REVIEW

Herbal Defenders of the Liver: Exploring Pakistan's Medicinal Flora for Hepatoprotection

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Abstract

Liver diseases are one of the leading global health risks with prevalence in developing countries. Indigenous medicinal plants remained promising, cost-effective, and culturally acceptable alternative therapy for hepatoprotection. This review provides an overview of several prospective indigenous medicinal plants having hepatoprotective efficacy with phytochemistry, potential anti-inflammatory activity, mechanism of action, as well as the key bioactive components such as curcumin from Curcuma longa and α-amyrin from Morus indica. Some case studies support the efficacy of Mangifera indica L., Kalanchoe pinnata (Lam.) Pers., Berberis lyceum Royle., Helianthus annus, and Cynodondactylon as therapeutic options. Other pharmacological studies were included to reiterate the efficacy of liver herbal remedies in curing hepatic damage with Cichorium intybus, Cinnamomum verum, and Andrographis paniculata. Although medicinal plants may have potential to ameliorate hepatic diseases, issues surrounding standardization, dosage, and clinical use remain challenging to utilize medicinal plants for hepatoprotective therapies. This review offers insights for future direction of the hepatoprotective drug discovery process by suggesting better ways of utilizing herbal compounds and a higher degree of integrated research that leads to exploration of herbal and natural compounds for the advancement of hepatoprotective drug discovery.

Key words: *Anti-inflammation, Hepatoprotection, Medicinal plants, Phytochemicals*

Introduction

Liver is the most important organ in the body due to its role in protein, lipid, and carbohydrate metabolism. Liver disease (acute or chronic) represents a global health issue, and effective medical treatment for hepatic diseases is not always readily available (Ali et al., 2019). Most liver diseases fall into one of the four categories: fatty liver, fibrosis, cirrhosis and hepatocellular carcinoma. Liver cancer and cirrhosis are among the most pressing global health concerns (Hussain et al., 2021). Natural medication from medicinal plants is increasingly being used to treat liver ailments, because of their effectiveness, affordability, and positive safety profiles. (Gonfa et al., 2024).

The World Health Organization (WHO) has estimated that more than 170 million people are suffering from hepatitis C with about 3-4 million are added each year. Besides, more than 2 billion people are suffering from HBV worldwide, and as many as 5 million are getting exposed to acute HBV every year (Mahmood et al., 2014). Thus, the role of complementary and alternative medicines to treat liver diseases has received much interest. About 80% of the population worldwide depends on indigenous medicinal plants for their healthcare requirements due to their enhanced tolerability, superior compatibility with the human body, and lesser adverse effects in both developing and industrialized countries (Mahmood et al., 2014). Another contributing factor for preference of using indigenous medicinal plants over conventional medication is the affordability in terms of financial burden (Kumar et al., 2011).

Herbal medicines are widely available and generally safe. Around 160 phytoconstituents from 101 plant species have been characterized with hepatoprotective activity (Handa et al., 1986). Although herbal medicines are usually safe; yet 30% of the patients can have serious negative effects on liver, kidney, perforation of the colon, carcinoma, coma or death (Raj et al., 2009). Patients turn to complementary medicines due to limited alternatives and low rate of treatment failure, including natural alternatives with limited scientific evidence regarding quality, safety a and efficacy (Ali et al., 2019). Hepatoprotective potential of 69 indigenous medicinal plant species from 38 families have been reported for the treatment of 15 particular liver diseases (Akhtar et al., 2023). *Nigella sativa* and *Piper nigrum* extracts have exhibited protective effects against concanavalin A induced liver injury in mice (Mushtaq, 2021). This article aims to discuss the indigenous hepatoprotective plants in terms of ethnopharmacological uses, active ingredients, chemical constituents, and pharmacological effects.

Phytochemical Properties of Medicinal Plants:

Phytochemicals, the bioactive molecules of herbal plants have hepatoprotective potential to counter the hepatic threats. Secondary metabolites such as alkaloids, flavonoids, phenolic compounds, terpenoids, steroids, saponins, tannins, and anthraquinones play crucial roles in hepatoprotection. Several prominent phytoconstituents, including silymarin, quercetin, luteolin, glycyrrhizin, curcumin, gallic acid, catechin, aloin, emodin, liquiritin, liquiritigenin, and karaviloside, have been identified as effective agents in treating hepatotoxicity (Figure 1; Gonfa et al., 2024).

Flavonoids:

A diverse subset of polyphenolic chemicals with antioxidant properties demonstrates many beneficial impacts on the human physiological system. They help in protecting against oxidative damage and promoting liver regeneration.

Silymarin: obtained from the seeds of *Silybum marianum*, normally referred to as milk thistle, is a bioflavonoid extensively studied for its liver-protective properties. It is considered to be effective against various toxins such as CCl_4 and alcohol, beneficial effects on antioxidant status, and on membrane stability (Ali et al., 2017).

