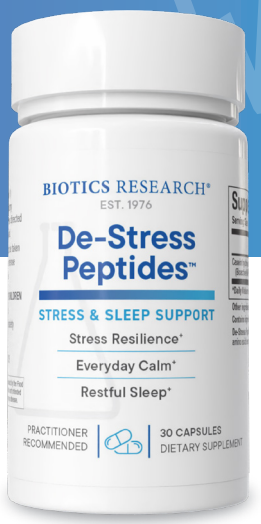
De-Stress Peptides™

Clinical Support for Stress Resilience & GABAergic Modulation



De-Stress Peptides™ available in 30 count bottle (#7707).

Overview

For mammalian species, including humans, the newborn functions as an external embryo, with milk serving as the umbilical cord linking the infant to maternal support. A baby's enzymatic system differs significantly from that of adults, particularly in exhibiting low pepsin levels and predominant tryptic activity. Observing infants' calm state after consuming warm milk, researchers investigated the connection between tryptic activity in milk and infant tranquility, leading to groundbreaking research on milk casein hydrolysate fractions and peptides with anxiolytic properties.

De-Stress Peptides™ Defined

De-Stress Peptides™ (U.S. Patent #5,846,939) is a patented, specially produced alpha-S1 casein hydrolysate (αS1-CH) derived from bovine milk protein. This ingredient constitutes a specific bioactive peptide concentrate demonstrating anxiolytic activity—referring to properties similar to medications prescribed for anxiety symptoms.

The active component has been characterized as a "benzodiazepine-like decapeptide" with GABA receptor modulating capabilities. A decapeptide is a peptide composed of exactly ten amino acids linked in a specific sequence. This decapeptide structure, determined through amino acid sequencing and confirmed by three-dimensional molecular modeling, enables the peptide to interact with GABA receptors in the brain and support the body's natural stress response mechanisms.[1,3,4]

What Is Alpha-Casozepine?

The primary bioactive compound in **De-Stress Peptides™** is alpha-casozepine, a decapeptide (10 amino acids) identified as the fragment αs1-CN(f91–100) from bovine alpha-s1 casein.[1] The name itself reflects its dual nature: "caso-" from casein (the milk protein it derives from) and "-zepine" referencing its benzodiazepine-like activity at GABA receptors.

Alpha-casozepine is produced through tryptic hydrolysis—the enzymatic cleavage of alpha-s1 casein by trypsin. This process mimics what occurs naturally in infant digestion, where trypsin activity is predominant. This is thought to be one reason infants become drowsy and calm after breastfeeding: their digestive systems naturally generate this bioactive peptide from milk protein in quantities that adults typically do not.

Alpha-Casozepine in the Context of Modern Peptide Therapies

With the growing interest in peptide-based therapies among healthcare practitioners, it is important to understand where alpha-casozepine fits within this landscape. A peptide is a short chain of amino acids—typically under 50—as distinct from full proteins, which can be hundreds or thousands of amino acids long. At 10 amino acids, alpha-casozepine falls in the same size class as many of the peptide therapies gaining clinical attention, such as BPC-157 (15 amino acids) and thymosin alpha-1 (28 amino acids).

Alpha-casozepine, however, differs from most trending peptide therapies in several important ways:

- **Food-derived, not synthetic.** Most clinical peptides are manufactured through chemical synthesis. Alpha-casozepine is a naturally occurring fragment liberated from a food protein through enzymatic hydrolysis.
- **Orally bioavailable.** A common limitation of peptide therapies is degradation by stomach acid, often requiring injection. Alpha-casozepine is created by enzymatic digestion (trypsin), so the hydrolysate form delivers it already cleaved and bioavailable. All clinical studies demonstrating cortisol reduction and sleep improvement used oral administration.
- **Regulatory clarity.** Unlike compounded synthetic peptides—some of which have faced FDA restrictions—alpha-casozepine is derived from milk protein and is available as a dietary ingredient.
- **Non-habit forming.** Alpha-casozepine's selective receptor binding does not produce tolerance, dependency, or withdrawal effects.

