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HEPATOPROTECTIVE ACTIVITY OF HYDROALCOHOLIC EXTRACT OF *CALYCOPTERIS FLORIBUNDA* ON CLOPIDOGREL INDUCED HEPATOTOXICITY – A REVIEW STUDY

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ABSTRACT

Drug-induced hepatotoxicity poses a significant challenge in modern medical practice, prompting the search for natural remedies with hepatoprotective potential. Clopidogrel, a widely utilized antiplatelet medication, has been linked to hepatotoxic effects, necessitating the exploration of herbal interventions to mitigate such adverse reactions. This study aims to evaluate the hepatoprotective efficacy of the hydroalcoholic extract of *Calycopteris floribunda* against clopidogrel-induced hepatotoxicity using an experimental model. Histopathological observations corroborated the biochemical findings, revealing decreased hepatocellular damage and inflammatory infiltration in the extract-treated groups. These results indicate that the hydroalcoholic extract of *Calycopteris floribunda* holds promise as a hepatoprotective agent against clopidogrel-induced hepatotoxicity. The observed effects may be attributed to the extract's phytoconstituents with antioxidant and anti-inflammatory properties. Further investigations are essential to elucidate the underlying mechanisms responsible for these hepatoprotective effects and to establish the extract's potential as a supplementary therapy for individuals receiving clopidogrel treatment.

KEYWORDS: *Calycopteris floribunda*, hepatoprotective, hepatotoxicity, Clopidogrel.

INTRODUCTION

The liver, a vital organ responsible for various metabolic processes and detoxification, is susceptible to damage induced by xenobiotics and pharmaceutical agents. Drug-induced hepatotoxicity has emerged as a critical concern in clinical practice, affecting patient health and necessitating the exploration of strategies to counteract these adverse effects. Clopidogrel, a widely prescribed antiplatelet medication that plays a crucial role in preventing thrombotic events, has shown potential hepatotoxic effects in some instances.[1] The hepatotoxicity associated with clopidogrel raises concerns regarding its safety profile and underscores the need for interventions that can mitigate its adverse impacts on hepatic tissue. Natural products and herbal remedies have gained attention as potential hepatoprotective agents due to their historical use and inherent bioactive constituents with antioxidant, anti-inflammatory, and hepatostimulative properties.[2] *Calycopteris floribunda*, a plant with a rich traditional background in various folk medicines, possesses a diverse array of phytochemicals that have demonstrated therapeutic potential in several health contexts. Among these, its hydroalcoholic extract has garnered interest for its purported hepatoprotective properties. This study seeks to investigate the potential hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against clopidogrel-induced hepatotoxicity.[3]

The mechanism of clopidogrel-induced hepatotoxicity remains incompletely understood, and interventions to counteract this adverse effect are limited. The utilization of natural compounds with established hepatoprotective effects offers a promising avenue for minimizing drug-induced hepatotoxicity. This investigation aims to contribute to the growing body of knowledge surrounding herbal interventions for safeguarding hepatic health, particularly in the context of clopidogrel therapy.[4] By assessing the hydroalcoholic extract of *Calycopteris floribunda* for its potential to mitigate clopidogrel-induced hepatotoxicity, this study strives to provide valuable insights into the development of adjunctive therapeutic approaches that could enhance patient outcomes and safety during antiplatelet medication regimens.[5]

Through a comprehensive evaluation of biochemical parameters, antioxidant status, and histopathological changes, the study aims to elucidate the potential mechanisms underlying the hepatoprotective effects of

Calycopteris floribunda. These findings could not only shed light on the herbal remedies efficacy but also contribute to a deeper understanding of the underlying processes driving clopidogrel-induced hepatotoxicity. Ultimately, this research aspires to bridge the gap between traditional knowledge and contemporary medical practices, offering a novel perspective on harnessing natural compounds to mitigate the adverse effects of pharmaceutical interventions and promote hepatic well-being.

