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Original Research

Effects of Green Tea Extract (Camellia sinensis L.) on Blood Biochemical Parameters in Paracetamol-Induced Wistar Rats

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ABSTRACT

Background: *Paracetamol is one of the analgesics and antipyretics that are widely traded freely, so it is possible that the use is not according to the recommended dose and consumption time. This can trigger liver damage and changes in blood biochemistry. Green tea has components such as antioxidants, anti-inflammatories, and hepatoprotectors. The study aimed to analyze the effect of green tea extract on the blood biochemistry of rats induced by paracetamol.*

Methods: *Laboratory experimental research with the Post-Test Control Group Design method, using 25 male Wistar rats, applying random sampling. Twenty-five rats were divided into 5 groups: K- (control), K+ (positive control), and treatment groups with green tea extract, respectively 175 mg (T1), 350 mg (T2), and 700 mg/kg bw (T3) for 24 days. The treatment group and K+ received paracetamol 600 mg/kg bw on the 14th day for 10 days, and green tea extract was still given. Data, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), total cholesterol, and leukocyte counts, were analysed using ANOVA and the Least Significant Difference (LSD) test.*

Results: *GTE significantly (p-value <0.05) reduced leukocytes and AST, but inadequate paracetamol induction failed to elevate ALT and lipids, masking GTE's measurable impact on those specific biochemical parameters.*

Conclusion: *Providing green tea extract was effective in declining the number of leucocytes and AST levels. The study concluded that green tea extract has the potential to influence the biochemical profile of rats induced by paracetamol. Further research is needed regarding the dose and period of administration and exposure.*

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INTRODUCTION

The widespread consumption of paracetamol (acetaminophen) as an over-the-counter analgesic and antipyretic agent poses a significant risk of liver damage. At therapeutic doses, paracetamol is predominantly metabolized through glucuronidation

and sulfation. Conversely, under conditions of high-dose or prolonged administration, the cytochrome P450 enzyme system, specifically CYP2E1, becomes more active, generating a highly reactive metabolite*: N-acetyl-p-benzoquinoneimine* (NAPQI) (Dear, 2023). Normally, NAPQI is conjugated and detoxified by hepatic glutathione (GSH) to form *3-(glutathione-S-yl)-APAP*. However, excessive or long-term paracetamol intake leads to a rapid depletion of GSH reserves. This lowering prevents adequate detoxification of NAPQI, initiating oxidative stress, mitochondrial dysfunction, and ultimately leading to hepatocellular necrosis and acute liver failure (Ayoub, 2021; Mitchell et al., 2020; Shivam et al., 2025).

Oral administration of paracetamol to Wistar rats at a dose of 600 mg/kg bw resulted in increased levels of AST and ALT, total protein, and bilirubin in the blood. This indicates that liver cell damage is occurring due to the metabolite NAPQI (Islam et al., 2021). Another research by 'aisy et al. (2021) stated that a dose of 600 mg for 7 days increased total bilirubin in the blood.

NAPQI accumulates in hepatocytes, binding to proteins that disrupt ATP production and cause intracellular hypercalcemia, which increases reactive oxygen species (ROS). This triggers oxidative stress, causing mitochondrial damage and inflammation. The accumulation of NAPQI leads to necrosis in liver cells, indicated by increased levels of AST, ALT, triglycerides, and total cholesterol. The increased ROS also enhances pro-inflammatory cytokines (TNF-α, IL-1β, IL-6, and IL-10), which activate white blood cells to migrate to the injury site, further indicating inflammation that damages tissues and organs (Ayoub, 2021).

Liver cell damage induced by NAPQI can be mitigated through the administration of antioxidant compounds. Regarding this, green tea extract has gained attention due to its potent antioxidant profile and proven hepatoprotective activity. In previous studies, green tea extract had been used as an anticholesterol (Sarel & Simanjuntak, 2020), with protective effects of EGCG from green tea against oxidative stress and kidney disease, while for hepatoprotective activity, the intervention of giving green tea extract significantly reduced paracetamol-induced liver injury (Ayusso et al., 2022; Lv et al., 2020).

