HERBS, SUPPLEMENTS AND HIV DISEASE

A PUBLICATION FROM
PROJECT inform
Information, Inspiration and Advocacy for People Living With HIV/AIDS

MAY 2004

issues to consider when deciding to use herbs, vitamins and nutritional supplements

Vitamins, supplements and herbs have long been used by people living with HIV to help manage the side effects of their therapies or improve their general health. In fact, studies suggest that almost 70% of people with HIV and about half the general population use some form of complementary therapy. The most common ones are massage and acupuncture.

Unfortunately, not many of these have been studied in people with HIV. They have not been studied to see how they interact with common medications or whether they add to the overall benefits of anti-HIV therapy. Recently, several reports have questioned the safety of some of these therapies in HIV and other diseases.

The intent of this publication is not to discourage using complementary therapies, but rather to supply some food for thought when making decisions about using them. Promoters of supplements and herbs are often the first to criticize prescription drugs as the products of "big business." However, supplements are themselves part of a huge industry—with annual sales of around $20 billion. This publication highlights some emerging concerns about using various therapies and ways to limit the possible risks when using them.

a little background on supplements

Under current law, vitamins, supplements and herbs do not have to be evaluated by any regulatory agency, like the Food and Drug Administration (FDA), prior to their sale. All they need to do is assert that the product is "generally regarded as safe." What this means is that studies are not required to show the effectiveness and safety of these products. This leaves the consumer with little or no meaningful information about their benefits or side effects.

Some manufacturers vaguely refer to "studies" in their literature, but these are seldom more than very small, uncontrolled studies. Also, these products do not have to be made according to the same *Good Manufacturing Practices* established for making prescription meds. As a result, these products vary widely in terms of their active ingredients, and even between batches of the same product. In fact, studies show that some products on the market today contain no active ingredients whatsoever.

Herbal supplements can actually contain dangerous chemicals, like arsenic and lead—both potentially deadly. Still others actually contain prescription meds. However, the best manufacturers make a serious effort to deliver the real product in the amounts claimed. But due to the lack of industry regulations, there's no simple way to know who is telling the truth.

People should be aware of these things and take measures to reduce their risk of buying contaminated products or ones without active ingredients. They can do this by seeking out reputable sellers. Seek guidance from a trained alternative medicine practitioner, like an herbalist or nutritionist who specializes in HIV, and gather information about the products you're considering. Only taking the word of people selling the products does not guarantee accurate information.

On their packages and even their websites, some manufacturers claim their products have been tested for active ingredients. Do a little research and see what you can learn. For example, some publications, like *Consumer Reports* and other groups like *www.consumerlab.com*, sometimes test supplements and list what is found in various brands. Even this, however, doesn't tell you whether you'll benefit from using the product.

Generally, if a company shows integrity in some of its products tested by consumer groups, it's a reasonable sign that they maintain similar standards for their other products. According to researchers who evaluate these therapies, the quality products that undergo evaluation by the manufacturer are, in general, not the ones you'll find at your average grocery store or pharmacy.

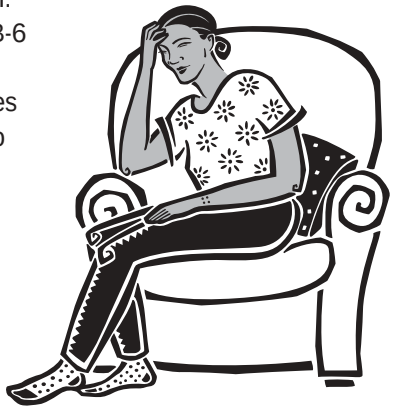
what about side effects?

The biggest myth about complementary therapies is that they're not toxic. Many people believe that because something is "natural" or sold over the counter that it doesn't have side effects. To the contrary, many people with HIV experience side effects from complementary therapies.

For example, Chinese herbal remedies that contain deer antler can cause nausea, diarrhea and other stomach upset. One man stopped all his anti-HIV meds to try to determine which had upset his stomach and quality of life. It turned out that when he stopped his herbal therapy (with deer antler), his problems cleared. It wasn't the anti-HIV drugs causing the problems at all.

High doses of vitamin C can cause severe diarrhea. Taking too many B-6 vitamins can lead to a complication that lands one in the hospital, and excessive levels of vitamin A can be highly toxic to the liver. These examples illustrate the need to be cautious when adding large doses of vitamins to your diet.

