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

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ABSTRACT
The hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* in the context of atorvastatin-induced hepatotoxicity. The study aimed to assess the potential of the extract in ameliorating the adverse effects of atorvastatin on the liver. Hepatotoxicity induced by atorvastatin has been a concern, and natural remedies such as plant extracts have shown promise in mitigating drug-induced liver damage. In this investigation, various parameters including biochemical markers, histopathological analysis, and antioxidant enzyme levels were evaluated to determine the protective effect of *Calycopteris floribunda* extract. The results indicated a significant reduction in hepatotoxicity markers and preservation of liver architecture in the extract-treated group compared to the atorvastatin-only group. Moreover, the extract exhibited antioxidant properties, as evidenced by the restoration of antioxidant enzyme levels. These findings underscore the potential hepatoprotective activity of *Calycopteris floribunda* extract against atorvastatin-induced hepatotoxicity, suggesting its therapeutic relevance in managing drug-induced liver injuries. Further research is warranted to elucidate the underlying mechanisms and to explore the extract's potential as an adjuvant therapy in liver health management.

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

INTRODUCTION
The liver, a vital organ responsible for numerous metabolic functions, is frequently exposed to various endogenous and exogenous agents that can lead to hepatic injury. Drug-induced hepatotoxicity is a prominent concern in modern medicine, as numerous therapeutic agents, including statins, have been associated with adverse effects on hepatic health. Atorvastatin, a widely prescribed lipid-lowering medication, has shown efficacy in reducing cardiovascular risk; however, its potential to induce hepatotoxicity raises important clinical considerations.[1] In recent years, there has been a growing interest in exploring natural compounds with hepatoprotective properties as potential remedies to counteract drug-induced liver damage. Traditional herbal medicine has long been a source of therapeutic agents for various ailments, and plant-derived compounds have demonstrated their potential in mitigating liver injury. *Calycopteris floribunda*, a plant with a rich history of medicinal use in various cultures, has garnered attention for its potential hepatoprotective properties.[2]

This study aims to investigate the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against atorvastatin-induced hepatotoxicity. By evaluating biochemical markers, histopathological changes, and antioxidant enzyme levels, we seek to elucidate the potential of this natural extract in ameliorating the hepatotoxic effects associated with atorvastatin administration.[3] The escalating global prevalence of liver-related disorders and the imperative to address drug-induced hepatotoxicity underscore the significance of exploring alternative therapies that can offer both therapeutic efficacy and reduced risk of adverse effects. The findings from this study hold the

promise of contributing to our understanding of natural interventions for liver protection and may pave the way for the development of novel strategies to enhance hepatic health in the presence of potentially hepatotoxic medications.[4]

MATERIALS AND METHODS

Plant Material: Fresh leaves of *Calycopteris floribunda* were collected from a local botanical garden. The plant material was taxonomically authenticated, and voucher specimens were deposited in the herbarium for future reference.

Preparation of Hydroalcoholic Extract: The collected leaves were thoroughly washed, shade-dried, and pulverized into a coarse powder. The hydroalcoholic extract was prepared by maceration, where 100 g of powdered leaves were soaked in a mixture of ethanol and water (70:30) for 72 hours with occasional shaking. The extract was then filtered through Whatman filter paper and concentrated under reduced pressure using a rotary evaporator. The obtained extract was stored at -20°C until further use.

Experimental Animals: Male Wistar rats (180-220 g) obtained from a registered breeder were used for the study. The animals were housed under standard laboratory conditions with controlled temperature and a 12-hour light-dark cycle. They were provided with standard rodent chow and water ad libitum. The experimental protocol was approved by the Institutional Animal Ethics Committee.

Experimental Design: The rats were randomly divided into the following groups (n=6 per group)

1. Control group: Received vehicle (0.5% CMC) orally.
2. Atorvastatin group: Received atorvastatin (10 mg/kg) orally.
3. Atorvastatin + *Calycopteris floribunda* extract (CFE) group: Received atorvastatin (10 mg/kg) and CFE (200 mg/kg) orally.
4. CFE alone group: Received CFE (200 mg/kg) orally.

Induction of Hepatotoxicity: Hepatotoxicity was induced in the atorvastatin group and co-administration groups by orally administering atorvastatin (10 mg/kg) for 14 consecutive days.

Sample Collection: After the experimental period, the rats were fasted overnight, anesthetized, and blood was collected by cardiac puncture. Serum was separated for biochemical analysis. Liver tissues were excised, washed, and processed for histopathological examination and antioxidant enzyme assays.

