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A Review: On Hepatoprotective Activity of Herbal Formulations

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ABSTRACT
Liver diseases are a major global health concern, caused by alcohol, drugs, toxins, viruses, and metabolic disorders. Conventional hepatoprotective drugs, while effective, are often limited by side effects, high cost, and variable therapeutic outcomes. Herbal formulations have emerged as safer, cost-effective alternatives with multi-targeted hepatoprotective potential. This review summarizes the major hepatoprotective herbal formulations used in traditional medicine, including Liv.52, Triphala, Phyllanthus-based preparations, PunarnavaMandur, Kalmegh syrups, Silymarin, and Ecliptaalba formulations. These formulations exert protective effects through diverse mechanisms such as antioxidant activity, anti-inflammatory action, antiviral effects, membrane stabilization, prevention of lipid peroxidation, enhancement of bile secretion, and activation of detoxification enzymes. Experimental and clinical evidence demonstrates their efficacy in preventing liver injury and restoring hepatic function. The review also highlights the bioactive phytochemicals responsible for these effects, including flavonoids, phenolics, alkaloids, terpenoids, and saponins. Despite promising results, further research is needed to standardize formulations, evaluate long-term safety, and conduct large-scale clinical trials. Collectively, herbal formulations represent a valuable and scientifically supported approach for liver protection and management of liver disorders.

Keywords: Hepatoprotective activity; herbal formulations; liver injury; phytochemicals; oxidative stress.

I. INTRODUCTION

The liver is a vital metabolic organ that performs numerous essential physiological functions, including carbohydrate, lipid, and protein metabolism, detoxification of xenobiotics, regulation of biochemical pathways, synthesis of plasma proteins, and bile secretion. Because it serves as the primary site for the metabolism of drugs, chemicals, and toxins, the liver is particularly vulnerable to damage from both endogenous and exogenous sources. Liver diseases continue to be a significant global health burden, contributing to high morbidity and mortality worldwide [1]. The major etiological factors responsible for hepatic injury include chronic alcohol consumption, prolonged use of hepatotoxic drugs like paracetamol and certain antibiotics, viral infections such as hepatitis B and C, aflatoxin exposure, autoimmune disorders, metabolic diseases including non-alcoholic fatty liver disease (NAFLD), and environmental toxins [2].

Conventional therapeutic approaches for liver disorders generally involve corticosteroids, antiviral drugs, immunomodulators, and antioxidants such as N-acetylcysteine. Although these drugs provide symptomatic relief or disease control, their long-term usage is often limited due to side effects, high cost, low patient compliance, and inadequate therapeutic response in chronic liver diseases [3].These challenges have driven increasing global interest in natural hepatoprotective agents derived from medicinal plants.

