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Dose-Responsive Mitigation of Hepatic Oxidative Stress and Histopathological Damage by Channa striata Extract in Post-Carbon Tetrachloride-Exposed Rats

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Abstract: Carbon tetrachloride (CCl_4) is widely used to induce experimental oxidative liver injury through the generation of free radicals that promote lipid peroxidation and hepatocellular damage. Natural products with antioxidant properties are being explored for their potential to mitigate such injury. This study aimed to evaluate the dose-responsive ameliorative effects of *Channa striata* extract on hepatic oxidative stress and histopathological alterations in rats following subacute CCl_4 exposure. Thirty male Wistar rats were divided into five groups: normal control (K1), CCl_4 control (K2), and three treatment groups receiving *C. striata* extract at 100, 150, and 200 mg/kg body weight/day for two weeks after six weeks of CCl_4 induction (K3–K5). Hepatic malondialdehyde (MDA) levels were measured as an indicator of lipid peroxidation. Liver histopathology was assessed for hepatocellular necrosis, congestion, and inflammatory cell infiltration using a semi-quantitative scoring system. CCl_4 exposure significantly increased hepatic MDA levels and caused severe histopathological damage in the control group. *C. striata* extract dose-dependently attenuated MDA levels ($p < 0.001$), with the 200 mg/kg/day group showing the lowest levels (2.80 ± 0.15 vs. 6.65 ± 0.13 nmol/g in CCl_4 control). Histopathological scores for necrosis, congestion, and inflammatory infiltration ameliorated progressively with increasing doses, with median total scores improving from 8.5 (CCl_4 control) to 2.0 (200 mg/kg/day). *Channa striata* extract demonstrates dose-dependent ameliorative activity against established CCl_4-induced oxidative liver injury, as evidenced by attenuation of lipid peroxidation and mitigation of histopathological damage. Further studies incorporating serum liver enzymes and molecular mechanisms are warranted.

Keywords: Ameliorative effect; Carbon tetrachloride; *Channa striata*; Dose-response; Hepatic oxidative stress; Histopathology; Malondialdehyde (MDA)

Introduction

Liver injury is an important biomedical problem because the liver is constantly exposed to xenobiotics, environmental toxins, drugs, and metabolic byproducts, which can disrupt redox homeostasis and damage hepatocytes (Sharma et al., 2023; Javed et al., 2023). Oxidative stress, triggered by excessive reactive oxygen species, accelerates lipid peroxidation, membrane instability, inflammatory responses, and structural injury in hepatic tissue (Mihajlovic & Vinken, 2022; Pomacu et al., 2021). This process is relevant to both experimental toxicology and the broader understanding of chronic liver disease progression in humans (Maran et al., 2022). Consequently, the search for bioactive compounds capable of mitigating oxidative hepatic damage continues to attract substantial research interest (Chupradit et al., 2022).

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Carbon tetrachloride (CCl_4) is a well-established chemical agent used in experimental hepatotoxicity models (Maran et al., 2022; Weber et al., 2003). During metabolism, CCl4 generates trichloromethyl and trichloromethyl peroxy radicals, which cause significant oxidative damage to the liver (Johra et al., 2023b). This model is useful for studying lipid peroxidation, hepatocyte degeneration, inflammation, and histological alterations following toxic exposure (Dai et al., 2023). Malondialdehyde (MDA) is a typical indicator of oxidative stress and lipid peroxidation in CCl_4-affected tissues (Javed et al., 2023; B. Wang et al., 2022). Furthermore, histopathological examination provides essential visual evidence of tissue damage and repair that biochemical markers alone cannot capture (Ogaly et al., 2022; Xue et al., 2020).

Natural compounds with antioxidant and anti-inflammatory properties are being investigated as potential agents to attenuate toxic liver damage (Algefare et al., 2024; Hasnat et al., 2024). The abundance of bioactive chemicals linked to tissue repair and inflammation management in *Channa striata*, for instance, has aroused much scientific attention (Lee et al., 2022; Yulizal et al., 2020). These molecules include albumin, amino acids, fatty acids, and others (Abdulgani et al., 2020; Zawawi et al., 2020). A recent systematic study by Lee et al. (2022) found that *C. striata* has favorable effects on various inflammatory conditions, including wound healing, stomach ulcers, osteoarthritis, and allergic reactions (Lee et al., 2022). This shows that *Channa striata* has broader pharmacological potential beyond nutritional advantages (Yulizal et al., 2020). However, existing literature primarily focuses on its anti-inflammatory and regenerative qualities, with limited direct evidence regarding its effects on toxic oxidative liver injury (Lee et al., 2022; Munakarmi et al., 2022).

Although multiple studies have examined the impact of plant-based antioxidants to CCl_4-induced liver damage, impact *C. striata* extract on oxidative liver damage remains mostly unknown (Dai et al., 2021; Wei et al., 2021). Most existing research on *Channa striata* has focused on inflammatory diseases, wound healing, and oxidative stress in tissues other than the liver (Lee et al., 2022; Yulizal et al., 2020). Few studies have targeted the liver. Furthermore, many experimental investigations of liver damage focus solely on serum biochemistry or general observations (Kabbashi et al., 2024; Ouais et al., 2023). Few studies investigate tissue oxidative stress markers in conjunction with a dose-response approach to histopathology (Liu et al., 2025; Y. Wang et al., 2025). Consequently, the precise effects of *C. striata* extract on reducing hepatic lipid peroxidation and mitigating microscopic liver damage following CCl_4 exposure remain unclear.

This research aimed addressing a research gap with investigating whether biochemical composition *Channa striata* could enhance antioxidant defenses and promote hepatic recovery from acute oxidative stress (Jahan et al., 2023; N. Li et al., 2024). Consequently, the examination is limited to toxicant-induced oxidative liver damage, ensuring that the study's objectives, methodology, and outcome measurements are aligned (Sarfo-Antwi et al., 2024). The study's uniqueness lies in its assessment of dose-dependent hepatic antioxidant responses using complementary endpoints: liver tissue MDA as a lipid peroxidation index and histopathological changes as markers of structural damage (J. Li et al., 2021; Ren et al., 2021). Though the methodology is simple, it provides a strong, publication-ready framework by maintaining consistency and preventing the overinterpretation of findings (Xu et al., 2022; Zhou et al., 2022).

