Maximizing the Use of Hepatoprotective Herbs

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Introduction

Botanical remedies can be used to treat a variety of issues and diseases. This report looks at ways to maximize the use of hepatoprotective herbs. Though there are many herbs that can help strengthen the liver, there are five herbs that are particularly effective medicinal agents for treating liver problems.

They are:

1. Milk thistle
2. Turmeric
3. Licorice
4. Schisandra
5. Chinese skullcap

Liver stimulants and general liver remedies

Liver stimulants and remedies are plants that can improve or increase liver function. They do this by increasing the production of bile, enhancing hepatic enzymatic activity and increasing blood flow to the liver. These plants can also have effects on stimulating bile from the gallbladder.

Some of the antiviral herbs that help protect liver cells from viral infection include:

- Lemon balm
- St. John's Wort
- Shiitake mushroom
- Garlic
- Reishi mushroom
- Licorice

Cholagogues

Cholagogues are used to stimulate the production and flow of bile. Some herbal cholagogues include:

- Artichoke leaf
- Yellow dock
- Burdock root
- Dandelion root
- Celandine
- Fringe tree
- Beet root
- Barberry
- Oregon grape
- Wild yam
- Maitake mushroom
- Reishi mushroom
- Siberian ginseng
- May apple
- Culver's root
- Rosemary
- Black radish

Five important liver herbs

Milk thistle (Silybum marianum)

Traditional uses

Milk thistle has been used as a medicinal agent for hundreds of years. Most commonly, it has been used for disorders of the liver and the gallbladder. In Europe, milk thistle has been used mostly to prevent or treat diseases including hepatitis, cirrhosis, gallstones, jaundice and toxin-induced liver damage. Other historical uses for milk thistle include treatment of: asthma, bladder cancer, breast cancer, bronchitis, cough, pleurisy, depression, diabetic neuropathy, dyspepsia, gynecological cancers, lactation stimulation, neuroprotection, peritonitis, prostate cancer, psoriasis, radiation toxicity, splenic disorders and varicose veins.

Composition

Milk thistle products come in all sizes and shapes; they are capsules, tinctures, extracts and powders. Whatever the form, most products are often standardized to contain 70% to 80% silymarin. Silymarin is a mixture of three flavonolignans: silybin, silidianin and silychristin. Different preparations and brands have different standardization and varying bioavailability.

Some research indicates that silymarin acts as an indirect antioxidant. A direct antioxidant neutralizes only one free radical molecule at a time. However, indirect antioxidants induce the activity of Phase II detoxification enzymes, subsequently neutralizing many free radicals.

Mechanisim of action/pharmacology

Milk thistle activates RNA polymerase, an enzyme responsible for making RNA from DNA, which in turn promotes hepatocellular regeneration. This ability to regenerate liver cells is one of the hallmarks of milk thistle. Other mechanisms of action for milk thistle include antifibrotic effects, antiviral effects, lipid oxidation, cholesterol synthesis and antineoplastic effects. It is also sometimes used to treat glucose metabolism issues.

Clinical applications

The clinical applications for milk thistle include:

- Chronic viral hepatitis
- Acute viral hepatitis
- Chronic alcoholic hepatitis
- Chronic alcoholic liver disease
- Alcoholic hepatitis
- Toxic hepatitis
- Autoimmune hepatitis
- Hepatitis (other)
- Cirrhosis
- Primary biliary cirrhosis

Systematic review

Sixteen randomized control trials (14 blinded) and 17 non-randomized control trials evaluated the effects of milk thistle. The majority of these studies used a silymarin product called Legalon. There were a number of different doses ranging from 240 up to 800 mg a day. The duration of treatment in these different trials was from one week to six years.

These trials looked at different etiologies of liver disease. Some of the trials were focused on chronic alcoholic liver disease, viral hepatitis (both acute and chronic) and cirrhosis (both alcohol and non-alcohol related). Three of the trials were related to hepatotoxins. Looking collectively at the results, milk thistle produced small effects that were not statistically significant; however, there were many therapeutic benefits that resulted from the studies.

Safety

Milk thistle is a safe herb for non-pregnant women. There is insufficient evidence surrounding milk thistle's use in pregnancy and lactation; however, it has historically been used during lactation and is often listed in some botanical texts as an herb that improves lactation. It has also been used to treat mothers who have suffered intrahepatic cholestasis during their pregnancy in treatment lengths of up to three weeks.