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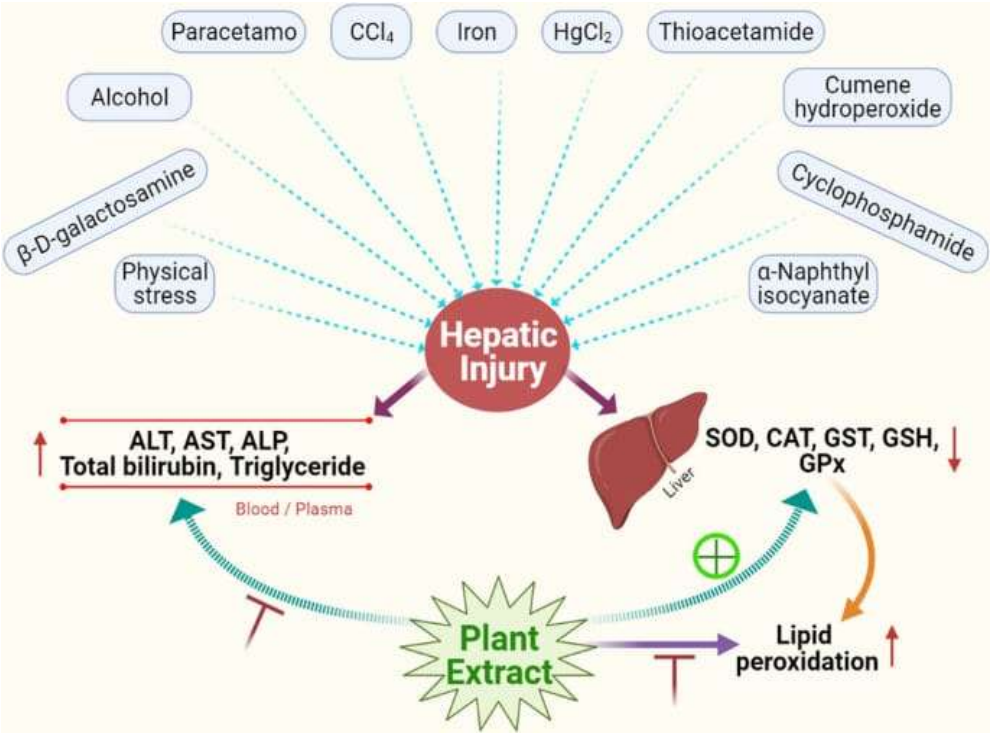

Figure 1 : Overview of Hepatotoxic agent and plant based Hepatoprotection

Herbal formulations especially polyherbal preparations used in Ayurveda, Siddha, and other traditional medicinal systems have gained considerable recognition for their hepatoprotective and restorative properties. Such formulations typically contain multiple plant ingredients rich in bioactive phytochemicals including flavonoids, alkaloids, phenolics, terpenoids, lignans, and saponins. These compounds act synergistically through multiple biological pathways to protect hepatocytes from oxidative stress, inflammation, fibrosis, viral infections, and toxin-induced damage [4].

Some of the most widely studied herbal formulations include Liv.52, Triphala, Phyllanthus-based preparations, Kalmegh syrups, PunarnavaMandur, Ecliptaalba formulations, Kutki preparations, Aloe vera extracts, and Silymarin-based syrups. These formulations have shown multiple pharmacological actions such as antioxidant defense enhancement, reduction of lipid peroxidation, membrane stabilization, anti-inflammatory activity, immunomodulation, bile secretion stimulation, and promotion of liver tissue regeneration. Several experimental and clinical studies have validated these effects, demonstrating that polyherbal combinations may provide therapeutic benefits comparable to or greater than individual plant extracts.

Given the rising incidence of liver diseases and the pressing need for safe, effective, and affordable hepatoprotective therapies, herbal formulations hold significant potential in both preventive and therapeutic contexts. This review aims to systematically summarize the key herbal formulations used for liver protection, their phytochemical constituents, mechanisms of action, and the supporting experimental and clinical evidence.

II. MATERIALS AND METHODS

Since this review does not involve experimental work, the methodology focuses on the systematic process used for literature collection and evaluation. A comprehensive literature search was conducted across major electronic databases including PubMed, ScienceDirect, Google Scholar, Scopus, Web of Science, Research Gate, along with relevant Ayurvedic classical texts. Keywords such as hepatoprotective activity, herbal formulations, Ayurveda,liver protection, phytochemicals, Liv.52, Triphala, Phyllanthusniruri, Picrorhizakurroa, oxidative stress, and drug-induced hepatotoxicity were used either singly or in combination to retrieve relevant studies.

To ensure scientific quality and relevance, studies published between 2000 and 2025 were

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considered and screened according to predefined inclusion criteria. Only research articles reporting hepatoprotective activity of herbal extracts or formulations, including in vitro assays, in vivo animal models, and clinical trials, were included. Studies describing phytochemical profiles and mechanisms of action were also selected, and only publications available in English were considered. Articles lacking scientific evidence, unrelated formulations, duplicate records, and non-English texts without translation were excluded.