Side effects from using herbs, vitamins and supplements may not reveal themselves immediately. It may take several weeks after starting a therapy for them to emerge. Keeping an accurate record of every therapy you take, including when you start and stop them. Documenting the onset of side effects may help sort out which one is causing the problem. (For a list of herbs with known side effects, see pages 6 & 7.)



drug interactions

St. John's Wort (hypericin), a popular herb used for mild depression, has possibly serious interactions with protease inhibitors and non-nucleoside reverse transcriptase inhibitors (NNRTI). St. John's Wort is processed in the body by the same enzyme used for processing many drugs, including protease inhibitors and most NNRTIs. This enzyme is called p450, and several diet supplements and herbs have reported effects on it. Depending on how these products interact with p450, using anti-HIV drugs with them could either raise or lower the blood levels of the anti-HIV drugs. Herbs with reported effects on p450 include St. John's Wort, garlic, ginseng, melatonin, milk thistle (silymarin), geniposide and scullcap. For more detailed information on St. John's Wort, read page 8.

At the National Institutes of Health's (NIH) HIV clinic, one woman who started a regimen with ritonavir (Norvir) and then started on garlic supplements developed severe nausea and vomiting, which resolved after stopping the garlic. The garlic may have increased the levels of ritonavir, and thus its side effects. A second case also reported that garlic supplements may have enhanced the side effects from using ritonavir. It is unclear, however, if garlic was increasing the risks of ritonavir-related side effects or if it was the actual cause of them. (See herbal side effects chart on pages 6 & 7.) Subsequently, small single-dose studies of ritonavir and garlic do not suggest a serious herb-drug interaction, but more research is needed.

Garlic may also increase the risk of side effects associated with other anti-HIV drugs. This information, coupled with knowing that garlic has an effect on p450, suggests that until more is known people should use caution when combining high doses of garlic with anti-HIV drugs that use p450. Moreover, people using the supplement with anti-HIV drugs who experience serious stomach problems (diarrhea, nausea or vomiting) might consider stopping it to see if these symptoms lessen.

A group in Pittsburgh has shown that the common herb, milk thistle, also interacts with the p450 enzyme. It may also interact with many drugs used to treat HIV.

A Canadian group has shown that vitamin A supplements (beta-carotene and other retinoids) have an effect on the p450 enzyme. While this was based on test tube studies, the information suggests that there might be possible vitamin-drug interactions as well. It's then easy to start wondering if food itself may interact with drugs. There are food-drug interactions, which is why certain drugs are absorbed better when taken with or without food.

Grapefruit inhibits the p450 enzyme system and in the early days of protease inhibitors some people drank grapefruit juice together with the older version of saquinavir (Invirase), which was poorly absorbed by the body, in hopes of increasing its blood levels and effectiveness. (The newer version, called Fortovase, has corrected this problem.) However, in general, drinking grapefruit juice with protease inhibitors might increase their blood levels to dangerously high levels and increase the risk of side effects.

Not a great deal is known about food-drug interactions in general. Does this mean that people should stop eating food? Absolutely not! But the point is that we don't know how food may cause various interactions. This underscores that supplementing with vitamins, in pill forms, could carry some risks along with its unknown benefits. The value of good nutrition for overall health is well known; the value of supplementing with vitamins is not. This doesn't mean that people should not use vitamins, but rather it means buyers beware!

An article in *The Lancet* reports a number of herb-drug interactions that include the following herbs:

- Betel Nut
- Chili Pepper
- Devil's claw
- Dong quai
- Garlic
- Ginkgo
- Ginseng
- Guar gum
- Kava
- Papaya
- Psyllium
- St. John's Wort
- Saiboku-to
- Shankhapushpi
- Sho-saiko-to
- Xiao chai hu tang
- Valerian
- Yohimbine

talking with your doctor

To lessen the chance of herb-drug interactions, experts encourage people to have more in-depth discussions about complementary therapy with their doctors and pharmacists. This may take some getting used to for both patients and doctors alike. Doctors may need to learn to listen and support their patients, in a non-judgmental way, about using these therapies. And it may very well be the patients who actually drive this learning curve.

However, patients also need to be open and honest about what they're using and considering. One way to capture information about drug interactions and side effects is to record all the supplements you use in a complete drug history. It's also important for patients, doctors and pharmacists to keep up to date on the latest drug-herb and drug-vitamin interaction studies.

conclusion

There are generally two schools of thought about using vitamins. One is that people should take vitamin supplements in pill form. The other is that people should simply improve their nutrition and increase their vitamin intake through better eating. Likely the best approach for people at risk for vitamin deficiencies is one that lies somewhere between these two approaches.

It's unknown if the body can really use vitamins that are delivered from pills. Some contend that in order for the body to optimally absorb and use vitamins they need to be delivered through better nutrition, in foods where they exist in complex forms which may help the body to better use the nutrients.

Herbal remedies and other vitamins are sold as "food supplements" and do not undergo the rigorous testing that prescription meds do. They're not regulated and may not reveal all of a product's contents on its label. They also may not contain the ingredient(s) listed or the amount(s) claimed. Don't assume that just because something is available over the counter or is "natural" that it doesn't have side effects or won't interact negatively with your other meds.

In the US alone, it's estimated that $20 billion was spent on complementary therapies in 2001. The use of these therapies has risen almost 400% in the past eight years, and it's estimated that half the people in the US use them. Currently, the industry has done very little to document the safe and effective use of its products. It's unlikely that it ever will.

