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Article

Effects of *Curcuma longa* Extract on Hepatic and Renal Biochemical Markers in Paracetamol-Induced Rats

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Abstract. Hepatic and renal disorders are major public health concerns. *Curcuma longa* contains bioactive compounds with antioxidant and anti-inflammatory properties that may improve hepatic and renal biochemical markers. This study evaluated these effects in paracetamol-induced rats. The extract was prepared by maceration using 96% ethanol. Twenty-four *Rattus norvegicus* were assigned to four groups (n = 6): a paracetamol-only control (PC) and three groups receiving extract at 300, 500, or 900 mg/kg body weight. Following three days of acclimatization, all rats received oral paracetamol (750 mg/kg) on day 4. Extract treatment was administered on days 5–11, and blood was collected on day 12. Biochemical markers were analyzed using one-way ANOVA followed by Tukey's test. Compared with PC, the 900 mg/kg group showed lower AST (193.67 versus 96.67 U/L) and ALT (145.33 versus 61.83 U/L; $p < 0.05$). Total/direct bilirubin decreased from 1.295/0.548 to 0.545/0.208 mg/dL ($p < 0.001$), while urea and creatinine decreased from 60.83 to 35.66 mg/dL and 1.23 to 0.71 mg/dL, respectively. The greatest reductions occurred at 900 mg/kg. These findings suggest beneficial effects on hepatic and renal biochemical markers. However, the absence of a normal healthy control group limits interpretation of injury severity and whether treatment restored markers to normal levels

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1. Introduction

The liver and kidneys are essential organs involved in metabolic regulation, detoxification, biotransformation, and the elimination of endogenous and exogenous compounds. Disturbances in these organs can be reflected by alterations in circulating biochemical markers. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are widely used biomarkers of hepatocellular injury, while bilirubin provides complementary information regarding hepatic functional and excretory disturbances [1]. Renal biochemical assessment commonly includes serum urea and creatinine as conventional markers of renal function. Creatinine is widely used as an endogenous marker for assessing glomerular filtration, whereas urea is a nitrogenous waste product eliminated through the kidneys [2]. Consequently, simultaneous assessment of hepatic and renal biochemical markers may provide a broader perspective on alterations affecting both organ systems.

Oxidative stress and inflammation are important mechanisms underlying cellular injury in both the liver and kidneys. An imbalance between reactive oxygen species production and antioxidant defenses may contribute to cellular dysfunction, while activation of inflammatory pathways can further amplify tissue injury. These processes are particularly relevant in experimental models of chemically induced organ injury and provide a biological basis for investigating compounds with antioxidant and anti-inflammatory properties. Excessive acetaminophen exposure is widely used as an experimental model of hepatic injury and has been associated with impaired antioxidant capacity, inhibition of Nrf2-mediated antioxidant signaling, activation of inflammatory pathways, and marked increases in circulating AST and ALT [3]. Recent experimental evidence also indicates that natural compounds possessing antioxidant and anti-inflammatory properties can attenuate acetaminophen-associated cellular and biochemical alterations by suppressing oxidative stress and inflammatory responses [4].

A single dose of paracetamol at 750 mg/kg body weight has been employed experimentally to induce acute hepatotoxicity in rats, providing a basis for evaluating hepatic biochemical alterations following toxic exposure [5]. Paracetamol-induced toxicity is associated with the formation of the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI), glutathione depletion, mitochondrial dysfunction, and oxidative stress, with potential renal involvement [6].

Among medicinal plants with potential antioxidant and anti-inflammatory activities, *Curcuma longa* L. (turmeric) has received considerable scientific attention. *C. longa* contains numerous bioactive constituents, with curcuminoids representing important bioactive components and curcumin being the most extensively investigated constituent [7]. In addition to curcumin, other constituents, including demethoxycurcumin, bisdemethoxycurcumin, and turmerone, may contribute to the antioxidant and anti-inflammatory activities of whole *C. longa* extract [8].

