

RESEARCH MONOGRAPH . COMPOUND PROFILE

Nebracetam

A 4-phenyl-pyrrolidinone with M1 muscarinic receptor agonist activity developed by Daiichi for cognitive impairment, discontinued in development.

DOCUMENT	KDC-MN-038
ISSUED	2026-05-09
REVISION	1.0
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COMPOUND CLASS	Phenyl-substituted aminomethyl pyrrolidinone

ABSTRACT

Nebracetam (WEB-1881-FU; 4-phenyl-2-pyrrolidinone-1-acetamide methyl derivative; CAS 97205-34-0; molecular formula $C_{13}H_{18}N_2O_2$; molecular weight 234.30) is a piracetam analog developed by Daiichi Pharmaceutical in Japan in the 1980s with structural features distinct from the classical racetam class. The compound includes a 4-phenyl group on the pyrrolidinone ring (similar to phenylpiracetam) and an aminomethyl modification on the acetamide side chain. Pharmacology shows partial M1 muscarinic acetylcholine receptor agonist activity in addition to the cholinergic facilitation typical of the racetam class. Phase 2 trials in mild cognitive impairment and elderly memory disorders showed positive but modest results; the development program was discontinued and the compound was never approved. The compound is sold as a research chemical in jurisdictions where it is not specifically scheduled. Pharmacokinetics include plasma half-life of approximately 4 hours and good oral bioavailability. The clinical evidence base is limited; the M1 muscarinic agonist activity introduces a distinct profile from the open-chain racetams.

1. Compound Identification

Nebracetam is described as phenyl-substituted aminomethyl pyrrolidinone. A 4-phenyl-pyrrolidinone with M1 muscarinic receptor agonist activity developed by Daiichi for cognitive impairment, discontinued in development.

1.1 Class summary

Phenyl-substituted aminomethyl pyrrolidinone

1.2 Subtitle

A 4-phenyl-pyrrolidinone with M1 muscarinic receptor agonist activity developed by Daiichi for cognitive impairment, discontinued in development.

2. Abstract

Nebracetam (WEB-1881-FU; 4-phenyl-2-pyrrolidinone-1-acetamide methyl derivative; CAS 97205-34-0; molecular formula C₁₃H₁₈N₂O₂; molecular weight 234.30) is a piracetam analog developed by Daiichi Pharmaceutical in Japan in the 1980s with structural features distinct from the classical racetam class. The compound includes a 4-phenyl group on the pyrrolidinone ring (similar to phenylpiracetam) and an aminomethyl modification on the acetamide side chain. Pharmacology shows partial M1 muscarinic acetylcholine receptor agonist activity in addition to the cholinergic facilitation typical of the racetam class. Phase 2 trials in mild cognitive impairment and elderly memory disorders showed positive but modest results; the development program was discontinued and the compound was never approved. The compound is sold as a research chemical in jurisdictions where it is not specifically scheduled. Pharmacokinetics include plasma half-life of approximately 4 hours and good oral bioavailability. The clinical evidence base is limited; the M1 muscarinic agonist activity introduces a distinct profile from the open-chain racetams.

3. Mechanism of Action

Partial M1 muscarinic agonist plus cholinergic facilitation typical of racetam class.

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

100 to 600 mg per day in Phase 2 trials.

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. Japanese Daiichi development program for WEB-1881-FU; sparse English literature.
2. Sakurai T, et al. Cholinergic effects of nebracetam. Neurosci Res 1990s.

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