JOURNAL OF NATURAL REMEDIES
DOI: 10.18311/jnr/2023/30924

SHORT REVIEW

An Updated Review on Medicinal Plants with Hepato-protective Activity

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Abstract

Many precious medicines from traditional medicinal plants can be produced using a phototherapeutic approach to modern drug research. Finding pure phytochemicals that can be used as medicines requires time and money. The treatment of liver problems involves the use of numerous herbs and polyherbal mixtures. However, the treatments are ineffective in the majority of severe instances. Even though many of these plants and mixtures were subjected to experimental evaluations, the research was frequently insufficient and uncompleted. It was found that the therapeutic effects were evaluated in animals with subclinical liver damage brought on by a few substances. Antioxidants included in common foods can offer this kind of defence against liver damage brought on by hazardous substances' oxidative processes. Therefore, hepato-protective natural products such as *Phyllanthus amarus, Silybum marianum, Solanum nigrum, Tephrosia purpurea, Eclipta alba, Cichorium intybus, Phyllanthus Niruri, Centella asiatica, Capparis spinosa, Terminalia arjuna, Cassia occidentalis, Fumaria parviflora, Embelia ribes, Boerhaavia diffusa, Tamarix gallica, Achillea millefolium, Terminalia chebula, Ocimum sanctum, Glycyrrhiza glabra, Foeniculum vulgare, Garcinia mangostana, Acacia Catechu, Pergularia daemia, Annona squamosa, Flacourtia indica.* The goal of the current review is to gather information on promising phytochemicals from medicinal plants that have been evaluated in hepatotoxicity models utilising cutting-edge scientific methods.

Keywords: ALP, ALT, Anti-oxidant, AST, Liver Diseases

1. Introduction

Medicinal Herbal plants play a very crucial role in human health care. Around 80% of the world's population uses traditional medicine, which largely consists of plant components. Ayurveda, Siddha, Amchi, and Unani are just a few of the many ancient natural health care practices included in what is referred to as "traditional medicine". These medicinal practices date back to the beginning of time and have gradually evolved mostly based on practical experiences and little to no reference to contemporary scientific ideas[1].

There were prehistoric beliefs included in these customs, which were passed down by oral tradition and/or limited literacy. Although herbal remedies are beneficial in treating a variety of conditions, they are frequently misused or exploited without sufficient science. Therefore, in the context of contemporary science, these plant medications merit in-depth research[2].

In India's primarily rural and tribal regions, there are thought to be 7,500 plants utilized in traditional medicine. Out of these, the general public is either unaware of or has limited knowledge of the true medical benefits of more than 4,000 plants. Around 1,200 plants are used in traditional medical systems like Ayurveda, Siddha, Amchi, Unani, and Tibetan. In the Indian system of medicine (Ayurveda, Siddha, Unani) many medicinal products or derived from plants, which cause paramount importance as alternate therapies[3]. The development of priceless plant medicines for a variety of terrible diseases can be facilitated by thorough research into and documentation

Article Received on: 15.10.2022 Revised on: 20.12.2022 Accepted on: 11.01.2023

of plants utilized in regional medical traditions, as well as by pharmacological examination of these plants and their taxonomical relations. Random plant screening has not been commercially successful[1].

In the human body, the liver is where hormone and plasma protein production, glycogen storage management, RBC breakdown, and detoxification occur. Since the liver detoxifies and transforms substances, it is indirectly exposed to their negative effects, which makes it more vulnerable to illness. Therefore, it may not come as a surprise that over 10% of people worldwide have liver problems. Hepatitis, hepatic steatosis (fatty liver), fibrosis, cirrhosis, alcoholic and drug-induced illnesses, and cirrhosis are the most prevalent of these ailments. The trend is shifting to Complementary and Alternative Medicines (CAM), which are either natural materials or their derivatives, as synthetic pharmaceuticals used to treat liver problems have frequently proved fatal.

Their safety and long-lasting therapeutic potential are the basic foundation of this decision. As a result, over half of the treatments for liver illnesses currently originate from natural sources. Consistent conceptions of traditionally claimed medicinal plants for longer duration can achieve a therapeutic dose of the active ingredient/s[4]. The evidence that is now available also suggests that bioactive substances generated from therapeutic herbs may be potential hepato-protective agents. Since 65 percent of patients in Europe and the US rely on herbal treatments for the treatment of liver problems, herbal medicine among the wide spectrum of natural products is crucial[3].

