

An Examination of Herbal Plants with Hepatoprotective Properties

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Abstract: *The liver is a vital organ responsible for maintaining numerous physiological processes within the human body. Excessive alcohol consumption, exposure to toxic substances including certain chemotherapeutic agents, antibiotics, thioacetamide (TAA), carbon tetrachloride (CCl₄), and various microorganisms have all been shown to cause significant hepatic cellular damage. In such circumstances, the use of conventional synthetic drugs for the treatment of liver disorders may further aggravate hepatic injury. Consequently, herbal medicines have gained increasing prominence and are now widely utilized as alternative therapeutic options. Herbal formulations have been traditionally employed for the management of hepatic ailments, as maintaining optimal liver function is essential for overall human health. A wide range of herbal preparations is currently available in the market for this purpose. The objective of the present study is to compile and evaluate existing data on potential phytochemicals derived from medicinal plants that have been scientifically investigated using contemporary hepatotoxicity models. Hepatitis refers to inflammation of the liver, characterized by the infiltration of inflammatory cells into hepatic tissue. There are five principal types of hepatitis viruses designated as A, B, C, D, and E which are of major global concern due to their significant contribution to morbidity and mortality. Liver injury or dysfunction represents a serious health challenge for healthcare professionals, drug regulatory authorities, and the pharmaceutical industry alike. Herbal medicines have long been employed in the management of liver disorders. The immune system plays a crucial role in recognizing pathogens through specific receptors, thereby initiating an immediate response via the activation of immune cells, chemokines, cytokines, and the release of inflammatory mediators. These processes collectively potentiate and modulate immune function. Plant-derived phytoconstituents such as polysaccharides, proteins, flavonoids, lignans, and rotenoids exert immunostimulatory effects and contribute to the maintenance of hepatic health. Numerous herbs with hepatoprotective and immunomodulatory properties have been identified and documented. The present review aims to compile and evaluate existing data on promising phytochemicals derived from such hepatoprotective and immunomodulatory medicinal plants.*

Keywords: Medicinal plants, Liver, Phytochemicals, Hepatotoxicity Hepatoprotective herbs, Immunomodulatory herbs, Nitric oxide

I. INTRODUCTION

Medicinal plants serve as a vital source for the development of innovative drugs utilized in traditional medicine, modern pharmaceuticals, nutraceuticals, dietary supplements, folk remedies, pharmaceutical intermediates, bioactive compounds, and as lead molecules in synthetic drug discovery. According to the World Health Organization (WHO), more than 80% of the global population relies on medicinal plants as a primary means of healthcare. However, the overexploitation of certain medicinal plant species has resulted in a significant decline in their natural populations, leading to the inclusion of many of these species in the Red Data Book due to their threatened status.

Nature has endowed our nation with an abundance of therapeutically valuable plant species.^{1,2} Historically, plants have been extensively employed as traditional healing agents across various cultures. The WHO has identified approximately



20,000 medicinal plant species worldwide, of which 15–20% are found in India. Furthermore, medicinal plants are utilized in healthcare systems in over 80% of countries globally. A substantial body of scientific evidence supports the therapeutic potential of medicinal herbs used across diverse traditional systems of medicine.

In recent years, more than 13,000 plant species have been investigated for their potential in the treatment of various diseases and disorders, demonstrating the vast pharmacological promise of plant-derived bioactive compounds.^{3,4} The liver is one of the most important organs in the human body. It performs many vital functions such as metabolism, secretion, and storage. The liver helps in detoxifying and removing harmful substances, both those produced by the body and those taken from outside, like drugs and chemicals. Because of these important functions, any damage to the liver can have serious effects on a person's health. Every year, about 18,000 people die from liver cirrhosis caused mainly by hepatitis.

The liver stores important nutrients such as proteins, glycogen, vitamins, and minerals. It also helps regulate blood flow between the portal and general circulation and plays a key role in the body's immune defense system. When the body takes in medicines or other foreign substances (called xenobiotics), it recognizes them as foreign and changes them chemically so they can be removed. This process mostly happens in the liver, which works like the body's main "metabolic center." It processes both natural substances (like cholesterol and hormones) and foreign chemicals (like drugs). Because of this, the liver is easily affected by drug-related damage.

Hepatitis is inflammation of the liver, caused by infection, toxins, or other factors. It is marked by the presence of inflammatory cells in the liver tissue. There are five main types of hepatitis viruses A, B, C, D, and E. These are the most serious because they cause many illnesses and deaths worldwide. Hepatitis can be acute (lasting less than six months) or chronic (lasting longer than six months). It may cause few or no symptoms at first, but common signs include yellowing of the skin and eyes (jaundice), loss of appetite, and tiredness (malaise). If not treated, hepatitis can lead to fibrosis (scarring) and cirrhosis (severe liver damage). The disease can also result from parasites, autoimmune disorders, alcohol, certain medicines, toxic chemicals, or environmental pollutants. Among the viral forms, hepatitis B and C are the most dangerous, leading to long-term liver damage, cirrhosis, and cancer. Globally, viral hepatitis causes about 1 million deaths each year. Hepatitis B and C together account for about 78% of liver cirrhosis and liver cancer cases.⁵

Around one-third of the world's population about 2 billion people has been infected with these viruses at some point. On World Hepatitis Day (July 28, 2013), the World Health Organization (WHO) emphasized that despite the large global impact, many people remain unaware of the risks and prevention methods for hepatitis. disease caused by viral hepatitis is growing, it remains largely ignored or unknown to many policymakers, health workers, and the public.⁶

