

Hepatotoxicity: A Study on Role of Some Herbal Hepatoprotective Plants and Natural Product with Hepatoprotective Effects

Md. Aftab Alam*

Associate Professor, Department of Pharmacy, Galgotias University, Greater Noida, Uttar Pradesh, India

Abstract – Hepatic disorders are one of the most serious challenges to public health as a result of these functions, and they appear to be a concern all over the planet. Despite tremendous advancements in modern medicine, there are no fully successful medications that stimulate hepatic activity, provide total organ defense, or aid in hepatic cell regeneration. As a result, it is essential to identify pharmaceutical alternatives, with the aim of making these alternatives more beneficial and less harmful. The usage of some plants and the use of various fruits have played important roles in human health care, and several experimental investigations have shown that the beneficial results of certain plants and fruits can be due to the existence of chemical compounds known as phytochemicals in certain plants and fruits.

Keywords – Hepatotoxicity, Natural Product, Herbal Hepatoprotective Plants, Hepatoprotective Effects

----- X -----

INTRODUCTION

In ethnobotanical literature, the common use of medicinal plants is implied. For health management, people in developing Asian and African countries depend primarily on natural herbs and plants. Modern clinical management schemes, on the other hand, use 25% plant-derived drugs, such as aspirin from *Salix alba* and quinine from *Cinchona* tree bark (1).

Because of its multibiological roles in protein, lipid, and carbohydrate metabolism, the liver significant body organs. Acute and persistent liver disorders are a worldwide problem, and prescription therapies for them are sometimes impossible to obtain and can be ineffective. As a result, complementary and natural therapies for the management of hepatic diseases have sparked a lot of concern. When these medications are used in clinical trials, developing therapeutically effective agents from natural products can reduce the risk of toxicity (2).

The assumption that herbal remedies are safe & have no serious side effects has led to a rise in the usage of herbal medicines to cure liver diseases around the world. Furthermore, they are willingly obtainable in nature and simple to remove. Furthermore, the usage of alternative medication, such as herbal formulations, has grown as a consequence of conventional medicine's limited care choices and sometimes unsatisfactory therapeutic outcomes (3).

A vast range of remedial plants and their preparations have been claimed to have hepatoprotective effectiveness all over the world. The flavonolignan silymarin, obtained from the herb "milk thistle" (*Silybum marianum*), is almost exclusively used to protect the liver.

Medicinal plants are used by a predictable 80% of the world's people, with physicians recommending 30% of them (4, 5).

The prevention of CCl₄-induced liver damage is commonly used as a marker of medication hepatoprotective function in general.

CURRENT TRENDS IN HERBAL MEDICINES

And if only a small percentage of medicinal plants may have been identified as sources of useful medicinal compounds. On a war footing basis, continuous and unbroken chains of studies are underway to assess their pharmacological ability. Through the ages, several medical systems have originated from Asia, including Unani, Siddha, and Ayurveda (6).

In the past, the Western medicinal culture underwent a series of transformations that focused on quick symptomatic therapies at the site of illness. Some of them are still unsuccessful or have negative side effects. The economy has played a role in the unpopularity of certain medications, especially those used to treat chronic diseases. Traditional drugs have grown in prominence in Western nations, resulting in modern terminology such as "alternative medicines," "complementary medicines," and also "integrative medicines." (7).

Liver

It is considered the body's main organ and workspace. About all biochemical processes are triggered by biochemical agents such as hepatic enzymes or arise in the liver. Males and females have different weights. It has two primary lobes, one on the right and one on the left (8).

Liver function tests

The liver is dependable of activities, including the production of a variety of biochemicals that enter the bloodstream. In the blood, these biochemicals are found in optimal concentrations. Their absorption in the blood, though, may be affected by hepatic disorders.

