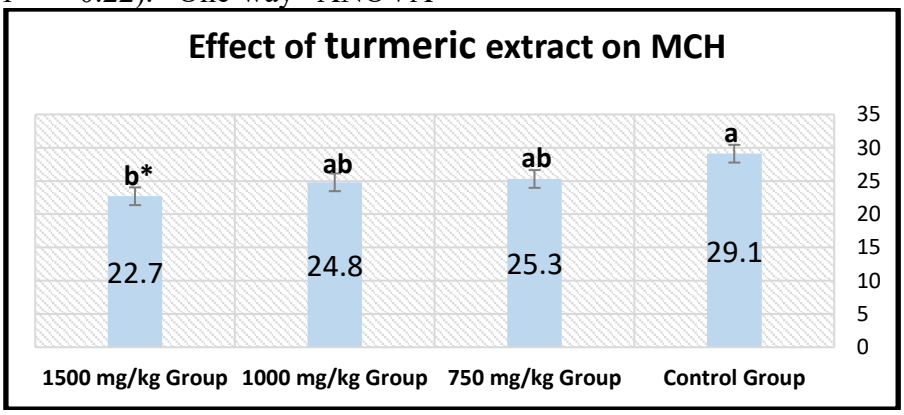

Fig. 5: Effect of turmeric root extract (*Curcuma longa L.*) on mean corpuscular hemoglobin (MCH) parameter in male hamsters treated for 60 days. Post hoc Tukey's test showed that the only significant difference was between the 1000 mg/kg and 1500 mg/kg groups.

1.6. Effect of Turmeric Root Extract (*C. longa* L.) on Mean Corpuscular Hemoglobin Concentration (MCHC):

As illustrated by Figure 6, the MCHC values showed a decrease in the treated groups (29.1 ± 0.21, 28.5 ± 0.43, and 28.7 ± 0.65) compared to the control group (32.5 ± 0.16). One-way Analysis of Variance (ANOVA) revealed significant overall differences among the groups. The use of superscript letters "a" and "b" indicates statistically significant differences between the groups. Tukey's post hoc test confirmed that MCHC levels were significantly reduced in all treatment groups (750, 1000, and 1500 mg/kg) compared to the control group ($p = 0.022$, $p = 0.008$, and $p = 0.013$, respectively). These statistical differences and

corresponding indicators suggest that the effects became more pronounced with increasing doses, highlighting the need for further studies to assess the physiological implications of these changes and their potential impact on animal health.

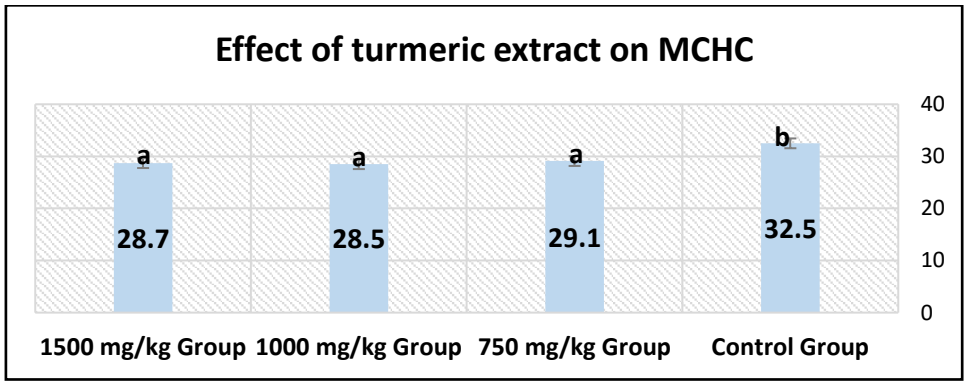

Fig. 6: Effect of *Curcuma longa* L. root extract on mean corpuscular hemoglobin concentration (MCHC) in male hamsters treated for 60 days. Tukey's test confirmed significant reductions in all treatment groups (750, 1000, and 1500 mg/kg) compared to the control group.

2. Effect of Turmeric Root Extract on White Blood Cells (WBCs) and Platelet (PLT) Indices:

Table 2 illustrates the effect of turmeric root aqueous extract (*Curcuma longa* L.) on white blood cell (WBC) and platelet parameters in male hamsters treated for 60 days.

Table 2: Effect of aqueous turmeric root extract (*Curcuma longa* L.) on white blood cells (WBCs) and platelet (PLT) indices in male hamsters treated for 60 days.

Parameter	Unit/ Type	Control (n = 8)	Turmeric extract (n=8)		
			1500 mg/kg	1000 mg/kg	750 mg/kg
WBCs (x 10^3 cells/mm^3)	Mean ± SE	6.94 ± 0.33[a]	6.73 ± 1.45[a]*	8.96 ± 1.45[a]*	9.13 ± 1.45[a]*
	% change	–	↓ 3.1%	↑ 29.0%	↑ 31.5%
Lymphocytes (%)	Mean ± SE	2.13 ± 0.11[a]	1.79 ± 0.34[a]*	3.23 ± 0.34[b]*	2.05 ± 0.34[a]*
	% change	–	↓ 16.0%	↑ 51.7%	↓ 3.8%
Monocytes (%)	Mean ± SE	0.47 ± 0.03[a]	0.88 ± 0.26[ab]*	0.94 ± 0.26[ab]*	1.41 ± 0.26[b]*
	% change	–	↑ 86.0%	↑ 100.0%	↑ 200.0%
Granulocytes (%)	Mean ± SE	4.34 ± 0.23[a]	3.98 ± 0.90[a]*	5.05 ± 0.90[a]*	5.89 ± 0.90[a]*
	% change	–	↓ 8.3%	↑ 16.4%	↑ 35.8%
PLT (x 10^6 platelet/mm^3)	Mean ± SE	263.1 ± 22.8[a]	615.0 ± 14.8[b]	610.0 ± 15.0[b]	601.8 ± 91.25[b]
	% change	–	↑ 133.8%	↑ 132.0%	↑ 110.4%
Mean platelet volume	Mean ± SE	8.36 ± 0.24[b]	6.86 ± 0.20[a]*	7.40 ± 0.20[a]*	7.13 ± 0.20[a]*
	% change	–	↓ 17.9+%	↓ 11.5%	↓ 14.7%
Platelet Distribution width	Mean ± SE	14.05 ± 0.28[a]	16.18 ± 0.28[b]*	16.91 ± 0.28[b]*	16.32 ± 0.28[b]*
	% change	–	↑ 15.1%	↑ 20.3%	↑ 16.1%
Plateletcrit	Mean ± SE	0.20 ± 0.01[a]	0.23 ± 0.06[a]*	0.37 ± 0.06[b]*	0.39 ± 0.06[b]*
	% change	–	↑ 15.0%	↑ 85.0%	↑ 95.0%

