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# Natural Hepatoprotective Agents: A Systematic Review of Plant-Based Therapies

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## Abstract

Liver diseases remain a major global health burden, driven by factors such as alcohol consumption, viral infections, drug-induced toxicity, and metabolic disorders. Conventional pharmacological treatments are often limited by adverse effects, high costs, and variable efficacy, prompting growing interest in plant-based alternatives. This systematic review aims to evaluate the hepatoprotective potential of medicinal plants and their bioactive constituents, with a focus on mechanisms of action, preclinical and clinical evidence, and therapeutic relevance. A comprehensive literature search was conducted across major scientific databases, including PubMed, Scopus, and Web of Science, selecting studies that investigated plant-derived extracts or compounds with demonstrated liver-protective activity. such as *Silybum marianum*, *Curcuma longa*, *Phyllanthus niruri*, and *Andrographis paniculata*, exhibit significant hepatoprotective effects. These effects are primarily mediated through antioxidant, anti-inflammatory, anti-fibrotic, and detoxification pathways, including modulation of oxidative stress markers, cytokine production, and hepatic enzyme activity. Additionally, certain phytochemicals, such as flavonoids, terpenoids, and polyphenols, play a crucial role in liver regeneration and cellular protection. Despite promising preclinical data, clinical validation remains limited and heterogeneous. plant-based therapies represent a valuable and promising approach for hepatoprotection, offering potential complementary or alternative strategies in the management of liver disorders.

**Keywords**

Antioxidant, Cirrhosis, Hepatoprotection, Liver function, Metabolic disorders

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## 1.INTRODUCTION:

Hepatoprotective agents are substances natural or synthetic that prevent or reduce damage to the liver caused by toxic agents, alcohol, drugs, or disease. They function by combating oxidative stress, neutralizing radicals, and promoting cell regeneration, often lowering liver enzymes like ALT and AST. Hepatoprotection Mechanism: These agents prevent cellular necrosis, reduce inflammation, and enhance anti-radical defenses, limiting damage from hepatotoxins. Sources Many natural products, including herbal medicines (e.g., *Amaranthus spinosus*, *Artemisia absinthium*) and antioxidant-rich foods, show hepatoprotective potential. Significance They are crucial for treating drug-induced liver injury, chronic alcohol-related damage, and managing diseases like cirrhosis. Evaluation Efficacy is often determined by measuring liver function improvement in experimental models. Hepatoprotective herbs are natural compounds that protect liver cells from damage caused by toxins, alcohol, and infections through antioxidant and anti-inflammatory mechanisms. Key examples include Milk Thistle (Silymarin), Bhumi Amla (Phyllanthus niruri), Kutki (Picrorhiza kurroa), Turmeric (Curcuma longa), and Giloy (Tinospora cordifolia). These plants are widely studied for aiding liver detoxification and supporting liver function [1].

**Hepatoprotective Herbs**

**Milk Thistle (Silybum marianum):** Often considered the most potent, its active component, silymarin, prevents toxin binding to liver cells and acts as an antioxidant.

**Bhumi Amla (Phyllanthus niruri):** Widely used in traditional medicine to fight hepatitis and reduce liver fibrosis.

**Kutki (Picrorhiza kurroa):** Contains kutkin, known for its strong antioxidant activity and ability to treat acute hepatitis.

**Turmeric (Curcuma longa):** Contains curcumin, which reduces inflammation and oxidative stress in liver tissue.

**Giloy (Tinospora cordifolia):** Known for its immunomodulatory properties, helping to protect the liver from toxins [2].