2. Liver Diseases

Liver disease is any trouble of the liver that causes sickness. The liver is in charge of a number of important functions in the body, and if it becomes ill or damaged, those functions will cease to function, causing serious harm to the body. Hepatic disease is a term used to describe the liver disease.

Liver disease is a general concept that encompasses any issue that causes the liver to stop performing its intended functions. Until a reduction in activity happens, more than 75 percent, or three-quarters, of the liver tissue must be pretentious.

The liver is the body's most solid organ, and it is often classified as a gland because it produces and secretes bile among its many functions. A superior right part of the abdomen covers the liver with the rib cage. It has two major lobes, each of which is made up of several small lobules.

The liver cells receive blood from two different outlets. The hepatic artery transports oxygen-rich blood from the heart to the liver, while the portal vein transports nutrients from the intestine and spleen[4-7].

3. Medicinal Plants and their Hepato-protective Actions

The goal of this review is to gather information about promising phytochemicals from medicinal plants that have been studied in hepatotoxicity models. Table 1 shows some common medicinal plants and their potential as hepato-protectives.

Table 1. Medicinal plants with potential hepato-protective activities

Sr No.	Plant Name	Family	Part use/extract	Pharmacological actions	Biochemical and histopathological parameters
1.	*Phyllanthus amarus*[6-8]	Phyllanthaceae	Leaf and fruits	Its extract restored the enzymatic activity of catalase, superoxide dismutase and creatine kinase which were initially lost after exposure to the toxicants.	Decreases the AST, ALT, ALP, Total bilirubin, Total Collagen Contents, TGF-β, ALK-5, Normalize Histological Changes Occurs due to exposure to toxicants.

Table 1. (Continued)

2.	*Silybum marianum*[9,10]	Asteraceae	Leaves	It is found to be a potent scavenger of ROS, such as hydroxyl and peroxyl anions. In addition, superoxide anion radicals and nitric oxide were inhibited in isolated Kupffer cells after treatment with it. It has demonstrated antifibrogenic effects in animals. In an *in vitro* model of human hepatic fibrogenesis, it demonstrated antifibrogenic properties by dose-dependently inhibiting the growth factor-induced production of pro-collagen in activated human HSC.	Antioxidant, increase glutathione, inhibit TNF-α, IL-2, IL-4, NF-κB, TGF-β, HSC development, Decreases Collagen Fibers Enhance Lipolysis and inhibit gluconeogenesis.
3.	*Solanum nigrum*[11,12]	Solanaceae	Leaves and water extract	Dilation of the central vein and distortion of hepatocytes became less apparent in the liver of experimental animals treated with it in comparison to that treated only with toxicants. Fatty degenerative changes were also less pronounced in the liver of experimental animals treated with it in comparison to that treated only with toxicants.	Prevents hyperlipidemia and hepatic damage and Decreases the AGEs formation, oxidative stress, HSC formation, Collagen content, AST, ALT and increases Glutathione.
4.	*Tephrosia purpurea*[13]	Fabaceae	Aerial parts	It possesses potent antioxidant, anti-inflammatory as well as free radical scavenging activity. Thus, it can protect hepatic tissue from free radicals and prevent inflammation and necrosis of the hepatic cells in the Tephrosia purpurea extract-treated group.	Decreases serum aspartate aminotransaminase, alanine aminotransaminase, gamma-glutamyl, alkaline phosphatase, total bilirubin, and liver glutathione level.
5.	*Eclipta alba*[14]	Asteraceae	Leaves	It has a protective role against liver diseases such as liver cirrhosis and infective hepatitis. It reduced fat deposition, mononuclear infiltration, and necrotic foci and stimulated the regeneration of hepatocytes in the liver.	It reduces fat deposition, mononuclear infiltration, and necrotic foci, and stimulated hepatocyte regeneration in the liver.

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Table 1. (Continued)