Although various studies have been conducted on the toxicity of paracetamol, most research focuses predominantly on liver enzyme markers (AST/ALT) without fully integrating the correlation between metabolic shifts (lipid profiles) and systemic inflammatory responses. In addition, the lack of clarity regarding the specific dose-response upon exposure to paracetamol and green tea extract treatment. Green tea extract contains flavonoids and L-theanine, which provide protective properties by analyzing the blood biochemistry of rats induced by paracetamol.

This study aims to investigate the potential of green tea extract in preclinical research and its effects on blood chemical levels, such as aspartate aminotransferase (AST), alanine aminotransferase (ALT), triglycerides (TG), total cholesterol, and leukocyte counts. The selection of doses in this study (175, 350, and 700 mg/kg bw) is explicitly justified based on Riyani et al. (2021), who exhibited the optimum dose at 50 mg/kg in mice, then converted into rats dose. The dose of 350 mg/kg bw is represented as a converted measure, while 175 mg/kg and 700 mg/kg bw served as lower and upper thresholds to determine the minimum effective dose and potential saturation effect, respectively.

MATERIALS AND METHOD

This research used an animal experiment with a post-test control group design. Green tea simplicity sourced from PT. Rumpun Sari Medini. The samples underwent a 5-day maceration process with 70% ethanol, followed by evaporation using a rotary evaporator at 45℃ and 50 rpm to yield a thick extract. The study, which was conducted on 25 male Wistar rats (weighing 190-200 grams).

The rats were divided into five groups using simple random sampling from the existing population: a control group (K-), a positive group (K+), and three treatment groups (T1, T2, T3) that received green tea extract at varying doses (175 mg, 350 mg, and 700 mg/kg bw, respectively) for a total of 24 days. This dose was based on the optimum measure in previous studies by Riyani et al. (2021) and Xu et al. (2019), which had converted into rats dosage. Starting on the 14th day, both the positive control and treatment groups were administered paracetamol at a dose of 600 mg/kg bw for 10 days, while the green tea extract administration continued. After the treatment finished, blood samples were drawn.

Blood profiles were analyzed to assess the impact of the treatment. Blood samples were collected from the orbital sinus, centrifuged at 3000 rpm for 15 minutes to obtain serum, and then used to measure levels of AST, ALT, cholesterol, and triglycerides. These measurements were performed using a hematology analyzer with the Electrical Impedance method, and a UV-VIS spectrophotometer at a wavelength of 340 nm. Cholesterol levels were specifically determined using the CHOD PAP Enzymatic Colorimeter Test and GPO-POD methods.

All collected data were statistically analyzed using the One-way ANOVA method with a 95% confidence level to test the differences in means between groups. This analysis was used to determine whether there were statistically significant differences in the variables studied. Furthermore, an LSD (Least Significant Difference) follow-up test was conducted to identify pairs of groups that showed significant differences in more detail.

This study has obtained animal ethics approval from the Health Research Ethics Committee of the Faculty of Sports Science with number 136/KEPK/EC/2023 and was conducted in accordance with the 3Rs principle (Replacement, Reduction, and Refinement). The principle of replacement was applied by considering alternatives to animals whenever possible, reduction through the use of the minimum number of animals necessary to meet the scientific strength of the research, and refinement by ensuring humane handling procedures to minimize pain, stress, and discomfort. The entire process of maintenance, treatment, and termination of test animals followed applicable animal welfare guidelines to ensure optimal ethical protection.

RESULTS

Measurement of blood biochemical levels of rats that had been injected with paracetamol and green tea extract was carried out at the Semarang Animal Health Laboratory and the Semarang City Health and Medical Device Testing Laboratory. The following table shows the results of the analysis of blood profile data, AST, ALT, total cholesterol, and triglyceride levels.

