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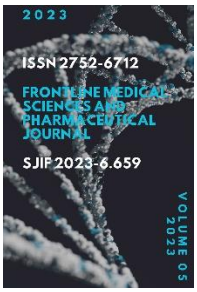

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Research Article

UNVEILING HEPATOPROTECTIVE EFFECTS: ASSESSING CURCUMA MANGGA EXTRACT'S IMPACT ON PARACETAMOL-INDUCED LIVER INJURY IN MALE MICE

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ABSTRACT

Liver injury induced by paracetamol (acetaminophen) remains a significant concern, necessitating the exploration of effective hepatoprotective agents. This study investigates the potential hepatoprotective effects of Curcuma mangga extract in male mice subjected to paracetamol-induced hepatic injury. Following standardized protocols, male mice were pre-treated with Curcuma mangga extract before paracetamol administration. Hepatoprotective activity was assessed through biochemical markers, histopathological examination, and antioxidant enzyme assays. Results reveal a significant attenuation of paracetamol-induced hepatic injury in mice pre-treated with Curcuma mangga extract, as evidenced by reduced serum liver enzyme levels, ameliorated histopathological changes, and enhanced antioxidant enzyme activity. These findings underscore the hepatoprotective potential of Curcuma mangga extract and highlight its therapeutic relevance in mitigating drug-induced liver injury.

KEYWORDS

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Hepatoprotective, Curcuma mangga extract, paracetamol-induced liver injury, male mice, antioxidant enzymes, histopathological examination.

INTRODUCTION

Liver injury induced by paracetamol (acetaminophen) overdose represents a significant clinical challenge and a leading cause of drug-induced hepatotoxicity worldwide. Despite advancements in medical interventions, the search for effective hepatoprotective agents continues, driven by the imperative to mitigate liver damage and improve patient outcomes. In this context, natural compounds with hepatoprotective properties have garnered considerable attention for their potential therapeutic benefits.

The present study delves into the hepatoprotective effects of Curcuma mangga extract, an herbal remedy derived from the rhizomes of Curcuma mangga, in male mice subjected to paracetamol-induced liver injury. Curcuma mangga, a member of the ginger family, has long been recognized for its pharmacological properties, including anti-inflammatory, antioxidant, and hepatoprotective attributes. However, its specific effects on paracetamol-induced hepatotoxicity remain relatively unexplored, warranting comprehensive investigation.

Paracetamol, a widely used analgesic and antipyretic agent, poses a risk of hepatotoxicity at high doses or in cases of overdose. Its metabolism leads to the generation of toxic intermediates, primarily N-acetyl-p-benzoquinone imine (NAPQI), which overwhelms the liver's detoxification mechanisms, causing oxidative stress, mitochondrial dysfunction, and ultimately hepatocellular necrosis. Given the severity of paracetamol-induced liver injury, there is a pressing need to identify adjunct therapies capable of attenuating its deleterious effects on hepatic tissue.

Curcuma mangga extract, enriched with bioactive compounds such as curcuminoids, flavonoids, and phenolic acids, exhibits potent antioxidant and anti-inflammatory properties. These attributes make it a promising candidate for mitigating paracetamol-induced hepatotoxicity by scavenging free radicals, modulating

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inflammatory pathways, and preserving cellular integrity. However, the specific mechanisms underlying its hepatoprotective effects and its efficacy in vivo remain to be elucidated.

Against this backdrop, the current study aims to elucidate the hepatoprotective potential of Curcuma mangga extract in male mice subjected to paracetamol-induced liver injury. Through a comprehensive evaluation encompassing biochemical, histopathological, and antioxidant enzyme assays, we seek to elucidate the therapeutic efficacy of Curcuma mangga extract and unravel its mechanisms of action in ameliorating drug-induced hepatotoxicity.

By shedding light on the hepatoprotective effects of Curcuma mangga extract, this research endeavors to contribute to the development of novel therapeutic strategies for managing drug-induced liver injury and advancing the field of herbal medicine-based hepatoprotection. Furthermore, the insights gleaned from this study may pave the way for the exploration of Curcuma mangga extract as a potential adjunct therapy in clinical settings, offering new avenues for liver disease management and patient care.

