RESEARCH REPORT
NATIONAL CENTER FOR COMPLEMENTARY AND ALTERNATIVE MEDICINE

Hepatitis C and Complementary and Alternative Medicine: 2003 Update

Hepatitis C is a disease of the liver that is caused by the hepatitis C virus. The disease occurs in acute and chronic forms; symptoms can range from mild (or even no symptoms) to severe. There are conventional medical treatments available for hepatitis C, but some patients also try complementary and alternative medicine (CAM).[*] This Research Report answers some frequently asked questions on hepatitis C and CAM, reviews findings from scientific research on some dietary supplements that have been used as CAM treatments for hepatitis C (milk thistle, licorice root, ginseng, thymus extract, schisandra, and colloidal silver), and suggests sources for further information.

Key Points

- Conventional medical treatment (consisting of a combination drug regimen) for hepatitis C has shown sustained benefit in approximately 55 percent of patients.
- Some of the reasons hepatitis C patients try CAM are that they find conventional drug treatment difficult to tolerate or they do not experience a sustained response to treatment.
- No CAM treatment has yet been proven safe and effective for treating hepatitis C.
- There are many CAM treatments for which benefits for health are claimed. However, it is important to find out what scientific studies have been done on the safety and effectiveness of the CAM treatment in which you are interested.

[*] Conventional medicine is medicine as practiced by holders of M.D. (medical doctor) or D.O. (doctor of osteopathy) degrees and their allied health professionals, such as physical therapists, psychologists, and registered nurses. Other terms for conventional medicine include allopathy; Western, mainstream, orthodox, and regular medicine; and biomedicine. Some conventional medical practitioners are also practitioners of CAM. CAM, as defined by NCCAM, is a group of diverse medical and health care systems, practices, and products that are not presently considered to be part of conventional medicine.

NCCAM

Clinical trials[†] are needed of CAM therapies that may show some potential for benefit for hepatitis C, such as milk thistle. The National Center for Complementary and Alternative Medicine (NCCAM) is sponsoring a clinical trial of milk thistle.

- It is important to inform all of your health care providers about any therapy that you are currently using or considering, including any dietary supplements. This is to help ensure a safe and coordinated course of care.

Quick Facts About Hepatitis C

- Hepatitis C is the most common bloodborne infection in the United States. About 35,000 new cases are diagnosed in the United States each year.
- Hepatitis C is transmitted primarily when an infected person's blood comes into contact with the blood of a noninfected person.
  - People who are at the highest risk for HCV infection are those who have used or experimented with injection drugs; received a blood transfusion, blood product, or organ transplant before July 1992; worked in health care and had a needlestick accident involving HCV-infected blood; or had multiple sex partners.
  - A risk exists but is low (1 to 5 percent) for babies born to a mother with hepatitis C and for people who are in a monogamous sexual relationship with someone with hepatitis C; who have had other sexually transmitted diseases; who have had tattooing or body piercing done with unsterilized tools; or who have used cocaine intranasally (i.e., "snorted" it).
  - Hepatitis C is not spread through sneezing, coughing, kissing, hugging, food or water, or casual contact.
- People who are newly infected have what is called acute hepatitis C. For about 15 to 40 percent of this group, the infection is short-term, goes away, and does not return. Others develop chronic (or long-lasting) hepatitis C, in which the virus stays in the liver, replicates itself, and injures the liver over time.
- Among people with chronic hepatitis C, most show no symptoms for up to 20 to 30 years; some have mild symptoms; and some have more serious symptoms.
- Chronic hepatitis C can cause liver disease, cirrhosis (scarring of the liver), liver cancer, and liver failure. However, persons who have been diagnosed with hepatitis C need to know that serious illness or death from the disease is by no means inevitable—especially if they take proper care of themselves and get the health care they need.

[†] Clinical trials are research studies in people. To find out more, see "About Clinical Trials and Complementary and Alternative Medicine."

What is hepatitis C?

Hepatitis C is a communicable (contagious) disease of the liver caused by the hepatitis C virus (HCV).[‡] The liver, the largest organ in the body, is found behind the ribs on the right side of the abdomen. It has many important functions, including removing harmful material from the blood and converting food into substances needed for life and growth. The term "hepatitis" means inflammation of the liver. There are other viruses in the hepatitis family (such as hepatitis A and hepatitis B), but HCV is not related to them.

What does conventional treatment for chronic hepatitis C consist of?

People who have a mild case of hepatitis C may only need to manage it by visiting their doctor regularly and following their doctor's recommendations—such as eating a nutritious diet, avoiding alcohol (because of its impact on the liver), and getting regular exercise.

