What is milk thistle?

Milk thistle (Silybum marinum) is a tall plant with a thistle-like appearance. Native to Europe, it now grows in North America. Although several parts of the plant may be used in herbal remedies, the active medicinal ingredients are concentrated in the seeds. Silymarin is a term used to describe three similar compounds considered primarily responsible for the plant’s medicinal action.

Why do people with HIV use this supplement?

1. To protect the liver and kidneys

Having a healthy liver and kidneys are crucial to the body's good health. The liver plays an important role in storing and releasing dietary nutrients. Both the liver and kidneys produce hormones and other chemical signals needed by the body. The liver and, to a lesser extent, the kidneys, modify and break down most drugs taken into the body. Both of these organs are places where waste materials are collected from other parts of the body. With HIV disease, the liver may be under increased strain for one or more of the following reasons:

- HIV infection increases the production of free radicals, which can damage the body's cells in the same way that rust damages a car. And PHAs have been found to have reduced defenses against free radicals. Because the liver is so heavily involved in detoxifying many of the substances that enter our body, a lot of free radicals are produced in this organ. Thus, HIV infection increases stress on the liver.
- The use of anti-HIV drugs may place an increased strain on the liver and kidneys because these organs help to detoxify medications.
- The livers of some PHAs have other stresses unrelated to HIV infection, including hepatitis B or C and the effects of current or past use and abuse of recreational drugs and alcohol.

Note: One early warning sign of liver distress or damage is an elevated level of liver enzymes. This can be detected by means of blood tests. These enzymes are usually monitored closely in people with HIV.
Milk thistle and HIV/AIDS

While milk thistle has not been studied in controlled clinical trials to find out its effect in helping heal liver damage caused by anti-HIV drugs, it has been tested for its ability to help people recover from liver damage in other chronic health conditions. PHAs who are considering the use of milk thistle or its extracts need to pay particular attention to the information in this Supplement Sheet's section on warnings.

Cautions and concerns

Although occasionally it has been said to cause mild diarrhea, milk thistle has no other reported direct side effects.

Warnings

1. Milk thistle and anti-HIV medications

Researchers at the University of Pittsburgh have suspected that milk thistle can slow down or reduce the activity of enzymes in the liver. What does this have to do with HIV? Enzymes in the liver break down many of the substances that we eat and drink, including medications. If the activity of these enzymes is reduced, then drugs remain in the blood longer than they otherwise might. This could lead to higher-than-expected levels of drugs in the body, causing side effects or intensifying already-existing side effects. Alternatively, if the activity of enzymes is increased, then the level of drugs in blood may fall to less-than-normal levels. This could help HIV resist the effect of the drugs you are taking and reduce your future treatment options.

Many medications taken by PHAs, such as protease inhibitors and non-nukes, are processed by this liver enzyme. If milk thistle is taken by someone using protease inhibitors or non-nukes, it has the potential to affect the levels of these medications.

To find out if milk thistle affects indinavir (Crixivan) levels in people, researchers at the National Institutes of Health (NIH) in Bethesda, Maryland, conducted a study. They used healthy, HIV negative subjects taking the protease inhibitor indinavir at a dose of 800 mg three times daily on an empty stomach. Milk thistle was taken at a dose of 175 mg three times daily with food. Overall, the researchers found that the total amount of indinavir that entered their blood was decreased by only 9% with use of milk thistle. Perhaps more significant were the changes in trough levels of indinavir.

"Trough levels" refers to the lowest level to which a drug in the blood falls over time. It's easiest for HIV to develop resistance when drug levels are at their lowest — at the trough. Levels of indinavir are at their lowest just before it's time to take the next dose — eight hours after the last dose was taken. In the study, milk thistle lowered indinavir trough levels by about 25% compared to their levels when indinavir alone was taken. This change was statistically significant, that is, not likely due to chance alone. In one subject, trough levels decreased by as much as 60%.

A decrease of 25% in trough levels may be a concern for some people who are using only one protease inhibitor in their treatment regimen. However, in North America and the European Union, more doctors are increasingly prescribing indinavir with another PI — ritonavir (Norvir). This is because Ritonavir can significantly increase and maintain high levels of indinavir. For the same reason, ritonavir is also used to boost other PIs including the following:

• amprenavir (Agenerase)
• lopinavir (in Kaletra)
• saquinavir (Fortovase or Invirase)

When taken with ritonavir, because it is such a powerful booster, indinavir levels may not be significantly affected by the dose of milk thistle used in the NIH study.

