

Medicinal Plant Extracts and Herbal Formulations to control hepatotoxicity: A Review

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CONTENTS

1. INTRODUCTION
2. DRUG TO TREAT HEPATOTOXICITY
3. TRADITIONAL MEDICINE AND ETHNOBOTANY
4. PLANTS WITH HEPATOPROTECTIVE POTENTIAL
5. CONCLUSIONS
6. REFERENCES

ABSTRACT

Hepatotoxicity, which arises from exposure to various toxins, pharmaceuticals, infections, or metabolic disorders, is a significant global health issue. Traditional treatment methods often come with considerable side effects, leading to increased interest in plant-based solutions recognized for their effectiveness and safety. Historically, medicinal plants have been used in traditional medicine systems for liver protection, providing bioactive compounds such as flavonoids, alkaloids and polyphenols that demonstrate anti-inflammatory, antioxidant, and hepatoprotective effects. This review aimed to show the potential of different plants by examining their phytochemical compositions and mechanisms through which they mitigate liver damage and additionally, it provides a list of potential plant species for liver health applications. By analysing scientifically validated research and identifying less-studied plant species, this study underscores the necessity for further exploration to incorporate these natural remedies into contemporary therapeutic practices. Such an approach could facilitate the creation of innovative and sustainable treatments for liver-related conditions.

Key words: Antioxidant, *Cuminum cyminum*, Hepatotoxicity, *Phyllanthus amarus*, Phytochemicals, *Silybum marianum*.

1. INTRODUCTION

The liver is an essential organ for preserving healthy physiological processes in living organisms. The digestion and metabolism of proteins, carbohydrates and fats, the excretion of endogenous and foreign metabolites, bile synthesis, urea production and the biotransformation and detoxification of xenobiotics are all carried out in this central hub. Any damage to the liver leads to changes in physiological processes resulting in hepatotoxicity (11). Certain pharmacological agents are associated with a high risk of

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inducing liver hepatotoxicity, a condition with potentially fatal outcomes. While it may initially present with mild or subclinical manifestations, severe cases can advance to hepatic fibrosis, acute liver failure, or mortality (43). The pathophysiology of drug-induced hepatotoxicity (DIH) is still unclear and diagnosis is extremely difficult due to the lack of reliable diagnostic indicators (28). DIH is mainly categorized as hepatocellular injury (characterized by elevated alanine aminotransferase (ALT) levels), cholestatic injury (marked by increased alkaline phosphatase (ALP) levels) and mixed injury (features elevations in both ALT and ALP) (27). The prevalence of hepatotoxicity is higher in tuberculosis patients undergoing treatment with first-line anti-tuberculosis agents. Thus, routine assessment of liver function is imperative, especially in patients of advanced age, those with underlying comorbidities, or cases involving extrapulmonary tuberculosis, to minimize the risk and severity of drug-induced hepatic injury (33). Environmental toxins [(heavy metals like cadmium (Cd), lead (Pb) and arsenic)] are the major contributors to hepatotoxicity, promoting liver diseases like Non-alcoholic fatty liver disease (NAFLD), fibrosis, cirrhosis and hepatocellular carcinoma (HCC). Cd disrupts liver function by altering cellular signalling and inducing defective autophagy, which can either mitigate or exacerbate hepatotoxicity. Normal autophagy protects against Cd toxicity, but impaired autophagy worsens liver damage. Strategies such as autophagy-targeting therapies, chelating agents and antioxidant phytochemicals show promise in mitigating Cd-mediated liver injury (38). Additionally, excessive alcohol intake, metabolic disorders like NAFLD and diabetes and chronic infections such as hepatitis B and C are key contributors to hepatotoxicity, causing liver injury via generating oxidative stress, lipid accumulation and inflammation. Genetic conditions like Wilson's disease and hemochromatosis lead to toxic metal buildup, while poor diets exacerbate oxidative damage. Pharmacological interventions targeting oxidative stress, inflammation, lipid metabolism, alongside chelating agents for metal detoxification, are crucial for managing and preventing DIH (4). Since ancient times, phytochemicals from plant-derived natural products have been extensively used for their therapeutic efficacy, as well as their roles in dietary formulations and as bioactive nutritional supplements. The diverse array of bioactive constituents, including essential vitamins, minerals, phenolic compounds, antioxidants and enzymatic components, underscores their significant pharmacological relevance and their integral contributions to the medicinal, nutraceutical and functional food industries (12). According to the literature, medicinal plants are rich sources of bioactive compounds including flavonoids, alkaloids, terpenoids, etc., has significant hepatoprotective potential. Flavonoids such as silymarin and quercetin, phenolic compounds like curcumin and ellagic acid and triterpenoids including glycyrrhizin and ursolic acid exhibit potent antioxidant and anti-inflammatory activities. Alkaloids such as berberine and piperine, along with saponins like diosgenin and coumarins such as scopoletin, play a critical role in enhancing hepatic detoxification and cytoprotection. Additional sterols, essential oils, polysaccharides and antioxidants like andrographolide and resveratrol, prevent hepatotoxicity by modulating oxidative stress, inflammation and cellular repair. These pharmacologically active compounds prevents liver injury and preservation of hepatic functioning (5,17,52).