Table 1. Mean and Standard Deviation of the Number of Leukocytes, Lymphocytes, and Neutrophils in the Control and Treatment Groups

Groups	Total Leukocyte (cells/mm3)	Lymphocyte (cells/mm3)	Neutrophil (cells/mm3)
K-	7520 ± 1215.3^{b}	5600 ± 809.3^{bc}	1560 ± 503^{ab}
K+	9440 ± 2032.9^{c}	6480 ± 1435.9^{c}	2400 ± 543.1^{c}
T1	6800 ± 1100.0^{ab}	4480 ± 749.7^{ab}	2060 ± 270.2^{bc}
T2	5180 ± 807.5^{a}	3480 ± 521.5^{a}	1420 ± 216.8^{ab}
T3	5000 ± 1585.9^{a}	3300 ± 989.9^{a}	1280 ± 759.6^{a}

Note: different letters (a, b, c) indicate significant differences, K-: normal control, K+: Control with paracetamol induction 600 mg/kg bb. T1, T2, and T3: paracetamol induction group and green tea extract 175 mg, 350 mg and 700 mg/kg bb.

The results of the ANOVA statistical test, as shown in Table 1, indicate that the administration of GTE had a significant effect ($p < 0.05$) on reducing the total number of leukocytes, lymphocytes, and neutrophils in rats. The number of total leukocytes in the K+ group was significantly different from all groups. The K- group was significantly different from T2 and T3. There was no significant difference in the number of lymphocytes between the treatment group and between treatment groups. The number of neutrophils in K+ was significantly different from all groups except T1.

Table 2. Mean and Standard Deviation of Transaminase Levels in All Groups

Groups	AST (U/L)	ALT (U/L)^{ns}
K-	134.92 ± 10.43^{a}	68.97 ± 18.12
K+	162.62 ± 16.39^{b}	79.30 ± 5.96
T1	202.66 ± 30.08^{c}	73.97 ± 5.26
T2	122.09 ± 16.56^{a}	57.44 ± 15.58
T3	118.00 ± 25.37^{a}	67.22 ± 10.30

Note: different letters (a, b, c) indicate significant differences, ns = no differences

The results of the homogeneity test of AST and ALT levels have homogeneous variations, $\alpha=0.625$ ($\alpha>0.05$). Furthermore, the normality test showed that the data was normally distributed ($\alpha>0.05$). The ANOVA test obtained data with $\alpha<0.05$, which showed that green tea extract had a significant effect on AST levels. Table 2 shows that group K was significantly different from groups K+ and T1. In group T1, it was significantly different from all groups. Groups T2 and T3 showed significant differences from group K+. This can be interpreted as green tea extract can reduce AST levels.

The results of the ALT level analysis showed that the data were homogeneous and normally distributed with $\alpha>0.05$. The ANOVA test to determine the effect of green tea extract obtained data, $\alpha>0.05$. This shows that the paracetamol dosage did not result in a significant enough baseline increase for GTE's protective effects to be statistically detected.

The total cholesterol's homogeneity test exhibited homogeneous variations, $\alpha=0.676$ ($\alpha>0.05$). Furthermore, the normality test showed that the data were normally distributed ($\alpha>0.05$). The ANOVA test obtained data $\alpha=0,077$ ($\alpha>0.05$), which illustrated

that cholesterol did not differ significantly between the control and treatment groups. Cholesterol levels were still within the normal range of 55-89 mg/dl.

Table 3. Mean and Standard Deviation of Lipid Profiles in All Groups

Groups	Total Cholesterol (mg/dl)^{ns}	Triglyseride (mg/dl)^{ns}
K	74.16 ± 12.06	85.00 ± 48.02
K+	66.70 ± 12.06	87.90 ± 21.56
T1	53.16 ± 17.80	64.03 ± 22.20
T2	76.78 ± 19.77	64.06 ± 23.801
T3	56.48 ± 10.21	57.50 ± 16.41

Note: ns = no difference

As for triglyceride testing, the data were homogenous and normally distributed with α=0.130 (α>0.05). The ANOVA statistical test presented that α=0.360 (α>0.05). Similar with cholesterol data, TG levels were in the range of 57.5 - 85.0 mg/dL, which according to Quesenberry et al. (2021), the normal triglyceride range of 62 - 92 mg/dL.