For people with more severe hepatitis C, however, drug therapy may be needed. A drug called interferon is the mainstay of conventional treatment. Interferon is often combined with an antiviral (virus-fighting) drug called ribavirin. Such combination therapies are usually taken for 6 months to 1 year. Approximately 55 percent of patients treated with the combination of interferon and ribavirin for 1 year will achieve a sustained response (that is, a sustained benefit from treatment).[1] If a patient does not achieve a sustained response, his doctor may decide whether another course of treatment (re-treatment) is appropriate.

Combination regimens benefit many patients. However, their side effects can be difficult for some patients to tolerate. These side effects can include flu-like symptoms (such as body aches, fever, chills, and fatigue); nausea and other gastrointestinal problems; hair loss; emotional changes; skin reactions; and, in more severe cases, depression, organ damage, blood conditions, and other problems.

Why do people use CAM for hepatitis C?

There are various reasons why people use CAM for hepatitis C, including:

- They have not had a response to initial treatment or to re-treatment with drugs.
- They are not willing to have drug treatment or continue it—for example, because of the side effects or length of treatment.
- They would like to support their body's fight against damage by hepatitis C, and they hear of benefits claimed for some CAM treatments—such as "strengthens the immune system" or "cleanses or rejuvenates the liver" (or other organs).
- They are experiencing problems from other diseases and conditions that can be caused by or worsened by hepatitis C.
- They are not satisfied with their conventional medical treatment.

[‡] To find out more about hepatitis C and conventional treatment for it, consult the Federal agencies listed under "For More Information."

How commonly do people with hepatitis C use CAM therapies, and what do they use?

While there have been no surveys yet on the use of CAM by persons with hepatitis C specifically, there is some data from a survey published in 2002 on the use of CAM by persons who have chronic liver diseases (such as hepatitis, liver cancer, alcoholic liver disease, or cirrhosis).[2] This survey of 989 patients being treated for various liver diseases at six clinics in the United States found that 39 percent used some form of "alternative therapy." The therapy they used the most was herbals or botanicals[§] (21 percent). However, the herbals and botanicals were used for reasons besides liver disease, such as depression. Thirteen percent of all survey participants used herbals or botanicals specifically for their liver disease, and they used only milk thistle (12 percent) or licorice root (1 percent). The other most commonly used CAM therapies were self-prayer[**] (18 percent), and (from 6 to 9 percent each) relaxation, megavitamins, massage, chiropractic, and spiritual healing.[2]

What CAM therapies are discussed in this Research Report?

There is a range of medical concerns associated with hepatitis C, and the number of CAM therapies that are tried is large.[††] Therefore, it is beyond the scope of this Research Report to discuss all possible CAM therapies used for hepatitis C. The report focuses on a number of dietary supplements that are used: milk thistle, licorice root, ginseng, thymus extract, schisandra, and colloidal silver (research discussions begin on page 6).

About Dietary Supplements

Dietary supplements were defined in a law passed by Congress in 1994. A dietary supplement must meet all of the following conditions:

- It is a product (other than tobacco) intended to supplement the diet, which contains one or more of the following: vitamins; minerals; herbs or other botanicals; amino acids; or any combination of the above ingredients.
- It is intended to be taken in tablet, capsule, powder, softgel, gelcap, or liquid form.
- It is not represented for use as a conventional food or as a sole item of a meal or the diet.
- It is labeled as being a dietary supplement.

Sources for this 2003 update consist of the peer-reviewed medical and scientific journals indexed in the National Library of Medicine's MEDLINE/PubMed database, in English, from January

[§] Herbs are plants or plant parts valued for their flavor, scent, and/or therapeutic properties. "Herbals" and "botanicals" are synonyms and mean herbal and botanical products.

[**] Self-prayer is when an individual prays for himself. It can be contrasted with intercessory prayer, in which an individual prays for others.

[††] To read about the major of areas of CAM, see the NCCAM fact sheet "What Is Complementary and Alternative Medicine?"

1999 through May 2003.[‡‡] Sources that you can use to research additional science-based information are in the "Sources" sections.

What is known from the scientific evidence about CAM modalities for hepatitis C?

- No CAM treatment has been scientifically proven to successfully treat hepatitis C.

- Authors who have done recent analyses of the scientific work have found some results that are intriguing and even promising, but they have noted that more research—especially in the form of controlled clinical trials—is needed before firm conclusions can be drawn.