The US government, through the NIH, has established two botanical centers to evaluate these types of therapies. A third center will be funded shortly. Every few years, new discussions are held about whether and how to better regulate the marketing of nutritional supplements and herbs.

There is a great difficulty in evaluating herbs and herb-drug interactions because often the active ingredient in the products and its dose are not known. Although drug interaction studies for medications typically take a matter of a week to ten days, drug-herb interaction studies are expected to take much longer. This is a more expensive process since people will probably have to take herbs for a few weeks before an effect is seen.

Even when the interactions are known for one particular product, it's unclear how they will relate to similar products because of the lack of control over dosing. Because no studies have determined the proper or best dose of many complementary therapies, researchers face another challenge in first selecting the dose of herbs to use in studies.

Funding for these studies still remains a problem and a limitation to moving forward rapidly. Many companies that sell complementary therapies are reluctant to fund studies which may reveal their products are not useful, have side effects or have interactions with common meds. This information could hurt their profit margins. Pharmaceutical companies are also unwilling to fund these studies for many of the same reasons, and the FDA does not require them.

Whatever the possible benefits of herbs, vitamins and supplements, there's simply no meaningful information to guide making decisions when using them. Be aware that using them entails some risk. For more information on studies of herbs and vitamins conducted in HIV disease, see pages 8–12.

buyer beware!

Some herbal remedies contain controlled and possibly dangerous substances banned by the FDA. The FDA readily admits that it doesn't have enough enforcement to ensure that these products stay off store shelves. Media exposés on this topic in California reveal countless tales of people harmed by products that contain lead, arsenic, anabolic steroids and other dangerous substances.

A few years ago a number of Chinese herb supplements to manage diabetes were pulled from the shelves by the California Food and Drug Board. This followed an incident when a person with diabetes was hospitalized after taking one of the supplements. It was tested and found to contain a medication used to treat diabetes. The additional medication in the claimed "natural" product led to an overdose for that person.

To protect yourself, seek reputable sellers, investigate the product and seek guidance from trained professionals. Other resources that may help are ones that address fraud issues, such as state AIDS Fraud Task Forces and Project Inform's publication, *How to Identify AIDS Fraud*, available at 1-800-822-7422 and *www.projectinform.org*.

vitamins and potential side effects

Vitamin A and beta-carotene	Perhaps the most toxic vitamin. At high doses (more than 25,000 IU per day) toxicities are more likely, including loss of appetite, weight loss, bone malformations, spontaneous fractures, internal bleeding, liver toxicities and birth defects.
Vitamin B-6 (pyridoxine)	Reversible neuropathy has been reported in people taking high doses (500mg to 6 grams a day) over extended periods of time. For people with previous side effects associated with taking higher doses, symptoms resumed at doses as low as 50mg per day. (NOTE: The recommended daily allowance of this vitamin is 2mg per day.)
Vitamin B-12	In very rare instances, allergic reactions have been reported.
Folate	High doses have been associated with reduced zinc absorption and have been shown to mask signs of vitamin B-12 deficiencies.
Vitamin C	High doses can cause diarrhea and gastrointestinal distress. Buffered formulas are available and may decrease stomach problems. People with a history of kidney stones should consult a doctor before taking high doses.
Vitamin D	Potentially very toxic, can cause bone lesions. Toxicities reported with a single high dose supplement.
Thiamin	Very high intravenous doses have caused intoxication, headache, convulsions, muscular weakness, paralysis and cardiac arrhythmias.
Biotin	No reported toxicities.
Vitamin E	At doses higher than 1,000mg (1,500 IU) it can interfere with blood clotting. Prolonged use of high doses (800–3,200mg/daily) has been associated with nausea, diarrhea, muscle weakness and fatigue.
Riboflavin	No reported toxicities.
Pantothenic Acid	No reported toxicities in humans.
Vitamin K	No reported toxicities at doses of up to 500 times the required daily allowance (0.5mg/kg/day).
Niacin	Toxicities may be related to formulation. Nicotinic acid can cause itching, nausea, diarrhea and vomiting at doses of 2 to 4 grams/day. Nicotinamide only rarely produces these toxicities. At high doses, less common but more serious side effects may include liver injury, muscle disease, vision problems, low blood pressure, heart disease and poor blood clotting.

Virtually any herb has the potential of causing side effects. For some, the risks are small and only occur when herbs are used in large quantities or for long periods of time. For others, severe and life-threatening side effects have been seen even at very low doses with a single use. A good herbal practitioner should discuss the potential risks of both side effects and herb-drug interactions with you. However, this shouldn't replace discussing these interactions and side effects with your doctor and pharmacist.

