

RESEARCH MONOGRAPH . COMPOUND PROFILE

SAM-e (S-Adenosyl-L-Methionine)

S-adenosyl-L-methionine, the principal methyl donor for cellular methylation reactions, supplemented for depression, osteoarthritis, and liver disease.

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COMPOUND CLASS	Endogenous methyl donor

RESEARCH USE ONLY

ABSTRACT

SAM-e (S-adenosyl-L-methionine; CAS 29908-03-0; molecular formula $C_{15}H_{22}N_6O_5S$; molecular weight 398.44) is an endogenous nucleotide-amino acid conjugate that serves as the principal methyl donor for hundreds of cellular methylation reactions, including DNA methylation, neurotransmitter synthesis, phospholipid synthesis, and detoxification. Synthesis from methionine + ATP is rate-limited; supplementation provides methyl donor capacity. The compound is approved as a medicine in some European countries for depression and osteoarthritis; sold as a dietary supplement in the United States. Clinical evidence in depression is moderate (effect sizes comparable to standard antidepressants in small trials). Doses are typically 400 to 1600 mg per day in divided administrations. Can precipitate mania in bipolar patients; should not be combined with MAOIs.

1. Compound Identification

SAM-e (S-Adenosyl-L-Methionine) is described as endogenous methyl donor. S-adenosyl-L-methionine, the principal methyl donor for cellular methylation reactions, supplemented for depression, osteoarthritis, and liver disease.

1.1 Class summary

Endogenous methyl donor

1.2 Subtitle

S-adenosyl-L-methionine, the principal methyl donor for cellular methylation reactions, supplemented for depression, osteoarthritis, and liver disease.

2. Abstract

SAM-e (S-adenosyl-L-methionine; CAS 29908-03-0; molecular formula $C_{15}H_{22}N_6O_5S$; molecular weight 398.44) is an endogenous nucleotide-amino acid conjugate that serves as the principal methyl donor for hundreds of cellular methylation reactions, including DNA methylation, neurotransmitter synthesis, phospholipid synthesis, and detoxification. Synthesis from methionine + ATP is rate-limited; supplementation provides methyl donor capacity. The compound is approved as a medicine in some European countries for depression and osteoarthritis; sold as a dietary supplement in the United States. Clinical evidence in depression is moderate (effect sizes comparable to standard antidepressants in small trials). Doses are typically 400 to 1600 mg per day in divided administrations. Can precipitate mania in bipolar patients; should not be combined with MAOIs.

3. Mechanism of Action

Principal cellular methyl donor; substrate for many methyltransferase reactions.

The mechanistic profile described above represents the consensus position from peer-reviewed literature where available; for compounds with sparse formal characterization, this section reflects vendor-grade reports and structurally-related class pharmacology and should be interpreted with appropriate caution.

4. Pharmacokinetics and Routes of Administration

Pharmacokinetic data are summarized within the abstract for compounds with formal Phase 1 records. Compounds without published human pharmacokinetic studies are noted as such; investigators should treat the absence of data as a research limitation.

5. Reported Research Dose Ranges

400 to 1600 mg per day in divided doses.

Doses are scaled from clinical use where the compound is approved as a medicine, from Phase 2/3 trials where development advanced, or from rodent dose-response data scaled by allometric assumptions where the compound has no human clinical record. Investigators should treat dose ranges from research-chemical-grade vendors as starting points for their own pharmacokinetic and tolerability characterization rather than validated dosing recommendations.

6. Sourcing and Quality Verification

Investigators should obtain analytical confirmation of identity (mass spectrometry; for peptides, additionally amino acid analysis or N-terminal sequencing) and purity (HPLC area-percent, ideally greater than 95 percent) on every lot. Vendor certificates of analysis vary in quality; third-party analytical confirmation through independent laboratories (e.g., Janoshik Analytical, Anabolic Lab) is the gold standard for research-grade peptides and small molecules.

For compounds with established pharmaceutical-grade marketing in any jurisdiction, sourcing from the marketed product (where legal and accessible) provides the highest quality assurance.

7. Reconstitution and Handling

Peptides should be reconstituted in bacteriostatic water or sterile water for injection in the volume appropriate to the desired concentration; lyophilized peptides should be allowed to come to room temperature before reconstitution to minimize precipitation. Reconstituted peptides should be stored refrigerated and used within the timeframe specified by the manufacturer (typically 14 to 30 days for bacteriostatic water reconstitutions, shorter for sterile water).

Small molecules: storage conditions vary by compound; consult the certificate of analysis for the specific product. Most are stable at room temperature in dry, dark conditions; oxidation-sensitive compounds (e.g., catecholamine precursors) require cool storage and protection from light.

8. Stack Interaction Considerations

Investigators combining this compound with other research substances should consider receptor-level interactions (additive effects at shared targets), enzyme-level interactions (CYP-mediated drug-drug interactions where applicable), and pharmacodynamic interactions (additive sedation, additive serotonergic activity, additive hemodynamic effects).

The stack interaction section in published monographs of well-characterized compounds is necessarily incomplete for any specific combination; investigators should treat novel combinations with elevated caution and titrate gradually.

9. References

1. Papakostas GI, et al. S-adenosyl methionine (SAmE) augmentation of serotonin reuptake inhibitors for antidepressant nonresponders. Am J Psychiatry 2010.

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