



## HERB - DRUG INTERACTIONS

### Summary

Many people living with HIV/AIDS (PHAs) use herbal therapies together with prescription and non-prescription medications. Although considered natural, many of these herbal therapies can interact with other medications, causing either potentially dangerous side effects and/or reduced benefits from the medications. Unfortunately, there is little available scientific research on herb-drug interactions; therefore, when combining herbal therapies with other medications, it is important to watch for potential interactions. Informing all your health care providers (doctors, nurses, pharmacists and complementary practitioners) about all the herbal therapies and medications you are taking can help reduce the risk of harmful interactions.

### What are herbal therapies?

Herbal therapies are plants or plant-based products that are used to treat or prevent illness. They can be referred to as herbs, herbal supplements, botanicals or biomedicines. Many plants have medicinal properties; in fact, numerous pharmaceutical drugs were originally derived from plants. Herbal therapies are usually prepared by grinding or steeping the parts of a plant that are believed to contain medicinal properties. The resulting therapies come several forms, including oral tablets, capsules, extracts and infusions. They are eaten, swallowed, inhaled or applied to the skin. (For more information, see CATIE's *Practical Guide to Herbal Therapies*, available at [www.catie.ca](http://www.catie.ca).)

### What are herb-drug interactions?

When herbal therapies and drugs (prescription or non-prescription medications) are used together, they can interact in your body, causing changes in the way the herbs and/or the drugs work. Such changes are called herb-drug interactions. They can be beneficial or harmful to you, depending on the type of interaction.

### Why is it important to know about herb-drug interactions?

Herb-drug interactions can impact your health and the effectiveness of your treatments. For example, some herbal therapies might:



- Increase the side effects of drugs, possibly leading to toxicity
- Decrease the therapeutic effect of drugs, possibly leading to treatment failure. (In the case of highly active antiretroviral therapy [HAART], such an interaction can also cause drug resistance, thereby limiting future options for treatment.)
- Modify the action of drugs, possibly leading to unexpected complications
- Enhance the therapeutic effect of drugs, possibly leading to over medication

Likewise, prescription and non-prescription drugs can alter the way your body reacts to herbal therapies.

## What are the mechanisms of herb-drug interactions?

### 1. Pharmacokinetic Interactions

Pharmacokinetic interactions involve changes in the way herbs and drugs move through your body and can alter the amount, or level, of drug(s) in your body. If the interaction increases the level of a drug, you might experience side effects and/or toxicity. If the interaction decreases the level of a drug, it might not work as well, possibly leading to treatment failure and/or drug resistance. There are several places in your body where such interactions can happen.

*Stomach (Gastro-intestinal tract)* — When herbs and drugs are taken orally, they are usually absorbed into the bloodstream through the stomach and intestines. Herbs can affect the way in which drugs are absorbed, leading to changes in the amount of drug that enters the bloodstream. For example, some herbs can change the physical environment of the stomach, such as the pH level, while others might chemically bind to drugs, causing them to remain in the stomach instead of entering the bloodstream. Some herbs, such as laxatives, can speed up the digestive process, reducing the amount of time a drug is present to be absorbed by the stomach.

*Liver* — Once in the bloodstream, many drugs need to be metabolized (chemically altered) by the liver either in order to become therapeutically active or to be removed from the bloodstream. Your liver, therefore, plays an important role in controlling the level and effectiveness of drugs in your body. Herbal therapies (and drug therapies, too) can change liver metabolism. By inducing or inhibiting liver enzymes, herbs can alter the amount of therapeutically active drug in the blood. This is the most important mechanism for interactions between herbal therapies and anti-retroviral drugs.

*Kidney* — Some drugs are eliminated from the bloodstream through the kidney. Herbs that affect the functioning of the kidney can change the level of drug in the blood. If the herb reduces kidney function, the level of drug may increase. If the herb increases kidney functioning, the level of drug may decrease.

### 2. Pharmacodynamic Interactions

Pharmacodynamic interactions refer to the mutual actions of herbs and drugs inside the body. When taken at the same time, herbs and drugs may work together (synergistically) or in opposition (antagonistically). For example, separately they can have the same toxic effects, so that when taken together, they cause increased side effects. Many herb-drug interactions fall into this category. Pharmacodynamic interactions are difficult to predict or prevent.

## What is known about herb-drug interactions?

Unfortunately, very little is known about herb-drug interactions. There are several reasons for this, including:

- Research on herbal therapies is not nearly as advanced as research on pharmaceutical drugs. Herbal products are not studied or monitored for safety and potential interactions to the same extent as prescription drugs. Studies of prescription drugs rarely consider potential interactions with herbs.



- Traditionally, herbal products have not been regulated for purity and potency. The ingredients of herbal products can vary greatly between manufacturers and even between batches from the same manufacturer. However, Health Canada, through the Natural Health Products Directorate, is currently in the process of implementing a new regulatory framework for licensing Natural Health Products.
- Most health care practitioners do not have clinical experience combining herbs and drugs.