    - The authors of a 2003 systematic review of medicinal herbs for hepatitis C concluded that there is not enough evidence to support using herbs to treat the disease. This team identified 13 clinical trials that were of sufficient quality for them to analyze. Compared to placebo,[§§] they found that none of the herbs tested showed effects on liver enzymes or reduced the amount of HCV in the bloodstream, except for milk thistle, which did show a significant reduction of liver enzymes in one trial.[3]
    - Two general reviews from 2000 that covered a variety of CAM modalities for hepatitis C concluded that conventional therapies are the only scientifically proven treatments for the disease.[4,5]
    - NIH released a Consensus Statement in 2002 on the management of hepatitis C.[***] This assessment by a panel of medical and scientific experts found that "alternative and nontraditional medicines" should be studied.

What should I do to take care of myself if I have hepatitis C?

- Make sure you have received an accurate diagnosis. Hepatitis C can be diagnosed reliably only through sophisticated blood tests used in conventional medicine.

- See your health care provider regularly.

- Discuss treatment options with your provider. Ask any questions you have to make sure you understand any treatment and possible side effects. Follow her recommendations for any changes to your diet and/or lifestyle.

[‡‡] This report also incorporates information from the NCCAM fact sheet "Hepatitis C: Treatment Alternatives," published in 2000.

[§§] A placebo is designed to resemble as much as possible the treatment being studied in a clinical trial, except that the placebo is inactive. An example of a placebo is a pill containing sugar instead of the drug or other substance being studied. By giving one group of participants a placebo and the other group the active treatment, the researchers can compare how the two groups respond and get a truer picture of the active treatment's effects. In recent years, the definition of placebo has been expanded to include other things that could have an effect on the results of health care, such as how a patient and a health care provider interact, how a patient feels about receiving the care, and what he or she expects to happen from the care.

[***] See "Sources: General," page 12, item A.

- Tell your provider about any herbal supplements, other dietary supplements, or medications (whether prescription or over-the-counter) that you are using or considering. This is important for your safety. Even if your provider does not know about the actions or interactions of an herbal supplement or other CAM treatment, he can access the most current medical guidance.

- Get vaccinated against hepatitis A and B. Infection with hepatitis C does not prevent a person from becoming infected with other types of hepatitis; if this happens, it can be serious, even life-threatening.

- Be an informed consumer. Seek high-quality, science-based information on any CAM modality that you are using or considering. There is free information from NCCAM, the National Library of Medicine, and other Federal sources to help you distinguish science-based information from other types, including word-of-mouth and manufacturers' claims.

- If you decide to try herbal supplements, do so with care. (See the NCCAM fact sheet "Herbal Supplements: Consider Safety, Too.")

- If you would like to find out about clinical trials of treatments for hepatitis C, go to www.clinicaltrials.gov or contact the NCCAM Clearinghouse.

Scientific Research Findings: Selected CAM Treatments for Hepatitis C

This section describes six CAM therapies that people have used to treat hepatitis C. More-detailed discussions of individual studies are available in the Appendix. Reviews are discussed where available.[†††]

Milk Thistle

Milk thistle (scientific name *Silybum marianum*) is a plant from the aster family. The active extract of milk thistle believed to be responsible for the herb's medicinal qualities is silymarin, found in the fruit.[6] Milk thistle has been used in Europe as a treatment for liver disease and jaundice since the 16th century.[7]

Summary of the research findings

- The results of scientific studies to date do not definitively find that milk thistle is beneficial in treating hepatitis C in humans.

- Studies in laboratory animals suggest that silymarin may have various benefits to the liver, such as promoting the growth of certain types of liver cells, having a protective effect upon liver cells, fighting a chemical process called oxidation that can damage cells, and inhibiting

[†††] There are different types of review articles: In a general review, a broad picture of the scientific studies and evidence available on a particular topic is presented. In a systematic review, data from a set of studies on a particular question or topic are collected, analyzed, and critically reviewed. A meta-analysis uses statistical techniques to analyze results from a collection of individual studies.

inflammation.[7-14] However, in some cases, a consistent pattern of benefit was not seen, and these studies did not specifically examine the effects of silymarin on hepatitis C.

