Biopress Journal of Advanced Pharmacology Vol.2 Issue. 9 (2026)

"HERBAL MEDICINES IN LIVER DISEASE: FRIEND OR FOE?"

Shaik Nafilun Shirina[1], Sania Mirza[1], Sofiya Begum[1]

[1]Rbvrr Women's College Of Pharmacy, Approved By Aicte, Pci. Affiliated To Osmania University, Accredited By Naac Grade B++

Corresponding author: shaikshirina42@gmail.com
Doi: https://doi.org/10.5281/zenodo.22685707
Received: 29 July 2026
Accepted: 2 September 2026

Abstract:

The review article examines the dual role of herbal medicines in liver disease management, highlighting both their therapeutic hepatoprotective benefits and their potential risks for herb-induced liver injury, <source type="bfd058e. Botanicals such as milk thistle, turmeric, licorice, and green tea contain bioactive compounds that exert antioxidant, anti-inflammatory, and anti-fibrotic effects, offering valuable adjunctive support for conditions like non-alcoholic fatty liver disease and viral hepatitis ac414c3, <source type="334393a, . However, unstandardized preparations, contaminants, and adverse herb-drug interactions present serious safety concerns that can precipitate acute liver damage, <source type="b0f81ae, <source type="6238d50. Ultimately, the authors emphasize that transitioning toward rigorous manufacturing standards and chemical standardization is essential to safely harness the therapeutic potential of traditional remedies in modern hepatology c8db47f, <source type="a12aa7f.

INTRODUCTION:

Herbal medicines are crude or processed medicinal substances obtained from plants or their parts that contain active constituents used for the prevention, diagnosis, or treatment of diseases.

People use them to support general health and well-being, or to help manage specific conditions such as trouble sleeping, low mood, menopause symptoms, digestive problems, joint pain and many other various disease conditions. Common examples include St. John's wort, turmeric, echinacea, valerian, ginkgo, and cranberry. Few examples of herbs used for their different properties include:

- Ginger – used for indigestion and nausea
- Turmeric – anti inflammatory properties
- Aloe vera – used for burns and skin healing
- Pepperment -relieves digestive discomfort

TYPES:

Depending on their source, processing, plant part used, chemical constituents, therapeutic action, and dosage form, herbal drugs are classified into different types

Table 1:Classification of Herbal drugs

CLASSIFICATION OF HERBAL DRUGS		
BASIS OF CLASSIFICATION	**TYPES**	**EXAMPLES**
1. Based on Degree of Processing	• Crude Herbal Drugs • Processed Herbal Drugs – Powdered drugs – Extracts (Aqueous, Alcoholic, Hydroalcoholic) – Tinctures – Essential oils – Standardized herbal preparations	*Senna leaves, Ginger rhizome, Cinnamon bark* *Triphala churna, Turmeric powder* *Green tea extract, Ginkgo extract* *Belladonna tincture, Ginger tincture* *Peppermint oil, Eucalyptus oil* *Milk thistle extract (Silymarin)*
2. Based on Plant Part Used	• Leaves • Roots • Rhizomes • Bark • Flowers • Fruits • Seeds • Whole plant	*Senna, Neem* *Ashwagandha, Liquorice* *Ginger, Turmeric* *Cinnamon, Cinchona* *Chamomile, Hibiscus* *Amla, Fennel* *Fenugreek, Coriander* *Brahmi, Andrographis*
3. Based on Chemical Constituents	• Alkaloid-containing drugs • Glycoside-containing drugs • Flavonoid-containing drugs • Tannin-containing drugs • Saponin-containing drugs • Volatile oil-containing drugs • Resin-containing drugs	*Cinchona, Belladonna, Rauwolfia* *Senna, Digitalis, Aloe* *Ginkgo, Green tea, Chamomile* *Witch hazel, Tea leaves, Catechu* *Liquorice, Ginseng, Fenugreek* *Clove, Peppermint, Cinnamon* *Asafoetida, Myrrh, Benzoin*
4. Based on Therapeutic Uses	• Anti-inflammatory • Antioxidant • Antidiabetic • Hepatoprotective • Antimicrobial • Immunomodulator • Adaptogen • Expectorant • Laxative	*Turmeric, Boswellia* *Green tea, Ginkgo, Amla* *Gymnema, Fenugreek* *Milk thistle, Phyllanthus* *Neem, Garlic, Tulsi* *Guduchi, Echinacea* *Ashwagandha, Rhodiola* *Vasaka, Liquorice* *Senna, Cascara*
5. Based on Dosage Form	• Fresh herbs • Dried herbs • Powders (Churna) • Tablets • Capsules • Extracts • Syrups • Decoctions (Kwath) • Infusions (Tea) • Tinctures • Essential oils • Ointments / Creams / Gels	*Powdered turmeric, Triphala tablets, Ashwagandha capsules, Aloe vera gel, Tulsi syrup, Neem oil, Belladonna tincture, Green tea infusion etc.*
6. Based on Source	• Wild Herbal Drugs • Cultivated Herbal Drugs	*Sandalwood, Neem, Guduchi* *Ashwagandha, Aloe vera, Turmeric*

DIFFERENT SYSTEMS OF HERBAL DRUGS

Herbal medicine has been practiced for thousands of years in different parts of the world. Each system has its own philosophy, methods of diagnosis, preparation of medicines, and treatment approaches. These systems primarily use medicinal plants, either alone or in combination with minerals and animal products, to maintain health and treat diseases.

India is known for its traditional medicinal systems Ayurveda, Siddha, and Unani. Medical systems are found mentioned even in the ancient Vedas and other scriptures. The Ayurvedic concept appeared and developed between 2500 and 500 BC in India.