From each selected study, essential information such as plant species, type of herbal formulation, active phytochemicals, experimental models of hepatotoxicity (e.g., CCl_4, paracetamol, alcohol), biochemical parameters (SGOT, SGPT, ALP, bilirubin), proposed mechanisms, and key findings were systematically extracted. The collected data were then synthesized into major thematic areas including common hepatoprotective formulations, phytochemical constituents, mechanisms of action, comparative efficacy, and existing research gaps. A qualitative synthesis approach was adopted to identify trends, summarize outcomes, and provide a comprehensive understanding of the hepatoprotective potential of herbal formulations.

Mechanisms of Hepatoprotection

The hepatoprotective effects of herbal formulations are mediated through multiple complementary mechanisms, as illustrated in Figure 1. These mechanisms include antioxidant activity, where bioactive compounds such as flavonoids and phenolics scavenge free radicals and enhance endogenous antioxidant enzymes like superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), thereby reducing oxidative stress [5].

Anti-inflammatory action is another critical mechanism, involving the inhibition of pro-inflammatory mediators such as TNF-α, IL-1β, and COX-2, which prevents inflammation-induced liver damage. Certain formulations, particularly Phyllanthus species, exhibit antiviral effects, protecting hepatocytes against hepatitis viruses. Membrane stabilization is a key protective mechanism that maintains hepatocyte integrity against toxin-induced injury. Additionally, herbal formulations help in the prevention of lipid peroxidation, reducing cell membrane damage caused by reactive oxygen species. Finally, they enhance detoxification enzyme activity and bile secretion, facilitating the metabolism and excretion of xenobiotics and toxins, which further supports liver function. Collectively, these multi-targeted mechanisms underscore the efficacy of herbal formulations in maintaining hepatic health and mitigating liver injury.