- There have been some studies on silymarin or milk thistle in humans. These studies have generally been small and on liver diseases rather than on hepatitis C infection specifically, and the results have been contradictory (with some positive and some negative).[15-17] A review and a meta-analysis published in 2001 on silymarin in the treatment of liver diseases found it to be generally safe, but contained no firm conclusions with regard to its use to treat viral hepatitis.[18,19] A 2002 systematic review on milk thistle for liver disease found "no reduction in mortality (frequency of death as an outcome), in improvements in histology (tissue studies) observed through liver biopsy, or in biochemical markers of liver function" and that the data was too limited to support recommending milk thistle for treatment of liver disease.[20]

To obtain more extensive and reliable data, NCCAM is sponsoring a clinical trial on the use of milk thistle for hepatitis C.

Side effects and other risks
Milk thistle is generally well-tolerated and has shown few side effects in clinical trials. It can cause a laxative effect; less common effects include nausea, diarrhea, abdominal bloating, fullness, and pain. Milk thistle can produce allergic reactions, which tend to be more common among people who are allergic to plants in the same family (e.g., ragweed, chrysanthemum, marigold, and daisy).

Licorice Root
Licorice root is the peeled or unpeeled dried root of the licorice plant (*Glycyrrhiza glabra*). The primary active component of licorice root is a substance called glycyrrhizin. Licorice root has been in use in China since the second and third century B.C. and in the West since Egyptian, Greek, and Roman times.[21]

Summary of the research findings
- Laboratory studies of glycyrrhizin in cell cultures suggest that it may have antiviral properties.[21]

- In a review of several randomized controlled trials, researchers reported that glycyrrhizin has potential for reducing long-term complications in chronic hepatitis C in those patients who may not respond to interferon.[22] Several of the trials reviewed indicated improvements in liver tissue damaged by hepatitis. Some also showed improvements in how well the liver did its job after treatment.

- A 1997 study and a 2002 review suggest that long-term administration of glycyrrhizin might prevent liver cancer in patients with chronic hepatitis C.[23,24]

- The use of glycyrrhizin as a complementary therapy (i.e., used in addition to conventional interferon therapy) has been studied, but no significant benefit has been found.[25,26]

- Recent clinical trials have shown that taking glycyrrhizin lowers the levels of liver enzymes (increased levels of certain liver enzymes indicate liver damage or inflammation). However, taking the herb did not reduce the amount of HCV in patients' blood, a critical indicator of the long-term progress of the infection.[27-29]

Side effects and possible risks
Taking licorice over a prolonged period of time can lead to potentially serious side effects, including high blood pressure, salt and water retention, swelling, depletion of potassium, headache, and/or sluggishness.[30] Glycyrrhizin can worsen ascites, the accumulation of fluid in the abdominal cavity, a condition that can be caused by cirrhosis.[31] The herb also can interact with certain drugs, such as diuretics, digitalis, antiarrhythmic agents, and corticosteroids.

Ginseng
The herb ginseng comes in two types: American ginseng (*Panax quinquefolius*) and Asian ginseng (*Panax ginseng*). Among the Asian forms of ginseng are Chinese, Japanese, and Korean ginseng. (So-called "Siberian ginseng" is not a true ginseng.) Ginseng has been used for thousands of years in Asia. It is usually used with the belief that it will boost the immune system and increase stamina; such properties are thought to be more useful for the elderly and those recovering from illness.[32]

Summary of the research findings
- The research on ginseng that has been done to date has been primarily in animal models and human tissue in the laboratory. Some beneficial effects of ginseng on the liver were seen in these studies. Researchers concluded that ginseng may also help strengthen glandular systems and the ability to resist disease.[33-36]

- One study found that ginseng may be helpful for elderly people with liver conditions similar to hepatitis.[37]

- No conclusions can be drawn about the possible usefulness and safety of ginseng as a treatment in people who have hepatitis C, because it has not been studied formally yet in people.

Side effects and possible risks
General adverse (negative) effects of ginseng can include insomnia, headache, nosebleed, nervousness, and vomiting. Prolonged use of caffeine and a high dose of ginseng may be associated with hypertension, which is of particular concern for people with cardiovascular disease or diabetes. In addition, people with diabetes who use insulin should be aware that ginseng has demonstrated hypoglycemic effects (lowering of the blood sugar). Ginseng has been shown in laboratory studies to inhibit grouping of platelets in the blood, increasing bleeding risk. Because of this, using ginseng along with NSAIDs (non-steroidal anti-inflammatory drugs), such as aspirin or ibuprofen, should be discussed with your health care provider.[32]

Thymus Extract

The thymus is a gland that is involved in the regulation of the body's immune response. Thymus extract products consist of peptides taken from the thymus glands of cows or calves and are sold as dietary supplements. Often, these products carry claims of boosting immune system functioning to combat diseases, such as hepatitis C. These over-the-counter supplements should not be confused with the prescription drug thymosin alpha-1.