Values are presented as Mean ± Standard Error (SE ± Mean).
Different letters (a, b) indicate statistically significant differences between groups at $p < 0.05$.
Identical letters denote no significant difference between those groups.
An asterisk (*) next to the letter indicates a statistically significant difference.
Arrows (↑, ↓) denote the percentage of increase or decrease relative to the control group.

2.1. Effect of *C. longa* L. Root Extract on Total White Blood Cells (WBCs) Count:

The group treated with 750 mg/kg of turmeric root extract exhibited a numerical increase of 31.5% in total white blood cell count (9.13 ± 1.45) compared to the control group (6.94 ± 0.33). A similar trend was observed in the 1000 mg/kg group, with an increase of 29.0% (8.96 ± 1.45). In contrast, the 1500 mg/kg group showed a slight decrease of 3.1% (6.73 ± 1.45). However, one-way ANOVA and Tukey's post hoc test revealed no statistically significant differences between any of the treated groups and the control group, or among the treated groups themselves, indicating a lack of significant effect on WBC count (Fig. 7).

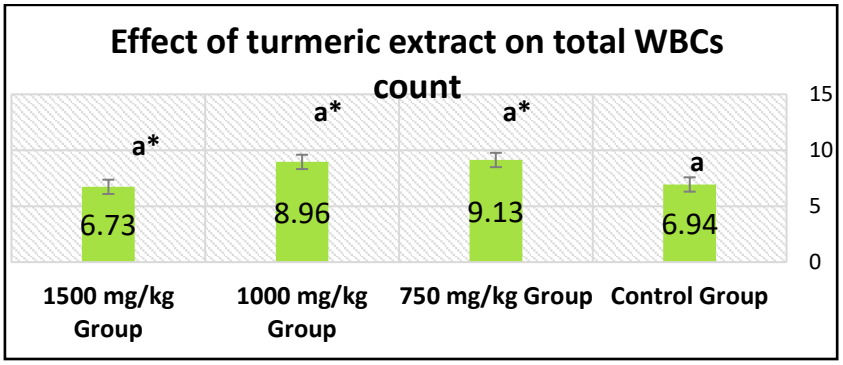

Fig. 7: Effect of *Curcuma longa* L. root extract on total white blood cells (WBCs) count in male hamsters treated for 60 days. Although a decrease was observed in the 1500 mg/kg group, Tukey's test indicated no statistically significant differences between the treated groups and the control.

2.2. Effect of *C. longa* L. Root Extract on Lymphocytes (Lymph):

As indicated by **Figure 8,** the 750 mg/kg group recorded a slight decrease in lymphocyte count (2.05 ± 0.34; −3.8%) compared to the control (2.13 ± 0.11). Conversely, the 1000 mg/kg dose resulted in a significant increase of 51.7% (3.23 ± 0.34), while the 1500 mg/kg group showed a reduction of 16.0% (1.79 ± 0.34). One-way ANOVA revealed overall significant differences, and Tukey's post hoc test confirmed that the 1000 mg/kg group had a statistically significant increase in lymphocyte count compared to the control group ($p = 0.015$), the 750 mg/kg group ($p = 0.009$), and the 1500 mg/kg group ($p = 0.001$).

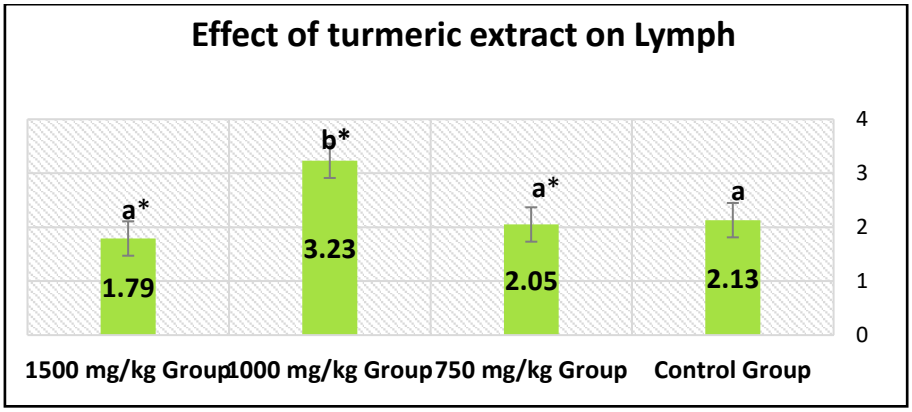

Fig. 8: Effect of *Curcuma longa* L. root extract on lymphocyte (Lymph) indices in male hamsters treated for 60 days. A notable reduction was observed in the 1500 mg/kg group, while the 1000 mg/kg group demonstrated a significant increase in lymphocyte count compared to the control group.