This research assessed the hepatic antioxidant properties of *C. striata* extract in a dose-responsive manner in rats exposed to carbon tetrachloride. The study examined liver malondialdehyde levels and histopathological changes. Specifically, this research evaluated whether increasing extract doses would result in lower tissue oxidative stress and progressive mitigation of microscopic liver injury (Alkinani et al., 2021; Dai et al., 2021, 2023). By addressing both biochemical and morphological signs of toxic liver damage, this work seeks to provide preclinical evidence regarding the ameliorative potential of *Channa striata* extract in CCl_4-induced liver damage (Almeer et al., 2019; Bedoui et al., 2024).

Method

Ethical Approval and Extract Preparation

Following clearance from Prima Indonesia University Health Research Ethics Committee (approved number 041/KEPK/UNPRI/X/2025), the experiment took place at the Ellio Laboratory in Medan from September to November 2025. The *Channa striata* extract powder was manufactured by PT Herbal Nusantara Solo and supplied by PT Mega Medica Pharmaceutical (POM HT. 203 300 841). Prior to oral administration, the extract was suspended in 0.5% carboxymethyl cellulose (CMC) and contained standardized albumin, also necessary amino acids indicated on research products (Yulizal et al., 2020; Zawawi et al., 2020).

Experimental Animals

Male Wistar rats (*Rattus norvegicus*) ranging in weight from 150 to 250 grams and six to eight weeks old were used in the research. None of the rats had ever been exposed to experimentation before. The sample size examined utilizing the Federer models, which stipulated

that eachgroup needed a minimum of five animals (Fahrudin et al., 2020). We increased the number of rats in each group from four to six in order to adjust for mortality. The animals were kept in standard polypropylene cages in a controlled environment with ambient temperature of 24 ± 2°C, a relative humidity of 50-60%, and a light/dark cycle occurring every 24 hours (Weber et al., 2003). The rats had free access to a standard pellet diet and water. To reduce stress-related variability and stabilize physiological adaptation to the laboratory setting, all rats were acclimated for seven days prior to the experiment (Sharma et al., 2023).

Randomization and Experimental Design

A random number sequence was used for the basic randomization, which included drawing lots, to split the animals into five groups (B. Wang et al., 2022). To make sure everyone was in an equal group, we utilized this strategy to prevent selection bias. A randomized control group design with just post-test factors was used in the investigation (Dai et al., 2023). There were thirty rats total, with six animals in each of the five groups: K1, the control group, K2, the group that received CCl_4, and K3, K4, and K5, the experimental groups that had 100, 150, 200 mg/kg body weight/day, dosages of *C. striata* extract, respectively.

The K1 group received 0.5% CMC orally in 1-mL doses. Over the course of six weeks, the K2 group was given a mixture of 0.1 mL/kg body weight of pure CCl_4 and 0.9 mL/kg body weight of coconut oil (1:9 v/v) orally twice weekly, followed by 0.5% CMC during weeks seven and eight (Fahrudin et al., 2020; Weber et al., 2003). Groups K3, K4, and K5 received an identical CCl_4 induction regimen for six weeks, followed by an oral dose of *Channa striata* extract at 100, 150, or 200 mg/kg body weight per day, respectively, as weeks seven through eight (Abdulgani et al., 2020; Lee et al., 2022). All animals were killed at the end of week 8 (Johra et al., 2023b).

Anesthesia, Termination, and Tissue Collection

The rats were anesthetized before the experiment ended. A commonly utilized anesthesia strategy in rat experimental research prior to tissue collection is intraperitoneal ketamine (70 mg/kg) combined with xylazine (7 mg/kg) (Jahan et al., 2023). As study did not report any blood collection for serum biochemical analysis, the primary biological material collected for outcome assessment was liver tissue (Abdulgani et al., 2025; Javed et al., 2023). A portion of the right lobe was removed for histological examination, and about 200 mg of liver tissue was collected for the MDA test after the compassionate termination was carried out (Mihajlovic et al., 2022). The abdominal cavity was then opened (Pomacu et al., 2021).

Measurement of Liver Tissue Malondialdehyde

Homogenized liver tissue from rats exposed to CCl_4 was tested for MDA levels using the TBARS method (Javed et al., 2023; B. Wang et al., 2022). Nearly two hundred milligrams of liver tissue was harvested, weighed, and cleaned with physiological saline after anesthesia and termination. Tissue was ground up in 2 milliliters of pH 7.4 cold phosphate buffer solution before being mixed with SDS, acetic acid, and thiobarbituric acid (TBA) (Algefare et al., 2024; Dai et al., 2021). The next stage was to heat the mixture in a water bath for 20 minutes until it reached a temperature ranging from 95 to 100 °C (Ogaly et al., 2022). After the samples cooled, they were spun in a centrifuge at 3,000 rpm for 10 minutes. Following this, the absorbance was measured at 532-535 nm relative to 1,1,3,3-tetramethoxypropane (TEP) (Xue et al., 2020). The results were quantified as nmol/g of liver tissue and presented as the mean ± SD for each group (Ouais et al., 2023).

Histopathological Examination

After anesthesia, a 1 × 1 × 1 cm specimen was taken from the right hepatic lobe for histopathological examination (Ogaly et al., 2022). After soaking in 10% neutral buffered formalin for 24 hours, the specimen was rinsed with physiological saline. After fixation, the specimens were immersed in progressively higher concentrations of alcohol to dry them (Pomacu et al., 2021). They were then cleaned with xylene and embedded in paraffin. Placing the paraffin blocks on glass slides, they were then stained with hematoxylin and eosin (HE) after being sectioned at a thickness of 4-5 µm (Kabbashi et al., 2024). The animals were examined under blindfolded circumstances using five high-power fields under a 400× magnification microscope (Y. Wang et al., 2025). An independent, single anatomical pathologist reviewed the histopathological slides. In order to reduce observer bias and maintain consistency in scoring, the pathologist was blinded to group allocation (Liu et al., 2025).

Hepatocellular necrosis, congestion, and inflammatory cell infiltration were all analyzed histopathologically and scored on a scale from 0 to 3 (J. Li et al., 2021; Sarfo-Antwi et al., 2024). If the score was 0, it meant that the histology results were normal. The severity of hepatocellular necrosis was determined by three scores: 1 for mild damage affecting 1–10% of the lobular area, 2 for moderate injury affecting 11–30% of the lobular area, and 3 for severe injury affecting more than 30% of the lobular area (Ren et al., 2021). Congestion was scored on a scale from 1 (representing minor sinusoidal or venous dilatation impacting less than 25% of the field) to 3 (representing substantial dilatation affecting more than 50% of the field) (Xu et al.,

2022). With a score of 1, we have 1–10 inflammatory cells per high-power field; with a score of 2, we have 11–30 cells per high-power field; and with a score of 3, we have more than 30 cells per high-power field (Almeer et al., 2019; Bedoui et al., 2024).