**Eclipta alba (Bhringraj):** Used in alcohol-induced liver damage treatment.

**Aegle marmelos (Bel):** Studied for hepatoprotective activity in hepatotoxicity models.

**Andrographis paniculata (Kalmegh):** Known to contain hepatoprotective compounds like andrographolide.

**Glycyrrhiza glabra (Licorice):** Used for its anti-inflammatory effects on the liver [3].

**Liver:** The liver is a well-known player in the metabolism and removal of drugs. Drug metabolizing enzymes in the liver detoxify drugs and xenobiotics, ultimately leading to the acquisition of homeostasis. However, liver toxicity and cell damage are not only related to the nature and dosage of a particular drug but are also influenced by other factors such as aging, immune status, environmental contaminants, microbial metabolites, gender, obesity, and expression of individual genes Furthermore, factors such as drugs, alcohol, and environmental contaminants could induce oxidative stress, thereby impairing the regenerative potential of the liver and causing several diseases. Persons suffering from other ailments and those with comorbidities are found to be more prone to drug-induced toxicities. Moreover, drug composition and drug-drug interactions could further aggravate the risk of drug-induced hepatotoxicity [4]. A plethora of mechanisms are responsible for initiating liver cell damage and further aggravating liver cell injury, followed by impairment of homeostasis, ultimately leading to the generation of reactive oxygen species, immune-suppression, and oxidative stress. The liver is located deep in the right upper quadrant and is well protected by the right ribcage. Its size, as measured in the right midclavicular line, is about 12–15 cm and its weight is about 1500 g. The weight of the liver is approximately 2.5% of the body weight. The right lobe of the healthy liver is not usually palpable. The left lobe may be palpable up to midway between the xiphisternum and umbilicus. This means that a palpable left lobe, in isolation, is not of clinical importance. In a patient, the consistency (normal consistency is firm), surface (normal is smooth, non-tender) and margins (normal is regular) of the liver are much more important features than the liver size alone. The liver is a very vascular organ. About 1500 mL of blood passes through the liver cardiac output (normal cardiac output is 5L/min). Compared to its weight (which is about 2.5% of the body weight), it receives a massive blood supply [5]. It is important to realize that the majority (about 65%) of the blood supplied to the liver is deoxygenated venous blood (which carries much less oxygen than arterial blood) from the small and large intestine. Only one third of the supply is oxygenated arterial blood and carries a high level of oxygen. This dual blood supply serves three important functions. First, the dual blood supply gives a safety cushion to the liver and keeps it alive even if one supply is terminated because of some pathological state. Second, the venous blood carries several harmful substances, toxins and biological products derived from food and gut bacteria present in the large intestine; the liver acts as a filter that prevents the systemic circulation from exposure to these substances; when this filter function of the liver is impaired, such as in patients with liver failure, these harmful substances reach to the brain and the patient becomes unconscious. Third, venous blood carries a lot of nutrients from the small intestine; these nutrients, if released unchecked into the circulation, will produce metabolic imbalance. The liver acts as a temporary warehouse to store excessive amounts of these nutrients and releases the mat the time of need (such as fasting). During normal blood circulation, deoxygenated blood is collected from all over the body by the venous system and is pumped by the right side of the heart into the lungs. In the lungs, oxygenation of blood takes place and oxygen-rich blood is returned to the left side of the heart and pumped through the arteries throughout the body. Capillaries connect arteries to veins. Oxygen and carbon dioxide is exchanged in arteries, and blood collected from the capillaries returns to the lungs through veins.

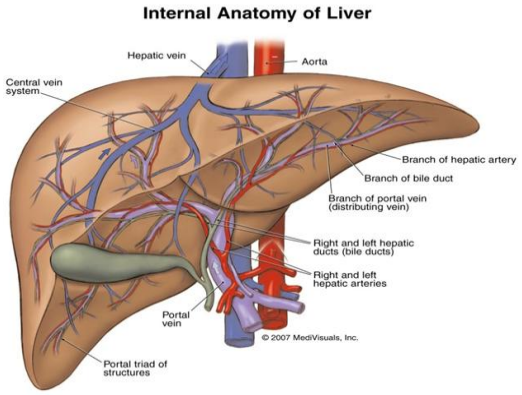


**Figure: 1: Human Liver**

In the portal system, the blood returning from the capillaries is not directly returned to venous system but is again passed through another set of capillaries in another organ or tissue. There are two portal systems in the human body: the pituitary–hypophyseal system in the brain and the second in the liver. The objective of this portal system is to provide the liver with extra circulation time and expose the blood to the extensive network of hepatocyte plates. It helps the liver to perform its metabolic and filtering activities more efficiently [6]. The liver is a vital organ located in the upper right abdomen, responsible for over 500 functions, including detoxification, metabolism, digestion, and energy storage. It is composed of four lobes right, left, caudate, and quadrate subdivided into functional lobules, and features a dual blood supply from the portal vein and hepatic artery [7].

**Liver Anatomical Parts**

**Lobes (Right, Left, Caudate, Quadrate):** The liver is divided into these four anatomical lobes, with the right being the largest. The liver is anatomically divided into four lobes—right, left, caudate, and quadrate—separated by ligaments and fissures. The large right lobe and smaller left lobe are separated anteriorly by the falciform ligament, while the caudate and quadrate lobes are visible on the visceral (underside) surface [8].

**Right Lobe:** The largest lobe, situated on the right side. It is functionally divided into anterior and posterior sectors.

**Left Lobe:** Smaller and more flattened, located on the left side of the falciform ligament.

**Caudate Lobe:** Located superiorly on the posterior (back) surface, nestled between the inferior vena cava and the fissure for the ligamentum venosum [9].