Milk thistle is likely unsafe:

- When taken in greater than recommended doses
- When taken for longer than four years
- In pregnancy/lactation (insignificant research to prove or disprove)
- In the inhibition of cytochrome P450 3A4 and 2C9
- In insulin-dependent DM associated with cirrhosis

Dosing

Milk thistle is most commonly prescribed in extract form standardized to 70% to 80% silymarin content, 140 mg three times per day. Higher doses might also be more effective. Fluid extracts are typically more concentrated and this form of the herb is typical given in 5 mL doses, three times per day.

A sample dosing of cirrhosis is demonstrated in figure 1.

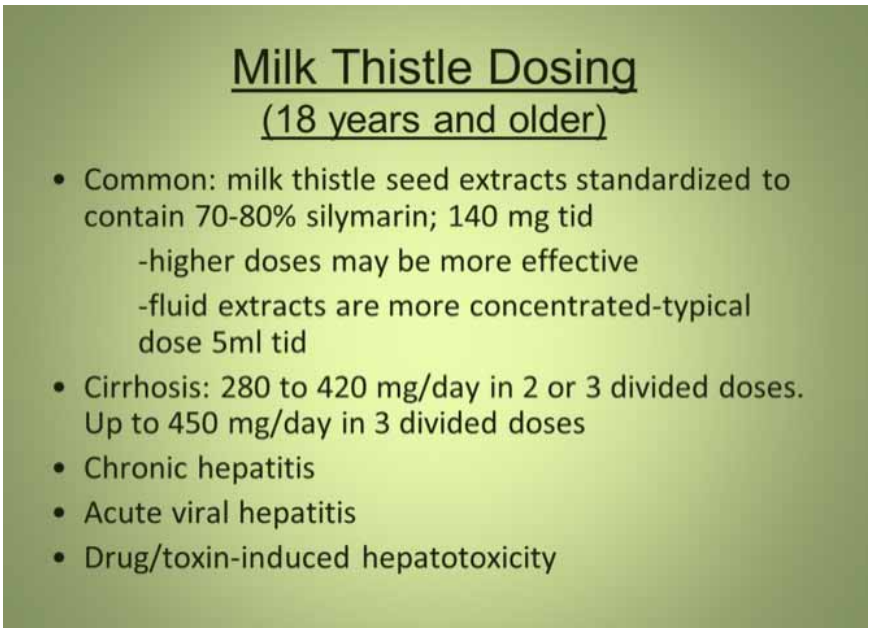

Figure 1

Adverse effects

Milk thistle is generally well-tolerated and most of the reported adverse reactions have been fairly mild. Those with allergies or hypersensitivity to the aster family might be vulnerable to allergic reactions. There are case studies that have reported some hypersensitivity or even anaphylactic reactions to milk thistle.

Occasional pruritus has been reported in several milk thistle trials; however, pruritus has also been found in many placebo trials. Milk thistle can sometimes cause mild gastrointestinal symptoms such as nausea, heartburn, diarrhea, dyspepsia and gas. A direct link between milk thistle and GI symptoms has not been established due to the fact that GI issues may be the result of underlying liver disease.

Cautions/contraindications

Milk thistle can decrease fasting plasma glucose. This can be a side effect, or a therapeutic effect depending on the patient. It may be necessary to adjust insulin doses in patients who are insulin-dependent diabetics. Milk thistle should be used cautiously with medications that are metabolized by the cytochrome P450 system. There has also been some in vitro observation that showed that milk thistle inhibited CYP3A4 and CYP2C9; therefore, increased concentrations of concomitant medications might occur when taking milk thistle. Theoretically, silymarin might decrease the clearance of drugs like Lorazepam or Lamotrigine. Silymarin has been reported to decrease fasting blood sugar, lower hemoglobin A1C and fasting insulin levels, especially in insulin-dependent diabetics who have cirrhosis. This is important to note as using milk thistle for this group may allow patients to decrease some of their medications. Milk thistle should also be avoided in patients with known allergies to the aster family, daisies, artichokes, common thistle and kiwi.