Statistical Analysis

It was decided to look at the quantitative data for MDA in liver tissue using one-way ANOVA. Next came Tukey's post hoc test (Dai et al., 2023; Xu et al., 2022). times A Kruskal-Wallis test applicable to ordinal histology was run. Bonferroni corrections were used to fix pairwise comparisons in the Mann-Whitney U test (Ogaly et al., 2022). SPSS version 25 was used for all of our analyses, and statistical significance was defined as p-values < 0.05. In contrast to ordinal variables (Jahan et al., 2023), which are represented as median (min-max) (Javed et al., 2023), continuous variables are expressed as mean ± standard deviation (Pomacu et al., 2021). The Mann-Whitney U test with Bonferroni correction was used to compare the two sets of data (Algefare et al., 2024). We achieved significance with a p-value less than 0.05.13 We used SPSS 25.(B. Wang et al., 2022) for all of our analyses. Mean ± standard deviation (SD) was used for continuous data, whereas median (minimum-maximum) was employed for ordinal variables (Hasnat et al., 2024).

Result and Discussion

Result

Liver Tissue Malondialdehyde Levels

The Shapiro-Wilk test confirmed normal distribution of MDA levels across all groups (all p > 0.05), which allowed for further investigation using parametric methods (Javed et al., 2023). One-way ANOVA revealed significant differences among groups (p < 0.001), as shown in Table 1 (Algefare et al., 2024; Dai et al., 2023). The CCl_4 control group (K2) exhibited the highest MDA concentration (6.65 ± 0.13 nmol/g) (B. Wang et al., 2022). There was a dose-responsive antioxidant activity, nevertheless, as treatment with increasing doses of *C. striata* extract progressively decreased MDA levels in liver tissue (Ogaly et al., 2022; Xue et al., 2020).

Comparing the groups treated with extracts to the CCl_4 control group revealed lower levels of malondialdehyde (MDA), as shown in Table 1 (Johra et al., 2023a). At 150 mg/kg body weight/day, there was a decline of 4.05 ± 0.13 nmol/g, reaching its maximum at 200 mg/kg body weight/day, with a decrease of 2.80 ± 0.15 nmol/g (Alkinani et al., 2021; Dai et al., 2021). The 200 mg/kg/day group (K5) demonstrated the greatest attenuation of lipid peroxidation, with MDA levels approaching those of the normal control group (2.05 ± 0.16 nmol/g) although the difference remained statistically significant (p < 0.05) (Kabbashi et al., 2024; Ouais et al., 2023). These results indicate a dose-responsive ameliorative effect on hepatic oxidative stress.

Table 1. Liver Tissue Malondialdehyde Levels Across Experimental Groups

Group	n	MDA (nmol/g liver tissue) mean ± SD	Significance
K1 Group	6	2.05 ± 0.16	e
K2 Group	6	6.65 ± 0.13	a
K3 Group	6	5.30 ± 0.15	b
K4 Group	6	4.05 ± 0.13	c
K5 Group	6	2.80 ± 0.15	d

The results are revealed as the average plus or minus the standard deviation. All groups were compared using one-way ANOVA, which revealed a significant disparity (p < 0.001). Statistically significant differences between groups are shown by different letters based on Tukey's post hoc test (p < 0.05).

Histopathological Findings

Representative histopathological findings are shown in Figure 1. The normal control group (K1) exhibited preserved hepatic architecture without evidence of necrosis, congestion, or inflammatory infiltration (Sarfo-Antwi et al., 2024). In contrast, the CCl_4 control group (K2) showed the most severe liver damage, characterized by extensive hepatocellular necrosis, marked congestion, and pronounced inflammatory cell infiltration (J. Li et al., 2021; Ren et al., 2021).

Treatment with *Channa striata* extract resulted in progressive mitigation of these histological alterations with increasing doses as illustrated in Figure 1 (Almeer et al., 2019; Bedoui et al., 2024). The 100 mg/kg body weight/day group (K3) showed liver damage compared to (K2) (Xu et al., 2022). The 150 mg/kg/day group (K4) demonstrated substantial recovery, while the 200 mg/kg/day group (K5) exhibited the mildest lesions, with histological features approaching normal architecture (Liu et al., 2025; Y. Wang et al., 2025).

A semi-quantitative analysis revealed significant differences in hepatocellular necrosis, congestion, and inflammatory infiltration among the groups (all p = 0.001) as summarized in Table 2 (Liao et al., 2024; Zhou et al., 2022). Median scores progressively decreased with increasing extract doses, corroborating the histopathological observation of dose-responsive hepatic mitigation (Jahan et al., 2023; Munakarmi et al., 2022). The 200 mg/kg/day group (K5) demonstrated the lowest total histopathological score among all treatment groups (median 2.0, range 1.0–3.0), compared to the CCl_4 control group (median 8.5, range 8.0–9.0) (Chupradit et al., 2022; Dai et al., 2023).

Overall, the histological and biochemical results were similar and complementary (J. Li et al., 2021; Wei et al., 2021). The CCl_4 control group exhibited the highest level of oxidative stress and the most severe microscopic liver injury (B. Wang et al., 2022). Conversely, the extract-treated groups showed a steady attenuation of hepatic MDA levels accompanied by progressive amelioration of necrosis, congestion, and inflammatory infiltration (Abdulkadir et al., 2024; Sarfo-Antwi et al., 2024). The most pronounced mitigation of liver injury was observed at a dose of 200 mg/kg body weight/day.