The precise effect of milk thistle on other single protease inhibitors without the ritonavir boost, and on non-nukes, until studied, is not clear.
2. Milk thistle and other medications

Below is a short list of some other medications that are processed through the CYP3A4 enzyme. Based on the effect of milk thistle on liver enzymes in the lab, it is possible that levels of these medications may increase if taken by people who are also using milk thistle. This list is not exhaustive:

- methadone
- heart drugs – Tambocor (flecainide), Rythmol (propafenone)
- antibiotics – erythromycin, rifampin
- anti-seizure drugs – carbamazepine (Tegretol)
- antidepressants – Zyban/Wellbutrin (bupropion), Paxil (paroxetine), Prozac (fluoxetine), Luvox (fluvoxetine). Serzone (nefazodone), Zoloft (sertraline), Effexor (venlafaxine)
- St. John's wort
- 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)
- erectile dysfunction drugs – Viagra (sildenafil)
- street drugs – ecstasy (MDMA)
- lipid-lowering drugs (statins) – Lescol (fluvastatin), Mevacor (lovastatin), Pravachol (pravastatin), Zocor (simvastatin)
- transplant drugs – cyclosporine (Neoral, Sandimmune), ProGraf (tacrolimus)

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

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

The research by the scientists in Pittsburgh and at the NIH should emphasize to readers that simply because a product is "natural" it does not mean it is safe when taken with other substances. This research also highlights the need to conduct further research on herb-drug interactions on liver cells as well as in people. Such studies may find combinations of herbs and drugs that can be safely used together.

The Pittsburgh researchers noted that "patients and health care professionals must be encouraged to discuss the use of herbs and be educated about the potential interactions between herbs and drugs." This cannot be stressed enough.

Available forms and usage

Milk thistle extracts are available in most health food stores and in drug stores that sell herbal products. Silymarin, the plant's active ingredient, does not dissolve easily in water and is extracted from the seeds with an alcohol solution. For this reason, milk thistle teas are likely not effective and should be avoided. A dried extract is usually sold in capsules containing a specified amount of silymarin (usually 70% or 80%). Germany's Commission E, an expert advisory panel of doctors, pharmacists and herbal practitioners, has approved milk thistle extracts standardized to at least 70% silymarin as a treatment for "toxic liver damage [and] for supportive treatment in chronic inflammatory liver disease and hepatic cirrhosis."

Commission E and some available studies recommend daily dosages of 200 mg to 400 mg or about three capsules a day. To check the dosage, multiply the percentage of silymarin by the number of milligrams of milk thistle in each capsule. For example, three 150 mg capsules of milk thistle standardized to 80% silymarin would contain \((3 \times 150) \times 0.8 = 360\) mg of silymarin. For optimum benefit, milk thistle should be taken three times a day, usually around meal times. Several weeks of regular use are necessary before liver enzymes are likely to decrease.

Milk thistle usually costs $15 to $20 for 60 capsules and may be stored at room temperature.
References


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.

The Canadian AIDS Treatment Information Exchange (CATIE) in good faith provides information resources to help people living with HIV/AIDS who wish to manage their own health care in partnership with their care providers. Information accessed through or published or provided by CATIE, however, is not to be considered medical advice. We do not recommend or advocate particular treatments and we urge users to consult as broad a range of sources as possible. We strongly urge users to consult with a qualified medical practitioner prior to undertaking any decision, use or action of a medical nature.

We do not guarantee the accuracy or completeness of any information accessed through or published or provided by CATIE. Users relying on this information do so entirely at their own risk. Neither CATIE nor Health Canada nor any of their employees, directors, officers or volunteers may be held liable for damages of any kind that may result from the use or misuse of any such information. The views expressed herein or in any article or publication accessed or published or provided by CATIE are solely those of the authors and do not reflect the policies or opinions of CATIE or the official policy of the Minister of Health Canada.

Permission to reproduce

This document is copyrighted. It may be reprinted and distributed in its entirety for non-commercial purposes without prior permission, but permission must be obtained to edit its content. The following credit must appear on any reprint: *This information was provided by the Canadian AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1.800.263.1638.*
Contact CATIE

by telephone
1.800.263.1638
416.203.7122

by fax
416.203.8284

by e-mail
info@catie.ca

on the Web
http://www.catie.ca

by mail
505-555 Richmond Street West
Box 1104
Toronto, Ontario
M5V 3B1
Canada

Funding has been provided by Health Canada, under the Canadian Strategy on HIV/AIDS.