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REVIEW ARTICLE

Medicinal Plants Used for Hepatoprotective Activity: A Focus on Picrorhiza kurroa Royle ex Benth. and Piper longum L.

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ABSTRACT

The liver is vital for numerous physiological functions, including metabolism, detoxification, and immune regulation. Hepatic diseases, which may arise from infections, drugs, alcohol, toxins, and metabolic disorders, represent a major global health challenge. Traditional medicine has provided a wealth of plant-based remedies for liver protection. This review aims to evaluate and compare the hepatoprotective activity of several medicinal plants in rats, with a focus on Picrorhiza kurroa, Piper longum, Silybum marianum, and Andrographis paniculata. By examining their phytochemical composition, mechanisms of action, and the experimental evidence from rat models, we present a comprehensive understanding of their hepatoprotective potential and therapeutic value.

1. INTRODUCTION

The liver is a highly regenerative organ but is prone to damage from various insults, including chemicals (e.g., CCl_4), drugs (e.g., acetaminophen), infections (e.g., hepatitis), and metabolic disturbances (e.g., fatty liver disease). Traditional medicinal plants have been used across cultures for centuries to support liver function and treat liver-related ailments.[1] This review focuses on evaluating medicinal plants with demonstrated hepatoprotective effects in experimental rat models. Rats are commonly used to study liver damage due to their physiological similarities with humans.[2] By comparing the hepatoprotective mechanisms, phytochemical profiles, and efficacy of plants like Picrorhiza kurroa, Piper longum, Silybum marianum, and Andrographis paniculata, this review provides valuable insights into the therapeutic potential of these plants.[3]

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2. MATERIALS AND METHODS

A comprehensive literature review was conducted to identify studies evaluating the hepatoprotective effects of Picrorhiza kurroa, Piper longum, Silybum marianum, and Andrographis paniculata in rat models. The search included peer-reviewed articles, research papers, and review articles published in scientific journals.

3. FINDINGS AND DISCUSSION

3.1 Mechanisms of Hepatoprotective Action

Hepatoprotective agents protect the liver from damage or help regenerate liver cells after injury. Various mechanisms contribute to their hepatoprotective action, including:

Antioxidant Activity: The liver is highly susceptible to oxidative stress, which leads to liver damage. Hepatoprotective plants reduce free radical formation and enhance antioxidant enzyme activity.[4]

Anti-inflammatory Effects:Inflammation plays a key role in liver damage. By suppressing pro-inflammatory cytokines and enzymes, hepatoprotective plants reduce liver inflammation.[5]

Liver Regeneration: Some plants stimulate hepatocyte regeneration by activating growth factors and transcription factors involved in cell proliferation and repair. [6]

Anti-fibrotic Activity: Chronic liver injury often leads to fibrosis, which can progress to cirrhosis. Some medicinal plants help prevent or reverse liver fibrosis by inhibiting collagen synthesis. [7]

Modulation of Lipid Metabolism: Hepatoprotective plants can regulate lipid metabolism, preventing fat accumulation and oxidative damage caused by fat storage in hepatocytes. [8]

3.2 Comparative Overview of Selected Medicinal Plants

3.2.1 *Picrorhiza kurroa* (Kutki)

Picrorhiza kurroa is a well-known herb in Ayurvedic medicine, commonly used to treat liver disorders such as jaundice, hepatitis, and cirrhosis.[8] Its hepatoprotective effects are attributed to its rich composition of iridoid glycosides, flavonoids, and triterpenoids.

Phytochemistry

Picrosides I and II: Iridoid glycosides are the primary bioactive compounds in Picrorhiza kurroa. These compounds possess potent antioxidant and anti-inflammatory activities. [9]

Triterpenoids: Known for its hepatoprotective and anti-inflammatory properties.

Flavonoids: Contributes to the antioxidant properties of the plant.

