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Phytopharmacology of herbs used in liver disorder

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Abstract
Researchers' interest in herbal therapy has been sparked by an increase in patients with liver disease as a result of heavy drug and alcohol use. This is due to the limited number of treatments are readily available for common liver illnesses such as cirrhosis, fatty liver, and chronic hepatitis. Globally, chronic liver dysfunction or injury is a severe health issue. Numerous liver diseases, such as fatty liver, hepatitis, fibrosis, cirrhosis, and hepatocellular cancer are all part of chronic liver disease. Current synthetic medications are not very effective at treating chronic liver disease, and they also have unfavourable side effects. In order to treat chronic liver illnesses, a wide variety of medicinal plants and phytochemicals have been researched as complementary and alternative therapies. For liver tonic, a variety of conventional herbal combinations are employed. The plants used to treat liver illness were discussed in this review. The rising popularity of herbal remedies is a reflection of both their alleged efficacy in the treatment and prevention of disease and the notion that they are secure because they are "natural." In order to treat severe liver problems, a combination of various herbal extracts is likely to deliver the required effects. Many phytochemicals found in medicinal plants have strong antioxidant properties, which result in antihepatotoxic action.

Keywords: liver, medicinal plant, diseases, hepatoprotective, phytochemicals

Introduction
The world's largest producer of medicinal plants, India is referred to as the "Botanical Garden of the World." The health and vitality of both humans and animals are significantly impacted by therapeutic herbs. The liver is the body's biggest organ. Liver aids in energy conservation and toxin removal. In addition, the liver performs approximately 500 other tasks, including being a key component of the digestive system, metabolism, and system for converting essential micronutrients into forms the body can use. Also, the liver is where bile, albumin, prothrombin, and complement are mostly produced and excreted, which makes them important components of the humoral branch of the immune system [1]. According to the WHO information sheets on hepatitis, more than 170 million individuals have long-term hepatitis C virus infections, and 60,000 people die each year from acute and chronic hepatitis B. The use of herbal therapy is widespread and is growing in acceptance.
Among other things, the liver's bile plays a significant part in digestion. One of the most dangerous conditions is liver disease. They can be divided into three categories: cirrhosis (a degenerative ailment that causes fibrosis of the liver), hepatosis (non-inflammatory disorders), and acute or chronic hepatitis (inflammatory liver diseases). Toxic chemicals (such as certain antibiotics, chemotherapeutics, peroxidised oil, aflatoxin, carbon tetrachloride, acetaminophen, chlorinated hydrocarbons, etc.), excessive alcohol use, infections, and autoimmune diseases are the main causes of liver problems [2-4]. The majority of hepatotoxic substances primarily harm liver cells by causing lipid peroxidation and other oxidative liver damage. Hepatitis and cirrhosis may occur from increased lipid peroxidation caused by the liver's microsomal breakdown of ethanol. About 90% of acute hepatitis is thought to be caused by viruses. Hepatitis B, A, C, D (delta agents), E, and G are the principal viral agents at play. Of them, Hepatitis B infection frequently causes chronic liver conditions and liver cirrhosis. These viruses have also been demonstrated to cause primary liver cancer. It has been reported that about 14-16 million people are infected with Hepatitis B virus in South East Asia region and approximately 6% of the total population in the region are carriers of this virus. A vaccine has become available for immunization against Hepatitis B virus. Hepatitis C and Hepatitis E infections are also common in countries of South East Asia region [4]

Liver diseases
A. Chronic hepatitis
The inflammation of the liver is known as chronic hepatitis, and its typical causes include viral infections, autoimmune disorders, and toxic chemicals like alcohol or narcotics. The most prevalent liver illnesses are viral hepatitis and cirrhosis, which can develop over time [5]. The well-known causes of chronic viral hepatitis are the hepatitis B and c viruses (HBV and HCV). Currently, 5% of the global population is thought to be a chronic HBV carrier and more than 30% of the population is infected with the virus. Since the 1980s, Hepatitis C has overtaken HBV as the most frequent cause of viral hepatitis in certain developed nations [6] as a result of the extensive use of the HBV vaccine.
The fundamental causes of the disease determine the precise mechanism of chronic hepatitis. Hepatic virus activation of the immune system causes inflammation and liver damage in viral hepatitis. In autoimmune hepatitis, an inappropriate immune reaction against liver cells is brought on by the autoimmune illness. The damage in alcoholic hepatitis is typically detected in conjunction with fatty liver [7, 8]. Inflammation, necrosis, and fibrosis in the liver tissues are the main traits of chronic hepatitis.
Drugs, alcohol, non-alcoholic steatohepatitis (NASH), and viral hepatitis are all causes of hepatitis.

