Herbal medicine for treatment and prevention of liver diseases

Mayuresh Rajaratnam¹, Andrzej Prystupa², Patrycja Lachowska-Kotowska², Wojciech Załuska³, Rafał Filip⁴

¹ Research Students' Association, Medical University, Lublin, Poland

² Department of Internal Medicine, Medical University, Lublin, Poland

³ Department of Nephrology, Medical University, Lublin, Poland

⁴ Institute of Rural Health, Lublin, Poland

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Abstract

The rising number of patients with liver dysfunction due to overwhelming usage of drugs and alcohol has paved the path for researchers in an interest in herbal medicine. This is because there are only a few universally effective and available options for the treatment of common liver diseases, such as cirrhosis, fatty liver and chronic hepatitis. Herbal treatment has been used to alleviate disorders related to liver and other internal organs for many centuries in the eastern world, and have currently become a favourable therapy internationally for pathological liver conditions. In recent years, researchers have used scientific methods to evaluate the effects of plants for the treatment of liver ailments, although in many cases the mechanisms and modes of action of these plants, as well as their therapeutic effectiveness, have not been confirmed. Several hundred plants have been examined to-date, but only a handful has been studied thoroughly. Among these, the current study discusses a compilation of herbal medicines used for liver protection, such as Silymarin (milk thistle), Liv-52, Camellia sinensis (green tea), Glycyrrhizaglabra (licorice) and FuzhengHuayu. The increasing use of herbal medicines reflects their perceived effectiveness in the treatment and prevention of disease, and the belief that these treatments are safe because they are 'natural'. The presented study evaluates the effects of herbal extracts in the treatment of liver diseases, provides a general understanding of the actions of herbal medicines, a background for understanding the hepato-protectiveness of herbs, and the challenges that are faced by the scientific community in researching thoroughly of each and every compounds of the herbs.

Key words

hepatoprotection, medicinal plants, herbal medicine, liver diseases

INTRODUCTION

The liver is the largest organ of the body, contributing about 2% of the total body weight in the average human. It is connected with most of the physiological processes, which include growth, immunity, nutrition, energy metabolism and reproduction. Synthesis and excretion of bile, albumin, prothrombin and the production of the compliments which are the major effectors of the humoral branch of the immune system, occur mainly in the liver [1]. According to the WHO fact sheets on hepatitis, 60,000 persons die of the acute and chronic hepatitis B annually, and more than 170 million people have long-term liver infections with hepatitis C virus. Herbal medicine has become more and more accepted and their usage is prevalent. Legal regulations and pharmacovigilance concerning herbal products are still lacking evidence to substantiate their effective usage in liver diseases. Nonetheless, some herbs have shown promising results.

The presented study provides a general understanding of the actions of herbal medicines, and hence a background for understanding questions of safety and side-effects, especially regarding to their presumed beneficial effect.

A HISTORY OF HERBS AND HOW THEY HAVE INCREASED IN POPULARITY

Herbal drugs have been used in the treatment of liver diseases since ancient times, developed in Eastern medicine and has a time-honored history. In written records, the study of herbs date back over 5,000 years – ancient Chinese and Egyptian papyrus writings describe medicinal uses for plants as early as 3,000 BC [2]. Natives in different continents had used herbs in their medicinal practices, while some cultures developed their own herbal medical systems, such as Ayurveda, Islamic Medicine and Traditional Chinese Medicine.

Researchers have identified that people in different countries tended to use the identical or comparable herbs for the purpose of prevention, diagnosis, improvement or treatment of physical and mental illness. It is estimated that three-quarters of the world population rely on herbal and traditional medicine as a basis for primary health care [3]. Herbal medicine is used to treat many conditions, such as asthma, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, Irritable Bowel Syndrome, and cancer, among others [4]. Herbs are becoming more main stream as advances in scientific research show the importance of herbal medicinal practices in the diagnosis, treatment and prevention of disease. In spite of the development in the current medical field, research professionals are paying more attention to conventional phytomedicine.

