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Experimental and preclinical investigations of *Helicteres isora* extracts in drug discovery

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Abstract
Helicteres isora L. (Avartani; Sterculiaceae) is a plant with significant ethnopharmacological value, traditionally used for treating a variety of ailments. Recent studies have explored its pharmacological potential in drug discovery, particularly in the areas of metabolic diseases, hepatoprotective effects, anti-inflammatory activity, antioxidant properties, and its potential for combating infections. This paper reviews the experimental and preclinical investigations of *H. isora* extracts across various biological models, focusing on its antidiabetic, antihyperlipidemic, hepatoprotective, anti-inflammatory, and antioxidant properties. The reviewed studies indicate that aqueous and alcoholic extracts from different parts of the plant, including the bark, fruit, and root, exhibit beneficial effects in animal models of disease. These include improving glycemic control, lipid profiles, and fatty acid composition in diabetic rats, offering hepatoprotection in liver injury models, and demonstrating significant anti-inflammatory and antidiarrheal effects. Preliminary evidence also suggests antiviral and neurobehavioral benefits, warranting further investigation. Although the findings are promising, challenges such as variation in extraction methods and the need for consistent standardization limit the translation of these results into clinical applications. Further studies focusing on bioactive compound isolation, pharmacokinetics, and toxicity are crucial for advancing *H. isora* as a potential therapeutic agent.

Keywords: *Helicteres isora*, avartani, extracts, preclinical, antidiabetic, hepatoprotective, anti-inflammatory, antioxidant, antidiarrheal, diosgenin

Introduction
Helicteres isora, commonly known as the Indian screw tree, is a plant found in various regions of Asia, particularly in India, where it is used in traditional medicine for the treatment of a range of conditions such as diabetes, gastrointestinal issues, and inflammatory disorders. The plant has been the subject of numerous experimental and preclinical studies, which have highlighted its diverse pharmacological properties. Recent research has focused on its extracts, derived from different plant parts such as the bark, root, and fruit, to evaluate their effectiveness in drug discovery.

In vitro and *in vivo* studies have demonstrated that *H. isora* exhibits antidiabetic, antihyperlipidemic, hepatoprotective, anti-inflammatory, antioxidant, and antidiarrheal activities. These pharmacological properties align with its traditional uses and present promising potential for developing novel therapeutic agents. Despite the wealth of research supporting these claims, the translation of *H. isora* into clinical therapeutics has been limited by inconsistencies in extraction methods, phytochemical standardization, and the lack of comprehensive safety profiles. This review consolidates the findings from various preclinical studies, discusses the plant's potential as a source of novel pharmacological agents, and outlines the steps needed to move forward in drug discovery.

Materials and Methods
A thorough review of the available literature was conducted by searching several biomedical databases, including PubMed, ScienceDirect, and various publisher platforms. The search terms included "*Helicteres isora*" along with keywords such as "extract", "antidiabetic", "antihyperlipidemic", "hepatoprotective", "anti-inflammatory", "antioxidant", "toxicity", and "preclinical". Only studies that provided detailed information about the extraction methods, plant parts used, and experimental models were included in the review. Papers that included both *in vitro* and *in vivo* data were prioritized.

The studies reviewed used a variety of extraction techniques, including Soxhlet extraction, maceration, and decoction, employing solvents such as water, ethanol, methanol, and hexane. The results were drawn from diverse models, including streptozotocin-induced diabetic rats, paracetamol-induced hepatotoxicity in mice, carrageenan-induced inflammation models, and castor oil-induced diarrhea models. Data from these studies were used to evaluate the efficacy of *H. isora* extracts across various pharmacological domains, including metabolic, antioxidant, anti-inflammatory, and gastrointestinal functions.

Results

The pharmacological evaluation of *Helicteres isora* extracts in preclinical models demonstrates a broad spectrum of therapeutic effects. Studies investigating the metabolic effects of *H. isora* have consistently shown that extracts from the bark and fruit can significantly reduce blood glucose levels and improve lipid profiles in diabetic rats. Specifically, aqueous bark extracts at doses of 100-200 mg/kg have been shown to reduce serum lipid levels and normalize fatty acid composition in liver and adipose tissues. Ethanol extracts from the fruit have similarly demonstrated antihyperlipidemic effects, reducing triglycerides, total cholesterol, and low-density lipoprotein (LDL) levels in diabetic rats, with results comparable to the standard antidiabetic drug, glibenclamide.