AYURVEDA

Ayurveda is the oldest traditional medical system in India, originating more than 5,000 years ago. The term *Ayurveda* comes from the Sanskrit words Ayur (life) and Veda (knowledge), meaning "the science of life."

The classical Ayurvedic literature includes:

- **Charaka Samhita** – Internal medicine (Kayachikitsa)

- **Sushruta Samhita** – Surgery (Shalya Tantra)
- **Ashtanga Hridaya** – Comprehensive medical text by Vagbhata

According to Ayurveda, everything in the universe, including the human body, is composed of **five basic elements**: pritvi(earth), jala(water), agni(fire), vayu(air), akash(ether).

Basic Principle: Health depends on the balance of the three Doshas (Tridosha):

- **Vata** – controls movement and the nervous system.
- **Pitta** – regulates metabolism and digestion.
- **Kapha** – provides structure, lubrication, and immunity.

Disease occurs when these doshas become imbalanced.

Few herbs used in Ayurveda include: Ashwagandha(Withania somnifera) used to reduce stress and anxiety, improve energy, supports immune health, Tulsi also known as holy basil, boosts immunity, relieves cold, cough and asthma, helps regulate blood sugar, Turmeric, Neem, and Amla are few other herbs used in Ayurveda.

SIDDHA SYSTEM:

The Siddha system of Medicine is one of the traditional medical system, providing preventive, promotive, curative, rejuvenative and rehabilitative health care by adopting scientific and holistic approach. The word ‘Siddha’ is derived from the root word ‘Citti’ meaning attainment of perfection, eternal bliss and accomplishment.

The Siddha system originated in Tamil Nadu, India, and is considered one of the oldest traditional medical systems.

Principles:

- **Mukkutram (Three Humors):** Imbalances in *Vali* (air), *Azhal* (fire), and *Iyyam* (earth/water) cause illness.
- **Pancha Boothangal:** The belief that the human body shares a direct link with the five basic elements (earth, water, fire, air, and space).
- **96 Tattuvam:** The foundational functional, psychological, and intellectual principles governing human life

Common medicinal herbs used in unani include: Nilavembu used to reduce fever, enhance immunity, protect the liver, and can be used in dengue and influenza management. Keezhanelli, also protects liver, used in jaundice, kidney stone management. Adathoda, karisalankanni, thoothuvalai, vasambu, nannari, musumusukkai etc.

UNANI SYSTEM:

It originated in ancient Greece (Yunani) and was later developed and enriched by Arab and Persian physicians. The term "Unani" is derived from the Arabic word "Yūnān," meaning Greece.

This system was introduced into India by the Mughals and has since become an important part of the AYUSH systems of medicine.

Basic elements of life:

Arkan- element

Mizaj - temperament

Akhlaat – humor

Aza – organ

Arwah – pneuma

Quwa – faculty

Af' aal- functions

Methods of Treatment

1. Ilaj-bil-Ghiza (Dietotherapy)

2. Ilaj-bid-Dawa (Pharmacotherapy)

3. Ilaj-bit-Tadbeer (Regimental Therapy)

4. Ilaj-bil-Yad (Surgery)

Different herbs used in Unani system include: Aslus soos, Senna, Kalonji, Zanjabeel, Haldi, Amla, Banafsha, Isabgol, etc.

TRADITIONAL CHINESE MEDICINE (TCM):

Traditional Chinese medicine (TCM) is an important example of how ancient and accumulated knowledge is applied in a holistic approach in present day health care. TCM has a history of more than 3000 years.

Basic Principle

Health depends on the balance of:

- **Yin and Yang**
- **Qi (vital life energy)**

Disease results from disruption of this balance.

Treatment Methods

- Herbal medicines
- Acupuncture

- Moxibustion
- Tai Chi
- Dietary therapy

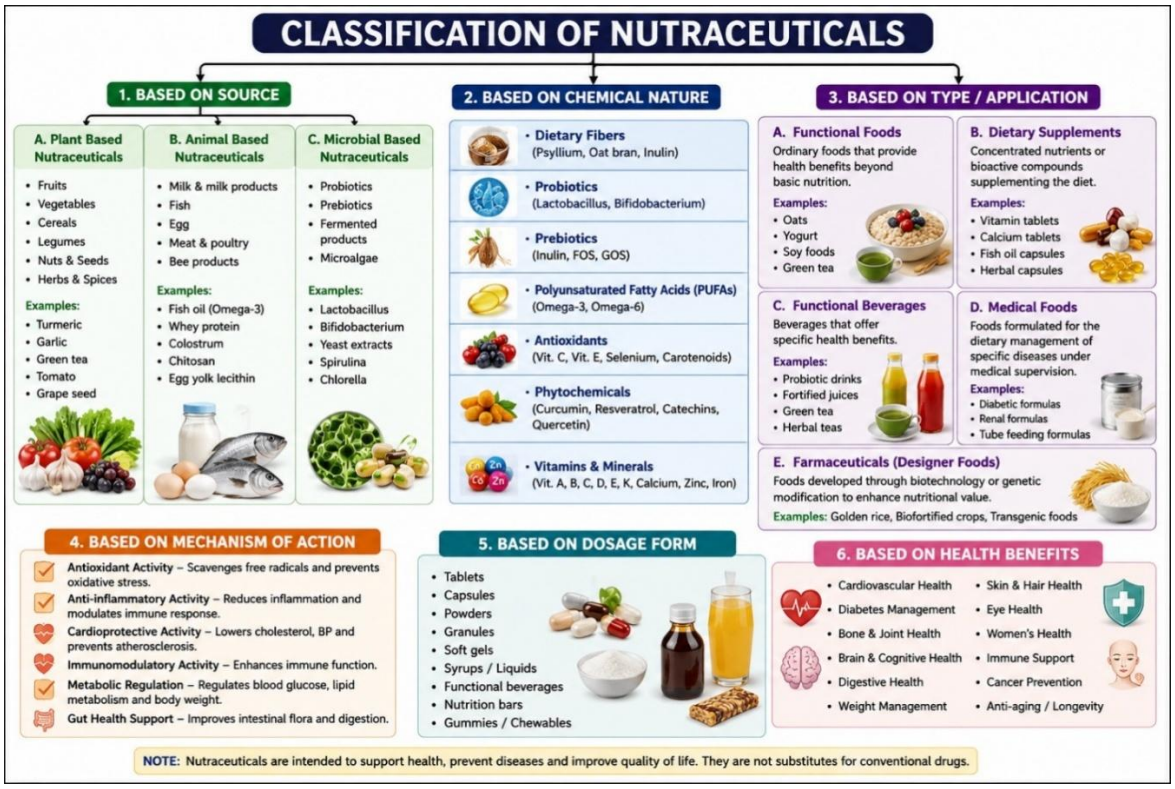
Different Herbal medicines used in TCM include: Ginseng, Astragalus, Goji berry, Licorice, Ginger, Chinese Skullcap, Reishi Mushroom, and Dong Quai etc.

