



Traditional Medicinal Plants and Liver Disease

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Abstract:

According to the World Health Organization, the global prevalence of liver cirrhosis ranges from 4.5% - 9.5% of the general population. Hence, estimated the > 50 million world population suffers from chronic liver disease. During 2001, the estimated worldwide mortality from cirrhosis was 771000 people, ranking 14th and 10th leading cause of death in developed countries like China, India, the U.S., Australia and the United Kingdom. Hepatocellular carcinoma, or cancer in the liver, is the 2nd most common cause of death due to malignancy in the world. At the turn of the 20th century, folk medicine was viewed as a practice used by poverty-stricken communities and quacks. The prevalence of folk medicine in certain areas of the world varies according to cultural norms. Some modern medicine is based on plant phytochemicals that have been used in folk medicine. Choice of plant species may be a crucial issue for the final word success of the investigation. Random choice provides some hint, targeted assortment supported chemotaxonomic relationships and ethno- medical data derived from ancient drugs are also possible to yield pharmacologically active compounds. Although advances in trendy medicines are important, there remains an ever-increasing demand for herbal medicines. Effective and potent herbal medicines need analysis by customary scientific strategies thus being valid for the treatment of diseases. Drug-induced liver toxicity is a major ill health that challenges healthcare professionals, the pharmaceutical trade, and drug regulatory agencies. The inhibition of atom generation will function facile model for evaluating the activity of hepatoprotective agents.

INTRODUCTION

The liver is the very important part of our body responsible for the maximum metabolic and secretary activities and therefore appears to be a sensitive target site for substances modulating biotransformation. The liver is also associated with detoxification from exogenous and endogenous challenges like xenobiotics, drugs, viral infections and chronic alcoholism. The period and intensity of the pharmacological response to drugs is influenced by their metabolic rate and hence substances capable of modifying drug metabolism would be able to change the result of drug therapy. During all such exposures to the above-mentioned challenges, if the usual defensive mechanisms of the liver are overpowered, the effect is liver damage. Liver injury or liver dysfunction is a major health problem that challenges not only medical professionals but also pharmaceutical companies and drug regulatory authorities. Liver cell injury caused by various toxic chemicals like certain antibiotics, chemotherapeutic agents, carbon tetrachloride, thioacetamide, excessive alcohol consumption and microbes.

Herbal medicines have been applied for the treatment of liver disorders for a lengthy period. Many herbal preparations are available in the market and therefore present review is aimed at compiling the data on promising phytochemicals from medicinal plants that have been tested in hepatotoxicity models using modern scientific Systems. Most ethnobotanical knowledge has existed in the world since ancient times. The Dictionary of World folk-medicine and ethno botany

includes more than 2532 plants. Even though early (4500-1500 BC) origins and a long history of usage in the last two centuries. The aim of the present article is to put the spotlight on some important medicinal plants that have ingredients effect on liver disease, and mechanism of this effect to cause the remedy of liver disease.

Nemours medicinal plants are mostly used in the traditional system of medicine for the treatment of liver disorder.

ETHANO MEDICINE OF MEDICINAL PLANTS

Ethno pharmacology can be an important element for developing nation's medical and economic system, Third World governments are being encouraged to seek a synthesis between modern and traditional medicine. Even though developing countries are providing many of the raw materials that considered column of drug manufacturing, in spite of tremendous strides in modern medicine, there are hardly any drugs that stimulate liver function, offer protection to the liver from damage or help regeneration of hepatic cell.

MEDICINAL PLANTS USED FOR LIVER DISEASE

India is the largest producer of medicinal plants and is rightly called the (Botanical Garden of the World). The medicinal plants have very important place in the health and vitality of human beings as well as animals. As per the WHO estimates, about three quarters of the world's population currently use herbs and other traditional medicines to cure various diseases, including liver disorders. Hence, several phytomedicines (medicinal plants or herbal drugs) are now used for the prevention and treatment of various liver disorders. Although experimental studies have been conducted on a number of these plants and their formulations, however, only some plants have clearly shown the hepatogenic / hepatoprotective effects against liver diseases or hepatotoxicity caused by variety of hepatotoxic agents such as chemicals, drugs, pollutants, and infections from parasites, bacteria or viruses (e.g., hepatitis A, B and C), etc. Indeed, to obtain satisfactory herbal drugs for treating severe liver diseases, the medicinal plants must be evaluated systematically for properties like antiviral activity (Hepatitis B, Hepatitis C, etc.), antihepatotoxicity activity (antioxidants and others), stimulation of liver regeneration and choleric activity. A combination of different herbal extracts / fractions is likely to provide desired activities to cure severe liver diseases. The medicinal plants contain several phytochemicals which possess strong antioxidant property, leading to antihepatotoxic activity, (Govind, 2014).

