

SAMe

❖ **Name of Supplement**
S-Adenosylmethionine

❖ **Also known As**

Ademetionine	S-Adenosylmethionine
Adenosylmethionine	SAMe, SAM-e
S-Adenosyl Methionine	Samyr
S-Adenosyl-L-Methionine	“Sammy”

❖ **Scientific Name**
S-Adenosyl-L-methionine

❖ **Description of Active Ingredients**

S-adenosylmethionine is a natural substance found in cells, tissue and body fluids. It is produced from methionine, an amino acid containing sulfur, and adenosine triphosphate (ATP). The nutritional supplement is harvested from yeast cell cultures. ^(1,2)

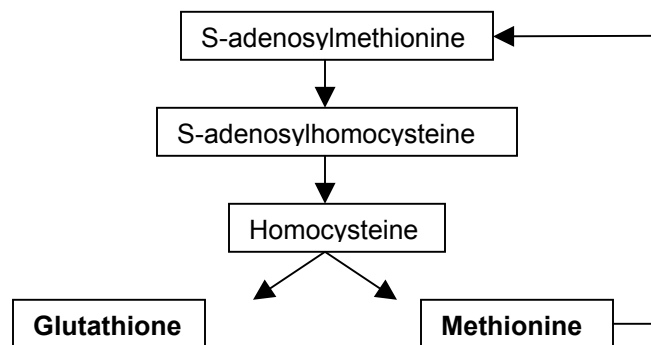
❖ **Mechanism of Action**

S-adenosylmethionine is a substrate in a variety of reactions involving transmethylation. It is linked to production and metabolism of many substances: hormones, neurotransmitters, nucleic acids, proteins and phospholipids. For example, SAMe is a precursor to glutathione, an important antioxidant found in the liver. Deficiencies in vitamin B12 and folate can result in decreased endogenous SAMe levels. ^(1,2)

Figure 1.

S-Adenosylmethionine Metabolism

(Adapted from SAMe monograph, Natural Medicine Comprehensive Database)¹



(Folate and B12 are required for these reactions)

❖ **Current Indications and Efficacy**

Depression –

The mechanism of S-adenosylmethionine's antidepressant effects is not yet well defined. Decreases in SAME serum levels has been associated with imbalances in serotonin, dopamine and norepinephrine.¹

Chiaie et al.³ a randomized, double-blind, placebo controlled, multicenter trial, conducted in Italy, compared the efficacy and safety of SAME to imipramine. This study included 576 patients, ages 18 to 70, who met the DSM-IV criteria for major, unipolar, non-psychotic depression. One arm of this trial compared treatment with imipramine 150mg po to SAME 1600mg po for 6 weeks. And the second arm of the trial compared treatment with imipramine 150mg po to SAME 400 IM for 4 weeks. In both arms, the imipramine dose was titrated up to 150mg over a period of 15 days.

The primary outcome of this trial was significant reduction in the Hamilton Depression (HAM-D) Rating Scale scores. All patients showed statistically significant reductions in HAM-D scores, with no significant difference between groups.

Secondary outcomes included: reduction in Montgomery-Asberg Depression Rating Scale (MADRS) scores, percent responders (those patients having a decrease of 50% or more in HAM-D scores), and improved Global Clinical Impression scores (GCI). Both imipramine and SAME groups achieved statistically significant improvements with regard to these secondary outcomes. There was no significant difference between groups except in the area of improved GCI. Imipramine was superior to the oral form of SAME in improving GCI scores, (no significant difference between imipramine and the intramuscular form of SAME was shown in this area). SAME had fewer drug-related adverse events compared to imipramine.