Plants reported for hepatoprotective activity

Table 1: List of plants reported for hepatoprotective properties

Medicinal Plant	Family	Hindi Name	Part Used
<i>Adhatoda zeylanica</i>	Acanthaceae	Adosa	Leaves
<i>Andrographis paniculata</i>	Acanthaceae	Kalmegh	Whole Plant
<i>Argyreia speciosa</i>	Convolvulaceae	Vriddadaru	Roots
<i>Aegle marmelos</i>	Rutaceae	Bael	Leaves
<i>Boerhaavia diffusa</i>	Nyctaginaceae	Punarnava	Roots
<i>Calendula officinalis</i>	Asteraceae	Zergul	Flowers
<i>Calotropis procera</i>	Asclepiadeceae	Aak	Flowers
<i>Coccinia grandis</i>	Curcubitaceae	Tindora	Fruits
<i>Ficus carica</i>	Moraceae	Anjir	Fruits

<i>Ficus carica</i>	Moraceae	Anjir	Fruits
<i>Pergularia daemia</i>	Asclepiadaceae	Sagovani	Aerial parts
<i>Phyllanthus niruri</i>	Euphorbiaceae	Bhumi amla	Whole plant
<i>Psidium guajava</i>	Myrtaceae	Amrood	Leaves
<i>Sapindus mukorossi</i>	Sapindaceae	Ritha	Fruit pericarp
<i>Wedelia chinensis</i>	Asteraceae	Pilabhingraj	Whole plant
<i>Trigonella foenum-graecum</i>	Leguminosae	Methi	Seed

Causes of liver diseases

Due to eating patterns, alcohol use, improper sanitation, unsupervised substance usage, and smoke, liver diseases are the most serious health concern in developing countries. Because of hepatic insufficiency, elevated levels of plasma total cholesterol (LDL-C) and triacylglycerols (TGs) are linked to an increased risk of atherosclerosis and cardiovascular disease. Hepatotoxicity can be activated by pollutants, like carbon tetrachloride (CCl₄), thioacetamide, acute or chronic alcohol intake, viruses such as hepatitis A, B, and C, and medications, with drugs becoming the more frequent perpetrator. As a consequence of caused by alcohol use, hepatitis develops, eventually contributing to cirrhosis (9).

Hepatoprotective plants

- **“Opuntia ficus-indica” nopal (cactus pear) and tuna (cactus pear fruit)**

The genus *Opuntia* is the most widely cultivated of the Cactaceae family, with plants grown throughout the American continent, as well as in the Mediterranean, Europe, Asia, Africa, and Australia. The fruits of this plant [also known as cactus pear fruits (tunas) or prickly pear fruits] are oval berries with a wide number of seeds and a semihard bark with thorns, and they are divided into four categories based on their color. Fruit with a white pulp and green skin is generally chosen for use as food, and domestic demand accounts for approximately 95% of global production (10).

- **Hepatoprotective evidence for *Opuntia ficus -indica*:**

Despite the many medicinal uses assigned to plants in the genus *Opuntia* for several years, prickly pear and cactus pear fruits (tunas) remained neglected by the scientific community until the early 1980s, when they began to attract recognition and various investigations and symposia were launched, culminating in reviews, books, and book pages. However, scientific study into this food's hepatoprotective properties remains lacking. Wiese et al. provided the first empirical proof for the usage of *Opuntia ficus-indica* against hepatotoxic agents. Their findings suggested that the duration of an alcoholic hangover could be triggered by inflammation triggered by impurities in drinks or alcoholic metabolism (11, 12).

- **Chamomile (Chamomile)**

While there is a significant body of evidence that drinking teas made from *Camilla sinensis* (black and green teas) has health benefits, there is no proof-based information about the effectiveness of the rest of herbal teas, or tisanes (12).

Chamomile and its phytochemicals have been shown to support the liver:

Chamomile is one of the most popular teas in the world, eaten as a single herbal portion, or tisane, and has long been used for medicinal purposes, as stated in the general comments. A large number of researchers have looked at it in order to thoroughly demonstrate its therapeutic value. In terms of its gastroprotective ability, research on the antispasmodic impact of various chamomile formulations in isolated guinea-pig ileum started in the 1980s. Atropine (7.0 g/L) changed the dosage reaction curves in a comparable way to chamomile, but it was unable to reduce the peak contraction in response to either acetylcholine or histamine, unlike chamomile. Both apigenin and -bisabolol inhibited the development of gastric ulcers in rats when they were given indomethacin, stress, or alcohol (13).