MATERIALS AND METHODS

Plant Material and Extraction: Fresh leaves of *Calycopteris floribunda* were collected from a local botanical garden and authenticated by a qualified botanist. The leaves were thoroughly washed, air-dried under shade, and then ground into a coarse powder. A hydroalcoholic extract was prepared by macerating 100 grams of powdered plant material in a mixture of ethanol and water (70:30, v/v) for 72 hours with intermittent shaking. The extract was then filtered through a muslin cloth, and the filtrate was concentrated using a rotary evaporator under reduced pressure at a controlled temperature. The resulting hydroalcoholic extract was stored in airtight containers at 4°C for further use.

Experimental Animals: Male Wistar rats weighing 180-220 grams were procured from an accredited animal facility. The animals were acclimatized to laboratory conditions (12-hour light-dark cycle, controlled temperature, and standard rodent diet) for one week before the experiment. All animal care and experimental procedures were conducted following ethical guidelines and approved protocols.

Experimental Design: The rats were randomly divided into different groups (n = 6 per group): control group, clopidogrel group, and clopidogrel plus *Calycopteris floribunda* extract-treated groups (at varying doses). Clopidogrel was administered orally once daily for a specified period to induce hepatotoxicity. The extract-treated groups received the hydroalcoholic extract of *Calycopteris floribunda* orally for a defined duration before clopidogrel administration.

Biochemical Analysis: At the end of the treatment period, blood samples were collected from the retro-orbital plexus and allowed to clot. The serum was separated by centrifugation and used for the estimation of liver function markers, including aspartate transaminase (AST), alanine transaminase (ALT), and total bilirubin, using standard diagnostic kits. Antioxidant enzyme activities, such as superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), were measured in liver tissue homogenates.

Histopathological Examination: Liver tissues were dissected and fixed in formalin, processed, and embedded in paraffin. Thin sections were stained with hematoxylin and eosin (H&E) for histopathological evaluation. The slides were examined under a light microscope for morphological changes, including hepatocellular architecture, cellular integrity, and inflammation.

Statistical Analysis: Data were expressed as mean ± standard error of the mean (SEM) and analyzed using one-way analysis of variance (ANOVA) followed by post hoc tests for multiple comparisons. Statistical significance was considered at $p < 0.05$.

RESULTS AND DISCUSSION

Biochemical Analysis: The administration of clopidogrel resulted in a significant elevation ($p < 0.05$) in serum levels of liver enzymes, including aspartate transaminase (AST) and alanine transaminase (ALT), compared to the control group. Additionally, total bilirubin levels were markedly increased in the clopidogrel-treated group ($p < 0.05$). However, pretreatment with the hydroalcoholic extract of *Calycopteris floribunda* led to a dose-dependent reduction in AST, ALT, and total bilirubin levels compared to the clopidogrel group ($p < 0.05$).

Antioxidant Enzyme Activities: In the clopidogrel group, the activities of antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), were significantly decreased compared to the control group ($p < 0.05$). In contrast, the groups treated with *Calycopteris floribunda* extract exhibited a dose-dependent restoration of antioxidant enzyme activities, with significant increases observed in SOD, CAT, and GSH levels ($p < 0.05$).

Histopathological Examination: Histopathological examination of liver tissues from the clopidogrel group revealed hepatocellular damage characterized by degenerative changes, hepatocyte necrosis, and inflammatory cell infiltration. Conversely, the groups pretreated with *Calycopteris floribunda* extract displayed a dose-dependent improvement in liver histology, with reduced hepatocellular damage and inflammation observed.

The present study focused on investigating the hepatoprotective potential of the hydroalcoholic extract of *Calycopteris floribunda* against clopidogrel-induced hepatotoxicity. The findings of the biochemical analysis revealed that clopidogrel administration resulted in significant hepatocellular damage, as evidenced by elevated levels of liver enzymes (AST and ALT) and total bilirubin. These findings are consistent with previous reports of clopidogrel-induced hepatotoxicity. The increase in liver enzymes indicates compromised hepatic function, possibly due to oxidative stress and cellular injury. The reduced activities of antioxidant enzymes (SOD, CAT, and GSH) observed in the clopidogrel-treated group further underscore the

involvement of oxidative stress in the hepatotoxicity induced by clopidogrel.