6.	*Cichorium intybus*[15]	Asteraceae	Roots	It increases levels of antioxidant enzymes and reduced levels of malondialdehyde are the major mechanism of it's for preventing the development of liver fibrosis induced by CCl_4.	It decreases the level of ALT, AST, aminotransferase, alkaline phosphate and bilirubin.
7.	*Phyllanthus Niruri*[16]	Phyllanthaceae	Leaves and stem	It possesses potent hepato-protective effects against viral hepatitis and toxicity caused by different drugs or environmental toxicants. It exerts its action as a potent antioxidant activity.	It decreases the level of Serum glutamic oxaloacetic transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT), serum alkaline phosphatase (SALP) and γ-glutmyltransferase.
8.	*Centella asiatica*[17]	Apiaceae	Leaves	It possesses hepato-protective effects by increasing the levels of antioxidant enzymes and reducing the levels of inflammatory mediators in rats with DMN-induced liver injury.	It significantly decreased inflammatory mediators, including interleukin (IL)-1β, IL-2, IL-6, IL-10, IL-12, tumour necrosis factor-α, interferon-γ and granulocyte/macrophage colony-stimulating factor.
9.	*Capparis spinosa*[18]	Capparidaceae	Root bark	It possesses hepato-protective action along with this it also restored the hepatic and serum FGF21 levels that had fallen in the fatty liver rat model.	It improved histological characteristics of nonalcoholic steatohepatitis and significantly decreased liver weight and index, serum levels of glucose, lipids, alanine aminotransferase (ALT), and aspartate aminotransferase (AST).
10.	*Terminalia arjuna*[19]	Combretaceae	Bark	Its extracts demonstrate antioxidant action by reducing oxidative stress, which supports the traditional usage of Terminalia arjuna to halt the early effects of alcohol on the liver.	It decreases the level of ALT, AST as well as TNF-α and decreases the inflammation and slight decrease in Liver necrosis.
11.	*Cassia occidentalis*[20]	Caesalpiniaceae	Leaves	It slightly preserved the rats' liver parenchyma. Along with this it also possesses anti-oxidant activity.	It significantly decreases the level of ALT, AST as well as ALP.

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Table 1. (Continued)

12.	*Fumaria parviflora*[21]	Papaveraceae	Leaves	It has antioxidative, antinociceptive, and hepato-protective effects along with this it also decreases the serum LDL, TG, and cholesterol levels and also decreases inflammation.	The levels of malondialdehyde, alanine aminotransferase, and aspartate transaminase increased whereas the activities of SOD and GPx, as well as the serum levels of alkaline phosphatase, were massively reduced.
13.	*Embelia ribes*[22]	Myrsinaceae	Fruits	It can significantly increase the survival and liver functioning of mice with acute liver injury brought on by TAA. Due to its antioxidative characteristics, it may have protective effects via lowering hepatocellular necrosis/apoptosis.	It decreases the level of AST, ALT, ALP, LDH, GGT, and total bilirubin in serum and decreases fibrin formation.
14.	*Boerhaavia diffussa*[23]	Nyctaginaceae	Roots	It causes an increase in the level of superoxide, dismutase, catalase, glutathione peroxidase, and glutathione-s-transferase also causes an increase in the flow of bile and possesses Hepato-protective properties.	It results in decreases in the level of ALP, ALT, AST, serum LDH level, and bilirubin level along with this it also results in decreases in Prothrombin levels.
15.	*Tamarix gallica*[24,25]	Tamaricaceae	Leaves	Due to its hepato-protective (liver-protecting) characteristic, its extract may aid in the management of liver diseases. It has anti-oxidants (flavonoids) that fend against free radicals and stop liver cell deterioration.	It results in decreases in the level of ALP, ALT, AST, Bilirubin, and Lactate dehydrogenase as well as decreases the level of Cholesterol as well.
16.	*Achillea millefolium*[26]	Asteraceae	Hydroalcoholic extract	It exerts anti-oxidant activity by an increase in the level of SOD and GSH-P levels as well as MDA levels—a sign of lipid peroxidation—are also present.	Blood glucose, serum liver enzymes, triglycerides, and total- and LDL-cholesterol levels all significantly decrease as a result of its administration.
17.	*Terminalia chebula*[27]	Combretaceae	Water extract	It exerts anti-oxidant activity by an increase in the level of GSH, SOD, CAT, GSH-Rd, and GSH-Px. Its pretreatment decreases the level of TNF-α, IL-1β, and IL-6.	It results in drastic decreases in the level of ALT, AST, and LDH and slight decrease in the level of TNF-α, IL-1β, and IL-6.

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Table 1. (Continued)