2.3. Effect of *C. longa* L. Root Extract on Monocytes (MID):

The 750 mg/kg treatment group showed a substantial increase of +200% in monocyte count (1.41 ± 0.26) compared to the control group (0.47 ± 0.03). The 1000 mg/kg and 1500 mg/kg groups also exhibited increases of 100% (0.94 ± 0.26) and 86.0% (0.88 ± 0.26), respectively. One-way ANOVA revealed statistically significant differences. Tukey's post hoc test confirmed that the 750 mg/kg group had a significant increase in monocyte count compared to the control group, while no other statistically significant differences were observed among the treated groups (Fig. 9).

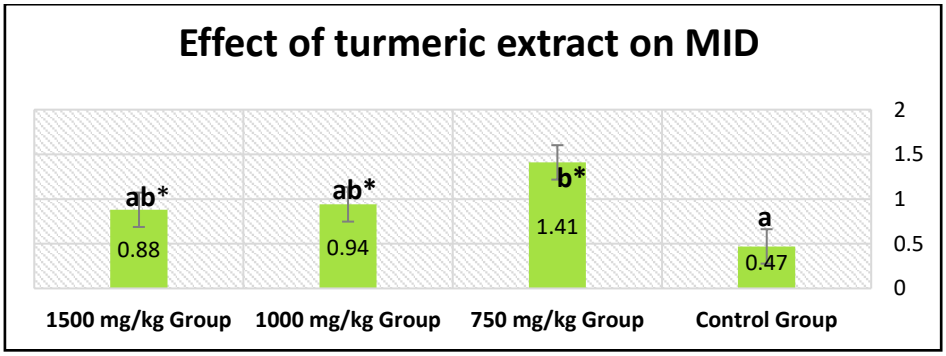

Fig. 9: Effect of *Curcuma longa* L. root extract on monocyte (MID) indices in male hamsters treated for 60 days. ANOVA showed significant differences, and Tukey's test confirmed that the 750 mg/kg group had a statistically significant increase compared to the control.

2.4. Effect of *C. longa* L. Root Extract on Granulocytes (GRAN):

Granulocyte count increased numerically in the 750 mg/kg and 1000 mg/kg groups by 35.8% (5.89 ± 0.90) and 16.4% (5.05 ± 0.90), respectively, compared to the control group (4.34 ± 0.23). Conversely, the 1500 mg/kg group exhibited a decrease of 8.3% (3.98 ± 0.90). However, all groups shared the same superscript letter ("a"), indicating no statistically significant differences. ANOVA and Tukey's test confirmed the absence of significant differences between any of the treatment groups and the control (Fig. 10).

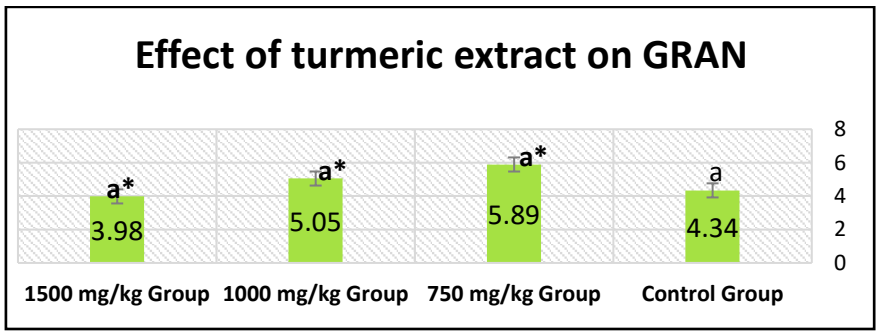

Fig. 10: Effect of *Curcuma longa* L. root extract on granulocyte (GRAN) indices in male hamsters treated for 60 days. ANOVA indicated no significant differences among the groups compared to the control.

2.5. Effect of *C. longa* L. Root Extract on Platelet (PLT) Count:

Figure 11 shows that a marked numerical increase in platelet count was observed in all treated groups compared to the control (263.1 ± 22.8). The increases were 110.4% (601.8 ± 91.25) for the 750 mg/kg group, 132.0% (610.0 ± 15.0) for the 1000

mg/kg group, and 133.8% (615.0 ± 14.8) for the 1500 mg/kg group. ANOVA revealed significant overall differences. Tukey's post hoc test confirmed statistically significant increases in platelet count for the 750 mg/kg (p = 0.038) and 1000 mg/kg groups (p = 0.004) compared to the control. However, no significant difference was found between the 1500 mg/kg group and the control (p = 0.847). Additionally, the 1000 mg/kg group showed a significant increase compared to the 1500 mg/kg group (p = 0.032).

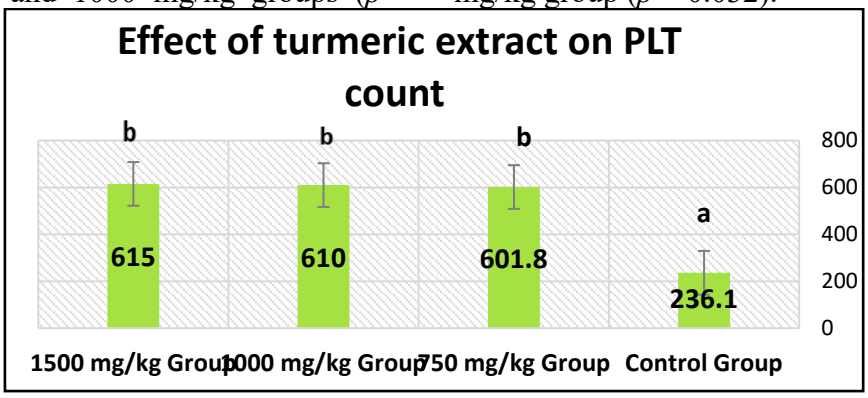

Fig. 11: Effect of *Curcuma longa* L. root extract on platelet (PLT) indices in male hamsters treated for 60 days. All treatment groups showed notable numerical increases compared to the control group.