Aside from above mentioned systems, herbs have found their way to be usefull in other systems as well, as mentioned below:

Nutraceuticals

The term nutraceutical was defined Dr. Stephen L.Defelice, the founder and chairman of the foundation for innovation in medicine in the year 1989. Nutraceutical is a term that combines nutrients as well as pharmaceuticals and is defined as a substance that provides nutrition when takes as food or food supplement and also possesses the ability to prevent diseases or to improve health.

Table 2:Classification of Neutraceuticals



Functional food:

Food is referred as functional food when it is cooked/ prepared with or without the knowledge of the purpose of its use. Such food products fulfil the requirements of protein, carbohydrates, vitamins, fats etc., to maintain a healthy body.

Most foods are functional because they are physiologically beneficial. Japan defined functional foods as the foods that provide health beyond nutrition.

Examples: Milk is fortified with vitamin D, Some foods and beverages are fortified with high amounts of added sugars or sodium.

The following functional foods are rich in nutrients:

- Sardines and salmon
- Nuts
- Whole grains
- Beans
- Berries

Limitations of Synthetic Drugs in Liver Diseases:

Drug induced Liver Injury (DILI):

One of the major drawbacks of synthetic drugs is that many have hepatotoxic property themselves and can cause damage to liver. Acetaminophen overdose is one the leading cause of acute liver failure in US and several other countries. Promptly treating with N- acetylcysteine(NAC) can prevent severe liver injury *. Most of the cases of DILI are benign and improve when the drug is withdrawn. It is also observed that NAFLD can increase susceptibility for DILI

No effective cure for Advanced Fibrosis or Cirrhosis:

Current synthetic drugs can slow down the progression of disease, but cannot completely reverse advanced liver fibrosis or cirrhosis. For which, liver transplantation remains the only treatment for end stage liver disease. Patients with compensated cirrhosis receive treatment with drugs such as non selective beta blockers to reduce hypertension and diuretics for ascites, hence they only give cure for the symptoms but do not regenerate scarred liver tissue or treat cirrhosis itself.

Drug Resistance:

Chronic hepatitis caused by viruses may develop resistance to antiviral drugs, thereby reducing the effectiveness of the treatment. This can be observed in Lamivudine Resistance in Hepatitis B, where long term treatment with Lamivudine led to mutations in the YMDD motif of the hepatitis B virus polymerase gene. These mutations caused viral resistance, resulting in treatment failure and disease progression.

Serious adverse effect:

Long terms use of certain drugs maybe limited due to the significant side effects produced by synthetic drugs. Before introduction of direct acting antivirals (DAA’s), interferon alpha based therapy was standard treatment but due to its side effect like, fever, depression, fatigue, bone marrow suppression and thyroid dysfunction, it is no longer prominently used. Immune check point inhibitors, used in cancer immunotherapy like Nivolumab, can cause immune-mediated hepatitis, elevated ALT and AST, in severe cases may lead to acute liver failure.

High Cost of Therapy:

Modern synthetic drugs used in liver diseases are highly effective but expensive, limiting access to many low and middle income countries. Sofosbuvir revolutionized hepatits C treatment achieved cured rates above 95%, however a 12 weeks course can cost up to USD 24,000 to $94,500, making it unaffordable for many patients before generic version became available. (afdhal N et)

Polypharmacy and Drug – Drug Interactions:

Patients with chronic liver disease (CLD) often have multiple complications such as portal hypertension, ascites, hepatic encephalopathy, diabetes, hypertension, and infections. As a result, they frequently require five or more medications simultaneously (polypharmacy). Because the liver is the primary site of drug metabolism, impaired hepatic function increases the risk of drug accumulation, adverse drug reactions (ADRs), and clinically significant drug–drug interactions. A cirrhotic patient is given Warfarin for atrial fibriallation develops a fungal infections and is prescribed Fluconazole. Fluconazole inhibits CYP2C9 decreasing warfarin metabolism which leads to warfarin increase causing excessive anticoagulation.

Why herbal medicines can be preffered over synthetic drugs? :

Multi-target mechanism of action:

Unlike most synthetic drugs, which usually act on a single receptor or pathway, herbal medicines contain multiple bioactive compounds that act on several disease mechanisms simultaneously. Silymarin (Milk Thistle) Scavenges free radicals, Increases glutathione, Inhibits NF-κB-mediated inflammation, Reduces hepatic fibrosis and Stabilizes hepatocyte membranes. This makes it useful in chronic liver diseases involving oxidative stress, inflammation, and fibrosis.

