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Herbal Technology For Liver Disease

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ABSTRACT :

One of the most dangerous health issues in the world is liver disease, which can be brought on by drugs, alcohol, viral infections, and exposure to harmful substances. Damage to the liver can result in serious health issues since it is essential for metabolism, detoxification, and general bodily functions. Even though there are many synthetic medications available in modern medicine to treat liver problems, many of these treatments have drawbacks such adverse effects, high prices, and poor efficacy in long-term therapy. In this regard, herbal technology has become a viable strategy for treating and preventing liver disorders.

The scientific investigation, extraction, formulation, and application of medicinal plants with hepatoprotective qualities are all part of herbal technology. Flavonoids, alkaloids, tannins, and phenolics are examples of bioactive substances found in many herbs that have detoxifying, anti-inflammatory, and antioxidant properties. Phyllanthus niruri (Bhumyamalaki), Silybum marianum (Milk Thistle), Andrographis paniculata (Kalmegh), Curcuma longa (Turmeric), and Glycyrrhiza glabra (Licorice) are a few examples of plants that have demonstrated considerable promise in preserving liver cells, promoting regeneration, and boosting liver function.

In order to boost the bioavailability of active plant chemicals, recent developments in herbal technology concentrate on enhancing extraction techniques, standardizing formulations, and creating innovative drug delivery systems. The effectiveness of herbal remedies in hepatoprotection has been reinforced by scientific validation through preclinical and clinical research. Additionally, combining ancient knowledge with contemporary science offers a safe and sustainable method of managing liver illness.

To sum up, herbal technology provides a safer, more economical, and natural substitute for traditional medications for liver disorders. To fully realize the therapeutic potential of medicinal plants and encourage their acceptability in contemporary healthcare systems, more research, standardization, and quality control are necessary.

Keywords: Hepatoprotective agents; Medicinal plants; Phytochemicals; Antioxidants;

1.Introduction

Insulin resistance, obesity, and diabetes mellitus are intimately linked to non-alcoholic fatty liver disease (NAFLD), a hepatic manifestation of the metabolic syndrome [1]. The pathophysiology of NAFLD is still poorly understood, and there are currently no viable treatments, despite the fact that it poses a serious threat to public health [2].

Recent research over the past 20 years suggests that gut bacteria may play a part in the development of non-alcoholic fatty liver disease [3]. Increased intestinal permeability, endogenous ethanol production, and choline insufficiency are all consequences of small intestine bacterial overgrowth, which is frequently observed in NAFLD patients [4,5,6]. Additionally, the gut microbiota stimulates de novo hepatic lipogenesis and improves fat storage via controlling lipoprotein lipase activity by promoting the absorption of monosaccharides and short chain fatty acids through fermentation [7]. Low-grade, chronic inflammation is commonly linked to NAFLD [9], and lipopolysaccharide (LPS), a significant component of Gram-negative bacteria's cell walls, is known to be highly effective at inducing inflammation [10]. A small amount of LPS from the gut microbiota can cause a number of inflammatory processes when it binds to CD14 and toll-like receptor 4 on the surface of immune cells [11,12], which further adds to the pathophysiology of NAFLD. As a result, probiotics, prebiotics, and antibiotics are being tested for the treatment or prevention of NAFLD [14,15,16], making the gut microbiota a novel target for potential therapies [13].

The most prevalent cause of malignant biliary obstruction (MBO) is pancreatic cancer, but it can also be brought on by other pancreatic tumors, ampullary cancer, cholangio-carcinoma, gallbladder cancer, malignant lymphadenopathy, or metastatic lesions [17]. Patients with MBO typically present late in their course, have either locally widespread or metastatic disease, and have a very poor prognosis; surgery is the only treatment option available to them [18]. Palliative care, which aims to alleviate symptoms and enhance quality of life, is all that remains [19]. There are three ways to palliate MBO: endoscopic stent implantation, percutaneous stent insertion, and surgical bypass.

One benefit of surgical palliation, which is accomplished by creating a hepatic jejunostomy, is that it allows for the simultaneous palliation of gastric and biliary outlet obstruction and pain management in one setting. Biliary blockage is typically palliated for the rest of one's life without the need for additional

treatments. Surgical palliation has the drawback of increased mortality, particularly in patients with advanced illness [20]. Palliation of hilar cholangio-carcinoma rarely involves surgery. Compared to distal biliary blockage, hilar obstruction has a poorer success rate for jaundice treatment, a greater complication rate, and a higher likelihood of jaundice recurrence [21].