Mechanisms of Action

Antioxidant Effects: Picrorhiza kurroa significantly reduces oxidative stress by scavenging free radicals and enhancing the activities of liver antioxidant enzymes (e.g., SOD, catalase, and glutathione).[10]

Anti-inflammatory Effects:It reduces pro-inflammatory cytokines (e.g., TNF-α, IL-6) and inhibits the activation of NF-κB, a key regulator of inflammation. [11]

Anti-fibrotic Action:Picrorhiza kurroa reduces liver fibrosis by inhibiting collagen deposition and downregulating α-SMA (a marker of hepatic stellate cell activation). [12]

Experimental Evidence

CCl_4-Induced Hepatotoxicity: In rats, Picrorhiza kurroa administration significantly reduces serum ALT, AST, and ALP levels, indicating a protective effect against liver damage. [13]

Liver Regeneration: Histopathological analysis in rats shows improved liver architecture and reduced necrosis following treatment with Picrorhiza kurroa. [14]

Fibrosis Models:In chronic models of liver injury, the plant reduced the accumulation of fibrotic tissue and prevented the progression to cirrhosis. [7]

3.2.2 Piper longum (Long Pepper)

Piper longum is another Ayurvedic herb known for its diverse biological activities, including hepatoprotective effects.[15] The primary active constituent, piperine, has demonstrated antioxidant and anti-inflammatory properties, which are key to its liver-protective effects.[16]

Phytochemistry

Piperine: The main bioactive alkaloid responsible for Piper longum's hepatoprotective effects.[17]

Flavonoids and Essential Oil: Contributes to its antioxidant, anti-inflammatory, and antimicrobial activities.[18]

Mechanisms of Action

Antioxidant Effects: Piper longum has been shown to significantly reduce lipid peroxidation in liver tissues and enhance the liver's antioxidant defense system.[19]

Anti-inflammatory Effects: It suppresses the expression of pro-inflammatory cytokines (e.g., TNF-α, IL-6) and inhibits COX-2 and iNOS, which are key drivers of liver inflammation. [20]

Liver Regeneration: Piper longum enhances hepatocyte proliferation and supports liver regeneration in rat models.

Experimental Evidence

CCl_4-Induced Hepatotoxicity: In rats, treatment with Piper longum significantly lowered liver enzyme levels and improved liver function markers (ALT, AST). [5]

Acetaminophen-Induced Liver Injury: Piper longum demonstrated protective effects against acetaminophen-induced oxidative stress, preventing hepatocellular necrosis and inflammation.[14]

Fibrosis Models: Piper longum inhibits liver fibrosis in rat models by reducing collagen deposition and

improving liver histopathology.

3.2.3 Silybum marianum (Milk Thistle

Silybum marianum is one of the most researched plants in hepatoprotection due to its primary active compound, silymarin. This plant has been widely studied for its effects on liver diseases such as cirrhosis, hepatitis, and drug-induced liver injury.[21]

Phytochemistry

Silymarin: A flavonoid complex consisting of silybin, silydianin, and silychristin, silymarin is the key bioactive component responsible for its hepatoprotective effects.[22]

Mechanisms of Action

Antioxidant Activity: Silymarin acts as a powerful free radical scavenger, significantly reducing oxidative stress in the liver and increasing intracellular glutathione levels.[23]

Regeneration of Hepatocytes: Silymarin stimulates liver cell regeneration by promoting protein synthesis in hepatocytes.
Anti-inflammatory Effects: It inhibits NF-κB activation, reducing the production of inflammatory cytokines and mediators involved in liver damage. [24]

Experimental Evidence

CCl_4-Induced Hepatotoxicity:In rats, Silybum marianum treatment resulted in significantly lower ALT, AST, and ALP levels. Histological studies showed improved liver architecture and reduced liver injury. [25]
Fibrosis Models: Silymarin prevents liver fibrosis by reducing collagen deposition and lowering liver stiffness in chronic liver injury models..