**Quadrate Lobe:** Located inferiorly on the visceral surface, positioned between the gallbladder and the fissure for the ligamentum teres

- **Lobules:** Thousands of small functional units forming the lobes. Liver lobules are the small, hexagonal functional units of the liver, with 50,000 to 100,000 packing the organ. They feature a central vein, radiating plates of hepatocytes, and portal triads (bile duct, portal venule, hepatic arteriole) at the corners. They process blood, produce bile, and metabolize
- **Hepatocytes:** Liver cells within the lobules that perform metabolic and detox functions. Hepatocytes are defined as the primary liver cells that comprise approximately 65% of all liver cells, playing essential roles in metabolism, detoxification, and protein production, while also participating in immunological functions by interacting with T cells and producing inflammatory cytokines [10].
- **Portal Vein:** Brings nutrient-rich blood from the intestines. The portal vein is a major blood vessel that carries nutrient-rich blood from the digestive organs (intestines, stomach, spleen, pancreas) directly to the liver. It provides about 75% of the liver's blood supply, enabling it to process nutrients, toxins, and medications before blood enters systemic circulation. Formation It is formed by the union of the splenic vein and the superior mesenteric vein behind the pancreas. Pathway It brings blood into the liver, which then divides into smaller branches (right and left) to distribute blood throughout the liver sinusoids. Blood Flow Normal flow is directed *into* the liver, known as hepatopetal flow [11].
- **Hepatic Artery:** Supplies oxygenated blood from the heart. The hepatic artery is a major blood vessel supplying oxygen-rich blood to the liver, providing about 25% of its total blood flow (300-500 mL/min), which is essential for hepatic metabolism and oxygenation. Originating from the celiac trunk, it divides into right and left

branches within the porta hepatis. Hepatic Artery Origin & Pathway The Common Hepatic Artery originates from the celiac artery (from the abdominal aorta). It becomes the "proper hepatic artery" after giving off the gastro duodenal artery. Branches The proper hepatic artery divides into the right hepatic artery and left hepatic artery to supply the liver and gallbladder. Anatomy & Supply The right hepatic artery supplies the right lobe, while the left supplies the left. The right hepatic artery often branches into the cystic artery to supply the gallbladder. Vascular Function While the hepatic portal vein provides nutrients, the hepatic artery provides the oxygen necessary for the liver tissue, complementing the deoxygenated, nutrient-rich blood from the portal vein. Anatomical Variation While a classic anatomy is standard, variations in hepatic arterial anatomy, such as replaced/accessory arteries, occur in 40-45% of individuals [12].

- **Bile Ducts:** Channels that transport bile to the gallbladder and small intestine. The liver bile ducts are a network of tubes—the biliary tree—that transport bile from the liver, where it is produced, to the gallbladder for storage and the small intestine to aid in fat digestion. They are divided into intrahepatic (inside the liver) and extrahepatic (outside) segments, merging into the common bile. Bile Duct System Anatomy Small channels called *canaliculi* collect bile, leading to interlobular ducts, which merge into the right and left hepatic ducts. Drainage The left and right hepatic ducts join outside the liver to form the common hepatic duct, which connects with the cystic duct from the gallbladder to form the common bile duct (CBD). Function Bile is essential for breaking down fats, absorbing fat-soluble vitamins, and removing waste products. Blockages & Symptoms Blocked bile ducts (caused by stones, tumors, or strictures) can lead to jaundice (yellow skin/eyes), dark urine, abdominal pain, nausea, and itching [13].

**FUNCTIONS OF THE LIVER include:**

**Detoxification & Filtration:** Filters all blood leaving the digestive tract, breaking down drugs, alcohol, and waste products (e.g., converting ammonia to urea).

**Production of Bile:** Produces bile, a fluid essential for breaking down fats in the small intestine and removing waste from the body [14].

**Metabolism & Storage:** Converts excess glucose into glycogen for storage (and back to glucose for energy), stores iron, and creates essential amino acids and proteins (like albumin).

**Blood Regulation:** Controls blood clotting and regulates the levels of amino acids, fats, and glucose in the blood.

**Immune System Support:** Removes bacteria from the bloodstream and produces immune factors [15].

**Maintaining a Healthy Liver:** The best way to avoid liver disease is to take active steps toward a healthy life. The following are some recommendations that will help keep the liver functioning as it should:

**Avoid Illicit Drugs**: Illicit drugs are toxins that the liver must filter out. Taking these drugs can cause long-term damage [16].

**Drink Alcohol Moderately**: Alcohol must be broken down by the liver. While the liver can moderate amounts, excessive alcohol use can cause damage.

