

Useful herbs for the liver disease treatment

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Abstract

The liver is a vital organ that plays an important role in the metabolism and excretion of xenobiotics from the body. Liver damage or liver dysfunction is a serious health concern that concerns not only medical professionals but also the pharmaceutical industry and drug regulatory agencies. Damage to liver cells caused by various toxic chemicals (certain antibiotics, chemotherapy agents, carbon tetrachloride (CCL₄), thioacetamide (TAA) etc.), excessive alcohol consumption and microbes are well studied. The synthetic drugs available to treat liver problems in this disease also cause further damage to the liver. As a result, herbal medicines have become increasingly popular and their use is widespread. Medicinal plants have long been used in the treatment of liver disease. Numerous herbal preparations are available in the market. In this review we are represented the most effective plant that can be used as therapeutic agent for the liver.

Keywords: *Herbal drugs, Liver Injury, Rosemary, Milk thistle, Nettle leaf, Turmeric, Artichoke, Chicory*

Introduction

Chronic liver diseases represent a heavy global health burden, with cirrhosis of the liver being the ninth leading cause of death in Western countries (1). Chronic viral hepatitis B and C, alcoholic liver disease, non-alcoholic fatty liver disease and hepatocellular carcinoma are important entities and many problems remain unresolved. Therapies developed according to the principles of Western medicine often have limited efficacy, carry risks of adverse effects and are often too expensive, especially for developing countries. Therefore, treating liver disease with plant-derived compounds that are affordable and do not require laborious pharmaceutical syntheses looks very appealing. Moreover, despite advances in conventional medicine in recent decades, professionals and the general public in developed countries are paying increasing attention to phytomedicine. Several recent surveys in Europe and the United States have shown a large increase in the use of botanical medicines in a few years, and up to 65% of patients with liver disease take herbal preparations (2). Similar figures exist for Europe, where spending on silymarin, a herbal preparation used to treat chronic liver disease, reaches \$180 million in Germany alone (3). The following review describes the current scientific evidence regarding herbal drugs and the liver

Rosemary

In general, flavonoids are an important group of antioxidants in plants and their antioxidant activities have been widely reported (4). 5-Hydroxy-7, 4-dimethoxyflavone (also called 4-methoxytecto-chrysin) isolated from rosemary has shown antioxidative activity (5).

Rosmarinus officinalis (rosemary) possesses antioxidant activity and hepatoprotective effects, and may therefore constitute a possible therapeutic alternative for chronic liver diseases. The effect produced by a methanol extract of *Rosmarinus officinalis* on cirrhosis of the liver induced by CCl_4 , the enzymatic activities of gammaglutamyl transpeptidase (GGT) and alanine aminotransferase (ALT), as well as the increase in bilirubin levels caused by the administration of CCl_4 have been prevented by the concomitant administration of

Rosmarinus officinalis. When oxidative stress cirrhosis was assessed as an increase in hepatic lipoperoxidation, total lipid peroxides, serum nitric oxide, and loss of erythrocyte plasma membrane stability, *R. officinalis* was shown to prevent these changes. In cirrhotic animals treated with CCl_4 , histological studies have shown massive necrosis, periportal inflammation and fibrosis modified by rosemary. These benefits on experimental cirrhosis suggest a potential therapeutic use of rosemary as an alternative to cirrhosis of the liver (6).

Rosmarinus officinalis (rosemary) oil is widely used by the cosmetics, food and pharmaceutical industries as a fragrance component of soaps, creams, lotions and perfumes. Although popular, the potential harmful side effects of the oil have been described (7).

Milk thistle

Milk thistle is a thistle of the genus *Silybum Adans.*, a flowering plant in the daisy family (Asteraceae). They are native to the Mediterranean regions of Europe, North Africa and the Middle East. The name "milk thistle" derives from two characteristics of the leaves: they are mottled with white spots and contain a milky sap (8). The extract is composed of approximately 65-80% silymarin (a flavonolignic complex) and 20-35% acids, including linoleic acid (8).

For many centuries, milk thistle extracts have been recognized as "liver tonics" (8). Milk thistle seeds have been used for 2000 years to treat chronic liver disease and protect the liver from toxins (9). Milk thistle has been reported to have protective effects on the liver and significantly improve its function. It is generally used to treat cirrhosis of the liver, chronic hepatitis (inflammation of the liver), toxin-induced liver damage (including the prevention of serious liver damage caused by *Amanita phalloides* (mushroom poisoning), and gallbladder (8,9).