Quercetin: found in fruits and vegetables, has strong antioxidant properties and has been used to minimize the deterioration of liver cells due to oxidative stress (Ali et al., 2017).

Terpenoids:

A highly important category of phytochemicals having significant hepatoprotective mechanism. These substances are highly appreciated for their ability to prevent inflammations and to act as antioxidants.

Oleanolic Acid: sourced from many plants, including olive tree (*Olea europaea*), oleanolic acid has been proved to possess hepatoprotective effects through the decrease of inflammation and fibrosis of liver tissue (Venmathi Maran et al., 2022).

Echinocystic Acid: from *Eclipta prostrata*, offers hepatic protection through the suppression of oxidative stress and inflammation in rats (Ali et al., 2017).

Phenolic Compounds:

The prevalent phenolics, such as tannins and phenolic acids are reported for their antioxidant property essential for the vital function of liver.

Gallic Acid: from plants like *Terminalia chebula* demonstrated ability in defending the liver against CCl_4 toxicity through suppression of oxidative stress caused by ROS and increasing the activity of antioxidants (Ali et al., 2017; Venmathi Maran et al., 2022).

Chlorogenic Acid: found in coffee and some fruits also shows the hepatoprotective activity because of their influence on liver enzymes and prevention of lipid peroxidation (Arman et al., 2022).

Alkaloids:

Phytochemicals also include alkaloids which have prevent the hepatotoxicity.

Berberine: derived from *Berberis vulgaris*, has the potential for the prevention of alcohol induced liver injury through mitigation of inflammation and oxidative stress (Ali et al., 2017; Arman et al., 2022).

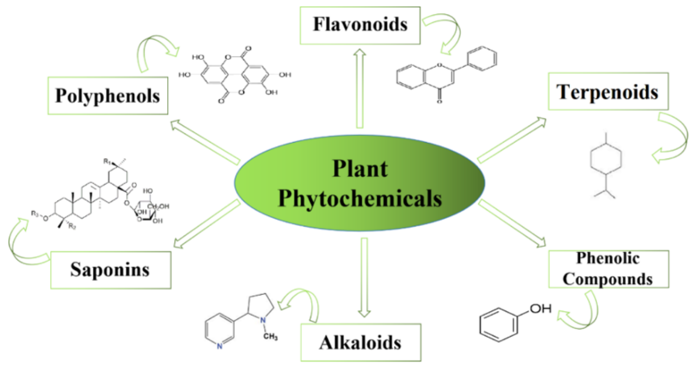

Figure 1: Plant phytochemicals and their common structures.

Saponins:

Saponins work as active substances to promote liver function and show the hepatoprotection effect by regulating lipid profile and decreasing the inflammation in the body.

Glycyrrhizin: A naturally occurring compound, glycyrrhizin is isolated from *Glycyrrhiza glabra*, also known as licorice, and acts as an anti-liver injury compound because of its anti-inflammatory capabilities as well as it stimulates liver cell division (Venmathi Maran et al., 2022).

Polyphenols:

Polyphenols are the phytochemicals with hepatoprotective potential.

Resveratrol: An antioxidant found in grapes and berries was proved effective to reduce liver inflammation, oxidative stress and initiating programmed cell death in liver cells. It manages the inflammations that occur and at the same time encourages antioxidant activity (Khan & Ibrahim, 2022).

Caffeic Acid: This phenolic compound possesses the ability to fight inflammation and act as an antioxidant as the main factor for the healing of the severe liver injuries. Thereby controlling key signaling particles to increase liver information data (Khan & Ibrahim, 2022).

Potential Hepatoprotective Activity of Medicinal Herbs:

Silybum marianum (milk thistle), *Glycyrrhiza glabra* (licorice), and *Phyllanthus amarus* have hepatoprotective potential via immunomodulation, increased DNA synthesis, and increased levels of antioxidants. These plants also reduce oxidative stress, decrease levels of intracellular ROS, and serve as inhibitors of ethanol-induced lipid accumulation in the liver, which can be helpful in treating liver disease (Ali et al., 2017).

Oral administration of *A. arvensis* to rats reduced the liver enzymes (ALT, AST, ALP, and bilirubin) and raised lipid profiles (cholesterol, TG, LDL, and VLDL), showing strong hepatoprotective action (Shabbir et al., 2022). Hepatoprotective potential of plants of Asteraceae and Fabaceae family has shown improvements in serum liver enzymes, oxidative stress indicators, and histopathological characteristics (Shawon et al., 2024).

Schaftoside and Echinocystic acid have been reported to have hepatoprotective activity in *in vivo* CCl_4 and paracetamol induced models (Arman et al., 2022). Pandey et al. (2023) has reported that phytoconstituents from plants have antioxidant, free radical scavenging, and lipid peroxidation reduction capabilities.