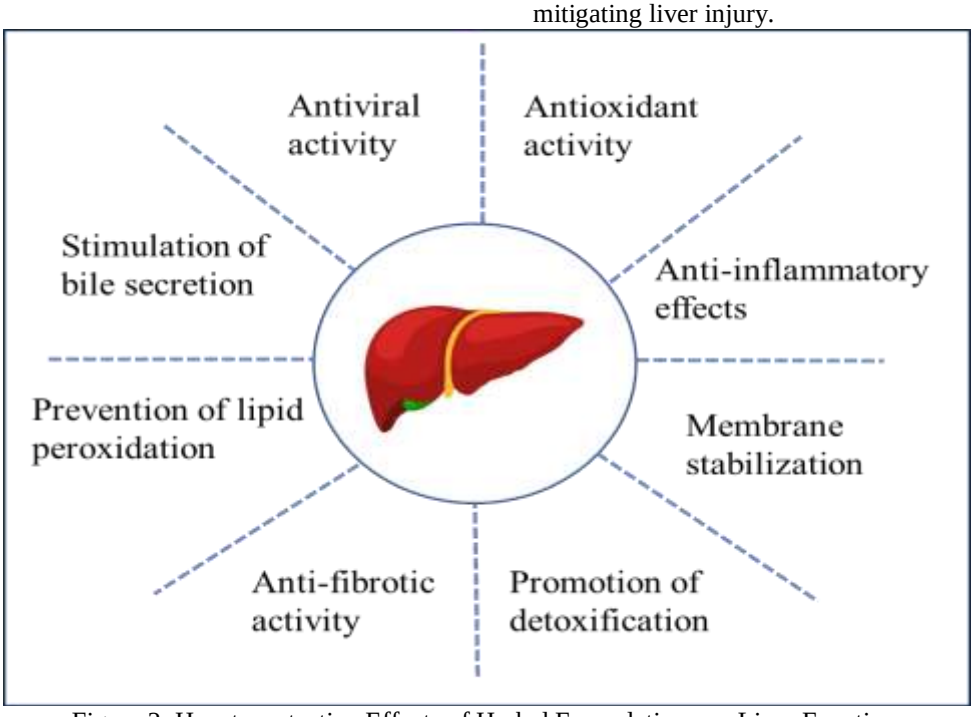

Figure 2 :Hepatoprotective Effects of Herbal Formulations on Liver Function

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III. REVIEW OF LITERATURE

Common Hepatoprotective Herbal Formulations

A wide range of herbal formulations from Ayurveda and traditional medicine systems have been studied for their hepatoprotective activity. Among them, Liv.52, Triphala, Kalmegh syrups, PunarnavaMandur, Phyllanthus-based preparations, Ecliptaalba formulations, Silymarin, and Kutki formulations are the most documented. These polyherbal and single-herb preparations contain mixtures of medicinal plants that act synergistically to protect liver tissue. Liv.52 is one of the most widely used formulations for alcohol-induced, viral, and drug-induced hepatotoxicity, while Triphala is known for its potent antioxidant activity. Similarly, Kalmegh formulations rich in andrographolide, as well as Phyllanthus species containing phyllanthin, have been extensively validated for hepatoprotective and antiviral effects. Additionally, Aloe vera and Giloy (Tinosporacordifolia) formulations have shown significant hepatoprotective and immunomodulatory effects, enhancing liver enzyme levels and reducing oxidative stress.

Table 1: Commonly used hepatoprotective herbal formulations, their key ingredients, major phytochemicals, and mechanisms of action:

Herbal Formulation	Key Ingredients	Major Phytochemicals	Mechanism of Action	Reference
Liv.52	Capparisspinosa, Cichoriumintybus, Solanum nigrum, etc.	Flavonoids, tannins	Antioxidant, membrane stabilization, enzyme restoration	Sharma et al., 2010[6]
Triphala	Terminalia chebula, T. bellirica, Emblica officinalis	Gallic acid, ellagic acid, ascorbic acid	Antioxidant, reduces lipid peroxidation	Peterson et al., 2017[7]
Phyllanthus-based formulations	Phyllanthusniruri	Phyllanthin, hypophyllanthin	Hepatitis B antiviral, antioxidant	Lee et al., 2011[8]
Kalmegh Syrups	Andrographispaniculata	Andrographolide	Anti-inflammatory, enhances bile secretion	Akbar, 2011[9]
PunarnavaMandu	Boerhaviadiffusa + polyherbal blend	Punarnavine, flavonoids	Diuretic, antioxidant, anti-inflammatory	Chandan et al., 2008[10]
Eclipta alba formulations	Eclipta alba	Wedelolactone, luteolin	Boosts SOD, CAT, protects	Singh et al., 2012[11]
Silymarin formulations (Milk Thistle)	Silybummarianum	Silymarin complex (silybin, silydianin, silychristin)	Antioxidant, anti-fibrotic, membrane stabilizer, increases glutathione	Flora et al., 1998[12]
Kutki formulations	Picrorhizakurroa	Picroside I & II, apocynin	Antioxidant, anti-inflammatory, stimulates bile flow	Dwivedi et al., 1991[13]

