

Herbal Medicine for Viral Hepatitis

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Abstract

Traditional and researched herbal treatments for acute and chronic viral hepatitis caused by hepatitis A, B, and C viruses are reviewed. Agents discussed include *Andrographis paniculata* (kalmegh) leaf, *Silybum marianum* (milk thistle) seed, silymarin, silibinin, Liv.52 formula, *Artemisia capillaris* (capillary wormwood, *yin chen hao*) leaf, *Yin Chen Hao Tang*, *Ligusticum porteri* (*oshá*) root, *Ligusticum grayi* (*oshala*) root, *Lomatium dissection* (desert parsley) root, *Forsythia suspensa* (*lian qiao*) herb, *Hypericum perforatum* (St. John's wort) herb, *Coptis chinensis* (gold thread, *huang lian*) root, *Artemisia ludoviciana* (western mugwort) leaf, *Glycyrrhiza glabra* (licorice) root, glycyrrhizin, *Schisandra chinensis* (*wu wei zi*) fruit, *Astragalus membranaceus* (*huang qi*) root, *Taraxacum officinale* (dandelion) root, *Arctium lappa* (burdock) root, *shosaiko-to*, *Xiao Chai Hu Tang*, *Salvia miltiorrhiza* (Chinese sage, *dan shen*) root, salvianolic acid B, *Fuzheng Huayu* formula, *Gynostemma pentaphyllum* (*jiao gu lan*) root, and *Ginkgo biloba* seed.

Introduction

Hepatitis viruses are a major problem around the world. Hepatitis A, a major cause of acute hepatitis in many parts of the world, has gone into serious decline in the developed world as the result of existence of an effective vaccine. The disease remains prevalent in the developing world. Hepatitis B has also been greatly inhibited by vaccination in the developed world, but remains a major cause of chronic hepatitis, cirrhosis, and liver cancer in parts of Africa and Asia. There is no vaccine against hepatitis C, and it remains rampant,

although effective screening of blood products for the virus has greatly reduced transmission of the agent in the developed world. Intravenous (i.v.) drug users are still at extremely high risk for hepatitis C infection.

Once acute hepatitis A occurs, there is no established, effective treatment. Chronic hepatitis B, once it becomes established, can be treated by a range of drugs, but they are expensive, carry risks of serious adverse effects, and confer uncertain long-term benefit. Chronic hepatitis C is primarily treated by a combination of pegylated interferon- α (pegIFN α) -2a or -2b and ribavirin. These drugs are very expensive, require administration by injection (in the case of pegIFN α), have a very high rate of adverse effects, and are frequently ineffective, particularly against the most common genotype of hepatitis C virus in the United States and Europe, genotype 1.

Herbal medicines offer new and interesting alternatives to expand the therapeutic options for people with the different types of hepatitis. While some treatments are well-established in many clinical trials as valuable, other herbal medicines have been shown to be ineffective or have simply not been studied and are used on a purely empirical basis. We review the most promising herbs in this article.

Acute Hepatitis

A hepatoprotective and antiviral herb would seem to be the ideal candidate for someone with acute infection by hepatitis A virus (HAV). *Andrographis paniculata* (*kalmegh* or *chuan xin lian*), a Southeast Asian herb in the Acanthaceae family, fits this bill. The leaf is intensely bitter and well-regarded in traditional medicine for problems associated with the liver. The leaf has been



Glycyrrhiza glabra (licorice) flower and root. Drawing © 2010 by Eric Yarnell, ND.

fairly extensively studied and shown to be helpful for people with acute viral upper respiratory infections (URIs), although most of the studies did involve a major manufacturer of *kalmegh* extracts and negative studies may not have been published.¹

In one open trial of 20 patients with acute hepatitis A, a decoction made from 40 g of leaf per day for 1 month increased the speed of symptom resolution and lowered serum alanine aminotransferase (ALT) levels in patients.² One other case series with 112 patients, conducted in China, reported that 83% of the subjects were “successfully treated” with *kalmegh*, although no details of this study were obtainable.³