2. DRUGS TO TREAT HEPATOTOXICITY

Hepatotoxicity (liver damage induced by chemicals, requires immediate intervention to avoid serious liver harm). The initial step in treatment is to stop exposure to the harmful substance and offer supportive care. For acetaminophen (paracetamol) toxicity, N-acetylcysteine (NAC) is the recommended antidote, as it helps restore glutathione levels, enhancing detoxification processes and minimizing liver injury (42). In management of other drug-induced liver injuries, the primary approach involves symptomatic treatment and continuous monitoring of liver function, as targeted antidotes are not available. Ongoing research is investigating novel therapeutic strategies, (hepatoprotective agents and antioxidants) to facilitate liver recovery in hepatotoxicity cases (15).

3. TRADITIONAL MEDICINE AND ETHNOBOTANY

Traditional medicines encompass a wealth of knowledge, practices and beliefs based on the use of plant-based remedies for various health conditions. Ethnobotany, focuses on the interactions between humans and plants, particularly their applications in local and indigenous medicinal practices. Together, these disciplines provide valuable insights into the natural remedies used to treat liver diseases and other ailments (9). Similarly, in Ethiopia, traditional medical practices utilize 276 plant species across 89 families to address hepatic disorders, underscoring the rich botanical diversity and indigenous knowledge in hepatoprotection (36). A prime example of the overlap between traditional wisdom and modern research is *Phyllanthus amarus*, a plant widely used in traditional systems like Ayurveda for liver ailments. Studies have demonstrated its hepatoprotective effects, attributed to compounds like phyllanthin and gallic acid (31). Likewise, plants such as *Silybum marianum* (milk thistle) and *Andrographis paniculata* (kalmegh) are known for their potent bioactive components, including silymarin and andrographolide, respectively, which support liver function through antioxidative and anti-inflammatory mechanisms (41). Ethnobotanical research serves as a bridge between age-old practices and contemporary medicine by identifying promising plants for further pharmacological exploration. As such, it plays a vital role in fostering the development of plant-based hepatoprotective drugs while emphasizing the need for sustainable use and conservation of these natural resources (10). List of plants used in traditional herbal formulations to treat hepatotoxicity is mentioned in Table 1.

Table 1. List of plants used in traditional herbal formulations to treat hepatotoxicity.

S. No	Source (Plant)	Traditional Use	Bioactive Compounds	Medicines/ Extracts	Mechanism of Action	Ref.
1	<i>Phyllanthus amarus</i>	Treats jaundice and liver disorders	Phyllanthin, gallic acid	Liv-52, <i>Phyllanthus amarus</i> herbal tea	Antioxidant, anti-inflammatory, hepatocyte repair	16
2	<i>Silybum marianum</i>	Protects liver from toxins	Silymarin	Legalon, Milk Thistle Extract	Antioxidant enhances glutathione synthesis	39