Medicinal plants Role in hepatotoxicity

Many medicinal plants found in various parts of India have been identified as hepatoprotective drugs and are extensively used to treat liver diseases. Hepatoprotective function can be seen in a variety of plants and polyherbal formulations. We examined some common herbal plants with hepatoprotective potential to highlight the value of their usage.

Allium cepa

The garden onion, *Allium cepa*, belongs to the Liliaceae genus. It is widely grown in China, India, and the United States. It has a high glucose, potassium, sodium, and phosphorus content. It's been use for centuries to cure stomach diseases, earaches, eye infections, headaches, drowsiness, urinary tract infections, burning ulcers, and cough. It has antiviral, antifungal, antibacterial, and antiparasitic properties, as well as hypoglycemic, antithrombotic, antihyperlipidemic, antiinflammatory, and antioxidant properties. Ige et al. discovered that *A. cepa* could shield rats from cadmium-induced hepatotoxicity. Lee et al. have discovered that *A. cepa* extract would shield mice from acetaminophen-induced liver damage (14).

Boerhavia diffusa

Because of their purity and potency, *Boerhavia diffusa* roots (Punarnava) are used to treat a variety of hepatic disorders. Punarnava is a Sanskrit term that means "body renewer." Purarnava has long been regard as a significant medicinal herb in India. In India, South America, and Africa, *B. diffusa* (family Nyctaginaceae) is an essential medicinal plant for treating liver diseases (15).

Azadiracta indica

The *Azadiracta indica* flower, also known as Nimba or Neem, is a popularly grown tree. It is a Meliaceae family member and is widely known as neem. A plant native to India and Burma, *A. indica* is a tropical and semi-tropical plant. Leprosy, intestinal worms, skin diseases, constipation, epistaxis, biliary affliction, anorexia, blood morbidity, and biliousness have also been linked to *A. indica*. Bitter active concepts can be found in various sections of the plant (16).

Trigonella-foecum-graecum

Trigonella (methi in Hindi, fenugreek in English) is a member of the Fabaceae genus. It is a popular annual herb in India, Pakistan, Egypt, and other Middle Eastern countries. *Trigonella* has grown in popularity as a result of its potent fragrance and therapeutic properties for treating a wide range of illnesses. *Trigonella* leaf is high in calcium, iron, beta-carotene, and other phytochemicals. Culinary uses include the leaves and plants. *Trigonella* leaf extracts have

cytoprotective, antioxidant, and hepatoprotective effects, according to Singh et al., and may be used as dietary supplements or in liver disease formulations. Tripathi and Chandra found that *Trigonella*'s antioxidative ability prevents liver tissue from deltamethrin (DM)-induced toxicity. Increased amounts of LPO and GSH, as well as lower antioxidant activities such as SOD, GST, and catalase, indicate that DM causes oxidative stress throughout the rat liver. The *Trigonella* exposure culminated in a substantial recovery in these parameters' altered stages. It can also help with hepatotoxicity caused by pesticides. *Trigonella* has anti-ulcer, wound-healing, CNS stimulant, immunomodulatory, antioxidant, antidiabetic, antineoplastic, anti-inflammatory, and antipyretic properties. *Trigonella* methanol extract has a strong hepatoprotective function against CCl₄-induced hepatotoxicity (17).

CONCLUSION

Drug and chemical-induced hepatotoxicity is the most prevalent form of iatrogenic disorder. Chronic liver disease is marked by fibrosis, cirrhosis, or neoplasia of varying degrees. According to a WHO survey, Approximately 80% of the world's population in developed countries uses herbal medicines for their essential healthcare needs. Even from medicines, modern medicine provides a very small variety of medications and treatments for liver safety. Thus, the usage of herbal medicines, which are simple to obtain and much easier to prepare formulations of any kind of hepatotoxicity, is gaining prominence across the world. These treatments are luckily both efficacious and cost-effective, attracting researchers in the quest for new drugs, more powerful plant active concepts, and more palatable formulations.