Impact of Anti-inflammatory Herbs in Hepatoprotection:

Medicinal plants remained effective in mitigating the toxicity in the liver caused by inflammation and injury induced by different hepatotoxic substances. The ethanolic extract of rooted bark from *Capparis spinosa* showed remarkable liver protective effects against CCl_4-induced liver injury in mice. The treatment reduced liver enzymes significantly, restored normal sleep duration, and improved liver histology with less necrosis and inflammation. The extract showed no evidence of toxicity at the doses used, likely due to its high antioxidant capacity (Aghel et al., 2010).

The anti-hepatotoxic activity of the dried hydro–alcoholic extract obtained from *Peumus boldus* (Monimiaceae) was evaluated *in vitro* against tert-butyl hydroperoxide and *in vivo* against CCl_4 induced toxicity, which showed the alkaloid boldine may have a major role in this line of action. Although some prophylactic choleretic properties were not observed in rats, the specific extract demonstrated the dose-related anti-inflammatory activity tests in edema induced by carrageenan. These outcomes confirm the protective effect of *P. boldus* for the liver and anti-inflammatory activity, suggesting the further use of this plant in therapeutic approaches (Lanhers et al., 1991).

A particular experiment analyzed the performance of *Sida rhombifolia* regarding drug and chemical induced hepatotoxicity as well as carrageenan induced paw edema in rat. The powder and aqueous extracts of the roots and aerial parts of plant possessed promising hepatoprotective effects against different hepatotoxicants like CCl_4, paracetamol and rifampicin. The methanolic extract of the aerial parts also revealed superior edema suppressant activity. The hepatoprotective effects were due to the ability of compounds to influence the process of hepatic regeneration and to scavenge free radicals, the anti-inflammatory role may be caused by blocking the release of histamine-like substances (Rao & Mishra, 1997).

The dichloromethane extract from the roots of *D. juxtapostia* showed strong anti-inflammatory activity both *in vitro* (urease blockage, 56.7% of the time) and *in vivo* (paw oedema caused by carrageenan and formaldehyde, 61.7–67.3% of the time). This indicates that anti-inflammatory mechanisms may complement its hepatoprotective potential (Rani et al., 2022).

Anti-inflammatory and hepatoprotective efficacy of Chinese herb Peh-Hue-Juwa-Chi-Cao (PHJCC), an extract from *Hedyotis diffusa*, *Hygrophila corymbosa*, and *Mollugo pentaphylla* revealed that all the three extracts possess anti-inflammatory property particularly *M. pentaphylla* having the highest inhibition activity against the induced paw edema using carrageenan by reducing the acute spike in sGOT and sGPT levels (Lin et al., 2002).

Hepatoprotective Plants of Pakistan

Several indigenous medicinal plants are used for their hepatoprotective activities. These medicinal properties, plant parts and their active ingredients are summarized in Table 1.

Table 1: Hepatoprotective Plants of Pakistan.

Scientific Name	Common Name	Family	Parts Used	Constituents	Properties
Azadirachta indica **(Nunes et al., 2020)**	Neem	Meliaceae	Leaf, root, oil, seed, gum, fruit, flower.	Margosine, Bitteroil, Azadirachtin	Medicinal properties, anti-inflammatory
Coriandrum sativum **(Nunes et al., 2020)**	Cilantro	Umbellifer aeapiacea e	Leaf, bark, flower	Tannin, cathartin, malic acid, cathartin, albuminoids	Anti- inflammatory, antioxidant, antidiabetic, antimicrobial
Cuscuta reflexa **(Nunes et al., 2020)**	Amarbail / dodder	Convolvula ceae	Plant, seed, fruit, stem.	Cuscutine, flavonoid, glucoside, bergenin, coumarin	Anti-inflammatory
Ficus benghalensis **(Nunes et al., 2020)**	Banyan	Moraceae	Aerial roots, bark, seeds, leaves, buds, fruits, latex.	Skin, fruits contain 10% tannin.	Anti-inflammatory or Phytochemical
Hibiscus rosa-sinesis **(Nunes et al., 2020)**	Chinese hibiscus / Shoe flower	Malvaceae	Buds, roots, leaves, flower	Quercetin, ascorbic acid.	Effective against liver toxicity, anti-inflammatory
Ocimum basilicum **(Nunes et al., 2020)**	Sweet basil	Lamiaceae	Whole plant	Acetic acid, Ascorbic acid, aspartic acid, apigenin, arginine.	Anti- inflammatory, hepatoprotective