The plant stimulates repair and detoxification of the liver through four main pathways: antioxidant, scavenging free radicals and regulating glutathione; stabilization of cell membranes and permeability, which limits the entry of hepatotoxins into hepatocytes; promotion of ribosomal RNA synthesis, stimulating liver

regeneration; and slowing down the transformation of stellate hepatocytes into myofibroblasts, slowing the onset of cirrhosis which occurs through collagen deposition (10).

Perhaps the most significant new applications of milk thistle stem from its role as an adjunct to chemoprevention, treatment and reduction of treatment side effects (9). When combined with omega-3 fatty acids, milk thistle reduces the number of radionecrosis sites in cancer patients and prolongs survival (8,9).

Nettle leaf

Stinging nettle (*Urtica dioica*), also known as stinging nettle, common nettle, devil's leaf, net plant, and stinging nettle, can be found in temperate climates growing as an herb around the world whole. The plant has many stinging hairs called trichomes on its leaves and stems, which act like hypodermic needles that inject histamine and other chemicals that produce a tingling sensation upon contact with humans and other animals (11).

Nettle is one of the plants with a long history as an herbal remedy and a nutritional supplement to diets. Young leaves cooked like a vegetable herb are added to soups and can also be dried for the winter. Nettle is a very nutritious food, easily digestible and rich in minerals (especially iron), vitamin C and provitamin A. Although the plants are mainly used in soup, a tea made from the leaves has traditionally been used (11). Previous studies show that nettle leaves are a good source of essential amino acids, ascorbic acid, available and unavailable carbohydrates, fatty acids and carotenoids, and various mineral elements (11,12). The root of the plant contains chemicals such as scopoletin, sterols, fatty acids, polysaccharides and isolectins (12).

Turmeric

Turmeric has historically been used as a component of Indian Ayurvedic medicine since 1900 BC. for the treatment of a wide variety of conditions. Research conducted in the second half of the 20th century identified curcumin as being responsible for most of the biological activity of turmeric (13). Curcumin is the main curcuminoid in

popular Indian turmeric, which belongs to the ginger family (14). The other two curcuminoids are desmethoxy curcumin and bisdesmethoxy curcumin. Curcuminoids are polyphenols and are responsible for the yellow color of turmeric. Curcumin can exist in at least two tautomeric forms, keto and enol. The enol form is energetically more stable in solid phase and in solution (13,14).

In vitro and animal studies have suggested a wide range of potential therapeutic or preventive effects associated with curcumin. At present, these effects have not been confirmed in humans. However, as of 2008, many human clinical trials were underway studying the effect of curcumin on various diseases, including multiple myeloma, pancreatic cancer, myelodysplastic syndromes, colon cancer, psoriasis, and Alzheimer's disease. Alzheimer's (15). In vitro and animal studies have suggested that curcumin may have antitumor effect (16) antioxidant, antiarthritic, antiamyloid, anti-ischemic properties (Shukla et al., 2008) and anti-inflammatory. The anti-inflammatory properties may be due to inhibition of eicosanoid biosynthesis (15). Curcumin acts as a free radical scavenger and antioxidant, inhibiting lipid peroxidation (15,16).

Curcumin, with its proven anti-inflammatory and antioxidant properties, has many therapeutic benefits. It has been shown to be a potent scavenger of a variety of reactive oxygen species, including superoxide anion radicals, hydroxyl radicals, and nitrogen dioxide radicals. It has also been shown to inhibit lipid peroxidation in several animal models (17). Vascular endothelial cells treated with curcumin prevent oxidative damage mediated by increased production of heme oxygenase (17). Curcumin (diferuloylmethane), an active ingredient in turmeric, obtained from the powder of the rhizomes of *Curcuma longa* Linn. Curcumin is considered to be a powerful anti-inflammatory and antioxidant agent. In addition, it is a powerful scavenger of superoxide anions, hydroxyl radicals and nitrogen dioxide and protects DNA from strand breaks induced by singlet oxygen. Turmeric has hepatoprotective and nephroprotective effects. These beneficial effects have been explained by the induction of antioxidant enzymes (18).