REFERENCES:

1. Yue J, Peng R, Chen J, Liu Y, Dong G. (2009). Effects of rifampin on CYP2E1-dependent hepatotoxicity of isoniazid in rats. *Pharmacol Res.*; 59(2): pp. 112–9.
2. Shih TY, Pai CY, Yang P, Chang WL, Wang NC, Hu OY (2013). A novel mechanism underlies the hepatotoxicity of pyrazinamide. *Antimicrob Agents Chemother.*; 57(4): pp. 1685–90.
3. Ramappa V, Aithal GP (2013). Hepatotoxicity related to anti-tuberculosis drugs: mechanisms and management. *J Clin Exp Hepatol.*; 3(1): pp. 37–49.
4. Tasduq SA, Peerzada K, Koul S, Bhat R, Johri RK (2005). Biochemical manifestations of anti-tuberculosis drugs induced hepatotoxicity and the effect of silymarin. *Hepatol Res.*; 31(3): pp. 132–5.
5. Shabbir M, Khan MR, Saeed N (2013). Assessment of phytochemicals, antioxidant, anti-lipid peroxidation and anti-hemolytic activity of extract and various fractions of *Maytenus royleanus* leaves. *BMC Complement Altern Med.*; 13: pp. 143.
6. Hussain M, Ghani A (2008). Herbal remedies used for gastrointestinal disorders in Kaghan valley, NWFP, Pakistan. *Pak J Weed Sci Res.*; 14(3–4): pp. 169–200.
7. Shabbir M, Syed DN, Lall RK, Khan MR, Mukhtar H (2015). Potent anti-proliferative, pro-apoptotic activity of the *Maytenus royleanus* extract against prostate cancer cells: evidence in in-vitro and in-vivo models. *PLoS One.*; 10(3): pp. e0119859.
8. Shabbir M, Khan MR, Saeed N (2013). *Medicine a*: Assessment of phytochemicals, antioxidant, anti-lipid peroxidation and anti-hemolytic activity of extract and various

- fractions of *Maytenus royleanus* leaves. *BMC Complement Alternat Med.*; 13(1): pp. 143–52.
9. Lowry OH, Rosebrough NJ, Farr AL, Randall RJ (1951). Protein measurement with the Folin phenol reagent. *J Biol Chem.*; 193(1): pp. 265–75.
 10. Afsar T, Razak S. (2017). Modulatory influence of *Acacia hydaspica* R. Parker ethyl acetate extract against cisplatin induced hepatic injury and dyslipidemia in rats. *BMC Complement Altern Med.*; 17(1): pp. 307.
 11. Chance B, Maehly AC (1955). Assay of catalase and peroxidases. *Methods Enzymol.*; 2: pp. 764–75
 12. Wiese J, McPherson S, Odden MC, Shlipak MG (2004). Effect of *Opuntia ficus indica* on symptoms of the alcohol hangover. *Arch Intern Med.*; 164: pp. 1334-1340
 13. Achterrath-Tuckermann U, Kunde R, Flaskamp E, Isaac O, Thiemer K (1980). [Pharmacological investigations with compounds of chamomile. V. Investigations on the spasmolytic effect of compounds of chamomile and *Kamillolan* on the isolated guinea pig ileum]. *Planta Med.*; 39: pp. 38-50
 14. Lee DY, Liu Y. (2003). Molecular structure and stereochemistry of silybin A, silybin B, isosilybin A, and isosilybin B, Isolated from *Silybum marianum* (milk thistle). *J. Nat. Prod.*;
 15. Ligeret H, Brault A, Vallerand D, Haddad Y, Haddad PS (2008). Antioxidant and mitochondrial protective effects of silibinin in cold preservation-warm reperfusion liver injury. *J. Ethnopharmacol.*; 115: pp. 507-514 [PMID: 18061382 DOI: 10.1016/j.jep.2007.10.024]
 16. Shaker E., Mahmoud H., Mnaa S. (2010). Silymarin, the antioxidant component and *Silybum marianum* extracts prevent liver damage. *Food Chem Toxicol.*; 48: pp. 803-806 [PMID: 20034535 DOI: 10.1016/j.fct.2009.12.011]
 17. Abou Zid S. (2012). Silymarin, Natural Flavonolignans from Milk Thistle. In: Venkateshwer R, editor. *Phytochemicals-A Global Perspective of Their Role in Nutrition and Health*. Rijeka: Croatia InTech, : pp. 255-272

Corresponding Author

Md. Aftab Alam*

Associate Professor, Department of Pharmacy, Galgotias University, Greater Noida, Uttar Pradesh, India