

a series of fact sheets written
by experts in the field of liver
disease

Herbs & Hepatitis C

2nd Edition

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A Word from the Author

Interest in herbs and supplements seems to be on the rise. When I first wrote this article, it was difficult to find reliable sources of information about herbs. As more information became available, it became clear it was time to update "Herbs and Hepatitis C." This article is not meant to be the final stop on the information highway. I hope the reader will use this as a tool towards gaining more insight and knowledge about the world of herbs. Of course, this information is not meant to be used for medical care. Always talk to your primary healthcare provider before using herbs.

The use of herbs for medicinal purposes has a long and interesting history. The origins of some modern

medications are actually plants, such as aspirin from white willow bark, digitalis from foxglove, morphine from poppies and warfarin (Coumadin) from sweet clover. Many cultures use indigenous plants for healing purposes. The use of herbs, however, is controversial in contemporary western medicine due to the lack of evidence-based research to support safety and efficacy. Couple this with the potential harm these substances can inflict and it is easy to see why physicians are reluctant to endorse herb use. Some patients are interested in alternative methods to use with or instead of the treatment their physicians have prescribed. This is particularly true for patients living with chronic hepatitis C virus (HCV). Although huge progress has been made in the HCV treatment arena, current antiviral therapy has many side effects and is not always effective. Add these elements to the symptoms some people experience from HCV and it is no wonder that herbs seem attractive.

Although herbs and other supplements may seem appealing, a number of herbs can cause harm. Some herbs are known to have potentially carcinogenic properties and to cause neurological damage. There are herbs that can be particularly harmful to the liver and can cause damage and death. It is because of the potential for hepatotoxicity (poisoning of the liver) that HCV patients are advised to avoid herbs or to use them cautiously.

The Food and Drug Administration (FDA) is the federal agency responsible for drug and food safety. Drugs undergo years of rigorous testing on animals and humans before the FDA allows them to be marketed. Herbs and supplements, on the other hand, are considered to be dietary supplements. This means that they are regulated by different standards, called the Dietary Supplement Health and Education Act of 1994 (DSHEA). Under this act, it is the manufacturer that ensures the safety of the dietary supplement. In general, the supplement manufacturers do not need FDA approval and do not need to register their product. They are required, however, to label the supplement in a truthful manner.

The point at which the FDA may become involved with herbs is after marketing. The FDA may monitor product labeling, information, and safety. Adverse event reporting is voluntary. Whether the FDA should regulate supplements is a hotly debated issue. The FDA has been criticized both for regulating and under regulating dietary supplements. For a variety of reasons, the FDA's involvement with herb use has been

minimal. To date, the notable exception to this is the sale of dietary supplements containing ephedrine alkaloids. Ephedra, also called Ma Huang, is one of the plants that are a source of ephedrine alkaloids. Its use has been associated with an increase in blood pressure, a condition which will increase the risk of heart attack, stroke, and death.

There is very little independent research involving the use of herbs. The gold standard randomized, controlled, double blind placebo controlled studies are few in the area of botanical remedies, let alone the use of herbs and HCV. In 1991, the U.S. Congress established the Office of Alternative Medicine (OAM) within the National Institutes of Health (NIH). In 1998 the National Center for Complementary and Alternative Medicine (NCCAM) became a new center of the NIH. Responding to the need for more research about the safety and efficacy of herbs and supplements, NCCAM and the NIH Office of Dietary Supplements established the first Dietary Supplements Research Centers with an emphasis on botanicals. The specific subject of herbs and viral hepatitis was included in the Complementary and Alternative Medicine in Chronic Liver Disease conference in 1999 and a few clinical trials are being conducted in this area. Unfortunately funding is limited and evidence-based data about herbs and HCV is largely unavailable.

