BIOMOD LABS · RESEARCH PEPTIDE CO.

RESEARCH COMPOUND MONOGRAPH · SERIES 1 · NO. SPR-004

Semax (Nasal Spray Preparation)

A single-component aqueous nasal spray preparation of the Russian Academy of Sciences ACTH(4-7)-Pro-Gly-Pro heptapeptide Semax — formulated for intranasal mucosal delivery via a 200-actuation metered-dose bottle at 0.20 mg active per spray.

CATALOG REFERENCE	FORM FACTOR	STRENGTH	DATE OF ISSUE
BM-SPR-004	Nasal spray · 40 mg / bottle · 200 sprays · 0.20 mg per spray	40 mg active per bottle	May 2026

Semax is a synthetic heptapeptide of sequence Met-Glu-His-Phe-Pro-Gly-Pro, developed at the Institute of Molecular Genetics of the Russian Academy of Sciences during the 1980s by Ivanov and colleagues. The molecule corresponds to ACTH residues 4-7 (the Met-Glu-His-Phe N-terminal segment common to ACTH and the melanocortin family) with a C-terminal Pro-Gly-Pro tripeptide extension that confers metabolic stability against plasma peptidase degradation. Semax is closely related to Selank (Monograph 006) in originating laboratory and design philosophy — both molecules are synthetic neuropeptide analogues with the C-terminal Pro-Gly-Pro stabilising motif appended to a parent neuroactive sequence. Semax has been characterised across multiple Russian and international laboratories in preclinical models for effects on brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF) gene expression, dopaminergic and serotonergic neurotransmission, and cognitive performance markers in rodent learning paradigms. ***This monograph summarises published cellular pharmacology and preclinical findings for laboratory research reference only.***

01 Compound Profile

COMMON DESIGNATION	Semax · ACTH(4-7)-Pro-Gly-Pro
PRIMARY SEQUENCE	Met-Glu-His-Phe-Pro-Gly-Pro (MEHFPGP)
PARENT SEQUENCE	ACTH(4-7) Met-Glu-His-Phe — the N-terminal segment of ACTH that is also conserved in α-MSH and other melanocortin family peptides
C-TERMINAL STABILISING MOTIF	Pro-Gly-Pro tripeptide extension — shared with Selank and characteristic of the Russian Academy of Sciences neuropeptide design philosophy[1]
CAS REGISTRY	80714-61-0
MOLECULAR FORMULA	$C_{39}H_{54}N_{10}O_{10}S$
AVERAGE MOLECULAR MASS	854.97 g · mol^{-1}
PROPOSED MOLECULAR ACTIONS	Modulation of BDNF and NGF gene expression in hippocampus and cortex; effects on dopaminergic, serotonergic, and noradrenergic neurotransmission; melanocortin-receptor-independent action despite parent ACTH-derived sequence[2]
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Water-soluble; the Pro-Gly-Pro C-terminal motif confers metabolic stability and good aqueous solubility
STORAGE (RESEARCH HANDLING)	Lyophilised solid: −18 °C, desiccated; reconstituted solution refrigerated 2–8 °C; long-term aliquots at −18 °C; **the N-terminal Met1 is oxidation-susceptible** — air-exposure minimisation recommended
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC (BIOMOD Labs internal release specification)

02 Origin and Chemistry

Semax was developed at the Institute of Molecular Genetics of the Russian Academy of Sciences (Moscow) during the 1980s by the laboratory of N. F. Myasoedov, drawing on the concept that short fragments of the larger ACTH polypeptide retain selected pharmacological properties of the parent hormone without the full corticotropic activity. The ACTH(4-10) heptapeptide had been characterised previously as a neuroactive fragment with effects on memory and learning in rodent preparations (the "ACTH(4-10) effect"); the Semax design simplified this to

ACTH(4-7) and appended the Pro-Gly-Pro C-terminal motif for plasma stabilisation. The design philosophy is closely parallel to that of Selank (Monograph 006), a related Russian Academy of Sciences neuropeptide built on tuftsin with the same Pro-Gly-Pro motif.[1]

Chemically, Semax is a small acidic heptapeptide with one methionine (oxidation-susceptible) at the N-terminus and no cysteine, tryptophan, or tyrosine. The two prolines (positions 5 and 7) and the C-terminal proline confer substantial conformational rigidity and protease resistance — proline-containing sequences are poor substrates for many plasma proteases owing to the restricted backbone geometry.

03 Proposed Mechanisms in Preclinical Models

Semax's preclinical pharmacology has been characterised across multiple parallel mechanisms in rodent brain preparations. **Neurotrophic factor expression** — Shadrina and colleagues reported upregulation of BDNF (brain-derived neurotrophic factor) and NGF (nerve growth factor) mRNA and protein in rat hippocampus and frontal cortex following Semax administration. **Neurotransmitter modulation** — effects on dopaminergic, serotonergic, and noradrenergic neurotransmission have been reported, with measurable changes in monoamine turnover in specific brain regions. **Melanocortin-receptor-independent action** — despite the parent sequence's derivation from ACTH (a melanocortin peptide), Semax is not characterised as a melanocortin-receptor agonist; its mechanism appears to involve direct effects on neuropeptide receptors and intracellular signalling cascades distinct from MC1R-MC5R engagement. **BDNF / trkB pathway downstream** — phosphorylation of trkB-pathway components following Semax has been reported in rodent brain preparations.[2,3] PRECLINICAL · RAT

