

RESEARCH MONOGRAPH . COMPOUND PROFILE

Cortagen

A four-residue synthetic peptide developed by the Khavinson group as a cerebral cortex bioregulator, part of the Russian short-peptide bioregulator class.

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COMPOUND CLASS	Khavinson tetrapeptide bioregulator (Ala-Glu-Asp-Pro)

ABSTRACT

Cortagen (Ala-Glu-Asp-Pro; CAS 254749-42-7; molecular weight 414.41) is a four-residue synthetic peptide developed at the St. Petersburg Institute of Bioregulation and Gerontology by Vladimir Khavinson as a representative of the short-peptide bioregulator class derived from cortexin (a porcine cerebral cortex extract registered as a medicine in the Russian Federation). The Khavinson program isolated active fragments from organ-specific peptide extracts and characterized synthetic tetrapeptide and tripeptide analogs as the molecular basis of the parent extract's activity, including Cortagen for cerebral cortex, Pinealon (Glu-Asp-Arg) for pineal/CNS, Epitalon (Ala-Glu-Asp-Gly) for pineal, Vilon (Lys-Glu) for thymus, and several others. The proposed mechanism is direct DNA binding of the short peptides at promoter regions of tissue-specific genes, modulating transcription in a cell-type-restricted manner; published Russian-language work characterizes binding to specific GC-rich regulatory regions and effects on transcription factor recruitment. Pro-cognitive and neuroprotective activities of Cortagen are reported in rodent models of cerebral hypoxia, traumatic brain injury, and stress; Russian clinical reports describe efficacy in vegetative-vascular dystonia, post-traumatic asthenia, and discirculatory encephalopathy at intramuscular doses of 5 to 10 mg over 5 to 10 day courses. The Khavinson bioregulator class is registered as medicines in the Russian Federation and a small number of CIS jurisdictions; FDA, EMA, and most Western regulatory authorities have not reviewed the class. The principal limitation on the evidence base is the dominance of the originating laboratory's publications and the limited scale of clinical evidence

relative to what would be required for Western regulatory approval. Investigators should weight the evidence accordingly.

1. Compound Identification

Cortagen is described as khavinson tetrapeptide bioregulator (ala-glu-asg-pro). A four-residue synthetic peptide developed by the Khavinson group as a cerebral cortex bioregulator, part of the Russian short-peptide bioregulator class.

1.1 Class summary

Khavinson tetrapeptide bioregulator (Ala-Glu-Asp-Pro)

1.2 Subtitle

A four-residue synthetic peptide developed by the Khavinson group as a cerebral cortex bioregulator, part of the Russian short-peptide bioregulator class.

2. Abstract

Cortagen (Ala-Glu-Asp-Pro; CAS 254749-42-7; molecular weight 414.41) is a four-residue synthetic peptide developed at the St. Petersburg Institute of Bioregulation and Gerontology by Vladimir Khavinson as a representative of the short-peptide bioregulator class derived from cortexin (a porcine cerebral cortex extract registered as a medicine in the Russian Federation). The Khavinson program isolated active fragments from organ-specific peptide extracts and characterized synthetic tetrapeptide and tripeptide analogs as the molecular basis of the parent extract's activity, including Cortagen for cerebral cortex, Pinealon (Glu-Asp-Arg) for pineal/CNS, Epitalon (Ala-Glu-Asp-Gly) for pineal, Vilon (Lys-Glu) for thymus, and several others. The proposed mechanism is direct DNA binding of the short peptides at promoter regions of tissue-specific genes, modulating transcription in a cell-type-restricted manner; published Russian-language work characterizes binding to specific GC-rich regulatory regions and effects on transcription factor recruitment. Pro-cognitive and neuroprotective activities of Cortagen are reported in rodent models of cerebral hypoxia, traumatic brain injury, and stress; Russian clinical reports describe efficacy in vegetative-vascular dystonia, post-traumatic asthenia, and discirculatory encephalopathy at intramuscular doses of 5 to 10 mg over 5 to 10 day courses. The Khavinson bioregulator class is registered as medicines in the Russian Federation and a small number of CIS jurisdictions; FDA, EMA, and most Western regulatory authorities have not reviewed the class. The principal limitation on the evidence base is the dominance of the originating laboratory's publications and the limited scale of clinical evidence relative to what would be required for Western regulatory approval. Investigators should weight the evidence accordingly.

3. Mechanism of Action

Proposed direct DNA binding at GC-rich promoter regions of tissue-specific genes, modulating transcription in cerebral cortex tissue. Pro-cognitive and neuroprotective activity in rodent hypoxia and TBI models.

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

Russian clinical use 5 to 10 mg intramuscular daily for 5 to 10 day courses, repeated as indicated.

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. Khavinson VK. Peptides and ageing. Neuroendocrinol Lett 2002.
2. Khavinson VK, Malinin VV. Gerontological aspects of genome peptide regulation. Karger 2005.
3. Anisimov VN, Khavinson VK. Peptide bioregulation of aging: results and prospects. Biogerontology 2010.

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