3.2.4 Andrographis paniculata (King of Bitters)

Andrographis paniculata is a well-known herb in Asia, traditionally used to treat a wide range of conditions, including liver diseases. Its major bioactive compound, andrographolide, has demonstrated significant hepatoprotective effects.[26]

Phytochemistry

Andrographolide: The primary diterpenoid lactone is responsible for most of the plant's therapeutic effects, including hepatoprotection.[27]

Mechanisms of Action

Antioxidant Activity: Andrographis paniculata reduces oxidative stress by increasing the levels of liver antioxidants, such as SOD and catalase.
Anti-inflammatory Effects: It suppresses the expression of inflammatory mediators, including TNF-α and IL-1β, and inhibits NF-κB signaling. [28]
Liver Regeneration: The plant promotes hepatocyte proliferation and accelerates liver regeneration in rat models. [29]

Experimental Evidence

CCl_4-Induced Hepatotoxicity:Rats treated with Andrographis paniculata demonstrated a significant reduction in liver enzyme levels, and liver histology revealed a decrease in necrosis and inflammatory cells. [30]
Alcohol-Induced Liver Injury: The plant reduced hepatic inflammation and oxidative stress in alcohol-induced liver injury models.

4. DISCUSSION

This review highlights the hepatoprotective potential of several medicinal plants, with Picrorhiza kurroa, Piper longum, Silybum marianum, and Andrographis paniculata standing out due to their strong therapeutic effects in rat models.
Picrorhiza kurroa is especially strong in its antioxidant and anti-fibrotic effects, making it ideal for treating chronic liver conditions. [9]
Piper longum offers a broader spectrum approach, with antioxidant, anti-inflammatory, and regenerative effects.[31]

Silybum marianum is the most clinically validated, with extensive research supporting its use in liver regeneration, antioxidation, and anti-inflammatory effects.[4]

Andrographis paniculata offers strong regenerative properties and antioxidant effects, though its use in liver fibrosis models is less studied compared to the other three.[26]

5.CONCLUSION

These plants, either individually or in combination, offer significant promise as natural hepatoprotective agents. Further clinical trials are needed to translate these findings into human therapies and fully explore the therapeutic potential of these medicinal plants.

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All the authors contributed equally to the design and execution of the article.

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This manuscript does not require ethical approval as it is a review study.

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This is an original manuscript, and all data are available for review purposes only from principal investigators.

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1. Comparison of Medicinal Plants for Hepatoprotective Activity

Property/Plant	*Picrorhiza kurroa*	*Piper longum*	*Silybum marianum*	*Andrographis paniculata*
Key Active Compounds	Picrosides I and II, Triterpenoids	Piperine, Flavonoids, Essential Oils	Silymarin (Silybin, Silychristin)	Andrographolide
Antioxidant Activity	Strong (reduces ROS and enhances antioxidants)	Moderate (reduces lipid peroxidation)	Very Strong (increases glutathione, reduces ROS)	Moderate (increases SOD, catalase)
Anti-inflammatory Activity	Strong (inhibits TNF-α, IL-6, COX-2)	Moderate (reduces lipid peroxidation)	Very Strong (inhibits NF-κB, reduces cytokines)	Strong (inhibits TNF-α, IL-1β, NF-κB)
Regeneration of Hepatocytes	Moderate to strong	Moderate	Strong (stimulates protein synthesis)	Strong (promotes cell proliferation)
Anti-fibrotic Activity	Strong (reduces collagen deposition)	Moderate (reduces fibrosis markers)	Moderate (reduces liver stiffness)	Moderate (reduces collagen deposition)
Hepatotoxicity Models Tested	CCl_4, Chronic Liver Injury	CCl_4, Acetaminophen	CCl_4, Alcohol, Chronic Liver Injury	CCl_4, Alcohol
Primary Mechanism	Antioxidant, Anti-fibrotic	Antioxidant, Regeneration	Antioxidant, Regeneration, Anti-inflammatory	Antioxidant, Anti-inflammatory
Overall Efficacy	High	High	Very High	Moderate to High