SAMe 200

SAM-e is the abbreviated name for a natural substance called S-adenosyl methionine. SAMe is present in all cells of the body and is crucial in maintaining proper methylation – one of the most important biochemical reactions in the entire body. SAM-e is considered to be a primary methyl donor, meaning that it can donate methyl groups (one-carbon molecules) to inactive compounds and thereby biologically activate them. This is extremely important for maintaining and accelerating many pathways, especially brain neurotransmitters, detoxification, DNA synthesis, immune system activity and joint health. Methylation promotes healthy cells, regulates the expression of genes (including cancer suppressor genes), and helps with the synthesis of various hormones and neurotransmitters, including serotonin, melatonin, dopamine and adrenaline.

An alarming fact is that the majority of people are lacking in optimal methylation, and this could be putting them at a disadvantage for coping with daily insults to the body. At least 50% of people carry what’s called a gene polymorphism (variant) that predisposes them to insufficient methylation. This gene polymorphism is a mutation of MTHFR and if present, it will result in the decreased ability to methylate and an “increased risk for the development of cardiovascular disease, Alzheimers, depression in adults, and of neural tube defects in the fetus” (Trimmer EE. Methylene tetrahydrofolate Reductase: Biochemical Characterization and Medical Significance, Curr Pharm Des 2012 Oct 31). This polymorphism is also associated with elevated homocysteine (linked to over 100 medical conditions).

“SAM-e is used for psychiatric illnesses, infertility, liver concerns, premenstrual disorders and musculoskeletal disorders, among others. SAM-e has been studied extensively in the treatment of osteoarthritis and depression. Many trials provide evidence that SAM-e reduces the pain associated with osteoarthritis and is well tolerated in this patient population… Anti-inflammatory and analgesic (pain relieving) activity has also been attributed to SAM-e.” (Mayo Clinic Monograph, Sept. 1, 2012)

SAM-e supplementation benefits are widespread; methylation affects so many pathways it is not surprising that the research holds so many diverse reports of favorable effects. More than 40 metabolic reactions involve the methyl transfer from SAM-e to various substrates, such as nucleic acids, proteins, lipids and secondary metabolites.
Web MD (2013) notes that “SAMe is used for depression, anxiety, heart disease, fibromyalgia, osteoarthritis, bursitis, tendonitis, chronic lower back pain, dementia, Alzheimer's disease, slowing the aging process, chronic fatigue syndrome (CFS), improving intellectual performance, liver disease... It is also used for attention deficit-hyperactivity disorder (ADHD), multiple sclerosis, spinal cord injury, seizures, migraine headache, and lead poisoning.”

**SAM-e and Depression:** SAM-e is one of the few heavily researched supplements for mood disorders such as depression. The Journal of Psychosocial Nursing and Mental Health Services notes that even though many dietary supplements are readily accessible and commonly used for the treatment of depression, few products have been adequately studied for their efficacy – except for SAM-e. Of the products they reviewed, they determined that SAM-e and omega-3 fatty acids had sufficient supporting evidence for their efficacy (Howland RH. J Psychosoc Nurs Ment Health Serv. 2012 Jun;50(6):13-6. Dietary supplement drug therapies for depression.)

The Canadian Family Physician reports that patients with depression exhibit low levels of SAM-e, and supplementation raises levels of SAM-e, dopamine, and other neurotransmitters in the brain. Additionally, they also report that a large study of 281 people generated a 12.5-point reduction in Ham-D scores in both groups after 6 weeks (Nahas R & Sheikh. O. Complementary and alternative medicine for the treatment of major depressive disorder. Can Fam Physician. 2011 June; 57(6): 659–663.)

Out of 6 published systematic reviews of SAM-e, all concurred that for mild to moderate depression, SAM-e “shows superior efficacy compared to placebo, and similar efficacy to tricyclic antidepressants (TCAs, usually imipramine)” (Ravindran A.V. et al. Journal of Affective Disorders. Volume 117, Supplement 1, October 2009, Pages S54–S64. Canadian Network for Mood and anxiety Treatments (CANMAT) Clinical Guidelines for the Management of Major Depressive Disorder in Adults. Clinical guidelines for the management of major depressive disorder in adults: Complementary and alternative medicine treatments).

**SAM-e and Brain Disorders:** Researchers indicate that SAM-e is involved in several metabolic processes and “its administration may have a role in the amelioration of several disorders” (Strous RD, et al. Improvement of aggressive behavior and quality of life impairment following S-adenosyl-methionine (SAM-e) augmentation in schizophrenia. Eur Neuropsychopharmacol. 2009 Jan;19(1):14-22.) SAM-e increases catechol-O-methyltransferase (COMT) enzyme activity, “which may ameliorate aggressive symptoms in certain patients... Eighteen patients with chronic schizophrenia were randomly assigned to receive either SAM-e (800 mg) or placebo for 8 weeks in double-blind fashion. Results indicated some reduction in aggressive behavior and improved quality of life following SAM-e administration” (Strous, RD et al. 2009 ibid).

