

# Epithalon

*Ala-Glu-Asp-Gly* — a synthetic tetrapeptide developed by Vladimir Khavinson and colleagues at the St. Petersburg Institute of Bioregulation and Gerontology, derived from the pineal-gland peptide preparation Epitalamin and characterised in preclinical models of telomerase activation, lifespan extension in rodents, and circadian gene expression.

**CAS REGISTRY**

307297-39-8

**CATALOG REFERENCE**

BM-LY0-016

**CLASS**Synthetic tetrapeptide  
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**E** pithalon (also spelled Epitalon) is a synthetic tetrapeptide with sequence Ala-Glu-Asp-Gly (AEDG), developed at the St. Petersburg Institute of Bioregulation and Gerontology by Vladimir Khavinson and colleagues as part of the short-peptide bioregulator programme. The molecule was derived from a polypeptide pineal-gland preparation (Epitalamin) by chemical fractionation, and is identified as the active short-peptide component. Across approximately three decades of investigation, Epithalon has been characterised in cell-culture and rodent preparations as a putative telomerase activator (Khavinson 2003, *Bull Exp Biol Med*), a modulator of circadian-rhythm gene expression including pineal-melatonin-synthesis enzymes, and a candidate lifespan-extending compound in rodent longevity studies from the originating laboratory. A 2025 study by Brunel University researchers independently confirmed dual telomerase / alternative-lengthening-of-telomeres (ALT) activity in human cell-line preparations, making Epithalon the more independently-validated of the two principal Khavinson pineal-tetrapeptides (the other being Pinealon / EDR, Monograph 005). **This monograph summarises published preclinical findings for laboratory research reference only.**

## 01 Compound Profile

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COMMON DESIGNATION	Epithalon · Epitalon · AEDG peptide
PRIMARY SEQUENCE	Ala-Glu-Asp-Gly (A-E-D-G)
CAS REGISTRY	307297-39-8
MOLECULAR FORMULA	$C_{14}H_{22}N_4O_9$
AVERAGE MOLECULAR MASS	390.35 g · mol <sup>-1</sup>
PARENT PREPARATION	Epitalamin – polypeptide pineal-gland preparation from which Epithalon was identified as the active short-peptide component
PROPOSED MOLECULAR ACTIONS	Telomerase enzymatic activation; ALT-pathway engagement (Brunel 2025); modulation of pineal melatonin-synthesis enzyme gene expression; circadian-rhythm gene modulation <sup>1, 4</sup>
PHYSICAL FORM	White lyophilised solid
SOLUBILITY (LAB RECONSTITUTION)	Highly water-soluble; small acidic tetrapeptide with no rigid secondary structure
STORAGE (RESEARCH HANDLING)	Lyophilised solid: -18 °C, desiccated; reconstituted solution refrigerated 2–8 °C short-term; aliquoted long-term at -18 °C
ANALYTICAL SPECIFICATION	≥ 99 % purity by HPLC (BIOMOD Labs internal release specification)

## 02 Origin and Chemistry

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EPITHALON EMERGED FROM THE LONG-RUNNING KHAVINSON PROGRAMME AT THE ST. PETERSBURG INSTITUTE OF Bioregulation and Gerontology investigating short tissue-derived peptides as putative regulators of tissue-specific gene expression. The starting material was Epitalamin, a polypeptide preparation derived from bovine pineal gland with reported geroprotective and circadian-rhythm-modulating activities in rodent studies. Chemical fractionation of Epitalamin identified the AEDG tetrapeptide as the active short-peptide component, which was subsequently synthesised and characterised as Epithalon.<sup>2</sup>

Chemically, Epithalon is a small acidic tetrapeptide (Asp and Glu contribute two acidic side chains; the molecule's net charge at neutral pH is approximately -1 to -2). The sequence is unusually proline- and aromatic-free, conferring substantial structural flexibility and water solubility. Khavinson's proposed mechanism for the short Khavinson peptides invokes direct cellular uptake, nuclear translocation, and interaction with DNA promoter regions — a hypothesis that distinguishes the Khavinson-peptide pharmacology from classical receptor-mediated signalling.<sup>3</sup>