The following is a list of herbs and their known side effects. Those with FDA warnings or heightened safety concerns are highlighted ***in grey***. This list is not comprehensive. If you don't see the herb(s) you may be taking on this list, it does not mean that there are no reported or possible side effects from using them. Many resources exist on the internet and elsewhere providing even more comprehensive information. One is *www.personalhealthzone.com/herbsafety.html*.

Akebia trifoliata caulis (Mu Tong)
Kidney toxicity, kidney failure. This herb contains aristolochic acid. In 2001 the FDA classified it as a Class 1 toxic substance and product recalls were started.

Aloe Vera (Carrisyn)
Severe diarrhea without proper preparation, must be processed properly. Refrain from ingesting aloe vera plant directly, or use proper preparations. **AB**

Apple seeds
May cause cyanide poisoning and death if consumed in large quantities. **C**

Apricot Seeds
May cause cyanide poisoning (possibly death) if consumed in large quantities. **C**

Asarum sieboldii herba cum Radix (Xi Xin)
Kidney toxicity, kidney failure. This herb contains aristolochic acid. In 2001 the FDA classified it as a Class 1 toxic substance and product recalls were started.

Astragalus (Huang-chi)
Low blood pressure, low blood sugar and increased urine production. May result in dizziness and fatigue. **AB**

Atractylodes (Bai-zhu, Pai-chu)
Liver toxicity, sedation, dehydration (diuretic), low blood sugar. **AB**

Bitter almond seeds
May cause cyanide poisoning (possibly death) if consumed in very large quantities. **C**

Black Tree Fungus
Can inhibit blood clotting and trigger hemorrhagic syndrome. **A**

Borage
Liver toxicity.

Buckthorn Bark (Rhamnus)
Increased bowel movements, diarrhea. **C**

Burdock (Arctium lappa)
Neurologic effects, blurred vision, dry mouth, constipation, bizarre behavior and speech (including hallucinations), increased urine (diuretic), low blood sugar and may impact estrogen activity. **BC**

Calamus
Kidney toxicity.

Cassava beans
May cause cyanide poisoning and death if consumed in large quantities. **C**

Chamomile
Belongs to ragweed family. People with allergies to ragweeds may experience allergic symptoms to chamomile. **A**

Chaparrel (Larrea divericata, Larrea tidentata, Creosote bush)
Nausea, vomiting, diarrhea, cramps, skin irritation, mouth sores and may promote tumor growth. The FDA issued a health warning in 1992 and many companies' voluntary removed chaparrel from their products or recalled products containing chaparrel. Some may still exist on the market, however. **B**

Cherry pits
May cause cyanide poisoning and death if consumed in large quantities. **C**

Choke cherry pits
May cause cyanide poisoning and death if consumed in large quantities. **C**

Coconoosis
(Codonopsis pilosula, Tang-shen)
Low blood pressure. **B**

Coltsfoot
Liver toxicity, light sensitivity.

Comfrey [Symphytum officionale (common comfrey), S. asperum (prickley comfrey), and S. x uplandicum (Russian comfrey)]
Liver toxicity: Vaso-occlusive disease, fatal liver intoxification. In 2001 the FDA's Center for Food Safety and Applied Nutrition sent letters to dietary supplement manufacturers advising that comfrey be removed from all nutritional health products due to potentially serious and life-threatening consequences of comfrey ingestion. **BE**

Compound Q (Trichosanthes, Guaiougen, GLQ223, Chinese cucumber root)
Severe neurologic side effects (ranging from dizziness to coma) at very high doses, low blood sugar, induces abortion. **B**

Dandelion (Taraxacum)
Excessive gas, nausea and vomiting; skin rashes, allergic reaction; increased urination (diuretic). Diuretic effect is likely no more than what is seen with coffee. **BC**

Devil's Claw Root
(Hapagophytum procumbens)
Induces abortion. **C**

Dock Roots
Increased bowel movements, diarrhea. **C**

Echinacea
Skin rash and insomnia. Allergic reaction. May aggravate auto-immune disorders (like lupus). **AB**

Ephedra
Heart failure, stroke, increased blood pressure.

Ganoderma (Ling-zhi, reishi)
Can inhibit blood clotting and trigger hemorrhagic syndrome. **AB**

Garlic (Allium sativum, Dasuan)
Can inhibit blood clotting and interfere with thyroid function. Diarrhea, vomiting, nausea, weight loss, loss of appetite and skin rashes have been reported. AB

Germander
Inflammation of the liver (hepatitis), liver injury and death. Early symptoms appear to resolve after stopping the herb. Re-starting herb appears to result in immediate return of the problem. The risk or degree of liver injury is not apparently associated with dose or duration of use. **E**

Ginseng (Wuchaseng, Siberian, wjuia, ren-shen)
Ginseng is touted the "most abused" or "mis-used" herb. Ginseng Abuse Syndrome (GAS) is associated with its long-term use. Various forms exist. *Panax* and *Eleutherococcus* ginsengs produce morning diarrhea, insomnia, nervousness, depression, confusion, skin rashes and high blood pressure. Ginsengs are known to increase effects of some antidepressants called Monoamine Oxidase Inhibitors (MOIs). Women may experience breast swelling or tenderness and changes in menstrual cycle (amenorrhea) due to impact on estrogen. **ABCD**

