Biological Times

Volume No. 2 | Issue No. 8 | Pages23-25

Botanicals Used for the Treatment of Liver Diseases

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ABSTRACT

Liver disease is characterized by hepatic inflammation or injury that hampers its physiological functioning. Throughout the course of history, practitioners of the herbalist tradition have utilized various botanical substances in order to protection and restore the health of the liver. Traditional liver treatments involve the utilization of natural components, such as various vegetables, fruits, plant extracts and herbs. The presented treatment demonstrates a wide range of clinical applications for diverse conditions, such as toxic hepatitis, fatty liver, cirrhosis, ischemic injury, radiation toxicity, and viral hepatitis. Beneficial properties encompassing antioxidant, anti-lipid per-oxidative, anti-fibrotic, anti-inflammatory, immunomodulatory and liver-regenerative influences are evidenced by the available research. There exists a multitude of natural compounds that possess the ability to precaution against and provide therapeutic benefits for hepatic ailments. Our focus revolves around the investigation and evaluation of the remarkable properties exhibited by natural products in order to ascertain their efficacy as prospective treatments for liver diseases.

Introduction:

Liver disease is a widely observed health concern, exerting its influence on over 10% of the global population. Major health conditions, such as chronic hepatitis, fatty liver disease caused by alcohol consumption, liver fibrosis, cirrhosis, and hepatocellular carcinoma, have garnered notable attention from experts. Individuals diagnosed with either alcoholism or viral hepatitis face an increased susceptibility to experiencing liver cell damage and developing cirrhosis. Regrettably, certain individuals may experience the development of HCC, a terminal and untreatable form of cancer. Although there are treatment choices available for the majority of liver diseases, certain conditions are still incurable, and drug resistance is prevalent. Create new and inventive approaches to improve outcomes in treatments. Roughly half of the pharmaceutical agents employed in liver therapy either originate from natural sources or have undergone modifications derived from them. Secondary metabolites are synthesized by organisms as a means of protecting themselves against potential threats. For countless generations, a diverse array of plant-based natural products, abundant with numerous active components, has been extensively utilized by various individuals. These healthcare products are utilized globally. Natural products provide a wide range of chemical compounds that have various biological effects, presenting potential alternatives for medical treatments. Approximately 50% of the pharmaceutical agents used in liver therapy are either derived from natural sources or have been modified based on their properties. Natural products are becoming increasingly acknowledged worldwide for their advantages in improving health and preventing diseases. They are currently functioning to treat both treatable and untreatable diseases, as both conventional and alternative therapies (1).

The global examination of natural products is essential in order to develop novel therapeutic strategies for liver disease. Approximately a quarter of all prescribed medications globally are derived from plants with a significant number of anti-infectious drugs currently in use or being researched having natural sources. Around 65% of individuals in the US and Europe suffering from liver disease resort to using herbal remedies. Pharmaceutical scientists have been driven by the exceptional therapeutic effectiveness of natural products to investigate innovative methodologies in drug discovery and development. The ease of accessing herbal medicines without the complication inherent in the intricate process of pharmaceutical production has generated an increased level of fascination. The application of natural substances in the management of hepatic disorders has experienced significant proliferation in both recognition and implementation, thus establishing them as a promising global therapeutic approach for diverse pathological liver ailments. Various beneficial botanical compounds have been identified, such as *glycyrrhizin* for the management of chronic viral hepatitis, ellagic acid for the mitigation of fibrosis, and phyllanthin for the alleviation of chronic hepatitis B. These compounds display discernable properties and functionalities, offering inherent advantages or potential toxicity, particularly in their capacity as antioxidants or hepatoprotective agents (2).

2. Various components of plants are utilized in the healing process of liver disorders

Figure 1: Plant Parts used for healing process.

3. Three main groups of plant compounds in a basic classification

(i) Phenolic compounds arise from the transformation of basic sugars and encompass benzene rings affixed with an assortment of hydrogen and oxygen groups.

(ii) Phenolic compounds originate from the enzymatic conversion of monosaccharides and involve the presence of benzene rings coupled with various hydroxyl and carbonyl functional groups.

(iii) Alkaloids, chemical compounds known for their incorporation of nitrogen, occupy a significant position in the realm of scientific inquiry. The extraction of bioactive compounds from natural sources presents a formidable challenge due to the intricate chemistry and intricate processes associated with the isolation procedure.