Silybum marianum (milk thistle) seeds—and more specifically the flavonolignan complex known as silymarin extracted from the seeds—have been studied in patients with acute viral hepatitis. The most recent and highest-quality study involved patients with acute hepatitis A, B, C, or E; cytomegalovirus; or Epstein-Barr virus-associated hepatitis in Egypt.⁴ Patients were treated either with 140 mg three times per day of silymarin or a multivitamin for 28 days. Jaundice was reduced more quickly in the silymarin than in the multivitamin group, and there was a trend toward a more-rapid reduction of other symptoms, such as fatigue and anorexia, favoring silymarin. In a much-less-rigorous and poorly reported trial, silymarin 140 mg, three times per day, lowered serum transaminase and bilirubin levels more effectively than placebo in patients with acute hepatitis A or B.⁵ Silymarin is extremely safe.

An herbal formula known as Liv.52 has also been studied in people with viral hepatitis, caused by HAV, hepatitis B, and hepatitis E. It is not clear if this is a traditional formula or a modern recipe; the ingredients are listed in Table 1 (though the formula is also often prepared in a base of many other undisclosed herbs). Several low-quality double-blinded trials conducted in India suggest that Liv.52 is effective for patients with acute hepatitis.^{6–8} Most of the formulas were not published in English originally or were in nonmainstream journals, so not all details were available. Given these limitations, it still appears that Liv.52 can clear symptoms more rapidly and reduce serum bilirubin, compared with placebo. A typical dose of Liv.52 is 275–550 mg three times daily in capsules or 5–10 mL of syrup three times daily.

Although there is no clear modern research supporting this, Chinese herbalists historically used *Artemisia capillaris* (capillary wormwood, *yin chen hao*) leaf and the herbal formula *Yin Chen Hao Tang* for people with acute viral hepatitis with jaundice.⁹ *Yin Chen Hao Tang* also contains *Gardenia jasminoides* (gardenia, *shan zhi zi*) fruit, *Rheum palmatum* (rhubarb, *da huang*) root, *Glycyrrhiza uralensis* (*gan cao*, Chinese licorice) root, and *Phellodendron amurense* (*huang bai*) bark. *Artemisia ludoviciana* (western mugwort) is an acceptable local substitute for capillary wormwood in the United States.

Table 1. Liv.52 Herbomineral Formula

Latin binomial	English and Hindi common names	% in formula
<i>Capparis spinosa</i>	Capers, <i>himsra</i>	25%
<i>Cichorium intybus</i>	Wild chicory, <i>kasani</i>	25%
<i>Terminalia arjuna</i>	Arjuna (in both languages)	11%
<i>Solanum nigrum</i>	Black nightshade, <i>kakamachi</i>	11%
<i>Achillea millefolium</i>	Yarrow, <i>branjasi</i>	11%
<i>Cassia occidentalis</i>	Senna, <i>kasamarda</i>	6%
<i>Tamarix gallica</i>	Tamarix, <i>jhavuka</i>	6%
Ferric oxide calx	Calcinated iron oxide, <i>mandur bhasma</i>	5%

Typical dose—275–550-mg capsules or 5–10 mL syrup t.i.d.



Zizyphus jujuba (jujube) tree fruit.



Zingiber officinale (ginger) leaf and root.

Various other Western and Eastern herbs are widely used as antiviral medicines during other acute infections and should be considered clinically and for research projects to help people recover from acute viral hepatitis more quickly. These herbs would include *Ligusticum porteri* (*oshá*) root, *Ligusticum grayi* (*osbala*) root, *Lomatium dissectum* (desert parsley) root, *Forsythia suspensa* (*lian qiao*) herb, *Hypericum perforatum* (St. John's wort) herb, and *Coptis chinensis* (gold thread, *huang lian*) root, to name just a few. For a review of a base formula, which can be individualized to a specific patient's symptoms and other factors, see Table 2.