Horsetail (Equisetum arvense)
Excitement, loss of appetite and muscle control, diarrhea, labored breath, convulsion, coma and death. **C**

effects chart

Hypericin (St. John's Wort)
May induce sensitivity to light (photosensitivity), resulting in severe rash following sun exposure. May also have interactions with some anti-depressants called Monoamine Oxidase Inhibitors (MOIs). In 2000, the FDA issued a warning about this herb and its interactions with anti-HIV drugs. **ABC**

Isatis (Pan-lan-ken, dyers' wood root)
Can inhibit blood clotting. **B**

Iscador (Mistletoe)
Liver toxicity, seizures, shock, heart failure. **BC**

Juniper Berry
Stomach upset. **C**

Kava (Piper methysticum)
Liver-related injuries including hepatitis, cirrhosis and liver failure. In at least eight cases liver failure resulting in liver transplantation was required and death has been reported in three. In 2002 the FDA issued a warning noting that while liver-related injury associated with kava use is low, consumers should be warned of risks. Further, those with liver disease or taking other drugs that affect the liver should be especially careful.

Kelp (Laminara japonica, Kombu)
Interferes with thyroid function. Goiters. **B**

Licorice
High blood pressure, water retention and even serious heart problems. **ABC**

Life root
Veno-occlusive disease.

Lobelia (Lobelia inflata)
Depending on the dose, lobeline can cause either autonomic nervous system stimulation or depression. At low doses, it produces bronchial dilation and increased respiratory rate. Higher doses result in respiratory depression, as well as sweating, rapid heart rate, hypotension, and even coma and death. As little as 50mg of dried herb or a single milliliter of lobelia tincture has caused these reactions. **E**

Lycium Fruit (Kuo-chi-tzu, gouqizi, wolfberry, false jessamine)
Low blood sugar, mouth sores. **B**

Magnolia
Adverse effects were published in February 1993, of 48 women identified with serious kidney disease associated with the use of a Chinese diet herbal product containing this herb. Eighteen had terminal kidney failure that will require either kidney transplantation or lifelong renal dialysis. **E**

Nutmeg
Very high doses can cause altered mental status, liver damage and death. Fairly small amounts can cause headaches, cramps and nausea. **C**

Pau d'Arco
Nausea, vomiting, weight loss and has been shown to inhibit blood clotting. **AB**

Peach pits
May cause cyanide poisoning (possibly death) if consumed in large quantities. **C**

Pear seeds
May cause cyanide poisoning (possibly death) if consumed in large quantities. **C**

Pennyroyal Oil (Hedeoma pulegiodes, Mentha pulegium)
Has been used to induce menstruation and induces abortion. Has caused death due to kidney and liver toxicity. **C**

Peony (Paeonia, Moutan bark, chi-shao, bai-shoa, mudan-pi)
Stomach upset, nausea, diarrhea, depression, low blood pressure, increased urination (diuretic). **B**

Plum pits
May cause cyanide poisoning (possibly death) if consumed in very large quantities. **C**

Poke Plant (pokeweed, inkberry)
The root is particularly toxic. Can cause severe stomach upset, shortness of breath and death. Children have died from eating the berries. **C**

Privet (Ligustrum, Nuzhenzi)
Kidney failure, low blood pressure. **B**

Propolis
Alleric reaction, skin rashes. **B**

Prunella (Xia-ku-cao, woundwort, allheal)
Low blood pressure, increased urination (diuretic), contractions of uterus, increased bowel movements. **B**

Red Clover
Interferes with blood clotting. **B**

Rehmennia (Sheng-ti-huang)
Low blood sugar. **B**

Salvia (Tan-shen)
Interferes with blood clotting, platelets, tiredness/fatigue, low blood pressure, low blood sugar, increased urination (diuretic). **B**

Sassafras Root Bark
Causes cancer and liver toxicity in animal studies. **C**

Schizandra (Gomishi)
Depression, low blood pressure, contractions of the uterus. **B**

Senna leaves (Cassia angustafolia)
Increased bowel movements, diarrhea. **C**

Shave Grass
Excitement, loss of appetite and muscle control, diarrhea, labored breath, convulsion, coma and death. Shave grass may lead to thiamine deficiency with symptoms. **C**

Shiitake Mushroom (Lentinus edodes, Xiangling)
Can inhibit blood clotting and trigger hemorrhagic syndrome. Skin rashes, low blood pressure. **AB**

Stephania
Adverse effects were published in February 1993, of 48 women identified with serious kidney disease associated with the use of a Chinese diet herbal product containing this herb. Eighteen had terminal kidney failure that will require either kidney transplantation or lifelong renal dialysis. **E**