Because there is so little research, information about herb-drug interactions is usually pieced together from several different sources; some of the most important are:

- Anecdotal information, clinical experience and reports of potential interactions in the literature
- Reasonable likelihood of an interaction based on knowledge of how specific drugs and herbs work together
- *In vitro* (test tube) studies — particularly studies of liver cell metabolism
- Observational studies regarding the use of herbal therapies by PHAs
- Pharmacokinetic studies that directly measured fluctuations in the amount of drugs in the blood

## Which herb-drug interactions are important for PHAs?

Listing all of the herb-drug interactions, that potentially impact PHAs, is not possible. Many considerations must be taken into account when making decisions about using herbs and drugs together. Discussing available options with all your health care providers, is a good idea. Here are only a few important interactions of which you should be aware.

### 1. General interactions

PHAs should be cautious about mixing herbs and drugs in any of the following situations:

- The herbal therapy can change digestion, kidney or liver functions
- The herbal therapy is reported to have similar side effects to the drug therapy
- The herbal therapy and the drug therapy are used to treat the same condition
- There is underlying impairment or damage to the stomach, liver or kidney as a result of illness or adverse drug reactions

### 2. Highly Active Antiretroviral Therapy (HAART)

The following combinations should **not** be taken together

- St. John's Wort (*Hypericum perforatum*) with any protease inhibitor or any non-nucleoside reverse transcriptase inhibitor (NNRTI)
- *Large quantities* of raw or processed garlic with any protease inhibitor (a few cloves of cooked garlic in food should not be a problem)

The following combinations *might* alter levels of antiretroviral drugs in the blood

- Milk thistle (*Silybum marianum*) with any protease inhibitor or any non-nucleoside reverse transcriptase inhibitor (NNRTI)

### 3. Other drugs

Many PHAs are taking other medications in addition to HAART. These can include antibiotics, medications for high blood pressure, depression, heart conditions and diabetes, to name a few. The following herb-drug combinations have the potential for significant interactions. This list is not exhaustive.

- Ginkgo biloba with anticoagulants
- St. John Wort (*Hypericum perforatum*) with antidepressants, oral contraceptives, anticoagulants and transplant medications
- Kava Kava (*Piper methysticum*) with alcohol or liver damage
- Devil's Claw (*Harpagophytum procumbens*), Ginseng (*Panax ginseng*) or Dong Quai (*Angelica sinensis*) with warfarin
- Hawthorn (*Crataegus* Species) with antihypertensive medications, digoxin or antidepressants



# How can herb-drug interactions be avoided?

[The following ten tips for avoiding herb-drug interactions is reprinted from *Living +*, a magazine published by British Columbia Persons with AIDS Society.]

## 1. Knowledge is power

Knowledge is your best defense against drug-herb and herb-herb interactions. Know what you are taking and why. Your alternative and conventional medical providers should provide you with the name of all the drugs and herbs, the reason for taking them, the expected benefit and potential side effects. Avoid anything that has a “secret formula”. If it works, there should be evidence that it does. Unfortunately, lack of knowledge about how medicinal plants and pharmaceutical drugs affect each other, and large variations between individuals make identifying adverse drug-herb interactions difficult. One of the key things you can do is to be proactive, and work closely with your doctor, pharmacists and complementary care practitioners to make sure each of them are aware of all the substances you are taking and to ensure you get the information you need to make informed treatment decisions.

## 2. Your pharmacist is your friend

Make all of your providers aware of everything you are taking. Project Inform suggests the “Brown Bag Medicine Check Up”. Put all of your medications, including over-the-counter, prescription and complementary products like herbs and vitamins, in a bag and take them to your various health care providers so that they can conduct a personalized review. Typing a list of all the supplements and herbs you take and providing that to your health care providers for your file can be helpful. New information on benefits, adverse effects and drug interactions with herbal remedies is being published in the medical and pharmaceutical literature all the time- your pharmacist or physician may be able to tell you of recent developments (or you may be able to tell them). Whichever way, you'll all be better off.

## 3. Buyer beware

Buy your herbal products from a reputable manufacturer, or a store that has been in business for some time. Ask your alternative medical provider to recommend a good source of high quality herbs. Products from less reputable manufacturers may be mislabeled, have variable (or incorrect) herb content or quality, or be contaminated with other ingredients. You can't predict or evaluate a drug interaction if you don't know what's in the product.

## 4. One thing at a time

Start one product at a time, and don't use in larger than recommended doses. Avoid combination products with a long list of ingredients. In general, don't start a new herbal regimen at the same time as you start a new antiretroviral regimen - wait until you are stabilized on your new HIV medications. There may be times when you will choose to take herbs to alleviate some of the short-term side effects of a new regimen, such as ginger for nausea, or raspberry tea for diarrhea.