Lower incidence of serious adverse effects (when standardized):

Standardized herbal extracts are generally well tolerated. Clinical studies have shown that silymarin causes mainly mild gastrointestinal complaints and is considered safe for long-term use in many patients with chronic liver disease.

May benefit diseases with limited synthetic treatment options:

Synthetic drugs cannot completely reverse liver fibrosis or cirrhosis. Experimental and early clinical studies suggest that Curcumin, Berberine, Silymarin, Glycyrrhizin may reduce oxidative stress, inflammation, and collagen deposition. Curcumin supplementation has shown improvements in liver enzymes and inflammatory markers in patients with non-alcoholic fatty liver disease (NAFLD), although larger trials are still needed.

Lower cost and greater accessibility:

Herbal medicines are often less expensive and more readily available, especially in developing countries, making them attractive as adjunctive therapies.

Some of the plant constituents and their uses in liver toxicity:

Milk Thistle is commonly noted for its ability to protect the liver due to its active ingredient silymarin which is made up of silibinin, silydianin, and silychristin. Silymarin is also known to be a very powerful antioxidant as it reduces inflammation and oxidative stress within the liver. It has multi target action and good safety profile

Ginger: Gingerol, shogaol, and zingerone found in ginger are considered bioactive and their antioxidant and anti-inflammatory properties make these compounds very helpful. These compounds also help reduce inflammation of the liver, protect the liver from oxidative stress, improve liver enzyme levels, insulin resistance and protect the liver from damage.

Mandarin oranges contain flavonoids such as hesperidin, naringenin, and limonene that have hepatoprotective properties. These inhibit fat storage in the liver, decrease fibrosis, and decrease inflammation. Hesperidin and naringenin also increase the detoxification function of the liver and are thus useful in the prevention of liver disease brought on by toxins.

Green tea is a strong liver-protective drink, primarily because of its high epigallocatechin gallate (EGCG), catechins, and theanine content. EGCG is a strong antioxidant that can decrease oxidative stress, inhibit liver steatosis (fat accumulation), and enhance liver detoxification.

Herbal medicines also have applications in various hepatic diseases, as follow:

Herbs in different liver diseases:

1. Polyphenolic Compounds: Mechanisms of Hepatoprotection

The therapeutic benefits of widely studied botanical extracts stem primarily from their capacity to suppress oxidative stress—a common final pathway driving hepatocyte necrosis, mitochondrial failure, and fibrogenesis across varied etiologies.

Quercetin: Quercetin is a naturally occurring dietary flavanol found in fruits and vegetables, particularly apples and onions. In its native aglycone form, pure quercetin exhibits limited systemic bioavailability. Glycosylated forms (conjugated with sugar residues) undergo enhanced uptake via intestinal transporters before entering Phase II biotransformation (glucuronidation, sulfation, and methylation) in the gut and liver.

Alcohol-Induced Injury (ALD): Chronic ethanol consumption triggers mitochondrial dysfunction, glutathione (GSH) depletion, and ROS overgeneration. Pre-clinical evidence shows that quercetin preserves mitochondrial membrane potential, attenuates lipid peroxidation, and modulates key antioxidant enzymes—including superoxide dismutase (SOD2) and glutathione peroxidase (GPX4)—thereby protecting primary hepatocytes against acute alcohol toxicity.

Metabolic Liver Disease (MASLD/NAFLD): In models of metabolic disease, quercetin administration attenuates hepatic fat accumulation and improves systemic insulin sensitivity. These metabolic benefits occur via the downregulation of lipogenic genes (such as PPAR-\alpha modulation) and the inhibition of pro-inflammatory signal cascades (including the amphiregulin/EGFR pathway involved in fibrotic remodelling).

Antiviral Modulatory Effects: Quercetin exhibits direct viral interaction in hepatitis C virus (HCV) models by inhibiting the HCV NS3 protease in a dose-dependent manner, suppressing viral RNA replication. In hepatitis B virus (HBV) models, related flavone glucosides demonstrate anti-HBV activity, though structural glycosylation appears essential for suppressing viral antigen secretion.

2. Curcumin

Curcumin is a lipophilic, low-molecular-weight polyphenol isolated from the rhizomes of Curcuma longa (turmeric). Despite showing robust anti-inflammatory, antioxidant, and anti-fibrotic activity in vitro, native curcumin demonstrates very poor oral bioavailability due to minimal intestinal absorption, rapid biotransformation, and swift systemic elimination. To overcome these pharmacokinetic barriers, modern delivery strategies utilize liposomal formulations, phospholipid complexes, nanoparticle carriers, structural analogues (e.g., bis-desmethoxy curcumin), or co-administration with glucuronidation inhibitors like piperine.

Anti-Fibrotic & Matrix Remodelling: In chronic liver damage—including alcohol- and toxin-induced injury—curcumin and its analogs modulate extracellular matrix (ECM) remodelling. They lower collagen accumulation, suppress tissue inhibitors of metalloproteinases (TIMPs), and restore active-matrix metalloproteinases (MMPs), directly counteracting hepatic stellate cell (HSC) activation.

3. Liv.52 (Standardized Polyherbal Formulation)

Liv.52 is a proprietary Ayurvedic polyherbal medicine used clinically for over five decades in the management and prevention of viral hepatitis, alcoholic liver disease, early cirrhosis, and protein-energy malnutrition. It combines several botanical ingredients, including Capparis spinosa, Cichorium intybus, Mandur Bhasma, Solanum nigrum, Terminalia arjuna, Cassia occidentalis, Achillea millefolium, and Tamarix gallica.