Interactions

Milk thistle may reduce hepatotoxicity associated with alcohol ingestion. It is theorized that silymarin may increase the clearance of estrogen by inhibiting bladed glucuronidases. One of the flavonolignans in the silymarin might increase the efficacy of certain platen compounds.

Turmeric (Curcuma longa)

Traditional uses

Turmeric is one of the fine spices in curry powder. Historical uses of turmeric are noted in figure 2.

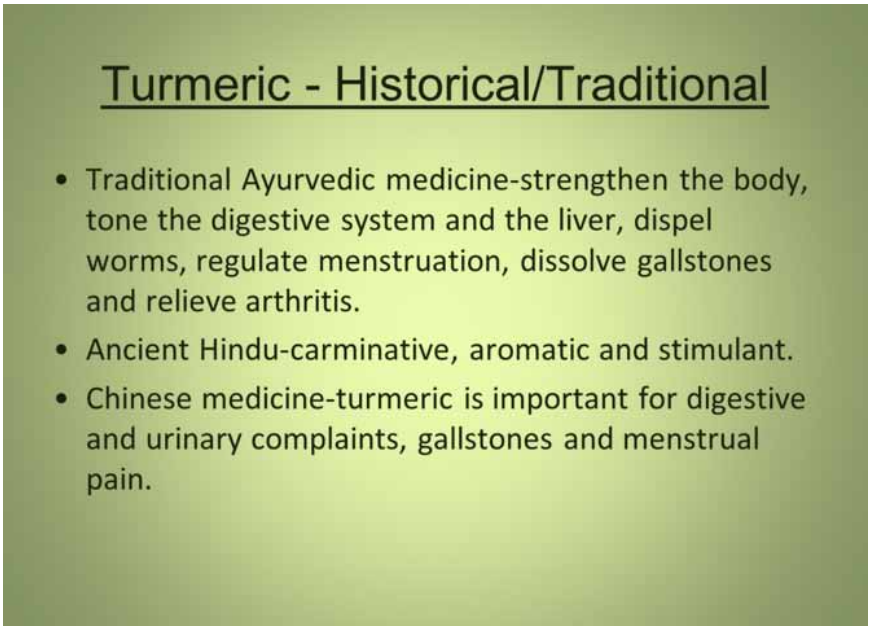

Figure 2

One of the most frequent indications on this list is GI-related issues. Turmeric has been used to tonify the digestive system and the liver, dissolve gallstones and in other situations.

In ancient Hindu text, turmeric is described as a carminative, aromatic and a stimulant. In Chinese medicine, turmeric is used for digestive complaints.

Pharmacology

Curcumin is a polyphenol compound that is responsible for turmeric's bright yellow color, and is believed to be the principle pharmacologic agent in turmeric. There are several curcuminoids in turmeric. There are also many different sugars, resins, proteins, vitamins, minerals and small levels of iron and potassium.

Clinical applications

Turmeric has been used in laboratory and animal studies to measure antiproliferative effects on malignant cells. The herb has shown lipid lowering effects and some ability to contract the gallbladder.

Some of the other clinical applications for turmeric include:

- Dyspepsia
- PUD
- Cholelithiasis, GB stasis
- Hyperlipidemia
- Inflammation
- Osteoarthritis
- Rheumatoid arthritis
- Scabies
- HIV
- Uveitis

Role in liver/gallbladder disease

Case study 1

A study of dyspepsia involved giving patients 250 mg of the dried root powder four times per day. After a week, almost three quarters of the turmeric patients showed clinical improvement, and 16% were cured, versus those in the placebo group where only 42% showed clinical improvement and an 11% cure rate.[1]

Case study 2

Preliminary human data suggests that curcumin has the ability to cause the gallbladder to contract and stimulate the flow of bile, an effective method of preventing gallstones. A randomized, double blind crossover study examined the effects of 20 mg of curcumin and placebo on gallbladder volume in 12 healthy people. During the study, 20 mg of curcumin or placebo were administered following a night of fasting. Gallbladder volume was measured with ultrasound. Following a one week washout period, subjects received alternate therapy. Gallbladder contraction occurred in the curcumin group 30 minutes after administration. After two hours, there was a 16% mean reduction in volume. In the placebo group, there was initial contraction similar to curcumin, but after two hours, the mean gallbladder volume increased by 31%. These results suggest an effect of curcumin on gallbladder function.[2]