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Like other bioactive peptides, alpha-casozepine's 10-amino-acid sequence gives it a specific three-dimensional shape that allows it to dock into the benzodiazepine binding site on the GABA-A receptor.[1,3] Its amphiphilic structure—with hydrophobic residues on one side and hydrophilic on the other—enables it to cross both types of biological membranes.[3] However, its shape is slightly different from pharmaceutical benzodiazepines, resulting in selective modulation of certain GABA-A receptor subtypes (particularly those with β1 subunits) rather than the broad, non-selective binding characteristic of drugs like diazepam.[9] This selectivity is the basis for its anxiolytic and sleep-supporting effects without sedation, cognitive impairment, or dependence.

From Milk Protein to Neuromodulatory Peptide

Casein, the predominant milk protein, serves as a source of bioactive peptides generated through enzymatic hydrolysis. The αS1-casein sequences in **De-Stress Peptides™** can interact with GABA receptors, the same inhibitory system targeted by certain anxiolytic agents. Clinical evidence suggests that this peptide may modulate GABAergic signaling, influence hypothalamic-pituitary-adrenal (HPA) axis activity, and support behavioral and physiological adaptation to stress without pharmacologic sedation.

Peptide Characterization & Mechanism

Molecular Structure

Identification of the active peptide began with laboratory production of an alpha-S1 casein tryptic hydrolysate, which demonstrated anxiolytic activity both in vitro (GABA-A receptor-binding test and peripheral-type benzodiazepine binding assays) and in vivo (elevated plus maze test and conditioned defensive burying test in rats).[1,2]

Amino acid sequencing identified the peptide as a benzodiazepine-like decapeptide.[1] Utilizing molecular separation techniques combined with circular dichroism, two-dimensional NMR spectroscopy, and molecular modeling, researchers characterized the peptide as a 310 helix structure, initiated and terminated by an alpha-turn.[3] The decapeptide exhibits amphiphilic characteristics, with hydrophobic side chains located on one side of the molecule and hydrophilic side chains on the opposite side, indicating it is "essentially flexible."[3] This structural feature suggests the peptide can cross both hydrophobic and hydrophilic membranes. Three-dimensional molecular modeling further confirmed the peptide structure.[4]

GABAergic Modulation

Compelling results from a pivotal 2018 preclinical study published in *Biomolecules & Therapeutics* demonstrated that oral administration of αS1-CH (120–300 mg/kg) modulates the brain's GABA receptor in rodent models.[9] The peptide was associated with:

- Increased theta (θ) wave activity on EEG
- Prolonged total sleep time
- Stabilized sleep-wake transitions
- Selective upregulation of the β1 subunit of the GABA receptor in the hypothalamus

These findings suggest receptor-specific modulation without sedative effects, indicating a mechanism distinct from traditional GABAergic medications.

Neurobiology of Stress & Clinical Relevance

HPA Axis & Autonomic Balance

Stress resilience depends on balanced communication among the limbic system, HPA axis, and autonomic nervous system. Chronic stress can weaken GABAergic tone and elevate corticotropin-releasing hormone (CRH) signaling, sustaining cortisol excess and sympathetic overdrive. By supporting GABA receptor integrity, αS1-CH may help restore inhibitory-excitatory balance, potentially mitigating hyperarousal and facilitating physiological recovery.

The hypothalamus integrates neural, hormonal, and metabolic signals that shape stress reactivity. αS1-CH's modulation of hypothalamic GABA receptors may recalibrate HPA axis output, attenuating corticotropin and cortisol responses during stress exposure.

Preclinical Evidence

The action of **De-Stress Peptides's** casein hydrolysate was demonstrated in randomized double-blind preclinical studies utilizing Wistar rats.[5] The anxiolytic activity was confirmed across multiple behavioral assessments.

Key Findings:

- At 3 mg/kg dosage, significant reductions were observed in:
  - Duration of probe burying ($P<0.005$)
  - Head stretches toward probe ($P<0.01$)
  - Percent approaches toward probe followed by retreats ($P<0.01$)
- Rats given 3 mg/kg **De-Stress Peptides™** showed significant reduction in pentylenetetrazole (PTZ) activity ($P<0.002$).
- Protective effect on sleep when subjects were exposed to chronic mild stress, observed as maintenance of slow-wave sleep duration with minor increases in paradoxical sleep duration.