Momordi cacharantia **(Nunes et al., 2020)**	Bitter gourd / Bitter melon	Cucurbitaceae	Whole plant	5-Hydroxytrypt amine, alkaloids, ascorbic acid, β-carotene, cholesterol, lutein, diosgenin, lanosterol, lycopene, momordicin, charantin niacin, momordicoside	Hepatoprotective, anti-inflammatory
Solanum melongena **(Nunes et al., 2020)**	Eggplant / Brinjal	Solanaceae	Roots, leaves, tender fruits.	Ascorbic acid, alanine, arginine, caffeic acid.	Have Anti-inflammatory properties
Tinospora cordifolia **(Balkrishna et al., 2024; Madhavi et al., 2024)**	Guduchi, giloy, amrita	Menispermaceae	Whole plant, leaves and fruit	Alkaloids (berberine), palmatine, jatrorrhizine and sinapic acid	Anti-inflammatory, anticancer, antioxidant, antimicrobial properties
Alhagi maurorum **(Cao et al., 2024; Mahboubi et al., 2025)**	Turanjabeen/ camel thorn	Legumes	Ethanol extract from aerial portions	Flavonoids, polysaccharides, alkaloids, sterols and amino acids.	Immunomodulator, anti-allergic, anti-inflammatory effects
Nigella sativa **(Aslani et al., 2024; Barik et al., 2024; Madhavi et al., 2024; Saleem et al., 2024)**	Kalonji/ black cumin	Ranunculaceae	Seeds	Quinine, thymoquinone, Polyphenol, α-spinasterol, ascorbic acid, β-sitosterol, carvone, D-limonene, linoleic acid, myristic acid, methionine, Nigellone, stearic acid, stigmasterol, tannin, hederagenin.	Anti-cancer, antioxidant, antimicrobial, suppresses liver inflammation.
Fagonia schweinfurthii **(Barik et al., 2024; Madhavi et al., 2024; Nayila et al., 2024)**	Dhamasa or Dhamasia	Zygophyllaceae	Whole plant (ethanolic extract)	Phenols and flavonoids	anticancer,laxatives,anti-leishmanial,antidiabetic,antipyretic,
Citrullus colocynthis Linn **(Attri et al., 2025; Barik et al., 2024; Shawon et al., 2024;)**	Bitter apple/ Bitter cucumber	Cucurbitaceae	Methanolic fruit extract	Flavonoids, isosaponarins, isovitexin, isoorientin 3′-O-Methyl ether	Anti-inflammatory and laxative. Soften bowel contents.
Basella alba L. **(Barik et al., 2024; Sutor-Świeży et al., 2024)**	Malabar spinach/ "Indian Spinach"/ pui shak	Basellaceae	leaf extracts Aqueous fractions	acylated gomphrenins(6′-*O*-*E*-caffeoyl-gomphrenin (malabarin) and 6′-*O*-*E*-4-coumaroyl-gomphrenin (globosin)), betacyanins	Anticonvulsant, antioxidant, analgesic
Hippophae rhamnoides **(Barik et al., 2024; Zargar et al., 2022)**	Sea buckthorn/ Mirghinz/ Chuk.	Elaeagnaceae	Berries,leaf-extract	Quercetin-3-O-galactoside,quercetin-3-O-glucoside,kaempferol, and isorhamnetin	Anti-inflammatory, antidiabetic
Pandanus odoratissimus **(Barik et al., 2024), (Sinaga et al., 2021)**	Screw pine, Ccrew tree, Kewra,	Pandanaceae	Ethanolic root extract	Phenolic derivatives (vanillin, 4-hydroxy-3-(2′,3′-dihydroxy-3′-methyl-butyl)-benzoic acid methyl ester), benzofuran derivative (methyl ester), and lignans (eudesmin, kobusin, pinoresinol, epipinoresinol)	Hepatoprotective and anthelmintic activities
Origanum vulgare **(Chabib et al., 2021; Madhavi et al., 2024; Tawffiq & Almulathanon, 2023)**	Wild marjoram	Lamiaceae	Leaves aqueous extract	Carvacrol and thymol, Terpenoids, tannins, saponins, phenolic compounds, flavonoids	Antidiabetic, analgesic, anti-inflammatory, anticancer and other potential properties

Hepatoprotective Mechanism

Morus indica **(α-amyrin):** Mango, or *M. indica*, belongs to the Anacardiaceae family and are utilized extensively in phytochemistry, folk medicine, and pharmacotherapeutics. Terpenes, sterols, polyphenols, carotenoids, amino acids, and vitamins are all found in the *M. indica* tree, which is utilized in ethnomedicine to treat a variety of ailments. The pharmacological actions of *M. indica* including hepatoprotective, radioprotective, cell migration, antidiarrheal, anticancer, and antibacterial properties, have extensively been reported (Kabbashi et al., 2024).

Anti-inflammatory Mechanism

In the cell, CCl_4 stimulates the activation of the cytochrome P450 enzyme system (CYP2E1) and generates trichloromethyl radicals (CCl_3^+). After undergoing reductive metabolism, these radicals produce a very reactive intermediate which induces the release of serum enzymes (AST, ALT, GGT), lipid peroxidation, liver cell death, and reduction of antioxidant defenses adjacent to the central vein due to the toxicity induced change of cellular membrane permeability (Boro et al., 2022). Ethanol root extracts of *M. indica* can significantly suppress acute liver damage caused by CCl_4 due to the presence of anti-inflammatory compound α-amyrin, which is three times superior to aspirin. Additional novel compounds investigated were 1,4-phenylenebis (trimethylsilane), 1,2-Bis (trimethylsilyl) benzene, and 3,5-bis-trimethylsilyl, 2,4,6-cycloheptatriene-1-one (Figure 2; Boro et al., 2022).