Liver & Liver Diseases

The liver is one of the most vital organs in the human body, responsible for numerous essential physiological functions. It plays a central role in metabolism, secretion, storage, detoxification, and excretion processes. The liver is instrumental in eliminating both endogenous (naturally occurring within the body) and exogenous (externally introduced) substances. Consequently, any damage to the liver or impairment of its functions can lead to severe health complications. Although viral infections remain among the predominant causes of hepatic injury, it is estimated that more than 18,000 individuals die annually due to liver cirrhosis induced by hepatitis. Due to its crucial role in the biotransformation and clearance of chemical substances, the liver is particularly susceptible to drug-induced toxicity and other forms of chemical damage.⁷

Liver disorders represent some of the most serious and life-threatening medical conditions. They are broadly classified into three major categories: hepatitis, hepatosis, and cirrhosis. Hepatitis refers to inflammatory liver diseases that may occur in acute or chronic forms; hepatosis encompasses non-inflammatory hepatic conditions; and cirrhosis is a degenerative disorder characterized by progressive fibrosis and loss of normal liver architecture. The primary etiological factors contributing to liver diseases include toxic substances such as certain antibiotics, chemotherapeutic agents, peroxidized oils, aflatoxins, carbon tetrachloride, and chlorinated hydrocarbons. In addition, excessive alcohol consumption, infections, and autoimmune disorders also play a significant role in the onset and progression of hepatic pathology.⁸



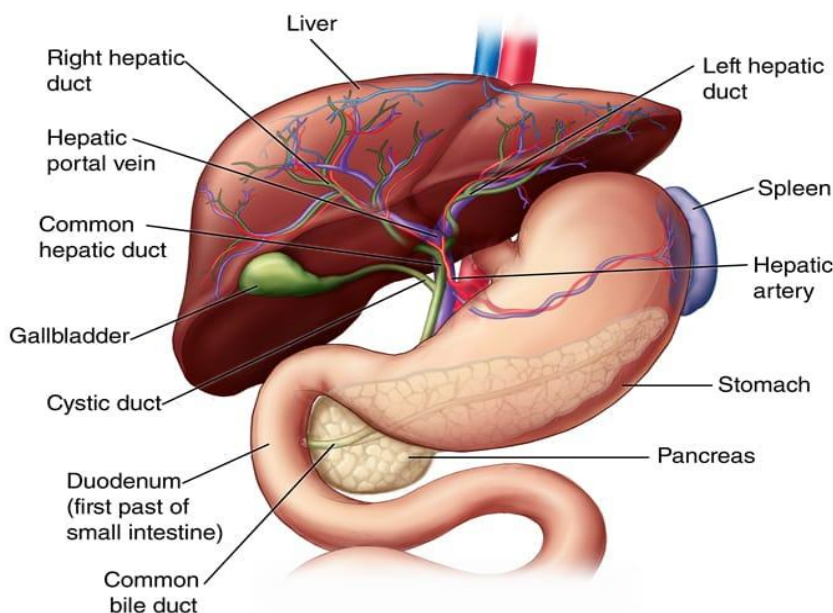


Fig.1. Structure of Liver

Causes of Liver Diseases

Liver disorders are among the most prevalent health concerns in developing countries, primarily due to unhealthy dietary habits, excessive alcohol consumption, poor hygiene, uncontrolled use of medications, and tobacco smoking. These factors contribute to the development of various hepatic conditions, which may be non-inflammatory, inflammatory, or degenerative in nature. Hepatic insufficiency has also been associated with an increased risk of developing atherosclerosis and cardiovascular diseases.^{9,10} A wide range of toxic agents can induce hepatotoxicity, including carbon tetrachloride (CCl₄), thioacetamide, excessive or prolonged alcohol intake, viral infections such as hepatitis A, B, and C, and numerous pharmaceutical agents, with drug-induced liver injury being among the most common causes. Furthermore, hepatitis and cirrhosis are often the result of free radical generation triggered by chronic alcohol consumption, which leads to oxidative stress and subsequent damage to hepatic cells.¹¹

Role of Medicinal Plants in Hepatotoxicity

Medicinal plants have been traditionally employed in Ayurveda for the protection of the liver against various toxins and dietary-related stressors. In recent years, herbal medicines have gained considerable attention due to their safety, therapeutic efficacy, and ability to treat a range of ailments. Additionally, these remedies are cost-effective, particularly for long-term use. Numerous medicinal plants indigenous to India have been identified as hepatoprotective agents and are widely utilized for the management of liver disorders. Both individual plant species and polyherbal formulations have demonstrated hepatoprotective activity. Approximately 160 phytoconstituents and other bioactive compounds have been reported to exhibit protective effects on the liver.¹² In India, over 87 plant species are employed in hepatoprotective therapy, with 33 of these incorporated into patented multi-ingredient formulations.¹³ The authors have systematically reviewed the available literature on the hepatoprotective properties of medicinal plants and organized the findings in a structured manner, as presented in Table 1.



Herbal Hepatoprotective Agents

Herbal hepatoprotective agents are generally classified into three major categories, as outlined below:

1. Antihepatotoxic Agents

These agents act by counteracting or neutralizing the harmful effects of hepatotoxins that cause hepatitis or other forms of liver disease. Their primary function is to mitigate liver damage induced by toxic substances.

2. Hepatoprotective Agents

These agents function primarily as preventive measures, protecting the liver from various infections and pathological conditions. They are used prophylactically to maintain hepatic health and prevent the onset of liver disorders.

Hepatotoxic Agents

These agents generally facilitate and promote the natural healing and regeneration processes of the liver.