The pharmacological properties attributed to *C. longa* and curcumin include antioxidant and anti-inflammatory activities, which provide a biological basis for their investigation in conditions involving oxidative and inflammatory disturbances. A systematic review and dose-response meta-analysis of randomized controlled trials demonstrated favorable effects of turmeric/curcumin supplementation on several inflammatory and oxidative stress biomarkers, including reductions in C-reactive protein, tumor necrosis factor-α, interleukin-6, and malondialdehyde, together with changes in antioxidant status [9].

Evidence regarding the effects of turmeric and curcumin on hepatic biochemical parameters has also continued to accumulate. A systematic review and dose-response meta-analysis of randomized controlled trials reported significant reductions in circulating ALT and AST following turmeric/curcumin supplementation, although considerable heterogeneity among studies was observed [10]. Experimental evidence using whole turmeric extract has similarly demonstrated modulation of hepatic biochemical parameters, oxidative stress, antioxidant defenses, and inflammatory responses [11].

These findings suggest that the biological effects of turmeric are not limited to isolated curcumin and support further evaluation of whole *C. longa* extract under controlled experimental conditions. Previous experimental research has evaluated the hepatoprotective activity of *C. longa* extract at doses of 200 and 400 mg/kg body weight [12]. These findings provide a reference for investigating graded doses of 300 and 500 mg/kg, while 900 mg/kg represents a higher exploratory dose intended to assess dose-associated biochemical responses.

Evidence regarding renal biochemical responses to curcumin is comparatively less consistent. A systematic review and meta-analysis of 14 studies demonstrated an overall significant improvement in serum creatinine following oral curcumin supplementation, whereas the effect on blood urea nitrogen varied according to intervention conditions, including treatment duration [13]. Previous experimental studies have similarly demonstrated that curcumin, a major bioactive constituent of *C. longa*, can attenuate paracetamol-associated alterations in both hepatic and renal biochemical parameters in experimental animals [14-15]. Collectively, these findings indicate potential effects of turmeric and curcumin on biochemical parameters related to both hepatic and renal function, although the magnitude and pattern of these responses may vary according to the preparation, dose, duration of exposure, and experimental conditions.

Despite the extensive literature on turmeric and curcumin, important gaps remain in understanding their biochemical effects across different experimental conditions. Previous studies have frequently investigated isolated curcumin, specific clinical conditions, or hepatic and renal outcomes separately. Whole *C. longa* extract contains curcumin together with other curcuminoids and phytochemical constituents, and its biological activity may differ from that of isolated curcumin because other constituents may contribute to the overall biological effects of the extract. Furthermore, evidence directly comparing graded doses of whole *C. longa* extract while simultaneously evaluating hepatic and renal biochemical parameters under the same experimental conditions remains limited. Consequently, evaluating graded doses of whole *C. longa* extract may provide additional evidence regarding dose-associated changes in hepatic and renal biochemical markers.

We hypothesized that whole *C. longa* extract would improve hepatic and renal biochemical markers in paracetamol-induced rats, with greater improvements at higher doses. Therefore, the present study aimed to evaluate the effects of whole *C. longa* extract administered at doses of 300, 500, and 900 mg/kg body weight on hepatic biochemical markers (AST, ALT, total bilirubin, and direct bilirubin) and renal biochemical markers (urea and creatinine) in paracetamol-induced rats.

2. Method

2.1 Research Design and Experimental Animals

This quantitative experimental study used a post-test-only control group design and was conducted at the Animal House Laboratory, Universitas Perintis Indonesia. Twenty-four male *Rattus norvegicus*, aged 8–12 weeks and weighing 190–210 g, were allocated to four groups (n = 6 per group). All groups received paracetamol at 750 mg/kg body weight (BW). The positive control group (PC) received no *Curcuma longa* extract, whereas groups P1, P2, and P3 received the extract at 300, 500, and 900 mg/kg BW, respectively. All animals were acclimatized for three days before induction and had access to food and drinking water during acclimatization.