Chronic Hepatitis C

Chronic hepatitis C (CHC) is an extremely common problem around the world. Originally spread by contaminated blood products in the United States, universal screening for the virus in 1991 eliminated this problem (although it remains a huge issue in the developing world). Now, i.v. drug users are the most likely to be infected in the United States. Hepatitis C is typically a very slow disease, and can have a wide range of manifestations. The main areas of therapeutic interest are to prevent progression of the disease to cirrhosis of the liver or hepatocellular carcinoma (HCC), and to decrease symptoms if they are present. IFN and ribavirin are currently used for most

patients to suppress the viral load, but the drugs are expensive, cause many adverse effects, and are not very effective for treating the most common hepatitis C virus (HCV) in North America, genotype 1.¹⁰ The very large HALT-C trial recently found that treatment with IFN- α -2a for many years was not effective for preventing progression of CHC.¹¹ Thus, herbal medicines have much to offer.

Many long-term trials have looked at the triterpenoid saponin, known as glycyrrhizin, found in the roots of *Glycyrrhiza glabra* (licorice) and *G. uralensis* (*gan cao*) for patients with CHC. Often, glycyrrhizin was given by i.v. injection along with glycine and cysteine, a product known as Stronger Neominophagen C (SNMC). In European populations, 200 mg of glycyrrhizin as SNMC six times per week for 26 weeks was associated with normalization of serum ALT levels, but no clear improvement appeared in liver histology assessed on biopsies.¹²

More impressively, at least three studies in Japan have shown that SNMC can cut the risk of developing cirrhosis or HCC.^{13,14} One of these studies was a retrospective analysis of 456 patients with CHC seen at hospitals, most of whom had not responded to IFN treatment.¹⁵ Risk of developing HCC in patients whose serum ALT fell to below 1.5, the upper limit of normal, was 60% less than patients who did not gain this reduction. Average duration of therapy was 4.1 years.

Table 2. Base Formula for Treating Acute Hepatitis A

Latin binomial (common name)	Part Used	% in formula	Rationale
<i>Taraxacum officinale</i> (dandelion)	Root	30%–40%	Hepatoprotective, antimicrobial, inflammation-modulator
<i>Andrographis paniculata</i> (<i>kalmegh</i>)	Leaf	10%–20%	Antiviral, hepatoprotective
<i>Artemisia ludoviciana</i> (western mugwort)	Leaf	10%–20%	Antiviral, inflammation-modulator
<i>Ligusticum porteri</i> (<i>oshá</i>)	Root	10%–15%	Antiviral
<i>Glycyrrhiza glabra</i> (licorice)	Root	10%–20%	Hepatoprotective, antiviral, corrigent, synergizer

Typical dose—5 mL 4–5 times per day until symptoms begin to abate.

Table 3. Contents of *Shosaiko-to* (*Xiao Chai Hu Tang*) Formula

<i>Bupleurum falcatum</i> (thorowax)—root, 16%
<i>Paeonia lactiflora</i> (peony)—root, 16%
<i>Pinellia ternata</i> (<i>ban xia</i>)—rhizome, 14%
<i>Cinnamomum cassia</i> (cassia)—bark, 11%
<i>Zingiber officinale</i> (ginger)—rhizome, 11%
<i>Zizyphus jujuba</i> (jujube)—fruit, 11%
<i>Panax ginseng</i> (Asian ginseng)—root, 8%
<i>Scutellaria baicalensis</i> (Chinese skullcap)—root, 8%
<i>Glycyrrhiza uralensis</i> (licorice, <i>gan cao</i>)—rhizome, 5%

Dosing

Typical doses—2.5 g t.i.d., or 2.7 g b.i.d.

