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A Promising Path for Gastritis Treatment: Policy Recommendation for the Integration of *Scrophularia striata* Based on Anti-Ulcer Scientific Evidence

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Abstract

This study investigated the therapeutic potential of the hydro-alcoholic extract of *Scrophularia striata* (*S. striata*) for treating ethanol-induced gastritis in Wistar rats. Gastritis was experimentally induced to assess the protective and healing effects of the extract. A total of 24 rats were treated with the extract at a dose of 100 mg/kg for 14 days. The ulcer index and gene expression levels of *Annexin A1 (AnxA1), Phospholipase A2* (*PLA2*), and *inducible nitric oxide synthase* (*iNOS*) were analyzed to evaluate the anti-inflammatory and tissue-repairing properties of the extract. Results showed a 52.77% reduction in ulcer severity, with significant upregulation of *AnxA1* and downregulation of *PLA2* and *iNOS*. These findings indicate that *S. striata* modulates key inflammatory pathways to promote gastric mucosal healing. The study supports the traditional use of *S. striata* in treating gastrointestinal disorders and highlights its potential as a natural therapeutic agent. It also emphasizes the importance of integrating traditional medicine with modern biomedical research to develop effective, plant-based treatments for common health issues like gastritis.

Keywords: Gastritis, *Scrophularia striata*, *Annexin-A1*, *Phospholipase-A2*, *iNOS*

1. Background

Gastritis is a widespread gastrointestinal disorder characterized by inflammation of the gastric mucosa, often caused by an imbalance between aggressive factors like gastric acid and the stomach's protective mechanisms.[1] Common causes include *Helicobacter pylori* infection and long-term use of NSAIDs. While current treatments such as proton pump inhibitors and H2 antagonists are available, they often fall short in terms of effectiveness and safety, prompting a growing interest in natural alternatives. Ethanol-induced gastritis models are widely used to study and test new therapeutic agents due to their similarity to human gastric injury.[2]

At the molecular level, the Annexin A1 (AnxA1)/ Phospholipase A2 (PLA2)/inducible nitric oxide synthase (iNOS) pathway plays a central role in gastric inflammation and tissue repair. AnxA1 promotes healing by inhibiting PLA2 and iNOS, which are involved in the production of harmful inflammatory mediators. This pathway is crucial for maintaining gastric mucosal integrity.[3]

Scrophularia striata (*S. striata*), a traditional medicinal plant in Iran, has been used for treating inflammatory and gastrointestinal conditions. However, its anti-ulcer mechanisms remain poorly understood.[4]

2. Methods

This experimental study followed ethical guidelines for animal care and used 24 male Wistar rats (180-230 g) housed under standard conditions. Animals were randomly divided into four groups of six: Control (no treatment), Sham (distilled water), Gastritis (ethanol-induced ulcer), and Treatment (ethanol-induced ulcer +100 mg/kg *S. striata* extract for14 days). After the treatment period, the rats were euthanized, and stomach tissues were collected for analysis.

Macroscopic evaluation was conducted to calculate the Ulcer Index and Ulcer Inhibition Percentage. RNA was extracted from the tissue, and cDNA was synthesized for Real-Time PCR analysis. The mRNA expression levels of *AnxA1*, *PLA2*, and *iNOS* were measured using the ΔΔCt method and normalized to a reference gene.

3. Results

Macroscopic results obtained from the examination of the gastric mucosa of the experimental rats revealed that the ethanol-induced gastritis group suffered severe, hemorrhagic lesions in the gastric mucosa. However, the animals in the treatment group, which received the Scrophularia striata extract (100 mg/kg), showed significant healing of

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the mucosal layer damage compared to the gastritis group. Based on calculations, the Ulcer Inhibition Percentage achieved by the *Scrophularia* extract was 52.77%, which indicates a potent anti-ulcer activity of the extract. In molecular evaluations using Real Time PCR, it was observed that ethanol-induced gastritis significantly increased the mRNA expression of the inflammatory genes *PLA2* and *iNOS* compared to the control and sham groups. Conversely, gavage of the *S. striata* extract for 14 days significantly decreased the mRNA levels of both *PLA2* and *iNOS* genes in comparison to the gastritis group. Furthermore, the *S. striata* extract significantly increased the mRNA level of the anti-inflammatory gene *AnxA1* in the stomach tissue of the treated rats, indicating the positive effect of the extract on healing and anti-inflammatory pathways.

4. Discussion and Conclusion

The findings of this study demonstrate that the hydro-alcoholic extract of *S. striata* exhibits significant anti-ulcer activity in an ethanol-induced gastritis model in laboratory rats. The extract effectively reduced gastric mucosal damage and enhanced healing, achieving a52.77% ulcer inhibition rate. Given that gastritis is a common gastrointestinal disorder, often caused by NSAIDs or *H. pylori* infection, and can progress to severe or pre-cancerous conditions, the development of safe and effective natural treatments is of high priority.

The therapeutic mechanism of *S. striata* involves the regulation of key inflammatory pathways. Molecular data show that the extract downregulates the expression of pro-inflammatory genes such as *PLA2* and *iNOS*, which are involved in the production of harmful mediators like reactive oxygen species and excessive nitric oxide. Simultaneously, it upregulates the expression of *AnxA1*, a well-known endogenous anti-inflammatory gene that supports mucosal repair and inhibits PLA2 activity. This suggests that the protective effect of the extract is mediated through the AnxA1/PLA2/iNOS axis, enhancing the body's natural defense mechanisms.

These results support the traditional use of *S. striata* in gastrointestinal treatments and highlight its potential as a natural therapeutic agent for acute gastritis. It is recommended that policymakers and health authorities consider this plant as a promising candidate for further pharmaceutical development. Future clinical trials in human subjects are necessary to confirm its efficacy and safety. Encouraging scientific research on native medicinal plants can contribute to the development of domestic pharmaceutical products and reduce dependence on foreign drugs.

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Author Contributions

Authors contributed equally to this work.

Conflict of Interest Disclosures

All authors declared that they have no conflict of interest.

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