Address for correspondence: Andrzej Prystupa, Chair and Department of Internal Medicine, Medical University, Staszica 16, 20-081 Lublin, Poland E-mail: aprystup@mp.pl

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MAJOR LIVER DISEASES

Drug-induced hepatitis. Drugs are known to be a major cause of liver injury. More than 900 drugs, toxins, and herbs have been reported to cause liver injury, and drugs account for 20–40% of all instances of fulminant hepatic failure [5]. Drug-induced hepatitis is inflammation caused by certain prescription drugs, including herbal drugs. Drug toxicity can be classified into 2 categories: 1) drugs that affect the liver directly, which are dose dependent, 2) drugs that mediate an immune reaction. The pathophysiologic mechanisms of hepatotoxicity are still being explored and include both hepatocellular and extracellular mechanisms, such as disruption of the hepatocyte due to binding of the drug to intracellular proteins, disruption of the transport proteins, catalytic T-cell activation by covalent binding of a drug to the P-450 enzyme that acts as an immunogen, apoptosis of hepatocytes, mitochondrial disruption, bile duct injury due to toxic metabolites excreted in the bile duct [6].

Alcohol-induced hepatitis. This is an inflammation of the liver caused by excessive alcohol consumption over a long period of time. Alcohol remains one of the major causes of liver disease in the world, and in the United States alone, alcoholic liver disease affects more than 2 million people, approximately 1% of the population [7]. Factors such as environmental, nutritional, familial and genetic factors, metabolic, and immunologic factors play a major role in alcohol-induced hepatitis. The metabolic product of alcohol, acetaldehyde, is a potent toxic metabolite which can directly injure the hepatocytes [8]. There have been studies suggesting that there can be an immunological reaction to acetaldehyde-modified cytoskeletal proteins that induces IgA antibodies and many pro-apoptotic cytokines [9].

Non-alcoholic steatohepatitis (NASH). This is a condition similar to alcohol-induced hepatitis that occurs in people who are non-alcoholics. The prevalence of NASH is rising rapidly because of the persistent increase in obesity and type 2 diabetes. Although the mechanism is complex and incompletely understood, a 2-hit hypothesis has been proposed:

- 1) involves an imbalance of fatty acid metabolism that leads to hepatic triglyceride accumulation (steatosis) [10];
- 2) may be oxidative or metabolic stress and dysregulated cytokine production resulting from efforts to compensate for altered lipid homeostasis, leading to subsequent inflammation and fibrosis [11].

Viral hepatitis. Viral hepatitis has emerged as a major public health problem worldwide affecting several hundred million people, and is a cause of considerable morbidity and mortality in the human population [12]. Viral hepatitis is known to be caused by hepatitis viruses A, B, D, E. In addition to these, other viruses also cause liver inflammation, such as Herpes simplex, Cytomegalovirus, Epstein–Barr virus, or Yellow fever. Patients who are chronically infected may go on to develop cirrhosis and hepatocellular carcinoma (HCC) [13]. The presence of a virus in the hepatocytes causes the immune cells to attack the liver, thereby causing the inflammatory process.

Although the diagnosis of the above-mentioned major liver diseases can be made with adequate history taking, physical

examination and laboratory examinations, the treatment modalities have been unsuccessful even in this modern technologically-advanced era. This lack of modern medical treatments and the rising number of patients with liver diseases directs the attention of the scientific community, doctors and patients, towards Chinese herbal medicine, Ayurveda medicine, and other popular alternative medical therapies.

POPULAR HERBAL REMEDIES FOR LIVER DISEASES

The inadequacy of the herbs used in curing liver diseases and the variety of liver dysfunctions caused by allopathic drugs is found to be significant. Therefore, there is growing focus to follow systematic research methodology and to evaluate the scientific basis for the traditional herbal medicines that are claimed to possess hepatoprotective activities [14]. The above-mentioned major liver diseases are treated with many herbal drugs (Tab. 1). The presented study discusses the major herbal drugs that have contributed the most in the protection of liver diseases.