The insufficiency of independent research does not mean that there is no value in herbs. Herbs have made a significant contribution to medicine. Herbal practice has been around for centuries and has produced some sound observations. Indigenous practitioners relied on botanicals for medicine. In these modern times it is common for people to self-treat mild sunburns with aloe vera, mild stomach aches with ginger, or mild colds with peppermint or chamomile tea. Generally these are assumed to be safe alternatives. However, the use of herbs for treatment of more serious conditions such as HCV is more complicated and raises a number of questions. For example, when choosing an herb, which part of plant is used, when is it harvested, and how is it processed? Botanicals are not made in a lab setting. This means that the consistency of the product is at risk. Is the herbal product safe, which brands are the best, and what is the recommended dose?

To answer these questions, start with the label. Herbs can vary in strength and purity, so it may be wise to take a standardized and certified form. Certification and standardization is voluntary. The goal of the United States Pharmacopeia (USP) is to set industry standards for drugs and dietary supplements in the U.S. The label of a supplement that displays the USP seal is worth considering. A product that is certified by NSF International (formerly the National Sanitation Foundation) is another indicator that the manufacturer complies with particular standards. A seal of approval from ConsumerLab.com (CL) also carries some distinction. Another standard is that of the world's leading authority on herbs, the German Commission E. This agency is the German equivalent of the Food and Drug Administration (FDA). The American Herbal Pharmacopoeia is also developing standardization guidelines for the American marketplace. ConsumerLab.com has provided a much-needed service by testing popular supplements. This company has discovered that many products do not contain the levels of key ingredients that are on the products' labels. A product that passes their inspection may carry the triangular label with the ConsumerLab.com quality of approval. The use of this service does have a fee associated with it. Companies that belong to the American Herbal Products Association and submit to this organization's code of ethics are another good choice.

Suggested Guidelines for Herbal Use

- Assess your overall health. If you smoke, drink alcohol, and have other unhealthy habits, do not expect herbs to offset the potential damage these habits can cause. Adopting healthy habits will provide far more benefit than any herb can possibly give.
- Discuss herb and supplement use with your healthcare provider. Identify all the herbs and supplements you take, even if you think your doctor might disapprove. Drugs and supplements can interact with each other as well as with other health conditions.
- Apply the same commonsense approach and standards to herbs as you would to any drug. If you are reluctant to take any prescription or over-the counter drug, be equally as reluctant to take an herb.
- Be informed and be sure your information is current.

- Before you take an herb or supplement, find out if it is compatible with other drugs or supplements you are taking. Verify that the supplement is not contraindicated for any other condition you may have (see “*A Warning about Milk Thistle and Drug Interactions*” below).
- Take extra precautions if you have a history of allergies. Botanical products can cause allergic reactions.
- Follow the label's dosage recommendations. ***More is not better.***
- Know your source. Herbs may be contaminated. Before ingesting anything, ask yourself what you know about what you are about to take.
- Choose herbs and supplements that are standardized.
- Buy products that submit to voluntary self-regulation.
- Natural does not equal healthy or safe. Snake venom is natural but not healthy.
- Do not be swayed by bargain prices. Herbs are not all equal.
- Check the expiration date on the container.
- Do not rely on the health food store staff for health care information. Although they may be helpful, remember that salespeople are usually not licensed to practice medicine. Do not treat your condition on the advice of a salesperson.
- Be skeptical. Claims made by the product manufacturer or seller may vastly differ from independent evidence-based research.
- Do not be swayed by personal testimonies. Although individuals may benefit from botanical use, the notion that "one size fits all" does not apply in medicine.
- Do not be influenced by the latest supplement to make headlines. Dietary supplements can be compared to cars. When new models are introduced, sometimes it takes time before problems develop. A product that really has value will be around for awhile.
- Herbs and supplements should not be given to children or taken by pregnant or nursing women without a physician's approval. Older adults and those with various health conditions should also exercise extra caution before taking non-prescribed supplements. Herbs should *never* be used with decompensated cirrhosis.

- Some herbs prolong bleeding times or interfere with anesthetics. Stop all herb use at least a week prior to any surgery or procedure that uses anesthesia. Tell your attending physician and anesthesiologist about any herbs you are using, particularly if the procedure occurs before you have sufficient time to observe this "wash-out" period.
- Report any suspected adverse reactions to an herb or supplement to the FDA's monitoring program, Medwatch. Call 800-322-1088 or www.fda.gov/medwatch.