Natural or self therapies (NST) techniques, such as relaxation, meditation, prayer, hypnosis, biofeedback, or physical strengthening, and exogenous chemicals, such as herbal supplements, vitamins, or plant extract, comprise the two main categories of complementary and alternative medicine (CAM) therapies [22]. Herbal medicine was first used in ancient China during the Xia dynasty and in India during the Vedic era [23]. The gap between Western and Eastern medicine seemed to widen with the advent of the natural sciences and evidence-based medicine, with CAM growing in popularity over time in Western nations (from 34% of the population in 1990 to 48% in 2004) [24]. Because of its long-lasting curative impact, ease of availability, natural healing method, and few side effects, the ancient system of herbal medicine is being revitalized by daily practice, and as a result, herbal medicines are becoming more and more popular worldwide [25].

Hepatic steatosis is the definition of non-alcoholic fatty liver disease (NAFLD), which does not include extensive alcohol consumption, steatogenic medications, or genetic abnormalities [26]. Steatosis is one of its histological characteristics [27]. NAFLD affects about 25% of individuals globally [28], and its incidence is still rising [29] despite known risk factors such diabetes, obesity, age, gender, and ethnicity. NAFLD increases the risk of cancer, diabetes, coronary artery disease, liver-related fatalities, and all-cause mortality [30].

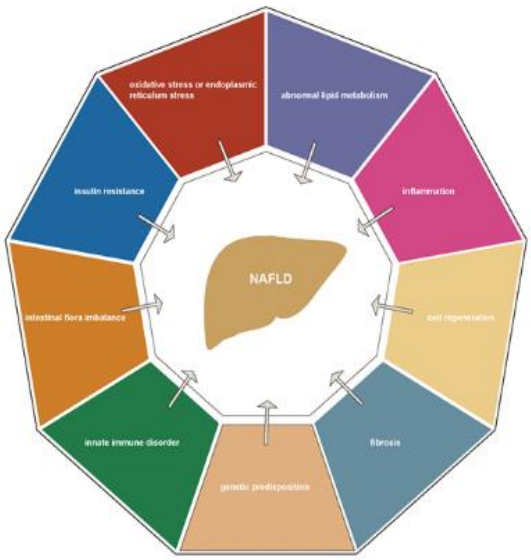


FIGURE 1
Current pathogenesis of NAFLD.

2.Materials and methods

2.1 Animal and Experimental Protocol

Statement of ethics The Shanghai University of Traditional Chinese Medicine's Animal Ethics Committee authorized all of the study's experimental protocols (Approval No. SCXK 2003-0003). The Shanghai University of Traditional Chinese Medicine's (Shanghai, China) Guidelines for Animal Experimentation were followed when caring for and using animals, and every attempt was made to reduce the number of animals and their suffering [31]. Twenty-six male Sprague-Dawley rats were grown in a particular pathogen-free barrier system at the Shanghai Traditional Chinese Medicine University's Laboratory Animal Center after being acquired from Shanghai Laboratory Animal Co. Ltd., China. Following acclimation, the rats were split into two groups: a control group (n = 5) was fed normal chow (NC) and a group (n = 21) was fed an HFD (w/w, 87.5% normal chow, 10% lard, 2% cholesterol, and 0.5% sodium cholate). HFD-fed rats were split into three subgroups at random after six weeks of the diet (n = 7). In addition to the HFD diet, two subgroups received intragastric administration of CHF (Qushi Huayu Fang) at high (H) and low (L) dosages (0.93 g/100 g body weight and 0.47 g/100 g body weight, respectively). The third subgroup continued to follow the HFD without receiving any additional care.

