

RESEARCH MONOGRAPH . COMPOUND PROFILE

NA-Semax Amidate

An N-terminal-acetylated, C-terminal-amidated variant of the heptapeptide nootropic Semax, designed to extend plasma and central nervous system exposure beyond both the parent and the simple N-acetyl variant.

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COMPOUND CLASS	N-acetylated and amidated Semax derivative

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ABSTRACT

NA-Semax Amidate (N-acetyl-Met-Glu-His-Phe-Pro-Gly-Pro-NH₂) is a doubly modified variant of Semax (the seven-residue ACTH(4-10) analog Met-Glu-His-Phe-Pro-Gly-Pro) developed at the Russian Academy of Sciences as a long-acting analog. Semax itself is registered in the Russian Federation as an intranasal nootropic and stroke treatment at 0.1 percent and 1 percent solutions, with a published pharmacological signature of BDNF and NGF transcriptional upregulation, neuroprotection in middle cerebral artery occlusion stroke models, and pro-cognitive effects in passive avoidance and operant conditioning paradigms. The parent Semax has a plasma half-life of minutes and a central nervous system exposure window of similarly short duration after intranasal administration. The N-acetyl variant of Semax (NA-Semax) extends plasma half-life by approximately 5-fold by blocking the aminopeptidase cleavage at the methionine N-terminus, and the C-terminal amidation in the Amidate variant additionally blocks the carboxypeptidase cleavage at the proline C-terminus, producing a peptide with the longest exposure in the Semax family. Comparative pharmacology in rodent models reports that NA-Semax Amidate at one-tenth the dose of parent Semax produces equivalent or greater BDNF mRNA elevation in cortex and hippocampus and equivalent neuroprotection in stroke models, with substantially longer duration of effect. Routes studied include subcutaneous, intramuscular, intranasal, and intraperitoneal administration. The compound is research-grade and not approved by any regulatory authority; the principal published record is in Russian-language journals from the Institute of Molecular Genetics RAS. Investigators should treat the

extended-PK variant as a research tool for studying long-duration ACTH-derived heptapeptide pharmacology where the brief pulse from intranasal Semax is operationally limiting.

1. Compound Identification

NA-Semax Amidate is described as n-acetylated and amidated semax derivative. An N-terminal-acetylated, C-terminal-amidated variant of the heptapeptide nootropic Semax, designed to extend plasma and central nervous system exposure beyond both the parent and the simple N-acetyl variant.

1.1 Class summary

N-acetylated and amidated Semax derivative

1.2 Subtitle

An N-terminal-acetylated, C-terminal-amidated variant of the heptapeptide nootropic Semax, designed to extend plasma and central nervous system exposure beyond both the parent and the simple N-acetyl variant.

2. Abstract

NA-Semax Amidate (N-acetyl-Met-Glu-His-Phe-Pro-Gly-Pro-NH₂) is a doubly modified variant of Semax (the seven-residue ACTH(4-10) analog Met-Glu-His-Phe-Pro-Gly-Pro) developed at the Russian Academy of Sciences as a long-acting analog. Semax itself is registered in the Russian Federation as an intranasal nootropic and stroke treatment at 0.1 percent and 1 percent solutions, with a published pharmacological signature of BDNF and NGF transcriptional upregulation, neuroprotection in middle cerebral artery occlusion stroke models, and pro-cognitive effects in passive avoidance and operant conditioning paradigms. The parent Semax has a plasma half-life of minutes and a central nervous system exposure window of similarly short duration after intranasal administration. The N-acetyl variant of Semax (NA-Semax) extends plasma half-life by approximately 5-fold by blocking the aminopeptidase cleavage at the methionine N-terminus, and the C-terminal amidation in the Amidate variant additionally blocks the carboxypeptidase cleavage at the proline C-terminus, producing a peptide with the longest exposure in the Semax family. Comparative pharmacology in rodent models reports that NA-Semax Amidate at one-tenth the dose of parent Semax produces equivalent or greater BDNF mRNA elevation in cortex and hippocampus and equivalent neuroprotection in stroke models, with substantially longer duration of effect. Routes studied include subcutaneous, intramuscular, intranasal, and intraperitoneal administration. The compound is research-grade and not approved by any regulatory authority; the principal published record is in Russian-language journals from the Institute of Molecular Genetics RAS. Investigators should treat the extended-PK variant as a research tool for studying long-duration ACTH-derived heptapeptide pharmacology where the brief pulse from intranasal Semax is operationally limiting.

3. Mechanism of Action

BDNF and NGF transcriptional upregulation in cortex and hippocampus. Neuroprotection in MCAO stroke models. N-acetyl and amidate modifications block aminopeptidase and carboxypeptidase cleavage, extending plasma half-life beyond both parent Semax and the simple N-acetyl variant.

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

Rodent and research-clinical doses 0.05 to 0.5 mg/kg subcutaneous, intranasal, or intraperitoneal. Equivalent activity to parent Semax at one-fifth to one-tenth the molar dose.

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. Levitskaya NG, et al. Nootropic and neuroprotective activity of N-acetyl-amidated Semax. Bull Exp Biol Med 2010.
2. Myasoedov NF, et al. Regulatory peptides Semax and Selank. Vestnik RAMS 2014.
3. Andreeva LA, et al. Long-acting Semax analogs. Russ J Bioorg Chem 2008.

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