2.6. Effect of *C. longa* L. Root Extract on Mean Platelet Volume (MPV):

As shown by **Figure 12,** a statistically and numerically significant reduction in mean platelet volume (MPV) was observed in all treated groups compared to the control group (8.36 ± 0.24). The treatment groups recorded lower values: 7.13 ± 0.20 (750 mg/kg), 7.40 ± 0.20 (1000 mg/kg), and 6.86 ± 0.20 (1500 mg/kg). One-way ANOVA showed highly significant differences. Tukey's test confirmed that all treated groups exhibited statistically significant decreases in MPV compared to the control (p < 0.001 for all comparisons).

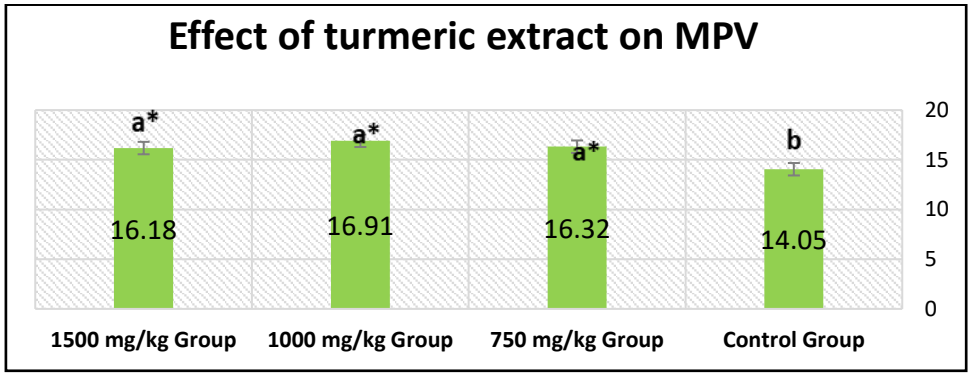

Fig. 12: Effect of *Curcuma longa* L. root extract on mean platelet volume (MPV) in male hamsters treated for 60 days. A clear and significant reduction in MPV was observed in all treated groups compared to the control.

2.7. Effect of *C. longa* L. Root Extract on Platelet Distribution Width (PDW):

The platelet distribution width (PDW) values increased in all treated groups by a range of 15.1% to 20.3% compared to the control group (14.05 ± 0.28). One-way ANOVA revealed highly significant differences (**Fig. 13**). Tukey's HSD post hoc test confirmed that all treatment groups (750, 1000, and 1500 mg/kg) exhibited statistically significant increases in PDW compared to the control group (p < 0.001 for all comparisons).

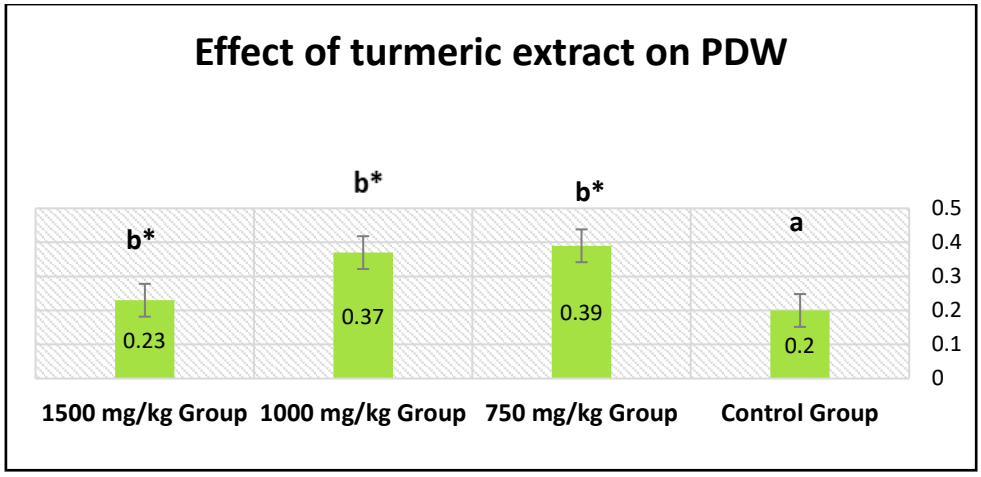

Fig. 13: Effect of *Curcuma longa* L. root extract on platelet distribution width (PDW) in male hamsters treated for 60 days. All treatment groups showed an increase in PDW values ranging from 15.1% to 20.3% compared to the control group.

2.8. Effect of *C. longa* L. Root Extract on Plateletcrit (PCT):

Numerical increases in plateletcrit (PCT) were observed in the 750 mg/kg and 1000 mg/kg groups, recording values of 0.39 ± 0.06 and 0.37 ± 0.06, respectively, corresponding to increases of 95.0% and 85.0% compared to the control group (0.20 ± 0.01). In contrast, the 1500 mg/kg group recorded a value of 0.23 ± 0.06, representing a smaller increase of 15.0%. ANOVA showed significant overall differences (Fig. 14). Tukey's test confirmed that the 750 mg/kg (p = 0.020) and 1000 mg/kg (p = 0.041) groups had statistically significant increases in PCT compared to the control group. However, the 1500 mg/kg group did not differ significantly from the control (p = 0.936).