Cytoprotective & Antioxidant Mechanisms: In vitro assays demonstrate that Liv.52 mitigates cellular toxicity induced by heavy metals (copper) and organic peroxides (tetra-butyl hydroperoxide) in HepG2 cells. It preserves hepatocyte viability by inhibiting lipid peroxidation, replenishing intracellular glutathione (GSH) reserves, and enhancing endogenous antioxidant enzyme activity.

Modulation of Inflammatory Pathways & Steatosis: In models of alcohol toxicity, Liv.52 blocks ethanol-induced suppression of peroxisome proliferator-activated receptor-gamma mRNA expression while simultaneously downregulating pro-inflammatory TNF-\alpha gene expression. Furthermore, preclinical dose-response studies show that pretreatment with Liv.52 significantly reverses acetaminophen (paracetamol)-induced hepatotoxicity in animal models.

Clinical Efficacy in Human Trials: While historical clinical data have occasionally shown mixed results, double-blind, placebo-controlled trials indicate tangible clinical benefits in advanced disease states. Cirrhotic patients receiving Liv.52 for 6 months demonstrated statistically significant improvements in Child-Pugh severity scores, reductions in ascites accumulation, and significant decreases in serum aminotransferases (ALT and AST) compared to placebo controls

4. Silymarin

Silymarin is a natural flavonolignan complex extracted from the seeds of milk thistle (Silybum marianum), a medicinal plant belonging to the Asteraceae family. It is composed mainly of silybin (the most active component), silydianin, silychristin, taxifolin, and quercetin. Silymarin is one of the most extensively studied herbal hepatoprotective agents and possesses antioxidant, anti-inflammatory, antifibrotic, antiviral, anticancer, and membrane-stabilizing properties. Although its oral bioavailability is low due to poor absorption and rapid metabolism, advanced formulations such as phytosomes, liposomes, nanoparticles, and β-cyclodextrin complexes have significantly improved its absorption. Because of its excellent safety profile and multiple mechanisms of action, silymarin is widely used as an adjunctive therapy for chronic liver diseases.

1. Alcoholic Liver Disease (ALD): Silymarin protects the liver against alcohol-induced injury by reducing oxidative stress, lipid peroxidation, inflammatory cytokines (TNF-α), and hepatocyte necrosis while restoring hepatic glutathione levels. Experimental studies have shown that nanosilibinin, due to its improved bioavailability, provides greater protection against ethanol-induced liver damage than conventional silibinin. Animal studies also demonstrated significant reductions in ALT and GGT levels and improvement in liver function following silymarin treatment. Overall, its antioxidant and anti-inflammatory effects help attenuate alcohol-induced liver injury.

2. Non-Alcoholic Fatty Liver Disease (NAFLD): In NAFLD, silymarin improves liver function by reducing hepatic fat accumulation, oxidative stress, inflammation, serum triglycerides, cholesterol, and liver enzyme levels (ALT and AST). Clinical studies have shown that a combination of silybin, vitamin E, and phospholipids significantly decreases liver steatosis, improves insulin resistance, reduces liver fibrosis markers, and lowers inflammatory cytokines. These findings suggest that silymarin serves as an effective complementary therapy for patients with fatty liver disease.

3. Hepatitis C Virus (HCV) Infection: Silymarin exhibits antiviral, antioxidant, and anti-inflammatory activities against HCV. Laboratory studies have shown that it inhibits viral entry into hepatocytes, viral RNA replication, viral protein synthesis, and cell-to-cell viral spread. It also modulates the JAK/STAT signaling pathway, suppressing HCV core gene expression. Clinical studies have reported improvements in ALT, AST, liver fibrosis markers, and quality of life, although sustained viral clearance remains lower than that achieved with standard antiviral therapy. Therefore, silymarin is mainly considered an adjunct rather than a replacement for conventional antiviral drugs.

4. Hepatitis B Virus (HBV) Infection: Evidence regarding silymarin in HBV infection is limited. Current studies suggest that its principal role is hepatoprotection rather than direct antiviral activity. Through its antioxidant and anti-inflammatory properties, silymarin may help reduce chronic liver injury and delay the progression to hepatocellular carcinoma (HCC). Thus, it has been proposed as a potential chemopreventive agent in patients with chronic HBV infection.

5. Glycyrrhiza glabra (Licorice)

Glycyrrhiza glabra (licorice) is a medicinal plant belonging to the Leguminosae (Fabaceae) family. Its major active constituent is glycyrrhizin (GL), which is metabolized to glycyrrhetinic acid (GA) in the body. Glycyrrhizin exhibits hepatoprotective, anti-inflammatory, antioxidant, antiviral, immunomodulatory, antifibrotic, and anticancer properties. It is widely used in Japan as Stronger Neo-Minophagen C (SNMC) for the treatment of acute and chronic hepatitis. Its hepatoprotective effects are mainly mediated through inhibition of NF-κB, MAPK, inflammatory cytokines, and oxidative stress.

Hepatitis C (HCV) and Hepatitis B (HBV): Glycyrrhizin exhibits antiviral activity by inhibiting viral replication, reducing HCV core gene expression, and decreasing HBsAg production. Clinical studies have shown improvement in ALT and AST levels, and long-term therapy has been associated with a reduced risk of hepatocellular carcinoma (HCC) in chronic hepatitis patients, particularly those who do not respond to interferon therapy.

Hepatic Fibrosis and NAFLD: Glycyrrhizin suppresses activation of hepatic stellate cells, inhibits collagen synthesis, promotes hepatocyte regeneration, and reduces liver fibrosis. It also improves hepatic steatosis by

decreasing lipid accumulation, oxidative stress, and mitochondrial damage, making it beneficial in non-alcoholic fatty liver disease (NAFLD).