B. Fatty liver disease

Steatosis, often known as fatty liver disease, is a degenerative condition in which the liver cells develop enormous vacuoles of triglyceride fat. Obesity, insulin resistance, and dyslipidemia are only a few metabolic conditions that can lead to fatty liver disease [9]. Alcohol-related steatosis is referred to as alcoholic fatty liver (AFL), whereas nonalcoholic fatty liver (NAFL) denotes that alcohol was not the initial cause of steatosis. The most prevalent liver illness in Western nations is fatty liver disease, which has a prevalence of 20% to 60% [10]. Recent research suggests that some herbal supplements may benefit this ailment that may be treatable. The use of herbal remedies for the treatment of fatty liver disease may have a small advantage, according to both scientific and clinical investigations.

C. Cirrhosis

Cirrhosis, a fatal complication of chronic liver illnesses, is a condition in which the liver does not function effectively as a result of long-term damage. More than 1,000,000 deaths from cirrhosis occurred in 2010, accounting for 1.95% of all deaths worldwide, up from around 676,000 cases in 1980, or 1.54% of all deaths worldwide [11]. The development of fibrosis in place of healthy parenchyma is the pathological sign of cirrhosis. In the case of fibrosis, excessive scar tissue accumulates in the liver as a result of wound and damage repair. Collagen and other extracellular matrix (ECM) proteins are overproduced or inadequately destroyed during this process, which may be brought on by chronic inflammation or a fatty liver. If the cause is addressed at this time, fibrosis may be curable but extensive fibrosis can progress to cirrhosis, which results in the loss of hepatic cells and permanently scarred liver. Except for liver transplantation, there is currently no treatment that can effectively repair cirrhosis [12]. However, there is a severe shortage of available liver allografts. Although no medications have been licenced for the treatment of cirrhosis or fibrosis in the United States, some herbal remedies have proven to be remarkably effective in avoiding cirrhosis, treating fibrosis, and reducing cirrhosis symptoms.

D. Primary liver cancer

Globally, liver cancer caused more than 750,000 fatalities in 2014 [13]. In nations where hepatitis virus infection is widespread, such as East Asia and sub-Saharan Africa, the prevalence of liver cancer is higher [14]. The most typical form of primary liver cancer is hepatocellular carcinoma (HCC). Cirrhosis brought on by viral hepatitis or fatty liver disease is the main contributor to liver cancer. Through repeatedly inducing the immune system to attack the hepatic cells, hepatitis or fatty liver promote the development of HCC. However, this continual cycle of damage followed by repair might result in errors during repair, which in turn promote carcinogenesis. The integration of the viral genome into the host liver cells can directly cause gene mutation in chronic hepatitis B, which leads to the development of HCC [15, 16].

Only 10% of patients are candidates for surgical resection since most patients are discovered at a late stage of the disease, despite the fact that it may be the greatest therapy for promoting long-term survival. In certain cases, herbal remedies are suggested as a complementary therapy for liver cancer patients in order to lessen the negative effects of conventional medication, increase survival time, and enhance quality of life.

Herbal remedies for liver diseases

Several different liver problems have been treated using a variety of herbs [18]. In India and China, where the majority of the research is unpublished, the use of herbal treatment for liver disease has been ongoing for millennia. A few new fields, including Phytopharmacology and Ethnopharmacology, have emerged as a result of the use of herbal therapy. The flora of many nations is now being highlighted as their cultural contribution to medicine. Numerous Phyto molecules from various plant sources, including as flavonoids, alkaloids, glycosides, and saponins, have been identified as powerful hepatoprotective agents [17]. Because herbs appear to be less poisonous and therefore less likely to have adverse effects, humans have employed plants as medicine from the dawn of time [19]. Numerous medications on the market have either been developed directly from or indirectly from medicinal plants. Researchers are now thinking about traditional herbal therapy because of the recent interest in natural therapies and alternative medications [20-28]. In this sense, ethnobotany is the study of how members of a particular culture, ethnic group, or geographic area make use of the local plants. The results of ethnobotanical studies can be very helpful in other fields, like pharmacognosy, and they may aid in eliciting native people's knowledge about the usage of plants to make goods for sale [29–34]. So, obtaining information on medicinal plants and how they are used in various settings is currently a useful medical resource that aids in the development of novel medications [35-42]. List of some medicinal plant which are effective on liver disease are given below.