3	<i>Cuminum cyminum</i>	Improves digestion and liver function	Cumin aldehyde, flavonoids	Cumin herbal supplements	Antioxidant, anti-inflammatory	31
4	<i>Boerhavia diffusa</i>	Reduces liver swelling	Punarnavoside alkaloids	Punarnava syrup, Ayurvedic tablets	Diuretic, antioxidant, hepatocyte regeneration	35
5	<i>Picrorhiza kurroa</i>	Manages bile flow disorders	Picrosides, kutkin	Picrorhiza capsules, Kutki powder	Enhances bile secretion, reduces oxidative stress	44
6	<i>Allium sativum</i>	Supports liver detoxification	Allicin, sulfur compounds	Garlic oil capsules, Herbal syrups	Antioxidant, antifibrotic	22
7	<i>Curcuma longa</i>	Reduces liver inflammation	Curcumin, volatile oils	Curcumin supplements, Turmeric extracts	Anti-inflammatory, antifibrotic	13
8	<i>Glycyrrhiza glabra</i>	Relieves liver inflammation	Glycyrrhizin, flavonoids	Licorice tablets, Herbal teas	Anti-inflammatory, hepatoprotective	53
9	<i>Terminalia chebula</i>	Supports digestion and liver health	Tannins, chebulagic acid	Triphala powder, Ayurvedic supplements	Antioxidant, hepatocyte regeneration	19
10	<i>Azadirachta indica</i>	Detoxifies the liver	Nimbin, azadirachtin	Neem capsules, Herbal extracts	Antioxidant, anti-inflammatory	54
11	<i>Eclipta prostrata</i>	Treats liver disorders and jaundice	Wedelolactone, flavonoids	Bhringraj oil, Herbal supplements	Antioxidant, anti-inflammatory	25
12	<i>Tinospora cordifolia</i>	Immunomodulator and liver protector	Alkaloids, diterpenoids	Giloy tablets, Guduchi extract	Antioxidant, anti-inflammatory	40
13	<i>Nigella sativa</i>	Supports liver detoxification	Thymoquinone, alkaloids	Black seed oil capsules	Antioxidant, hepatoprotective	18
14	<i>Solanum nigrum</i>	Treats liver inflammation	Solanine, saponins	Black nightshade extracts	Antioxidant, anti-inflammatory	37
15	<i>Berberis aristata</i>	Improves liver function	Berberine	Berberine supplements	Antioxidant, bile secretion	7
16	<i>Cichorium intybus</i>	Protects the liver from oxidative stress	Chicoric acid, flavonoids	Chicory root powder, Herbal teas	Antioxidant, hepatocyte repair	49
17	<i>Emblica Officinalis</i>	Protects liver from damage	Ascorbic acid, polyphenols	Amla juice, Herbal capsules	Antioxidant, anti-inflammatory	32

18	<i>Zingiber officinale</i>	Reduces liver inflammation	Gingerol, shogaol	Ginger tablets, Ginger extracts	Antioxidant, anti-inflammatory	46
19	<i>Fumaria indica</i>	Treats liver and bile disorders	Alkaloids, fumaric acid	Fumaria herbal extracts	Enhances bile secretion, antioxidant	47
20	<i>Acacia catechu</i>	Treats liver inflammation	Catechins, flavonoids	<i>Acacia Catechu</i> Extract Capsules, Herbal decoctions	Antioxidant, anti-inflammatory	1
21	<i>Adhatoda vasica</i>	Relieves liver congestion	Vasicine, alkaloids	Herbal syrups (Himalaya Liv.52 Syrup)	Anti-inflammatory, antioxidant	48
22	<i>Aegle marmelos</i>	Supports liver detoxification	Marmelosin, tannins	Bael juice, Herbal powders	Antioxidant, hepatocyte repair	26
23	<i>Aloe vera</i>	Detoxifies and soothes the liver	Aloin, polysaccharides	Aloe juice, Aloe extracts	Antioxidant, hepatoprotective	20
24	<i>Bacopa monnieri</i>	Improves liver function	Bacosides, alkaloids	Brahmi tablets, Herbal teas	Antioxidant, anti-inflammatory	34
25	<i>Carica papaya</i>	Treats liver disorders	Papain, flavonoids	Papaya leaf extracts	Antioxidant, anti-inflammatory	50
26	<i>Cassia occidentalis</i>	Detoxifies the liver	Chrysophanol, emodin	Herbal teas, Organic Cassia Occidentalis Powder	Antioxidant, bile secretion	21
27	<i>Centella asiatica</i>	Improves liver repair	Asiaticoside, madecassoside	Gotu Kola capsules, Herbal powders	Antioxidant, hepatocyte regeneration	24
28	<i>Citrus limon</i>	Detoxifies liver	Vitamin C, limonene	Lemon juice, Herbal extracts	Antioxidant, bile flow enhancer	8
29	<i>Coriandrum sativum</i>	Supports liver function	Coriandrol, flavonoids	Coriander herbal capsules	Antioxidant, anti-inflammatory	47

4. PLANTS WITH HEPATOPROTECTIVE POTENTIAL

Throughout history, plants have been used in treating various illnesses, as they have lower toxicity and minimal side effects (6). Human health greatly benefits from medicinal plants and around 80 % of people worldwide in underdeveloped nations use traditional

plant-based treatment (14). Historically, these plants have been used to treat liver disorders, with numerous studies highlighting their significant hepatoprotective effects. Hepatoprotective compounds help safeguard the liver or reduce damage and many phytoconstituents have demonstrated effectiveness in both *in-vitro* and *in-vivo* experiments (2). Traditional herbal remedies are highly regarded due to their diverse chemical composition, cost-effectiveness, low toxicity and wide-ranging pharmacological benefits, making them a crucial asset for developing new drugs (29). Numerous plants are reported as hepatoprotective Table 2.

Table 2. List of plants reported as hepatoprotective in experimental studies.