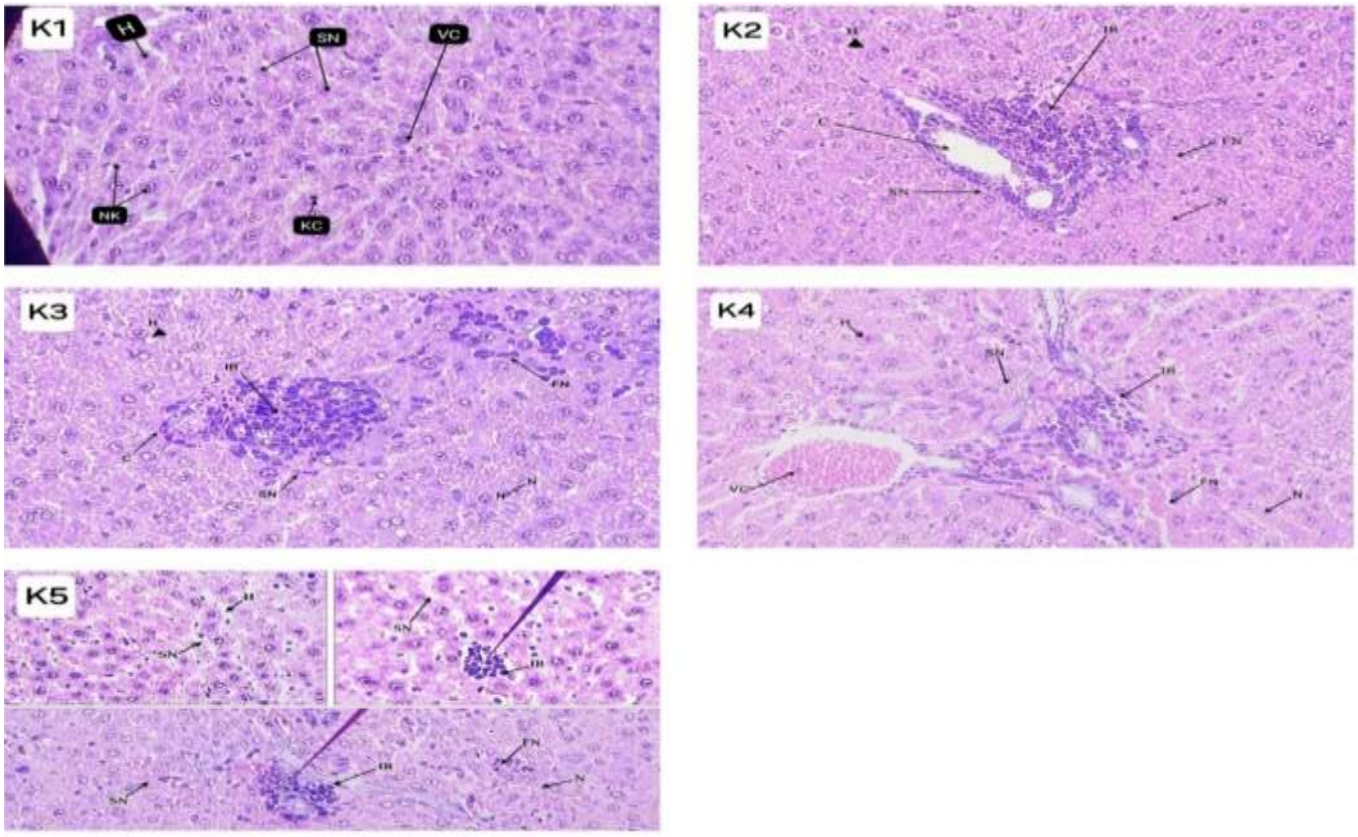

Figure 1. Representative histopathological appearance of liver tissue in each experimental group. K1: normal control; K2: CCl_4 control; K3: CCl_4 + *Channa striata* 100 mg/kg body weight /day; K4: CCl_4 + *Channa striata* 150 mg/kg body weight /day; K5: CCl_4 + *Channa striata* 200 mg/kg body weight /day. (H: Hepatocyte; SN: Liver sinusoid; VC: Central vein; NK: Nuclear Hepatocyte; KC: Kupffer Cell; C: Congestion; IR: Infiltration; N: Diffuse Necrosis; FN: Focal Necrotic). Representative findings include preserved hepatocyte architecture in K1; marked hepatocellular necrosis, congestion, and inflammatory infiltration in K2; and gradual histological improvement in K3–K5, with K5 exhibiting the mildest lesions. Hematoxylin-eosin staining at 400× magnification

Table 2. Histopathological Scores of Liver Injury Across Experimental Groups

Group	Necrosis median (min-max)	Congestion median (min-max)	Inflammatory infiltration median (min-max)	Total score median (min-max)
K1 Group	0 (0-0)[a]	0 (0-0)[a]	0 (0-0)[a]	0 (0-0)[a]
K2 Group	3 (2-3)[d]	3 (2-3)[d]	3 (2-3)[d]	8.5 (8.0-9.0)[d]
K3 Group	2 (1-3)[c]	2.5 (2-3)[c]	2 (1-2)[c]	7.0 (6.0-8.0)[c]
K4 Group	1.5 (1-2)[b]	2 (1-2) [b]	1 (1-2)[b]	4.5 (3.0-6.0)[b]
K5 Group	1 (0-2)[ab]	1 (1-2)[ab]	0.5 (0-1)[ab]	2.0 (1.0-3.0)[ab]
p-value	0.001	0.001	0.001	<0.001*

In this data set, the median (lowest to highest) is used for presentation. After that, the Kruskal-Wallis test was used to examine the overall comparisons. Pairwise differences that are statistically significant, as determined by Mann-Whitney U tests with Bonferroni correction ($p < 0.05$), are indicated by different superscript letters within the same column. Serious histopathological damage is indicated by higher scores. The overall score is the result of adding the scores for necrosis, congestion, and inflammatory infiltration.

Discussion

This research showed that *Channa striata* extract reduced MDA levels and minimized histopathological liver damage on rats revealed carbon tetrachloride (CCl_4) (Abdulgani et al., 2020, 2025; Lee et al., 2022). The most pronounced effects were observed at a daily dose of 200 mg/kg body weight. Groups receiving the extract exhibited progressively lower MDA levels and correspondingly lower scores for hepatocellular necrosis, congestion, and inflammatory infiltration (Algefare et al., 2024; Dai et al., 2023). These findings suggest a dose-related ameliorative effect on established liver injury rather than a single laboratory change (Ogaly et al., 2022; B. Wang et al., 2022). The alignment between oxidative stress markers and tissue-level histology enhances the biological credibility of the observed effects (Javed et al., 2023; Sharma et al., 2023).

These results align with the established pathogenesis of CCl_4-induced liver injury (Venmathi Maran et al., 2022; Weber et al., 2003). Hepatic cytochrome P450 enzymes activate CCl_4, producing highly reactive radicals that cause lipid peroxidation, membrane damage, and inflammatory amplification (Hasnat et al., 2024; Johra et al., 2023a). Ultimately, this results in hepatocellular necrosis and architectural disruption (Chupradit et al., 2022; Jahan et al., 2023). Malondialdehyde (MDA) is one of the most frequently used indices of lipid peroxidation, and higher hepatic MDA levels have been associated with CCl_4-mediated oxidative damage in rodents (Javed et al., 2023; Pomacu et al., 2021). The substantial increase in MDA levels observed in the toxic control group, followed by a progressive reduction across the three extract-treated groups, aligns with the hypothesized injury-recovery continuum of this model (Alkinani et al., 2021; Dai et al., 2021).