Table 1: Medicinal plants effective on liver diseases arranged in alphabetical order of their family.

Sr no.	Botanical name	family	Common name	Part of plant used	Ref. no.
1.	*Cynara scolymus* L.	Asteraceae	Kangar Farangi	Aerial part	45
2.	*Gundelia tournefortii* L.	Asteraceae	kangar	Aerial part	45
3	*Silybum marianum* (L.) Gaertn	Asteraceae	Khare Maryam	seed	45
4	*Cichorium intybus* L	Asteraceae	Casni	Root, leaf, apical part.	46, 48
5	*Centaureabehen*	Asteraceae /Compositae	Safedbaman	Root	49
6	*Berberis integerrima* Bunge	Berberidaceae	Zereshk	Fruit	44, 45
7	*Berberis vulgaris* L.	Berberidaceae	Zereshk	Fruit	46
8	*Berberis sp*.	Berberidaceae	Zereshk	Fruit	45
9	*Berbarisaristata*	Berberidaceae	Barberry	Root bark	49
10	*Cadaba farinosa*	capparaceae	Indian cadaba	Root	43
11	*Cordiamacleodii*	Boraginaceae	Dhaiman	Stem bark, leaf	49

12	*Tecomella undulate* (Roxb.) G. Don.	Bignoniaceae	Anare sheytani, anare aboojah	Whole plant	47
13	*Descurainia sophia* (L.) Webb ex Prantl	Brassicaceae	Khakshir	Seed	45
14	*Balanitesaegyptiaca*	Balanitaceae	Hing	Stem bark, leaf, fruit	49
15	*Bixaorellana*	Bixaceae	Annatto tree	Leaf	49
16	*Capparis spinosa* L.	Capparaceae	Kavar	Fruit-Root	45
17	*Terminalia chebula* Retz.	Combretaceae	Halileh Siah, harra	Fruit	45
18	*Terminaliaarjuna*	Combretaceae	Arjun	Stem bark, fruit	49
19	*Agrostemmagithago*	Caryophyllaceae	Corn cockle	Seeds	49
20	*Lychniscoronaria*	Caryophyllaceae	Rose campion	Root	49
21	*Polycarpaeacorymbosa*	Caryophyllaceae	Machechi	Leaf	49
22	*Capparisspinosa*	Capparidaceae	Caper bush	Root bark	49
23	*Citrulluscolocynthis*	Cucubitaceae	Indrayan	Root, fruit	49
24	*Momordicacharantia*	Cucurbitaceae	Karela	Leaf, fruit, seed	49
25	*Trichosanthescordata*	Cucurbitaceae	Bhumikumra	Root	49
26	*Aporosalindieyana*	Euphorbiaceae	Valaka	Root	49
27	*Baliospermummontanum*	Euphorbiaceae	Danti	Root	49
28	*Croton oblongifolius*	Euphorbiaceae	Chucka	Stem bark, aerial part	49
29	*Emblicaofficinalis*	Euphorbiaceae	Amla	Fruit	49
30	*Phyllanthusniruri*	Euphorbiaceae	Jangliamli	Root	49
31	*Ricinuscommunis*	Euphorbiaceae	castor	Leaf	49
32	*Aloe barbadensis*	Liliaceae	Indian aloe	Root, pulp, aerial part	49
33	*Asparagus officinale*	Liliaceae	Asparagus	Root	49
34	*Asparagus recemosus*	Liliaceae	Satawar	Whole plant	49
35	*Colchicum luteum*	Liliaceae	Hirantutiya	Corm	49
36	*Ocimum sanctum*	Labiatae/lamiaceae	Tulsi	Leaf	49
37	*Orthosiphonspiralis*	Labiatae/lamiaceae	Java tree	Leaf	49
38	*Glycyrrhiza glabra*	leguminosae	Liquorice	Root	49
39	*Marrubium vulgare* L	Lamiaceae	Ferasion	Aerial parts	45
40	*Moringaoleifera*	Moringaceae	Mungna	Fruit	49
41	*Tinosporacordifolia*	Menispermaceae	Giloe	Stem bark, fruit	49
42	*Abelmoschusesculentus*	Malavaceae	Lady's Finger	Root, fruit, seed	49
43	*Aphanamixispolystachya*	Meliaceae	Amoora	Stem bark	49
44	*Azadirachtaindica*	Meliaceae	Neem	Whole plant	49
45	*Boerhaaviadiffusia*	Nyctaginaceae	Punarnava	Root, whole plant	49
46	*Plantago major*	Plantaginaceae	Ispaghula	Seed	49
47	*Picrorrhiza kurroa*	Scrophulariaceae	Kutki	Root, rhizome	49
48	*Withania somnifera*	Solanaceae	Ashwagandha	Root	49
49	*Zingiberofficinale*	Zingiberaceae	Ginger	Rhizome	49
50	*Curcuma longa*	Zingiberaceae	Turmeric	Rhizome(tuber)	49