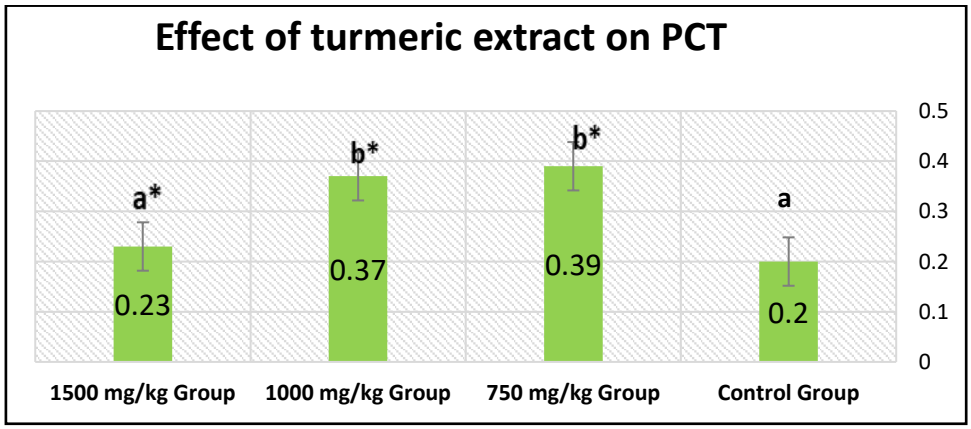

Fig. 14: Effect of *Curcuma longa* L. root extract on plateletcrit (PCT) in male hamsters treated for 60 days. Notable numerical increases were observed in the 750 mg/kg and 1000 mg/kg groups, while the 1500 mg/kg group showed only a slight increase compared to the control group.

3. Effect of *C. longa* L. Root Extract on Liver Function Biomarkers:

Table 3 and Figures 15, 16, 17 & 18 illustrate the effect of turmeric root aqueous extract (*Curcuma longa* L.) on Liver function biomarkers in male hamsters treated for 60 days.

Table 3: Effect of Aqueous extract of *Curcuma longa* L. roots on liver function biomarkers in male hamsters treated for 60 days.

Parameter	Unit/ Type	Control (n=8)	Turmeric extract (n=8)		
			1500 mg/kg	1000 mg/kg	750 mg/kg
AST (U/L)	Mean ± SE	83.8 ± 10.3[a]	201.8 ± 92.2[a]	208.7 ± 92.2[a]	233.5 ± 92.2[a]
	% change	–	↑ 140.9%	↑ 149.2%	↑ 178.7%
ALT (U/L)	Mean ± SE	57.6 ± 10.4[a]	246.6 ± 80.4[a]*	116.0 ± 80.4[a]	140.7 ± 80.4[a]
	% change	–	↑ 327.8%	↑ 101.3%	↑ 144.2%
T. Bil (mg/dl)	Mean ± SE	0.255 ± 0.04[a]	0.168 ± 0.04[a]	0.220 ± 0.04[a]	0.160 ± 0.04[a]
	% change	–	↓ 34.1%	↓ 11.5%	↓ 37.3%
ALB (mg/dl)	Mean ± SE	4.25 ± 0.45[a]	4.10 ± 0.45[a]	3.25 ± 0.45[a]	3.85 ± 0.45[a]
	% change	–	↓ 3.5%	↓ 23.5%	↓ 9.4%

Values are presented as Mean ± Standard Error (SE ± Mean).
Different letters (a, b) indicate statistically significant differences between groups at $p < 0.05$.
Identical letters denote no significant difference between those groups.
An asterisk (*) next to the letter indicates a statistically significant difference.
Arrows (↑, ↓) denote the percentage of increase or decrease relative to the control group.

The results of Table 3 suggest that turmeric root extract influences certain liver function biomarkers. Significant increases in AST and ALT levels were observed, with a statistically significant elevation in ALT at the high dose (1500 mg/kg), potentially indicating hepatotoxicity or liver stress at this concentration. In contrast, no significant changes were found in total bilirubin or albumin levels, reflecting the relative stability of these indicators. These findings recommend caution when using high doses of the extract and emphasize the need for careful monitoring of liver function in future studies.

3.1. Effect of *C. longa* L. Root Extract on Aspartate Aminotransferase (AST) Activity:

The groups treated with turmeric extract exhibited substantial numerical increases in AST levels compared to the control group (83.8 ± 10.3). The increase reached 178.7% in the 750 mg/kg group (233.5 ± 92.2), 149.2% in the 1000 mg/kg group (208.7 ± 92.2), and 140.9% in the 1500 mg/kg group (201.8 ± 92.2). Despite these large numerical increases, analysis of variance (ANOVA) and Tukey's test showed no statistically significant differences between any of the treated groups and the control, nor among the treated groups themselves (Fig. 15).

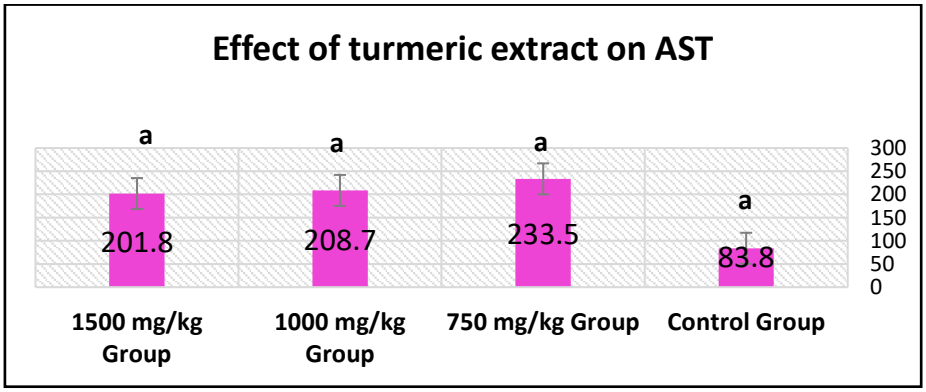

Fig. 15: Effect of *Curcuma longa* L. root extract on the mean aspartate aminotransferase (AST) activity in male hamsters treated for 60 days. No statistically significant differences were observed between the treated groups and the control.

3.2. Effect of *C. longa* L. Root Extract on Alanine Aminotransferase (ALT) Activity:

ALT activity showed a pattern similar to AST, with noticeable numerical increases. ALT levels increased by 144.2% in the 750 mg/kg group (140.7 ± 80.4), 101.3% in the 1000 mg/kg group (116.0 ± 80.4), and 327.8% in the 1500 mg/kg group (246.6 ± 80.4), compared to the control group (57.6 ± 10.4). However, ANOVA revealed no overall statistically significant differences among the groups (Fig. 16).

