

# A Warning about Milk Thistle and Drug Interactions



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The seeds of the milk thistle plant are commonly used to protect the liver from damage caused by hepatitis viruses as well as alcohol and other substances. Compounds found in milk thistle — silybin, silymarin — act as antioxidants and also stimulate the repair of the liver. But now it appears that these and possibly other compounds in milk thistle can have other effects.

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? you might ask. Well, enzymes in the liver break down many of the substances that we eat and drink, including medications. If the activity of these enzymes are reduced, then drugs remain in the blood longer than they otherwise might. This could lead to having higher-than-expected levels of drugs in the body, causing side effects or intensifying already-existing side effects. Indeed, in recent experiments using milk thistle and human liver cells, the researchers found that relatively small concentrations of milk thistle did significantly slow down the activity of the liver enzyme CYP3A4 by 50% to 100%.

Many medications taken by people with HIV/AIDS (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 raise levels of these drugs, causing unpleasant or even dangerous side effects. Below is a short list of some other medications that are processed through the CYP3A4 enzyme. 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 – St. John's wort, Zyban/Wellbutrin (bupropion), Paxil (paroxetine), Prozac (fluoxetine), Luvox (fluvoxetine) 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

The research by the scientists in Pittsburgh 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 shows 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.

## REFERENCE

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.

*This information was provided by the Community AIDS Treatment Information Exchange (CATIE). For more information, contact CATIE at 1-800-263-1638.*