Update on dietary supplements for depression

When does an alternative therapy become mainstream? When enough studies show that it’s safe and effective. For mild to moderate depression, a handful of supplements seem headed in that direction.

Although dietary supplements such as vitamins, minerals, herbs, and enzymes are regulated more like food than drugs, they constitute much of the pharmacopeia of complementary and alternative medicine. Valerian is popular for improving sleep. Some women use the herb black cohosh to relieve hot flashes. And many people take specific vitamins, minerals, or other supplements in hopes of warding off various ills—from colds to cancer.

Dietary supplements can be marketed without proof of safety or effectiveness. However, some have generated so much scientific interest that they’re being put to the test in clinical trials, a prerequisite for acceptance in mainstream medical practice. Depression is one of the conditions that has generated the most data on some of these supplements, says Dr. Andrew Nierenberg, associate director of the Depression Clinical and Research Program at Massachusetts General Hospital. That’s important, because depression is an enormous source of disability. In the United States alone, about 19 million people each year—two-thirds of them women—have an episode of depression. The supplements of particular interest for the treatment of this condition are St. John’s wort, folate, SAM e, and omega-3 fatty acids.

Supplements no substitute for professional help

Depression has many causes and severity ranges widely, so if you experience certain symptoms (see “Features of major depression”), it’s important to seek help first from a qualified professional. Major depression usually requires psychiatric medications and/or psychotherapy. But depression may also be mild to moderate, resembling a low mood more than a full-blown clinical disorder.

The supplements currently under study may be good for such low-grade depression (sometimes called minor depression, to distinguish it from major depression). If proved effective, they might improve mood without some of the side effects that accompany most prescription antidepressants. An important caveat: If you want to try a supplement, discuss it first with your clinician, because they’re active in the brain, have side effects, and can interact with other medications.

If any medication doesn’t help relieve depression within four weeks, see your physician or another professional. You may need a different medication or therapeutic approach.

The trials of St. John’s wort

St. John’s wort (Hypericum perforatum) is the most popular supplement for depression. Many small studies conducted mostly in Europe over the past two decades suggested that in treating mild to moderate depression, it was comparable to tricyclic antidepressants, an older class of medications.

But many scientists in the United States have questioned these small studies because of flaws in their experimental designs. Most were brief; their doses and preparations were inconsistent; and they didn’t test St. John’s wort against the newer selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine (Prozac) and sertraline (Zoloft).

The herb suffered a further setback in 2002, when a well-designed NIH-sponsored study found it to be no better than a placebo in treating major depression. But the study also raised questions. It found not only St. John’s wort but also Zoloft to be ineffective, although some thought the drug hadn’t been given at optimal doses. Moreover, critics pointed out, St. John’s wort has generally not been recommended as a treatment for major depression.

A four-year, NIH-sponsored study begun last year will test St. John’s wort against placebo and citalopram (Celexa), an SSRI antidepressant, in the treatment of minor depression.

Although its biological activity is not completely understood, St. John’s wort resembles an SSRI, minus the side effect of decreased libido. Its most common side effects include stomach upset, fatigue, and sun sensitivity. Because it affects the liver, St. John’s wort can decrease the effectiveness of a long list of medications, including blood thinners, digoxin (a heart drug), immunosuppressant drugs, oral contraceptives, and certain HIV medications. It may also decrease the absorption of iron. Do not take St. John’s wort with an SSRI or...
Folate and SAMe

Dr. Nierenberg says folate and SAMe look highly promising, although they haven’t yet been tested in large clinical trials.

Folate. Also called folic acid, folate is a B vitamin best known for preventing certain neurological defects in the developing fetus. There’s some evidence, although no proof, that it may also help protect against heart disease and certain cancers. In older people, especially deficiencies in vitamin B12 and folate can contribute to cognitive problems. Low folate is also known to cause depressive symptoms, including apathy, fatigue, and trouble concentrating.

Researchers believe the folate link to mood comes, in part, from the vitamin’s role in metabolizing certain brain chemicals. Numerous trials over the years have focused on folate taken along with a conventional antidepressant drug. In 2000, a well-designed study involving patients with moderate to severe depression found that 500 mcg of folic acid plus Prozac improved the women’s response to therapy by more than 30% over Prozac alone — but only in women, not in men. If larger studies can replicate these intriguing results, folate may gain acceptance as an inexpensive and relatively safe way to improve the effects of other depression medications, at least in women.

The risk of toxicity from folate is very low. However, taking large amounts (more than 1,000 mcg per day) can mask a vitamin B12 deficiency.

SAMe. S-Adenosyl-L-methionine (SAMe) is a substance made in the body that’s involved in dozens of processes, including the production of serotonin, norepinephrine, and dopamine — brain chemicals that may be low in depressed people. Its manufacture depends on adequate folate and vitamin B12 in the body. Like St. John’s wort, SAMe is widely used in Europe as a natural antidepressant. Since 1999, when it became available in an oral form, SAMe has been popular in the United States as well. A recent meta-analysis of 28 studies suggests that patients taking SAMe improve as much as they would on certain conventional antidepressants, such as tricyclic antidepressants; in some, it seemed to work faster.

There’s a lot of uncertainty about the right therapeutic dose of SAMe, which in research studies has varied from 400 mg per day by injection for six weeks to 1,600 mg per day taken orally for four weeks. SAMe has never been compared directly to SSRIs. Its interactions (if any) with other drugs and its long-term safety are unknown. It’s also expensive — about $1 for a 200-mg tablet. SAMe’s most common side effects are headaches, insomnia, jitteriness, and loose stools.

Omega-3 fatty acids

Clinical trials and international surveys of fish consumption have raised the hope that the omega-3 fatty acids found in fish oils could help prevent or relieve depression. There’s biological evidence to support the idea. Brain cell membranes contain high concentrations of certain omega-3 fatty acids, and omega-3s affect processes such as nerve cell communication that can go wrong in mood disorders like depression.

Research with depressed patients has used two different forms of omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), to boost the activity of antidepressant drugs. In some studies, EPA looks more effective than DHA for treating mood disorders, but there aren’t enough data yet to be sure, or to suggest an optimal dose of either type of fatty acid.

Meanwhile, dietary omega-3s are good for general health, because they help prevent heart attacks and strokes and may be beneficial for inflammatory diseases such as rheumatoid arthritis. Fish oil preparations, which include both DHA and EPA, can provide 1–2 mg per day of omega-3 fatty acids — an amount found to be helpful in depression studies. A drawback of these capsules is a fishy taste in the mouth. Refrigerating the capsules may help.

Selected resources

National Center for Complementary and Alternative Medicine (NCCAM) Clearinghouse
888-644-6226 (toll free)
nccam.nih.gov

Office of Dietary Supplements, NIH
ods.od.nih.gov/databases/ibids.html

Complementary and Alternative Medicine on PubMed

Food and Drug Administration
www.fda.gov

Buyer’s Guide to Herbs and Supplements, a Special Health Report from Harvard Health Publications, available for $16 from Harvard Health Publications, P.O. Box 421073, Palm Coast, FL 32142-1073 or online at www.health.harvard.edu
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