***Ecballium elaterium* (EE) and Virus**

Ecballium elaterium (EE) is one of the cucurbitaceous family. It is known as a squirting cucumber. It is abundant in North Africa and South- West Europe and the Mediterranean countries (Greige-Gerges et al., 2007). It grows in Egypt in north Sinai and El-Dabaa (Saker et al, 2012). In Jordan, it is founded in many places, including the waysides and cultured areas (Salhab, 2013). The fruits of the plant contain black seeds and juice. It has been known as a natural remedy for the treatment of several diseases (Raikhlin-Eisenkraft and Bentur, 2000). It has been used as a traditional medicine to treat rhino sinusitis (Uslu et al., 2006). EE also has antimicrobial and anticancer activities (Abbassi et al., 2014).

Alternative medicine is used for the treatment of several diseases worldwide. Numerous publications, about the complications of different plant usage for different treatment goals are present in literature. *Ecbalium elaterium* belongs to Cucurbitaceae family, takes place in alternative medicine because of cytotoxic, analgesic and purgative effects of the bioactive

materials included. (Salhab, 2013 and Satar et al., 2001). The plant's juice is used as diluted nose drip for the treatment of rinosinusitis in the community. Uvula edema is a life-threatening condition that occurs as a result of several reasons such as trauma, infection and allergic reactions (Alcoceba, 2010). In this paper, a severe uvula edema case, after using E. Elaterium for sinusitis treatment is presented.

Stephen et al., 2017, published that derivatives or component of Ecballium elaterium (A. Richard, "Squirting" or "Jumping" Cucumber, family Curcubitaceae have been used as a natural medicine in Mediterranean and African countries for centuries. The described actions of this herb include: antihepatotoxicity, the prevention of hepatitis induced liver cirrhosis and the treatment of jaundice in rats or humans, the effective management of sinusitis or nasal obstruction and reversal of tissue edema in mice. The crude juice of Ecballium elaterium (Ee) has been used most often in herbal medicinal practice, but it is often toxic. Reports of variable toxicity exist with crude concentrates of Ee, including: has included antifertility effects in female mice, cytotoxicity, and occasional deaths from poisoning. In contrast, water-distilled fractions of Ee juice given at approximate homeopathic dilutions 1x (LD times) are considered safe with retention of efficacy for several designated uses (vide infra). Ecballium elaterium has been widely used as a treatment for Hepatitis C (viral infection (HCV) in Egypt.

This use of Ee in treating liver disease is deeply rooted in Egyptian folklore medicine. The interest in Ee has been reactivated largely as a consequence of the emerging epidemic of Hepatitis C virus infection (HCV) in Middle Eastern countries, especially Egypt. Hepatitis C virus infection produces an indolent disease or diathesis that accounts for a large proportion of all patients with chronic liver disease. Hepatitis C is anticipated to cause major global increases in morbidity and mortality in the future.

Current treatments for HCV possess major disadvantages and limitations. While PEGylated interferon alpha combined with ribavirin are preferred treatments for HCV, these interventions are expensive, difficult to tolerate and limited in safety and effectiveness. Interferon/ribavirin treatments have unpredictable outcomes¹³ in patients with HCV.

Hepatitis C virus infection is a recalcitrant disorder that afflicts tens of millions of individuals worldwide. The emergence of HCV in third world countries cannot be impacted readily by expensive, high-technology approaches, such as those that utilize interferon and antiviral drugs (ribavirin). These treatments require skilled administration and extensive monitoring. In addition, these management strategies are not portable and they are often prohibitively expensive. Any alternative, low-cost intervention for HCV, with even partial effects on the clinical course of HCV, would represent a major breakthrough in therapeutics. This article describes the ethnobotanical discovery of derivatives of Ee as a potentially-viable, natural treatment for HCV and other disorders.

Glycyrrhizin

Felix and (2015), cited that Glycyrrhizin is extracted from liquorice root (*Glycyrrhiza glabra*) and comprises glycyrrhetic acid, flavonoids, hydroxycoumarins, and beta-sitosterol as the major constituents. In experimental models, glycyrrhizin alleviates toxic liver injury, possibly through antioxidant properties (Li et al., 2014). Before the advent of potent virostatics, an intravenous preparation (Stronger Neo-Minophagen C) containing glycyrrhizin, cysteine, and glycine was an established treatment for chronic hepatitis in Japan. Numerous studies, mostly from Asia, tested

glycyrrhizin formulations in various chronic liver diseases. Most trials were open label or pilot studies; only a few were placebo controlled (Stickel and Schuppan 2007). Efficacy was limited to improvements of serum liver enzyme levels, whereas no effect on viral markers was recorded. Retrospective data show a significant reduction of the risk for development of HCC in patients with hepatitis C virus (HCV). Potential negative side effects are hypokalemia, sodium retention, worsening of ascites, and hypertension caused by aldosterone-like activities. Glycyrrhizin is currently not recommended because of the lack of compelling evidence and the availability of better alternatives.