04 Preclinical Findings

SYSTEM	ANIMAL MODEL / PREPARATION	REPORTED OBSERVATION	REF.
Neurotrophic factor expression	Rat hippocampus & cortex preparations	BDNF and NGF mRNA upregulation	2
Monoamine neurotransmission	Rat brain region homogenates	Modulation of dopaminergic, serotonergic, noradrenergic markers	3
Learning & memory paradigms	Rodent passive avoidance and maze tasks	Effects on learning and memory consolidation markers	1
Cerebral ischaemia models	Rat focal cerebral ischaemia preparations	Reduced infarct volume; preserved neurological function markers	4
Plasma stability	Plasma protease stability assays	Pro-Gly-Pro C-terminal motif confers substantial peptidase resistance	1

05 Research Synthesis & Limitations

METHODOLOGICAL NOTES

Semax has a substantial published preclinical literature, with much of the foundational work in Russian-language journals and a growing body of English-language characterisation. Researchers should be aware that (a) the N-terminal Met1 is oxidation-susceptible — air-exposure minimisation and antioxidant excipients are common in cited methodology; (b) the molecule is closely related to Selank in design philosophy and originating laboratory, and some published comparisons treat the two compounds in parallel; and (c) despite the ACTH-derived parent sequence, Semax does not appear to engage melanocortin receptors significantly — its mechanism operates through different molecular targets that remain incompletely characterised compared with classical receptor pharmacology.

06 Laboratory Handling, Reconstitution, and Storage

Lyophilised Semax is supplied under research-use specifications. The small proline-rich peptide is water-soluble. **The N-terminal Met1 is oxidation-susceptible** — air-exposure minimisation is recommended; antioxidant excipients are sometimes used in cited methodology. Lyophilised storage at −18 °C, desiccated; reconstituted solutions held refrigerated 2–8 °C for short-term work; aliquoted long-term storage at −18 °C with minimised freeze–thaw. Working concentrations are determined by the investigator's experimental design.

07 References

1. Ashmarin IP, Nezavibatko VN, Levitskaya NG, Koshelev VB, Kamensky AA. Design and investigation of an ACTH(4-10) analog lacking D-amino acids and hydrophobic radicals (Semax). *Neurosci Behav Physiol.* 1995;25(3):243–250. pubmed.ncbi.nlm.nih.gov/8527826

2. Shadrina MI, Dolotov OV, Grivennikov IA, Slominsky PA, Andreeva LA, Inozemtseva LS, Limborska SA, Myasoedov NF. Rapid induction of neurotrophin mRNAs in rat glial cell cultures by Semax, an adrenocorticotropic hormone analog. *Neurosci Lett.* 2001;308(2):115–118. pubmed.ncbi.nlm.nih.gov/11457574

3. Eremin KO, Kudrin VS, Saransaari P, Oja SS, Grivennikov IA, Myasoedov NF, Rayevsky KS. Semax, an ACTH(4-10) analogue with nootropic properties, activates dopaminergic and serotoninergic brain systems in rats. *Neurochem Res.* 2005;30(12):1493–1500. pubmed.ncbi.nlm.nih.gov/16362768

4. Skvortsova VI, Raevsky KS, Kovalenko AV, Kudrin VS, Malyshev VV, Sokolov MA, Alekseev AA, Bashkatova VG. Levels of neurotransmitter amino acids in the cerebrospinal fluid of patients with acute ischemic insult treated with Semax. *Neurosci Behav Physiol.* 2000;30(5):553–558. pubmed.ncbi.nlm.nih.gov/11037151

5. Dolotov OV, Karpenko EA, Inozemtseva LS, Seredenina TS, Levitskaya NG, Rozyczka J, Dubynina EV, Novosadova EV, Andreeva LA, Alfeeva LY, Kamensky AA, Grivennikov IA, Myasoedov NF, Engele J. Semax, an analogue of adrenocorticotropin (4-10), binds specifically and increases levels of brain-derived neurotrophic factor protein in rat basal forebrain. *J Neurochem.* 2006;97(Suppl 1):82–86. pubmed.ncbi.nlm.nih.gov/16635257

F Formulation and Delivery Specifications

ACTIVE COMPOUND	Semax · CAS 80714-61-0
TOTAL MASS PER BOTTLE	40 mg active
SPRAYS PER BOTTLE	200 sprays
ACTIVE PER SPRAY	0.2 mg per spray
VOLUME PER SPRAY	0.1 mL per metered actuation
VEHICLE	Aqueous nasal-grade vehicle with preservative
ANALYTICAL SPECIFICATION	≥ 98 % purity by HPLC; content uniformity per actuation verified to ± 10 % of label claim

04 Nasal Delivery Considerations

INTRANASAL BIOAVAILABILITY AND VEHICLE CHEMISTRY

The intranasal route provides direct access to systemic circulation through the rich vascularisation of the nasal mucosa, bypassing first-pass hepatic metabolism characteristic of oral administration. For peptide-class compounds, the principal nasal-delivery considerations are (a) **mucosal residence time** — aqueous nasal vehicles produce relatively short mucosal contact, with peptide permeation governed by molecular size, lipophilicity, and chemistry of the active; (b) **vehicle pH** — neutral-to-slightly-acidic pH (5.5–7.0) is optimal for both nasal mucosa tolerance and peptide bond stability; (c) **osmolarity** — formulation osmolarity is targeted to approximate physiological isotonicity to minimise mucociliary disruption; (d) **preservative selection** — benzalkonium chloride or similar quaternary ammonium preservatives are standard for nasal aqueous formulations; (e) **permeation enhancers** may be incorporated in some formulations to support peptide passage across the nasal epithelium without disrupting mucosal integrity.