In India, the use of herbal formulations for disease management has a long-standing tradition, originating from the Ayurvedic system of medicine and extending to other ancient systems such as European and Chinese traditional medicine. Medicinal plants represent an important source of hepatoprotective agents. It is estimated that more than 700 mono- and polyherbal preparations—available in various forms such as decoctions, tinctures, and tablets—are utilized for the treatment of different liver disorders. The 21st century has witnessed a significant paradigm shift toward the scientific evaluation of herbal products for liver diseases.¹⁴ This has been achieved through an integration of traditional medicinal knowledge with modern, evidence-based approaches such as therapeutic screening, pharmacological authentication, and randomized placebo-controlled clinical trials to validate clinical efficacy. Numerous plants and herbal formulations have been reported to possess hepatoprotective activity. Approximately 160 active phytoconstituents derived from 101 plant species have been identified as having liver-protective properties. In India alone, 87 plant species are used in 33 patented multi-ingredient formulations with recognized hepatoprotective potential. Despite significant advancements in medical science, no completely safe and effective hepatoprotective agents are currently available in modern allopathic medicine. Consequently, global attention has increasingly shifted toward the development of plant-based hepatoprotective drugs, which are expected to be effective against a broad spectrum of liver disorders. A drug that exerts beneficial effects on the liver is termed a hepatoprotective agent, whereas substances that exert harmful effects on the liver are known as hepatotoxic agents. Clinical studies have demonstrated the genuine therapeutic potential of herbal medicines in managing liver diseases.¹⁵ Over the past three decades, several hepatotoxins—such as D-galactosamine, carbon tetrachloride, acetaminophen, and thioacetamide—have been extensively used to study liver damage. More recently, Concanavalin A (ConA) and lipopolysaccharide (LPS) have been introduced as experimental models. Although ConA and LPS do not perfectly mimic the clinical presentation of human hepatic disorders, they offer considerable advantages for investigating cellular mechanisms underlying autoimmune liver diseases.¹⁶ Among these, the D-galactosamine model is considered highly specific for hepatotoxicity, as it induces liver injury similar to human viral hepatitis by depleting uridine nucleotides, thereby inhibiting RNA and protein synthesis. In experimental animals, particularly rats, galactosamine intoxication alters plasma membrane permeability, leading to enzyme leakage and elevated serum transaminase levels, which serve as reliable biochemical markers of liver damage. Galactosamine exhibits a high degree of liver specificity compared to other hepatotoxins such as paracetamol, acetaminophen, and carbon tetrachloride, owing to the abundance of galactokinase and galactose-1-uridyltransferase enzymes in hepatocytes. Consequently, galactosamine-induced toxicity primarily affects the liver while sparing other organs. Histopathological findings include hepatocellular necrosis, portal and parenchymal inflammation, and spotty hepatocyte degeneration. Furthermore, galactosamine promotes the depletion of uridine diphosphate (UDP) through enhanced synthesis of UDP-sugar derivatives, thereby inhibiting RNA and protein synthesis, which leads to cell membrane deterioration. The present review aims to compile and analyze data from previous studies on promising phytochemicals derived from medicinal plants that have been evaluated using various hepatotoxicity models. This compilation seeks to highlight the investigative work carried out on herbal remedies beneficial in the management of hepatic disorders. The limitations of synthetic drugs in treating liver diseases, combined with the growing demand for potent immunomodulatory agents, have redirected scientific focus toward herbal medicine as a natural alternative for the prevention and treatment of severe hepatic disorders. At present, only



one naturally derived protective drug is available; however, it is not curative and offers limited protection against viral-induced hepatic injury.

What is liver disease?

Your liver is a large and powerful organ that performs hundreds of essential functions in your body. One of its most important functions is filtering toxins from your blood. While your liver is well-equipped for this job, its role as a filter makes it vulnerable to the toxins it processes. Too many toxins can overwhelm your liver's resources and ability to function. This can happen temporarily or over a long period of time.

What are the stages of chronic liver disease?

Chronic liver disease progresses in roughly four stages:

Hepatitis.

Fibrosis.

Cirrhosis.

Liver failure.

Stage 1: Hepatitis

Hepatitis means inflammation in your liver tissues. Inflammation is your liver's response to injury or toxicity. It's an attempt to purge infections and start the healing process. ¹⁷Acute hepatitis (an immediate and temporary response) often accomplishes this. But when the injury or toxicity continues, so does the inflammation. Chronic hepatitis causes hyperactive healing that eventually results in scarring (fibrosis).

Stage 2: Fibrosis

Fibrosis is a gradual stiffening of your liver as thin bands of scar tissue gradually add up. Scar tissue reduces blood flow through your liver, which reduces its access to oxygen and nutrients. This is how your liver's vitality begins to gradually decline. Remarkably, some amount of fibrosis is reversible. Your liver cells can regenerate, and scarring can diminish if the damage slows down enough for it to recover.

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Stage 3: Cirrhosis

Cirrhosis is severe, permanent scarring in your liver. This is the stage where fibrosis is no longer reversible. When your liver no longer has enough healthy cells left to work with, its tissues can no longer regenerate. But you can still slow or stop the damage at this stage. Cirrhosis will begin to affect your liver function, but your body will attempt to compensate for the loss, so you might not notice at first.

Stage 4: Liver failure

Liver failure begins when your liver can no longer function adequately for your body's needs. This is also called "decompensated cirrhosis" — your body can no longer compensate for the losses. As liver functions begin to break down, you'll begin to feel the effects throughout your body. Chronic liver failure is a gradual process, but it is eventually fatal without a liver transplant. You need a liver to live.