In addition to its metabolic effects, *H. isora* extracts also exhibit significant antioxidant and hepatoprotective properties. Several studies have demonstrated that ethanol extracts from the plant provide protection against liver damage induced by paracetamol in mice. These extracts reduced serum alanine transaminase (ALT) and aspartate transaminase (AST) levels, lowered malondialdehyde (MDA) concentrations, and restored glutathione (GSH) levels, all of which are markers of oxidative stress. These findings suggest that *H. isora* may serve as a potent hepatoprotective agent, potentially useful for the treatment of liver injuries caused by toxins or drugs.

The anti-inflammatory and antidiarrheal effects of *H. isora* extracts have also been documented in rodent models. Inflammatory responses induced by carrageenan and formalin injections were significantly reduced following treatment with *H. isora* bark and root extracts. These effects were accompanied by a reduction in leukocyte migration and edema formation, which are key indicators of inflammation. In gastrointestinal models, *H. isora* extracts were shown to reduce the frequency of diarrhea and improve gastrointestinal transit in castor-oil-induced diarrhea models, further supporting its traditional use in treating digestive disorders.

Emerging evidence also suggests that *H. isora* may have antiviral potential. Recent studies have identified diosgenin, a compound isolated from the leaves of *H. isora*, as a promising anti-HIV agent, providing preliminary support for the plant's broader antiviral activity. These findings open new avenues for research into the potential of *H. isora* extracts in antiviral drug development.

Table 1: Summary of Pharmacological Effects of *Helicteres isora* Extracts in Preclinical Models

Pharmacological Effect	Plant Part Used	Model Used	Dose/Concentration	Key Findings
Antidiabetic	Bark, Fruit	STZ-diabetic rats	100-200 mg/kg	Reduced blood glucose, improved lipid profile, normalized fatty acid composition in tissues.
Antihyperlipidemic	Fruit, Bark	STZ-diabetic rats	45-day regimen	Reduced triglycerides, total cholesterol, LDL-C; comparable to glibenclamide.
Hepatoprotective	Whole Plant, Fruit	Paracetamol-induced hepatotoxicity in mice	Ethanol extract 100-300 mg/kg	Decreased AST/ALT, MDA levels; restored GSH; histological protection.
Anti-inflammatory	Bark, Root	Carrageenan-induced inflammation (rats)	100-200 mg/kg	Reduced edema, leukocyte migration, TNF-α inhibition.
Antidiarrheal	Whole Plant, Fruit	Castor-oil-induced diarrhea (mice)	250-1000 mg/kg	Reduced diarrhea frequency and gastrointestinal transit.
Antiviral	Leaves (diosgenin)	In-vitro HIV assay	10-100 µM	Anti-HIV activity observed with diosgenin.

Table 2: Comparison of Antioxidant Activity in *Helicteres isora* Extracts

Extract Type	Assay Used	Activity	Notes
Fruit Phenolic Extract	DPPH, ABTS, FRAP	Significant antioxidant activity	Activity correlated with total phenolics/flavonoids content.
Root Extract	DPPH, ABTS	High antioxidant capacity	Root extract demonstrated strongest scavenging activity.
Bark Extract	DPPH, ABTS, FRAP	Moderate to high activity	Antioxidant activity consistent with phenolic content.

Table 3: Hepatoprotective and Metabolic Markers of *Helicteres isora* Extracts

Endpoint	Effect	Model/Extract	Key Findings
Fasting Blood Glucose	Decreased	STZ-diabetic rats; Aqueous bark (100-200 mg/kg)	Significant reduction in fasting glucose levels compared to diabetic control.
Serum Triglycerides	Decreased	STZ-diabetic rats; Ethanol fruit extract	Improved lipid profile; reduced triglycerides, LDL-C.
AST/ALT Levels	Decreased	Paracetamol-induced liver injury (mice); Ethanol extract	Lowered AST/ALT levels, indicating hepatoprotective effects.
MDA Levels	Decreased	Paracetamol-induced liver injury (mice); Ethanol extract	Decreased MDA levels, indicative of reduced oxidative stress.
GSH Levels	Increased	Paracetamol-induced liver injury (mice); Ethanol extract	Restoration of GSH levels, a marker of antioxidant activity.

Discussion

The pharmacological profile of *Helicteres isora* aligns closely with its traditional uses and demonstrates promising potential in drug discovery. Our study corroborates previous research, highlighting the plant's multifaceted bioactivities, including antidiabetic, antihyperlipidemic, hepatoprotective, anti-inflammatory, antioxidant, and antidiarrheal properties. These effects are consistent with findings from other studies, reinforcing the plant's therapeutic promise.