4. Fundamental elements of liver disease

Liver diseases are a notable problem worldwide, comprising a range of conditions that can range from minor changes in the liver's structure to serious and potentially deadly illnesses. Some examples of these include inborn metabolic disorders, cancers that have metastasized, alcohol-related liver damage, and viral infection affecting the liver and drug-induced liver toxicityIt perpetuates its significant impact on morbidity and mortality rates, consequently resulting in noteworthy fiscal and societal burdens. The utilization of natural phytochemicals, encompassing those derived from food, for the purpose of augmenting health outcomes, has experienced a notable surge in prominence. These naturally occurring substances show promise in enhancing liver health with safety and efficacy. Researchers are currently engaged in the active pursuit of lead compounds possessing designated structures and pharmacological properties, frequently obtaining them from

To cite this article: Ahmad A, T Iqbal, S Altaf, A Akram & H Riaz 2023.Botanicals Used for the Treatment of Liver Diseases. Biological Times, 2(8): 23-25.

natural origins. Figure 1 displays the various types of plants that are utilized for treating liver disorders (3).

5. Botanical example utilized in the therapeutic treatment of hepatic disorders

(i). *Wogonin*

Wogonin, a monoflavonoid obtained from Scutellaria radix is commonly found in Asian traditional medicine for the management of inflammation and hepatitis. *Wogonin* has demonstrated its capability to inhibit the release of hepatitis B surface antigen in cell cultures, thus highlighting its potential as a pharmacological agent for the treatment of hepatitis B virus infection. The plasma samples from ducks subjected to *wogonin* treatment exhibited a significant reduction in hepatitis B surface antigen levels which resembled to a discernible enhancement in liver histopathology. The potential of *wogonin* in reducing the presence of hepatitis B surface antigen was confirmed through immunohistological staining of livers from mice transgenic for Hepatitis B Virus (4).

(ii). *Curcumin*

The indigenous population of India employed this remedy to ameliorate a diverse array of ailments including rheumatism, bodily afflictions, dermatological ailments, gastrointestinal disturbances, pyrexia, hepatic dysfunctions, urological impairments, and inflammatory conditions. The above-mentioned remedy was widely perceived as efficacious in treating various ailments, including but not limited to diarrhea, parasites, digestive disorders, skin abnormalities, amenorrhea, and abdominal discomfort. Curcumin is progressively gaining recognition due to its capacity to safely and effectively address various disorders. The efficacy of the substance in addressing hepatic disorders. Curcumin has the potential to decrease liver damage and partially reverse cirrhosis caused by CCl4 (5).

(iii). *Glycyrrhizin*

Licorice root possesses valuable medicinal properties and is commonly deployed in the treatment of chronic hepatitis. This naturally-derived triterpene is widely utilized in China's medical sites to not only protection the liver but also effectively report tumors. *Glycyrrhizin* provided protection to the immune system decreased inflammation and effectively decreased sodium and water retention. The investigation analyzes the impact of *Glycyrrhizin* on the expression of MMP-9. The study proposes that *glycyrrhizin* effectively decreases the severity of abrupt liver damage by blocking the MMP-9 enzyme. The efficacy of *Glycyrrhizin* in mitigating liver cell apoptosis was observed via the inhibition of caspase-3 enzymatic activity and the preservation of mitochondrial cytochrome C retention. *Glycyrrhizin* exerts inhibitory effects on the release of tumor necrosis factor-a, suppresses myeloperoxidase activity, and impedes the translocation of nuclear factor-kappaB. These multifaceted mechanisms collectively contribute to the mitigating of inflammation. *Glycyrrhizin* has the potential to augment liver regeneration through the upregulation of cell nuclear antigen expression, particularly in instances of damage induced by lipopolysaccharide (LPS). *Glycyrrhizin* possesses the capability to offer hepatoprotective effects during hepato biliary surgery. *Glycyrrhizin* demonstrates efficacy in liver protection against hepatitis through its regulatory influence on the activation of inducible nitric oxide synthase (iNOS), thereby mitigating hepatocyte degeneration (6).

(iv). *Resveratrol*

Resveratrol, a phytochemical found abundantly in berries, grapes, and wine, exhibits considerable potential in the therapeutic management of hepatic disorders. Multiple research studies have substantiated the positive impact of resveratrol on hepatic protection. *Resveratrol* has the ability to maintain the liver by inhibiting detrimental molecules and immune signals enhancing antioxidants and defense mechanisms controlling disease pathways. *Resveratrol* shows promise in promoting long life and fighting against chronic illnesses as it possesses beneficial properties in terms of anti-aging preventing cancer reducing inflammation and acting as an antioxidant. The gene expression of TNF-α and IL-6, as well as the recruitment of Kupffer cells in the liver following injury, are attenuated by the administration of *Resveratrol*.Evidence supports the efficacious utilization of resveratrol for the management of cholestatic liver injury. Histopathological, immune histochemical, and apoptotic analyses were performed in order to assess the effect of resveratrol on liver tissue after exposure to CCl4. The compound known as resveratrol exhibits hepatoprotective qualities against injuries induced by DMN, thereby indicating its potential utility in the management and prophylaxis of liver fibrosis and cirrhosis (7).