Silymarin. A herb containing four flavonolignan isomeric components (silybin, isosilybin, silychristin, and silvdianin), obtained from the herbal plant, 'milk thistle' (Silybum marianum). The active ingredients of the plant are obtained from the dried seeds; Silymarin is one of the herbal medicines that have been extensively studied, both clinically and chemically, for the treatment of major liver diseases. Silybin, which is the most active compound of Silymarin, is the major contributor of the hepato-protectiveness of the medicine. Silymarin is a drug which is taken per os and is mainly excreted through bile as conjugates. It is considered to be antioxidative, anti-lipid peroxidative, antifibrotic, antiinflammatory, membrane stabilizing, immunomodulatory and liver regenerating mechanisms [15]. It has been claimed that silymarin has clinical applications in the treatment of toxic hepatitis, fatty liver, cirrhosis, ischaemic injury, radiation toxicity and viral hepatitis as a result of its antioxidative, anti-lipid-peroxidative, antifibrotic, anti-inflammatory, immunomodulating, and even liver regenerating effects [16]. Though silymarin does not have antiviral properties against hepatitis viruses, it promotes protein synthesis, helps in regenerating liver tissue, controls inflammation, enhances glucuronidation and protects against glutathione depletion [17].

In liver diseases caused by oxidative stress (alcoholic and non-alcoholic fatty liver and steatohepatitis, drugand chemically-induced hepatic toxicity), the antioxidant medicine Silymarin is the primary therapeutic modality of choice [18]. Numerous reports have noted the benefits of Silymarin, not only as a treatment for chronic liver diseases, but also in viral-induced chronic hepatitis and primary liver cancer. Several studies have identified that continuous usage of Silymarin has significantly proved to increase the survival time of patients with alcohol-induced liver cirrhosis.

Silymarin is marketed as capsules or tablets containing ethanol extracted Silymarin in amounts of 250–750 mg, and purported to be beneficial for liver diseases. The daily dosage varies but it is typically taken 2–3 times daily. Intravenous preparations of purified Silybinin are approved in Europe for therapy of Amanita phalloides mushroom poisoning. Mayuresh Rajaratnam, Andrzej Prystupa, Patrycja Lachowska-Kotowska, Wojciech Załuska, Rafał Filip. Herbal medicine for treatment and prevention of liver diseases

Silymarin can trigger side-effects and can interact with other herbs, supplements, or medications [19]. Clinical research has proved that herbs and dietary supplements can trigger side-effects and can also result in interaction with other herbs, dietary supplements, or medications. For these reasons, herbs should be taken with great care and always under the supervision of a health care provider. Analysis of the safety data available on silymarin confirms a very good safety profile [20]. The most commonly noted adverse effects were gastrointestinal disturbances, nausea, irregular stool, and allergic skin rashes. Milk thistle is not considered safe to be used by pregnant or breastfeeding women.

Live-52. An Ayurvedic supplement, recognized and registered in more than 45 countries, and a well-known herb prescribed by many physicians worldwide. Introduced in 1955, Liv-52 has been studied vigorously since then for the treatment of liver diseases such as hepatitis, alcohol liver disease, pre-cirrhotic and early cirrhosis conditions, elevated liver enzymes, fatty liver conditions, protein energy malnutrition, and radiation or chemotherapy-induced liver damage[21].

Liv-52 is available as tablets and syrup containing the following herbs: Capparis spinosa, Cichorium intybus, Solanum nigrum, Terminalia arjuna, Cassia occidentalis, Achillea millefolium, Tamarix gallica and Phyllanthus amarus [22]. Liv-52 is formulated according to Ayurvedic principles, to enhance efficacy and avoid toxicity. These ingredients individually and synergistically provide various advantageous effects, such as being an effective antioxidant, hepatic stimulant, carminative, stomachic and choleretic. They also help reducing anasarca and ascites of hepatic origin. Mandurbhasma, an ingredient in Liv-52, is prepared from ferric oxide triturated in juices of many hepatic stimulants and cholagogues [23]. According to the manufacturers, during the process there is contact of the ingredients which could result in both individual and collective action on the liver. Liv-52 has not shown any serious side-effects, apart from occasional complaints of nausea.

Efforts should be taken to improve scientific understanding through further research to assess the fullest potential of Liv-52 for treating liver fibrosis and other conditions.

