

## Dietary Supplements for Mood Disorders

What's the science behind the claims?

Although a full arsenal of prescription medications are available for depression and anxiety, some people are still curious about using various dietary supplements as an alternative, perhaps thinking these products are more "natural" or "safe." In reality, however, supplements are potentially more hazardous, as the U.S. Food and Drug Administration (FDA) holds them to a much lesser standard than prescription drugs. Specifically, the FDA does not require research on safety, dosage, or effectiveness before they are marketed.

That means it remains largely unknown how well any given product works or how it interacts with prescription drugs. What's more, the quality and strength of products can vary not only between brands but also from batch to batch by the same manufacturer.

Unfortunately, that doesn't seem to be stopping the 38 million American adults who self-treat with supplements for a variety of conditions. What exactly is the scientific evidence, if any, supporting the use of supplements for mood disorders?

### St. John's Wort

For centuries, St. John's wort (*Hypericum perforatum*) has served as a folk remedy for a variety of ailments; the ancient Greeks first recorded its healing benefits in 400 B.C. Today, the herb is widely used to treat depression, anxiety, and sleeping disorders in Europe and particularly in Germany, where the supplement is regulated as a drug and available via prescription. While it is not fully known how St. John's wort exerts its effects, preliminary

research suggests that it may prevent nerve cells in the brain from reabsorbing the neurotransmitter serotonin.

Some clinical trials, mostly from Germany, show that St. John's wort may be effective for mild to moderate depression. In a randomized, placebo-controlled study of 388 people with moderate depression, 900 mg of St. John's wort was almost as effective as 20 mg of citalopram (Celexa) over six weeks of treatment: 54% of the St. John's wort group improved, compared with 56% of the Celexa takers and 39% on the placebo. The St. John's wort group did experience fewer adverse effects—17% versus 53% of the Celexa group.

However, for severe depression, St. John's wort appears to be minimally effective. A 2005 review of 37 clinical trials reinforced earlier findings that the herb provides little or no benefit for people with major depression. Individuals with clinical depression may put themselves in danger of self-harm or suicide by self-treating with St. John's wort instead of antidepressants.

And St. John's wort is not without other risks. Taking it with an antidepressant can decrease the drug's effectiveness and increase side effects, such as nausea, anxiety, headache, and confusion. When taken alone, it has been shown to lower blood levels (and thus effectiveness) of these drugs:

- cyclosporine (Sandimmune), which prevents rejection of transplanted organs
- digoxin (Lanoxin), which strengthens heart muscle contractions

- indinavir (Crixivan), a treatment for HIV
- irinotecan (Camptosar), a cancer treatment
- warfarin (Coumadin) and other anticoagulants, which prevent blood clots
- birth control pills.

### SAM-e

Another supplement touted for the treatment of depression is S-adenosylmethionine, better known as SAM-e (pronounced "sammy"). The SAM-e found in supplements is a synthetic, stabilized form of a substance that we naturally manufacture in our bodies. SAM-e forms when the amino acid methionine combines with adenosyl-triphosphate (ATP). It is involved in the synthesis of neurotransmitters like serotonin and dopamine that are known to regulate mood.

Since the 1970s, SAM-e has been available (by prescription only) in some European countries for the treatment of a variety of diseases, including depression and arthritis. In 1999, it became available in the United States as a dietary supplement that promotes "emotional well-being" and "joint health."

Some evidence suggests that SAM-e may be helpful for depression. A 2002 review by the U.S. Agency for Healthcare Research and Quality examined 28 clinical trials and found that SAM-e was more effective than a placebo and equally effective as antidepressants, though the studies were limited in size and quality and involved varying levels of depression. The researchers acknowledged a need for further studies to determine

exactly how SAM-e works and to assess its risk-benefit ratio compared with antidepressants.

One small, preliminary study suggests that adding SAM-e to antidepressant treatment may improve results in people who haven't responded to the medication. Researchers added SAM-e to the medication regimen of 30 people with severe depression who were not responding to treatment with a selective serotonin reuptake inhibitor (SSRI) or venlafaxine (Effexor). After six weeks, 50% of the participants had improved significantly, and 43% saw their symptoms resolve completely. No serious side effects were reported.

Despite these findings, larger controlled trials are needed to confirm whether using SAM-e alone or with antidepressants should be endorsed as a treatment.

### **Kava Kava and Valerian**

Even less solid evidence exists to support the use of these two herbal treatments, the most commonly used supplements for anxiety and insomnia. Kava kava (*Piper methysticum*) is purported to promote relaxation without compromising mental sharpness, and a review of six randomized, placebo-controlled trials found that it was an effective option for anxiety. But in 2002 the FDA issued a warning about kava kava's potential for severe liver damage after adverse effects were widely reported. Since then, research into the herb's benefits has sharply declined and some countries (not including the United States) have banned its use.

Valerian, which comes from the *Valeriana officinalis* plant, appears to be free of major adverse effects.

### **Supplement Precautions**

If you are interested in trying a supplement, take the following steps:

- Tell your doctor about any supplements you are taking or plan to take. He or she can help you determine whether it will interact with any of your medications.
- Avoid products that contain more than one herb.
- Look for products that list the name and address of the manufacturer, a batch and lot number, expiration date, dosage guidelines, and side effects.
- Stop taking the supplement and call your doctor if you experience nausea, vomiting, rapid heartbeat, anxiety, insomnia, diarrhea, or skin rash.

Some randomized, placebo-controlled studies show it to be helpful for insomnia, though they are faulted for their small sample sizes or other biases. Overall, the evidence for the sleep-inducing effects of valerian remains inconclusive.

Should you decide to take kava kava or valerian—which we do not recommend—it should be taken instead of, rather than in addition to, prescription anti-anxiety drugs. That's because these supplements can interact dangerously with sedatives, such as benzodiazepines, barbiturates, narcotics, antidepressants, and antihistamines.

### **The Bottom Line**

While evidence exists that some alternative remedies may be helpful for mild to moderate depression or anxiety, you should consider a number of factors before taking a supplement.

First, aside from the few placebo-controlled, randomized studies mentioned earlier, much of the evidence for supplements comes from small studies, many of which used different experimental methods and even different forms of the supplement. Thus, there simply isn't enough evidence to show whether

these supplements will work as well as standard medications.

Second, it can be difficult to know exactly what you're taking. In 2007, the FDA began requiring herbal supplement manufacturers to evaluate the purity, quality, strength, and composition of their products and to report any adverse effects to the FDA. In addition, manufacturers usually have proprietary formulas for their products, meaning that the amount of active ingredient in each can vary greatly. So don't forget to read labels carefully. Cost also can be a factor. While prescription medications are likely to be covered by medical insurance, supplements are not.

Lastly, an individual may choose a supplement to self-medicate—and that can be hazardous. In contrast, when working with a mental health professional, the person has the benefit of someone carefully monitoring his or her symptoms in addition to potentially prescribing medications. Ultimately, keep in mind that both depression and anxiety are serious conditions that are best treated by a qualified physician. Always talk to your doctor before adding a supplement to your treatment regimen. ■