## 5. Watch the kids!

Use herbal products in children or infants only under the care of a trained practitioner. Children are more likely to have adverse effects due to altered metabolism. Avoid herbal treatments if you are pregnant, or planning a pregnancy. Some herbs like feverfew and goldenseal can cause premature labour, others such as hawthorn and kava kava decrease the tone of the uterus.

## 6. Write it down

Keep a diary of your response to each treatment you try, and don't continue use for more than a few weeks if you are not achieving the desired benefit. There are very few long-term studies on most herbal remedies. Minimizing the number of herbs taken decreases the chance of interaction.

## 7. Timing is important

Because we have limited information of drug-herb interactions due to altered absorption, try to separate your doses of antiretrovirals and herbs/



supplements by at least an hour. This is especially important for drugs with food restrictions such as didanosine (DDI) and indinavir (Crixivan) or those sensitive to changes in stomach pH, such as itraconazole and ketoconazole.

## 8. Have a healthy respect for nature

Just because it's natural doesn't mean it's harmless. Many people assume that because they are taking a "natural" product that there are no potential adverse effects, and that dosing recommendations are to be ignored. There are a wide variety of toxic effects of herbs. Avoid taking herbs that have known toxic effects, such as pennyroyal, comfrey, germander and liferoot. HIV infected persons should avoid the long-term use of echinacea, as it may increase the rate of replication of the HIV virus.

## 9. An ounce of prevention

Be especially careful when adding herbal treatments if you are on medication for the treatment of other chronic medical conditions such as: high blood pressure, high cholesterol or triglycerides, diabetes, heart failure or rhythm disturbances, seizure disorders, Parkinson's disease, rheumatoid arthritis or gout, or cancer chemotherapy. Be really, really careful if you are taking blood thinners such as warfarin (Coumadin). Some herbs can increase the toxicity of drugs used to treat these conditions, or counteract their effectiveness. Examples include: Ayurvedic Shankapushpi can decrease the effectiveness of phenytoin in the treatment of seizures, wormwood can lower seizure threshold, black cohosh can antagonize the effects of some high blood pressure medications, figwort can increase possibility of side effects to digoxin, red clover, chamomile and many others can affect anticoagulants.

## 10. Use common sense

If something seems too good to be true, it usually is. The most expensive products are not always the best. No drug or herb has "no known side effects". Even water is toxic if you give enough of it. Follow directions - if you are boiling herbs in water (making a decoction) or making teas (infusions) follow measurement and preparation instructions carefully.

## Where can I get more information?

**CATIE** — <http://www.catie.ca> or call 1-800-263-1638

A wealth of resources on complementary therapies, including the *Positive Side* magazine on holistic health, *Practical Guides* on nutrition, complementary therapies and herbal therapies, *Fact Sheets* on specific herbs and supplements, and links to other reviewed articles and Web sites on the Internet. *CATIE-News*, *TreatmentUpdate* and *Innovations* cover new developments in research on complementary therapies.

**CAM PubMed** — <http://www.nlm.nih.gov/nccam/camonpubmed.html>  
Free online searching of the medical literature for information on complementary therapies.

**Natural Health Products Directorate, Health Canada** — <http://www.hc-sc.gc.ca/hpfb-dgpsa/nhpd-dpsn/> or call 1-888-774-5555

Information on the federal regulatory framework for natural health products.

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## Credits

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## References

Eisenberg DM, Kaptchuk TJ. The Risk-benefit profile of commonly used herbal therapies: ginko, St. John's Wort, Ginseng, Echinacea, Saw Palmeto and Kava. *Annals of Internal Medicine* 2002;136:42-53.

Elion RA, Cohen C. Complementary Medicine and HIV Infection. *Primary Care* 1997; 24(4): 905-19.

Ernst E, Pittler MH. Herbal Medicine. *Medical Clinics of North America* 2002; 86(1): 149-61.

Fugh-Berman A. Herb-drug interactions. *Lancet* 2000; 355: 134-38.

Horowitz S. 2000. Combining Supplements and Prescription Drugs: what your patients need to know. *Alternative and Complementary Therapies*. 2000; Aug: 177-183.

Langerwitz W, Ruttimann S, Laifer G, Maurer P, Kiss A. The integration of alternative treatment modalities in HIV infection - patient's perspective. *Journal of Psychosomatic Research* 1994; 38:687-93.

Meneilly [MacDonald] G. Top ten tips for avoiding drug-herb interactions. *Living +* 2000;6 [http://www.bcpwa.org/issue6/tentips.htm accessed 2004 January].

Piscitelli SC. Indinavir concentrations and St John's Wort. *Lancet* 2000;355(9203):547-8.

## Disclaimer

**Decisions about particular medical treatments should always be made in consultation with a qualified medical practitioner knowledgeable about HIV-related illness and the treatments in question.**

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