

RESEARCH MONOGRAPH . COMPOUND PROFILE

Agmatine

An endogenous decarboxylated arginine derivative with NMDA receptor antagonism, alpha-2 adrenergic agonism, and imidazoline receptor binding.

DOCUMENT	KDC-MN-075
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	Endogenous polyamine / NMDA modulator

ABSTRACT

Agmatine ((4-aminobutyl)guanidine; CAS 306-60-5; molecular formula $C_5H_{14}N_4$; molecular weight 130.19) is an endogenous polyamine produced by decarboxylation of arginine. The compound is present in plasma and brain at micromolar concentrations and acts at multiple receptor systems: NMDA receptor antagonism (at the polyamine site), alpha-2 adrenergic receptor agonism, imidazoline I1 and I2 receptor binding, and modest opioid receptor effects. Agmatine has been investigated as adjunct therapy for opioid withdrawal, neuropathic pain, depression, and cognitive enhancement. The compound is sold as a dietary supplement in the United States. Pharmacokinetics: oral bioavailability moderate; plasma half-life of exogenous agmatine approximately 2 hours; the compound is hepatically metabolized by agmatinase to putrescine. Doses for cognitive/anxiolytic applications are typically 1 to 3 grams per day in divided administrations.

1. Compound Identification

Agmatine is described as endogenous polyamine / nmda modulator. An endogenous decarboxylated arginine derivative with NMDA receptor antagonism, alpha-2 adrenergic agonism, and imidazoline receptor binding.

1.1 Class summary

Endogenous polyamine / NMDA modulator

1.2 Subtitle

An endogenous decarboxylated arginine derivative with NMDA receptor antagonism, alpha-2 adrenergic agonism, and imidazoline receptor binding.

2. Abstract

Agmatine ((4-aminobutyl)guanidine; CAS 306-60-5; molecular formula C₅H₁₄N₄; molecular weight 130.19) is an endogenous polyamine produced by decarboxylation of arginine. The compound is present in plasma and brain at micromolar concentrations and acts at multiple receptor systems: NMDA receptor antagonism (at the polyamine site), alpha-2 adrenergic receptor agonism, imidazoline I1 and I2 receptor binding, and modest opioid receptor effects. Agmatine has been investigated as adjunct therapy for opioid withdrawal, neuropathic pain, depression, and cognitive enhancement. The compound is sold as a dietary supplement in the United States. Pharmacokinetics: oral bioavailability moderate; plasma half-life of exogenous agmatine approximately 2 hours; the compound is hepatically metabolized by agmatinase to putrescine. Doses for cognitive/anxiolytic applications are typically 1 to 3 grams per day in divided administrations.

3. Mechanism of Action

NMDA polyamine site antagonism, alpha-2 adrenergic agonism, imidazoline I1/I2 binding, modest opioid effects.

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

1 to 3 grams 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. Reis DJ, Regunathan S. Is agmatine a novel neurotransmitter in brain? Trends Pharmacol Sci 2000.

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