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Pomegranate formulations	Punicagranatum peel extract	Punicalagin, ellagic acid	Antioxidant, hepatocyte protection, increases SOD/CAT/GSH	Aviram et al., 2000[14]
Neem formulations	Azadirachtaindica	Azadirachtin, nimbin, nimbidin	Antioxidant, anti-inflammatory, protects against CCl_4 toxicity	Chattopadhyay, 1996[15]
Licorice Syrup	Glycyrrhizaglabra	Glycyrrhizin, liquiritin	Anti-inflammatory, antiviral, membrane stabilizer	Fiore et al., 2005[16]
Guduchi/Giloy formulations	Tinosporacordifolia	Tinosporaside, berberine	Immunomodulatory, antioxidant, protects from alcohol & paracetamol toxicity	Rege et al., 1999[17]
Boerhaviadiffusa Rasayana	Boerhaviadiffusa	Punarnavine, boeravinones	Anti-fibrotic, anti-inflammatory	Chandan et al., 2008[18]
Daruharidra formulations	Curcuma longa	Curcumin, demethoxycurcumin	Anti-inflammatory, anti-fibrotic, antioxidant	Aggarwal et al., 2007[19]
Aloe vera formulations	Aloe barbadensis	Aloin, emodin, polysaccharides	Antioxidant, membrane repair, protects against paracetamol toxicity	Pandey & Mishra, 2010[20]
Spirulina capsules	Spirulina platensis	Phycocyanin, carotenoids	Antioxidant, anti-inflammatory, reduces liver enzymes	Khan et al., 2005[21]
Chicory formulations	Cichoriumintybus	Chicoric acid, inulin, coumarins	Antioxidant, anti-inflammatory, protects from CCl_4 toxicity	Ahmed et al., 2003[22]
Fenugreek formulations	Trigonellafoenum-graecum	Diosgenin, saponins	Anti-lipid peroxidation, improves liver enzymes, reduces fat accumulation	Kaviarasan et al., 2007[23]

IV. DISCUSSION

The findings from various experimental and clinical studies highlight the broad-spectrum hepatoprotective potential of herbal formulations. Their effectiveness is primarily attributed to the presence of multiple phytochemicals that act synergistically, targeting several pathological processes involved in liver injury. This multi-targeted approach is especially important because liver diseases often arise from complex interactions between oxidative stress, inflammation, metabolic disturbances, and membrane damage.

One of the most clinically validated formulations, Liv.52, demonstrates hepatoprotection through enhancement of antioxidant enzymes, stabilization of hepatocyte membranes, and restoration of hepatic function markers such as ALT and [24].

Its multi-herb composition enables reduction of lipid peroxidation, prevention of free radical accumulation, and improvement of liver histology in alcohol- and toxin-induced liver damage models. Triphala, a classical Ayurvedic formulation, is rich in phenolic compounds including gallic acid, ellagic acid, and ascorbic acid, which confer strong antioxidant activity. By reducing oxidative stress, Triphala effectively prevents cellular damage in CCl_4- and paracetamol-induced hepatotoxicity [25]. Its ability to modulate detoxifying enzymes further supports its hepatoprotective properties.

Kalmegh (Andrographispaniculata)-based formulations exhibit potent anti-inflammatory and hepatostimulant effects. Andrographolide, the main bioactive compound, inhibits inflammatory cytokines such as TNF-α and IL-6, which are major

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mediators in toxin-induced liver injury [26]. Studies show that Kalmegh extracts significantly reduce necrosis, restore glutathione levels, and improve bile flow. Phyllanthus species, particularly Phyllanthusniruri, have gained prominence due to their antiviral activity against hepatitis B virus. The lignansphyllanthin and hypophyllanthin inhibit viral DNA polymerase, reduce oxidative stress, and protect hepatocytes from inflammation-mediated damage [27].

PunarnavaMandur and Boerhaviadiffusa-based preparations exert hepatoprotection predominantly through antioxidant and diuretic actions while also reducing tissue edema and inflammation [28]. Their role in preventing fibrosis and promoting regeneration makes them valuable in chronic liver diseases. Ecliptaalba (Bhringraj) formulations significantly enhance the activities of antioxidant enzymes such as superoxide dismutase (SOD) and catalase (CAT). Wedelolactone and luteolin contribute to membrane stabilization, reduced lipid peroxidation, and restoration of liver architecture in toxin-induced models [29].

Formulations containing Silymarin, derived from Silybummarianum, are among the most scientifically validated hepatoprotective agents. Silymarin stabilizes hepatocyte membranes, enhances protein synthesis, reduces fibrosis, and scavenges reactive oxygen species. Its role in restoring hepatic glutathione levels makes it particularly useful in cases of alcohol- and drug-induced liver injury.