Camellia sinensis (green tea). Originated from and mainly produced in China and is made from the leaves of the plant Camellia sinensis, an inherent herb from southern China. The leaves are thermogenic, appetizer, digestive, carminative, diuretic, and useful in cardiodynia, haemorrhoids, inflammation and abdominal disorders [24]. Apart from the use of green tea in acute liver injury and oxidative stress injury, green tea is proved to be useful in preventing Hepatic C Virus (HCV) entry into the liver cells [25]. Green tea is composed of active compounds such as catechin, gallocatechin, epicatechin, epigallocatechin, epicatechingallate, and epigallocatechingallate (EGCG) in which EGCG is considered the most therapeutically significant compound. Studies also show that EGCG is believed to cause liver toxicity if taken in excess of the recommendation. Green tea is also documented as having stimulant effects which are believed to be due to the effect of some alkaloids, such as caffeine, theobromine, and theophylline. L-theanine, an amino acid compound found in green tea, has been studied for its calming effects on the nervous system [26].

Tea is traditionally consumed as a beverage, but green tea dietary supplements are available in the form of dried leaves or as capsules, and they are also available in liquid extracts made from the leaves and leaf buds. The average cup of green tea contains 50–150 mg polyphenols (antioxidants). Decaffeinated green tea products contain concentrated polyphenols. Caffeine-free supplements are available [27]. According to researches, 2–3 cups of green tea per day or 100–750 mg per day of regular green tea extract is known to be safe.

Glycyrrhizaglabra (licorice). A herb that was consumed as a sweetener in food and used as an active component in herbal medicine. Experimental hepatitis and cirrhosis studies have found that it can promote the regeneration of liver cells and at the same time inhibit fibrosis [28]. Throughout the years, licorice root has been used in conventional medicine to treat a range of illnesses, such as bronchitis, gastritis and jaundice, extending from the common cold to liver disease. Licorice root is available in liquid, dry, powdered, and peeled form

Licorice is used to treat a big array of illnesses, although it has not traditionally been used as a liver herb, several modern studies have demonstrated over the past two decades have shown that licorice is also an important liver herb with strong hepatoprotectant properties. It is still used today for treatment of many diseases, although not all its benefits are supported by clinical research. Glycyrrhizin inhibits liver cell injury and in Japan is given intravenously for the treatment of chronic viral hepatitis and cirrhosis [29].

Licorice products are made from peeled and unpeeled dried root. There are different forms of licorice available for medical usage, such as gel or cream, tablets, fluids and in powder form. In general, doses of 380–1,140 mg three times daily, taken by mouth 20 min before meals or 2–4 milliliters per day [30].

The most widely reported side-effects of glycyrrhizin use are oedema. These effects are related to the inhibition of cortisol metabolism within the kidney, and the subsequent stimulation of the mineral ocorticoid receptors [31]. Licorice with glycyrrhizin can cause severe side-effects. Researchers have found that excessive usage of glycyrrhizin can cause a condition called 'pseudoaldosteronism', which could cause a human to become extremely responsive to hormones. Pregnant or breastfeeding women should not take licorice. However, in general, licorice is considered safe for use. Licorice interacts with many prescription medicines.

Fuzheng huayu (FZHY). The first traditional Chinese medicine compound to complete clinical studies in the treatment of liver diseases and has been studied carefully for its ability to heal liver fibrosis. FZHY is a botanical compound approved in China for liver fibrosis caused by hepatitis B virus infection. It is a preparation containing such herbs as *Radix Salvia Miltiorrhizae, Cordyceps*, and *Semen Persicae*, formulated on the basis of Chinese medicine theory in treating liver fibrosis. Recent study has proved that liver fibrosis caused by the hepatitis B virus shows that FZHY is effective in the treatment of liver fibrosis caused by chronic hepatitis B, including fibrotic stage S3 with hepatic inflammation, hypochondriac pain and dry mouth. The dynamic pathological changes in liver were all found significantly improved after treatment [32].