The current findings are consistent with previous open-access studies on natural substances tested in CCl_4 liver injury models (J. Li et al., 2021; Wei et al., 2021). For instance, a 2023 study in *Scientific Reports* on *Ganoderma lucidum* found that CCl_4 exposure increased oxidative stress and inflammation, while treatment reduced MDA levels and alleviated histological abnormalities, including inflammatory infiltration and structural injury (Johra et al., 2023a). Similarly, recent experimental investigations employing various natural products in CCl_4, models have revealed a consistent pattern: decreased hepatic MDA levels, enhanced endogenous antioxidant balance, and reduced necrosis or inflammatory alterations in histology following treatment (Kabbashi et al., 2024; Ouais et al., 2023; Xiao et al., 2025). Although these experiments employ many agents, the consistency of results is notable (Algefare et al., 2024; Dai et al., 2023). This suggests that the observed reaction with *C. striata* is biologically plausible within a broader antioxidant-ameliorative context rather than being an isolated or atypical finding (Ogaly et al., 2022; Xue et al., 2020).

At the same time, this study offers a more specific contribution (Lee et al., 2022). Prior literature on *Channa striata* has primarily focused on inflammatory conditions, wound healing, edema reduction, and tissue repair outside the liver (Yulizal et al., 2020; Zawawi et al., 2020). This study, however, directly examines toxic oxidative liver injury with both hepatic MDA and structured histopathology as outcomes (Abdulgani et al., 2020). A 2022 systematic review by Lee et al. concluded that *C. striata* exhibits promising anti-inflammatory activity in various experimental and clinical settings, including dermatitis, gastric lesions, osteoarthritis, allergic rhinitis, and wound-related conditions (Lee et al., 2022). However, the review also emphasized that the underlying mechanisms are not fully understood and that most studies employed crude extracts rather than isolated active compounds (Lee et al., 2022). This review is useful for interpreting these findings (Munakarmi et al., 2022). While the review does not directly establish hepatoprotection, it supports the premise that *C. striata* contains bioactive constituents capable of modulating inflammation and tissue injury *in vivo* (Chupradit et al., 2022; Hasnat et al., 2024).

The histopathological findings of this study support this interpretation (J. Li et al., 2021; Sarfo-Antwi et al., 2024). The toxic control group exhibited the highest scores for necrosis, congestion, and inflammatory infiltration (Ren et al., 2021; Xu et al., 2022). In contrast, the extract-treated groups showed gradual improvement with increasing doses (Almeer et al., 2019; Bedoui et al., 2024). This is significant because histology reflects the combined effects of oxidative damage, vascular disruption, and inflammatory cell recruitment downstream (N. Li et al., 2024; Zhou et al., 2022). The 200 mg/kg body weight/day group showed most comparable microscopic profile to normal control pattern when compared to 100 also 150 mg/kg body weight/day groups (Liu et al., 2025; Y. Wang et al., 2025). The dose-response relationship strengthens the argument that the extract's effects were not random (Dai et al., 2023; Ogaly et al., 2022).

Several mechanisms may underlie these observations (N. Li et al., 2024; Zhou et al., 2022). *Channa striata* contains albumin, amino acids, and fatty acids that may contribute to antioxidant defense and tissue repair (Abdulgani et al., 2020; Yulizal et al., 2020). Systematic reviews further identify albumin and fatty acids as key contributors to the fish's anti-inflammatory activity, potentially through free-radical scavenging and modulation of inflammatory pathways (Lee et al., 2022; Zawawi et al., 2020). The manuscript also implicates Nrf2-mediated antioxidant signaling and suppression of

inflammatory mediators as potential mechanisms (Munakarmi et al., 2022; Rahman et al., 2018). This interpretation aligns with recent CCl_4-induced hepatotoxicity studies, wherein effective ameliorative or reparative interventions typically involve reducing oxidative stress, mitigating pro-inflammatory signaling, and preserving hepatic microarchitecture (Algefare et al., 2024; Dai et al., 2021; B. Wang et al., 2022). However, these mechanistic conclusions must be interpreted with caution since the current investigation did not explicitly evaluate antioxidant enzymes, cytokines, or Nrf2 pathway components (N. Li et al., 2024; Zhou et al., 2022).

Not all past evidence regarding *Channa striata* is uniformly favorable, and this complexity should be acknowledged (Lee et al., 2022). Some clinical trials in the systematic review indicated minimal or statistically insignificant changes in inflammatory markers despite improvements in symptoms or wound-related outcomes (Lee et al., 2022). Others demonstrated more definitive effects, depending on the model used, dosage, and measured outcomes (Abdulgani et al., 2020, 2025; Yulizal et al., 2020). This varied pattern is not inherently contradictory (Venmathi Maran et al., 2022). Rather, it implies that the impact of *C. striata* may depend on context and be influenced by formulation, disease model, method of administration, and selection of endpoints (Weber et al., 2003; Xue et al., 2020). The current study may have revealed more distinct effects because it employed a carefully controlled experimental toxicology model focusing on direct hepatic outcomes rather than generalized systemic clinical markers (Dai et al., 2023; Johra et al., 2023a).

The correspondence between reduced tissue MDA and reduced histopathological severity strengthens the reliability of interpretation (Kabbashi et al., 2024; Ouais et al., 2023). Nonetheless, significant limitations must be acknowledged (Jahan et al., 2023). Since the trial did not include serum ALT and AST levels, it remains unclear whether the tissue-level effect translates into improved liver biochemistry in routine clinical assessments (Chupradit et al., 2022; Hasnat et al., 2024). Additionally, the study did not examine fibrosis-specific indicators or molecular mediators (N. Li et al., 2024; Munakarmi et al., 2022). Therefore, the findings should be viewed as evidence of attenuation of CCl_4-induced oxidative liver injury rather than as evidence of antifibrotic efficacy or reversal of advanced cirrhosis (J. Li et al., 2021; Ren et al., 2021). This distinction is critical for ensuring that the conclusions are proportionate to the measured outcomes and for achieving publication quality (Abdulkadir et al., 2024).

A further limitation is that the extract was administered after the cessation of CCl_4 exposure (weeks 7–8), whereas CCl_4 induction was completed at week 6. Therefore, the observed effects reflect reparative mechanisms, specifically the mitigation of established liver injury, rather than true preventive (hepatoprotective) activity. Future studies involving concurrent administration of CCl_4 and the extract are needed to determine whether the extract can prevent or attenuate liver damage during ongoing toxic exposure (Pandey et al., 2023; Ugwu et al., 2021). Additionally, the absence of a positive control group, such as silymarin, limits the comparative interpretation of the extract's efficacy because silymarin is widely used as a reference agent in CCl_4-induced liver injury models (El-Kot et al., 2023; B. Wang et al., 2022).