Sweet wormwood (Artemisa, Quindhaosu, mugwort)
Allergic reactions, skin rashes, altered mental status. **B**

Tang-kuei (Angelica, Du-huo, bai-zhi)
Interferes with blood clotting and platelets, depression, sensitivity to light. **B**

Tremella (Auriculariaceae, Bai-mur, white tree ear)
Inhibits platelets. **B**

Yarrow (Achillea millefoleum, Milfoil)
Interferes with blood clotting, allergic reactions, skin rashes, sensitivity to light. **BC**

Yohimbe (Pausinystalia yohimbe)
Kidney failure, seizures and death. Should also be avoided by individuals with low blood pressure, diabetes, and heart, liver or kidney disease. Symptoms of over dosage include weakness and nervous stimulation followed by paralysis, fatigue, stomach disorders and ultimately death. Certain foods (cheese, red wine, liver) can increase likelihood of side effects, as can concurrent use of over-the-counter therapies (diet aids, decongestants). **E**

SOURCES: A: Stephan Korsia. IHITTG, September 1992. (IHITTG was a publication of AIDS Project Los Angeles dedicated to alternative and complementary therapy.) B: Kassier, W.J., et. al., Arch Intern Med-Vol. 151, November 1991. C: The Medical Letter, Vol. 21, No. 7 (Issue 528), April 1976. D: Siegel, R., JAMA, Vol. 24, No. 15, April 1979. E: FDA Document, Illnesses and Injuries Associated with the Use of Selected Dietary Supplements, May 2000.

NIH study cautions use of St. John's Wort with anti-HIV drugs

A study conducted by the NIH found a significant interaction between the popular herbal therapy, St. John's Wort (*Hypericum perforatum*), and the protease inhibitor, indinavir (Crixivan). Indinavir blood levels were greatly decreased when the two were used together, greatly reducing indinavir's anti-HIV activity. This can quickly lead to developing resistance to indinavir. People commonly use St. John's Wort as a mild anti-depressant.

St. John's Wort is also likely to have the same effect on other protease inhibitors as well as NNRTIs. People who take these drugs are advised not to use St. John's Wort. Similar problems with drug interactions may occur between the herb and drugs used to treat other life-threatening illnesses, such as heart disease.

One possible limitation of the finding is that it is not clear how it applies to the various forms of St. John's Wort on the market. There is no way of knowing its quality or how much St. John's Wort is actually present in the products. Different brands may have a stronger or weaker effect. Also, the methodology of the study has not been fully described yet.

As this study shows, it's very possible for some herbal and nutritional supplements to lower the effectiveness of anti-HIV drugs or other medications. People who use complementary therapies should always discuss possible interactions with their doctors and pharmacists.

vitamin A (beta-carotene and retinoids) and anti-HIV drug interactions

In general, when used at reasonable doses on their own, nutritional products like vitamin A supplements are considered safe. New information suggests that when used with other therapies, including anti-HIV drugs and other nutritional products, interactions may occur that alter a product's effectiveness and safety.

Deficiencies in vitamin A (retinol, beta-carotene) have been associated with advanced HIV disease. It remains unclear if taking vitamin A supplements such as retinoids or beta-carotene helps people with HIV beyond correcting the deficiency. Moreover, questions remain as to whether or not vitamin A supplements cause vitamin-drug interactions.

A team in Canada set out to evaluate whether or not different vitamin A supplements interact with the p450 enzyme. The team evaluated four tablets and two soft gel capsules. All of the tested products had lower beta-carotene content than stated on their labels. One product had ten-fold less beta-carotene than advertised, and most were at least half as much than stated.

All forms of vitamin A (retinal, retinol, retinate and beta-carotene) as well as all the products tested had moderate (45–65%) to strong (65–100%) inhibitory effect on the p450 enzyme. Therefore, these products (and possible other nutritional health products) are very likely to interact with anti-HIV drugs. However, human studies are needed to understand the extent of these findings.

These data suggest that there are possible, real vitamin-drug interactions with potentially harmful results for people taking anti-HIV drugs. Much more information is needed to fully understand the scope of these interactions and their impact on the effectiveness and side effects of therapies. This information would also be needed on how to modify doses of either therapy to reduce the risk of developing drug resistance and increase the chances of benefiting from both.

selenium and hiv

Controversy remains over using selenium in people with HIV. Selenium is a toxic substance that gets spread into the environment through the burning of fossil fuel and other industrial processes. Trace amounts of it is often found in drinking water. Symptoms from consuming too much selenium include brittleness and loss of hair and nails, skin redness, blisters, vomiting, fatigue, neurological defects and damage to the liver and spleen.

Trace amounts of selenium are in the foods we eat. At these low levels, selenium is essential for proper immune function. The US Recommended Daily Allowance of selenium (all ages and genders) is 55 micrograms (mcg). Levels are slightly higher for pregnant (60mcg) and lactating (70mcg) women. The Institute of Medicine has proposed that the *maximum* daily intake before causing toxic effects is roughly 400mcg for adults.