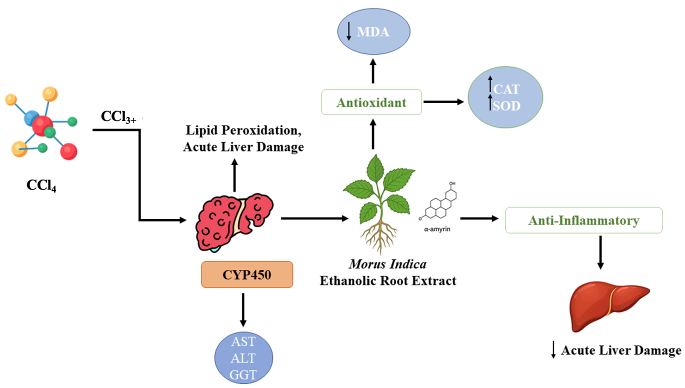

Figure 2: Schematic representation of Anti-inflammatory and Antioxidant Mechanism of Morus indica

Antioxidant Defense Mechanism

The antioxidant potential of *Morus nigra* extracts has been reported to increase the activity of antioxidant enzymes such as catalase (CAT) and superoxide dismutase (SOD), decreased malondialdehyde (MDA) levels, and inhibited lipid peroxidation enabling the plant to combat free radicals and minimize the oxidative damage (Figure 3; Ahmed et al., 2025).

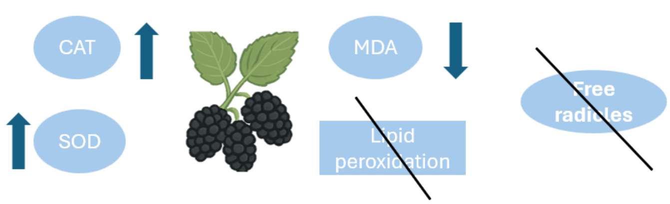

Figure 3. Schematic Representation of Antioxidant Defense Mechanism of Morus nigra

***Curcuma longa* (Curcumin):** The flowering plant *C. longa*, commonly known as "turmeric", of Zingiberaceae family, is indigenous to South Asia. For thousands of years, people have grown it for its rhizomes, which are full of bioactive substances that are utilized in both traditional medicine and cooking. About 2-5% of turmeric's weight is made up of curcumin, the main biologically active ingredient with health benefits. The varied phytochemical profile of *C. longa*, which consists of curcuminoids, essential oils, and polysaccharides, is thought to be responsible for its medicinal value (anti-inflammatory and antioxidant qualities). It contains 3% bis-demethoxycurcumin, 77% curcumin, and 17% demethoxycurcumin (Boudou et al., 2025; Ruiz De Porras et al., 2023).

Immunomodulatory mechanism

Curcumin inhibits the release of TNF-α, as well as other proinflammatory cytokines and chemokines controlled by NF-κB, such as IL-1β (interleukin-1 beta), IL-8, and IL-6. By specifically targeting NF-κB and suppressing the secretion of pro-inflammatory substances, curcumin effectively regulates the inflammatory conditions in the liver, hence, averting harm to tissues.

Furthermore, curcumin can suppress the production of cyclooxygenase-2 (COX-2), a well-recognized pro-inflammatory NF-κB target that triggers the secretion of prostaglandins. This reduction in the metabolism of prostaglandins and lipoxygenases consequently decreases inflammation and reactive oxygen species (ROS). Diet containing 1% curcumin reduces liver inflammation in mouse models of steatohepatitis by inhibiting NF-κB. This inhibition diminishes the subsequent activation of pro-inflammatory regulators such as ICAM-1, MCP-1, and COX-2. Oral curcumin treatment at a dosage of 18 mg/day may alleviate steatohepatitis by inhibiting TNF-α and increasing mitochondrial antioxidants (α-tocopherol and retinol), reducing aminotransferases, decreasing mitochondrial ROS, and enhancing mitochondrial activity in NASH mouse models produced via providing the animals a diet high in fat (Figure 4; Ruiz De Porras et al., 2023).