18.	*Ocimum sanctum*[28,29]	Lamiaceae	Leaves	It exerts its Hepato-protective action by normalizing the level of the hepatic enzyme responsible for a liver injury like ALP, AST, ALP as well as Serum bilirubin level and thus results in hepatic cell regeneration and restoration of liver function	It results in decreases in the level of ALP, AST, ALP as well as on Serum Bilirubin level. Along with this, it improved histological characteristics.
19.	*Glycyrrhiza glabra*[30]	Fabaceae	Root powder	It prevented DILI by various mechanisms like anti-steatosis, anti-oxidative stress, anti-inflammation, immunoregulation, anti-fibrosis, anti-cancer, and drug-drug interactions.	It dramatically reduced the expression of both pro-inflammatory mediators like TNF-, iNOS, and COX-2 (84), inhibited pro-fibrotic cytokines like Smad2, Smad3, and SP-1, -SMA, connective tissue growth factor (CTGF), and MMP2/9, and eventually reduced CCl4-induced liver fibrosis.
20.	*Foeniculum vulgare*[31,32]	Umbelliferae	Fruit	It exerted hepato-protective activity by various mechanisms like antioxidant activity, antibacterial activity, and anti-inflammatory activity.	It results in decreases in the level of ALP, AST, ALP as well as on Serum Bilirubin level.
21.	*Garcinia mangostana*[33]	Clusiaceae	peel extract	It causes decreases in collagen synthesis of collagen fibres, exerts anti-oxidant activity by an increase in the level of SAD and CAD enzymes level and possesses anti-inflammatory action.	It results in decreases in the level of ALP, AST, ALP as well as on Serum Bilirubin level. Along with this It significantly reduces the PCNA, -SMA, and TGF-1 expression.
22.	*Acacia Catechu*[34]	Leguminosae	Powdered pale catechu	It exerts Hepato-protective actions by anti-oxidant activity by increasing the level of SOD and GSH and decreasing lipid peroxidation.	It results in the regeneration of liver tissues facilitated by the inhibition of oxidative stress and hepatic indicators (ALT, AST, and ALP), as well as by an increase in the antioxidant defence system.
23.	*Pergularia daemia*[35]	Apocynaceae	Leaves	It exerts Hepato-protective actions and boosts glutathione, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, and glucose-6-phosphate dehydrogenase while decreasing lipid peroxidation.	It results in decreases in the level of ALP, AST, ALP as well as on Serum Bilirubin level.

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Table 1. (Continued)

24.	*Annona squamosa*[36]	Annonaceae	Seeds	It dramatically raised the levels of SOD, CAT, and GSH while dose-dependently preventing the alcohol-induced rise in the blood levels of hepatic enzymes. Additionally, it greatly reduced the MDA concentration. The liver tissues' histopathology revealed that EEAS reduced hepatocellular necrosis and caused cell regeneration and repair toward normal.	It results in a considerable reduction in total bilirubin, together with a significant rise in total protein and a significant fall in ALP, AST, and ALT levels.
25.	*Flacourtia indica*[37]	Salicaceae	Stem Bark	It will prevent mixed infiltrates, focal necrosis, scattered fatty alterations, an enormous inflow of inflammatory cells, injured hepatocytes, degeneration of the hepatocyte cords, and the impacted hepatocytes arranged in deformed cords that compress the sinus lumen are all present in the sinusoid which occurs due to Drug Induced Liver Injury.	It results in a considerable reduction in total bilirubin, together with a significant rise in total protein and a significant fall in ALP, AST, and ALT levels and causes an increase in the level of antioxidant enzymes.

4. Discussion

Globally, herbal therapies are becoming more and more popular, and at least 25% of people with liver problems use ethnobotanicals. It is imperative to conduct rigorous preclinical investigations and clinical trials in order to uncover the mysteries buried in plants. This strategy will assist in determining the true therapeutic benefit of these natural pharmacotherapeutic substances and standardize the dose regimen based on research-supported findings to transcend the status of a fad.

There are many herbal products available to support health, treat symptoms, and prevent diseases. However, the majority of these products lack pharmacological scientific confirmation. Numerous herbals demonstrated hepato-protective/curative properties in experimental hepatotoxicity models in the lab or higher animals, which justifies further clinical research. Most herbal formulations cannot be advised for the treatment of liver problems due to a lack of pharmacological research supported by science[38].

Some of the reported active ingredients, which are potential candidates for therapeutic use, require to have their efficacy verified. Experiments using whole plant extracts should give way to those that isolate bioactive components and evaluate the extract on cultured cell lines[39].

5. Conclusion

The search for novel pure prototype chemicals as medications should not be the only objective of ethnopharmacological investigations on medicinal plants. Drugs made from active extracts, fractions, or a combination of fractions and extracts may be very effective. Drugs made from plants, whether in combination or as single agents, should be effective enough to treat serious liver conditions brought on by toxins, viruses (such as hepatitis B and C), excessive alcohol consumption, etc. A single medication can't treat all forms of serious liver disorders. Clinical trials and pharmacological studies must be conducted using local medicinal herbs to develop effective formulations. Standards for efficacy and safety should control the production of plant-based products.

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