S.no	Plant Name	Family	Plant Part	Ref
1	<i>Silybum marianum</i>	<i>Asteraceae</i>	Seeds	2
2	<i>Glycyrrhiza glabra</i>	<i>Fabaceae</i>	Roots	2
3	<i>Phyllanthus amarus</i>	<i>Euphorbiaceae</i>	Whole Plant	2
4	<i>Salvia miltiorrhiza</i>	<i>Lamiaceae</i>	Roots	23
5	<i>Astragalus membranaceus</i>	<i>Fabaceae</i>	Whole Plant	2
6	<i>Capparis spinosa</i>	<i>Capparidaceae</i>	Whole Plant	2
7	<i>Cichorium intybus</i>	<i>Asteraceae</i>	Leaves	51
8	<i>Solanum nigrum</i>	<i>Solanaceae</i>	Whole Plant	2
9	<i>Ginkgo biloba</i>	<i>Ginkgoaceae</i>	Leaves	2
10	<i>Tecomella undulata</i>	<i>Bignoniaceae</i>	Stem Bark	2
11	<i>Andrographis paniculata</i>	<i>Acanthaceae</i>	Whole Plant	52
12	<i>Bauhinia purpurea</i>	<i>Fabaceae</i>	Leaves	52
13	<i>Commelina nudiflora</i>	<i>Commelinaceae</i>	Whole Plant	52
14	<i>Dillenia suffruticosa</i>	<i>Dilleniaceae</i>	Whole Plant	52
15	<i>Elaeis guineensis</i>	<i>Arecaceae</i>	Fruit	52
16	<i>Lygodium microphyllum</i>	<i>Lygodiaceae</i>	Whole Plant	52
17	<i>Morinda citrifolia</i>	<i>Rubiaceae</i>	Fruit	52
18	<i>Phyllanthus muellarianus</i>	<i>Euphorbiaceae</i>	Leaves	2
19	<i>Picrorhiza kurroa</i>	<i>Scrophulariaceae</i>	Roots	23
20	<i>Cochlospermum vitifolium</i>	<i>Cochlospermaceae</i>	Whole Plant	53
21	<i>Heterotheca inuloides</i>	<i>Asteraceae</i>	Whole Plant	53
22	<i>Hibiscus sabdariffa</i>	<i>Malvaceae</i>	Flowers	53
23	<i>Leucophyllum frutescens</i>	<i>Scrophulariaceae</i>	Whole Plant	53
24	<i>Prosthechea michuacana</i>	<i>Orchidaceae</i>	Whole Plant	53
25	<i>Psidium guajava</i>	<i>Myrtaceae</i>	Leaves	53
26	<i>Rosmarinus officinalis</i>	<i>Lamiaceae</i>	Leaves	53
27	<i>Verbena caroliniana</i>	<i>Verbenaceae</i>	Whole Plant	53
28	<i>Centaurea americana</i>	<i>Asteraceae</i>	Whole Plant	53
29	<i>Juglans mollis</i>	<i>Juglandaceae</i>	Leaves	53
30	<i>Krameria ramosissima</i>	<i>Krameriaceae</i>	Roots	53
31	<i>Turnera diffusa</i>	<i>Passifloraceae</i>	Whole Plant	53
32	<i>Eclipta alba</i>	<i>Asteraceae</i>	Whole Plant	3

5. CONCLUSIONS

Plant-based remedies for hepatotoxicity offers a valuable pathway to enhance liver health through holistic and sustainable methods. The wide range of bioactive compounds present in medicinal plants, including flavonoids, alkaloids and polyphenols, demonstrates considerable potential for protecting the liver due to their anti-inflammatory and antioxidant activity. This review underscores the significance of merging traditional medicinal practices with modern scientific research to deepen our understanding of these natural treatments. By focusing on lesser-known plant species, we can discover new therapeutic options that may work alongside existing liver treatments. The necessity for additional research is paramount, to find innovative strategies that not only reduce the impact of hepatotoxicity but also support overall liver wellness. Embracing these natural remedies, can facilitate the development of effective, safe and sustainable treatment options that meet contemporary healthcare demands. Ultimately, fostering collaboration between traditional knowledge and scientific exploration may unlock breakthroughs in liver therapy, significantly improving patient outcomes on a global scale.

AUTHOR'S CONTRIBUTION

In this review, AB, AM, PB and S have made a significant contribution to prepare the manuscript, conducted the systemic evaluation and provided detailed conclusions. All authors have carefully examined and approved the final article.

DECLARATION

The authors declare that the review paper contains tables are prepared originally and all references are cited throughout the manuscript.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ETHICAL APPROVAL

This manuscript did not involve any use of animals and humans, hence no ethical approval is required from the concerned committee.

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