There is some evidence that SAM-e may provide memory support (Tchantchou F, et al. “S-adenosyl methionine: A connection between nutritional and genetic risk factors for neurodegeneration in Alzheimer's disease.” J Nutr Health Aging. 2006 Nov-Dec;10(6):541-4.) SAM-e was studied in major depressive disorder (often accompanied by significant cognitive impairment) in 46 serotonin-reuptake inhibitor (SRI) non-responders during a 6-week, double-blind, randomized trial. Data from the trial suggest “that SAM-e can improve memory-related cognitive symptoms in depressed patients” (Levkovitz Y, et al. Effects of S-adenosylmethionine augmentation of serotonin-reuptake inhibitor antidepressants on cognitive symptoms of major depressive disorder. J Affect Disord. 2012 Feb;136(3):1174-8.)

SAM-e can exert a direct effect on GST (glutathione enzyme) activity. Since Alzheimer's disease is accompanied by reduced GST activity, diminished SAM-e and increased SAH (s-adenosyl homocysteine),” these findings underscore the critical role of SAM-e in maintenance of neuronal health” (Tchantchou F, et al. S-adenosylmethionine mediates glutathione efficacy by increasing glutathione S-transferase activity: implications for S-adenosyl methionine as a neuroprotective dietary supplement. J Alzheimers Dis. 2008 Jul;14(3):323-8.)
**SAM-e and Joint Health:** Knee osteoarthritis is a common disabling condition that affects more than one-third of persons older than 65 years. SAM-e is cited for its beneficial effects (Ringdahl E, Pandit S. Treatment of knee osteoarthritis. Am Fam Physician. 2011 Jun 1;83(11):1287-92.) In fact, a meta-analysis of randomized, controlled clinical trials found that SAM-e is “as effective as NSAIDs in reducing pain and disability, and has a better safety profile” (Soeken KL, et al. Safety and efficacy of S-adenosylmethionine (SAMe) for osteoarthritis. J Fam Pract. 2002;51(5):425-430.)

**SAM-e, Detoxification and the Liver:** SAM-e facilitates the pathway that produces cysteine and glutathione, (one of the most important antioxidants in the body), and certainly the most important antioxidant in the liver. The same pathway produces sulfur, which is significantly important in the detoxification process (and serves as a substrate for joint cartilage; glucosamine sulfate, chondroitin sulfate, etc.). A normal SAM-e level has been determined “necessary to maintain liver health and prevent injury and hepatocellular carcinoma” (Lu SC, Mato JM. S-adenosylmethionine in liver health, injury, and cancer. Physiol Rev. 2012 Oct;92(4):1515-42.) In fact, SAM-e is so efficient at raising glutathione levels that it has been demonstrated to be comparable to N-acetyl cysteine in its ability to raise glutathione levels in the liver after depletion by acetaminophen (Termeux MV, et al. Comparison of S-adenosyl-L-methionine (SAMe) and N-acetylcysteine (NAC) protective effects on hepatic damage when administered after acetaminophen overdose. Toxicology. 2008 Feb 3;244(1):25-34.)

SAM-e supplementation is “effective in the treatment of a variety of liver injuries”, and was evaluated in the prevention of chemotherapy-induced liver damage in 145 patients (Vincenzi B, et al. The role of S-adenosyl methionine in preventing FOLFOX-induced liver toxicity: a retrospective analysis in patients affected by resected colorectal cancer treated with adjuvant FOLFOX regimen. Expert Opin Drug Saf. 2011 May;10(3):345-9.) The results of the study demonstrated a protective effect of SAM-e administration. SAM-e is also a key metabolite that regulates hepatocyte growth, differentiation and death. Another review “describes the protection by SAM-e against alcohol and cytochrome P450 2E1-dependent cytotoxicity both in vitro and in vivo and evaluates mechanisms for this protection” (Cederbaum AI. Hepatoprotective effects of S-adenosyl-L-methionine against alcohol- and cytochrome P450 2E1-induced liver injury. World J Gastroenterol. 2010 Mar 21;16(11):1366-76.) Studies also show that the decreased liver SAM-e concentration and the associated liver lesions, including mitochondrial injury, can be corrected with SAM-e supplementation (Lieber CS. S-Adenosyl-L-methionine and alcoholic liver disease in animal models. Alcohol. 2002; Jul;27(3):173-7.)

In a placebo-controlled study, 16 patients with liver disease (both alcoholic and non-alcoholic) were given 1,200 mg of SAM-e per day for six months. Liver biopsies showed a significant increase in glutathione, and a significant reduction in oxidized glutathione. In the non-alcoholic, liver-damaged subjects, alanine aminotransferase (ALT, a liver enzyme indicating damage) was reduced (Vendemiale G, et al. Effects of oral S-adenosyl-L-methionine on hepatic glutathione in patients with liver disease. Scand J Gastroenterol 1989; 24:407-14.)

**Contraindications/Side Effects:** Side effects are uncommon, but occasionally gastrointestinal upset and anxiety can occur (Can Fam Physician. 2011 June; 57(6): 659–663.) There are no confirmed drug interactions with SAM-e, but caution is advised with the use of antidepressants, including serotonin re-uptake inhibitors and MAO inhibitors, due to potentially enhanced serotonin. Some recommend avoiding SAM-e for individuals with bipolar disorder or manic depression. Some recommend avoiding SAM-e for individuals with bipolar disorder or manic depression (this is controversial and at least one trial studied those with MDD (manic depressive disorder)) (Levkovitz Y, et al. J Affect Disord. 2012 Feb;136(3):1174-8.)
The above statements have not been evaluated by the FDA. The nutritional information, suggestions, and research provided are not intended to diagnose, treat, cure, or prevent disease and should not be used as a substitute for sound medical advice. Please see your health care professional in all matters pertaining to your physical health.