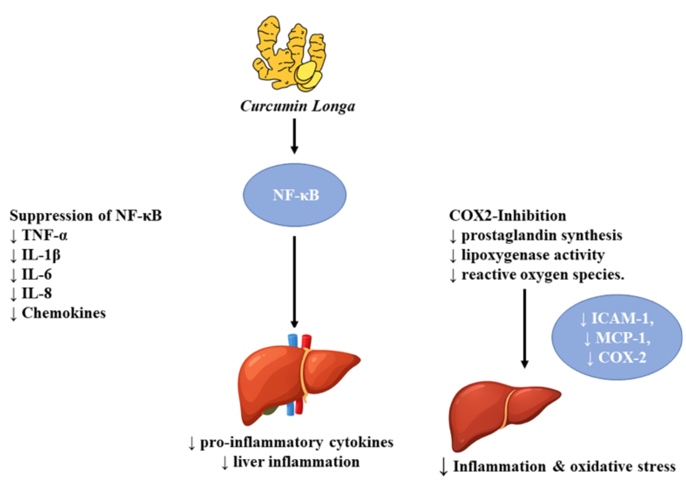

Figure 4: Schematic representation of Immunomodulatory Mechanism of Curcumin longa.

Case Studies of Hepatoprotective Plants

***Mangifera indica*:** The hepatoprotective effects of the plant components have been investigated against the synthetic phytochemical silymarin. In male Sprague–Dawley rats, the aqueous fruits extract effectively reversed oxidative stress-induced hepatotoxicity resulted from cumene hydroperoxide, and subsequently decreased levels of cellular glutathione degradation, ROS production, oxidized lipid, and liver tissue failure (Arman et al., 2022).

In one investigation, albino rats given CCl_4 were used to evaluate the ethanolic seed extract of *Mangifera indica*. Body weight and histological investigation revealed the restoration of normal liver architecture, and doses of 50 mg/kg and 100 mg/kg effectively reduced increased serum levels of ALT, AST, and

ALP. In the DPPH experiment, the extract demonstrated extremely high antioxidant activity (IC_{50} ~ 8 µg/mL), which was comparable to propyl gallate. Protected hepatocytes confirmed antioxidant-mediated hepatoprotection (Kabbashi et al., 2024).

Kalanchoe pinnata: Fresh leaf juice and ethanolic extract of *K. pinnata* were tested for their hepatoprotective qualities both *in vitro* and *in vivo* for CCl_4 induced liver toxicity (Arman et al., 2022). Male Wistar rats with hepatotoxic conditions caused by Carbon tetrachloride (CCl_4) and gentamicin were treated with *K. pinnata* juice and extract and found to have. The results showed that rats with CCl_4 and gentamicin-induced toxicity had lower levels of bilirubin, aspartate aminotransferase, alkaline phosphatase, and alanine transaminase in contrast to the rats given *K. pinnata* had considerably higher serum levels of albumin, globulin, and total protein after receiving a therapeutic beverage (Saeed et al., 2025).

Moreover, liver cells treated with extract from rats poisoned with CCl_4 showed a little lack of clarity compared to normal hepatocytes. In contrast the quantity of hepatocytes with intact nucleus was far greater (Arman et al., 2022). The butyl alcohol and acetic ester components of the methanolic leaf extract demonstrated significant efficacy in inhibiting the growth of hepatitis C virus (HCV) in a laboratory setting. Additional research on the secondary metabolites gallic acid, quercetin, and quercitrin revealed considerable antiretroviral therapy against HCV effects, with the first two showing the greatest benefit (Arman et al., 2022).

Berberis lycium Royle: *Berberis lycium Royle* is an indigenous perennial plant of the Berberidaceae family, native to the Himalayan region, particularly Nepal, and at high altitudes in Pakistan. It is widely used in conventional therapies to treat diabetes, ulcers, skin conditions, jaundice, muscular dystrophy and rheumatism (Verma et al., 2021). Although *B. lycium* contains many biologically active compounds such as alkaloids, saponins, tannins, vitamins, proteins, carbohydrates, lipids, berberine, berbamine, and sindamine, its main component is berberine, an isoquinoline alkaloid (Anjum et al., 2023).

Male Swiss albino mice with alloxan-induced liver injury were given aqueous extract of *B. lycium*, using an 18-gauge oral feeding syringe. Intraperitoneal administration of alloxan at a dosage of 150 mg/kg body weight results in elevated plasma levels of ALAT, ASAT, ALP, and LDH (Mughal et al., 2024). The alloxan's induced enzyme activity was decreased by administration of *B. lycium* root extract at a dosage of 200 mg/kg for 28 successive days. *B. lycium* extract considerably reduced the elevated blood glucose levels caused by Alloxan. Alloxan induction results in elevated bilirubin and MDA levels, and reduced total protein content, GSH and catalase levels, which can be reversed by administering 150 mg/kg body weight of *B. lycium* extract to diabetic mice. Administration of *B. lycium* extract before treatment effectively averts liver damage caused by alloxan in mice, thereby establishing its preventive role against liver damage (Mughal et al., 2024). Histological studies revealed the acute damage produced by acetaminophen, and the administration of the aqueous *Berberis vulgaris* fruit concentrate considerably decreased the severity. Hence, the water-based extracts of *B. vulgaris* may exhibit a hepatic protection against acetaminophen-induced liver injury, perhaps owing to their antioxidant properties (Kouchaki et al., 2023).

