

RESEARCH MONOGRAPH . COMPOUND PROFILE

D-Cycloserine

An antibiotic with NMDA receptor partial agonist activity; investigated as an extinction-learning enhancer in exposure therapy for anxiety disorders.

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ABSTRACT

D-cycloserine ((4R)-4-amino-1,2-oxazolidin-3-one; CAS 68-41-7; molecular formula C₃H₆N₂O₂; molecular weight 102.09) is a cyclic amino acid antibiotic isolated from *Streptomyces orchidaceus* and approved by the FDA in 1956 for second-line tuberculosis treatment. The compound is a partial agonist at the NMDA receptor glycine site (intrinsic activity approximately 40 to 60 percent), and the partial agonism produces dose-dependent NMDA receptor modulation: at low concentrations relative to endogenous glycine/D-serine, D-cycloserine functions as a positive modulator (enhancing NMDA function); at higher concentrations it competes with the full-agonist endogenous co-agonists and behaves as a functional antagonist. The lower-dose facilitating effect underlies use as an extinction-learning enhancer in exposure therapy for phobia, PTSD, OCD, and social anxiety; clinical trials have shown modest effects with timing-dependent results (administration shortly before therapy session is critical). Plasma half-life is approximately 10 hours. Used as the canonical NMDA glycine-site partial agonist in research.

1. Compound Identification

D-Cycloserine is described as nmda receptor glycine-site partial agonist. An antibiotic with NMDA receptor partial agonist activity; investigated as an extinction-learning enhancer in exposure therapy for anxiety disorders.

1.1 Class summary

NMDA receptor glycine-site partial agonist

1.2 Subtitle

An antibiotic with NMDA receptor partial agonist activity; investigated as an extinction-learning enhancer in exposure therapy for anxiety disorders.

2. Abstract

D-cycloserine ((4R)-4-amino-1,2-oxazolidin-3-one; CAS 68-41-7; molecular formula C₃H₆N₂O₂; molecular weight 102.09) is a cyclic amino acid antibiotic isolated from *Streptomyces orchidaceus* and approved by the FDA in 1956 for second-line tuberculosis treatment. The compound is a partial agonist at the NMDA receptor glycine site (intrinsic activity approximately 40 to 60 percent), and the partial agonism produces dose-dependent NMDA receptor modulation: at low concentrations relative to endogenous glycine/D-serine, D-cycloserine functions as a positive modulator (enhancing NMDA function); at higher concentrations it competes with the full-agonist endogenous co-agonists and behaves as a functional antagonist. The lower-dose facilitating effect underlies use as an extinction-learning enhancer in exposure therapy for phobia, PTSD, OCD, and social anxiety; clinical trials have shown modest effects with timing-dependent results (administration shortly before therapy session is critical). Plasma half-life is approximately 10 hours. Used as the canonical NMDA glycine-site partial agonist in research.

3. Mechanism of Action

NMDA receptor glycine-site partial agonist (intrinsic activity 40 to 60 percent); facilitates NMDA function at low doses, antagonizes at high doses.

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

Antibiotic 250 to 500 mg per oral administration twice daily; extinction learning 50 to 250 mg before therapy session.

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. Ressler KJ, et al. Cognitive enhancers as adjuncts to psychotherapy: use of D-cycloserine in phobic individuals to facilitate extinction of fear. Arch Gen Psychiatry 2004.
2. Hofmann SG, et al. D-Cycloserine augmentation of cognitive behavioral therapy for anxiety disorders. JAMA Psychiatry 2013.
3. Mataix-Cols D, et al. D-Cycloserine augmentation of exposure-based cognitive behavior therapy for anxiety, obsessive-compulsive, and posttraumatic stress disorders: a systematic review and meta-analysis. JAMA Psychiatry 2017.

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