Other formulations such as Kutki (Picrorhizakurroa), Aloe vera, Neem (Azadirachtaindica), Pomegranate peel extracts, Giloy (Tinosporacordifolia), Chicory, and Fenugreek further contribute to hepatoprotection through diverse mechanisms including anti-fibrotic activity, enhanced detoxification, immunomodulation, membrane repair, and metabolic regulation.

Overall, the reviewed herbal formulations demonstrate promising hepatoprotective effects due to their rich phytochemical diversity and multifaceted mechanisms of action. These combinations not only prevent toxin-induced damage but also promote the healing and regeneration of liver tissue. However, despite encouraging evidence, challenges such as a lack of standardization, variability in phytochemical content, and limited large-scale clinical trials still restrict their widespread therapeutic use. Future research should prioritize quality control, dose standardization, mechanistic studies, and well-designed clinical trials to firmly establish their efficacy and safety.

V. FUTURE SCOPE

Despite substantial evidence supporting the hepatoprotective potential of herbal formulations, several gaps remain that provide opportunities for future research. First, there is a need for standardization of herbal extracts and formulations, as variations in cultivation conditions, extraction methods, and phytochemical concentrations can significantly influence therapeutic activity. Future studies should focus on establishing consistent quality control parameters, including marker compounds and validated analytical profiles.

Secondly, although numerous preclinical studies have demonstrated strong hepatoprotective effects, there is a shortage of large-scale, randomized clinical trials to confirm safety and efficacy in human populations. Conducting well-designed clinical studies will be essential to translate traditional herbal knowledge into evidence-based therapeutic options. Advancements in molecular biology and omics technologies offer opportunities to uncover precise mechanisms of action of herbal constituents. Future investigations should incorporate genomics, proteomics, metabolomics, and network pharmacology to understand the multi-targeted interactions of phytochemicals at cellular and molecular levels.

These approaches can also help identify novel bioactive compounds with potent hepatoprotective properties. Another promising direction is the development of herbal-nanoparticle formulations, which can enhance bioavailability, targeted delivery, and therapeutic efficacy. Incorporating nanotechnology into herbal medicine may overcome limitations related to poor solubility or low absorption of certain phytochemicals.

Additionally, exploring synergistic combinations of polyherbal formulations with standard hepatoprotective drugs may improve clinical outcomes while minimizing adverse effects. This integrative approach could open new avenues in personalized medicine for liver disorders. Finally, research should address long-term safety profiling, herb–drug interactions, and toxicological evaluations to ensure the safe use of herbal formulations. Collectively, these future directions can significantly strengthen the scientific foundation of herbal hepatoprotective therapies and support their integration into modern healthcare.

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VI. CONCLUSION

Herbal formulations play a significant and scientifically supported role in protecting the liver against a wide range of chemical, microbial, and metabolic insults. The reviewed literature clearly demonstrates that medicinal plants rich in flavonoids, phenolics, alkaloids, terpenoids, glycosides, and lignans exert potent antioxidant, anti-inflammatory, antiviral, and membrane-stabilizing effects. These bioactive compounds restore hepatic enzymes, prevent lipid peroxidation, enhance bile secretion, and support detoxification pathways, thereby promoting overall hepatocyte health and regeneration. Polyherbal formulations such as Liv.52, Triphala, Phyllanthusniruri, Boerhaviadiffusa, Picrorhizakurroa, and Glycyrrhizaglabra have been widely validated through in vitro studies, animal models, and limited clinical trials. Their multi-targeted actions make them safer and more holistic alternatives to synthetic hepatoprotective drugs, which often cause side effects. However, challenges remain in terms of standardization, dose consistency, active component isolation, and large-scale clinical validation. Future studies should focus on molecular pathways, formulation optimization, toxicity profiling, and controlled human trials to strengthen their therapeutic acceptance. Overall, the evidence supports that herbal formulations are effective, economical, and promising hepatoprotective agents, with strong potential for integration into modern healthcare and complementary therapeutic strategies.

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