DISCUSSION

Paracetamol as a trigger for hepatotoxicity occurs due to the formation of a reactive metabolite called N-acetyl-p-benzoquinone imine (NAPQI). Normally, NAPQI is detoxified into harmless metabolites by glutathione S-transferase into mercapturic acid and excreted in the urine. However, glutathione will decrease after excessive use of paracetamol (Ohashi & Kohno, 2020; Sestili & Fimognari, 2020). This causes the concentration of NAPQI to increase, which produces reactive oxygen species (ROS) (L. Xu & Wang, 2023).

The release of massive ROS causes mitochondrial dysfunction, which is the starting point for the degradation of liver cell membrane integrity, so that inflammation, apoptosis, and necrosis occur (Rotundo & Pyrsopoulos, 2020). These cell membrane leaks directly correlate with the biochemical parameters AST and ALT. These enzymes, which are normally found in the cytoplasm and mitochondria of hepatocytes, are released into the bloodstream immediately after cell damage occurs. The increase in AST and ALT levels in this study is an objective indicator of the severity of liver injury by NAPQI.

In the study, it was found that there was a significant increase in AST levels due to paracetamol induction. This indicates inflammation in hepatocytes (Islam et al., 2021; Shen et al., 2023). Inflammation will reduce the permeability of the cell membrane, allowing the AST and ALT enzymes to exit the cell (Dias & Nylandsted, 2021). Increased levels of these liver enzymes can be used to diagnose organ damage, especially the liver. After damage by paracetamol occurs, the range of AST and ALT levels increases in the blood (Shen et al., 2023).

The figure also showed the increasing number of ALT, but not significantly compared to the normal group (K). The more significant increase in AST compared to ALT indicates that liver damage by paracetamol occurred at an early stage or mild occasion, and is commonly used as an additional or supporting data for the study that showed a normal range of ALT (X. Li et al., 2023; Ndrepepa, 2021). The initial stage of liver damage is liver inflammation due to hepatic cell destruction and AST release from mitochondria. This problem phase is the first trigger of liver injury and fibrosis (Derosa et al., 2021; Roehlen et al., 2020).

Simultaneously, hepatocyte necrosis releases damage-associated molecular patterns (DAMPs) into the extracellular environment, which activate Kupffer cells to produce pro-inflammatory cytokines (such as TNF-α and IL-1β) (Shen et al., 2023; L. Xu & Wang, 2023). This process bridges oxidative stress with systemic inflammation, which is manifested through changes in the white blood cell profile. The accumulation of ROS and cytokines triggers chemotaxis, which is the mobilization of lymphocytes, neutrophils and leukocytes from the blood circulation and damaged liver tissue to perform phagocytosis of necrotic cells (Liu et al., 2021).

Administration of paracetamol at a dose of 600 mg/kg for 10 days in the study had an effect on increasing the number of leukocytes, lymphocytes, and neutrophils in rats. According to He et al.(2023), the increased number of lymphocytes indicates the inflammatory status that can occur, including chronic. An increase in total leukocytes, lymphocytes, and neutrophils is one indicator of an inflammatory response triggered by paracetamol metabolism. The results of the study are consistent with previous studies, namely that paracetamol in rats caused a significant increase in the number of leukocytes (Latif et al., 2021). Another study also stated that inflammation can be caused by the administration of high doses of paracetamol, so that neutrophils will be active and migrate to liver cells to make repairs (Guo et al., 2021).

The increase in free radicals by paracetamol will inhibit the citric acid cycle and fatty acid oxidation in the mitochondria. This results in fatty acids not being oxidized properly in the mitochondria and fat synthesis occurs in the cytoplasm (Ganetsky et al., 2020; Luo et al., 2023). In the signaling pathway, high ROS levels in hepatocytes will activate SREBP1 (Sterol Regulatory Element Binding Protein). This protein is a protein that will affect lipid metabolism and synthesis (Ma et al., 2022).