Briefly, the current data suggest that *Channa striata* extract has ameliorative potential in rats previously exposed to CCl_4, as demonstrated by dose-dependent attenuation of hepatic lipid peroxidation and mitigation of histological damage (Lee et al., 2022). These results align with the existing open-access literature on oxidative liver injury and the broader anti-inflammatory profile of *C. striata* (Dai et al., 2023; Fahrudin et al., 2020). However, additional mechanistic and translational research is necessary (J. Li et al., 2021; Zhou et al., 2022). Future studies should incorporate serum liver enzymes, antioxidant enzyme panels, inflammatory cytokines, and pathway-level indicators to determine whether the observed effects are primarily due to redox modulation, inflammatory suppression, or a combination of bot (Bedoui et al., 2024; Munakarmi et al., 2022; Rahman et al., 2018).

Conclusion

Channa striata extract attenuates CCl_4-induced hepatic oxidative stress and tissue damage in rats, as evidenced by dose-dependent reduction in malondialdehyde levels and mitigation of histopathological features, including reduced scores for hepatocellular necrosis, congestion, and inflammatory infiltration. The 200 mg/kg body weight/day group demonstrated the most pronounced ameliorative effects among the treatment groups. The current data suggest that *C. striata* extract may reduce established CCl_4-induced hepatic oxidative stress and tissue injury. However, since the study did not include serum liver enzymes or molecular pathway analysis, further research incorporating ALT, AST, antioxidant enzyme profiles, inflammatory mediators, and mechanistic markers is necessary before drawing broader conclusions. Future studies with concurrent CCl_4 and extract administration, as well as positive control groups, are warranted to confirm the full therapeutic potential of this natural product.

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Author Contributions
Conceptualization, methodology, software, validation, formal analysis, investigation, resources, data curation, writing—original draft preparation, OK.Y.; writing—review and editing, visualization, supervision, project administration, S.G.B.S. and Y.E.P.L. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest
The authors declare no conflict of interest.

References

Abdulgani, N., Hidayati, D., Adinovitasary, R., Oliviatie, V., & Sekartaji, A. D. (2020). MDA levels in the pancreas, testes, liver, and plasma of diabetic rats: The effect of snakehead (Channa striata) extract. *Nusantara Bioscience*, *12*(1), 50–54. https://doi.org/10.13057/nusbiosci/n120109

Abdulgani, N., Winarni, D., Darmanto, W., Hidayati, D., & Rojafi, M. Z. (2025). Antioxidant Effect of Snakehead Fish (Channa Striata) Albumin Extract on Diabetic Rats (Rattus Norvegicus). *Trends in Sciences*, *22*(12). https://doi.org/10.48048/tis.2025.10834

Abdulkadir, M., Adam, A., Daniya, Z., & Sani, M. (2024). Hepatoprotective Effect of Ethanolic Extract of Rosemarinus officinalis (Rosemary) Leaves Against CCL4-induced Hepatic Damage in Albino Rats. *Journal of Environmental Bioremediation and Toxicology*, *7*(2), 58–62. https://doi.org/10.54987/jebat.v7i2.1038

Algefare, A. I., Alfwuaires, M., Famurewa, A. C., Elsawy, H., & Sedky, A. (2024). Geraniol prevents CCl4-induced hepatotoxicity via suppression of hepatic oxidative stress, pro-inflammation and apoptosis in rats. *Toxicology Reports*, *12*(May 2023), 128–134. https://doi.org/10.1016/j.toxrep.2024.01.007

Alkinani, K. B., Ali, E. M. M., Al-Shaikh, T. M., Awlia Khan, J. A., Al-Naomasi, T. M., Ali, S. S., Abduljawad, A. A., Mosa, O. F., & Zafar, T. A. (2021). Hepatoprotective Effects of (-) Epicatechin in CCl4-Induced Toxicity Model Are Mediated via Modulation of Oxidative Stress Markers in Rats. *Evidence-Based Complementary and Alternative Medicine*, *2021*, 4655150. https://doi.org/10.1155/2021/4655150

Almeer, R. S., Albasher, G., Alotibi, F., Alarifi, S., Ali, D., & Alkahtani, S. (2019). Ziziphus spina-christi Leaf Extract Suppressed Mercury Chloride-Induced Nephrotoxicity via Nrf2-Antioxidant Pathway Activation and Inhibition of Inflammatory and Apoptotic Signaling. *Oxidative Medicine and Cellular Longevity*, *2019*, 5634685. https://doi.org/10.1155/2019/5634685

Bedoui, A., Mufti, A., Feriani, A., Baccari, H., Bouallegue, A., Kharrat, M., Sobeh, M., Amri, M., & Abbes, Z. (2024). Unlocking the hepatoprotective potential of the parasitic plant Orobanche foetida Poir. aqueous extract against CCl4-induced liver injury in rat. *Frontiers in Pharmacology*, *14*, 1320062. https://doi.org/10.3389/fphar.2023.1320062

Chupradit, S., Bokov, D., Zamanian, M. ., Heidari, M., & Hakimizadeh, E. (2022). Hepatoprotective and therapeutic effects of resveratrol: A focus on anti-inflammatory and antioxidative activities. *Fundamental & Clinical Pharmacology*, *36*(3), 468–485. https://doi.org/10.1111/fcp.12746

Dai, C., Li, H., Wang, Y., Tang, S., Velkov, T., & Shen, J. (2021). Inhibition of Oxidative Stress and ALOX12 and NF-κB Pathways Contribute to the Protective Effect of Baicalein on Carbon Tetrachloride-Induced Acute Liver Injury. *Antioxidants*, *10*(6), 976. https://doi.org/10.3390/antiox10060976

Dai, C., Zhang, X., Lin, J., & Shen, J. (2023). Nootkatone supplementation ameliorates carbon tetrachloride-induced acute liver injury via inhibition of oxidative stress, NF-κB pathways, and activation of Nrf2/HO-1 pathway. *Antioxidants*, *12*(1), 194. https://doi.org/10.3390/antiox12010194