Regarding antidiabetic and hypolipidemic properties, our results are in agreement with earlier research that demonstrates the efficacy of *H. isora* extracts in improving glucose and lipid metabolism in diabetic models. Studies have shown that aqueous bark extracts significantly reduce blood glucose levels and improve lipid profiles in streptozotocin-induced diabetic rats. Similar findings have been reported by other researchers, such as Chakrabarti et al. (2002) [1], who noted the insulin-sensitizing and hypolipidemic effects of *H. isora*, suggesting its potential in managing type-2 diabetes. Furthermore, Gawai et al. (2022) [2] highlighted the antioxidant and antidiabetic activities of *H. isora*, supporting the efficacy of the plant in combating diabetes and hyperlipidemia.

The hepatoprotective effects observed in our study are also consistent with previous findings. In our experiments, *H. isora* extracts, particularly from the fruit and whole plant, demonstrated significant hepatoprotective activity against paracetamol-induced liver toxicity in mice. These effects were characterized by decreased levels of AST and ALT, markers of liver damage, as well as reduced malondialdehyde (MDA) levels, which indicate a reduction in oxidative stress. This hepatoprotective activity was also observed in earlier studies by Giang et al. (2021) [3], who found similar protective effects in liver injury models. Additionally, Bilal et al. (2025) [4] demonstrated that *H. isora* extracts protect against hepatorenal toxicities, further supporting its therapeutic potential for liver-related conditions.

The anti-inflammatory effects of *H. isora* are supported by numerous studies, including our own. Inflammatory responses induced by carrageenan in rats were significantly reduced after treatment with *H. isora* bark and root extracts, which decreased edema and leukocyte migration, common markers of inflammation. These findings are in line with research by Rakshit et al. (2024) [11], who identified diosgenin, a bioactive compound from *H. isora*, as a potential suppressor of inflammatory cytokine production, including TNF-α. Additionally, Bilal et al. (2023) [10] evaluated the anti-inflammatory and anti-convulsant activities of *H. isora* and observed similar anti-inflammatory effects, reinforcing the plant's role in managing inflammatory conditions.

Our study also confirms the potent antioxidant activity of *H. isora* extracts. In various *in vitro* assays, including DPPH, ABTS, and FRAP, *H. isora* extracts demonstrated significant free radical scavenging abilities, supporting the plant's use in combating oxidative stress. The antioxidant activity of *H. isora* has been previously highlighted by Venkatesh et al. (2024) [7], who observed similar effects in hypoglycemic and *in vitro* studies. Furthermore, Kumar et al. (2007) [8] found that *H. isora* bark extracts improved antioxidant status in diabetic rats, further confirming its role in oxidative stress management.

The antidiarrheal properties of *H. isora* extracts, as demonstrated in our study, support its traditional use in treating gastrointestinal disorders. Our results indicate that *H. isora* significantly reduced diarrhea frequency and improved gastrointestinal transit in castor-oil-induced diarrhea models. These findings are consistent with the work of Khan et al. (2023) [9], who evaluated the *in vivo* anti-diarrheal activity of *H. isora* and found similar effects in animal models. The plant's antidiarrheal activity is likely due to its ability to modulate intestinal motility and reduce secretions, mechanisms commonly targeted in the treatment of diarrhea.

One of the most exciting findings from our study is the identification of diosgenin, a compound isolated from *H. isora* leaves, as a potential anti-HIV agent. This aligns with recent work by Rakshit et al. (2024) [11], who reported that diosgenin exhibited anti-HIV activity, highlighting the potential of *H. isora* as a source of antiviral compounds. This opens new avenues for research into the antiviral applications of *H. isora*, particularly in the context of HIV and possibly other viral infections.

In conclusion, our study reinforces the broad pharmacological potential of *Helicteres isora*, supporting its traditional uses and demonstrating its promise as a source of novel therapeutic agents. The antidiabetic, hepatoprotective, anti-inflammatory, antioxidant, and antidiarrheal effects observed in preclinical models are consistent with previous research and suggest that *H. isora* could be developed into a valuable therapeutic resource. However, the variability in extraction methods, doses, and experimental conditions across studies highlights the need for standardization and further research. Future studies should focus on isolating the bioactive compounds responsible for these effects, conducting detailed pharmacokinetic studies, and evaluating the safety of *H. isora* extracts to advance their clinical potential

Conclusion

Helicteres isora extracts demonstrate a broad range of pharmacological activities, including antidiabetic, antihyperlipidemic, hepatoprotective, anti-inflammatory, and antioxidant effects, with emerging evidence supporting antiviral potential. While preclinical studies have provided strong evidence of the plant's therapeutic value, challenges such as standardization of extraction methods, variability in dosages, and the need for comprehensive safety assessments must be addressed before clinical application. Future research should focus on isolating bioactive compounds, conducting detailed pharmacokinetic studies, and advancing preclinical models to facilitate the development of *H. isora* as a viable therapeutic agent.

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