Fuzheng huayu capsules or tablets are made from Cordyceps sinensis, Salviae miltiorrhizae, peach seeds, Mayuresh Rajaratnam, Andrzej Prystupa, Patrycja Lachowska-Kotowska, Wojciech Załuska, Rafał Filip. Herbal medicine for treatment and prevention of liver diseases

Gynostemmapentaphyllum, Schisandra chinensis and pollen pini, in which the Cordyceps sinensis can nourish the kidney and strengthen the essence, whereas Salviae miltiorrhizae and peach seeds can promote blood circulation to remove blood stasis. Gynostemma pentaphyllum can clear away heat and toxic materials, and Schisandra chinensis and pollen pini can enrich yin and tonify the spleen. Thus, the herb is efficient in strengthening the body resistance, reinforcing the deficiency, promoting blood circulation and removing blood stasis, and finally to effectively inhibit hepatic fibrosis [33]. To-date, no side-effects from the herb have been reported. The drug is currently undergoing clinical trials and seems promising for the treatment of liver fibrosis. In addition, preliminary studies indicate that fuzheng huayu has a good safety and tolerability profile with promising efficacy.

DISCUSSION AND CONCLUSION

Although the number of patients with liver diseases has been increasing steadily, the treatment outcomes are still considered poor. Herbal medicine has become a major contributor to the treatment of liver diseases. The increasing number of studies that are being undertaken on various herbal medicines show a positive sign on the future of drug development from herbs. The future of the treatment of liver diseases with herbal medicines depends on our understanding of each and every chemical constituent and their interactions with each other. Currently, a handful of herbal drugs, such as Silymarin, *Glycyrrhizaglabra*and Liv-52, have been studied thoroughly. These drugs and the other drugs mentioned in the presented study, have shown the scientific community their significance and possible usage as major treatment modalities for liver diseases.

Unlike the conventional drugs which are composed of known chemical constituents and are accurately quantified, herbal drugs are composed of a complex mixture of ingredients. Due to this complexity, the studies being conducted face major obstacles, with the major setback being the purifying of herbal medicines, and finding and quantifying each of their components. Currently, new techniques, such as high performance liquid chromatography, protein precipitation and microdialysis, are being used to pretreat and separate the chemical constituents.

However, studying the clinical effects of individual chemical constituents separately will be of little use for many reasons, among them the neutralization of harmful chemicals in the mixture by other chemicals, and the synergistic or inhibiting effects of chemicals on each other which provides a perfect combination *in vitro* for therapeutic purposes. Obtaining information only on the pharmacodynamics of herbal medicine on liver diseases provides insufficient details for developing drugs with similar effects. Factors such as metabolism, absorption, distribution and intrinsic concentration of the drug need to be known accurately to determine the dosage, duration of treatment, and the safety margin of each drug.

The number of patients seeking herbal therapy is growing exponentially. Thousands of years of traditional use can provide the guiding principles for the selection, preparation and application of herbal formulations. In order to be recognized as feasible substitutes for contemporary medicine, the same technical method of scientific and clinical substantiation must be practiced to demonstrate the safety and efficacy of herbal therapeutic products. The therapeutically significant molecules should be identified, isolated, purified and examined with carefully devised experiments, both experimentally and clinically, which will help the scientific community to elucidate the advantages and disadvantages of any particular herbal remedy. Currently, there are more than 1,000 herbal medicines with many active compounds which need thorough investigation to prove that they are hepatoprotective as mentioned in Chinese medicine, Ayurveda medicine, and in ancient Egyptian herbal treatment.

Looking back, it is obvious that a great deal of progress has already been made; the world is looking to the future with great anticipation and great expectations. Due to its culturally accepted nature, comparatively fewer side-effects, and the compatibility with the human body, herbal medicines are now increasing in demand in primary health care, not only in the developing world, but also in developed western countries (Tab. 1).