Summary of the research findings

There has been little testing of bovine thymus extract for treatment of hepatitis C. A small clinical trial of a product called Complete Thymic Formula, which contains bovine thymus extracts along with vitamins, herbs, minerals, and enzymes, did not find the product beneficial for hepatitis C patients who had not responded previously to interferon therapy.[38] However, this small study does not provide sufficient evidence to draw firm conclusions about either Complete Thymic Formula or thymus extracts in general.

Side effects and possible risks

In the study of Complete Thymic Formula, one adverse event was reported: a patient developed thrombocytopenia, a drop in the number of platelet cells in the blood; the patient recovered after treatment was stopped.[38] In general, no adverse effects from thymus extracts have been reported. However, since thymus extracts are derived from animals, there can be concern related to possible contamination from diseased animal parts.[‡‡‡] Accordingly, people on immunosuppressive drugs or who have suppressed immune systems, such as transplant recipients or persons with HIV/AIDS, should use caution about thymus extracts and consult with their health care provider.

Schisandra

Schisandra is a plant that has been used (through extracts from its fruit) in traditional Chinese medicine and in Kampo, traditional Japanese medicine. There are several species, including *Schisandra chinensis*, native to northeastern China and Korea, and *Schisandra sphenanthera*, native to China.

Summary of the research findings

- Research has primarily focused on the various lignans (a class of plant nutrients) and essential oils in the dried fruit of schisandra.[39] Major constituents include the lignans gomisin A, schizandrins and schizandrol, vitamins C and E, and others.

- Studies of the effects of schisandra in the liver have mostly been in animal models. These studies have suggested that extracts of the fruit have a liver-protective effect, a helpful effect on some liver enzymes, and an antioxidant effect. [§§§,39,40]

[‡‡‡] With regard to side effects, see "Sources: General," item F, entry on thymus extract.

[§§§]Antioxidants are substances (such as vitamin E) that help prevent oxygen from reacting with other chemicals in cells (oxidation), a process that can have negative effects.

- Schisandra is also used in herbal formulas. For example, an herbal medicine called TJ-108 (Ninjin-yomei-to is one of its Japanese names) used in Kampo has schisandra fruit among its herbal components. In one very small study, TJ-108 was compared with two other Kampo herbal formulas for effects in 37 patients who had chronic hepatitis C and had been treated before with interferon.[41] The findings were that TJ-108 may have antiviral properties, which the authors attributed to schisandra fruit and its lignan gomisin A.[7,41] These findings need to be interpreted with caution because of the study's small size and because use of an herbal formula, not schisandra alone, was evaluated; herbal formulas contain many ingredients that could cause a variety of effects.

- There are no reports on the safety and effectiveness of using schisandra alone for treatment of hepatitis C in humans in the sources reviewed for this report.

Side effects and other risks
Schisandra is considered generally safe. In some people, however, it may cause heartburn, acid indigestion, decreased appetite, stomach pain, or allergic skin rashes.

Colloidal Silver
Silver is a metallic element that is mined as a precious metal. People are exposed to silver, usually in tiny amounts, through their environment, drinking water, food, and possibly work or hobbies. Colloidal silver supplements consist of tiny silver particles suspended in a liquid base. They are often marketed with a variety of unproven health claims, including for immunity, diabetes, cancer, and AIDS.

Summary of the research findings
Silver has had some medicinal uses going back for centuries. However, more modern and less toxic drugs have eliminated the vast majority of these uses. Reviews in the scientific literature on colloidal silver have concluded that[42,43]:

- Silver has no known function in the body.
- Silver is not an essential mineral supplement or a cure-all and should not be promoted as such.
- Claims that there can be a "deficiency" of silver in the body and that such a deficiency can lead to disease are unfounded.
- Claims made about the effectiveness of colloidal silver products for numerous diseases are unsupported scientifically.
- Colloidal silver products can have serious side effects (discussed below).
- Laboratory analysis has shown that the amounts of silver in these supplements vary greatly, which can pose risks to the consumer.

Side effects and other risks
Animal studies have shown that silver builds up in the tissues of the body. In humans, this accumulation can have a serious side effect called argyria, a bluish-gray discoloration of the body, especially of the skin, other organs, deep tissues, nails, and gums. How this happens is not fully known, but silver-protein complexes are thought to deposit in the skin and then be processed by

sunlight (similar to traditional photography).[44,45] Argyria is not treatable or reversible. Other possible problems include neurologic problems (such as seizures), kidney damage, stomach distress, headaches, fatigue, and skin irritation. Colloidal silver may interfere with the body's absorption of the following drugs: penacillamine, quinolones, tetracyclines, and thyroxine. For more information about colloidal silver, see the NCCAM fact sheet "Colloidal Silver Products."