Glycyrrhizin by injection has been safely and successfully combined with the bile acid ursodeoxycholic acid, ribavirin, and phlebotomy for systemic iron depletion and reduced oxidative load.^{16–18} The latter is particularly interesting, as many studies have shown that phlebotomy and a low-iron diet are quite effective for reducing progression of HCC.¹⁹

It is unknown if oral licorice products would be helpful for people with CHC, although the herb is definitely a traditional treatment for liver problems. Hints of its potential value come from use of the formula *shosaiko-to* in patients with chronic hepatitis B, which is discussed later in this article. At present, there is no published research on this question, but it would be worth considering if patients would or could not handle, or did not have access to, i.v. glycyrrhizin.

Glycyrrhizin acts as a weak mineralocorticoid by elevating cortisol levels in the kidney.²⁰ High doses of glycyrrhizin can cause pseudohyperaldosteronism, increasing sodium retention while depleting the body of potassium, thereby causing edema, hypertension, muscle damage, and kidney failure. Not everyone is equally sensitive to the effect and toxic outcomes are clearly dose-related.

Glycine and potassium are both believed to help prevent symptoms from occurring. Patients who are taking licorice or glycyrrhizin in any form should be warned to have their blood pressure (BP) and serum or urine potassium levels monitored regularly, and doses should be reduced or treatment stopped if these parameters become imbalanced to avoid catastrophe. Potassium-depleting diuretics, such as thiazides, loop diuretics, and corticosteroids, augment the toxicity of glycyrrhizin and should not be combined with it except under very careful monitoring.²¹

Some older clinical trials (often published before there was technology available to distinguish hepatitis B from hepatitis C clearly) showed that silymarin extracts of *S. marianum* could lengthen the lifespans of people with apparent CHC, and the latest Cochrane meta-analysis of trials found that silymarin can prevent death from liver disease overall.^{22,23} However,

when just the highest quality trials are examined, no benefit emerges for using silymarin. An ongoing problem with silymarin trials is that they lump together people with many different diseases (CHC, hepatitis B, and alcoholic-liver disease). Ultimately, much more research is needed, but the safety and potential life-lengthening effects of silymarin still support its use in patients with CHC. The usual dose is 420 mg per day of a 70%–80% silymarin extract.

There is an urgent need to study immunomodulating herbs in patients with CHC, which induces a state of systemic inflammation and appears to cause or increase the risk of many extrahepatic autoimmune and inflammatory diseases.²⁴ Herbs such as *Schisandra chinensis* (*wu wei zi*) fruit and *Astragalus membranaceus* (*huang qi*) root are historically considered at least somewhat supportive of the liver and are also said to decrease overactive immunity and inflammation, although other adaptogens may also be of use.²⁵

It is also surprising that so little work has been done with traditional hepatoprotective herbs, such as *Taraxacum officinale* (dandelion) root and *Arctium lappa* (burdock) root.²⁶ These herbs are commonly used clinically by herbalists and naturopathic doctors in North America and Europe for patients with CHC and should be looked at in research.

The antiviral herbs mentioned under this article's section on acute hepatitis should also be considered clinically and, they too, deserve more research. Various herbs that counter inflammation should also be seriously considered, particularly *Curcuma longa* (turmeric) rhizome, which also has a strong history of use as a hepatoprotective agent and has been shown both to decrease inflammation in hepatocytes and to protect these cells against iron overload.^{27,28}

Chronic Hepatitis B

The hepatitis B virus (HBV) is epidemic in Asia and Africa, although the availability of a vaccine in starting to decrease incidence of this disease. Unlike CHC, chronic hepatitis B (CHB) is much more likely to progress to cirrhosis and HCC. Thus, there is a strong need for an effective, safe alternative to drug therapies (to which the virus often evolves resistance if they are taken long-term) for this complex and difficult disease. It is still relatively uncommon in the United States, particularly compared with CHC, although HBV must be considered in anyone who has lived or traveled extensively in Asia or Africa and was not vaccinated.