What are the first signs and symptoms of liver disease?

Chronic liver disease often won't cause symptoms in the early stages. But sometimes it begins with an episode of acute hepatitis. For example, if you get a viral hepatitis infection, there's an acute phase before the chronic phase sets in. You might have a fever, stomachache or nausea for a brief period while your immune system works to defeat the infection. If it doesn't defeat it, it becomes a chronic infection. Some other causes of liver disease might also begin with more acute symptoms or have occasional episodes of acute symptoms. Early symptoms of liver disease tend to be vague. They might include:

Upper abdominal pain.

Nausea or loss of appetite.

Fatigue and malaise (feeling generally tired and ill).



What are the causes of liver disease?

There are over 100 types of liver disease, but they fall into a handful of subtypes. Causes include:

Viral infections. Viral hepatitis infections that become chronic can cause chronic hepatitis, including hepatitis B and hepatitis C. Alcohol-induced hepatitis.¹⁸ Heavy alcohol use can cause acute or chronic hepatitis. If it goes on long enough, it can cause cirrhosis and liver failure. Toxic hepatitis. Chronic overexposure to toxins, such as industrial chemicals or drugs, can cause acute or chronic hepatitis. Non-alcohol related fatty liver disease. Metabolic conditions associated with obesity, high blood sugar and high blood lipids can cause excess fat storage in your liver, which can cause inflammation (non-alcohol related steatohepatitis).

Biliary stasis. Congenital (present at birth) conditions that obstruct or stall the flow of bile through your bile ducts can cause bile to build up and injure your liver, including biliary atresia and cystic fibrosis. Non-congenital causes include biliary stricture and gallstones. Autoimmune diseases. Autoimmune conditions can cause chronic inflammation and scarring in your liver or your bile ducts, including autoimmune hepatitis, primary biliary cholangitis and primary sclerosing cholangitis.

Inherited metabolic disorders. Disorders that cause toxic products to build up in your blood — such as glycogen storage disease (GSD), Wilson disease, hemochromatosis and Gaucher disease — can cause chronic liver damage.

Cardiovascular diseases. Conditions that affect blood flow to and from your liver — including Budd-Chiari syndrome, ischemia, arterial diseases and right-sided heart failure — can cause chronic liver damage.

What are the risk factors for acquiring liver disease?

You may be more likely to get liver disease if you:

Drink alcohol heavily.

Use intravenous drugs.

Use pain relievers like aspirin or acetaminophen

Have metabolic syndrome.

Are regularly exposed to toxic chemicals.

Are regularly exposed to other people's blood or body fluids.

Diagnosis and Tests

How do you test for liver disease?

A healthcare provider checking for liver disease will begin by physically examining you. They'll look for visible signs and ask about your symptoms. They may also ask about your diet, lifestyle and health history. Finally, they'll use lab tests and imaging scans to check for liver disease. These may include: Blood tests. A panel of liver function tests can show signs of liver disease, liver disease severity and liver failure. These measure liver products like liver enzymes, proteins and bilirubin levels in your blood. Blood tests may also indicate inflammation, specific diseases or side effects, like reduced blood clotting. Imaging tests. An abdominal ultrasound, CT scan (computed tomography scan) or MRI (magnetic resonance imaging) can show the size, shape and texture of your liver. This can reveal inflammation and swelling, growths and fibrosis.

Elastography. A special type of imaging test called elastography uses ultrasound or MRI technology to measure the level of stiffness or fibrosis in your liver. Endoscopy. If your provider needs to see inside your biliary tract, they might need to use a type of endoscopic imaging. Endoscopy involves passing a tiny camera (endoscope) through your upper GI tract. From the endoscope, they can use EUS or ERCP to see your bile ducts. Nuclear medicine imaging.¹⁹ A nuclear liver and spleen scan uses a gamma camera to detect a (harmless) radioactive tracer material that's injected into your body. How your liver absorbs the tracer will highlight the areas that aren't functioning normally. Liver biopsy. A liver biopsy is a minor procedure to take a small tissue sample from your liver to test in a lab. A healthcare provider can usually take the sample through a hollow needle. You might need a liver biopsy to check for cancer or confirm cirrhosis and help determine the cause.



Management and Treatment

How do you treat liver disease?

Some types of liver diseases have specific medical treatments. For example, antivirals treat viral hepatitis, while corticosteroids and immunosuppressants treat autoimmune diseases. But in many cases, lifestyle changes are the primary treatment for liver disease.²⁰ Reducing the toxic load on your liver is important with any type of liver disease, but essential for those caused by excess fat storage, alcohol or other toxins. However, early recognition is key to treating liver disease effectively before permanent damage is done. Unfortunately, not everyone discovers liver disease in time to reverse its course. If you already have cirrhosis or liver failure, you might need additional treatments for complications like portal hypertension or liver cancer. Your liver might not be able to recover, and you might eventually need a liver transplant.

Prevention

How can I lower my risk of liver disease?