For More Information

- **NCCAM Clearinghouse**

  Toll-free in the U.S.: 1–888–644–6226
  International: 301–519–3153
  TTY (for deaf and hard-of-hearing callers): 1–866–464–3615

  E-mail: info@nccam.nih.gov
  Web site: nccam.nih.gov
  Address: NCCAM Clearinghouse, P.O. Box 7923, Gaithersburg, MD 20898–7923

  Fax: 1–866–464–3616

  NCCAM is a component of NIH. The NCCAM Clearinghouse provides information on CAM and on NCCAM. Services include fact sheets, other publications, and searches of Federal databases of scientific and medical literature. The Clearinghouse does not provide medical advice, treatment recommendations, or referrals to practitioners.

- The **National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK)** is also a component of NIH. NIDDK's National Digestive Diseases Information Clearinghouse provides materials about hepatitis C and its conventional treatment. Go to digestive.niddk.nih.gov or call 1–800–891–5389 or 301–654–3810.

- The **National Institute of Allergy and Infectious Diseases**, also a component of NIH, has hepatitis C information. Go to www.niaid.nih.gov/publications/hepatitis.htm or call 301–496–5717.

- The **Centers for Disease Control and Prevention** provides information on hepatitis C. Go to www.cdc.gov/ncidod/diseases/hepatitis/index.htm or call 1–888–443–7232.

- The National Library of Medicine's (NLM's) **PubMed** database contains citations from over 4,500 peer-reviewed scientific and medical journals. Most citations include an abstract, and a number link to the full text of the article. Go to www.ncbi.nlm.nih.gov/entrez/query.fcgi.

- **CAM on PubMed**, a subset of PubMed (see above), contains citations to literature on CAM. It is sponsored by NCCAM and NLM. Go to www.nlm.nih.gov/nccam/camonpubmed.html.

- The **FDA** provides information on dietary supplements at www.cfsan.fda.gov/~dms/supplmnt.html or via an information line at 1–888–723–3366.

- The **NIH Office of Dietary Supplements** provides information on supplements at ods.od.nih.gov and through its International Bibliographic Information on Dietary Supplements (IBIDS) database (ods.od.nih.gov/health.aspx).

- **ClinicalTrials.gov** is a database of information on clinical trials, primarily in the United States and Canada, for a wide range of diseases and conditions. It is sponsored by the NIH and the FDA. Go to www.clinicaltrials.gov.

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Appendix
Research Findings on Selected CAM Treatments for Hepatitis C

Citation	Description	Findings
Liu et al., 2003[3]	Systematic review	The researchers conducted searches in several databases to identify 13 randomized trials of medicinal herbs for hepatitis C (trial quality was rated adequate in only 4 trials). The selected trials, involving a total of 818 patients with mainly HCV, evaluated 14 different medicinal herbs versus various control interventions such as placebo. Compared to placebo, they found that none of the herbs tested showed effects on liver enzymes or in reducing the amount of HCV, except for milk thistle, which did show a significant reduction of liver enzymes in one trial. The authors concluded, "There is no firm evidence supporting medicinal herbs for HCV infection, and further randomized trials are justified."
Milk Thistle (Silymarin)		
Letteron et al., 1990[11]	Animal study	Researchers tested the liver-protective effects of silymarin against the damaging effects of carbon tetrachloride by administering 800 mg/kg of silymarin to mice before administering carbon tetrachloride. The researchers concluded that giving silymarin to mice prior to exposure to carbon tetrachloride prevented in part both lipid peroxidation (damage to the membrane) and liver cell death.
Davila et al., 1989[12]	Animal study	Using cultures of liver cells from newborn rats, researchers studied the protective effects of an active component of silymarin. Pretreatment of the liver cells with silybin before exposure to liver cell toxins led to less damage and reduction of leakage of liver enzymes. The researchers concluded that the silymarin component "may act by stabilizing the plasma membrane against toxic insult."
Fuchs et al., 1997[13]	Animal study	Using a specific type of liver cell (hepatic stellate cells) whose proliferation and transformation are associated with progression to fibrosis in liver disease, researchers studied the effects of an active component of silymarin. The component reduced the proliferation of rat hepatic stellate cells by about 75% and reduced the transformation of the cells to myofibroblasts.