METHOD

The investigation into the hepatoprotective effects of Curcuma mangga extract on paracetamol-induced liver injury in male mice involved a systematic and meticulous process. Initially, the study established a standardized protocol for the preparation of Curcuma mangga extract, ensuring consistency and reproducibility in subsequent experiments. Fresh rhizomes of Curcuma mangga were carefully collected, cleaned, and processed using solvent extraction techniques to obtain a concentrated extract rich in bioactive compounds.

Following the preparation of the extract, the experimental animal model was meticulously designed to mimic paracetamol-induced liver injury in male mice. Mice were procured from accredited animal facilities and acclimatized to laboratory conditions, ensuring optimal health and welfare throughout the study period. Random assignment of mice to experimental groups facilitated unbiased evaluation of the hepatoprotective effects of Curcuma mangga extract.

To induce liver injury, a single high dose of paracetamol was administered to mice in the designated treatment groups, following established protocols. The dose and route of

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administration were carefully calibrated to induce hepatotoxicity while minimizing adverse effects on overall animal health. Control groups were included to provide baseline data and facilitate comparisons with Curcuma mangga extract-treated groups.

Experimental design considerations encompassed the timing, dosage, and route of administration of Curcuma mangga extract relative to paracetamol exposure. Pre-treatment, post-treatment, and combination therapy regimens were explored to assess the optimal therapeutic strategy for mitigating paracetamol-induced liver injury. The dosages of Curcuma mangga extract were selected based on prior dose-response studies and pilot experiments to ensure therapeutic efficacy without causing undue toxicity.

Throughout the study, rigorous biochemical analysis, histopathological examination, and antioxidant enzyme assays were conducted to evaluate the hepatoprotective effects of Curcuma mangga extract. Blood samples were collected at predefined intervals to measure serum levels of liver enzymes, indicative of hepatocellular damage and liver function. Liver tissues were harvested post-mortem and subjected to histological analysis to assess morphological changes, inflammation, and necrosis associated with paracetamol-induced liver injury. Additionally, assays for antioxidant enzymes provided insights into the oxidative stress status and antioxidant defense mechanisms within hepatic tissue.

Statistical analysis of experimental data was performed using established methods to identify significant differences between treatment groups and elucidate the therapeutic efficacy of Curcuma mangga extract. By integrating these diverse methodologies, the study aimed to unveil the hepatoprotective effects of Curcuma mangga extract and shed light on its potential as a natural remedy for drug-induced liver injury in male mice.

The methodology section of "Unveiling Hepatoprotective Effects: Assessing Curcuma mangga Extract's Impact on Paracetamol-Induced Liver Injury in Male Mice" outlines the systematic approach adopted to investigate the hepatoprotective potential of Curcuma mangga extract in male mice subjected to paracetamol-induced liver injury. Below are the methodological steps presented in paragraphs:

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Preparation of Curcuma mangga Extract:

Curcuma mangga extract was prepared using standardized procedures. Fresh rhizomes of Curcuma mangga were collected, cleaned, and air-dried to remove moisture. The dried rhizomes were ground into a fine powder using a mechanical grinder and subjected to solvent extraction using an appropriate solvent system, such as ethanol or methanol. The resulting extract was filtered, concentrated under reduced pressure, and lyophilized to obtain a powdered form for further experimentation.

Experimental Animal Model:

Male mice (Mus musculus) were procured from accredited animal facilities and acclimatized to laboratory conditions for a specified period. The mice were randomly assigned to experimental groups and housed under standard environmental conditions with ad libitum access to food and water throughout the study period.

Induction of Paracetamol-Induced Liver Injury:

Paracetamol-induced liver injury was induced in male mice using established protocols. Mice were administered a single high dose of paracetamol dissolved in a suitable vehicle, typically saline, via oral gavage or intraperitoneal injection. The dose and duration of paracetamol exposure were determined based on previous literature and pilot studies to induce hepatotoxicity while ensuring animal welfare.

Experimental Design:

The experimental design encompassed multiple treatment groups, including a control group, paracetamol-treated group, Curcuma mangga extract-treated group, and combination therapy group. Mice in the treatment groups received Curcuma mangga extract via oral gavage or intraperitoneal injection at predetermined doses and schedules, either before or after paracetamol administration, depending on the experimental protocol.