### 03 Proposed Mechanisms in Preclinical Models

THE DEFINING PRECLINICAL OBSERVATION FOR EPITHALON IS TELOMERASE ACTIVATION. KHAVINSON AND COLLEAGUES (2003) reported that Epithalon exposure increased telomerase activity in cell-culture preparations of human somatic cells, with parallel telomere-elongation observations across multiple cell types.<sup>1</sup> A 2025 study from Brunel University extended this characterisation in human cell-line preparations and confirmed both classical telomerase activation and engagement of the alternative-lengthening-of-telomeres (ALT) pathway — providing independent corroboration of the dual-mechanism telomere-maintenance pharmacology attributed to the molecule.<sup>4</sup>

Beyond telomerase chemistry, the Epithalon literature documents preclinical effects on circadian-rhythm gene expression, particularly in pineal-gland tissue preparations from rodents. The molecule has been reported to modulate the expression of melatonin-synthesis enzyme genes including arylalkylamine N-acetyltransferase (AANAT) and hydroxyindole-O-methyltransferase (HIOMT), and to normalise circadian patterns disrupted by age in rat pineal preparations. Anisimov and colleagues have published a series of rodent lifespan studies reporting modest lifespan extension in animals exposed to Epitalamin / Epithalon, with corresponding histological and biochemical indices of slowed age-related decline.<sup>5</sup> PRECLINICAL · RAT

### 04 Preclinical Findings

SYSTEM	ANIMAL MODEL / PREPARATION	REPORTED OBSERVATION	REF.
Telomerase activity	Human somatic cell culture preparations	Increased telomerase activity; telomere elongation observations	<a href="#">1</a>
ALT pathway engagement	Brunel 2025 human cell-line study	Dual telomerase / ALT activation independently confirmed	<a href="#">4</a>
Pineal melatonin genes	Rat pineal preparations	Modulation of AANAT and HIOMT gene expression; circadian rhythm normalisation	<a href="#">5</a>
Rodent lifespan	Anisimov long-term studies in rats	Modest lifespan extension; slowed age-related decline markers	<a href="#">5</a>
Retinal preservation	Retinal cell culture & rat retinitis-pigmentosa preparation	Preservation of retinal cellular structure markers	<a href="#">3</a>
Pineal-aging biology	Aged rat pineal tissue analyses	Restoration of pineal melatonin synthesis markers in aged animals	<a href="#">2</a>

## 05 Research Synthesis & Limitations

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### METHODOLOGICAL NOTES

Epithalon's published literature is concentrated in the Khavinson laboratory and Russian-affiliated research groups, with the recent 2025 Brunel University study providing one of the first substantive independent biophysical validations of the telomerase-activation mechanism in human cell-line preparations. The dual telomerase / ALT-pathway engagement adds an additional dimension of telomere-maintenance pharmacology that should be considered in any experimental design involving the molecule. Researchers should note that the proposed mechanism of direct short-peptide–DNA promoter binding remains the central but not fully validated mechanistic hypothesis of the Khavinson programme, and that lifespan-extension studies in rodents have not been independently replicated outside the originating laboratory network at comparable methodological depth.

## 06 Laboratory Handling, Reconstitution, and Storage

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LYOPHILISED EPITHALON IS SUPPLIED UNDER RESEARCH-USE SPECIFICATIONS. THE SMALL ACIDIC TETRAPEPTIDE IS highly water-soluble and reconstitutes readily in sterile water for injection, physiological saline, or bacteriostatic water. The absence of cysteine (no disulfide considerations), methionine (no oxidation), or tryptophan/tyrosine (no photo-oxidation) makes Epithalon one of the more handling-tolerant peptides in the BIOMOD catalog. Lyophilised storage at  $-18\text{ }^{\circ}\text{C}$ , desiccated; reconstituted solutions at refrigerated  $2\text{--}8\text{ }^{\circ}\text{C}$  for short-term work; aliquoted long-term storage at  $-18\text{ }^{\circ}\text{C}$  with minimised freeze–thaw. Working concentrations are determined by the investigator's experimental design.

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## 07 References

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