The traditional Oriental formula known in Chinese as *Xiao Chai Hu Tang* and in Japanese as *shosaiko-to*, which translates in English to Minor Bupleurum Decoction, was first written down in the *Shang Han Lun* (*Treatise on Cold-Induced Disorders*). This treatise was written prior to 220 AD by Zhang Zhongjing. Obviously, therefore, this formula has been in continuous use for at least 2000 years and probably predated Zhang's text by longer than that. The ingredients of the formula are listed in Table 3. We have previously written about this amazing formula's ability to help people with epilepsy.²⁹



Glycyrrhiza glabra (licorice) root.

In a large double-blinded trial, 222 patients with CHB were randomly assigned to take *shosaiko-to* at a dose of 5.4 or g 0.5 g (a placebo dose) daily for 24 weeks.³⁰ Serum transaminase levels declined significantly in the reasonable dose group, compared with the controls, while HBe antigen levels fell and anti-HBe antibodies rose nonsignificantly in the therapeutic group.

Two randomized trials have evaluated the long-term potential of this formula to prevent HCC in patients with chronic hepatitis B (CHB) in Japan. In the first trial, 260 patients with cirrhosis caused by CHB were treated with conventional therapies, and some subjects were also randomized to take 7.5 g daily of *shosaiko-to* for 34 months.³¹ HCC rates at the end of the follow-up period were significantly lower in the *shosaiko-to* group, compared with the patients in the control group. In what appears to be an extension of the original study to 60 months, HCC rates were still lower and survival was better in the *shosaiko-to* group than in the conventional therapies group.³² Patients without hepatitis B surface antigen (HBs) had even better results from *shosaiko-to* treatment.

There are reports of interstitial pulmonary fibrosis developing in patients simultaneously treated with *shosaiko-to* and IFN.³³ This adverse effect sometimes occurs when IFN is given by itself, so it is still not clear if *shosaiko-to* might enhance the risk or merely act as a bystander to an IFN-related adverse effect.

Salvia miltiorrhiza (Chinese sage, *dan shen*) root is an important Chinese herbal medicine. It has long been used for conditions characterized in modern times as involving excessive inflammation. A crude extract of the root inhibited HBV in vitro.³⁴ An injection of a crude extract of the herb has previously been reported to help reduce fibrosis caused by CHB.³⁵

A polyphenolic, water-soluble compound present in the *S. miltiorrhiza* root and associated with many actions is salvianolic acid B. In a double-blinded trial, 60 Chinese patients with CHB and liver fibrosis were randomly assigned to either IFN- γ intramuscular (i.m.) injections plus oral placebo or placebo injections plus oral salvianolic acid B, 60 mg t.i.d., for 6 months.³⁶ The two treatments were similar in their efficacy for reducing liver fibrosis as shown by repeat liver biopsy, although, on liver ultrasound, the salvianolic acid B-group