Safety

Turmeric is considered safe, especially when consumed as a spice in culinary uses. It appears to be a non-toxic herb and likely safe even in large doses. Some patients report gastric irritation in some therapeutic doses, so caution should be used when prescribing turmeric to patients with PUD or GERD. If a patient has gallstones or signs of obstruction of 3 mm or more, turmeric should not be used. If the patient has a gallstone that is less than 3 mm, turmeric is likely safe since the stone will be able to pass through the duct and not cause an obstruction. If the patient has right upper quadrant pain, before using turmeric an ultrasound of their gallbladder should be performed. Caution should also be used with patients who are taking immunosuppressant medications because it is unclear if some of the mechanisms in turmeric impact the immune system or metabolism of some of these drugs.

Dosing

Turmeric products are often standardized to contain 95% curcuminoids per dose. Turmeric dried root capsules usually contain about 3% to 5% curcumin. Traditionally doses range from 1.5 to 3 g per day. Research suggests using 750 to 1,500 mg per day in three to four divided doses.

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[1] Thamlikitkul V, et al.J Med Assoc Thai 1989;72(11):613-620

[2] Rasyid A, Lelo A. Aliment Pharmacol Ther 1999;13(2): 245-249

Adverse effects

Some patients report allergic reactions to turmeric. Turmeric can be applied topically, and there have been cases of contact dermatitis. This situation is usually characterized by erythema or itching. Transient hypertension has been reported in animal studies.

Turmeric can cause GI irritation in some patients, but this is rare. If a patient has allergies to ginger, they may have an allergy to turmeric. As noted earlier, for patients with gallstones, caution should be used when using turmeric. Turmeric inhibits platelet aggregation, so it is important to discontinue use two weeks prior to any operation where there might be an increased risk of bleeding.

Cautions/contraindications

One study looked at patients with duodenal ulcers who were given 6 g of turmeric per day. The treatment plan was associated with epigastric burning in 27% of the patients. Based on this information, it is not recommended to use turmeric for patients who have ulcers.

Interactions

Turmeric may potentiate the effect of some anti-coagulants and can inhibit cytochrome P450. It is a mild inhibitor of CYP 2B1/2B2 and a weak inhibitor of CYP 2E1. Turmeric reduces reserpine induced ulcers and protects against acute doxorubicin-induced myocardial toxicity.

Licorice (Glycyrrhiza glabra)

Traditional uses

Licorice has a long history of medicinal use in Europe and Asia. In Europe, it has been used to treat cough, bronchitis, gastritis and peptic ulcer disease. In China, licorice has been used to treat diseases such as hepatitis B. It is also used in conjunction with chi, to tonify the spleen and to detoxify and moisten the lungs. Licorice is also traditionally used in China to treat sore throat, skin eruptions, abdominal pain, abscesses and sores, gastric and duodenal ulcers, malaria and tuberculosis.

In Ayurvedic medicine, licorice is used to treat ulcers, inflammation and constipation. Eclectics use licorice to reduce irritation of mucosal membranes, urinary, respiratory and digestive and to treat chronic gastritis, peptic ulcer disease and Addison's disease.

Composition

The unpeeled roots of licorice contain at least 4% glycyrrhizic acid and 25% water soluble matter. Licorice root contains triterpenoid saponins, most which are glycyrrhizin and salts of glycyrrhizic acid. The root contains flavanones, isoflavanones, glucose, sucrose and starch. Small amounts of phytosterols, polysaccharide sterols and coumarins can be found in licorice root.

Pharmacology

The pseudo-aldosterone-like effects of licorice are generally attributed to the glycyrrhizic acid component. Recent research suggests that the glycyrrhetinic acid is most likely the primary active component that causes peripheral metabolism of cortisol, which then binds to the mineral corticoid receptors in the same way as aldosterones. The blocking of the 11-beta hydroxysteroid dehydrogenase is temporary; after this occurs, the pseudo-aldesteronism is directly related to increased plasma concentration of licorice metablites and their binding to mineralocorticoid receptors.

