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COMPLEMENTARY AND ALTERNATIVE THERAPIES IN LIVER DISEASES

Complementary or alternative medicine (CAM) therapies are "medical and health care practices that are not an integral part of conventional (Western) medicine." They can be classified into five categories: biologically based therapies, mind-body medicine, alternative medical systems, manipulative and body-based systems, and energy-based systems.

Many people with chronic liver disease, particularly hepatitis C, are interested in CAM remedies, especially when the virus has failed to respond to antiviral treatment. However, the expanded use of CAM by patients often occurs without the advice or knowledge of their health care provider.

A huge variety of herbs have been suggested as useful in the prevention, treatment, and maintenance of patients with a spectrum of chronic liver diseases. These botanicals are derived from a worldwide pharmacopoeia, including those of Western Europe, China, and India. In general, herbs used in liver conditions are classified as cholagogues, which induce the liver to produce bile; choloretics, which increase the flow of bile from the gallbladder; and cholekinetics, which stimulate bile duct contraction. Most herbalists prescribe a combination of many botanicals, making appraisal of the effect of any given preparation problematic.

Following are a list of botanicals that have been used in the treatment of liver disease:

Carrot (*Daucus Carota*): experiments in animals have shown protection against experimental injury by extracts of carrot.

Chicory (*Cichorium Intybus*): crude extracts of *Cichorium intybus* (Chicory) have been shown to inhibit free-radical-mediated DNA damage in lab animals.

Chinese Angelica (*Angelica Sinensis*): known as dang quai, angelica is a very popular Chinese woman's herb. Sodium ferulate, one of the effective components of *Angelica sinensis*, has prevented acetaminophen-induced injury in rats.

Dandelion (*Taraxacum Officinale*): leaves and roots have been suggested as a diuretic, treatment of jaundice. Traditional remedy in many cultures including, Chinese, Indian,

and European. Dandelion is classified as a choloretic, cholagogue, diuretic, and mild laxative.

Licorice (*Glycyrrhiza Glabra*): the active ingredient, glycyrrhizin, has been shown to have hepatocellular protective properties in experimental animals. A recent retrospective Japanese trial has demonstrated that HCV patients taking a licorice extract (Stronger Neo-Minophagen C) were less likely to develop hepatocellular carcinoma (HCC).

Milk Thistle (*Silybum Marianum*): the fruit of the milk thistle (*silybum marianum*) has been used for many years in the treatment of a variety of liver diseases. This is the most commonly used and best tested herb in the category of liver diseases. Evidence suggests widespread use of silymarin compounds among patients diagnosed with chronic HCV. Extract of the milk thistle fruit, a cousin of the daisy, contains 4-6% silymarin, a mixture of flavonolignans including silibinin, silychristin and silydianin. The effects of silymarin are assumed to be due to antioxidant and hepatoprotective properties. Actions ascribed to silymarin include alteration of the hepatocyte membrane, stimulation of nucleolar polymerase A with a resulting increase in protein synthesis, free-radical scavenging, and inhibition of peroxidizing enzymes. The potential antifibrotic properties of silibinin might be due to the inhibition of hepatic stellate cell proliferation and transmutation.

A single long-term randomized trial suggested survival benefit when silymarin was given to a group of patients with cirrhosis. A study of twenty patients with chronic hepatitis treated with seven days of silymarin-phosphatidylcholine complex showed decreased measures of lipid peroxidation and transaminases. There are no published reports of silymarin toxicity.

Phyllanthus (*Phyllanthus Amarus, P. gastroemii*): phyllanthus are low shrubs common across southern Asia and Australia. In parts of India the herb is renowned for its success in treating hepatitis and jaundice. Classified as a cholagogue and antiviral, clinical trials have shown clinical improvement in patients with chronic hepatitis B infection, while animal studies have shown viral replicative inhibition.

Schizandra (*Schizandra Sinensis*): used in China to treat viral hepatitis. Studies in small animals have shown protective properties in carbon tetrachloride toxicity. Some studies have shown significant decrease in liver enzymes in various forms of hepatitis.

Syo-saiko-to: this Japanese herbal preparation contains a combination of botanicals. Recent reports have noted a decrease in HCC in patients treated for longer than five years.

NATUROPATHIC THERAPIES IN CHRONIC HEPATITIS C

No herbal, diet supplement or alternative medicines have been proven to cure or even relieve symptoms of hepatitis C. At this point, all such treatments should be considered experimental. Safety is the first concern. However, many people see these

products as safe because they are "natural". As part of the nutrition assessment, it is important to determine the type of herbal preparations and supplements used, the extent to which these replace nutrition intake, the risk of interactions or potential toxicities with conventional antiviral treatment, and the risk of damage to the compromised liver. As well, potential harmful effects of herbal preparations and mega-doses of vitamins/minerals must be discussed with the patient. CAM therapies that are safe should be taken only under the guidance of a health care provider.

