

RESEARCH MONOGRAPH . COMPOUND PROFILE

Sarcosine

N-methylglycine; an endogenous methylglycine that inhibits glycine reuptake at GlyT1, elevating synaptic glycine.

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COMPOUND CLASS	Glycine reuptake inhibitor (GlyT1)

ABSTRACT

Sarcosine (N-methylglycine; CAS 107-97-1; molecular formula $C_3H_7NO_2$; molecular weight 89.09) is an endogenous N-methylated derivative of glycine and a competitive substrate of the glycine transporter type 1 (GlyT1). Pharmacologically, sarcosine inhibits glycine reuptake at GlyT1, elevating extracellular glycine concentrations near NMDA receptors and consequently enhancing NMDA receptor function via the glycine co-agonist site. The mechanism complements direct D-serine administration. Phase 2 trials in schizophrenia (as adjunct to risperidone or olanzapine) and major depressive disorder have shown small to moderate effects on negative symptoms and depressive symptoms. Plasma half-life is approximately 7 hours; the compound is well tolerated. The selective GlyT1 inhibitor bitopertin (RG1678) was developed as a more potent alternative but failed phase 3 trials. Used as the canonical GlyT1 substrate inhibitor in NMDA receptor research.

1. Compound Identification

Sarcosine is described as glycine reuptake inhibitor (glyt1). N-methylglycine; an endogenous methylglycine that inhibits glycine reuptake at GlyT1, elevating synaptic glycine.

1.1 Class summary

Glycine reuptake inhibitor (GlyT1)

1.2 Subtitle

N-methylglycine; an endogenous methylglycine that inhibits glycine reuptake at GlyT1, elevating synaptic glycine.

2. Abstract

Sarcosine (N-methylglycine; CAS 107-97-1; molecular formula C₃H₇NO₂; molecular weight 89.09) is an endogenous N-methylated derivative of glycine and a competitive substrate of the glycine transporter type 1 (GlyT1). Pharmacologically, sarcosine inhibits glycine reuptake at GlyT1, elevating extracellular glycine concentrations near NMDA receptors and consequently enhancing NMDA receptor function via the glycine co-agonist site. The mechanism complements direct D-serine administration. Phase 2 trials in schizophrenia (as adjunct to risperidone or olanzapine) and major depressive disorder have shown small to moderate effects on negative symptoms and depressive symptoms. Plasma half-life is approximately 7 hours; the compound is well tolerated. The selective GlyT1 inhibitor bitopertin (RG1678) was developed as a more potent alternative but failed phase 3 trials. Used as the canonical GlyT1 substrate inhibitor in NMDA receptor research.

3. Mechanism of Action

Competitive substrate of glycine transporter type 1 (GlyT1); elevates extracellular glycine near NMDA receptors and enhances NMDA function via glycine co-agonist site.

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

Clinical trials 1 to 2 g per oral administration daily.

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. Tsai G, et al. Glycine transporter I inhibitor, N-methylglycine (sarcosine), added to antipsychotics for the treatment of schizophrenia. Biol Psychiatry 2004.
2. Lane HY, et al. Sarcosine or D-serine add-on treatment for acute exacerbation of schizophrenia. Arch Gen Psychiatry 2005.
3. Huang CC, et al. Sarcosine as add-on therapy in major depressive disorder. J Clin Psychiatry 2013.

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