Some Herbs Associated with Liver Toxicity

This list is primarily liver specific and by no means exhaustive. The substances on this list are referred to in their oral form only.

- Blue-green Algae
- Borage (*Borago officinalis*)
- Bupleurum
- Chaparral (*Larrea tridentata*)
- Comfrey (*Symphytum officinale* and *S. uplandicum*)
- Dong Quai (*Angelica polymorpha*)
- Germander (*Teucrium chamaedrys*)
- Jin Bu Huan (*Lycopodium serratum*)
- Kava
- Mistletoe (*Phoradendron leucarpum* and *viscum album*)
- Pennyroyal (*Mentha pulegium*)
- Sassafras (*Sassafras albidum*)
- Shark Cartilage
- Skullcap (*Scutellaria lateriflora*) Valerian

Ephedra

Although not specifically associated with liver toxicity, products containing ephedrine alkaloids (ephedra) should be avoided. Reports of heart attacks, strokes, seizures, psychosis, and death have been linked to the use of ephedrine alkaloids. The FDA has banned the sale of dietary supplements containing ephedrine alkaloids, including ephedra and Ma Huang.

Milk Thistle

Milk thistle, *Silybum marianum*, is the most commonly used herb for liver problems. A frequently asked question regarding chronic hepatitis C viral (HCV) infection concerns the use of this herb. If you are considering taking a milk thistle product, talk to your doctor and find out if it is compatible with other drugs or supplements you are taking. Verify that the supplement is not contraindicated for any other condition you may have (see "A Warning about Milk Thistle and Drug Interactions" below). Do not use milk thistle if you have decompensated cirrhosis.

Medical consultants for the Consumers Union recommended the following in the April 2001 issue of *Consumer Reports On Health*:

- Patients should not use milk thistle to replace a conventional treatment for viral hepatitis;
- Patients should not take milk thistle while on a conventional treatment for viral hepatitis;
- Milk thistle is probably safe and no one should be discouraged from taking it if there are no other options;
- Choose a brand that contains silibin and phosphatidyl choline, which may be better absorbed.

There is insufficient research to establish a suggested daily dose of milk thistle. Typical dosages are in the range of 140-420 mg in divided doses, 2-3 times a day of 70-80% silymarin. See the section "*Suggested Guidelines for Herbal Use*" (above) for more information on choosing milk thistle along with other herbal products.

A Warning About Milk Thistle and Drug Interactions

Raman Venkataramanan and colleagues¹ at the University of Pittsburg reported observations about silymarin, a compound found in milk thistle. In short, this report raised concerns that silymarin may impair the metabolism of certain drugs when taken together. Further, the potential exists for increased toxicity of co-administered drugs in the presence of silymarin.

The medications levels of the following **may** increase if taken by people who are also using milk thistle. The source for this list is the Community AIDS Treatment Information Exchange (CATIE) and is not meant to be complete.

- *protease inhibitors*
- *non-nucleoside analogues*
- *methadone*
- *heart drugs* - Tambocor (flecainide), Rythmol (propafenone)
- *antibiotics* - erythromycin, rifampin
- *anti-seizure drugs* - carbamazepine (Tegretol)
- *antidepressants* - St. John's wort, Zyban/Wellbutrin (bupropion), Paxil (paroxetine), Prozac (fluoxetine), Luvox (fluoxetine) Serzone (nefazodone), Zoloft (sertraline), Effexor (venlafaxine)
- *antihistamines* - Hismanal (astemizole), Seldane (terfenadine)
- *antifungals* - itraconazole (Sporanox), Ketoconazole (Nizoral)
- *gastrointestinal motility agents* - Prepulsid (Cisapride)
- *ergot drugs* - Ergonovine, Ergomar (ergotamine)
- *anti-psychotics* - Clozaril (clozapine), Orap (pimozide)
- *sedatives/sleeping pills* - Ambien (zolpidem), Halcion (triazolam), Versed (midazolam)
- *lipid-lowering drugs (statins)* - Lescol (fluvastatin), Mevacor (lovastatin), Pravachol (pravastatin) and Zocor (simvastatin), Baycol (cerivastatin)
- *transplant drugs* - cyclosporine (Neoral, Sandimmune), ProGraf (tacrolimus)