2.2 Preparation of *Curcuma longa* Extract

Fresh *Curcuma longa* rhizomes (3 kg) were washed to remove adhering soil and other impurities, cut into small pieces, and dried under direct sunlight for three days. The dried rhizomes were ground using a mortar and pestle to obtain a coarse powder. A total of 100 g of the powder was macerated in 96% ethanol at a solid-to-solvent ratio of 1:10 (w/v) for three days with periodic stirring. The mixture was filtered, and the filtrate was concentrated using a rotary evaporator at 40°C to obtain a

concentrated extract. The extract was used for administration to the treatment groups at the designated doses [16].

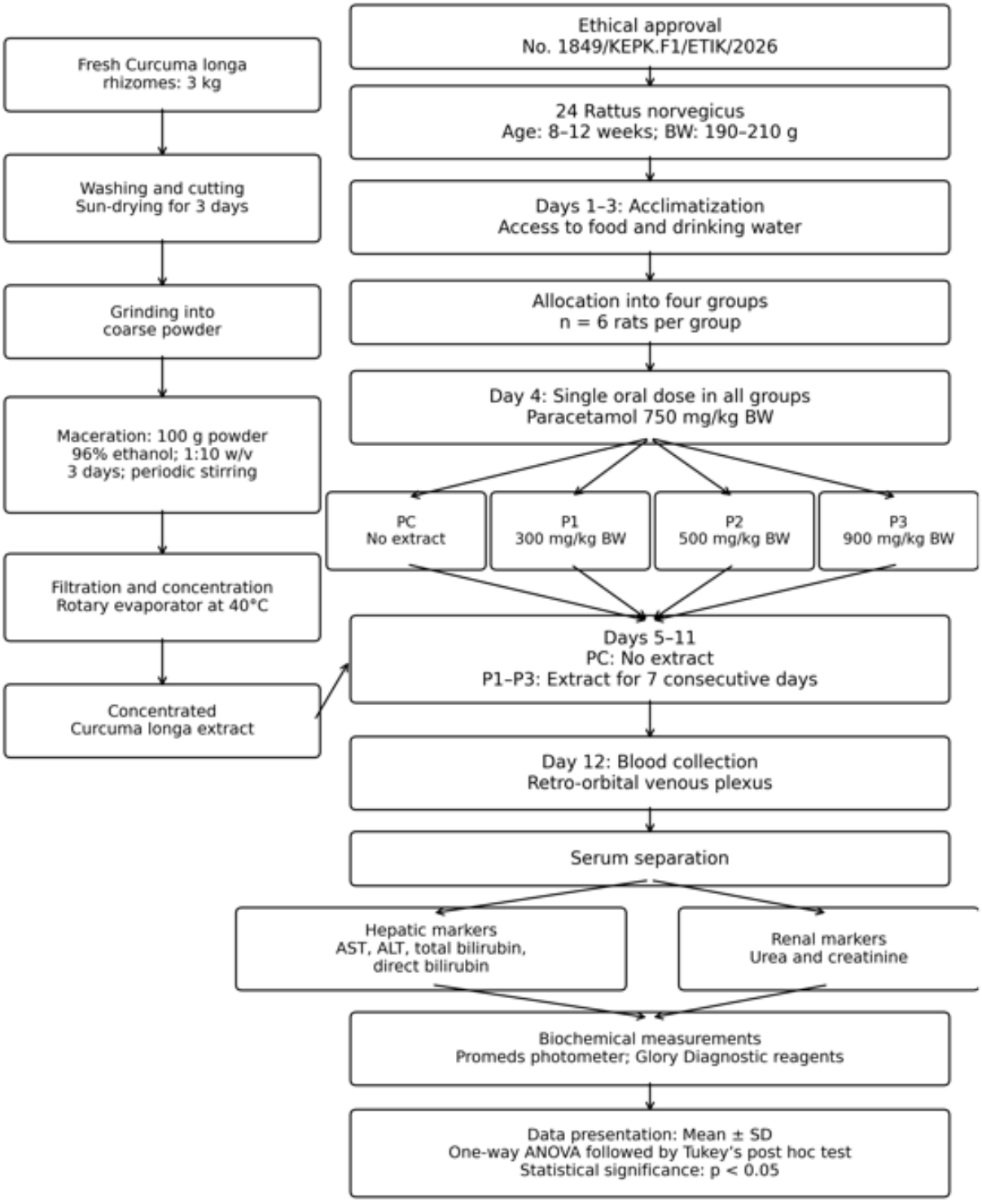


Figure 1. Flowchart of Curcuma longa extract preparation and experimental procedures