You can help prevent liver disease by:

Getting vaccinated. Vaccines are available to prevent viral hepatitis A and B. Practicing good hygiene. Handwashing after using the bathroom, safe food handling and safe needle use can help prevent infections from spreading. Drinking alcohol in moderation and using medications as directed. If you have a substance use disorder (SUD), treatment can help prevent toxic hepatitis. Managing metabolic factors such as your blood lipids and blood sugar. A healthcare provider can help with this.²¹

Plant Name	Plant Part	Extract	Active constituents	Mchanism
Allium sativum (Alliaceae)	Bulb	-	Organosulfur compounds	Prevention of GSH depletion, alteration of GSH dependent Enzymes 22
Azadirachta indica (Meliaceae)	Leaf	70% ethanol	Flavonoids	(Glutathione peroxidase (GPx), glutathione-S transferase (GST), superoxide dismutase (SOD) and catalase (CAT) 23
Arachniodes exilis (Dryopteridaceae)	Rhizomes	Ethanol	Polyphenols	Lipid peroxide, DPPH, ABTS, superoxide anion, hydroxyl radical and hydrogen peroxide, glutamate oxaloacetate transaminase, glutamate pyruvate transaminase, malondialdehyde and superoxide dismutase 24
Asparagus racemosus (Liliaceae)	Whole plant	purified aqueous fraction	Polysaccharides	Lipid peroxidation, protein oxidation 25
Baliospermum montanum (Euphorbiaceae)	Roots	Alcohol, chloroform	-	SGPT, SGOT and alkaline phosphate, Histopathological changes in liver. 26
Buddleja officinalis (Loganiaceae)	flowers and buds	-	Phenyl ethanoid Glycoside (Acteoside)	Decreased levels of AST, ALP 27
Boerhaavia diffusa (Nyctaginaceae)	Roots	Aqueous	-	GOT, GPT, ACP and ALP, but not GLDH and bilirubin 28
Cassia tora (Caesalpinaceae)	Leaves	Ethyl acetate	-	Glutathione enzyme activities. 29
Camellia sinensis	Leaves	-	Polyphenols (Catechin)	Inhibited hepatocellular



(Theaceae)				apoptosis and unregulated Bcl-2 protein expression 30
Cistus laurifolius L. (Cistaceae)	Leaves	Ethanol	Flavonoid (Quercetin)	MDA, AST, GSH levels decreased 31
Corydalis saxicola (Papaveraceae)	Whole plant	Ethanol	Alkaloid Dehydrocavidine	Decreased levels MDA, SOD, GPx 32
Cordia macleodii (Boraginaceae)	Leaves	Ethanol	Flavonoids and triterpenoids	Increased Glutamate pyruvate transaminase (GPT), serum glutamate oxaloacetate transaminase (GOT), Alkaline Phosphatase (ALP) and total bilirubin 33
Cassia fistula (Leguminosae)	Leaf	Methanol	Anthraquinone and steroids	Lowering the serum levels of transaminases (SGOT and SGPT), bilirubin and alkaline phosphatase (ALP). 34
Cochlospermum Planchoni (Coclospermaceae)	Rhizomes	Aqueous	tannins, carotenoids, flavonoids and triterpenes	Total bilirubin Alkaline phosphatase Alanine aminotransferase 35
Egletes viscosa Less. (Asteraceae)	Whole plant	Hexane and Ethanol	Flavonoid (Ternatin)	Decreased lipid peroxidation 36
Gardenia jasminoides (Rubiaceae)	Fruit	-	Iridoid Glycoside Geniposide	Antioxidant 37
Ginkgo biloba L. (Ginkgoaceae)	Leaves	Petroleum ether	Polyphenols	ALT, AST, ALP, ALB, TP, HA, LN, TG, and CHO levels decreased 38
Gossypium herbaceum (Malvaceae)	Root, leaves, stem	-	Polyphenols Gossypol	Antioxidant 39
Hibiscus sabdariffa L. (Malvaceae)	flowers	Ethanol, chloroform	Polyphenols Protocatechuic acid	LDH, AST, ALP, MDA levels decreased 40
Kalanchoe pinnata Pers. (Crassulaceae)	Leaves	Juice of the fresh leaves and ethanolic extract	-	Decreased Serum glutamyl oxalacetic acid transaminase (SGOT), serum glutamyl pyruvate transaminase (SGPT) alkaline phosphatase (ALKP), serum bilirubin (SBLN) 41
Larrea tridentata (Zygophyllaceae)	Leaves	-	Resin Nordihydroguaiaretic acid	Antioxidant 42
Magnolia officinalis (Magnoliaceae)	Bark, root, stem	-	Polyphenols Magnolol	Antioxidant 43
Momordica dioica (Cucurbitaceae)	Leaves	Ethanol and aqueous	-	Decreased serum glutamate oxaloacetate transaminase (AST), serum glutamate pyruvate transaminase (ALT), serum alkaline phosphatase



				(SALP) and total 44
Mangifera indica (Anacardiaceae)	-	-	Triterpene (Lupeol)	Decreased levels of SGOT, SGPT, ALP, bilirubin 45
Nigella sativa (Ranunculaceae)	-	-	Quinones Thymoquinone (TQ)	Scavenger of superoxide, hydroxyl radical, and singlet molecular oxygen 46
Ocimum basilicum (Lamiaceae or Labiatae)	-	-	Phenolic Acids (Rosmarinic acid)	AST, ALP, SGOT levels decreased 47
Orthosiphon stamineus (Lamiaceae)	Leaves	Methanol	-	AST, ALT and ALP 48
Peumus boldus (Monimiaceae)	-	-	Alkaloid BoldineLipid	peroxidation 49
Pinus maritima (Pinaceae)	Roots	50% aqueous ethanolic	Glycoside (Rubiadin)	SGOT, SGPT, SALP, and gamma-GT levels decreased 50
Schisandra chinensis (Schisandraceae)	Bee pollen	-	Lignans (Wuweizisu)	Antioxidant 51
Sida cordifolia (Malvaceae)	Leaves	Aqueous	Organic compound (Fumaric acid)	Antioxidant 52
Silybum marianum (Asteraceae)	-	-	Lignans (Silymarin)	Antioxidant 53
Tridax procumbens (Asteraceae)	Leaves	Ethanolic	-	Decreased Glutathione, superoxide dismutase and catalase 54
Vitis vinifera (Vitaceae)	Leaves	Chcl3, etoac, n buoh, and water	Phenolic compounds	Decreased (plasma and liver tissue MDA [malondialdehyde], transaminase enzyme levels in plasma [AST-aspartate transaminase, ALT-alanine transferase] and liver GSH [glutathione] levels) 55
Zanthoxylum armatum (Rutaceae)	Bark	Ethanolic	Isoquinoline alkaloid, berberine, as well as flavonoids and phenolic compounds,	Decreased serum transaminases, alkaline phosphatase and total bilirubin and antioxidant enzymes superoxide dismutase, catalase and glutathione 56