Milk thistle also has the potential to lower levels of the following drugs:

- *anti-parasite drugs* - Mepron (atovaquone)
- *sedatives/sleeping pills* - Ativan (lorazepam)
- *hormones* - estrogen

HCV Treatment and Herbs

There is virtually no research on the safety of herbs and supplements co-administered with peginterferon/ribavirin therapy. Because of this, it is common for patients to abstain from milk thistle and herb use while undergoing antiviral therapy. Even commonly used botanicals need to be used

with caution. Some herbs and supplements can hinder the ability of the blood to clot. For instance, ginger is widely used to relieve nausea. However, patients with gallstones should talk to their health care provider prior to using ginger. Additionally, ginger has an anticlotting action and should not be taken if you have reduced blood clotting ability. Interferon therapy and/or cirrhosis can also interfere with blood clotting, so there may be an increased risk if some herbs are used simultaneously under these conditions. Other commonly used herbs, such as chamomile and St. John's Wort carry a warning of potential drug interactions. The rule of thumb is to be informed and talk to your healthcare provider prior to using any botanical product.

Warning: *Bupleurum* is a popular herb used in a variety of Traditional Chinese and Japanese Medicine Mixtures for liver conditions. At least 16 deaths have been reported in Japan for HCV patients being treated simultaneously with alpha interferon and Xiao Chai Hu Tang (Minor Bupleurum).

Final Words

Herbs have been part of the healing arts for centuries. Clearly more information and research needs to be conducted in this area in order to better understand and incorporate the use of botanical products into current health practices. In the meantime, make informed decisions regarding your health. Your future depends on it.

¹ Venkataramanan R, Ramachandran V, Komoroski BJ, et al. Milk thistle, a herbal supplement, decreases the activity of CYP3A4 and uridine diphosphoglucuronosyl transferase in human hepatocyte cultures. *Drug Metabolism and Disposition* 2000;28(11):1270-1273.

Resources:

- *The American Pharmaceutical Association Practical Guide to Natural Medicines* by Andrea Peirce.
- *The ABC Clinical Guide to Herbs* edited by Mark Blumenthal, et al at the American Botanical Council.
- *ConsumerLab.com's Guide to Buying Vitamins & Supplements: What's Really in the Bottle* by Tod Cooperman, M.D., William Obermeyer, Ph.D., Denise Webb, R.D., Ph.D.
- *The Green Pharmacy* by James A. Duke.
- *Herbs of Choice* by James E. Robbers and Varro E. Tyler

PDR for Herbal Medicines published by the Medical Economics Company.

- *Tyler's Honest Herbal: A Sensible Guide to the Use of Herbs and Related Remedies* by Stephen Foster and Varro E. Tyler, Ph.D.
- American Botanical Council - 512-926-4900
www.herbalgram.org
- American Herbal Products Association - www.ahpa.org
- ConsumerLab.com - www.consumerlab.com
- FDA Dietary Supplement website - vm.cfsan.fda.gov/~dms/supplmnt.html
- HerbMed - www.herbmed.org
- Memorial Sloan-Kettering Cancer Center - www.mskcc.org/aboutherbs
- National Center for Complementary and Alternative Medicine - 888-644-6226 http://nccam.nih.gov
- National Institutes of Health Clinical Trial Information - www.clinicaltrials.gov
- National Sanitation Foundation - http://www.nsf.org
- NSF International - www.nsf.org
- The United States Pharmacopeia - 800-822-8772
www.usp.org
- UC Berkeley Wellness Letter - www.wellnessletter.com
- United States Pharmacopeia - www.usp.org

For more information about hepatitis C, hepatitis B and HCV coinfections, please visit www.hcvadvocate.org.

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A publication of the Hepatitis C Support Project

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