Helianthus annus and Cynodon dactylon: CCl_4-induced hepatotoxicity in mice treated either with 200 mg/kg body weight of ethanolic or aqueous liquid extracts of *H. annus* flowers significantly lowered serum ALP, AST, and ALT ($p<0.001$) compared to the group treated with CCl_4 suggests a decrease in oxidative damage caused by CCl_4. Similar observations were made in rabbits with liver damage induced by CCl_4 when given 100 mg/kg body weight of alcoholic root extracts from *C. dactylon* (Mughal et al., 2024). In another experiment, hepatotoxicity was caused by oral administration of acetaminophen to rats once a day for a week at dosage of 100, 300, and 500 mg/kg of *H. annus* methanolic extract. The methanolic seed extract of *H. annuus* was found to have antioxidant and hepatoprotective capabilities due to triterpenoids, glycosides, saponins, alkaloids, flavonoids, triterpenoids, and tannins. Administering acetaminophen raises blood levels of normally absent or low-concentration serum enzymes, including lactate dehydrogenase, phosphatases, aminotransferases, and gamma-glutamyl transferase, which assess liver damage and function. There was a significant decrease in indirect bilirubin when extract was administered with 100 and 300 mg/kg of body weight. The rats receiving extract coupled with paracetamol showed a notable reduction in ALT, AST, and ALP levels, suggesting that the extract safeguards the hepatic cells in oxidative damage generated by paracetamol (Brobbey et al., 2020).

Pharmacological evidence of hepatoprotective effects of medicinal plants:

Cichorium intybus (Chicory): *C. intybus* exhibits antioxidant properties due to the existence of polyphenolic compounds. The presence of inulin in 40% of chicory root pulp significantly enhances the synthesis of iron genes, proteins, and ferritin in intestinal absorptive cells. As a result, the liver enzymes were regulated and blood ferritin levels were decreased (Służały et al., 2024). An analysis conducted on 374 persons with NAFLD, cirrhosis, or hepatobiliary problems to assess their liver parameters after consuming chicory. The chicory was available in several forms, including a water-soluble concentrate, chicory leaves, powdered root concentrate, and pulverized seed. A variety of dosages of the extracts administered throughout a time span from 4 weeks to 6 months. NAFLD patients receiving 500 mg/day of dry crushed chicory root, didn't exhibit any appreciable improvement in liver markers (Służały et al., 2024).

HECL (hydroethanolic leaf extract) of chicory was tested in male Wistar rats subjected to lead and nickel toxicity using *in vitro, in vivo*, and *in silico* methods. HECL enhanced histological integrity, liver enzymes, and antioxidant status at 250 mg/kg. Cyanidin and rutin were named by molecular docking revealed cyanidin and rutin as the best interactors with liver-protective enzymes out of 28 phytocompounds (Pathak et al., 2024).

Cinnamon (Cinnamomum verum J. Presl): Cinnamon is a culinary spice effective in treatments of certain ailments and inflammations. It is used in confectionery, dental hygiene products, and fragrances. Cinnamaldehyde, the primary constituent of cinnamon, exhibits immune modulatory ability by influencing the expression of both anti- and pro-inflammatory genes evidenced in several cell cultures and in a living thing experiment. Conventionally it has been used for the control of lipid and blood sugar levels. The influence of cinnamon upon liver's functioning has been investigated in a single, double-blind randomized controlled trial (RCT) conducted on 45 Iranian patients diagnosed with non-alcoholic fatty liver disease (NAFLD). The study found a relationship among the control group (n = 22, 13 F, 9 M mean age 45.4, and BMI 30.3) and the regular consumption of 1.5 grams of undiluted extract of cinnamon (n = 23, 10 F, 13 M mean age 44.8, and BMI 29.9) over a 12-week period. These findings indicated a significant enhancement in each of the liver indices (enzymes including AST, ALT, and GGT). 37.25% reduction in ALT levels compared to 2.07% in the placebo group, 36.73% reduction in AST levels contrary to 2.77% in the control group, 32.47% reduction in GGT levels contrary to 3.46% in the control group (Służały et al., 2024).

Andrographis paniculata (Andrographolide):

Andrographolide is the bioactive compound from the leaf and aerial parts of *Andrographis paniculata*, exhibits profound liver-protection properties for APAP-generated impairment in *ex-vivo* preparations of rat liver tissues. It is a component in over 26 distinct ayurvedic preparations developed for the treatment of jaundice and hepatitis. Andrographolide administration has shown to enhance gallbladder function, promoting bile flow, and have comparable efficacy to silymarin in liver protection. Furthermore, it demonstrates antidiabetic properties in rats with chronic hypoglycemia produced by streptozotocin and diabetic nephropathy (Shakya, 2020).