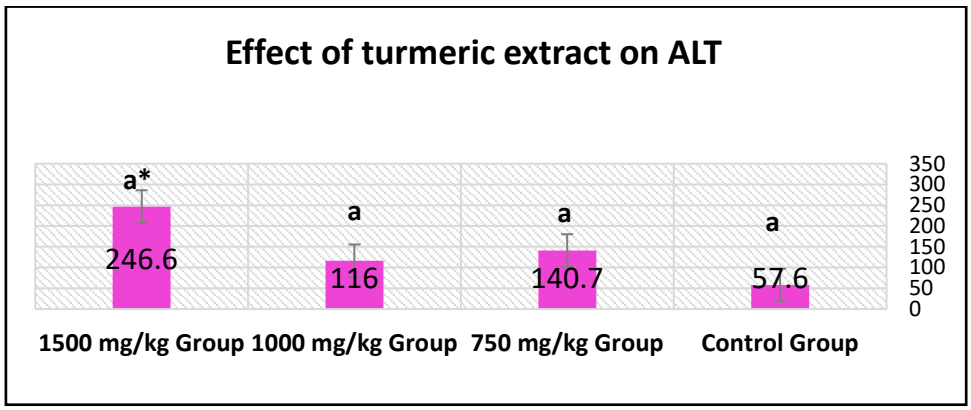

Fig. 16: Effect of *Curcuma longa* L. root extract on mean alanine aminotransferase (ALT) activity in male hamsters treated for 60 days. No statistically significant differences were found between the treated and control groups.

3.3. Effect of *C. longa* L. Root Extract on Total Bilirubin (T. Bil) Levels:

A numerical decrease in total bilirubin levels was observed in all treated groups compared to the control. The decreases were 37.3% in the 750 mg/kg group (0.160 ± 0.04), 11.5% in the 1000 mg/kg group (0.22 ± 0.04), and 34.1% in the 1500 mg/kg group (0.168 ± 0.04), compared to the control (0.255 ± 0.04). However, ANOVA and Tukey's test showed no statistically significant differences among the groups (**Fig. 17**).

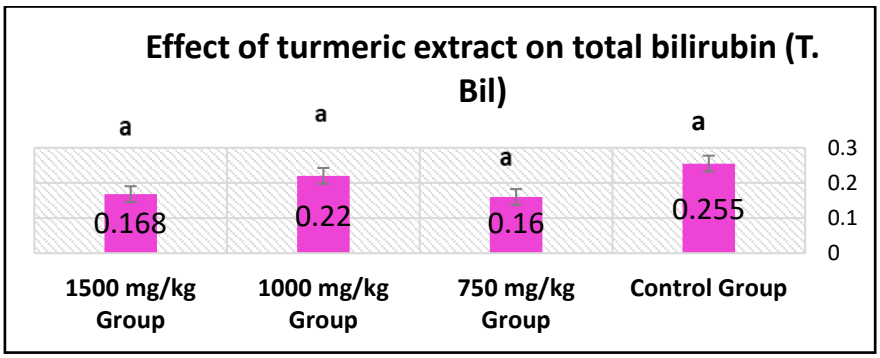

Fig. 17: Effect of *Curcuma longa* L. root extract on mean total bilirubin (T. Bil) levels in male hamsters treated for 60 days. No statistically significant differences were detected.

3.4. Effect of *C. longa* L. Root Extract on Albumin (ALB) Levels:

A slight decrease in albumin levels was noted in the treated groups: 9.4% in the 750 mg/kg group, 23.5% in the 1000 mg/kg group, and 3.5% in the 1500 mg/kg group, compared to the control. The repeated appearance of the same superscript letter "a" indicates no statistically significant differences among the groups, suggesting that the extract had no significant effect on albumin levels (Fig. 18).

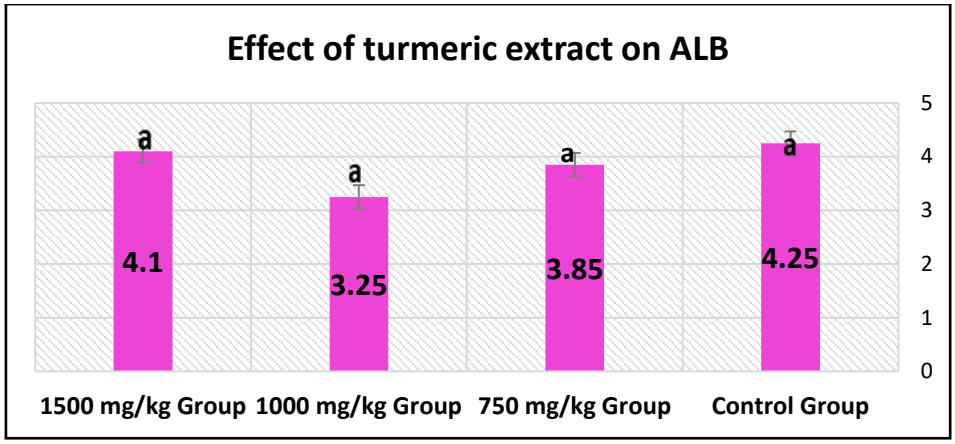

Fig. 18: Effect of *Curcuma longa* L. root extract on mean albumin (ALB) levels in male hamsters treated for 60 days. No statistically significant differences were found among the groups.

4. Effect of *C. longa* L. Root Extract on Kidney Function Indicators:

Table 4 and Figures 19 & 20 show the effect of turmeric extract on kidney function indicators.