2.2 PCR-DGGE and multivariate analysis of the 16S rRNA gene V3 region

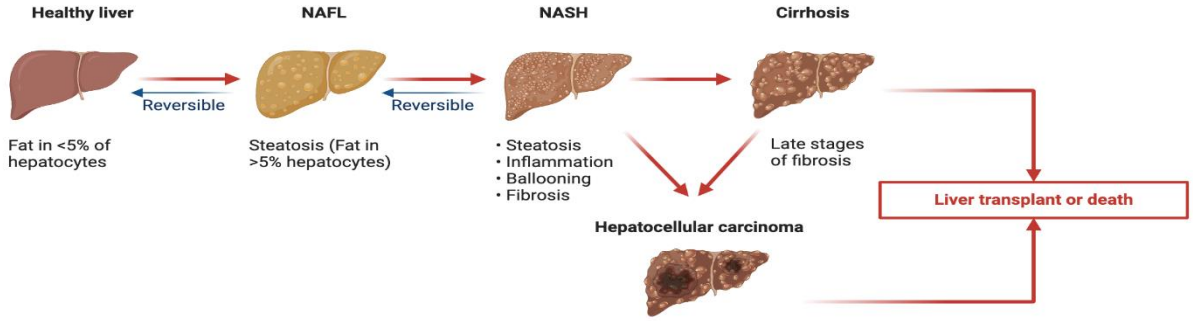
Each fecal sample had its DNA extracted using the bead-beating technique [32]. The 16S rRNA gene V3 region was amplified from each DNA sample using hot-start touchdown PCR using bacterial universal primers P2 (5 ATTACCGCGGCTGCTGG-3) and P3 (5-CGCCCGCCGCGCGCGGC GGGCGGGGCGGGGGCACGGGGGGCCTACGGGAGGCAGCAG-3) [33]. The DGGE denaturing gradient of 30–54% (7 M urea and 40% deionized formamide were thought to represent the 100% denaturant). PCR amplification processes, DGGE analysis, and phylogenetic identification of significant

bands were carried out as previously described [34]. With accession numbers JF729214–JF729235, the sequences extracted from significant DGGE bands have been added to GenBank (http://www.ncbi.nlm.nih.gov/Genbank/).

3.Historical Background

Every culture has investigated and employed plants for therapeutic purposes. Herbs may have been used medicinally for almost 60,000 years, according to the discovery of various plants with therapeutic qualities in a Neanderthal tomb in Iraq. [35] The earliest records originate from China, when around 3000 BC, Emperor Shen Nung assembled Pen Tsao, often known as Chinese Materia Medica or The Great Herbal. Numerous editions of this book have been published, and many of the thousands of medications it describes are still in use in China. [36]

The earliest surviving medical literature is the Ebers Papyrus, which was found in an Egyptian tomb in 1862 and dates to 1550 BC. It has hundreds of herbal medicines, such as a decoction of cumin, goose fat, and milk for numerous stomach issues and castor seeds and senna for constipation. 6 Over 200 plant-derived medications, including castor oil and senna as laxatives, are recorded in a thousand clay tablets from the 7th century BC. [37]



4.Adverse hepatic reactions from herbal drugs

Conventional medications are known to cause hepatic damage, and most doctors are aware of this. A new publication [38] provides an update on the role of herbal remedies in adverse liver responses. Acute and chronic hepatitis, cholestasis, drug-induced autoimmunity, vascular lesions, and even liver failure have all been linked to a number of herbal remedies.

4.1 Chinese herbs

Chinese remedies frequently comprise a variety of plants or components, making it very challenging to identify the causative compounds. Because of its calming properties, Jin BuHuan (Lypocodium serratum) has been used extensively in the United States. Depending on the period of consumption, case reports have shown both acute and chronic hepatitis with localized necrosis and moderate portal fibrosis [39,40]. Ephedrin-containing Ma-Huang (Ephedra sp.) was marketed in the United States to aid in weight loss treatments. After just three weeks of using Ma-Huang, a patient experienced acute hepatitis with increased antinuclear and smooth muscle antibodies [41]. A 57-year-old lady who took "Qialbai Biyan Pian," which contains seven different herbs, including Herba senecionis and Herba ephedra, was reported to have acute liver failure that required liver transplantation [42].