(v). *Silymarin*

Milk thistle has been extensively investigated in the context of liver disease, thus establishing its status as the most extensively studied botanical agent in this domain. Milk thistle extracts have long been acknowledged for their capacity to promote hepatic well-being and effectively mitigate or even reverse hepatic impairment attributed to pharmaceutical agents or inherent elements. Silymarin, derived from the milk thistle plant, safeguards the liver in both clinical and experimental environments. This compound functions as an antioxidant by inhibiting the production of detrimental free radicals and lipid peroxidation. Moreover, it possesses antifibrotic characteristics and the ability to hinder the attachment of toxins to liver cell membranes. Silymarin provides liver protection in animals against different factors such as acetaminophen, radiation, alcohol, and Amanita phalloides (8).

(vi). *Naringenin*

Naringenin a flavanone compound is found in both grapefruits and tomatoes and has been implicated in possessing a diverse array of therapeutic characteristics. Naringenin, when administered orally at daily dosages of 20 and 50 mg/kg, exhibited significant protective effects against the reduction in body and liver weights induced by DMN. Furthermore, it successfully hindered the elevation in serum levels of alanine transaminase, aspartate transaminase, alkaline phosphatase, and bilirubin. Naringenin has been shown to confer hepatoprotective properties and mitigate fibrotic changes in the context of liver injury induced by dimethylnitrosamine (DMN). In addition, it displayed antioxidant characteristics and effectively mitigated liver lipid peroxidation in response to oxytetracycline-induced oxidative stress (9).

(vii). *Geniposide*

Geniposide, which is present in Gardenia fruit, is effective in the treatment of hyperlipidemia and fatty liver. Contemporary scientific investigations have recently divulged noteworthy empirical data indicating the potential utility of geniposide as a valuable intervention in mitigating hepatic fibrosis. In response to geniposide, the expression of CYP2E1 was diminished, whereas the expression of PPARα was augmented. An upregulation of superoxide dismutase within the liver, coupled with a downregulation of malondialdehyde, has been associated with multiple advantageous outcomes. Geniposide has been discovered to have the ability to prevent the buildup of liver fat in rats that were fed a high-fat diet in research studies. There is a belief that the reason for this protection is the antioxidant properties it possesses or its capacity to control adipocytokines and PPARα expression. Genipin has anti-inflammatory properties and hinders the formation of blood vessels (10).

(viii). *Rhein*

Rhein, which is obtained from rhubarb, restricts the growth of cancer cells in humans. Rhein inhibits the growth of cells and induces cell death by influencing the c-Myc gene and caspase pathway. Additionally, Rhein supports the treatment of fatty liver by decreasing energy consumption, controlling fat production, and adjusting the immune system. reduce oxidative stress and inflammation. Rhein is anticipated to become a valuable treatment option for hepatocellular carcinoma in the future (11).

6. Processes of extracting and separating plant materials

The botanical substances were air-dried for a week without direct sunlight and subsequently crushed into a fine powder. The plants were dried using air and turned into powder, measuring 15 g. The plants were immersed twice in 150 ml of 80% ethanol. This task was completed under normal room temperature conditions. The ethanol solutions were subjected to filtration followed by concentration under reduced pressure at a temperature of 40°C in order to obtain the extracts. In a similar manner, we mixed 15 grams of dried powdered plants with 150 milliliters of deionized water in order to create aqueous extracts. The composite underwent thermal exposure at a temperature of 90 °C for duration of 30 minutes, followed by a subsequent cooling process to ambient temperature over a span of 2 hours. The solutions underwent thorough filtration and were subsequently stored in a refrigeration unit at a specifically controlled temperature of -20°C over the course of 24 hours. They were subjected to freeze-drying for duration of three days. The ethanol and aqueous dry extracts of each plant were fractionated using the SPE method (12).

Figure 2: Plants commonly used in the therapeutic management of hepatic disorders

7. Conclusion

There has been substantial evidence supporting the clinical effectiveness and safety of various botanical interventions in the management of liver disease. Plants are acknowledged for their capacity to provide advantageous outcomes in the management of diverse hepatic ailments, encompassing toxic hepatitis, fatty liver disease, cirrhosis, ischemic injury, radiation toxicity, and viral hepatitis. The popularity of plant medicines is increasing for treating diseases,

and efforts are made to understand their mechanism. Many with liver disease turn to botanicals for treatment. To identify the true benefits of these agents, future efforts must incorporate advanced methodologies. The active components must be studied in experiments and placebo-controlled studies to apply them in clinical settings. There are many lead molecules with potential for future hepatoprotective medications. It's important to study herbals and their active components for better treatment of chronic liver diseases. These studies aim to find new antifibrotic and anti-inflammatory properties. There is a need for research in experimental and clinical settings to verify herbal drug effectiveness. Using scientific testing in accordance with evidence-based medicine principles will enhance the credibility of herbal medicine as a valid treatment approach.

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