Table 1. List of Plant has Hepatoprotective Activity

II. CONCLUSION

Since ancient times, herbal and traditional botanical medicines have been employed to treat a wide range of ailments and diseases. Active extracts, fractions, or combinations thereof have the potential to serve as highly effective therapeutic agents. In the context of liver disorders, plant-based medications whether as single agents or in combination should possess sufficient efficacy to address severe hepatic conditions caused by toxic chemicals, viral infections (such as Hepatitis B and C), excessive alcohol consumption, and other etiological factors. Given the complexity of severe



liver diseases, no single therapeutic agent is capable of providing a comprehensive cure. Therefore, effective formulations should be developed using indigenous medicinal plants, supported by rigorous pharmacological evaluations and clinical studies.

The manufacture of plant-based products must adhere to stringent standards of safety and efficacy to ensure reliable therapeutic outcomes. Herbal and traditional botanical products have been employed since ancient times for the management and treatment of a variety of disorders and diseases. The present review highlights medicinal plants that have been previously investigated for their hepatoprotective and immunomodulatory properties. Numerous medicinal plants demonstrate not only hepatoprotective and immunomodulatory effects but also exhibit a broad spectrum of additional pharmacological activities, including anticancer, cardiogenic, diuretic, antiarrhythmic, and other therapeutic effects.

The identification and development of novel immunomodulatory and hepatoprotective plants are essential for the discovery of therapeutic agents that are cost-effective, potent, and associated with fewer adverse effects, thereby enabling more effective interventions for liver protection and immune modulation. Unlike conventional allopathic medicines, herbal therapies are generally considered to be non-toxic and free from significant side effects. Research on hepatoprotective and immunomodulatory medicinal plants is expected to benefit populations requiring herbal treatment, providing effective management of these conditions without reliance on synthetic drugs and reducing the potential adverse effects associated with conventional pharmacotherapy.

REFERENCES

- [1]. Ahmedullah M and Nayar MP: Red data book of Indian plants, (Peninsular India), Calcutta: Botanical Survey India. 1999.
- [2]. Bijauliya RK, Alok S, Chanchal DK, Sabharwal M and Yadav RD: An updated review of pharmacological studies on *Azadirachta indica* (neem). *Int J Pharm Sci & Res* 2018; 9(7): 2645-55. doi: 10.13040/IJPSR.0975-8232.9(7).2645-55
- [3]. Gupta R and Chadha KL: Medicinal and aromatic plants in India. In: Gupta R, Chadha KL, editors. *Advances in horticulture: medicinal and aromatic plants*. New Delhi: Malhotra Publishing House; 1995
- [4]. Pareek SK: Medicinal plants in India: Present status and future prospects. In: *Prospects of medicinal plants*. New Delhi: Indian Society for Plant Genetic Resources NBPGR Campus; 1996, p. 14.
- [5]. Dahanukar A, Kulkarni RA, Rege NN: Pharmacology of medicinal and natural products. *Indian J Pharmacol* 2000; 32: 81-118.
- [6]. Bijauliya RK, Alok S, Jain SK Singh VK, Singh D and Singh M: Herbal and allopathic medicine for kidney, gallbladder and urinary stones: a review. *Int J Pharm Sci Res* 2017; 8(5): 1935-52. doi: 10.13040/IJPSR.0975-8232.8(5).1935-52
- [7]. Ilyas U, Katore DP, Aeri V, Naseef PP: A review on hepatoprotective and immunomodulatory herbal plants. *Phcog Rev* 2016; 10: 66-70.
- [8]. Kumar CH, Ramesh A, Suresh Kumar JN, And Ishaq BM: A review on hepatoprotective activity of medicinal plants. *International Journal of Pharmaceutical Sciences and Research*. 2011; 2(3): 501-515.
- [9]. Dominiczak MH: Lipids, lipoproteins In: Baynes JW, Dominiczak MH (eds.) *Medical biochemistry*, Elsevier Mosby. Philadelphia 2005; 234-242
- [10]. Ekaideem IS, Akpan HD, Usuh IF, Etim OE, Ebong PE: Effects of Ethanolic Extract of *Azadirachta indica* Leaves on Lipid Peroxidation and Serum Lipids of Diabetic Wistar Rats. *Acta Biologica Szegedensis* 2007; 51: 17-20.
- [11]. Anand K and Lal UR: Hepatitis and medicinal plants: An Review 2016; 5: 408-415.
- [12]. Jannu V, Baddam PG, Boorgula AK, Jambula SR: A review on hepatoprotective plants. *Inter J Drug Development Res* 2012; 4 : 1-8.
- [13]. Handa SS, Sharma A, Chakarborty KK: Natural Products and plants as liver protecting drugs. *Fitoterapia* 1986; 57: 307-51.