Selenium deficiencies are rarely seen in the US, though they have been seen among people on Total Parental Nutrition (TPN), or intravenous nutrition. TPN is sometimes used to treat wasting syndrome in people with HIV. It is standard practice for doctors to check selenium levels in people on TPN and supplement as necessary.

Selenium toxicity has been seen in people using selenium supplements. In one case, high levels led to selenium poisoning in a man using supplements as a way to manage his fatigue. Investigators analyzed the over-the-counter product and found selenium levels of 500–1,000 times the amount labeled for each pill. This led to warnings noting that unusual diets and vitamin supplements are the most common causes of selenium toxicity in the US.

Several studies suggest that low levels of selenium are related to HIV disease progression. One study of 24 children and another of 125 adults has shown that those with these deficiencies were at a greater risk for disease progression and death. However, it's unknown whether or not selenium supplements would make a difference.

Other studies suggest that HIV needs selenium in order to reproduce. Some have proposed that when HIV uses all the selenium in a given cell, it may leave that cell to find more selenium by infecting other cells. Interestingly, HIV-positive women with low selenium levels have higher rates of HIV in vaginal secretions. Again, it remains unclear if selenium deficiency is a cause or an effect of HIV disease progression and if supplements will help or hurt.

A study conducted at the University of Miami compared selenium supplements (200µg/day) to placebo in 259 people living with HIV (147 men, 112 women). Information about CD4+ cell count, viral load and other parameters were collected at the first study visit and then every six months thereafter for two years.

One component of the study was to evaluate the frequency of hospitalizations among those receiving selenium compared to placebo. Unfortunately, sloppy data reporting leaves results of this aspect of the study completely uninterpretable currently.

Additionally, researchers examined blood levels of selenium in 112 HIV-positive women on anti-HIV therapy. They looked for links between selenium levels and the risk for pre-cancerous cervical cells (*cervical dysplasia*). While selenium levels were lower in women who developed dysplasia, using supplements made no difference in the risk of developing dysplasia. Five women who used selenium supplements and seven on placebo developed dysplasia.

In short, the most that can be concluded from these reports is that it remains entirely unknown if selenium supplements offer any benefit or harm, whatsoever. Risks for cervical dysplasia appear slightly higher when selenium levels are lower, but selenium supplements do not appear to eliminate this risk. This sloppy data reporting is a tragedy. Well-designed research is critical to evaluating the possible benefits (and risks) of selenium supplements.

amounts of selenium in various foods:

Food	Micro-grams	% Daily Value
Brazil nuts, dried, unblanched, 1 oz	840	1,200
Tuna, canned in oil, drained, 3.5 oz	78	111
Beef / calf liver, 3 oz	48	69
Cod, cooked, dry heat, 3 oz	40	57
Noodles, enriched, boiled, 1 c	35	50
Macaroni & cheese (box mix), 1 c	32	46
Turkey, breast, oven roasted, 3.5 oz	31	44
Macaroni, elbow, enriched, boiled, 1 c	30	43
Spaghetti w/ meat sauce, 1 c	25	36
Chicken, meat only, 1/2 breast	24	34
Beef chuck roast, lean only, oven roasted, 3 oz	23	33
Bread, enriched, whole wheat, 2 slices	20	29
Oatmeal, 1 c cooked	16	23
Egg, raw, whole, 1 large	15	21
Bread, enriched, white, 2 slices	14	20
Rice, enriched, long grain, cooked, 1 c	14	20
Cottage cheese, low-fat 2%, 1/2 c	11	16
Walnuts, black, dried, 1 oz	5	7
Cheddar cheese, 1 oz	4	6

vitamin E, vitamin A and anti-HIV therapies

Previous reports suggest that vitamin E levels are decreased in people living with HIV. Also, low levels of vitamin E have been associated with increased risk of disease progression. Researchers in the United Kingdom sought to evaluate vitamin E levels among 33 people before and six weeks after starting anti-HIV therapy. They compared levels to those seen in otherwise healthy HIV-negative people. Those taking multivitamins were not eligible.

Investigators found that before starting anti-HIV therapy, vitamin E levels were lower (21 µmol/l) among people with HIV compared to HIV-negative people (30 µmol/l). Contrary to earlier reports, people with AIDS had slightly higher vitamin E levels (24 µmol/l) than people with HIV who did not have AIDS (19 µmol/l). After six weeks of therapy, vitamin E levels normalized among people with HIV (28 µmol/l) compared to the HIV-negative people (26 µmol/l).

Vitamin A levels were also evaluated. No differences were seen in vitamin A levels either before or six weeks after starting anti-HIV therapy. Moreover, vitamin A levels were in normal healthy ranges, roughly equivalent to those seen in HIV-negative people, both before and after therapy. Further, no differences were seen in vitamin A levels between healthy HIV-positive people and those with AIDS.