**Exercise Regularly**: A regular exercise routine will help promote general health for every organ, including the liver.

**Eat Healthy Foods**: Eating excessive fats can make it difficult for the liver to function and lead to fatty liver disease.

**Practice Safe Sex**: Use protection to avoid sexually transmitted diseases such as hepatitis C.

**Vaccinate**: Especially when traveling, get appropriate vaccinations against hepatitis A and B, as well as diseases such as malaria and yellow fever, which grow in the liver [17].

**Types of Liver Disease:**

- **Hepatitis (Viral & Infectious):** Inflammation of the liver caused by viruses. Types A and E are usually acute (contaminated food/water), while B, C, and D can become chronic, causing long-term damage.
- **Fatty Liver Disease:**

Excessive fat accumulation in liver cells.

- **Nonalcoholic Fatty Liver Disease (NAFLD/MASLD):** Linked to obesity, diabetes, and metabolic syndrome.
- **Alcohol-Related Liver Disease (AFLD):** Caused by excessive alcohol consumption [18].
- **Cirrhosis:** Advanced scarring of the liver caused by long-term liver damage (e.g., from chronic hepatitis or alcohol abuse).
- **Autoimmune Liver Diseases:** The immune system attacks the liver or bile ducts.
  - **Autoimmune Hepatitis:** Immune system attacks liver cells.
  - **Primary Biliary Cholangitis (PBC):** Damage to bile ducts.
  - **Primary Sclerosing Cholangitis (PSC):** Inflammation/scarring of bile ducts.
- **Genetic/Inherited Diseases:** Metabolic disorders that cause toxic buildup.

- **Hemochromatosis:** Causes excess iron accumulation.
- **Wilson Disease:** Causes copper accumulation.
- **Alpha-1 Antitrypsin Deficiency:** A genetic condition affecting protein production.

- **Liver Cancer:**
  - **Hepatocellular Carcinoma (HCC):** The most common form of primary liver cancer, often arising from cirrhosis.
  - **Cholangiocarcinoma:** Bile duct cancer.
- **Vascular Diseases:** Conditions restricting blood flow to/from the liver, such as **Budd-Chiari syndrome**.
- **Acute Liver Failure:** Sudden, severe liver damage caused by drug overdoses (e.g., acetaminophen) or toxins [19].

**Herbal treatment of Liver Disease:**

**a. Silymarin:** Silymarin, often called milk thistle, consists of a group of compounds extracted from milk thistle (Silybum marianum) seeds, including silybin, silychristin, and silydianin. Milk thistle has been used for over 2,000 years Trusted Source to treat bile duct and liver conditions, and research shows that it may have liver-protective properties. It has been suggested that silymarin has strong antioxidant effects and may help promote liver cell regeneration, reduce inflammation, and benefit those with liver disease. However, results from human studies Trusted Source have been mixed. For example, some studies Trusted Source have shown that taking a silymarin supplement may help protect against liver disease progression, prolong life in people with alcoholic cirrhosis, and enhance overall quality of life in people with liver disease. Yet, other studiesTrusted Source indicate that silymarin is no more effective than placebo treatments, highlighting the need for additional research. Regardless, silymarin is considered safe and has not been associated with adverse side effects, even when used at high doses [20].

**b. Ginseng:** Ginseng is a popular herbal supplement known for its powerful anti-inflammatory properties. A number of test-tube and animal studies Trusted Source have demonstrated that ginseng has antioxidant effects and may help protect against liver injury caused by viruses, toxins, and alcohol. Plus, it may boost liver cell regeneration after surgery. some human Trusted Source studies Source have shown that ginseng treatment may improve liver function and reduce fatigue and inflammation in people with liver disease and liver dysfunction. For example, a study Source in 51 men with elevated levels of alanine transaminase (ALT), a marker for liver damage, found that those who took 3 grams of ginseng extract per day for 12 weeks experienced significant reductions in ALT, compared with a placebo group. Levels of gamma-glutamyl transferase (GGT), another marker for liver damage, were also reduced significantly. Although these results are promising, more research investigating the effects of ginseng on liver health is needed. When used on its own, ginseng is thought to be relatively safe for liver health. However, ginseng has the potential to react with medications, which can lead to liver injury and other potentially dangerous side effects [21].