Many people are turning to herbs for relief. They use herbs either to help with hepatitis itself or to deal with side effects of interferon. These harmful side effects can include: sudden hearing loss; anemia and other forms of low blood cell counts; headaches; heart, eye, liver, or kidney problems; and disorders of the mind, including depression. Among potential herbal therapies (including licorice root, ginseng, ginger, and St. John's wort) for hepatitis C, the most promising alternative treatment seems to be the herb commonly called milk thistle.

Preliminary studies in animals show that milk thistle may help protect the liver from injury by a variety of toxins ("poisons" such as drugs, viruses, alcohol, radiation, and poisonous mushrooms) and limit the damage from them. To date, the most reliable, and also quite preliminary, studies on people show that milk thistle does not cure liver disease, but that it may improve the way the liver works in patients with cirrhosis. However, there is no current evidence to indicate that milk thistle directly affects HCV.

In Germany, where many herbs are regulated and prescribed like drugs, health authorities have approved milk thistle as a complementary treatment (given in addition to conventional drugs) for cirrhosis, hepatitis, and similar liver conditions. But a great deal of research still is needed before this alternative therapy could be considered a standard treatment option in the United States.

Milk Thistle

Milk thistle originally is from Europe, but now it also is grown in the United States. Its scientific name is *Silybum marianum*. The ingredient that experts believe is responsible for its medicinal qualities is called silymarin. Silymarin is found in the fruits of the milk thistle plant. Studies in animals have shown that this active ingredient promotes the following activities:

Liver Cell Growth—Silymarin appears to promote the growth of some types of cells in the liver.

Antioxidation—Silymarin may be an effective "antioxidant," which means it may help fight a destructive chemical process in the body known as "oxidation." In oxidation, harmful substances produced in the body (called free radicals) can damage cells. Some studies suggest that silymarin can prevent these substances from damaging liver cells.

Antihepatotoxic Activity—Studies suggest that silymarin can block various types of toxins from entering and injuring liver cells.

Inflammation Inhibition—Silymarin is thought to prevent inflammation (swelling) of the liver; this may be described as displaying anti-inflammatory properties.

Milk thistle is not used to prevent HCV from causing liver disease. Rather, it is used with the hope that it would minimize the damage to the liver that HCV can cause.

Studies of Milk Thistle in People

Although studies in animals provide a good deal of information on potential new treatments, studies in humans are needed before it can be determined if these therapies are appropriate, safe, and effective in people. The most rigorous type of study to establish a scientific basis for use of a new therapy in people is a randomized, double-blind, placebo-controlled (RDBPC) trial.

Although not focused primarily on HCV disease, the most relevant existing research data regarding milk thistle's use as a therapy for hepatitis comes from two RDBPC trials of silymarin's effects on cirrhosis. The two studies produced conflicting results.

The first, reported in 1989, examined 170 patients with cirrhosis from various causes, including alcohol abuse. Approximately half (87) of the patients received silymarin (140 milligrams 3 times a day for 2 years). The others (83 patients) received a placebo. Because 24 patients dropped out of the study, a total of 146 patients (73 in each group) finished the 2-year study.

The doctors in this study noted that the number of patients who died in the 4 years after the study was 31 percent lower in the group that received the silymarin than in the group of patients who received the placebo. The beneficial effects of silymarin were especially seen in the patients who had cirrhosis as a result of alcohol abuse. The doctors did not report that any patients experienced side effects from silymarin treatment.

A more recent RDBPC trial, however, did not find silymarin to have any significant benefits for patients with cirrhosis. In this study, reported in 1998, doctors examined 200 patients with cirrhosis caused by alcohol abuse. Approximately half (103) of the patients received silymarin (150 milligrams 3 times a day for 2 years). The other half (97) received a placebo. A total of 125 patients (57 in the treatment group and 68 in the placebo group) finished the 2-year study. To measure effectiveness, the doctors measured (1) time to death and (2) the worsening of the disease.

Survival was similar in both the silymarin and placebo groups, and silymarin did not seem to improve the course of the disease in the treatment group. The doctors who performed the experiment did not note side effects in any of the patients.

Although small, one randomized controlled trial on hepatitis patients suggests that a specific component in silymarin may be beneficial in managing chronic hepatitis. In this study, reported in 1993, 10 patients with chronic hepatitis were assigned to the treatment group and 10 others were assigned to the placebo group. The treatment group received 240 milligrams of silybin, a component of silymarin, two times a day for 1 week. The results of tests that measure how well the liver is functioning showed significant improvement in the treatment group, suggesting that silybin may help treat chronic hepatitis.

Milk thistle in the treatment of liver disease needs to be studied further. Fortunately, negative side effects have not yet been reported, and this herbal therapy may be much less expensive than conventional drug therapies. Yet, it should be mentioned that conventional therapies have been proven to work in a substantial portion of patients.