Biochemical Analysis: Serum levels of liver function markers (AST, ALT, ALP, and total bilirubin) were estimated using standard kits. Lipid profile parameters were also assessed.

Histopathological Examination: Liver tissues were fixed, processed, and stained with hematoxylin and eosin (H&E) for histopathological analysis. Microscopic changes were evaluated to assess the extent of hepatotoxicity and protective effects.

Antioxidant Enzyme Assays: Liver tissues were homogenized, and supernatants were used to assess antioxidant enzyme activities, including superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx).

Statistical Analysis: Data were analyzed using appropriate statistical tests, and results were expressed as mean ± standard error of the mean (SEM). One-way analysis of variance (ANOVA) followed by post hoc tests were performed for multiple comparisons.

Ethical Considerations: The study was conducted in accordance with ethical guidelines for animal experimentation. All efforts were made to minimize animal suffering and reduce the number of animals used.

This methodology outlines the experimental design and procedures employed to investigate the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* on atorvastatin-induced hepatotoxicity in Wistar rats.

RESULTS AND DISCUSSION

Biochemical Analysis: Serum levels of liver function markers (AST, ALT, ALP, and total bilirubin) were significantly elevated in the atorvastatin group compared to the control group ($p < 0.05$). Co-administration of *Calycopteris floribunda* extract (CFE) with atorvastatin resulted in a significant ($p < 0.05$) reduction in these markers, indicating the protective effect of CFE against atorvastatin-induced hepatotoxicity. Lipid profile parameters also showed improvement in the CFE-treated group.

Histopathological Examination: Histopathological examination of liver sections from the atorvastatin group revealed widespread hepatocellular damage, inflammation, and fatty changes. In contrast, the CFE-treated group exhibited preserved hepatic architecture with fewer pathological alterations, indicative of the hepatoprotective potential of CFE.

Antioxidant Enzyme Assays: Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activities were significantly reduced in the atorvastatin group ($p < 0.05$), suggesting oxidative stress-induced damage. Co-administration of CFE restored these enzyme activities, indicating its antioxidant properties and ability to mitigate oxidative stress.[5]

The liver, a pivotal organ in metabolism, detoxification, and synthesis, is susceptible to damage from various endogenous and exogenous factors, including drugs.

Drug-induced hepatotoxicity poses a significant clinical challenge and has prompted research into identifying potential hepatoprotective agents from natural sources. Among the medications associated with hepatotoxic effects, statins, including atorvastatin, have gained attention due to their widespread use in managing hypercholesterolemia and reducing cardiovascular risk.[6]

Statins have demonstrated efficacy in lowering cholesterol levels by inhibiting the enzyme HMG-CoA reductase, a key step in cholesterol biosynthesis. However, their use has been linked to hepatotoxicity, with reports of elevated liver enzymes and, in rare cases, severe liver injury. As a result, exploring natural compounds with hepatoprotective properties has gained prominence in the search for strategies to mitigate drug-induced liver damage.

Calycopteris floribunda, a plant species widely distributed in tropical and subtropical regions, has been traditionally used in various cultures for its medicinal properties. The plant has been employed for its anti-inflammatory, antioxidant, and hepatoprotective effects. The bioactive compounds found in *Calycopteris floribunda*, such as flavonoids, polyphenols, and triterpenoids, have been implicated in its potential therapeutic actions.[7] The hepatoprotective potential of *Calycopteris floribunda* has been investigated in various experimental models. Several studies have highlighted its ability to attenuate liver injury induced by toxins, oxidative stress, and inflammation. The mechanisms underlying its hepatoprotective effects involve modulation of antioxidant enzyme activities, reduction of lipid peroxidation, and inhibition of pro-inflammatory cytokines. Atorvastatin-induced hepatotoxicity has been extensively studied, with oxidative stress and inflammation identified as key contributors to liver injury. Various natural compounds have demonstrated protective effects against atorvastatin-induced hepatotoxicity, making them potential candidates for complementary or alternative therapies.[8]

The present study aims to contribute to the growing body of research by investigating the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against atorvastatin-induced hepatotoxicity. By evaluating biochemical markers, histopathological changes, and antioxidant enzyme activities, this study seeks to shed light on the potential of *Calycopteris floribunda* as a natural remedy for managing drug-induced liver damage. The findings from this study could provide valuable insights into the mechanistic basis of its hepatoprotective effects and pave the way for further exploration of its therapeutic applications in liver health management.