2.3 Paracetamol Induction and *Curcuma longa* Extract Administration

The experimental period lasted 12 days. Following acclimatization on days 1–3, all rats received a single oral dose of paracetamol (750 mg/kg BW) on day 4 [17]. Groups P1, P2, and P3 then received *C. longa* extract at 300, 500, and 900 mg/kg BW, respectively, on days 5–11, for seven consecutive days. The PC group received no extract. Blood samples were collected on day 12 for assessment of hepatic and renal biochemical markers.

2.4 Blood Collection and Biochemical Analysis

On day 12, blood samples were collected from the retro-orbital venous plexus of the rats. Serum was separated from the blood samples and analyzed for aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, direct bilirubin, urea, and creatinine. Measurements were performed using a Promeds photometer and Glory Diagnostic reagents, according to the reagent manufacturer's instructions. The catalog number provided for the reagents was GD-POT025. The resulting values were used to compare hepatic and renal biochemical markers among the four groups.

2.5 Statistical Analysis

Data were expressed as mean ± standard deviation (SD). Differences among the four groups were assessed using one-way analysis of variance (ANOVA), followed by Tukey's post hoc test for pairwise comparisons. Statistical significance was set at $p < 0.05$.

2.6 Ethical Approval

This study was approved by the Health Research Ethics Committee of Universitas Perintis Indonesia (Ethical Approval No. 1849/KEPK.F1/ETIK/2026; Protocol No. 26-07-2239) on July 24, 2026. All procedures involving animals were conducted in accordance with the ethical principles and guidelines for animal research.

3. Results and Discussion

A total of 24 rats were included in the analysis, with six rats in each group. Hepatic and renal biochemical markers were assessed after the seven-day intervention. The mean ± SD values for each group, together with the overall *p*-values from one-way ANOVA, are presented in Table 1.

Table 1. Hepatic and Renal Biochemical Markers in Paracetamol-Induced Rats Following *Curcuma longa* Extract Administration

Biochemical marker	PC (n = 6) Mean ± SD	P1 (n = 6) Mean ± SD	P2 (n = 6) Mean ± SD	P3 (n = 6) Mean ± SD	ANOVA *p*-value
AST (U/L)	193.67 ± 12.85[a]	158.17 ± 9.91[b]	125.00 ± 9.14[c]	96.67 ± 7.09[d]	<0.001
ALT (U/L)	145.33 ± 8.82[a]	113.17 ± 7.57[b]	84.33 ± 6.47[c]	61.83 ± 5.19[d]	<0.001
Total bilirubin (mg/dL)	1.295 ± 0.090[a]	1.047 ± 0.078[b]	0.775 ± 0.071[c]	0.545 ± 0.056[d]	<0.001
Direct bilirubin (mg/dL)	0.548 ± 0.043[a]	0.425 ± 0.033[b]	0.310 ± 0.032[c]	0.208 ± 0.029[d]	<0.001
Urea (mg/dL)	60.83 ± 4.17[a]	51.00 ± 3.16[b]	42.00 ± 2.61[c]	35.67 ± 2.16[d]	<0.001
Creatinine (mg/dL)	1.232 ± 0.074[a]	1.028 ± 0.062[b]	0.852 ± 0.054[c]	0.713 ± 0.049[d]	<0.001

SD: standard deviation. The ANOVA p-value indicates the overall difference among the four groups. Within each row, different superscript letters (a–d) indicate significant differences between groups according to Tukey's post hoc test ($p < 0.05$). PC: paracetamol-only positive control; P1, P2, and P3: paracetamol followed by 300, 500, and 900 mg/kg body weight of *C. longa* extract, respectively.