The results of measuring triglyceride and total cholesterol levels have not shown any effect of green tea extract, although there has been a tendency to decrease. Giving a dose of paracetamol at a dose of 600 mg/kg for 10 days is considered not to interfere with fat metabolism. In Islam's study (2021), using a dose of 640 mg/kg of Sprague Dawley rats for 14 days, cholesterol levels and triglyceride levels can be significantly increased. Singh & Shukla's study (2020), stated that paracetamol can increase cholesterol levels and triglyceride levels at a dose of 3000 mg/kg. Paracetamol affects the increase in triglyceride and cholesterol levels indirectly, so it takes a long time and a large dose. Increased cholesterol and triglyceride levels were supported by a high-cholesterol diet for 2 weeks (Begriche et al., 2023).

The increase in AST and leukocyte counts reflects acute cellular rupture and the immediate systemic inflammatory response, alterations in lipid profiles, such as hypercholesterolemia or hypertriglyceridemia, seemingly require more chronic exposure or a more profound disruption. In acute settings, the liver may still maintain its capacity to regulate lipid homeostasis, or the duration of the study may not have been sufficient to manifest significant dyslipidemia (Garcia et al., 2023; Masenga et al., 2023; Shahdkar et al., 2025).

Green tea leaves mainly contain polyphenols, amino acids, L-theanine, caffeine, and organic acids. Polyphenols are the main active compounds found in tea. Catechins are the main polyphenol compounds in green tea, which include epigallocatechin-3-gallate (EGCG), epigallocatechin, epicatechin-3-gallate and epicatechin, gallocatechins and gallocatechin gallate (Cardoso et al., 2020). Catechin can act as an anti-inflammatory by suppressing the expression of COX-2 transcription process so that the inflammatory process is inhibited (S. Li et al., 2020). In addition, Li et al (2020) stated that alkaloids

play a role in inhibiting the COX-2 pathway, iNOS (nitric oxide synthase) and NF-kB activation so that the release of TNF-α and cytokines IL-1, IL-2, IL-6, IL-8 is inhibited.

L-theanine in tea will be hydrolyzed into glutamic acid and ethylamine with glutamate acting as a precursor for glutathione (GSH) synthesis (Saeed et al., 2020; Wang et al., 2025). This confirms the research of Xu et al. that giving green tea extract for 7 days can significantly increase GSH (Zheng et al., 2024) . The decrease in AST enzyme levels in this study indicates that the antioxidant compounds in green tea extract prevent liver damage. This statement confirms the research of Riyani et al. (2021) that green tea extract can provide liver protection from AST, ALT enzyme analysis.

The role of catechins in reducing total cholesterol levels is not only related to cholesterol synthesis, but also to cholesterol excretion. Catechins stimulate the 7α-hydrolase enzyme which increases the rate of conversion of cholesterol to bile acids (Sarel & Simanjuntak, 2020). Catechin compounds also play a role in helping to reduce the expression of SREBP 1c (Sterol Regulatory Element Binding Protein-1c), FAS (Fatty Acid Synthase), and SCD1 (Stearoyl-CoA desaturase) where these genes and enzymes support the lipogenesis process (Tindage et al., 2021).

This study has certain limitations, including the absence of histopathological analysis to confirm the extent of tissue damage or regeneration visually, and a relatively short exposure period for paracetamol induction, which may not fully reflect chronic liver toxicity. Future research is needed to optimize the dosage, extend the administration period, and include tissue-level analysis to fully establish the efficacy of paracetamol-induced injury and green tea across a wider range of metabolic and structural parameters.

CONCLUSION

The administration of green tea extract (GTE) demonstrated significant potential in preventing liver injury and systemic inflammation in paracetamol-induced Wistar rats. Specifically, GTE effectively suppressed the elevation of AST enzyme activity and restored the counts of leukocytes, neutrophils, and lymphocytes into normal ranges, indicating potent hepatoprotective and anti-inflammatory effects through the inhibition of oxidative stress. Nevertheless, further research is required to optimize dosage and duration to fully establish its efficacy across a broader range of metabolic parameters.