Osteoarthritis –

S-adenosylmethionine is associated with increased proteoglycan synthesis and therefore may be chondroprotective. It may also have analgesic and anti-inflammatory effects.²

Soeken et al.⁴ conducted a meta-analysis published in the Journal of Family Practice in May of 2002. The analysis included 11 randomized controlled trials comparing SAME to either placebo or NSAIDs for the treatment of OA. Collectively, the analysis included 1442 subjects with a diagnosis of OA, 54% of whom had OA of the knee. The mean age of subjects was 60 years, and the mean duration of OA was 5.7 years. The average study duration was 30 days.

Primary outcomes of the study were: pain, functional limitation and adverse effects. SAME showed to be superior to placebo in reducing functional limitations. It did not prove to be superior to placebo in reducing pain. SAME appeared to be comparable to NSAIDs in reducing functional limitation and reducing pain. There were fewer adverse effects reported with SAME compared to NSAIDs. The duration of treatment with SAME in these studies was short, further study is needed to determine the long-term effects of SAME in the treatment of OA.

Liver Disease –

Methionine is an essential amino acid that is not produced endogenously in the human body. Once taken in, it must be activated via methylation in the liver and/or other tissue before it can be utilized. Upon methylation, methionine is converted to SAME. SAME is then utilized as a methyl donor in a number of vital reactions.⁵

In patients with liver disease, conversion of methionine to SAME can be impaired. SAME is needed to form glutathione, which protects the body from free radicals. Supplementation with exogenous SAME, the activated form of the essential nutrient, may improve liver function and reduce tissue damage. This theory is currently being tested in animal models in the US.⁵

Uses listed in tertiary sources: (no primary literature found)

Fibromyalgia

AIDS Related Myelopathy

Migraine Headache

Sleep Modulation

❖ **Contraindications/Allergies**

Bi-polar disorder – SAME can cause mania in these patients

❖ **Dosage Forms**

Tablets: 200mg and 400mg

Parenteral solution: (not available in the US)

❖ **Recommended Doses, Duration**

Depression: Oral dose - 200mg to 1600mg daily
(800mg po bid - Chiaie et al³)

Osteoarthritis: Oral dose - 400mg to 800mg daily
(200mg po tid - typical dosing regimen¹)

Liver Disease: Oral dose - 800mg daily for 7 days^{1,6}

Fibromyalgia: Oral dose – 600mg to 800mg daily⁶

❖ **Drug Interactions and Drug-Disease Interactions**

Antidepressants – Additive neurotransmitter modulation

Levodopa – Additive/competitive dopamine modulation

MAOI's – Avoid in patients taking MAOI's or within 2 weeks of discontinuing MAOI

Bi-polar disorder – Can convert bi-polar patients from depression to mania

Pregnancy – Safety in pregnancy not yet confirmed

Lactation – Safety during lactation not yet confirmed

❖ **Other Safety Issues**

Most common side effects:

Headache

GI disturbances – nausea, diarrhea

❖ **References**

1. Natural Medicine Comprehensive Database. SAME monograph.

Available at www.naturaldatabase.com

2. Burnham TH, editor. Facts and Comparisons, The review of Natural Products: Updated monthly. St. Louis: Facts and Comparisons®; Oct 1999: SAME.

3. Delle Chiaie R, Pancheri P, Scapicchio P. Efficacy and tolerability of oral and intramuscular S-adenosyl-L-methionine 1,4-butanedisulfonate (SAME) in the treatment of major depression: comparison with imipramine in 2 multicenter studies. American Journal of Clinical Nutrition 2002;76(suppl):1172S-6S.

4. Seken KL, Lee WL, Bausell RB, Agelli M, Berman BM. Safety and efficacy of S-adenosylmethionine (SAME) for osteoarthritis: A meta-analysis. The Journal of Family Practice 2002 May;51(5):425-30.

5. Lieber CS. S-adenosyl-L-methionine: its role in the treatment of liver disorders. American Journal of Clinical Nutrition 2002;76(suppl):1183S-7S.

6. Abt L & Hammerly M (Eds): AltMedDex® System. MICROMEDEX, Greenwood Village, Colorado. Expires 3/2003.