This study suggests that for people taking anti-HIV therapy, vitamin E supplements are likely not necessary. Moreover, vitamin A deficiencies were not noted with HIV infection, regardless of stage of disease. It remains unknown if vitamin E supplements will benefit people not on anti-HIV therapy.

vitamin supplements and HIV in women (implications for everyone)

Vitamin deficiencies have been seen in people even at early stages of HIV infection. This has led to an interest in using multivitamins, particularly in resource poor settings and those where malnutrition is a problem. A study in Tanzania, Africa among HIV-positive pregnant women showed that using multivitamins led to fewer deaths of unborn children, increased birth weights and fewer pre-term births.

However, trends were noted that children born to HIV-positive mothers who took multivitamins during pregnancy were more likely to be infected with HIV. Because of this, another study was started in Kenya to examine the impact of using daily multivitamins (or placebo) and evaluate its impact on vaginal and cervical presence of HIV.

The use of multivitamins was associated with slightly higher CD4+ and CD8+ cell counts and no overall changes in HIV levels in the blood. However, it was also associated with increased vaginal presence of HIV, with about 1/2 log higher levels of HIV in vaginal swabs. The percentage of vaginal cells with HIV was higher among those taking daily multivitamins (31%) than those on placebo (17%). The differences were less striking in cervical cells.

Researchers speculate that using daily multivitamins among women is unlikely to protect them from HIV disease progression and may increase the chances of passing HIV onto others. The results are perhaps more relevant to places where anti-HIV therapies are not available or to those who choose not to use them together with multivitamins. The use of multivitamins was linked to improved markers of immune health (slight increases in both CD4+ and CD8+ cell counts). It remains unknown whether the increased vaginal presence of HIV from using multivitamins would be controlled while using anti-HIV therapy. (The women in this study were not on anti-HIV therapy.)

Another Kenyan study found that vitamin A deficiencies in blood were associated with increased vaginal presence of HIV during pregnancy, increased HIV in breast milk, higher rates of mother-to-child HIV transmission, lower CD4+ cell counts and more rapid disease progression. Four hundred women took either placebo or vitamin A at the dose recommended by the World Health Organization for correcting symptomatic vitamin A deficiencies in women of child-bearing potential. The study found that the supplements had no effect whatsoever on vaginal presence of HIV, blood levels of HIV, or CD4+ or CD8+ cell counts.

These findings held true even among the 59% of women with notable vitamin A deficiencies at the start of the study. They suggest that while vitamin A deficiencies may be associated with poorer outcomes in passing HIV from mother to child and of HIV disease in general, supplements are unlikely to address these problems. As with the other study, this study did not evaluate using supplements together with anti-HIV therapy.

zinc deficiencies and HIV

Deficiencies in dietary zinc have been associated with decreased immune function and possibly increased HIV reproduction. Drug users are at particular risk for zinc deficiencies for a number of reasons. These include poor diets, poor absorption of nutrients and poor processing of nutrients by the body.

A team in Florida examined the nutritional and immunologic status of 118 HIV-positive injection drug users. They found that people whose diets included foods with higher levels of zinc showed higher levels of zinc in their blood. This suggests that, in general, improving a person's diet results in more normalized zinc levels.

The study also showed that people with lower zinc levels had somewhat lower CD4+ cell counts and were more likely to have counts below 200. It would be rash to suggest, however, that low zinc levels are the cause of lower CD4+ cell counts and not merely an effect of disease progression. In general this study is encouraging in that it shows that simply improving diet, without supplements, leads to increased zinc levels in the blood and better immune status. Another study is ongoing to see if zinc supplements will result in improved blood levels of zinc and to see if it has any effect on HIV or immune markers.

For more treatment information, call Project Inform's toll-free National HIV/AIDS Treatment Information Hotline at 1-800-822-7422.

YES, I WANT TO HELP PROJECT INFORM! OUR MAILING LIST IS CONFIDENTIAL.

☐ WISE WORDS ☐ EN ESPAÑOL
Three-times yearly newsletter with information by, for and about women.

☐ PI PERSPECTIVE ☐ EN ESPAÑOL
Three-times yearly cutting-edge HIV treatment journal.

☐ INTRO PACKET ☐ EN ESPAÑOL
Beginning HIV treatment information to help you make decisions.

☐ TAN ALERT
Grassroots advocacy network newsletter (email only).

☐ Enclosed is my donation of $_____ to help Project Inform.
☐ I can't help right now, but I would like to receive the free publications checked at left.
☐ Please take me off your mailing list.

_____
Mr. / Ms. / Mrs.

_____ ☐ This is a new address.
Address

_____
City State Zip Email FACT

Project Inform 205 13th Street, Suite 2001 San Francisco, CA 94103-2461 TEL 415.558.8669 FAX 415.558.0684 HOTLINE 1.800.822.7422