- [15]. Mueller MM, Fusenig NE. Friends or foes bipolar effects of the tumour stroma in cancer. *Nat Rev Cancer* 2004;4:839-49
- [16]. Hussain SP, Harris CC. Inflammation and cancer: An ancient link with novel potentials. *Int J Cancer* 2007;121:2373-80
- [17]. Schottenfeld D, Beebe-Dimmer J. Chronic inflammation: A common and important factor in the pathogenesis of neoplasia. *CA Cancer J Clin* 2006;56:69-83
- [18]. Friedman, S. L., Neuschwander-Tetri, B. A., Rinella, M., & Sanyal, A. J. (2018). Mechanisms of NAFLD development and therapeutic strategies. *Nature Medicine*, 24(7), 908–922. <https://doi.org/10.1038/s41591-018-0104-9>
- [19]. Asrani, S. K., Devarbhavi, H., Eaton, J., & Kamath, P. S. (2019). Burden of liver diseases in the world. *Journal of Hepatology*, 70(1), 151–171. <https://doi.org/10.1016/j.jhep.2018.09.014>
- [20]. European Association for the Study of the Liver (EASL). (2018). EASL Clinical Practice Guidelines: Management of chronic liver diseases. *Journal of Hepatology*, 69(1), 182–236. <https://doi.org/10.1016/j.jhep.2018.03.018>
- [21]. World Health Organization (WHO). (2023). Liver diseases: Key facts. Retrieved from <https://www.who.int>
- [22]. Mayo Clinic Staff. (2024). Liver disease – Symptoms and causes. Mayo Clinic. Retrieved from <https://www.mayoclinic.org>.
- [23]. Sabayan B, Foroughinia F, Chohedry A: A postulated role of garlic organosulfur compounds in prevention of valproic acid hepatotoxicity. *Med Hypotheses* 2007; 68: 512-4.
- [24]. Chattopadhyay RR and Bandyopadhyay M: Possible Mechanism of Hepatoprotective Activity of *Azadirachta indica* Leaf Extract Against Paracetamol-Induced Hepatic Damage In Rats: Part III, *Indian J Pharmacol*, June 2005; 37: 184-185.
- [25]. Zhoua BD, Ruana J, Caia Y, Xionga Z, Weifua, Weia A: anti- antioxidant And Hepatoprotective Activity of Ethanol Extract of *Arachniodes exilis* (Hance) Ching, *Journal of Ethanopharmacology* 2010; 129: 232–237.
- [26]. Jayashree P, Kamat A, Krutin K, Bolor A, Thomas PA, Devasagayam A, Venkatachalam B: antioxidant Properties of *Asparagus racemosus* against Damage Induced By G Radiation in Rat Liver Mitochondria, *Journal of Ethnopharmacology* 2000; 71: 425–435.
- [27]. Wadekar RR, Supale RS, Tewari KM, Patil KS, Jalalpure SS: Screening of Roots of *Baliospermum montanum* for Hepatoprotective Activity Against Paracetamol Induced Liver Damage In Albino Rats, *International Journal Of Green Pharmacy*, 2010; 220-223.
- [28]. Lee KJ, Woo ER, Choi CY, Shin DW, Lee DG, You HJ. Protective effect of acteoside on carbon tetrachloride-induced hepatotoxicity. *Life Sci* 2004; 74: 1051-64.
- [29]. Rawat KS, Mehrotra AS, Tripathi SC and Shome BU: Hepatoprotective Activity of *Boerhaavia diffusa* L. Roots - A Popular Indian Ethnomedicine, *Ethnopharmacology* 1997; 56: 61- 66. *Journal Of*
- [30]. Dhanasekarana M, Ignacimuthua S, Paulagastianb, Potential Hepatoprotective Activity of Ononitol Monohydrate Isolated from *Cassia tora* L. On Carbon tetrachloride Induced Hepatotoxicity In Wistar Rats, *Phytomedicine* 2009; 16: 891–895.
- [31]. Xu C, Shu WQ, Qiu ZQ, Chen JA, Zhao Q, Cao J: Protective effects of green tea polyphenols against subacute hepatotoxicity induced by microcystin-LR in mice. *Environ Toxicol Pharmacol* 2007; 24 :140-8.
- [32]. Kupeli E, Orhan DD, Yesilada E. Effect of *Cistus laurifolius* L. leaf extracts and flavonoids on acetaminophen-induced hepatotoxicity in mice. *J Ethnopharmacol* 2006; 103: 455 60.
- [33]. Wang T, Sun NL, Zhang WD, Li HL, Lu GC, Yuan BJ: Protective effects of dehydrocavidine on carbon tetrachloride-induced acute hepatotoxicity in rats. *J Ethnopharmacol* 2008; 117: 300-8.
- [34]. Naseem N, Qureshi A, Bhanudansh S, Kuchekar B, Nadeem A, Logade A, Majid A, Haleem A, Antioxidant And Hepatoprotective Activity of *Cordia macleodii* Leaves, *Saudi Pharmaceutical Journal*, 2009; 17: 299–302.
- [35]. Bhakta T. A et al., Evaluation of Hepatoprotective Activity of *Cassia Fistula* Leaf Extract, *Journal of Ethnopharmacology* 1999; 66: 277–282.



