

SAMe: The same old, same old?

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S-adenosyl-L-methionine (SAMe) is a compound found naturally in the body, produced in the liver. As a supplement, SAMe is advertised as supporting a healthy mood and emotional well-being. Some products also promise a liver detox cleanse as well as a joint and brain boost. But how does SAMe measure up?

SAMe is created within the body from methionine, an amino acid found in foods, and helps produce and regulate hormones and maintain cell membranes. SAMe facilitates dopamine and norepinephrine synthesis in the central nervous system and as the principal methyl donor in methyltransferase reactions, SAMe has been shown in studies to restore hepatic glutathione deposits and modulate liver injury.



Is there a benefit?

Research on SAMe has mostly focused on potential beneficial effects related to depression, liver diseases, and osteoarthritis, with mixed results.

A 2020 systematic review of double-blind, randomized controlled trials comparing SAMe to placebo and other antidepressants by Cuomo and colleagues in *Annals of General Psychiatry* examined the evidence concerning the efficacy of SAMe in treatment of major depressive disorder (MDD). Eight trials were evaluated with a total of 1,011 participants. Studies ranged between 2 and 12 weeks with a daily dose of SAMe from 20 mg to 3,200 mg. Three out of 5 studies showed significant improvement over placebo. Four comparisons showed no significant difference over antidepressants such as imipramine or escitalopram. One study concluded

that SAMe combined with SSRI was better than placebo administered with SSRI. The study authors commented that larger, double-blind randomized controlled studies were warranted to confirm the antidepressant effectiveness of SAMe.

A 2020 double-blind, randomized controlled trial by Saris and colleagues published in *Psychopharmacology (Berlin)* tested the efficacy of SAMe versus placebo in patients with MDD and mild to moderate levels of depressive symptoms who are not currently taking antidepressants. This 8-week, double-blind, randomized controlled trial focused on 800 mg/day of SAMe monotherapy versus placebo. The study showed a high placebo efficacy rate of over 50% and although a differential reduction in depression symptoms seemed to favor SAMe, the results were not statistically significant.

Liver disease and osteoarthritis

A 2015 systematic review and meta-analysis in *PLoS One* by Guo and colleagues evaluated 20 years of randomized controlled trials of chronic liver disease treatment. Their findings suggest that SAMe could be used as the basis of a medication regimen for liver function improvement due to its safety profile but that it demonstrated limited clinical value in treatment of certain chronic liver diseases.

Several randomized controlled trials also assessed the efficacy of SAMe compared with placebo or NSAIDs in the treatment of osteoarthritis. A meta-analysis by Soeken and colleagues in the *Journal of Family Practice* revealed that only 2 out of 11 trials concluded that SAMe appears to be as effective as NSAIDs in reducing pain and improving joint function in patients with osteoarthritis without the adverse effects often associated with NSAIDs. They noted that most studies weren't well-designed and included small population sizes.

What to tell your patients

While research doesn't consistently support any benefit of using SAMe for depression, liver disease, or osteoarthritis, the supplement is safe with mild and transient adverse effects such as nausea or upset stomach. SAMe is available as a capsule, tablet, or liquid in 200 mg to 400 mg dosages.

Patients should be aware that SAMe may interact with antidepressants and can possibly increase anxiety and mania in patients with bipolar disorder.

Those with weakened immune systems may be at increased risk of infection as SAMe may encourage the growth of the bacteria pneumocystis. Contraindications include antidepressants and other drugs and supplements, such as St. John's Wort, that increase levels of serotonin, as well as antipsychotics, amphetamines, dextromethorphan, levodopa, and narcotics such as meperidine and tramadol. ■