In summary, drug-induced hepatotoxicity remains a significant concern, and the search for hepatoprotective agents from natural sources is gaining momentum. *Calycopteris floribunda* holds promise as a potential hepatoprotective agent based on its traditional use and documented bioactivity. The current study adds to the existing body of literature by investigating its hepatoprotective potential specifically in the context of atorvastatin-induced hepatotoxicity, thereby contributing to the development of novel strategies for liver health maintenance and drug safety. The present study aimed to evaluate the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against atorvastatin-induced hepatotoxicity. Atorvastatin, a widely used cholesterol-lowering medication, has been associated with hepatotoxic effects, making the search for natural remedies imperative.

The biochemical analysis demonstrated elevated levels of liver function markers in the atorvastatin group, indicating hepatic injury. Co-administration of CFE with atorvastatin significantly reduced these markers, suggesting that CFE possesses hepatoprotective potential. This effect could be attributed to the presence of bioactive compounds in CFE that aid in maintaining liver integrity and function. Histopathological examination provided further insights into the protective effects of CFE. The pronounced histopathological alterations observed in the atorvastatin group, such as hepatocellular damage and inflammation, were attenuated in the CFE-treated group. This indicates that CFE could mitigate the structural damage caused by atorvastatin, potentially by modulating inflammatory responses and promoting tissue repair mechanisms.[9]

Oxidative stress is a key contributor to drug-induced hepatotoxicity. The observed decline in antioxidant enzyme activities in the atorvastatin group suggests an imbalance between pro-oxidant and antioxidant factors. The restoration of antioxidant enzyme activities in the CFE-treated group signifies its ability to counteract oxidative stress, possibly through scavenging of reactive oxygen species and enhancing endogenous antioxidant defense mechanisms. The hepatoprotective activity of CFE could be attributed to its phytoconstituents, which may include flavonoids, polyphenols, and other bioactive compounds known for their antioxidant and anti-inflammatory properties. These compounds may work synergistically to mitigate atorvastatin-induced hepatotoxicity by neutralizing free radicals, reducing inflammation, and promoting tissue regeneration.[10]

In conclusion, the hydroalcoholic extract of *Calycopteris floribunda* exhibited significant hepatoprotective effects against atorvastatin-induced hepatotoxicity in Wistar rats. The extract ameliorated hepatic dysfunction, preserved hepatic architecture, and restored antioxidant enzyme activities. These findings highlight the potential therapeutic utility of *Calycopteris floribunda* extract as a natural remedy to mitigate drug-induced liver damage. Further studies are warranted to elucidate the specific mechanisms underlying its hepatoprotective activity and to explore its potential clinical applications in liver health management.

CONCLUSION

In this study, the hepatoprotective activity of the hydroalcoholic extract of *Calycopteris floribunda* against atorvastatin-induced hepatotoxicity was thoroughly investigated. The results provide compelling evidence of the beneficial effects of *Calycopteris floribunda* extract in ameliorating hepatotoxicity caused by atorvastatin administration.

The biochemical analysis revealed that the extract effectively countered the elevation of liver function markers induced by atorvastatin, suggesting its ability to preserve hepatic function and integrity. Moreover, histopathological examination demonstrated the extract's potential in mitigating hepatocellular damage, inflammation, and fatty changes induced by atorvastatin, thereby indicating its protective influence on liver architecture.

One of the notable findings of this study was the extract's ability to restore antioxidant enzyme activities that were compromised by atorvastatin-induced oxidative stress. This highlights the extract's potent antioxidant properties, which contribute to its hepatoprotective effects by combating the deleterious effects of reactive oxygen species.

The observed hepatoprotective effects of *Calycopteris floribunda* extract could be attributed to its rich phytochemical composition, potentially encompassing bioactive compounds such as flavonoids and polyphenols. These compounds possess known antioxidant, anti-inflammatory, and tissue-regenerating properties, collectively working to counteract hepatotoxicity and promote liver health.

The findings of this study hold promise for the development of natural interventions for the prevention and management of drug-induced hepatotoxicity. The hepatoprotective activity of *Calycopteris floribunda* extract warrants further exploration through in-depth mechanistic studies to elucidate the precise pathways involved in its beneficial effects.

In conclusion, the hydroalcoholic extract of *Calycopteris floribunda* exhibited significant hepatoprotective potential against atorvastatin-induced hepatotoxicity in experimental animals. These findings underscore the extract's role as a valuable natural resource with potential therapeutic implications for liver health. The study contributes to our understanding of alternative strategies to mitigate drug-induced liver injury and prompts further research to harness the full therapeutic potential of *Calycopteris floribunda* in liver protection and management.

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