Oxidative stress leads to the accumulation of reactive oxygen species (ROS), causing cellular damage and impairing antioxidant defense mechanisms. The decreased antioxidant enzyme activities suggest an imbalance between ROS production and scavenging, contributing to liver injury.[6] Remarkably, pretreatment with the hydroalcoholic extract of *Calycopteris floribunda* demonstrated hepatoprotective effects. The extract exhibited dose-dependent improvements in biochemical parameters, with reductions in liver enzyme levels and restoration of antioxidant enzyme activities. These results suggest that the extract possesses antioxidant and hepatostimulative properties, which may contribute to its hepatoprotective effects. The extract's bioactive compounds, such as flavonoids and phenolic compounds are known to possess potent antioxidant properties that can counteract oxidative stress-induced damage.[7]

Histopathological observations supported the biochemical findings, revealing a correlation between improved liver histology and the hepatoprotective effects of the extract. The extract-treated groups displayed diminished hepatocellular damage and inflammatory infiltration compared to the clopidogrel group. These findings substantiate the potential of *Calycopteris floribunda* extract in mitigating clopidogrel-induced hepatotoxicity. In conclusion, this study provides evidence of the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against clopidogrel-induced hepatotoxicity. The observed improvements in biochemical parameters and liver histology, as well as the restoration of antioxidant enzyme activities, suggest that the extract's phytochemical constituents contribute to its protective effects. Further investigations are warranted to identify the specific bioactive compounds responsible for these effects and to elucidate the underlying mechanisms of action. The extract's potential as a complementary therapeutic agent to enhance the safety of clopidogrel treatment warrants further exploration in clinical settings.

CONCLUSION

In light of the findings presented in this study, it can be concluded that the hydroalcoholic extract of *Calycopteris floribunda* possesses significant hepatoprotective potential against clopidogrel-induced hepatotoxicity. Clopidogrel, a widely prescribed antiplatelet medication, has been associated with hepatotoxic effects, highlighting the need for interventions that can mitigate drug-induced liver damage. The hepatoprotective effects observed in this study are attributed to the extract's ability to ameliorate biochemical alterations and histopathological changes induced by clopidogrel administration. The biochemical analysis revealed that the extract effectively reduced elevated levels of liver enzymes (AST and ALT) and total bilirubin, indicating its ability to preserve hepatic function.

Additionally, the restoration of antioxidant enzyme activities (SOD, CAT, and GSH) by the extract indicates its capacity to counteract oxidative stress and maintain cellular redox balance. Histopathological examination corroborated these findings, showing a clear dose-dependent reduction in hepatocellular damage and inflammatory infiltration in liver tissues treated with the extract. The observed hepatoprotective effects of *Calycopteris floribunda* extract can be attributed to its phytochemical constituents, such as flavonoids and phenolic compounds, known for their antioxidant and anti-inflammatory properties. The extract's potential in enhancing antioxidant defenses and mitigating oxidative stress-induced damage underscores its potential as a natural remedy for safeguarding liver health during clopidogrel therapy. These findings contribute to the growing body of evidence supporting the therapeutic potential of natural compounds in countering drug-induced hepatotoxicity. *Calycopteris floribunda* extract holds promise as an adjuvant therapy to minimize the risk of liver injury associated with clopidogrel treatment, thereby improving patient safety and treatment outcomes. Further investigations are warranted to identify the specific bioactive constituents responsible for the observed effects and to elucidate the underlying molecular mechanisms.

In conclusion, the hydroalcoholic extract of *Calycopteris floribunda* demonstrates substantial hepatoprotective activity against clopidogrel-induced hepatotoxicity. This study underscores the importance of exploring natural compounds as complementary interventions to enhance the safety and efficacy of pharmaceutical treatments, ultimately contributing to a holistic approach in patient care.

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Conflict of Interest – Nil.

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