El-Kot, S. M., Wanas, W., Hafez, A. M., Mahmoud, N. A., Tolba, A. M., Younis, A. H., El Sayed, G., & Abdelwahab, H. E. (2023). Effect of silymarin on the relative gene expressions of some inflammatory cytokines in the liver of CCl4-intoxicated male rats. *Scientific Reports*, *13*, 15245. https://doi.org/10.1038/s41598-023-42250-7

Fahrudin, F., Ningsih, S., Wardhana, H. I., Haribowo, D. R., & Hamida, F. (2020). Efektivitas Dosis Karbon Tetraklorida (CCl4) Terhadap Tikus (Rattus norvegicus L.) Sebagai Hewan Model Fibrosis Hati. *Berita Biologi*, *19*(3B), 411422. https://doi.org/10.14203/beritabiologi.v19i3b.3961

Hasnat, H., Shompa, S. ., Islam, M. ., Alam, S., Richi, F. ., Emon, N. ., Ashrafi, S., Ahmed, N. ., Chowdhury, M. N. ., Fatema, N., Hossain, M. ., Ghosh, A., & F, A. (2024). Flavonoids: A treasure house of prospective pharmacological potentials. *Heliyon*, *10*(6), e27533. https://doi.org/10.1016/j.heliyon.2024.e27533

Jahan, I., Islam, M., Sarif, S., Amena, I., Shuvo, A., Akter, N., Chowdhury, F., Akter, R., Ahmed, I., Khan, F.,

Subhan, N., & Alam, M. (2023). Tempol Alters Antioxidant Enzyme Function, Modulates Multiple Genes Expression, and Ameliorates Hepatic and Renal Impairment in Carbon Tetrachloride (CCl4)-Intoxicated Rats. *Livers*, *3*(1), 105–120. https://doi.org/10.3390/livers3010010

Javed, A., Mehboob, K., Rashid, A., Majid, A., Khan, S., & Baig, Z. (2023). Oxidative Stress and Lipid Peroxidation in NAFLD with and without Type 2 Diabetes Mellitus. *Journal of the College of Physicians and Surgeons Pakistan*, *33*(11), 1254–1258. https://doi.org/10.29271/jcpsp.2023.11.1254

Johra, F. T., Hossain, S., Jain, P., Bristy, A. T., Emran, T., Ahmed, R., Sharker, S., Bepari, A. K., & Reza, H. M. (2023a). Amelioration of - CCl 4 - induced oxidative stress and hepatotoxicity by Ganoderma lucidum in Long Evans rats. *Scientific Reports*, 1–13. https://doi.org/10.1038/s41598-023-35228-y

Johra, F. T., Hossain, S., Jain, P., Bristy, A. T., Emran, T., Ahmed, R., Sharker, S., Bepari, A. K., & Reza, H. M. (2023b). Amelioration of _ CCl 4 _ induced oxidative stress and hepatotoxicity by Ganoderma lucidum in Long Evans rats. *Scientific Reports*, 1–13. https://doi.org/10.1038/s41598-023-35228-y

Kabbashi, A. S., Eltawaty, S. A., Ismail, A. M., Elshikh, A. A., Alrasheid, A. A., Elmahi, R. A., Koko, W. S., & Osman, E. E. (2024). Ethanolic Extract of Mangifera indica Protects against CCl4-Induced Hepatotoxicity via Antioxidant Capabilities in Albino Rats. *Journal of Toxicology*, *2024*, 5539386. https://doi.org/10.1155/2024/5539386

Lee, V. L. L., Choo, B. K. M., Norazit, A., Noor, S. M., & Shaikh, M. F. (2022). Channa striatus in inflammatory conditions: A systematic review. *Frontiers in Pharmacology*, *13*, 1–10. https://doi.org/10.3389/fphar.2022.1076143

Li, J., Song, D., Zhang, B., Guo, J., Li, W., Zhang, X., & Zhao, Q. (2021). Hepatoprotective Effects of Heracleum candicans Against Carbon Tetrachloride-Induced Acute Liver Injury in Rats. *Dose-Response Hyphen*, *19*(3), 15593258211029510. https://doi.org/10.1177/1559325821102951

Li, N., Hao, L., Li, S., Deng, J., Yu, F., Zhang, J., Nie, A., & Hu, X. (2024). The NRF-2/HO-1 Signaling Pathway: A Promising Therapeutic Target for Metabolic Dysfunction-Associated Steatotic Liver Disease. *Journal of Inflammation Research*, *17*, 8061–8083. https://doi.org/10.2147/JIR.S490418

Liao, Y., Lv, F., Quan, T., Wang, C., & Li, J. (2024). Flavonoids in natural products for the therapy of liver diseases: progress and future opportunities. *Frontiers in Pharmacology*, *15*, 1485065. https://doi.org/10.3389/fphar.2024.1485065

Liu, H., Zhang, Y., & Ning, S. (2025). ScRNA-seq combined with ATAC-seq analysis to explore the metabolic balance mechanism of CCl4-induced liver inflammatory injury. *Frontiers in Immunology*, *16*, 1600685. https://doi.org/10.3389/fimmu.2025.1600685

Mihajlovic, M., & Vinken, M. (2022). Mitochondria as the Target of Hepatotoxicity and Drug-Induced Liver Injury: Molecular Mechanisms and Detection Methods. *International Journal of Molecular Sciences*, *23*(6), 3315. https://doi.org/10.3390/ijms23063315

Munakarmi, S., Gurau, Y., Shrestha, J., Risal, P., Park, H. S., Shin, H. B., & Jeong, Y. J. (2022). Hepatoprotective Effects of a Natural Flavanol 3,3'-Diindolylmethane against CCl4-Induced Chronic Liver Injury in Mice and TGFβ1-Induced EMT in Mouse Hepatocytes via Activation of Nrf2 Cascade. *International Journal of Molecular Sciences*, *23*(19), 11407. https://doi.org/10.3390/ijms231911407

Ogaly, H. A., Aldulmani, S. A. A., Al-Zahrani, F. A. M., & Abd-Elsalam, R. M. (2022). D-Carvone Attenuates CCl4-Induced Liver Fibrosis in Rats by Inhibiting Oxidative Stress and TGF-ß1/SMAD3 Signaling Pathway. *Biology*, *11*(5), 739. https://doi.org/10.3390/biology11050739

Ouais, G. N., & Hassan, D. M. (2023). A comparative study on the hepatoprotective effect of selenium-nanoparticles and dates flesh extract on carbon tetrachloride induced liver damage in albino rats. *Antomy & Cell Biology*, *56*(4), 583–551. https://doi.org/10.5115/acb.23.101