- [36]. Roseline Aliyu A, Okoye ZSC, Thomas Shier B: The Hepatoprotective Cytochrome P-450 Enzyme Inhibitor Isolated From The Nigerian Medicinal plant *Cochlospermum planchonii* Is A Zinc Salt, *Journal Of Ethnopharmacology* 1995; 48: 89-97.
- [37]. Souza MF, Rao VS, Silveira ER: Prevention of acetaminophen-induced hepatotoxicity by ternatin, a bioflavonoid from *Egletes viscosa* less. *Phytother Res* 1998; 12: 557-61.
- [38]. Tseng TH, Chu CY, Huang JM, Shiow SJ, Wang CJ: Crocetin protects against oxidative damage in rat primary hepatocytes. *Cancer Lett* 1995;97:61-7.
- [39]. Yang L, Wang CZ, Ye JZ, Li HT. Hepatoprotective effects of polyphenols from *Ginkgo biloba* L. leaves on CCl₄-induced hepatotoxicity in rats. *Fitoterapia* 2011; 82: 834-40.
- [40]. Randel RD, Chase CC Jr, Wyse SJ: Effects of gossypol and cottonseed products on reproduction of mammals. *J Anim Sci* 1992; 70: 1628-38.
- [41]. Tseng TH, Hsu JD, Lo MH, Chu CY, Chou FP, Huang CL. Inhibitory effect of *Hibiscus protocatechuic* acid on tumor promotion in mouse skin. *Cancer Lett* 1998; 126: 199-207.
- [42]. Yadav NP and Dixit VK: Hepatoprotective Activity of Leaves of *Kalanchoe pinnata* Pers, *Journal of Ethnopharmacology* 2003; 86: 197–202.
- [43]. Arteaga S, Andrade-Cetto A, Cardenas R. *Larrea tridentata* (Creosote bush), an abundant plant of Mexican and US American deserts and its metabolite nordihydroguaiaretic acid. *J Ethnopharmacol* 2005; 98: 231-9.
- [44]. Lin YR, Chen HH, Ko CH, Chan MH: Neuroprotective activity of honokiol and magnolol in cerebellar granule cell damage. *Eur J Pharmacol* 2006; 537: 64-9.
- [45]. Jain A, Soni M, Deb L, Jain A, Roul AP, Gupta VB, Krishna KL: Antioxidant and Hepatoprotective Activity of Ethanolic and Aqueous Extracts of *Momordica dioica* Roxb. Leaves, *Journal of Ethnopharmacology* 2008; 115: 61–66.
- [46]. Kumari A and Kakkar P: Lupeol prevents acetaminophen induced in vivo hepatotoxicity by altering the Bax/Bcl-2 and oxidative stress-mediated mitochondrial signalling cascade. *Life Sci* 2012; 90: 561-70.
- [47]. Abdel-Wahab WM: Protective effect of thymoquinone on sodium fluoride-induced hepatotoxicity and oxidative stress in rats. *J Basic Appl Zoo* 2013; 66: 263-70. 39. Liu Y, Flynn TJ, Ferguson MS, Hoagland EM: Use of the Combination Index to determine interactions between plant-derived phenolic acids on hepatotoxicity endpoints in human and rat hepatoma cells. *Phytomedicine* 2013; 20: 461-8.
- [48]. Chin JH, Hussin AH And Ismai :, Anti-Hepatotoxicity Effect of *Orthosiphon Stamineus* Benth Against Acetaminophen Induced Liver Injury In Rats By Enhancing Hepatic GST Activity, *Pharmacognosy Research*, March-April 2009; 1: 53 58.
- [49]. Lanhers MC, Joyeux M, Soulimani R, Fleurentin J, Sayag M, Mortier F: Hepatoprotective and anti-inflammatory effects of a traditional medicinal plant of Chile, *Peumus boldus*. *Planta Med* 1991 ;57: 110-5.
- [50]. Yang YS, Ahn TH, Lee JC, Moon CJ, Kim SH, Jun W: Protective effects of pycnogenol on carbon tetrachloride-induced hepatotoxicity in Sprague-Dawley rats. *Food Chem Toxicol* 2008; 46: 380-7.
- [51]. Rao GM, Rao CV, Pushpangadan P, Shirwaikar A: Hepatoprotective effects of rubiadin, a major constituent of *Rubia cordifolia* Linn. *J Ethnopharmacol* 2006; 103: 484-90.
- [52]. Cheng N, Ren N, Gao H, Lei X, Zheng J, Cao W: Antioxidant and hepatoprotective effects of *Schisandra chinensis* pollen extract on CCl₄-induced acute liver damage in mice. *Food Chem Toxicol* 2013; 55: 234-40.
- [53]. Silva RL, Melo GB, Melo VA, Antonioli AR, Michellone PR, Zucoloto S: Effect of the aqueous extract of *Sida cordifolia* on liver regeneration after partial hepatectomy. *Acta Cir Bras* 2006; 21(Suppl 1): 37-9.
- [54]. Upadhyay G, Kumar A, Singh MP: Effect of silymarin on pyrogallol- and rifampicin-induced hepatotoxicity in mouse. *Eur J Pharmacol* 2007; 565: 190-201.
- [55]. Reddipalli H: Anti-Hepatotoxic and Anti-Oxidant Defense Potential of *Tridax Procumbens*, *International Journal of Green Pharmacy*, 2010; 164-169
- [56]. Didem DO, Nil Ufer O, Ender E, Fatma E: Hepatoprotective Effect of *Vitis vinifera* L. Leaves on Carbontetrachloride Induced Acute Liver Damage In Rats, *Journal of Ethnopharmacology* 2007; 112: 145–151.



- [57]. Singh L, Ranawat, Bhatt J, Paetl J, Hepatoprotective activity of Ethanolic Extracts of Bark of Zanthoxylum armatum DC In CCl₄ Induced Hepatic Damage in Rats, Journal of Ethnopharmacology 2010; 127: 777–780.