Table 4. Contents of Fuzheng Huayu Formula Ingredients

Salvia miltiorrhiza (Chinese sage, *dan shen*)—root 33.3%

Gynostemma pentaphyllum (*jiao gu lan*)—root 25%

Fermentation Mycelium Powder—16.7%

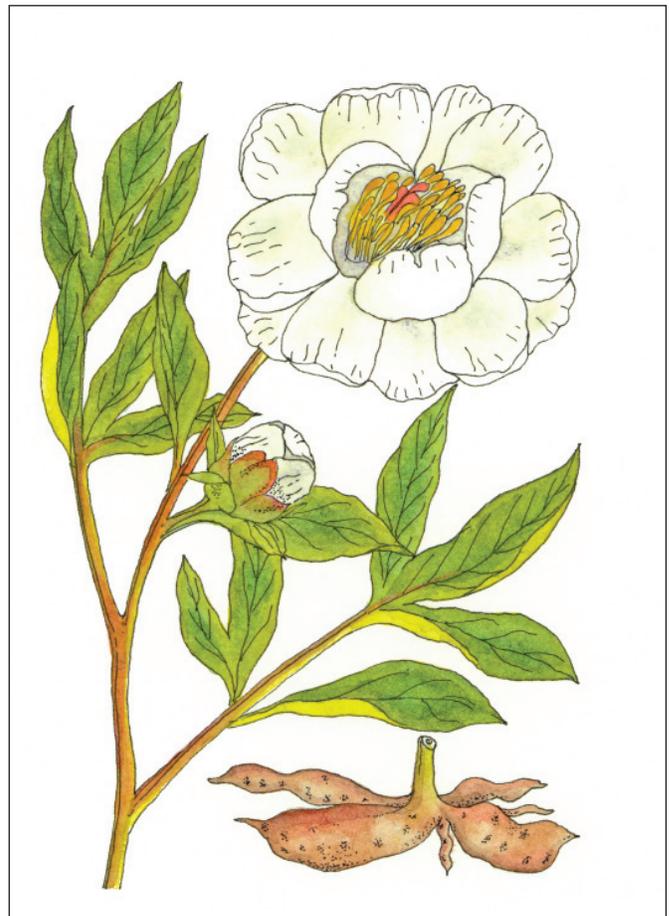
Schisandra chinensis (*schisandra*, *wu wei zi*)—fruit 8.3%

Prunus persica (peach, *tao ren*)—seed 8.3%

Pinus spp. (pine, *song hua fen*)—pollen 8.3%

Dosing

Typical doses—8 g t.i.d. or 12 g b.i.d.



Paeonia lactiflora (peony) root.

had significantly better improvement. Reduction of symptoms and improvement in serum transaminases were similar between the groups.

There were no obvious adverse effects of the salvianolic acid B. Another trial, about which no details were available, apparently showed that crude extracts of *dan shen* combined with the anti-HBV drug lamivudine were more effective than either agent alone for patients with CHB.³⁷ *S. milti-*

orrhiza and salvianolic acid B appear to be promising ways to prevent and treat progressive CHB. A typical dose of the whole herb would be 1–2 g as powder or a 3–5 mL tincture three times per day.

A Chinese formula known as *Fuzheng Huayu*, developed in modern times—based on herbs used traditionally for liver problems and shown experimentally to be antifibrotic and helpful for patients with cirrhosis—has been studied in patients with CHB. The formula's ingredients are listed in Table 4. *Fuzheng Huayu* contains both *dan shen* and schisandra, two herbs already mentioned as being potentially valuable for patients with chronic viral hepatitis, as well as the immunomodulator *Gynostemma pentaphyllum* (*jiao gu lan*) root. Several clinical trials have shown that *Fuzheng Huayu* is effective for reversing hepatic fibrosis and inflammation in patients with CHB.³⁸ Most of the trials were published only in Chinese, so the cited review article³⁸ is the best way to learn more about this combination.

S. marianum has also been studied in patients with CHB. Older studies suggest that this herb can reduce mortality caused by the disease.³⁹ Much more research will be needed to clarify completely the role of silybum and milk thistle in patients with CHB, as most of the studies done to date have not focused on CHB. Glycyrrhizin and SNMC injections are helpful for patients with CHB just as these injections help patients with CHC.^{40,41} The seed of *Ginkgo biloba* has been used to reverse early cirrhosis in patients with CHB in an open trial.⁴² No details of this study were available as it was published only in Chinese, although it appears to have lasted 3 months and to have involved 86 patients.

Conclusion

Many promising herbal treatments exist for people with acute and chronic viral hepatitis. Preliminary and, in some cases, advanced clinical trials have demonstrated efficacy and safety. Much more work remains to be done to determine optimal treatments, doses, and formulas. In the meantime, practitioners can enhance their existing approaches to patients with viral hepatitis and improve outcomes with little risk. ■

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