Clinical applications

Clinical applications for licorice include:

- Atopic dermatitis
- Dyspepsia
- Hepatitis B and C
- Muscle cramps
- Aphthous ulcers
- Peptic ulcers
- Weight loss
- Hyperandrogenism
- Herpes simplex
- IV Viral hepatitis

Glycyrrhizin shows potential for reducing long-term complications from hepatitis C. Some evidence suggests that long-term use of glycyrrhizin might prevent liver cancer in patients with hepatitis C. Several clinical trials found that taking glycyrrhizin reduced the levels of liver enzymes such as ALT, but did not reduce the amount of hepatitis C virus in the blood. These studies, however, gave glycyrrhizin in intravenous (IV) form, not as a dietary supplement.

These studies demonstrate some of the beneficial effects of IV glycyrrhizin in the treatment of chronic viral hepatitis. In Japan, a preparation of GL, cysteine and glycine is administered by injection to treat acute hepatitis, chronic hepatitis, including hepatitis C and subacute hepatic failure due to viral hepatitis.[3,4,5,6,7]

Safety

Licorice is likely safe when used orally in amounts commonly found in foods. It is possibly safe when taken orally and appropriately as a medicine for short term use. Long term use may cause adverse side effects. Licorice should not be used in pregnancy because it has abortifacient, estrogenic and steroid effects that can cause uterine stimulation. Heavy consumption of licorice during pregnancy has been found to increase the risk of delivery before gestational age of 38 weeks. Licorice's safety in lactation is unknown; therefore, it is advisable to avoid prescribing this herb for lactating mothers.

Dosing

Licorice is prescribed as a:

- Powdered root (4% to 9% glycyrrhizin): 1-4 g per day in three divided doses
- Fluid extract (10%-20% glycyrrhizin): 2-4 mL per day
- Deglycyrrhinated licorice: 380 mg-1140 mg three times per day, 20 minutes before meals
- Gel or cream: 2% cream or gel five times per day

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[3] Fortschr Med 1992

[4] Asian Med J 1980

[5] Am J Gastroenterol 1993

[6] Cancer 1997

[7] Ind J Med Res 1993

Adverse reactions

Occasionally, elevated blood pressure may result from licorice use. This can happen in patients who are hypertensive. Higher levels of licorice may cause hypokalemia, CHF, rhabdomyolysis, pulmonary edema, hypertensive encephalopathy, pseudoaldosteronism and hypermineralocorticoidism. It can also cause headaches.

Cautions/contraindications

Some cautions and contraindications for licorice include:

- CHF
- Arrhythmias
- ER positive breast cancer
- Consider estrogenic effects in general
- Hypertonia
- Hypokalemia
- Kidney insufficiency
- HSDD
- ED

Licorice is contraindicated in breast cancer patients whether the patient is ER positive or negative because it has been shown to increase proliferation of ER positive cells in vitro.

Possible interactions

Licorice has possible interactions with some medications. Licorice can cause these medications to work improperly and can make side effects worse, including a build-up of potassium in the body. If a patient is taking angiotensin converting enzyme (ACE) inhibitors or diuretics for high blood pressure, licorice products should not be used.

ACE inhibitors include:

- Captopril (Capoten)
- Benazepril (Lotensin)
- Enalapril (Vasotec)
- Lisinopril (Prinivil, Zestril)
- Gosinopril (Monopril)
- Ramipril (Altace)
- Perindopril (Aceon)
- Quinapril (Accupril)
- Moexipril (Univasc)
- Trandolapril (Mavik)

Additional potential interactions are noted in figure 3.