As shown in Table 1, the mean values of AST, ALT, total bilirubin, direct bilirubin, urea, and creatinine decreased progressively from the paracetamol-only positive control group (PC) through P1 and P2 to P3, which received 900 mg/kg body weight of *Curcuma longa* extract. All six markers differed significantly among the four groups (one-way ANOVA, all $p < 0.001$), and Tukey's post hoc test showed significant differences between every pair of groups for each marker, as indicated by the different letters within each row. These findings show a dose-associated pattern across the tested extract doses, with the lowest mean values consistently observed in P3. Previous experimental studies have also reported that curcumin-related interventions attenuated acetaminophen-associated changes in hepatic aminotransferases, oxidative stress measures, urea, and creatinine [18-19].

The significant reductions in AST and ALT observed in the present study are particularly relevant because increased circulating aminotransferase activities are commonly associated with hepatocellular injury [20]. Paracetamol toxicity results in hepatocellular injury accompanied by leakage of intracellular enzymes into the circulation, leading to increased AST and ALT levels [21]. In the present study, both enzymes were progressively lower from PC through P1 and P2 to P3, and all pairwise differences were statistically significant. The present findings are consistent with Zhai et al. (2024), who demonstrated that acetaminophen exposure increased serum AST and ALT levels in mice, whereas co-treatment with curcumin and berberine significantly attenuated these elevations. The combined treatment also suppressed inflammatory responses, suggesting that modulation of inflammation may contribute to the improvement in hepatic biochemical alterations [22-23].

A hydroethanolic *Curcuma longa* extract was evaluated at doses of 200 and 400 mg/kg body weight in paracetamol-induced rats. The reduction in ALT was greater at 400 mg/kg body weight, whereas the reductions in AST were not statistically significant [24]. The progressively lower AST and ALT values across the treatment groups are consistent with a meta-analysis reporting reductions in both enzymes following curcumin supplementation in patients with fatty liver disease [25]. A review of acetaminophen-induced liver injury further suggests that curcumin may limit oxidative stress and support glutathione availability, although these mechanisms were not measured in the present study [26].

The observed reductions in total and direct bilirubin complement the aminotransferase findings. Bilirubin is influenced by hepatic uptake, conjugation, and biliary excretion; consequently, alterations in circulating bilirubin can provide additional information regarding hepatic functional disturbances. In this study, total bilirubin decreased from 1.295 ± 0.090 mg/dL in PC to 0.545 ± 0.056 mg/dL in P3, while direct bilirubin decreased from 0.548 ± 0.043 to 0.208 ± 0.029 mg/dL. The reductions in total and direct bilirubin observed in the present study are consistent with experimental findings reported by Wu et al. (2023), who demonstrated that curcumin supplementation reduced circulating total bilirubin and ALT in animals subjected to experimentally induced hepatic oxidative stress. These findings support the potential of curcumin to favorably influence hepatic biochemical alterations, although the experimental model differed from that used in the present study [27]. The concordant reductions in AST, ALT, total bilirubin, and direct bilirubin in the present study therefore provide a consistent biochemical pattern rather than an alteration restricted to a single hepatic marker.

One biologically plausible explanation for the hepatic findings involves the antioxidant properties of curcumin and its metabolites. Excessive paracetamol exposure is associated with formation of the reactive metabolite N-acetyl-p-benzoquinone imine (NAPQI), depletion of glutathione, oxidative stress, and subsequent hepatocellular injury [28]. Experimental evidence has demonstrated that curcumin can attenuate hepatic oxidative stress by reducing lipid peroxidation and restoring glutathione and antioxidant enzyme activity, providing a plausible mechanism for its favorable effects on hepatic biochemical alterations [29].

The renal biochemical findings followed a pattern comparable to the hepatic markers. Urea decreased from 60.83 ± 4.17 mg/dL in PC to 35.67 ± 2.16 mg/dL in P3, while creatinine decreased from 1.232 ± 0.074 to 0.713 ± 0.049 mg/dL. One-way ANOVA demonstrated significant differences

among the groups for both parameters, and Tukey's post hoc analysis showed significant differences across all pairwise comparisons. The difference between P2 and P3 remained significant for urea ($p = 0.011$) and creatinine ($p = 0.004$), indicating that the biochemical responses remained distinguishable between the two highest extract doses. These findings are consistent with Alqahtani et al. (2023), who demonstrated that acetaminophen administration significantly increased serum urea and creatinine levels in rats, whereas curcumin treatment significantly reduced both renal biochemical markers [30]. Hamdy et al. (2024) demonstrated that curcumin reduced serum urea and creatinine and attenuated oxidative and inflammatory responses in experimentally induced renal injury [31]. A meta-analysis found that curcumin supplementation reduced serum creatinine, but had no significant effect on blood urea nitrogen in patients with diabetic kidney disease [32].