Liver Cancer (Hepatocellular Carcinoma): Glycyrrhizin possesses anticancer activity by inducing apoptosis, arresting the cell cycle, and inhibiting NF-κB-mediated oncogenic signalling. Experimental studies have demonstrated its ability to suppress the growth of hepatocellular carcinoma cells.

6. Phyllanthus amarus (Bhumi Amla):

Phyllanthus amarus is a small annual herb belonging to the Phyllanthaceae family. It is widely distributed in tropical and subtropical regions of Asia, Africa, and South America. In Ayurveda, it is known as Bhumi Amla and has traditionally been used for the treatment of jaundice, hepatitis, kidney stones, and other liver disorders. The herb is rich in lignans such as phyllanthin and hypophyllanthin, which are responsible for its hepatoprotective, antiviral, antioxidant, and anti-inflammatory activities. **Chronic Hepatitis B**: Phyllanthus amarus is one of the best-studied herbs for chronic hepatitis B. Clinical studies have shown that it can reduce hepatitis B surface antigen (HBsAg) levels and suppress HBV replication in some patients. By decreasing viral load, it reduces chronic inflammation and slows the progression of hepatitis to fibrosis and cirrhosis. Although antiviral drugs remain the standard treatment, Phyllanthus has been investigated as an adjunct therapy to improve viral clearance and liver enzyme levels. **Drug-induced liver injury**: In experimental models, Phyllanthus protects hepatocytes from toxic drugs by reducing oxidative stress and maintaining hepatocyte membrane integrity. Liver enzymes (ALT and AST) are significantly reduced, indicating protection against hepatocellular damage.

7. Picrorhiza kurroa (Kutki)

Picrorhiza kurroa commonly known as Kutki, is a perennial medicinal herb belonging to the Plantaginaceae family. It grows in the alpine Himalayan regions of India, Nepal, and Tibet. Kutki has been used extensively in Ayurveda for centuries as a liver tonic and is regarded as one of the most effective herbal remedies for liver diseases. Its major bioactive constituents, picroside I and picroside II, possess potent antioxidant, hepatoprotective, choleretic, and anti-inflammatory property

Non-alcoholic Fatty Liver Disease (NAFLD): In NAFLD, excessive triglycerides accumulate inside hepatocytes, leading to steatosis and inflammation. Picrorhiza reduces hepatic fat accumulation by improving fatty acid oxidation and decreasing lipid synthesis. It also lowers inflammatory cytokines, preventing progression from simple steatosis to non-alcoholic steatohepatitis (NASH).

Alcoholic Liver Disease: Alcohol metabolism generates acetaldehyde and reactive oxygen species that damage hepatocytes. Picrorhiza neutralizes these free radicals, restores antioxidant enzymes, decreases inflammation, and reduces alcohol-induced necrosis.

Cholestatic Liver Disease: Kutki stimulates bile secretion (choleretic effect), improving bile flow and reducing the accumulation of toxic bile acids, thereby relieving cholestatic liver injury.

8. Tinospora cordifolia (Guduchi)

Tinospora cordifolia commonly known as Guduchi or Giloy, belongs to the Menispermaceae family. It is a climbing shrub widely distributed throughout India. In Ayurveda, Guduchi is classified as a Rasayana (rejuvenating herb) due to its immunomodulatory and restorative properties. It contains alkaloids, diterpenoid lactones, glycosides, and polysaccharides that contribute to its antioxidant, anti-inflammatory, hepatoprotective, and immunomodulatory effects.

Drug-induced Liver Injury (DILI): Tinospora is mainly used for hepatotoxicity caused by drugs such as paracetamol, antitubercular drugs, and certain chemotherapeutic agents. It restores glutathione levels depleted by toxic metabolites, thereby protecting hepatocytes from necrosis and accelerating liver regeneration.

Fatty Liver Disease: Tinospora reduces oxidative stress and inflammatory cytokines associated with fatty liver, resulting in improved liver enzymes and reduced fat accumulation in experimental studies.

9. Nigella sativa (Black Seed):

Nigella sativa L., commonly known as Black Seed or Black Cumin, belongs to the Ranunculaceae family. It has been used for more than 2,000 years in Unani, Ayurveda, and Middle Eastern traditional medicine. The seeds are rich in thymoquinone, the major bioactive compound responsible for its antioxidant, anti-inflammatory, antimicrobial, immunomodulatory, and hepatoprotective properties**.**

Non-alcoholic Fatty Liver Disease: Several randomized clinical trials have shown that Nigella sativa supplementation reduces liver fat, lowers ALT and AST, improves insulin resistance, and decreases body mass index. These effects make it particularly useful in metabolic-associated fatty liver disease.

Alcoholic Liver Disease: Alcohol increases oxidative stress and lipid peroxidation. Thymoquinone protects hepatocytes by reducing oxidative damage and inflammatory cytokines, thereby decreasing alcohol-induced liver injury**.**

Drug-induced Liver Injury: Animal studies demonstrate protection against hepatotoxic drugs by restoring antioxidant capacity and preventing hepatocyte apoptosis.

10. Berberine:

Berberine is a naturally occurring isoquinoline alkaloid isolated from several medicinal plants, including Berberis aristata, Coptis chinensis, and Hydrastis canadensis. It has been widely used in Traditional Chinese Medicine and Ayurveda for treating metabolic disorders, infections, and gastrointestinal diseases. In recent years, berberine has gained considerable attention for its beneficial effects in metabolic dysfunction-associated steatotic liver disease (MASLD/NAFLD) because of its lipid-lowering, antidiabetic, anti-inflammatory, antioxidant, and hepatoprotective activities.