Table 4: Effect of *Curcuma longa* L. root extract on kidney function indicators {blood urea (BU) and creatinine (Crea)} in male hamsters treated for 60 days

Parameter	Unit/ Type	Control (n=8)	Turmeric extract (n=8)		
			1500 mg/kg	1000 mg/kg	750 mg/kg
Blood urea (mg/dl)	Mean ± SE	25.4 ± 3.91a	26.78 ± 3.91a	42.3 ± 3.9b*	30.2 ± 3.91a
	% change	–	↑ 5.1%	↑ 66.1%*	↑ 18.7%
Creatinine (mg/dl)	Mean ± SE	0.45 ± 0.15a	0.39 ± 0.15a	0.44 ± 0.15a	0.47 ± 0.15a
	% change	–	↓ 13.3%	↓ 2.2%	↑ 4.4%

Values are expressed as mean ± standard error (SE ± Mean).
Different letters (a, b) indicate significant differences between groups at $p < 0.05$.
Same letters indicate no significant difference between those groups.
The asterisk (*) indicates statistical significance.
Arrows ↑ ↓ indicate percentage increase or decrease compared to the control group.

4.1. Effect of *C. longa* L. Root Extract on Blood Urea (BU) Concentration:

As shown in Figure 19, an increase in the average urea level was observed in the treated groups. The 750 mg/kg group recorded an 18.7% increase (30.2 ± 3.91) compared to the control group (25.4 ± 3.91). The 1000 mg/kg group showed a significant increase of 66.1% (42.3 ± 3.91). Meanwhile, the 1500 mg/kg group showed a slight increase of 5.1% (26.78 ± 3.91). ANOVA and Tukey tests showed that the 1000 mg/kg group had a statistically significant increase in urea levels compared to the control group ($p = 0.001$), the 750 mg/kg group ($p = 0.022$), and the 1500 mg/kg group ($p = 0.002$).

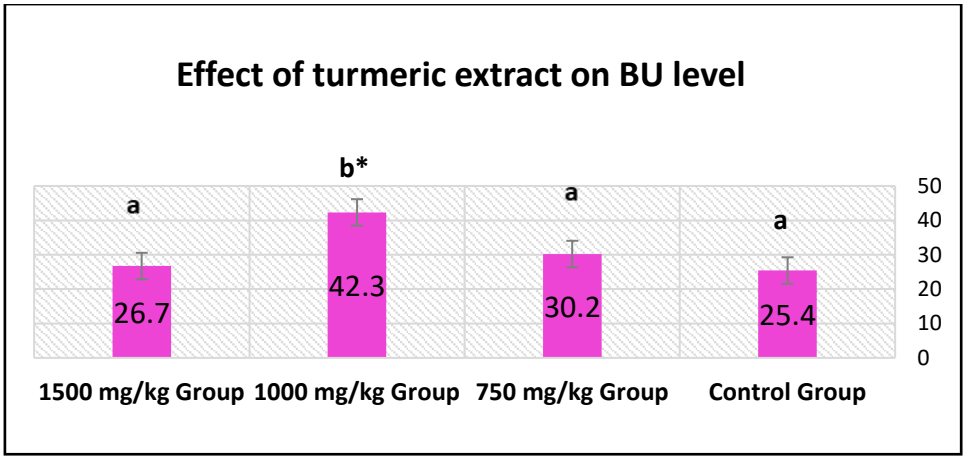

Fig. 19: Effect of *Curcuma longa* L. root extract on the average blood urea (BU) activity level in male hamsters treated for 60 days, showing a statistically significant increase in urea levels compared to the 750 mg/kg and 1500 mg/kg groups.

4.2. Effect of *C. longa* L. Root Extract on Creatinine (Crea) Concentration:

Regarding creatinine, the results in Figure 20 showed a slight numerical variation between groups. The 750 mg/kg group recorded a non-significant increase of 4.4% (0.47 ± 0.15) compared to the control group (0.45 ± 0.15). The values in the 1000 and 1500 mg/kg groups were 0.44 ± 0.15 and 0.39 ± 0.15, respectively, with relative decreases of 2.2% and 13.3%. These differences were not statistically significant in ANOVA or Tukey tests. The results of Table 4 indicate that Curcuma longa root extract significantly affects urea levels, especially at the medium dose (1000 mg/kg), which may reflect an impact on kidney function or protein metabolism. However, no significant effects were observed on creatinine levels, indicating relative stability in kidney function regarding this indicator. Based on these results, further studies are recommended to evaluate the safety of the extract and its potential effects on the kidneys, especially at medium doses.

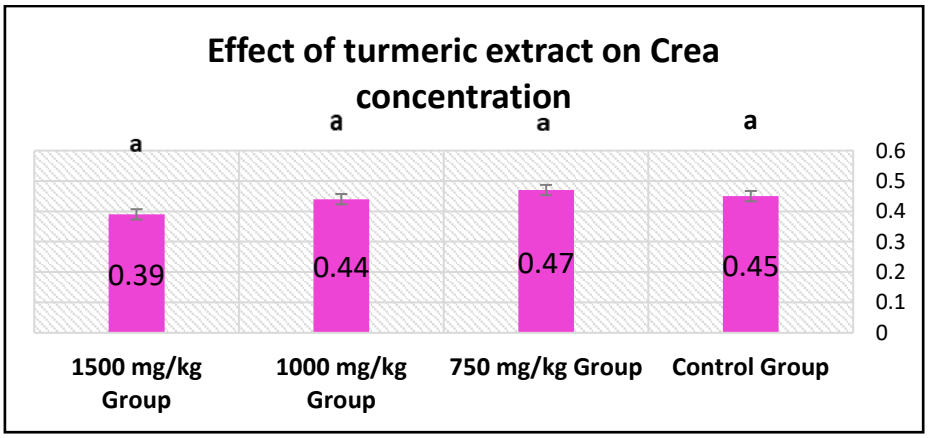

Fig. 20: Effect of *Curcuma longa* L. root extract on creatinine (Crea) concentration in male hamsters treated for 60 days, with no statistically significant differences observed between any treated groups and the control or among themselves.