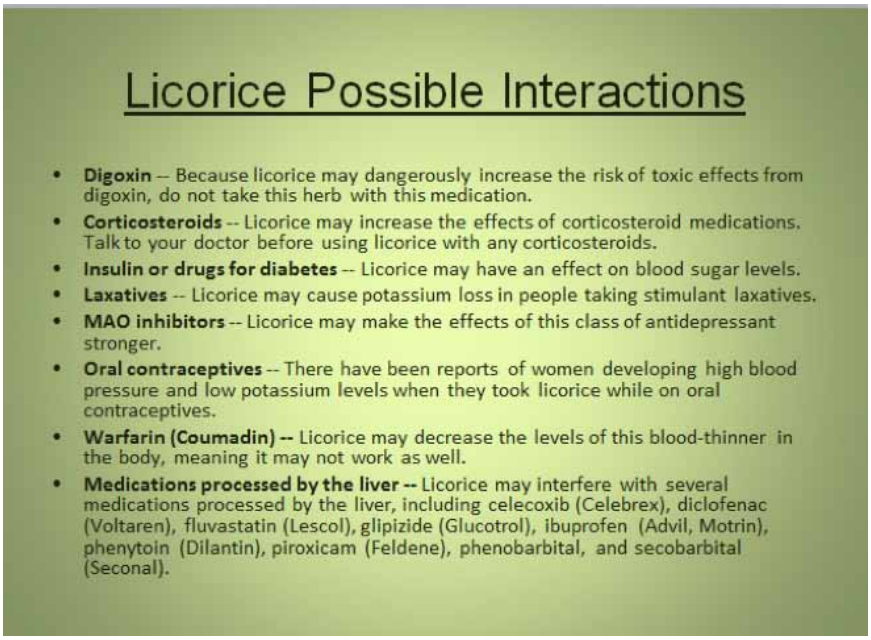

Figure 3

Schisandra (Schisandra chinensis)

Traditional use

Schisandra is one of the 50 fundamental herbs in Chinese medicine. Traditionally, it has been used either in dry form or as a tea. It is known to have a tonic restorative adaptogenic effect. It is most notable in its liver protecting effects. The primary hepatoprotective and immunomodulated constituents in schisandra are the lignins. Lignins are found in the seeds of the fruit. Schisandra is an antioxidant. It is hepatoprotective and reduces damage and aids in regeneration. It also induces Phase I liver enzymes, increases Phase II enzymes-glutathione reductase and glutathione-s-transferase. Schisandra has been shown to improve mental performance, physical endurance and resistance to the effects of stress. The traditional uses for schisandra reside around the herb's adaptogenic properties. Figure 4 illustrates some of the herb's traditional uses.

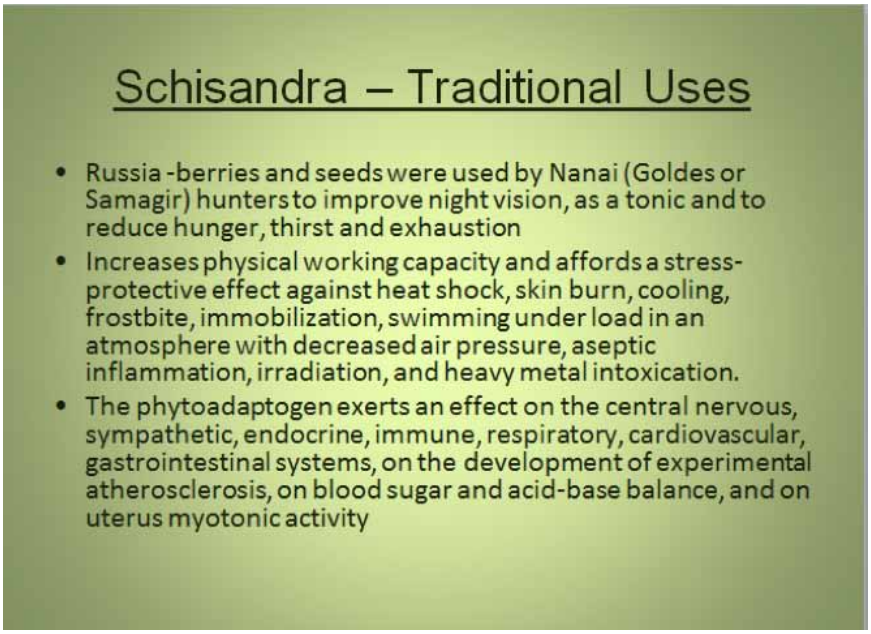

Figure 4

Pharmacology

The two major lignins, schizandrin and gomisin have been shown to induce interleukin 8, macrophage inflammatory protein, granulocyte-macrophage-colony stimulating factors. Schisandra may be beneficial in promoting the body's humoral and immune responses. There have been some documented antioxidant effects and in vitro hepatoprotective antiviral effects noted.

Dosing

Schisandra can be prescribed as a liquid extract in 3-10 mLs per day as a 1:3 extract. It can also be consumed as a fruit in 2-6 g per day. This plant should be avoided in pregnancy. No negative effects have been observed in the somatic state of patients.