4.2 Pyrrolizidine alkaloids

Hepatotoxicity may be dose-dependent in plants that contain pyrrolizidine alkaloids. Although the first historical accounts were from South Africa [43], Jamaica [44], India [45], and Afghanistan [46], Arizona [47,48] and Europe [49,50] also reported cases of pyrrolizidine alkaloid overdose causing liver injury. Veno-occlusive disease (VOD), a non-thrombotic obliteration of the lumen of terminal centrilobular hepatic veins that resembles Budd Chiari syndrome, is the usual liver damage caused by pyrrolizidine alkaloids. Because they are biotransformed into pyrrole derivatives by cytochrome P450s, pyrrolizidine alkaloids isolated from heliotropium, senecio, symphytum (comfrey), and crotalaria species exhibit unique toxicity [51]. Drugs that stimulate cytochrome P450 3A4, such as phenobarbital, can increase toxicity.

4.3 Germander

Germander (Teucrium chamaedrys) was authorized in France in 1986 as a remedy for moderate diarrhea and obesity [52]. The French Pharmacovigilance Authorities were subsequently notified of several cases of acute, chronic, and even fulminant hepatitis linked to Germander [53,54]. Hepatitis was cytolytic on histology, and cirrhosis developed in certain patients whose liver disease progressed more slowly [53,55]. After unintentional reexposure, a number of patients experienced relapses [55]. According to Fau et al., cytochrome P450 3A produces furano neo-clerodane diterpenoids, which mediate the toxicity [56]. Teucrium polium consumption was linked to fulminant liver failure in another study [57].

5.Popular Herbal Remedies For Liver Disease

The range of liver dysfunctions brought on by allopathic medications and the insufficiency of herbs used to treat liver disorders are shown to be considerable. As a result, there is an increasing emphasis on using systematic research methods and assessing the scientific foundation of traditional herbal remedies that are said to have hepatoprotective properties [58]. Numerous herbal medications are used to treat the primary liver illnesses listed above. The main herbal medications that have made the most contributions to the prevention of liver illnesses are covered in the study that is being presented.

5.1 Silymarin

A herb derived from the herbal plant known as "milk thistle" (Silybum marianum) that contains four flavonolignan isomeric components: silybin, iso-silybin, silychristin, and silydianin. The dried seeds contain the plant's active compounds. Silymarin is one of the herbal remedies that has been thoroughly investigated for the treatment of serious liver conditions, both chemically and clinically. The primary component of Silymarin's hepatoprotective properties is silybin, the drug's most active ingredient. The medication silymarin is taken according to OS and is primarily eliminated as conjugates through bile. It is thought to have immunomodulatory, membrane-stabilizing, anti-inflammatory, antioxidative, anti-lipid peroxidative, antifibrotic, and liver-regenerating properties [59]. Because of its antioxidative, anti-lipid-peroxidative, antifibrotic, anti-inflammatory, immunomodulating, and even liver-regenerating properties, silymarin has been suggested to have clinical uses in the treatment of toxic hepatitis, fatty liver, cirrhosis, ischemic injury, radiation toxicity, and viral hepatitis [60]. Silymarin increases protein synthesis, aids in liver tissue regeneration, reduces inflammation, improves glucuronidation, and guards against glutathione depletion, although it lacks antiviral capabilities against hepatitis viruses [61].

5.2 Live-52

An Ayurvedic supplement that is approved and registered in over 45 countries, as well as a popular herb that many doctors throughout the world prescribe. Since its introduction in 1955, Liv-52 has been extensively researched for the treatment of liver diseases, including hepatitis, alcohol-related liver disease, pre-cirrhotic and early cirrhosis conditions, elevated liver enzymes, fatty liver conditions, protein energy malnutrition, and liver damage caused by radiation or chemotherapy [62]. Capparis spinosa, Cichorium intybus, Solanum nigrum, Terminalia arjuna, Cassia occidentalis, Achillea millefolium, Tamarix gallica, and Phyllanthus amarus are among the herbs found in Liv-52 tablets and syrup [63]. Ayurvedic principles are used in the formulation of Liv-52 to improve efficacy and prevent toxicity. Both separately and in combination, these components have a number of beneficial benefits, including being a powerful antioxidant, liver stimulant, carminative, stomachic, and choleretic. Additionally, they aid in the reduction of hepatic ascites and anasarca. Ferric oxide triturated in the juices of several hepatic stimulants and cholagogues is used to make mandurbhasma, an ingredient in Liv-52 [64].