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CONFLICT OF INTERESTS

The author declares that there is no conflict of interest in this research.

REFERENCES

’aisy, A. R., Ratnaningrum, K., & Nugraheni, D. M. (2021). Hepatoprotective effects of papaya leaves extract (*Carica Papaya* L.) with increased dose: A Study of total bilirubin levels of wistar rats that given paracetamol. *Ahmad Dahlan Medical Journal*, *2*(2), 46–57. https://doi.org/10.12928/admj.v2i2.5063

Ayoub, S. S. (2021). Paracetamol (acetaminophen): A familiar drug with an unexplained mechanism of action. *Temperature*, *8*(4), 351–371.

https://doi.org/10.1080/23328940.2021.1886392

Ayusso, L. L., Girol, A. P., Neto, L. A., Gomes, I., & Burdmann, E. A. (2026). Protective effect of green tea *(Camellia Sinensis)* against kidney diseases. *December*, S196. https://doi.org/10.65034/bjnabstract-cpn25196

Begriche, K., Penhoat, C., Bernabeu-Gentey, P., Massart, J., & Fromenty, B. (2023). Acetaminophen-induced hepatotoxicity in obesity and nonalcoholic fatty liver disease: A critical review. *Livers*, *3*(1), 33–53. https://doi.org/10.3390/livers3010003

Cardoso, R. R., Neto, R. O., dos Santos D'Almeida, C. T., do Nascimento, T. P., Pressete, C. G., Azevedo, L., Martino, H. S. D., Cameron, L. C., Ferreira, M. S. L., & Barros, F. A. R. de. (2020). Kombuchas from green and black teas have different phenolic profile, which impacts their antioxidant capacities, antibacterial and antiproliferative activities. *Food Research International*, *128*, 108782. https://doi.org/10.1016/j.foodres.2019.108782

Dear, J. W. (2023). Fomepizole should not be used more liberally in paracetamol overdose. *British Journal of Clinical Pharmacology*, *89*(2), 599–601. https://doi.org/10.1111/bcp.15596

Derosa, Y., Zubir, N., & Arnelis, R. (2021). The differences of t-regulator cells, alanine aminotransferase serum and aspartate aminotranspherase between hepatitis b chronic patients with and without liver fibrosis. *The Indonesian Journal of Gastroenterology, Hepatology, and Digestive Endoscopy*, *22*(2), 116–123. https://doi.org/10.24871/2222021116-123

Dias, C., & Nylandsted, J. (2021). Plasma membrane integrity in health and disease : signi fi cance and therapeutic potential. *Cell Discovery*. https://doi.org/10.1038/s41421-020-00233-2

Garcia, C., Andersen, C. J., & Blesso, C. N. (2023). The role of lipids in the regulation of immune responses. *Nutrients*, *15*(18). https://doi.org/10.3390/nu15183899

Guo, H., Chen, S., Xie, M., Zhou, C., & Zheng, M. (2021). The complex roles of neutrophils in APAP-induced liver injury. *Cell Proliferation*, *54*(6), 1–7. https://doi.org/10.1111/cpr.13040

He, L., Xie, H., Du, Y., Xie, X., & Zhang, Y. (2023). The relationship between C-reactive protein to lymphocyte ratio and the prevalence of myocardial infarction in US adults: A cross-sectional study. *Heliyon*, *9*(7). https://doi.org/10.1016/j.heliyon.2023.e17776

Islam, M. T., Quispe, C., Islam, M. A., Ali, E. S., Saha, S., Asha, U. H., Mondal, M., Razis, A. F. A., Sunusi, U., Kamal, R. M., Kumar, M., & Sharifi-Rad, J. (2021). Effects of nerol on paracetamol-induced liver damage in Wistar albino rats. *Biomedicine and Pharmacotherapy*, *140*, 111732.

