

## **S-adenosyl-L-methionine (usually pronounced "Sammy")**

### **Acclaimed Natural Antidepressant Offers Numerous Benefits and Uses**

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#### **Introduction**

S-adenosyl-L-methionine, or SAM-e (usually pronounced "Sammy"), a natural constituent of the brain and other tissues, has been known for decades in biochemistry as the body's ultimate methyl donor. The transfer of methyl groups -- which is so critical for detoxification, neurotransmitter synthesis, fat metabolism, and much else -- depends on the presence of methyl groups, which are in turn "passed" or donated by way of SAM-e. What only became known in recent years, however, was the activity of supplemental SAM-e as a natural agent to promote health.

#### **Clinical Emergence of SAM-e**

The first serious application of supplemental SAM-e was depression, but as many thousands of cases were treated with SAM-e it became evident that the compound also had anti-arthritis activity -- an unexpected but gratifying "side effect."

It is now clear, from over a decade of rigorous clinical studies in Europe and elsewhere, that SAM-e is a useful medical adjunct in depression [1], osteoarthritis [2] and liver disease [3,4]. The research suggests other exciting applications as well, such as fibromyalgia [5,6] and migraine headache [7].

#### **Roles in Neuropsychiatry, Rheumatology, and Hepatology**

##### **-- Brain Function and Mood**

SAM-e increases cell membrane fluidity, upregulates neurotransmitter receptor number, and enhances neurotransmitter receptor affinity. In other words, SAM-e effectively enhances the action of all the critical antidepressant neurotransmitters: serotonin, dopamine and norepinephrine. It is free from the side effects that are typical with conventional pharmaceutical antidepressant drugs. Numerous clinical trials over many years have demonstrated SAM-e to be a safe and effective treatment for most varieties of depression, excluding manic depression [1,8-11]. SAM-e may also be useful in a range of other neuropsychiatric disturbances [12].

##### **-- Connective Tissue Repair and Joint Health**

SAM-e stimulates growth of chondrocytes and the synthesis of proteoglycans therein. Proteoglycans are huge, critically-important molecules for joint integrity. SAM-e also downregulates enzymes that attack cartilage. Clinically, SAM-e is mildly analgesic and anti-inflammatory. All that adds up to an exceptional anti-arthritic profile, which has been born out in large-scale clinical trials over many years [13-19]. SAM-e is clearly a useful medical adjunct in osteoarthritis [13-16] -- and it lacks the GI and other side effects so common with the NSAIDs typically used in arthritides. Indeed, SAM-e compares favorably in the rheumatology clinic with NSAIDs such as ibuprofen and naproxen [17-19].

##### **-- Liver Protection**

SAM-e is a precursor of the critical antioxidant tripeptide glutathione [20] -- the primary protector of cells from free radical damage, and a key molecule in the detoxification process in the liver. Indeed, SAM-e appears to be capable of regenerating diseased livers, and the clinical results with SAM-e in liver disease have been remarkable [3,4].

### **Biosynthesis, Sources and Precursors**

The body manufactures SAM-e and there is no formal nutritional requirement for it. But inadequate supply of its precursors, or substances which are required for its formation -- methionine, folate, or vitamin B12 -- can limit endogenous SAM-e synthesis [21]. And, an abundant supply of nutritional methyl donors such as choline and betaine are also required. There are no good food sources of SAM-e.

### **Practical Pharmacy and Dosing**

SAM-e is expensive. It is a highly unstable substance which oxidizes rapidly when exposed to air and moisture. The manufacturing process must be very specialized and highly regulated to assure potency, which is one of the reasons for the high cost.

To ensure clinical efficacy with this expensive material, proper manufacturing is vital. Oral SAM-e, given unprotected, is largely demethylated in the stomach, thereby losing much of its unique character and medicinal value. SAM-e tablets **MUST** be enteric-coated.

Last, to further enhance efficiency, SAM-e is best given with other ingredients involved in methyl-group supply and metabolism such as folic acid, vitamin B12, choline, niacinamide and pyridoxine.

A typical maintenance dose of SAM-e is 200 mgs taken twice daily. Larger doses are used in the initial phases of treatment: 400 mg taken 2-3 times daily. Some users have experienced mild GI upset at the higher dose levels; this can be avoided by starting low and working up to the full dosage gradually.

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