Pandey, B., Baral, R., & Kaundinnyayana, A. (2023). Promising hepatoprotective agents from the natural sources: a study of scientific evidence. *Egyptian Liver Journal*, *13*, 14. https://doi.org/10.1186/s43066-023-00248-w

Pomacu, M. M., Traşcă, M. D., Pădureanu, V., Bugă, A. M., Andrei, A. M., Stănciulescu, E. C., Baniţă, I. M., Rădulescu, D., & Pisoschi, C. G. (2021). Interrelation of inflammation and oxidative stress in liver cirrhosis. *Experimental and Therapeutic Medicine*, *21*(6), 602. https://doi.org/10.3892/etm.2021.10034

Rahman, M., Molla, M., Sarker, M., Chowdhury, S., & Shaikh, M. (2018). Snakehead Fish (Channa striata) and Its Biochemical Properties and Health Benefits. *SF Journal of Biotechnology and Biomedical Engineering*, *1*(1), 1–5. Retrieved from https://www.semanticscholar.org/paper/Snakehead-Fish-(Channa-striata)-and-Its-Biochemical/a0bc6c4fcaa273ee9a34eaf7d1e7834c600967ed

Ren, Z., Huo, Y., Zhang, Q., Chen, S., Lv, H., Peng, L., Wei, H., & Wan, C. (2021). Protective Effect of Lactiplantibacillus plantarum 1201 Combined with Galactooligosaccharide on Carbon Tetrachloride-

Induced Acute Liver Injury in Mice. *Nutrients*, *13*(12), 4441. https://doi.org/10.3390/nu13124441

Sarfo-Antwi, F., Larbie, C., Emikpe, B., & Appiah-Opong, R. (2024). Pericopsis laxiflora (Baker) stem bark extract is protective against carbon tetrachloride-induced acute liver damage by modulation of oxidative stress and inflammation. *Journal of Taibah University for Science*, *18*. https://doi.org/10.1080/16583655.2024.2354569

Sharma, P., Nandave, M., Nandave, D., Yadav, S., Vargas-De-La-Cruz, C., Singh, S., Tandon, R., Ramniwas, S., & Behl, T. (2023). Reactive oxygen species (ROS)-mediated oxidative stress in chronic liver diseases and its mitigation by medicinal plants. *American Journal of Translational Research*, *15*(11), 6321–6341. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/38074830%0Ahttp://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=PMC10703659

Ugwu, C. E., & Suru, S. M. (2021). Medicinal plants with hepatoprotective potentials against carbon tetrachloride-induced toxicity: a review. *Egyptian Liver Journal*, *11*, 88. https://doi.org/10.1186/s43066-021-00161-0

Venmathi Maran, B. A., Iqbal, M., Gangadaran, P., Ahn, B., Rao, P. V., & Shah, M. D. (2022). Hepatoprotective Potential of Malaysian Medicinal Plants: A Review on Phytochemicals, Oxidative Stress, and Antioxidant Mechanisms. *Molecules*, *27*(5), 1533. https://doi.org/10.3390/molecules27051533

Wang, B., Cui, S., Mao, B., Zhang, Q., Tian, F., Zhao, J., Tang, X., & Chen, W. (2022). Cyanidin Alleviated CCl4-Induced Acute Liver Injury by Regulating the Nrf2 and NF-κB Signaling Pathways. *Antioxidants*, *11*(12), 2383. https://doi.org/10.3390/antiox11122383

Wang, Y., Zhang, Y., He, Y., Zhang, S., Huang, B., Wang, Y., Lin, W., Xiao, W., Zou, Z., & Cui, G. (2025). GGV formula attenuates CCl4-induced hepatic injury in mice by modulating the gut microbiota and metabolites. *Frontiers in Nutrition*, *12*, 1564177. https://doi.org/10.3389/fnut.2025.156417

Weber, L. W., Boll, M., & Stampfl, A. (2003). Hepatotoxicity and mechanism of action of haloalkanes: carbon tetrachloride as a toxicological model. *Critical Reviews in Toxicology*, *33*(2), 105–136. https://doi.org/10.1080/713611034

Wei, X., Luo, C., He, Y., Huang, H., Ran, F., Liao, W., Tan, P., Fan, S., Cheng, Y., Zhang, D., Lin, J., & Han, L. (2021). Hepatoprotective Effects of Different Extracts From Triphala Against CCl4-Induced Acute Liver Injury in Mice. *Frontiers in Pharmacology*, *12*, 664607. https://doi.org/10.3389/fphar.2021.664607

Xiao, J., Li, C., Pei, Y., Xu, S., Zhao, H., Xiang, W., & Wei, J. (2025). Lycium ruthenicum Polysaccharides Alleviate CCl4-Induced Acute Liver Injury Through Antioxidant and Anti-Inflammatory Effects. *Nutrients*, *17*(21), 3359. https://doi.org/10.3390/nu17213359

Xu, Y., Zhang, Z., Wang, B., He, X., Tang, J., Peng, W., Zhou, J., & Wang, Y. (2022). Flammulinavelutipes Polysaccharides Modulate Gut Microbiota and Alleviate Carbon Tetrachloride-Induced Hepatic Oxidative Injury in Mice. *Frontiers in Microbiology*, *13*, 847653. https://doi.org/10.3389/fmicb.2022.847653

Xue, Y., Deng, Q., Zhang, Q., Ma, Z., Chen, B., Yu, X., Peng, H., Yao, S., Liu, J., Ye, Y., & Pan, G. (2020). Gigantol ameliorates CCl4-induced liver injury via preventing activation of JNK/cPLA2/12-LOX inflammatory pathway. *Scientific Reports*, *10*(1), 22265. https://doi.org/10.1038/s41598-020-79400-0

Yulizal, O., Lelo, A., Ilyas, S., & Kusumawati, R. L. (2020). The effect of Channa striata extract and standard eradication regimen on asymmetric dimethylarginine in Helicobacter pylori gastritis rat model. *Veterinary World*, *13*(8), 1605–1612. https://doi.org/10.14202/vetworld.2020.1605-1612

Zawawi, N. Z. M., Shaari, R., Luqman Nordin, M., Hayati Hamdan, R., Peng, T. L., & Zalati, C. W. S. C. W. (2020). Antibacterial and cytotoxic activity assessment of Channa striatus (Haruan) extract. *Veterinary World*, *13*(3), 508–514. https://doi.org/10.14202/vetworld.2020.508-514

Zhou, J., Zheng, Q., & Chen, Z. (2022). The Nrf2 Pathway in Liver Diseases. *Frontiers in Cell and Developmental Biology*, *10*, 826204. https://doi.org/10.3389/fcell.2022.826204