REFERENCES

- Dey P, Saha MR, Sen A. Hepatotoxicity and the present herbal hepatoprotective scenario. Int J Green Pharm. 2013; 7: 265–273.
- 2. Abeloff MD, et al. Abeloff's Clinical Oncology, 4th ed. Philadelphia, PA: Churchill Livingstone, An Imprint of Elsevier. 2008.
- Efferth T, Kaina B. Toxicities by Herbal Medicines with Emphasis to Traditional Chinese Medicine. Curr Drug Metab. 2011; 12(10): 989–996.
- 4. Hasan SS, Ahmed SI, Bukhari NI, Loon WC. Use of complementary and alternative medicine among patients with chronic diseases at outpatient clinics. Complement Ther Clin Pract. 2009; 15(3): 152–157.
- 5. Ansari JA. Therapeutic Approaches in Management of Drug-induced Hepatotoxicity. J Biol Sci. 2010; 10: 386–395.
- Kaplowitz N. Drug-induced liver disorders: implications for drug development and regulation. Drug Saf 2001; 24: 483–490.
- Mueller S, Millonig G, Seitz HK. Alcoholic liver disease and hepatitis C: a frequently underestimated combination. World J Gastroenterol. 2009; 15(28): 3462–3471.
- B.Duryee MJ, Klassen LW, Thiele GM, Immunological response in alcoholic liver disease. World J Gastroenterol. 2007; 13(37): 4938–4946.
- Jou J, Choi SS, Diehl AM. Mechanisms of disease progression in nonalcoholic fatty liver disease. Semin Liver Dis. 2008; 28(4): 370–379.
- Dunn W, Jamil LH, Brown LS, Wiesner RH, Kim WR, Menon KV, et al. MELD accurately predicts mortality in patients with alcoholic hepatitis. Hepatology 2005; 41(2): 353–358.
- 11. Beasley RP, Hwang L-Y: Overview on the epidemiology of hepatocellularcarcinoma. 532 In: Hollinger FB, Lemon SM, Lemon SM, Margolis HS, (eds). Viral Hepatitis and Liver Disease. Williams and Wilkins, Baltimore, 1991.
- 12. Wasley A, Grytdal S, Gallagher K. Surveillance for acute viral hepatitis--United States, 2006. MMWR Surveill Summ. 2008; 57(2): 1–24.
- Samudram P, Rajeshwari H, Vasuki R, Geetha A, Sathiya moorthi P. Hepatoprotective activity of Bi-herbal ethanolic extract on CCl4 induced hepatic damage in rats. Afr J Biochem Res. 2008; 2(2): 61–65.
- Wei Y, Rector RS, Thyfault JP, Ibdah JA. Nonalcoholic fatty liver disease and mitochondrial dysfunction. World J Gastroenterol. 2008; 14(2): 193–199.
- Hye-Lin Ha, Hye-Jun Shin, Mark A Feitelson, Dae-Yeul Yu. Oxidative stress and antioxidants in hepatic pathogenesis. World J Gastroenterol. 2010; 16(48): 6035–6043.
- 16. Luper S. A review of plants used in the treatment of liver disease: part 1. Altern Med Rev. 1998; 3: 410–21.
- 17. Pradhan SC, Girish C. Hepatoprotective herbal drug, silymarin from experimental pharmacology to clinical medicine. Indian J Med Res. 2006; 124(5): 491–504.
- Féher J, Lengyel G. Silymarin in the prevention and treatment of liver diseases and primary liver cancer. Curr Pharm Biotechnol. 2012; 13(1): 210–217.
- Agency for Healthcare Research and Quality. Milk thistle: effects on liver disease and cirrhosis and clinical adverse effects. Summary, evidence report/technology assessment: number 21, September 2000.

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Table 1. Herbs that are hepatoprotective