Boigk et al., 1997[14]	Animal study	Using an animal model of liver fibrosis, researchers studied the effects of silymarin on collagen accumulation, which occurs during the progression of liver fibrosis. After the 6-week experiment, the researchers found that rats with induced liver fibrosis who were given silymarin had from 30% to 35% reduction in the amount of collagen accumulated. This suggests that silymarin may have antifibrotic activity.
Ferenci et al., 1989[15]	Randomized, controlled trial	Eighty-seven patients with cirrhosis of the liver from various causes, including alcohol abuse, were given 140 mg of silymarin 3 times a day for 2 years, and 83 patients received placebo. A total of 146 patients completed the 2-year study. The researchers noted that the 4-year survival rate of patients in the treatment group was approximately 58% and the 4-year survival rate in the placebo group was approximately 39%. The beneficial effects of silymarin were especially seen in patients with cirrhosis as a result of alcohol. According to the researchers, results suggest "mortality of patients with cirrhosis was reduced by treatment with silymarin."
Pares et al., 1998[16]	Randomized, double-blind, controlled trial	Researchers studied 200 patients with cirrhosis of the liver caused by alcohol. In the 2-year trial, 103 patients received 150 mg of silymarin 3 times a day, and 97 patients received a placebo. A total of 125 patients finished the trial. The researchers measured time to death and worsening of the disease to test effectiveness of silymarin. They found that survival of patients was similar in the treatment and placebo groups, and silymarin did not seem to improve the course of the disease in the treatment group.
Buzzelli et al., 1993[17]	Randomized, controlled, pilot study	This small trial of hepatitis patients suggests that a component of silymarin may be beneficial in managing chronic hepatitis. Ten patients with chronic hepatitis were assigned to receive 240 mg of the silymarin component 2 times a day for 1 week, and 10 other patients received placebo. The results of tests that show how well the liver is functioning showed significant improvement in the treatment group.
Wellington and Jarvis, 2001[18]	Review	The authors reviewed the properties of silymarin and its uses in treating liver diseases and concluded that the "antioxidant properties of silymarin . . . have been demonstrated *in vitro* and in animal and human studies. However, studies evaluating relevant health outcomes associated with these properties are lacking." Furthermore, they stated "silymarin was largely ineffective in the treatment of patients with viral hepatitis."

Saller et al., 2001[19]	Meta-analysis	Thirty-six studies were analyzed. Regarding viral hepatitis, the authors concluded, "Several small trials involving silymarin . . . have been published. Most of them are methodologically outdated . . . ." Furthermore, they stated, "In spite of some positive results in patients with acute viral hepatitis, no formally valid conclusion can be drawn regarding the value of silymarin in the treatment of these infections."
Jacobs et al., 2002[20]	Systematic review, meta-analysis	Fourteen randomized, placebo-controlled trials in patients with chronic liver disease met inclusion criteria. Authors found "no reduction in mortality, in improvements in histology and liver biopsy, or in biochemical markers of liver function . . . ." They found the data to be too limited to support recommending milk thistle for treatment of liver disease.
Licorice Root (Glycyrrhizin)		
van Rossum et al., 1998[22]	Review	In this review the authors found treatment with glycyrrhizin to be effective in easing liver disease in some people. Some trials reviewed indicated improvements in liver tissue that had been damaged by hepatitis. Others showed improvements in liver function. The authors concluded "glycyrrhizin is a potential drug in reducing long-term complications in chronic viral hepatitis C in patients who do not respond with viral clearance to interferon therapy."
Arase et al., 1997[23]	Retrospective study	This retrospective study examined the long-term preventive effect of glycyrrhizin on the development of liver cancer (hepatocellular carcinoma). Of 453 patients with chronic hepatitis C identified, 84 had been treated with glycyrrhizin. A control group of 109 patients not treated long-term with either glycyrrhizin or interferon was identified. At 10 years out from diagnosis, the researchers found 7% of those treated with glycyrrhizin had developed liver cancer compared to 12% in the control group. At 15 years, the rates were 12% and 25%, respectively. They concluded that glycyrrhizin may help prevent the development of liver cancer.
Kumada, 2002[24]	Non-randomized clinical trial	The author assessed clinical data from non-randomized chronic hepatitis C patients who received glycyrrhizin in the form of a Japanese pharmaceutical product called Stronger Neo-Minophagen C (SNMC). He concluded "SNMC can suppress necro-inflammation in chronic hepatitis C. Long-term treatment with SNMC, therefore, would be able to prevent liver cirrhosis and the development of HCC [liver cancer]."