5.3 Camellia sinensis (green tea)

Made from the leaves of the Camellia sinensis plant, an indigenous herb from southern China, it originated and is primarily produced in China. In addition to being beneficial for cardiodynia, hemorrhoids, inflammation, and abdominal diseases, the leaves are thermogenic, appetizing, digestive, carminative, and diuretic [65]. Green tea has been shown to be helpful in inhibiting Hepatic C Virus (HCV) entry into the liver cells in addition to its usage in acute liver injury and oxidative stress injury [66]. Active chemicals found in green tea include catechin, gallocatechin, epicatechin, epigallocatechin, epic a tech in gal late, and epi gallocatechin ching al late (EGCG), of which EGCG is thought to be the most therapeutically relevant. Additionally, research indicates that excessive consumption of EGCG may result in liver damage. Additionally, green tea has been shown to have stimulant effects, which are thought to be caused by certain alkaloids like caffeine, theobromine, and theophylline. Green tea contains an amino acid molecule called L-theanine, which has been researched for its potential to relax the nervous system [67].

5.4 Glycyrrhizaglabra (licorice)

A herb that was utilized as an active ingredient in herbal medicine and as a food sweetener. Studies on experimental cirrhosis and hepatitis have shown that it can both prevent fibrosis and encourage liver cell regeneration [68]. Licorice root has been used in traditional medicine over the years to treat everything from the common cold to liver disease, including pneumonia, gastritis, and jaundice. Liquid, dry, powdered, and peeled licorice root are all available. Although licorice has not historically been utilized as a liver herb, several recent studies conducted over the past 20 years have indicated that it is an important liver herb with potent hepatoprotective qualities. Licorice is used to treat a wide range of ailments. Even though not all of its advantages are backed by clinical studies, it is nonetheless used today to treat a wide range of illnesses. In Japan, glycyrrhizin is used intravenously to treat cirrhosis and chronic viral hepatitis because it prevents liver cell damage [69].

6.Discussion

India is one of the world's richest nations in terms of genetic resources for medicinal plants and a diversity of herbal plants. The present prevalent idea that "green medicine" is safer, more accessible, and less expensive than expensive synthetic pharmaceuticals, many of which have negative side effects, is the reason for the increased knowledge of herbal medicines [70]. One of the most deadly diseases in the world today is liver disease. They pose a significant threat to global public health. There isn't much that modern medications can do to lessen liver problems. Due to their therapeutic efficiency, plant-based herbal medications are now quite popular and utilized all over the world. Numerous bioactive chemical components, such as flavonoids,

tannins, polyphenolic compounds, etc., are present in such plant-based medications and are responsible for their antioxidant qualities. However, there aren't many drugs available to address liver problems [71]. For this reason, a lot of traditional medicines are tested on various experimental animal models to determine their hepatoprotective efficacy. Models of hepatotoxicity caused by carbon tetrachloride [72], paracetamol [72], diclofenac [73], thioacetamide [74], cadmium [75], alcohol [75], isoniazid [76], and other substances are frequently used to examine the hepatoprotective effectiveness of both synthetic and herbal medications. Despite the widespread use of herbal remedies, there were certain gaps in the research on them. The widespread belief that herbal medications are safe and natural is refuted by several studies on negative pharmacological effects. According to a National Poison Information Service survey conducted between 1991 and 1995, there were 785 instances of both proven and suspected adverse reactions linked to herbal medications. Therefore, safety studies are crucial to gathering enough information that could aid in the development of herbal medications in the future [77].

7.Conclusion

A useful and long-lasting method for managing and preventing liver problems is provided by herbal technology. Strong hepatoprotective, antioxidant, and anti-inflammatory benefits are provided by the usage of medicinal plants high in bioactive substances such flavonoids, alkaloids, and phenolics, which aid in the preservation and regeneration of liver tissues. Herbal formulations are typically less expensive, safer, and have less adverse effects than synthetic medications. The scientific legitimacy of herbal remedies has increased due to developments in extraction techniques, standardization, and clinical assessment. Treatments for liver diseases that are efficient, dependable, and easily available can be created by combining ancient herbal knowledge with contemporary technological research. The safety, effectiveness, and widespread adoption of herbal technology in the treatment of liver disease depend on ongoing study and quality assurance.

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