Chinese skullcap (Scutellaria baicalensis)

Traditional use

Chinese skullcap is also considered one of the 50 fundamental herbs used in traditional Chinese medicine. Scutellaria baicalensis, also called Chinese skullcap, is a member of the mint family. It has been incorporated into many different herbal formulas and is used to treat a variety of conditions including cancer, liver disease, allergies, skin conditions and epilepsy. The root is the part of the plant most commonly used medicinally.

Pharmacology

The root of Chinese skullcap contains flavonoids. For this reason, studies have isolated and studied the flavonoids of Chinese skullcap more than the herb itself. Preliminary evidence suggests that one flavanoid, baicalein, can enhance the activity of antibiotics against antibiotic resistance staff bacteria. Preliminary evidence also suggests that these flavonoids have anti-inflammatory and anti-cancer liver protective properties.

Dosing

The optimum doses of Chinese skullcap have not been established. Typically it is prescribed in traditional Chinese medicine at about 3-9 grams per day as part of an herbal combination.

Safety

Chinese skullcap appears to have a good safety profile and low levels of toxicity. Case reports of liver injury have been associated with use of skullcap products, but these may have been due to adulteration by the herb germander. Chinese skullcap may reduce the absorption of cyclosporine and it may reduce the blood level of drugs in the statin family. There has not been much research regarding its safety in young children, pregnant or nursing women or people with severe liver or kidney disease.

Interactions

Chinese skullcap should not be prescribed to patients who are taking cyclosporine or statins.

Herbal treatment options

The following are several herbal treatment options for a variety of conditions.

Hepatitis C

For patients with hepatitis C, it can be effective to use plants that have antiviral, anti-inflammatory, antioxidant, antifibrotic and regeneration abilities of the hepatocytes. Four effective treatment options would be the use of milk thistle, turmeric, licorice and globe artichoke. Milk thistle provides anti-inflammatory, hepatocyte re-generation and anti-fibrotic benefits. Turmeric provides anti-inflammatory and anti-oxidant benefits. Licorice provides anti-viral, anti-inflammatory and anti-oxidant benefits. Globe artichoke provides antioxidant and regenerate function benefits.

Cholestatis

Cholestatis is best treated with cholagogues. The best treatment option would be:

- Equal parts celandine with dandelion root, 20 drops three times a day
- Wild yam tincture, 30 drops with each meal

This treatment plan will help ease a patient's discomfort in the right upper quadrant after eating.

Choledocolithiasis (gall bladder duct spasms)

For patients with gallbladder duct spasms who have gallstones that are less than 3 mm, using wild yam and supplemental bile salts can be an effective treatment method. It is also beneficial for the patient to avoid triggers such as sulfur-containing foods and high fat foods. Other cholagogues to consider including in a treatment plan include:

- Artichoke leaf
- Yellow dock
- Burdock root
- Dandelion root
- Celandine
- Fringe tree
- Beet root
- Barberry
- Oregon grape

Elevated LFTs idiopathic

Patients with elevated liver function (LFTs) who have not been found to consume high levels of alcohol or to have hepatitis or obstruction can benefit from the following:

- Milk thistle (70-80% silymarin; >140 mg three times a day)
- Turmeric
- Artichoke
- Licorice

Conclusion

Hepatoprotective herbs can be a viable and effective treatment method when used in the correct doses and situations. Milk thistle, turmeric, licorice, schisandra and Chinese skullcap are herbs that can help treat liver problems and other conditions. Understanding how these herbs function and what their limitations are can help the practitioner develop a customized treatment plan to benefit the patient.

Contributor

Dr. Tori Hudson is a naturopathic physician and a graduate of the National College of Naturopathic Medicine. She is currently a clinical professor at NCNM and Bastyr University and has served as medical director, associate academic dean and academic dean for NCNM. She is also the program director for the Institute of Women's Health and Integrative Medicine. Hudson also sits on the scientific advisory boards for Gaia Herbs Professional Solutions, Nordic Naturals, Integrative Therapeutics Inc., and Natural Health International. She has more than 28 years of experience and expertise in women's health and is the director of her own clinic in Portland, Oregon, A Woman's Time, as well as serves as the program director for the Institute of Women's Health & Integrative Medicine, as well as the director of research and development for Vitanica. She is the publisher of several publications including the *Women's Encyclopedia of Natural Medicine*.