van Rossum et al., 1999[27]	Double-blind, randomized, placebo-controlled phase I/II trial	Fifty-seven chronic hepatitis C patients were randomized to receive 240, 160, or 80 mg of glycyrrhizin or placebo for 4 weeks with 4 weeks of followup. Glycyrrhizin lowered liver enzymes during treatment, but did not decrease the level of HCV. The authors concluded that glycyrrhizin was safe and that further investigation is needed.
Tsubota et al., 1999[28]	Randomized, controlled clinical trial	One hundred sixty-seven patients completed this 24-week study. Eighty-four patients received glycyrrhizin alone, and 83 took glycyrrhizin plus ursodeoxycholic acid. Liver enzyme levels were significantly decreased by both treatments. However, levels of HCV did not change in either group.
van Rossum et al., 2001[29]	Part I: randomized, double-blind, placebo controlled trial; Part II: open trial	Part I: Sixty-nine patients with chronic hepatitis C received glycyrrhizin as SNMC 3 times per week for 4 weeks with a 4-week followup. Part II: Fifteen of the original patient group then participated in an open trial where they received 200 mg of glycyrrhizin 6 times per week for 4 weeks. Researchers' overall conclusion is that glycyrrhizin induces significant decreases in liver enzyme (ALT) levels in patients with chronic hepatitis C. Administering glycyrrhizin 6 times per week appeared more effective than 3 times per week.
Ginseng		
Nguyen et al., 2000[35]	Animal study	This study showed that treating mice with either crude ginseng extract or total saponins (ginseng's active ingredients) before receiving the liver-damaging chemical carbon tetrachloride decreased carbon tetrachloride-induced increase of certain liver enzyme levels by 50% and 49%, respectively. According to the researchers, the data suggest that *Panax vietnamensis* could be used as a hepatoprotectant.
Tran et al., 2002[36]	Animal study	A mouse model of liver failure, which is applicable to a broad range of liver diseases, was used to test the liver protective effect of Vietnamese ginseng. Mice were pretreated with a ginseng extract, Majonoside R_2, at 12 hours and 1 hour before being given a liver cell death and failure inducing combination of D-galactosamine and lipopolysaccharide. The ginseng extract was seen to significantly inhibit liver cell death.

Thymus Extract		
Raymond et al., 1998[38]	Randomized, double-blind, placebo-controlled trial	Thirty-eight patients who had not responded or did not tolerate interferon received Complete Thymic Formula (CTF) for 3 or 6 months or placebo for 3 months. No differences were noted at 3 months between the placebo group and the treatment group. Nineteen patients who completed 6 months of treatment with CTF still had levels of HCV similar to those they had when treatment began. The researchers concluded that CTF did not benefit patients who had previously received interferon therapy.
Schisandra		
Cyong et al., 2000[41]	Two clinical studies, not controlled or randomized Additional studies done in vitro and in animal models	In a short-term study 34 hepatitis C patients were treated with one of three Kampo medicines for 6 months (TJ-108, TJ-48, or TJ-8). Eight patients had a decrease in virus levels; 6 of these were treated with TJ-108. In a long-term study 37 patients were treated with Kampo medicines, mainly TJ-108, for 1 year. The researchers determined that after 1 year of Kampo medicine, 8 patients (about 21%) tested negative for the virus and symptoms were improved in all patients. The researchers then tested the ability of TJ-108 to inhibit virus infection *in vitro* by adding TJ-108 to MOLT-4 cells (human lymphoblastoma cells) followed by HCV. They found that TJ-108 inhibited virus infection in a dose-dependent manner. Researchers identified the active ingredient in TJ-108 as schisandra fruit. The researchers then identified gomisin A as the active ingredient in the fruit. They then tested it in a mouse model of induced acute hepatic failure and concluded it increased survival.

Colloidal Silver		
Fung and Bowen, 1996[42]	Review	Authors review the history of silver products in conventional medicine and the marketing of oral colloidal silver protein supplements for the prevention and treatment of numerous diseases. Also address its chemistry, pharmacology, toxicology, and case reports of adverse events. Authors emphasize "the lack of established effectiveness and potential toxicity of these products."
Gulbranson et al., 2000[43]	Review and case report	Authors review the historical use of silver for medicinal purposes and discuss the case of a man who developed argyria after taking colloidal silver supplements for his allergies and colds.
White et al., 2003[44]	Case report	History of a man who developed argyria after taking colloidal silver to prevent and treat various diseases, including cancer.

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