

Supplement Sampler

SAMe: S-Adenosyl-L-Methionine

Best Indications

- Depression
- Joint Pain
- Intrahepatic cholestasis (decreasing symptoms in chronic liver disease, pregnancy)
- Fibromyalgia

Mechanism of Action

S-Adenosyl-L-Methionine, pronounced “Sammy” is present in nearly all tissues and fluids in the body. It is involved in over 100 methyl group transfer reactions and influences reactions related to neurotransmitters, nucleic acids, proteins, hormones, and multiple other chemical compounds. How it works for depression is unknown; it may alter cell membrane fluidity to affect receptors, and it may change neurotransmitter turnover rates. With joint pain, SAMe may help by working as an anti-inflammatory, increasing cartilage growth and repair, and antagonizing TNF-alpha.

Low CSF levels have been linked to depression, and with improvement in levels, depression symptoms seem to improve. Oral and IV forms of SAMe cross the blood brain barrier and increase levels.

Best Studies

Hundreds of studies of SAMe have been done, many of which are in the European literature. The Agency for Healthcare Research and Quality (AHRQ) summarized the studies up through the year 2000 nicely in a review available at the website:

<http://www.ahrq.gov/clinic/epcsums/samesum.pdf>

Highlights of the meta-analyses performed for SAMe include:

1. Depression: 28 studies that met criteria for meta-analysis indicate that SAMe was associated with a change of 6 points on the Hamilton Depression Scale, which is equivalent to a partial response to treatment. SAMe was not found to be significantly better than “conventional” depression treatments (but often performed equally as well in studies when they were compared with tricyclics; few if any SSRI studies have been done).
2. Osteoarthritis: 13 studies were used to indicate an effect size in favor of SAMe of 0.20 relative to placebo (95% CI, -0.39, -0.02). There were no statistically significant outcomes differences when compared with NSAIDs. (Note that many studies have shown equivalence or superiority of SAMe compared to such drugs as celecoxib.)
3. Cholestasis: A meta-analysis of 8 studies indicated that SAMe had a significant effect size of nearly a full standard deviation for decreasing pruritus and over a standard deviation for decreasing serum bilirubin in cholestasis of pregnancy. Usodeoxycholic acid had a better effect. Similarly, 6 studies of SAMe with pruritus for intrahepatic cholestasis caused by other liver diseases indicated that SAMe was twice as likely as placebo to reduce pruritus symptoms.



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Dose

For depression, consider 400-1600 mg daily. 1600 mg in divided doses is the most common dose for use in trials. 400 mg TID is a common dose. For osteoarthritis, 200 mg three times a day is a typical dose. Fibromyalgia dosing is often in the 800 mg daily range. SAMe is also given parenterally with good effect in some clinics. Avoid dosing close to bedtime since it can cause insomnia.

Side Effects

There are surprisingly few. Natural Database (naturaldatabase.com) notes that in studies lasting as long as 2 years in over 22,000 patients, no serious toxicities have been reported. Small studies of 800 mg daily in pregnancy for 2-3 weeks in the third trimester for cholestasis found no adverse effects, but proceed with caution. At high doses, GI effects, nervousness, decreased appetite, dry mouth, insomnia and headache may occur.

Also use caution if someone is already taking antidepressant medications or is bipolar. It can trigger serotonin syndrome and mania.

Cost

Most supplements come as 200 or 400 mg tabs or capsules, with an average cost on iherb.com or drugstore.com of 50 cents to a dollar per capsule. Not a cheap one! Buy in blister packs since oxidation can render the product inactive. *Natures Made* is one product that is reasonably priced and comes in blister packs.

Comments

SAMe has prescription drug status in Italy, Spain, and Germany. Some supplement gurus recommend its use as a relatively rapid treatment of depression while waiting for St. John's wort to take effect. Two fibromyalgia studies (n=17 and n=44) showed some improvements in some measures, but not in others. SAMe has orphan drug status for AIDS-related myelopathy.

Clinical Bottom Line

SAMe is worth considering, particularly in patients who want supplements for depression or osteoarthritis. It is worth a try in fibromyalgia and intrahepatic cholestasis as well. Its safety profile is reassuring, but tread cautiously in pregnancy with any supplement if it is not being used at food-level doses or has limited research surrounding its use.

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