Studies have shown that curcumin pretreatment resulted in significant restoration of

hepatic cytokines IL1 α , IL1 β , IL2, IL6, and IL10 to normal levels increased by the hemorrhage/resuscitation regimen in rats. Indeed, IL1 β levels were lower than sham levels. NF-kappa B and AP1 were differentially activated at 2 and 24 hours after bleeding and were inhibited by pretreatment with curcumin. Estimates of serum aspartate transaminases indicated reduced liver damage in curcumin-pretreated animals prone to hemorrhage. These results suggest that protection by curcumin pretreatment against resuscitation bleeding/injury may have resulted from inactivation of involved transcription factors and regulation of cytokines to beneficial levels (19).

In 2010, a food grade polymeric micellar encapsulation system was shown to increase curcumin water solubility and anti-tumor activity *in vitro*. It has been found that hydrophobically modified starch, generally used to encapsulate flavors, is capable of forming polymeric micelles. homogenization method, it can load curcumin into its hydrophobic core and then solubilize curcumin. Cell culture experiments revealed increased anti-tumor activity on the HepG2 cell line. However, further *in vivo* studies are needed to further demonstrate its efficacy from a bioavailability perspective (20).

Artichoke

The artichoke is a perennial herbaceous plant native to North Africa, the Canary Islands and southern Europe, the countries of this zone being the main world producers. Artichoke leaves were used in ancient herbal medicine for various diseases: they were widely used in Europe mainly for the treatment of dyspepsia; indeed, it has a documented choleric effect both in healthy volunteers and in people suffering from non-specific digestive disorders (21). In addition, artichoke extracts exhibit antioxidant properties in endothelial cell and monocyte cultures, primarily antagonizing lipid peroxidation (22).

The chemical components of the artichoke have been widely studied; in particular, the leaves of this plant are rich in phenolic compounds, such as mono and dicaffeoylquinic acids and flavonoids, which have been extracted, isolated and identified as main chemical components (21,22). Flavonoids

are a heterogeneous group of phytochemicals that can act as potent inhibitors of LDL oxidation through various mechanisms: scavenging of free radicals by acting as reducing agents; chelation of transition metal ions, thereby reducing the generation of free radicals; economy of vitamin E and carotenoids (β carotene, lycopene) in the LDL particle, thus protecting LDL from oxidation; and by promoting the activity of serum paraoxonase, thereby antagonizing lipid peroxidation (23). Additionally, previous studies on artichoke extract have shown that due to its content of flavonoids like luteolin, it delays LDL oxidation (22,23) and reduces oxidative stress in cells. endothelial cells stimulated by tumor necrosis factor alpha and oxidized LDL (23). The artichoke leaf extracts have hepatoprotective properties and are used by patients with chronic liver disease. In recent years, artichoke extracts have been tested for various pharmacological activities. In humans, randomized controlled trials have shown a moderate cholesterol-lowering effect (24).

Chicory

Chicory (*Cichorium intybus*, Asteraceae) is a root vegetable whose green tops are also used in salads or as a supplement to coffee. The pharmacological actions of chicory have attracted the attention of many researchers. Chicory is one of the most promising new carbohydrate candidates with both food and non-food potential. It has been used in folk medicine from North Africa to South Asia for several hundred years (25).

Fresh chicory typically contains 68% inulin, 14% sucrose, 5% cellulose, 6% protein, 4% ash, and 3% other compounds, while dried chicory contains around 98% inulin and 2% other compounds (Meehye and Shin, 1996). is a naturally occurring linear fructose with 9 (2-1) glycosidic bonds which is not digested in the upper gastrointestinal tract but which is fermented in the coecocolon (26).

Inulin is water soluble and not hydrolyzed by human digestive enzymes; it is expected to behave like soluble fiber and have a lipid-lowering effect. It could treat jaundice, hepatitis, liver congestion, etc. Moreover, by stimulating the flow of bile, chicory would treat gallstones, biliary insufficiency, gastritis and splenomegaly (27). A mechanism of action of

oligofructose has been associated with the modulation of cholesterol synthesis by short chain fatty acids produced by the intestinal microflora during the fermentation process (Wagner et al., 1983). Chicory has a powerful hepatoprotective, antioxidant, hypoglycemic, diuretic, antitesticular and immunomodulatory effect (28).

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