https://doi.org/10.1016/j.biopha.2021.111732

Latif, A. A. El, Assar, D. H., Elkaw, E. M., Hamza, H. A., Alkhalifah, D. H. M., Hozzein, W. N., & Hamouda, R. A. (2021). Protective role of *Chlorella vulgaris* with thiamine against paracetamol induced toxic effects on haematological, biochemical, oxidative stress parameters and histopathological changes in wistar rats. *Scientific Reports*, *11*(1), 1–16. https://doi.org/10.1038/s41598-021-83316-8

Li, S., Liu, X., Chen, X., & Bi, L. (2020). Research progress on anti-inflammatory effects and mechanisms of alkaloids from chinese medical herbs. *Evidence-Based Complementary and Alternative Medicine*, 1–10. https://doi.org/10.1155/2020/1303524

Li, X., Ni, J., & Chen, L. (2023). Advances in the study of acetaminophen-induced liver injury. *Frontiers in Pharmacology*, *14*, 1–13. https://doi.org/10.3389/fphar.2023.1239395

Liu, K., Wang, F. S., & Xu, R. (2021). Neutrophils in liver diseases: Pathogenesis and therapeutic targets. *Cellular and Molecular Immunology*, *18*(1), 38–44. https://doi.org/10.1038/s41423-020-00560-0

Lv, L., Xu, C., Mo, X., Sun, H. Y., & Bi, H. (2020). Green tea polyphenols protect against acetaminophen-induced liver injury by regulating the drug metabolizing enzymes and transporters. *Evidence-Based Complementary and Alternative Medicine*, *2020*. https://doi.org/10.1155/2020/2696432

Masenga, S. K., Kabwe, L. S., Chakulya, M., & Kirabo, A. (2023). Mechanisms of oxidative stress in metabolic syndrome. *International Journal of Molecular Sciences*, *24*(9). https://doi.org/10.3390/ijms24097898

Mitchell, R. A., Rathi, S., Dahiya, M., Zhu, J., Hussaini, T., & Yoshida, E. M. (2020). Public awareness of acetaminophen and risks of drug induced liver injury: Results of a large outpatient clinic survey. *PLoS ONE*, *15*(3), 1–9. https://doi.org/10.1371/journal.pone.0229070

Ndrepepa, G. (2021). Aspartate aminotransferase and cardiovascular disease - A narrative review. *Journal of Laboratory and Precision Medicine*, *6*(January). https://doi.org/10.21037/jlpm-20-93

Ohashi, N., & Kohno, T. (2020). Analgesic Effect of Acetaminophen: A Review of Known and Novel Mechanisms of Action. *Frontiers in Pharmacology*, *11*(November), 1–6. https://doi.org/10.3389/fphar.2020.580289

Quesenberry, K. E., Orcutt, C. J., Mans, C., & Carpenter, J. W. (Eds.). (2021). *Ferrets, rabbits, and rodents: Clinical medicine and surgery* (4th ed.). Elsevier.

Riyani, A., Firman Solihat, M., & Rohdiana, D. (2021). Hepatoprotector activity test of green tea (*Camellia Sinensis*, L) gambung variety ethanol extract in Balb/C mouse

induced with Ccl4. *International …*, *December*, 14–16. http://conference.juriskes.com/index.php/IC/article/view/116

Roehlen, N., Crouchet, E., & Baumen, T. E. (2020). Liver fibrosis : Mechanistic Concepts and. In *Cells* (Issue 9).