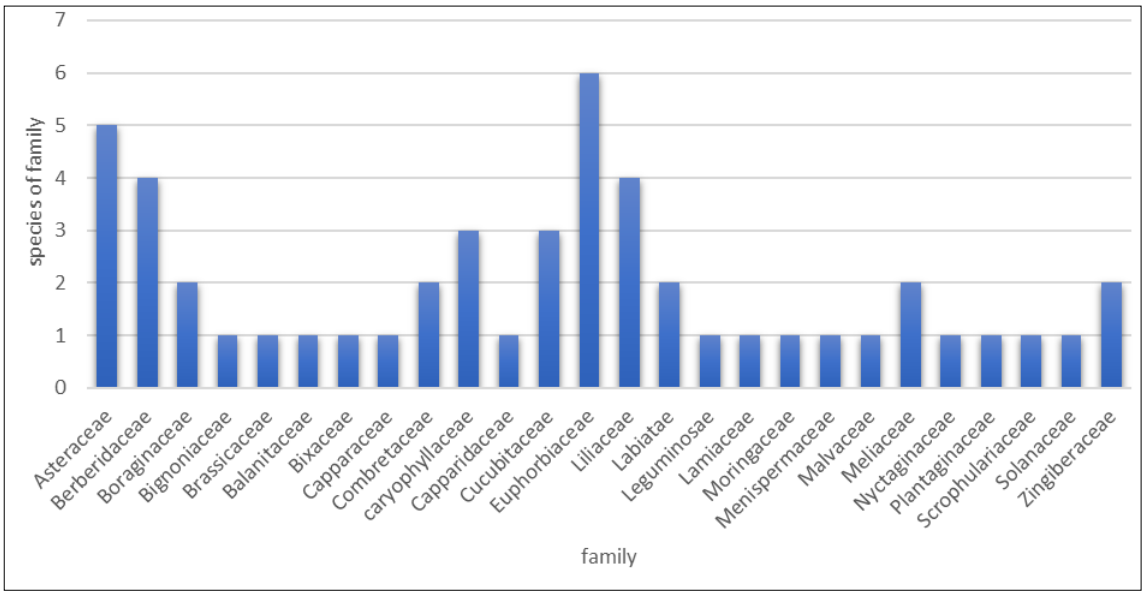

Fig 1: The number of medicinal species effective on liver diseases in each family

Conclusion

Herbal medications produced from plant extracts are used more frequently to treat a wide range of clinical disorders, and great efforts are being made to understand how they work. Slowing oxidative damage, reducing fibrogenesis, eradicating viral infection, and preventing or slowing tumour growth are among ways that medicinal plants and phytochemicals can cure chronic liver disease. Future

research is likely to uncover more medicinal plants and phytochemicals that can treat chronic liver disease safely and effectively. This review provides the report of herbal medicines which are frequently used for treatment of liver disorders. We mentioned 50 plants belonging from different families. As noted in Chinese medicine, Ayurveda medicine, and ancient Egyptian herbal treatments, there are currently more than 1,000 herbal medications on the market with a variety of active ingredients. These medications require rigorous analysis to demonstrate their hepatoprotective potential. Herbal medications are currently more in demand in primary health care, not just in underdeveloped nations but also in developed countries, due to its cultural acceptance, relative lack of adverse effects, and compatibility with the human body.

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