An important feature of the present findings is the consistency of the biochemical response across hepatic and renal parameters. All six markers showed progressively lower mean values across P1, P2, and P3, while the highest values occurred in the paracetamol-only positive control group. This pattern agrees with the study by Yousef et al. (2010), in which paracetamol increased bilirubin, hepatic transaminases, urea, and creatinine, while curcumin mitigated biochemical alterations in both organs. Similarly, Kheradpezhouh et al. (2010) reported that curcumin reduced acetaminophen-induced hepatic and renal biochemical abnormalities and that these effects were supported by oxidative stress measurements and histopathological findings. Taken together, the agreement between the present biochemical results and previous experimental studies supports a potential role of *C. longa*-derived bioactive compounds in modulating paracetamol-associated hepatorenal biochemical alterations [33].

The progressive differences observed across the three treatment groups may reflect differences in exposure to the bioactive constituents of *C. longa*. Curcumin, one of the major bioactive curcuminoids in turmeric, has well-established antioxidant and anti-inflammatory properties. Recent experimental evidence indicates that curcumin can attenuate acetaminophen-induced hepatic and renal biochemical alterations, supporting the biological plausibility of the dose-associated pattern observed in the present study (30). *Curcuma longa* extract contains curcuminoids, including curcumin, which have been widely studied for their antioxidant activity. Curcumin has been associated with reduced markers of lipid and protein oxidation and increased activity of antioxidant enzymes, including superoxide dismutase and glutathione peroxidase [34].

The present study used *C. longa* extract rather than purified curcumin. Therefore, the observed biochemical responses may reflect the combined effects of naturally occurring curcuminoids and other bioactive constituents of turmeric. The progressive changes across the treatment groups suggest that increasing doses of the extract may enhance exposure to these bioactive constituents and potentially contribute to favorable changes in hepatic and renal biochemical markers. the present study demonstrates a consistent dose-associated pattern in hepatic and renal biochemical responses following *C. longa* extract administration in paracetamol-induced rats. The progressive reductions in AST, ALT, total bilirubin, direct bilirubin, urea, and creatinine across the treatment groups provide integrated biochemical evidence of favorable changes in both hepatic and renal profiles, with the greatest changes observed at 900 mg/kg BW. These findings strengthen the experimental evidence supporting the biological potential of *C. longa* as a source of bioactive compounds capable of modulating biochemical alterations associated with hepatic and renal injury.

This study has an important limitation: it did not include a normal control group of rats that received neither paracetamol nor *Curcuma longa* extract. Consequently, no concurrent baseline values were available to determine whether the hepatic and renal biochemical markers in P3 returned to normal levels. The findings at 900 mg/kg body weight should therefore be interpreted as statistically significant improvements compared with the paracetamol-only positive control group, rather than evidence of complete restoration of liver and kidney function.

4. Conclusion

Curcuma longa extract was associated with dose-related reductions in hepatic and renal biochemical markers in paracetamol-induced rats. At 900 mg/kg body weight, the dose with the greatest response among those tested, AST decreased from 193.67 to 96.67 U/L and ALT from 145.33 to 61.83 U/L compared with the paracetamol-only control group. Total bilirubin decreased from 1.295 to 0.545 mg/dL, direct bilirubin from 0.548 to 0.208 mg/dL, urea from 60.83 to 35.67 mg/dL, and creatinine from 1.232 to 0.713 mg/dL. These findings demonstrate improvement across both hepatic and renal biochemical indicators, but do not establish restoration to normal values because the study lacked a normal control group.

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