NAFLD: Berberine is considered one of the most promising phytochemicals for NAFLD. Clinical trials have shown that it reduces liver fat content, Improves insulin sensitivity, Lowers ALT and AST, Decreases serum triglycerides and cholesterol, Improves ultrasound evidence of fatty liver. Because NAFLD is closely linked to obesity and diabetes, berberine targets the underlying metabolic abnormalities rather than simply protecting hepatocytes.

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD): Berberine improves glucose metabolism and lipid homeostasis, thereby slowing progression to steatohepatitis and fibrosis.

Limitations of herbal medicines:

1. Lack of robust clinical evidence:

Most synthetic drugs are approved only after extensive Phase I–IV clinical trials. Many herbal medicines rely on animal studies, small clinical trials, and heterogeneous study designs. Therefore, they cannot completely replace evidence-based pharmacotherapy. Conduct large, multicenter randomized controlled trials (RCTs) with standardized herbal formulations. Long-term studies are needed to establish efficacy, optimal dosage, and safety comparable to synthetic drugs

2. Poor standardization:

Herbal preparations vary according to plant species, growing conditions, harvesting time, extraction methods, and storage. This causes inconsistent potency and unpredictable clinical effects. Two commercial milk thistle products may contain different concentrations of silymarin despite having the same label. Standardize cultivation, harvesting, extraction, and manufacturing processes using Good Agricultural and Collection Practices (GACP) and Good Manufacturing Practices (GMP). This ensures consistent concentrations of active constituents.

3. Herb-induced liver injury (HILI):

Herb-Induced Liver Injury (HILI) is liver damage caused by herbal medicines, herbal supplements, or traditional herbal products. In the liver, herbal compounds are metabolized by cytochrome P450 (CYP450) enzymes. While many are converted into harmless metabolites, some are transformed into reactive toxic metabolites that generate excessive reactive oxygen species (ROS), leading to oxidative stress, mitochondrial dysfunction, depletion of glutathione, lipid peroxidation, and ultimately hepatocyte apoptosis or necrosis. In some cases, herbal constituents bind to liver proteins and form antigenic complexes that trigger an immune-mediated response, activating Kupffer cells and T lymphocytes, which release inflammatory cytokines such as TNF-α and IL-6, resulting in hepatitis. Giloy (Tinospora cordifolia), During the COVID-19 pandemic, Giloy was widely promoted as an immune booster in India. A nationwide multicenter study found cases of autoimmune-like hepatitis, acute liver injury, liver failure, and liver transplantation in severe case. Green Tea contains large amounts of EGCG, which at high doses acts as pro-oxidant instead of antioxidant, causing mitochondrial damage and acute hepatocellular injury. Implement routine pharmacovigilance and monitor liver function during herbal therapy, especially in high-risk patients. Herbs with known hepatotoxic potential should be used only under medical supervision.

4. Herb–drug interactions:

Many herbs alter cytochrome P450 enzymes. St. John's Wort(Hypericum perforatum) induces CYP3A4, reducing the effectiveness of cyclosporine, oral contraceptives, warfarin, antiretroviral drugs which may result in treatment failure or toxicity. Curcumin also interacts with warfarin to produce similar effect. Glycyrrhiza glabra interacts with Digoxin which results in hypokalemia and increased risk of digoxin and cardiac arrhythmia. Evaluate potential interactions through clinical and pharmacokinetic studies. Patients should always inform healthcare providers about herbal supplement use before starting conventional medications.

5. Quality control and contamination:

Some herbal products have been found to contain heavy metals, pesticides, undeclared pharmaceutical ingredients (intentional adulteration), and incorrect plant species. These contaminants may themselves cause liver injury. Different Phyto-hepatotoxinS include, pyrrolizidine alkaloids (Symphytum officicale), kavalactones(kava), catechins(green tea extract), anthraquinones(aloe, senna). Different non- phytohepatotoxins include, aflatoxins (poorly stored herbs), Mycotoxins(mold contamination), industrial solvents, microbial toxins etc. Screen herbal products for heavy metals, pesticides, microbial contamination, aflatoxins, and adulterants. Regulatory agencies should enforce strict quality testing before products reach the market.

6. Overestimation of efficacy:

Many herbal products are marketed as "liver detoxifiers." However, recent reviews conclude that evidence for many products remains modest, benefits are generally adjunctive, and they do not replace antiviral drugs, immunosuppressants, or liver transplantation when these are indicated. Promote evidence-based use of herbal medicines and avoid exaggerated marketing claims. Herbal products should be recommended only when supported by scientific and clinical evidence and used as adjuncts, not replacements, for standard therapy.

Conclusion:

Ultimately, whether herbal medicines act as a therapeutic "friend" or a dangerous "foe" in managing liver disease hinges entirely on the implementation of strict quality control. While many botanicals offer genuine antioxidant and anti-inflammatory benefits for the liver, the lack of standardization opens the door to severe risks, including species misidentification, heavy metal contamination, and toxic adulteration that can trigger herb-induced liver injury. For these traditional remedies to be safely integrated into modern hepatology, the industry must transition toward rigorous, phytopharmaceutical-grade manufacturing standards. Only through mandatory authentication, contaminant screening, and chemical standardization can the true medical potential of herbs be realized without compromising the very organ they are meant to protect.

Reference:

1. World Health Organization. WHO global report on traditional and complementary medicine 2025. Geneva: World Health Organization; 2025.
2. World Health Organization. Traditional medicine in the WHO South-East Asia Region. Geneva: World Health Organization; 2025.
3. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 59th ed. Pune: Nirali Prakashan; 2023.
4. Trease GE, Evans WC. Trease and Evans Pharmacognosy. 16th ed. Edinburgh: Elsevier; 2009.
5. Wallis TE. Textbook of Pharmacognosy. 5th ed. New Delhi: CBS Publishers & Distributors; 2005.