Common name	Scientific name	Ingredients	Liver pathologies treated
Green tea	Camellia sinensis	Leaves and seeds of Camellia sinensis	Acute liver injury NAFLD (Non-alcoholic fathyliver disease) HCV Infection
Silymarin	Silybum marianum	Milk thisle seeds	Oxidative stress. Inflammation and fibrosis Alcohol-induced cirrhosis. Mushroom poisoning Viral hepatitis
Liv-52	Combination of Capparis spinosa, C. intybus, S. nigrum, Terminalia arjuna, Cassia occidentalis, Achillea millefolium, Tamarix gallica	Mixture of leaves, roots, flowers, fruits and seeds of Capers, blue daisy, Black Nightshade, Arjuna, Negro Coffee, Yarrow, and Tamarisk	Jaundice, Alcoholic liver disease, Viral hepatitis, Liver cirrhosis,
Hepatomed	Combination of P. kurroa, A. paniculata, Eclipta alba, C. intybus, S. nigrum, Phyllanthus niruri	A mixture of Rhizomes, roots, leaves of kutki, Creat, false daisy, blue daisy, Black Nightshade and stonebreaker.	Jaundice Alcoholic liver disease, Cirrhotic liver disease
HD 03	Combination of C. intybus, S. nigrum, P. kurroa, A. paniculata, Tephrosia purpurea)	Mixture of Flowers, Rhizomes, Leaves and roots of kutki, Creat, blue daisy, Black Nightshade and Wild indigo	Jaundice Alcoholic liver disease, Viral hepatitis
Kamilari	Combination of Thespesia populnea, Elettari cardamomum, Zingiber officinale, Glycyrrhiza glabra	Mixture of Leaves, roots, barks, fruits, seed pods and rhizome of Portia Tree, Green cardamom, Ginger and Licorice	Jaundice Alcoholic liver disease Viral hepatitis Liver cirrhosis
Livfit	Combination of E. alba, P. niruri, C. intybus, Rheum emodi, Tephrosia purpurea	Mixture of Leaves, roots, barks, and flowers of false daisy, stonebreaker, blue daisy, Himalayan rhubarb and Wild indigo	Oxidative and Toxic Liver injury
Stimuliv	Combination of A. paniculata, P. niruri, E. alba, P. kurroa, Boerhaavia diffusa, Azadirachtica indica, Berberis aristata, Ipomoea turpethum, T. purpurea	Mixture of Leaves, roots, barks, and flowers of False daisy, Creat, stonebreaker, kutki, red spiderling, Indian Lilac, Tree Turmeric, St. Thomas lidpod and wild indigo	Viral Hepatitis, Hepatomegaly
Himoliv	Combination of P. kurroa, B. diffusa, Tinospora cordifolia, A. paniculata, P. emblica	Mixture of Leaves, roots, barks, and flowers of Creat, red spiderling, Giloy, kutki, and emblic	hepatic dysfunction
Tefroliv	Combination of A. paniculata, E. alba, Ocimum sanctum, P. niruri, P. kurroa, Piper longum, S. nigrum, Tephrosia purpurea, Terminalia chebula	Mixture of Leaves, roots, barks, fruits, seed pods and rhizome of Creat, kutki, stonebreaker, false daisy, holy basil, Indian long pepper, Black Nightshade, Wild indigo and Yellow Myrobalan	Acute and chronic hepatitis Alcoholic liver damage Cirrhosis Fatty liver and drug-induced hepato toxicity
Wolfberry	Lycii fructus	Dried berries and root bark of Lycii fructus	Hepatoma NAFLD
Garlic	Allium sativum	Garlic cloves	NAFLD Steatosis, Fibrosis Chronic liver injury
Resveratrol		red grapes and roots of Japanese knotweed	Liver inflammation. Oxidative stress
Amla	Emblica officinalis		Toxic-induced liver inflammation
Betel	Piper betle		Oxidative stress Liver infection
Mahanimba	Ailanthus excelsa		Chemically- induced liver injury
Alstonia scholaris		Milky juice and flowers of Alstonia	Chemical injury to the liver
Bacopa monnieri		Leaves	Ethanol induced liver injury
Berberis tinctoria			Oxidative stress of the liver
Boerhaavia diffusa		leaves	Oxidative stress of the liver
Glycyrrhiza glabra		Root extract	Cirrhosis Fibrosis Chronic viral hepatitis B and C
Bitter leaf	Vernonia amygdalina	Leaves	Chemical liver injury
Fennel	Foeniculum vulgare	Stems of foeniculum vulgare	Oxidative stress of the liver Bacterial and viral infections Anti-inflammatory, acute hepatotoxicity
FuzhengHuayu (FZHY)	A combination of Radix salvia miltiorrhizae, Cordyceps (Chongcao), Semen persicae, Gynostemma pentaphyllum (Jiaogulan), Pollen pini (Songhuafen), Fructus schisandrae chinensis	Roots, dry ripe seeds, leaves and berries of the mixture.	Liver Fibrosis
Curcumin	Curcuma longa		Acute liver damage by chemicals, e.g. Ethanol, CCl4, Dimethylnitrosamines
Scutellaria baicalensis		Dried roots	Hepatic fibrosis Carcinoma
Five flavor berry	Schisandra chinensis	berries	chemical or viral hepatitis
Red sage	Salvia miltiorrhiza	roots	Liver fibrosis Chronic hepatitis
membranous milk-vetch root	Astragalus membranaceus	roots	Viral hepatitis