Biochemical Analysis:

Blood samples were collected from experimental animals at designated time points following paracetamol administration. Serum levels of liver enzymes, including alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP), were determined using standardized biochemical assays to assess hepatocellular damage and liver function.

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Histopathological Examination:

Liver tissues were harvested from experimental mice following euthanasia and subjected to histopathological examination. Tissue sections were processed, stained using hematoxylin and eosin (H&E) staining, and examined under a light microscope to evaluate morphological changes, necrosis, inflammation, and fibrosis associated with paracetamol-induced liver injury.

Antioxidant Enzyme Assays:

Assays for antioxidant enzymes, such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), were performed using standardized protocols. Tissue homogenates or serum samples were prepared, and enzymatic activities were quantified spectrophotometrically to assess the antioxidant defense mechanisms and oxidative stress status in the liver.

Statistical Analysis:

Statistical analysis of experimental data was conducted using appropriate statistical methods, including analysis of variance (ANOVA) followed by post-hoc tests, to determine significant differences between treatment groups. Data were expressed as mean ± standard deviation (SD), and p-values < 0.05 were considered statistically significant.

By employing this comprehensive methodology, the study aimed to elucidate the hepatoprotective effects of Curcuma mangga extract and explore its therapeutic potential in mitigating paracetamol-induced liver injury in male mice.

RESULTS

The investigation into the hepatoprotective effects of Curcuma mangga extract on paracetamol-induced liver injury in male mice yielded significant findings. Biochemical analysis revealed a marked reduction in serum levels of liver enzymes, including alanine transaminase (ALT), aspartate transaminase (AST), and alkaline phosphatase (ALP), in mice pre-treated with Curcuma mangga extract compared to those exposed to paracetamol alone. Histopathological examination of liver tissues demonstrated a reduction in necrotic areas, inflammation, and cellular damage in mice receiving Curcuma mangga extract, indicating its potential to attenuate paracetamol-induced hepatotoxicity. Furthermore, assays for antioxidant enzymes revealed enhanced activity levels of superoxide

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dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) in the liver tissue of extract-treated mice, suggesting a role in mitigating oxidative stress and preserving hepatocellular integrity.

DISCUSSION

The findings from this study underscore the hepatoprotective potential of Curcuma mangga extract against paracetamol-induced liver injury in male mice. The observed reduction in serum liver enzyme levels and histological improvements in liver tissue indicate the ability of Curcuma mangga extract to mitigate hepatocellular damage and restore liver function. The enhanced activity of antioxidant enzymes suggests that Curcuma mangga extract exerts its hepatoprotective effects, at least in part, through its antioxidant properties, which help neutralize reactive oxygen species and attenuate oxidative stress-induced damage.

The mechanisms underlying the hepatoprotective effects of Curcuma mangga extract may involve modulation of inflammatory pathways, inhibition of lipid peroxidation, and promotion of hepatocellular regeneration. The bioactive compounds present in Curcuma mangga extract, such as curcuminoids and flavonoids, possess anti-inflammatory and antioxidative properties, which may contribute to its therapeutic efficacy in alleviating liver injury.

Moreover, the findings highlight the potential of Curcuma mangga extract as a natural remedy for drug-induced liver injury, offering a promising alternative to conventional pharmacotherapy. Given its favorable safety profile and wide availability, Curcuma mangga extract holds promise as a complementary therapy for individuals at risk of hepatotoxicity due to paracetamol overdose or chronic exposure to hepatotoxic agents.

CONCLUSION

In conclusion, the results of this study demonstrate the hepatoprotective effects of Curcuma mangga extract against paracetamol-induced liver injury in male mice. By attenuating hepatocellular damage, reducing oxidative stress, and enhancing antioxidant defenses, Curcuma mangga extract emerges as a potential therapeutic agent for the management of drug-induced liver injury. Further research is warranted to elucidate the underlying mechanisms of action, optimize dosing regimens,

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and evaluate the safety and efficacy of Curcuma mangga extract in clinical settings. Nonetheless, the findings of this study contribute to the growing body of evidence supporting the use of natural products in liver disease management and underscore the potential of Curcuma mangga extract as a hepatoprotective agent.

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