Rotundo, L., & Pyrsopoulos, N. (2020). Liver injury induced by paracetamol and challenges associated with intentional and unintentional use. *World Journal of Hepatology*, *12*(4), 125–136. https://doi.org/10.4254/wjh.v12.i4.125

Saeed, M., Khan, M. S., Kamboh, A. A., Alagawany, M., Khafaga, A. F., Noreldin, A. E., Qumar, M., Safdar, M., Hussain, M., Abd El-Hack, M. E., & Chao, S. (2020). L-theanine: An astounding sui generis amino acid in poultry nutrition. *Poultry Science*, *99*(11), 5625–5636. https://doi.org/10.1016/j.psj.2020.07.016

Sarel, Z., & Simanjuntak, K. (2020). Pengaruh pemberian ekstrak teh hijau (*Camellia sinensis* L.) terhadap penurunan kadar kolesterol total tikus wistar (rattus norvegicus) diabetes induksi aloksan. *Jurnal Sehat Mandiri*, *15*(1), 98–111. https://doi.org/10.33761/jsm.v15i1.195

Sestili, P., & Fimognari, C. (2020). Paracetamol-induced glutathione consumption: Is there a link with severe COVID-19 illness? *Frontiers in Pharmacology*, *11*(October), 1–7. https://doi.org/10.3389/fphar.2020.579944

Shahdkar, M., Orang Goorabzarmakhi, M., Shafizadeh, M., Joukar, F., Maroufizadeh, S., Faraji, N., Zeinali, T., & Mansour-Ghanaei, F. (2025). Association between dyslipidemia and elevated liver enzymes: A cross-sectional study from the PERSIAN Guilan cohort study. *Endocrine and Metabolic Science*, *19*(July), 100272. https://doi.org/10.1016/j.endmts.2025.100272

Shen, X. L., Guo, Y. N., Lu, M. H., Ding, K. N., Liang, S. S., Mou, R. W., Yuan, S., He, Y. M., & Tang, L. P. (2023). Acetaminophen-induced hepatotoxicity predominantly via inhibiting Nrf2 antioxidative pathway and activating TLR4-NF-κB-MAPK inflammatory response in mice. *Ecotoxicology and Environmental Safety*, *252*, 114590. https://doi.org/10.1016/j.ecoenv.2023.114590

Shivam, K. S., Gourav, D. K., Kumar, M., Prajapati, K., Nag, G., Verma, A., Kumar, M., Minz, S., Yadav, J. K., Kumari, T., Singh, K., Kumari, P., Gupta, P. K., & Kumari, K. (2025). paracetamol-induced toxicity : A review of the side effects associated with excessive consumption and mishandling. *International Journal of Scientific Research and Technology, 2*(7), 427–436.

Singh, R., & Shukla, R. (2020). Anti hyperlipidemic activity of *Saccharum officinarum* Linn fresh juice in paracetamol induced hyperlipidemic rats. *International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)*, *9*(10), 2557–2566. https://doi.org/10.31032/IJBPAS/2020/9.10.5201

Tindage, D. P., Dewi, R., Manalu, J. L., Kedokteran, F., & Kesehatan, I. (2021). Green tea and black tea can lower the levels of ldl cholesterol in hyperlipidemic animal model. *Damianus Journal of Medicine*, *20*(1), 40–45.

Wang, Q., Yu, J., Lin, W., Ahammed, G. J., Wang, W., Ma, R., Shi, M., Ge, S., Mohamed, A. S., Wang, L., Li, Q., & Li, X. (2025). L-theanine metabolism in tea plants: Biological functions and stress tolerance mechanisms. *Plants*, *14*(3). https://doi.org/10.3390/plants14030492

Xu, L., & Wang, H. (2023). A dual role of inflammation in acetaminophen-induced liver injury. *Liver Research*, *7*(1), 9–15. https://doi.org/10.1016/j.livres.2023.03.001

Xu, X. Y., Zheng, J., Meng, J. M., Gan, R. Y., Mao, Q. Q., Shang, A., Li, B. Y., Wei, X. L., & Li, H. Bin. (2019). Effects of food processing on in vivo antioxidant and hepatoprotective properties of green tea extracts. *Antioxidants*, *8*(12). https://doi.org/10.3390/antiox8120572

Zheng, X. Q., Zhang, X. H., Gao, H. Q., Huang, L. Y., Ye, J. J., Ye, J. H., Lu, J. L., Ma, S. C., & Liang, Y. R. (2024). Green tea catechins and skin health. *Antioxidants*, *13*(12). https://doi.org/10.3390/antiox13121506