**c. Green tea:** Although it isn't technically an herb, green tea and its main polyphenol compound epigallocatechin-3-gallate (EGCG) are often included in literature reviews Trusted Source focusing on herbal remedies for liver conditions. Some studies have found that supplementing with green tea extract may help treat those with liver disease. Study with 80 people with nonalcoholic fatty liver disease (NAFLD) found that supplementing with 500 mg of green tea extract per day for 90 days significantly reduced the liver damage markers ALT and aspartate aminotransferase (AST). Although the placebo group also noticed a reduction in AST and ALT levels, they were not significant. Another 12-week study Source in 80 people with NAFLD observed that those who took 500 mg of green tea extract daily experienced significant improvements in AST, ALT, and inflammatory markers, compared with a placebo. The treatment also reduced fatty changes in the liver. Green tea intake has likewise been shown to Trusted Source protect against various liver conditions, including liver cancer, hepatitis, cirrhosis, fatty liver (hepatic steatosis), and chronic liver disease. While drinking green tea is considered safe for most people, in rare cases Trusted Source, green tea extract supplements have been linked to acute liver injury [22].

**d. Licorice:** It was the most prescribed herb in Ancient Egyptian, Roman, Greek, East China, and the West from the Former Han era. There are various beneficial effects of licorice root extracts, such as treating throat infections, tuberculosis, respiratory, liver diseases, antibacterial, anti-inflammatory, and immunodeficiency. Although chewy candy often comes to mind when thinking of licorice (Glycyrrhiza glabra), it's really an herb with powerful medicinal properties. Licorice root to have anti-inflammatory, antiviral, and liver-protective effects in scientific studies. The main active component in licorice root is the saponin compound glycyrrhizin, which is commonly used in traditional Chinese and Japanese medicine to treat many ailments, including liver disease. Some studies have demonstrated that

treatment with licorice extract may benefit those with certain liver conditions. An study in 66 people with fatty liver disease found that supplementing with 2 grams of licorice root extract per day for 2 months significantly reduced ALT and AST, compared with a placebo treatment. In another small study Trusted Source, 6 healthy people took a glycyrrhizin product before drinking vodka every night for 12 days, and 6 people only drank vodka nightly for 12 days. In the vodka-only group, liver damage markers, including ALT, AST, and GGT, significantly increased. In the glycyrrhizin group, these markers did not significantly increase, suggesting that glycyrrhizin may help protect against alcohol-related liver damage [23].

**e. Ginger:** Ginger root is a popular culinary ingredient and also commonly used as a medicinal treatment for many health conditions, including liver disease. A 12-week study Trusted Source in 46 people with NAFLD found that supplementing with 1,500 mg of ginger powder per day significantly reduced ALT, total and LDL (bad) cholesterol, fasting blood sugar, and the inflammatory marker C-reactive protein (CRP), compared with placebo treatment. Another study Trusted Source observed similar results. People with NAFLD who supplemented with 2 grams of ginger for 12 weeks experienced significant reductions in ALT, GGT, inflammatory markers, and fat accumulation in the liver, compared with a placebo group. Ginger root contains powerful compounds, including gingerols and shogaols, that help inhibit inflammation and protect against cellular damage, which may help support liver health. Plus, ginger may help protect your liver against toxins like alcohol [24].

**f. Astragalus:** Astragalus is an edible herb commonly used in traditional Chinese medicine. It's loaded with medicinal compounds, including saponins, iso-flavonoids, and polysaccharides, which have powerful therapeutic properties. It's generally considered safe and hasn't been associated Trusted Source with liver injury. However, it can interact with certain medications. Rodent Trusted Source Studies Trusted Source indicateTrusted Source that astragalus may help protect against fibrosis and high fat diet-induced fatty liver when used alone or in combination with other herbs [25].

**g. Danshen:** Danshen is a substance that's commonly used in traditional Chinese medicine. It's the dried roots of the herb Salvia miltiorrhiza Bunge. Human and animal studies have shown that danshen may have positive effects on liver health. Animal studies indicate danshen may help protect against alcohol-related liver disease and promote liver tissue regeneration, while some human studies suggest danshen injections may help treat liver fibrosis when used alongside other herbal remedies [26].

**Conclusion:** Natural hepatoprotective agents derived from medicinal plants offer significant promise in the prevention and management of liver disorders. This review highlights that a wide range of plant species and their bioactive constituents possess notable liver-protective properties, primarily through antioxidant, anti-inflammatory, anti-fibrotic, and detoxifying mechanisms. These effects contribute to the stabilization of hepatic function, reduction of cellular damage, and promotion of liver regeneration. Liver-protective (hepatoprotective) plants play an important role in supporting liver health and managing liver-related disorders. A wide variety of medicinal plants have demonstrated protective effects against liver damage caused by toxins, drugs, alcohol, and metabolic stress. These beneficial effects are largely attributed to the presence of bioactive compounds such as flavonoids, alkaloids, phenolics, and terpenoids, which exhibit strong antioxidant and anti-inflammatory properties.

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