DISCUSSION

The results of this study demonstrated that chronic administration of turmeric root extract (*Curcuma longa L.*) at doses of 750, 1000, and 1500 mg/kg for 60 days caused notable effects on hematological, immunological, hepatic, and renal parameters in male hamsters. These effects were dose-

and time-dependent, highlighting the importance of evaluating dosage and exposure duration in toxicological and pharmacological studies.

Red blood cell (RBC) count increased by 22.8% in the 750 mg/kg dose group, while the increase was less pronounced in the 1000 and 1500 mg/kg groups, with no statistically significant differences. This pattern suggests that lower doses may stimulate erythropoiesis over time by enhancing bone marrow activity and protecting red cells from oxidative stress due to curcumin's antioxidant properties (Samarghandian *et al.,* 2014). In contrast, higher doses with prolonged exposure may inhibit iron absorption or induce metabolic stress, leading to decreased erythrocyte production (Hussain *et al.,* 2015). Hemoglobin (Hb) and hematocrit (HCT) levels decreased in most dose groups, except for the highest dose (1500 mg/kg), which showed a significant increase in HCT. The decline in Hb after 60 days may reflect a cumulative effect on iron stores or hemoglobin synthesis. The elevated HCT at 1500 mg/kg may indicate an increase in cell volume or blood viscosity (Manjunatha & Srinivasan, 2007). Mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC) all decreased significantly with increasing dose, especially after 60 days, suggesting a microcytic hypochromic anemia pattern. This may be linked to the chronic effects of curcumin on iron absorption (Ganga *et al.,* 2013; Hussain *et al.,* 2015).

In addition, the total white blood cell (WBC) count increased at low and moderate doses, but decreased at the high dose, reflecting a biphasic effect of curcumin immunostimulatory at moderate doses and immunosuppressive at higher doses (Sharma *et al.,* 2010). A significant increase in lymphocytes at 1000 mg/kg after 60 days suggests this dose may optimize adaptive immune stimulation (Antony *et al.,* 2015), whereas reductions in other doses may reflect either weak stimulation or immune-suppression (Jagetia & Aggarwal, 2007). Monocytes showed a marked increase at 750 mg/kg, indicating activation of innate immune responses (Bruck *et al.,* 2016).

In this study, all treated groups showed significant increases in platelet count (PLT), exceeding 110% after 60 days, accompanied by a decrease in mean platelet volume (MPV) and an increase in platelet distribution width (PDW). This pattern suggests enhanced production of small-sized platelets from the bone marrow in response to chronic stimulation, possibly a protective mechanism to enhance coagulation or inflammatory response (Srivastava *et al.,* 1985). Processed forms of curcumin (e.g., nanocurcumin) enhance platelet production through activation of ERK and JNK signaling pathways. A recent study reported an improvement in platelet count following treatment (Mortazavi Farsani *et al.,* 2020). Some reviews (e.g., Hassani *et al.,* 2023). also indicated that the curcumin has strong antiplatelet effects, modulating inflammatory and exosomal responses

Liver enzymes (AST and ALT) showed noticeable elevations. ALT was significantly elevated in the 1500 mg/kg group, suggesting possible hepatic stress or cell injury following chronic administration. As shown in the study by Soleimani *et al.* (2018), increased ALT is a sensitive marker of liver damage. However, no significant changes in total bilirubin or albumin were observed, indicating the liver retained much of its synthetic and detoxifying function in most cases.

Blood urea (BU) showed a significant increase at 1000 mg/kg (+66.1%), while creatinine remained statistically unchanged. This may indicate that potential renal effects are more related to increased protein breakdown or changes in nitrogen metabolism rather than impaired glomerular filtration (Panda *et al.,* 2013). These findings suggest that the hematological, immunological, hepatic, and renal effects of turmeric root extract are strongly dependent on dose and exposure duration. Low and moderate doses over 60 days appeared beneficial in boosting immunity and

increasing RBC and platelet counts, whereas high doses were linked to signs of liver stress and changes in blood parameters. This emphasizes the need to determine an optimal dose and safe duration of curcumin use to prevent potential adverse effects.

Conclusions

This study provided a comprehensive evaluation of the chronic effects of whole turmeric root extract on hematological, hepatic, and renal parameters in male hamsters over 60 days, addressing key knowledge gaps regarding long-term exposure and escalating doses. Low and moderate doses (750 and 1000 mg/kg) demonstrated beneficial effects on specific immune markers, including significant increases in lymphocytes at 1000 mg/kg and monocytes at 750 mg/kg. A notable rise in platelet count was seen across most treatment groups, along with a decrease in mean platelet volume and an increase in platelet distribution width. High doses (1500 mg/kg) were associated with blood changes indicative of microcytic hypochromic anaemia, with significant reductions in MCV, MCH, and MCHC, particularly at higher doses. Liver enzymes (AST and ALT) exhibited numerical increases, suggesting potential hepatic stress, although Tukey's post hoc test did not consistently confirm statistical significance. A significant increase in blood urea level was observed at 1000 mg/kg, whereas creatinine levels showed no statistically significant changes. This points to a metabolic effect on kidney function rather than a direct impact on glomerular filtration. These results indicate that turmeric extract may offer hematological and immunomodulatory benefits at moderate doses. However, chronic exposure to higher doses may lead to hepatic stress and undesirable blood changes, emphasizing the need to define a safe and effective dosage regimen.

Recommendation

Further investigations were needed to clarify the relationship between dose and time. Understanding the dose-time relationship is crucial for identifying physiological responses that may initially appear benign but evolve into gradual toxicity over time.

Declarations:

Ethical Approval and Consent to Participate: Protocols for collection of samples as well as the experiment plan and all methods were performed in accordance with the guidelines and regulations of Al-Asmarya Islamic University.

Competing interests: The authors have no competing interests to declare that are relevant to the content of this article.

Availability of Data and Materials: All data generated or analyzed during this study are included in this published article.

Authors' Contributions: Authors equally shared in the data collection, wrote, revised the manuscript, and approved its publication.

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