Table 2: Key Hepatoprotective Plants

Scientific Name	Common Name	Family	Major Bioactive Constituents	Key Hepatoprotective / Biological Actions
Alhagi maurorum	Camel Thorn	Leguminosae	Flavonoids, alkaloids, polysaccharides	Immunomodulator, anti-allergic, anti-inflammatory
Azadirachta indica	Neem	Meliaceae	Margosine, aodaarichlim, bitter oil	Anti-inflammatory, antioxidant, detoxifying
Basella alba	Malabar Spinach	Basellaceae	Betacyanins, gomphrenins	Antioxidant, analgesic, anti-cancer
Berberis lycium	Mango	Berberidaceae	Gallic acid, quercetin, flavonoids	Protection against CCl_4 and drug-induced toxicity
Citrullus colocynthis	Bitter Apple	Cucurbitaceae	Flavonoids, isovitexin, isoorientin	Anti-inflammatory, laxative, liver protection
Coriandrum sativum	Cilantro	Apiaceae	Tannins, malic acid, albuminoids	Anti-inflammatory, antioxidant, antidiabetic
Cuscuta reflexa	Dodder Amarbal	Convolvulaceae	Cuscutine, flavonoids, coumarins	Anti-inflammatory, hepatoprotective
Fagonia schweinfurthii	Dhamasa	Zygophyllaceae	Phenols, flavonoids	Antioxidant, anti-leishmanial, hepatoprotective
Ficus benghalensis	Banyan Tree	Moraceae	Tannins, phenolics	Anti-inflammatory, wound healing
Hibiscus rosa sinensis	Chinese Hibiscus	Malvaceae	Quercetin, ascorbic acid	Effective against liver toxicity, anti-inflammatory
Hippophae rhamnoides	Sea Buckthorn	Elaeagnaceae	Quercetin glycosides, isorhamnetin	Anti-inflammatory, antioxidant, anti-diabetic
Momordica charantia	Bitter Melon	Cucurbitaceae	Charantin, momordicosides, alkaloids	Hepatoprotective, antioxidant
Nigella sativa	Black Cumin	Ranunculaceae	Thymoquinone, polyphenols, sterols	Strong antioxidant, anti-inflammatory,
Ocimum basilicum	Sweet Basil	Lamiaceae	Ascorbic acid, apigenin, amino acids	Anti-inflammatory, antioxidant, hepatoprotective
Origanum vulgare	Miei Marjoram	Lamiaceae	Carvacrol, thymol, tannins, flavonoids	Anti-inflammatory, anticancer, antioxidant
Pandanus odoratissimus	Kewra	Pandanaceae	Phenolics, lignans, benzaturin derivatives	Hepatoprotective, antioxidant
Solanum melongena	Eggplant	Solanaceae	Caffeic acid, ascorbic acid, arginine	Reduces inflammation, antioxidant
Tinospora cordifolia	Giloy	Menispermaceae	Berberine, palmatine, jatrorrhizine	Anti-inflammatory, antioxidant, immunomodulatory

Potential challenges in Hepatoprotective Drug Development from Medicinal Plants:

Even though modern medicine has developed rapidly, there is no complete effective drug available to rebuild or protect liver function or stimulate liver replication. Therefore, plant-based alternatives containing phytoconstituents can provide safer and more effective alternatives for the treatment of hepatic diseases (Datta et al., 2023). Phytochemicals can provide health benefits; however, if used excessively or for a prolonged period, they can be hepatotoxic. Some compounds may induce hepatotoxicity by promoting oxidative stress, inflammation, mitochondrial dysfunction, and fibrosis. Understanding these mechanisms may provide valuable information for the development of safe and effective phytochemical hepatoprotective agents (Namazzi Apiyo, 2025).

The development of drugs from natural phytonutrients is lacking preclinical and clinical studies. Multi-omics and network pharmacology in combination with genomic and metabolomic approaches can improve the rigor with which research is conducted on natural products, including potentially establishing the basis for their use as therapeutics (Datta et al., 2023).

Future directions in the field of hepatoprotection using medicinal flora:

More clinical studies are warranted to establish and authenticate hepatoprotective abilities on bioactive substance sources of natural origin; preclinical studies are also required to authenticate different treatment modalities as having hepatoprotective activities. Molecular docking, machine learning, and deep learning have unique scopes to investigate the potential hepatoprotective effects of new bioactive molecules, while the mechanisms underlying those activities can be pursued with advanced biophysical and biochemical experimental methodologies. In addition, further investigations are urgently required to identify and validate potential hepatoprotective action of new bioactive substances of natural resources (Pandey et al., 2023).

Summary of Review

Table 2 summarizes the hepatoprotective plants with their bioactive constituents and their mode of actions, which can be a ready reference for researchers for further studies.

Author contributions

HA: Data acquisition and manuscript write-up; ZA: Data acquisition and manuscript write-up; NS: Data acquisition and manuscript write-up; MA: Data acquisition and manuscript write-up; NN: Conceived the idea, Intellectual input, manuscript review.

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