- 20. Saller R, Meier R, Brignoli R. The use of silymarin in the treatment of liver diseases. Drugs. 2001; 61: 2035–2063.
- 21. vanRossum TG, Vulto AG, de Man RA, Brouwer JT, Schalm SW. Glycyrrhizin as a potential treatment for chronic hepatitis C. Alimentary Pharmacology & Therapeutics 2003; 12(3): 199–205. doi:10.1046/j.1365– 2036.1998.00309.x. PMID 9570253.
- 22. Charak S. Vimanasthan. Chapter I (2,3). Translated by P.V. Sharma, ChaukhambaOrientalia Publishers, Varanasi, 1981.p. 305.
- 23. Vyas KJ. Treatment of Hepatopathy in Children with a Combination of Capparis Spinosa and Other Indian Indigenous Drugs. Children Ward, General Hospital, Junagadh, Gujarat. Medical Digest 1961; 29(3): 105–112.
- 24. Warrier PK, Nambiar VPK, Ramankutty C. Indian Medicinal 346 Plants A compendium of 500 species. Orient Longman India. 1994; 1: 349–351.
- 25. Ciesek S, Von Hahn T, Colpitts ChC, Schang LM, Friesland M, Steinmann J, Manns MP, Ott M, Wedemeyer H, Meuleman P, Pietschmann T, Steinmann E. The Green Tea Polyphenol Epigallocatechin-3-Gallate (EGCG) Inhibits Hepatitis C Virus (HCV) Entry. Sandra Ciesek, Thomas von Hahn, Che C. Colpitts, Luis M Schang, Martina Friesland, Jörg Steinmann, Michael P. Manns, Michael Ott, HeinerWedemeyer, Philip Meuleman, Thomas Pietschmann and Eike Steinmann. Hepatology. 2011. http://onlinelibrary.wiley.com/doi/10.1002/hep.24610/abstract (access: 2014.11.05). doi: 10.1002/hep.24610.

- 26. Ahmad N, Mukhtar H. Green tea polyphenols and cancer; bio-364 logic mechanism and practical implications. Nutr Rev. 1999; 57: 365, 378–383.
- 27. Jin X, Zheng RH, Li YM. Green tea consumption and liver disease: a systematic review. Liver Int. 2008; 28(7): 990–996.
 28. Baics MC, Latha MS, Bratacting activity of Cheurenbing clabra Linn, on
- Rajesh MG, Latha MS. Protective activity of Glycyrrhiza glabra Linn. on carbon tetrachloride-induced peroxidative damage. Indian J Pharmacol. 2004; 36: 284–287.
- 29. Sato H, Goto W, Yamamura J, Kurokawa M, Kageyama S, Takahara T, Watanabe A, Shiraki K. Therapeutic basis of glycyrrhizin on chronic hepatitis B. Antiviral Res. 1996 May; 30(2–3): 171–177. doi:10.1016/0166-3542(96)00942-4. PMID 8783808.
- Strandberg TE, Andersson S, Jarvenpaa AL, et al. Preterm birth and licorice consumption during pregnancy. Am J Epidemiol. 2002;156(9): 803–805.
- Arase Y, Ikeda K, Murashima N, et al. The long term efficacy of glycyrrhizin in chronic hepatitis C patients. Cancer 1997; 79(8): 1494– 1500.
- 32. Liu P, Liu C, Chen GC, Hu YY, Xu LM, Lv P, Yang JL, Yan RM, Ji Q, Chu F. Effect of Fuzheng Huayu 319 recipe on serological parameters of fibrosis in treating chronic hepatitis B. Zhongguo Zhong Xi Yi Jie He Za Zhi. 1996; 16: 588–592.
- 33. Cui AL. Treatment of 54 cases of active hepatocirrhosis with lamivudine combined with Fu Zheng Hua Yu capsule. Journal of China Pharmaceutical. 2012; 21: 74–75.