Phyllanthus amarus

Phyllanthus contains phyllantins, hypophyllanthins, and several polyphenols for which data indicate an interference with the hepatitis B virus (HBV) life cycle. Clinical trials with *phyllanthus* species in patients with chronic HBV infection were recently reviewed in a Cochrane analysis (Xia et al., 2011). In total, 16 trials with 1326 patients were included of which 15 trials tested *Phyllanthus* in combination with other antivirals, whereas 1 trial tested against placebo. The combined results showed that *Phyllanthus* species had a favorable effect on HBV DNA levels and hepatitis B e antigen seroconversion when given together with conventional antivirals. A second Cochrane metaanalysis examined five clinical trials comparing *Phyllanthus* species with antiviral drugs (lamivudine, interferon-alpha, and thymosin) in patients with HBV and found no superior effect from phyllanthus (Xia et al., 2013). No trials with entecavir or tenofovir have been conducted yet. Altogether, *Phyllanthus* could be an interesting candidate for further testing in rigorously designed trials with clear endpoints.

Silymarin

Silybum marianum (Milk thistle) has been used to treat liver diseases since the 16th century. Its major constituents are the flavonoids silibinin, silidianin, silichristin, and isosilibinin of which silibinin is the biologically most active compound and used for standardisation of pharmaceutical products (Wagner et al., 1976). The pharmacological profile of silymarin has been well defined and hepatoprotective properties of silymarin were investigated both *in vitro* and *in vivo*. Experimental studies demonstrated antioxidant and free radical scavenging properties, improvement of the antioxidative defence by prevention of glutathione depletion, and antifibrotic activity.

A number of well-designed experimental studies suggest that silymarin might exert beneficial effects in chronic liver diseases through antifibrotic properties. For example, silymarin interferes with leukotriene formation in Kupffer cell cultures and may thereby inhibit hepatic stellate cell (HSC) activation, which is a crucial event in fibrogenesis (Dehmlow et al., 1996). In addition, silymarin at 10^{-4} mol/l blocked the proliferation of HSC cultures and their transformation to myofibroblasts (Fuchs et al., 1997). Experimental models included fibrosis induced by carbon tetrachloride (CCl₄) and secondary biliary fibrosis, while results from CCl₄-induced rat liver fibrosis are controversial, likely due to the inhomogeneity of the model, dosing during gavage of the free radical inducer CCl₄ and low numbers of animals. Mourelle et al. found that silymarin dosed at 50 mg/kg body weight reduced fibrosis by 30% as measured by relative collagen content (per g of liver) (Mourelle et al., 1989), which could not be confirmed by others (Hall et al., 1994). In a study by Boigk et al. in representative groups of 20 rats in which secondary biliary fibrosis was induced following complete bile duct occlusion, silymarin at 50 mg/kg/day reduced total (per liver) and relative (per g of liver) hepatic collagen content by 35% which was mirrored by decreased serum levels of the aminoterminal propeptide of procollagen type III (PIIINP), a surrogate marker of

hepatic fibrogenesis (Boigk et al., 1997). Silymarin prevented further progression when fibrosis was advanced, a situation encountered in many patients. Furthermore, the number of activated HSCs was markedly reduced (Boigk et al., 1998) and transcription of hepatic procollagen type I and TIMP-1 mRNA was decreased by 50% (Jia et al., 1998). However, compared to the recommended dose for patients (400–450 mg daily) the applied dose of silymarin was eight-fold higher, and hepatic levels were likely further increased due to retarded biliary secretion in this model of secondary biliary fibrosis.

CONCLUSION

Medicinal herbal drugs have gained importance and recognition in recent years as a result of their safety, effectuality and value effectiveness. From this review study, it is clear that the medicinal plants play a significant role against on various diseases. Different medicinal herbs and plants extracts have potent hepatoprotective activity in various animal models. The hepatoprotective activity is probably due to the presence of flavonoids, phenolic compounds, polyphenols etc in all few herbal plants. The results of this study indicate that extracts of leaves and plants extracts of some medicinal plant have good potentials for use in hepatic disease.

The predicted mechanism of action of various plant extracts may be attributed to antioxidant properties and the presence of flavonoids, to increase the reduced level of blood glutathione in experimental animal models, to increase total proteins, to inhibit lipid peroxidation and increase in the antioxidant enzymatic activity, to decrease the hepatic marker enzymes (AST, ALT, ALP, and arginase) and total bilirubin in plasma, to enhance antioxidative enzymes, including SOD, GPx, CAT and GST, to decrease MDA level, SGOT, SGPT etc.

Clinical studies analyzing the efficacy of herbals in the treatment of liver diseases provided only moderate evidence. Future efforts will have to implement extensive methodological improvements to separate the real therapeutic value from unfounded hopes. Rigorous scientific testing along the principles of evidence-based medicine is required for herbal medicine to become more than a fashionable trend.

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