Because milk thistle does not dissolve well in water, the herb is not effective in the form of a tea. It currently is marketed in the United States as a dietary supplement in the form of capsules containing 200 milligrams of a concentrated extract with 140 milligrams of silymarin.

Other Herbs That May Help

Licorice Root—Herbalists use tea made with licorice root to manage some of the effects hepatitis has on the liver. The scientific name for licorice root is *Glycyrrhiza glabra*, and its active component is called glycyrrhizin. Studies suggest that licorice root displays antiviral and anti-inflammatory properties.

Licorice root does come with a warning, however. If taken regularly (more than 3 grams of licorice root a day for more than 6 weeks, or more than 100 milligrams of glycyrrhizin a day), this herb can cause the following conditions in some people: high blood pressure, sodium and water retention, low potassium levels in the bloodstream, and disturbance of an important electrolyte balancing system in the body.

Signs and symptoms of excessive licorice root consumption may include headache, sluggishness, puffiness and swollen ankles, and even heart failure or cardiac arrest (when the heart suddenly stops beating).

Glycyrrhizin has been used in Japan for more than 20 years as a treatment for chronic hepatitis. In a 1998 review of several randomized controlled trials, researchers reported that treatment with glycyrrhizin is effective in easing liver disease in some people. Several of the trials reviewed indicated improvements in liver tissue that had been damaged by hepatitis. Some of them also showed improvements in how well the liver does its job.

A 1997 experiment suggested that glycyrrhizin also may help prevent the development of liver cancer in patients with chronic hepatitis C. The use of glycyrrhizin as a

complementary therapy (in addition to conventional use of interferon drugs) has been studied, but no significant benefit has been found yet.

Ginseng—Tests on animals and on human tissues suggest that ginseng may help the body's disease-fighting and glandular systems. Tests in small animals also suggest that ginseng may help improve the way the liver works and reduce damage to liver tissue caused by hepatitis and similar conditions. However, a search of the current literature shows no studies in people that test ginseng's helpfulness for hepatitis. Only one study, conducted in Italy, shows that ginseng may be helpful for elderly people with liver conditions similar to hepatitis.

There are two true ginsengs—American ginseng (*Panax quinquefolius*) and Asian ginseng (*Panax ginseng*), which includes Chinese, Japanese, and Korean ginseng. Siberian ginseng (*Eleutherococcus senticosus*) is not a true ginseng. It is hard to get authentic ginseng products. Companies that market herbs for sale have poor quality control, so the quality of the different brands varies widely. A 1990 analysis of 54 available ginseng products revealed that 85 percent of them contained little or no ginseng at all! Ginseng most often is taken as a tea.

Herbs That May Ease Interferon's Effects

Ginger—For 2,500 years, the Chinese have used ginger (*Zingiber officinale*) to treat nausea. Some, but not all, research studies confirm that ginger may reduce nausea. This herb may relieve nausea and vomiting caused by interferon drug therapy in some patients with hepatitis C. Ginger generally is recognized as safe and is not known to cause any serious side effects. Ginger is relatively inexpensive and readily available. It most commonly is taken in the form of a tea.

St. John's Wort—Some patients with hepatitis C take the herb St. John's wort (*Hypericum perforatum*) to treat depression caused by interferon drug therapy. Although St. John's wort is not a proven treatment for depression, studies have shown that it does have antidepressive effects over the short term. Although research largely has been done using capsules of this herb, St. John's wort also is taken as a tea. There is no proof yet that St. John's wort is effective and safe over the long term.

St. John's wort does not require a prescription, and it is less expensive and may have fewer side effects than prescription antidepressant drugs. Tests in people reveal it may cause side effects such as fatigue, dry mouth, dizziness, digestive tract symptoms, and increased sensitivity to sunlight.

HERBS KNOWN TO BE TOXIC

A key concern is that some plant substances are hepatotoxic. Some herbs may be an added stress to an already compromised liver, thereby increasing liver damage. Because

the evidence is so limited, the only way to reduce the risk of liver damage is to limit the use of herbal products, and to avoid the herbs that are known to be hepatotoxic.

Herbs That Are Hepatotoxic

Artemesia	Kombucha mushroom (tea)
<i>Atractylis gummifera</i>	Ma-Huang (<i>Ephedra sinica</i>)
Bush tea	Margosa oil
<i>Callilepis laureola</i>	Mate (Paraguay) tea
Chapparal leaf (creosote bush, greasewood)	Mistletoe
Comfrey (<i>Symphytum officinale</i>)	Pennyroyal (squawmint oil)
Crotalaria	Sassafras
Germander	<i>Senecio aureus</i>
Gordolobo herbal tea	Senna
Heliotropium	Skullcap
Jin-Bu-Huang	Symphytum
Kava (<i>Piper methysticum</i>)	Valerian root