

RESEARCH MONOGRAPH . COMPOUND PROFILE

Ketamine

A non-competitive NMDA receptor antagonist FDA-approved as a dissociative anesthetic since 1970, with rapid antidepressant activity at sub-anesthetic doses.

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ABSTRACT

Ketamine (CAS 6740-88-1; molecular formula $C_{13}H_{16}ClNO$; molecular weight 237.73) is a non-competitive NMDA receptor antagonist developed in 1962 by Calvin Stevens at Parke-Davis and approved by the FDA in 1970 as a dissociative anesthetic. The compound is used clinically for anesthesia, procedural sedation, and analgesia. Sub-anesthetic doses (0.5 mg/kg IV or equivalent) produce rapid antidepressant effects in treatment-resistant depression, an indication for which the (S)-enantiomer (esketamine) is FDA-approved as Spravato. Mechanism includes NMDA receptor blockade, AMPA receptor potentiation through downstream signaling, and modest opioid receptor effects. Schedule III in the United States.

1. Compound Identification

Ketamine is described as nmda receptor antagonist / dissociative anesthetic. A non-competitive NMDA receptor antagonist FDA-approved as a dissociative anesthetic since 1970, with rapid antidepressant activity at sub-anesthetic doses.

1.1 Class summary

NMDA receptor antagonist / dissociative anesthetic

1.2 Subtitle

A non-competitive NMDA receptor antagonist FDA-approved as a dissociative anesthetic since 1970, with rapid antidepressant activity at sub-anesthetic doses.

2. Abstract

Ketamine (CAS 6740-88-1; molecular formula $C_{13}H_{16}ClNO$; molecular weight 237.73) is a non-competitive NMDA receptor antagonist developed in 1962 by Calvin Stevens at Parke-Davis and approved by the FDA in 1970 as a dissociative anesthetic. The compound is used clinically for anesthesia, procedural sedation, and analgesia. Sub-anesthetic doses (0.5 mg/kg IV or equivalent) produce rapid antidepressant effects in treatment-resistant depression, an indication for which the (S)-enantiomer (esketamine) is FDA-approved as Spravato. Mechanism includes NMDA receptor blockade, AMPA receptor potentiation through downstream signaling, and modest opioid receptor effects. Schedule III in the United States.

3. Mechanism of Action

Non-competitive NMDA receptor antagonist; rapid antidepressant effects through downstream AMPA potentiation and BDNF release.

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

0.5 mg/kg IV for depression; higher doses for anesthesia.

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. Berman RM, et al. Antidepressant effects of ketamine in depressed patients. Biol Psychiatry 2000.

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