6. Sharma PV. Charaka Samhita. Varanasi: Chaukhambha Orientalia; 2014.
7. Sushruta. Sushruta Samhita. Varanasi: Chaukhambha Sanskrit Sansthan; 2015.
8. Vagbhata. Ashtanga Hridaya. Varanasi: Chaukhambha Surbharati Prakashan; 2016.
9. Ministry of AYUSH, Government of India. The Ayurvedic Pharmacopoeia of India. New Delhi: Ministry of AYUSH; various volumes.
10. Ministry of AYUSH, Government of India. The Siddha Pharmacopoeia of India. New Delhi: Ministry of AYUSH.
11. Ministry of AYUSH, Government of India. The Unani Pharmacopoeia of India. New Delhi: Ministry of AYUSH.
12. Ministry of AYUSH, Government of India. National Institute of Siddha – Reference Documents. Chennai: National Institute of Siddha.
13. DeFelice SL. The nutraceutical revolution: its impact on food industry research and development. Trends Food Sci Technol. 1995;6(2):59–61.
14. Brower V. Nutraceuticals: poised for a healthy slice of the healthcare market? Nat Biotechnol. 1998;16(8):728–31.
15. Pandey MM, Rastogi S, Rawat AKS. Indian traditional Ayurvedic system of medicine and nutritional supplementation. Evid Based Complement Alternat Med. 2013;2013:376327.
16. Patwardhan B, Vaidya ADB, Chorghade M. Ayurveda and natural products drug discovery. Curr Sci. 2004;86(6):789–99.
17. Patwardhan B, Warude D, Pushpangadan P, Bhatt N. Ayurveda and traditional Chinese medicine: a comparative overview. Evid Based Complement Alternat Med. 2005;2(4):465–73.
18. Mukherjee PK. Quality Control and Evaluation of Herbal Drugs. 2nd ed. New Delhi: Elsevier; 2019.
19. Mukherjee PK. Quality Control of Herbal Drugs: An Approach to Evaluation of Botanicals. New Delhi: Business Horizons; 2002.
20. Vaidya ADB, Devasagayam TPA. Current status of herbal drugs in India: an overview. J Clin Biochem Nutr. 2007;41(1):1–11.
21. Grander, C., Grabherr, F., & Tilg, H. (2023). Non-alcoholic fatty liver disease: pathophysiological concepts and treatment options. Cardiovascular Research, 119(9), 1787–1798. https://doi.org/10.1093/cvr/cvad095
22. Walsh K, Alexander G. Alcoholic liver disease. Postgrad Med J. 2000;76(895):280–286. doi:10.1136/pmj.76.895.280
23. Nirali Prakashan. Pathophysiology: Inflammatory Bowel and Liver Diseases. Pune: Nirali Prakashan; 2020. p. 11.11–11.17.
24. Sharma B, John S. Hepatic Cirrhosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482419/
25. Jogu P, Zubair M, Minter DA. Liver Function Tests. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482419/
26. Del Prete A, Scalera A, Iadevaia MD, Miranda A, Zulli C, Gaeta L, Tuccillo C, Federico A, Loguercio C. Herbal Products: Benefits, Limits, and Applications in Chronic Liver Disease. Evid Based Complement Alternat Med. 2012;2012:837939. doi:10.1155/2012/837939.

27. William M. Lee, Acetaminophen (APAP) hepatotoxicity—Isn't it time for APAP to go away? Journal of Hepatology, Volume 67, Issue 6, 2017, Pages 1324-1331, ISSN 0168-8278, https://doi.org/10.1016/j.jhep.2017.07.005.
28. European Association for the Study of the Liver. EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. J Hepatol. 2018 Aug;69(2):406-460. doi: 10.1016/j.jhep.2018.03.024. Epub 2018 Apr 10. Erratum in: J Hepatol. 2018 Nov;69(5):1207. doi: 10.1016/j.jhep.2018.08.009. PMID: 29653741.Devarbhavi H. A comprehensive review on the hepatotoxicity of herbs used in the Indian (AYUSH) systems of alternative medicine. J Clin Exp Hepatol. 2024;14(2):101-121.
29. Navarro VJ, Khan I, Björnsson E, Seeff LB, Serrano J, Hoofnagle JH. Herbal and dietary supplement-induced liver injury. Hepatology. 2017;65(1):363-373.
30. Izzo AA, Ernst E. Interactions between herbal medicines and prescribed drugs: An updated systematic review. Drugs. 2009;69(13):1777-1798.
31. Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. Front Pharmacol. 2014;4:177.
32. Pradhan SC, Girish C. Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. Indian J Med Res. 2006;124(5):491-504.
33. Flora K, Hahn M, Rosen H, Benner K. Milk thistle (Silybum marianum) for the therapy of liver disease. Am J Gastroenterol. 1998;93(2):139-143.
34. Saller R, Melzer J, Reichling J, Brignoli R, Meier R. An updated systematic review of the pharmacology of silymarin. Drugs. 2008;68(15):2035-2063.
35. Lee WM. Acetaminophen (APAP) hepatotoxicity—Isn't it time for APAP to go away? J Hepatol. 2017;67(6):1324-1331.
36. European Association for the Study of the Liver (EASL). EASL Clinical Practice Guidelines: Management of decompensated cirrhosis. J Hepatol. 2018;69(2):406-460.
37. Lok ASF, McMahon BJ. Chronic hepatitis B: Update 2009. Hepatology. 2009;50(3):661-662.
38. Ghany MG, Strader DB, Thomas DL, Seeff LB. Diagnosis, management, and treatment of hepatitis C: An update. Hepatology. 2009;49(4):1335-1374.