Human Clinical Trials

Lactium®, the trademarked casein hydrolysate found in **De-Stress Peptides™**, has been evaluated in 9+ clinical studies spanning over two decades (1999–2021), enrolling more than 800 participants across multiple countries. These trials range from small pilot studies to large multi-country consumer trials, covering acute stress, chronic stress, sleep disturbances, and psychodermatology. The following sections highlight the pivotal trials in detail, with additional supporting studies summarized thereafter.

Study 1: Stress-Related Symptoms in Women[6]

In a double-blind, randomized, crossover, placebo-controlled trial, 63 female volunteers were randomly assigned to receive either αS1-casein (150 mg/day) or placebo for 30 days, followed by a three-week washout period before crossing over.

Results: The αS1-casein hydrolysate group demonstrated reduced stress-related symptoms with significant improvements in:

- Digestive function ($P<0.05$)
- Cardiovascular symptoms ($P<0.05$)
- Intellectual performance ($P<0.05$)
- Emotional state ($P<0.05$)
- Social functioning ($P<0.05$)

In subjects with the highest initial symptom intensities (>4/day), even more pronounced improvements were noted:

- Digestive: 66.1% vs. 36% for placebo
- Cardiovascular: 48% vs. 35.5% for placebo
- Intellectual: 64.8% vs. 36.7% for placebo
- Emotional: 43.8% vs. 23.5% for placebo
- Social: 36.7% vs. 22.5% for placebo

Study 2: Hemodynamic Responses to Stress[7]

In a subsequent double-blind, placebo-controlled trial, 42 healthy male volunteers participated in a randomized study assessing physiological stress responses. Participants received 1,200 mg/three sessions of αS1-casein hydrolysate over ~36 hours while exposed to successive mental and physical stress situations.

Results demonstrated significant "antistress activity":

- **Cortisol reduction:** Plasma cortisol decreased 20.69% in the αS1-casein group (t=3.73; P=0.001) compared to only 3.39% in placebo (t=1.05; P=0.30)
- **Blood pressure:** Both systolic and diastolic blood pressures were significantly lower in the αS1-casein group compared to placebo
- **Heart rate:** Significant decrease (P=0.05) in the αS1-casein group versus placebo

These findings are consistent with modulation of HPA axis activity and improved autonomic balance, as reported in subsequent research.

Study 3: Sleep Quality Support[11]

In a 2019 four-week, double-blind, placebo-controlled, randomized crossover clinical study of 48 adults with mild to moderate sleep disturbances, 150 mg/day αS1-CH was associated with:

- Increased total sleep time
- Shorter sleep latency
- Improved sleep efficiency
- Enhanced sleep patterns confirmed by both actigraphy (objective movement tracking) and polysomnography (gold-standard sleep assessment measuring brain waves, eye movements, and muscle activity)

Participants also reported improvements in subjective sleep quality via sleep diaries, suggesting that αS1-CH may support improved sleep patterns and overall stress resilience.

Broader Clinical Evidence

Beyond the three pivotal trials detailed above, Lactium® has been evaluated in seven additional human studies (1999–2021) enrolling a combined 600+ participants across multiple countries. Dosing ranged from 150–300 mg/day over 15 days to 6 weeks. Results were consistent: significant improvements in stress-related symptoms and sleep quality across diverse populations, dosing regimens, and geographic regions. The most recent multi-country consumer study (n=300; France, USA, China) confirmed significant improvements in both perceived stress (PSS-10, P<0.001) and sleep quality (PSQI, P<0.001), with an overall satisfaction rate of 8 in 10 consumers.

Stress, Skin & Immune Interactions

Beyond central nervous system effects, αS1-casein hydrolysate may influence multiple interconnected systems affected by stress. Chronic stress can heighten inflammatory signaling, disrupt immune function, and contribute to conditions such as acne through neuroendocrine-immune pathways.[12,13]

In a 2022 randomized, controlled, multicenter trial of 100 patients with moderate-to-severe acne vulgaris, supplementation with αS1-CH alongside standard care led to:[13]

- Reductions in serum cortisol
- Decreased perceived stress and anxiety
- Decreases in both inflammatory and non-inflammatory acne lesions
- Improvements in quality of life and acne severity scores

These findings suggest that αS1-CH may help support skin health and systemic balance by modulating stress-related physiological pathways, reflecting the complex interconnections between neuroendocrine, immune, and dermatologic systems.[13]

Integrated Perspective on Stress Resilience

Across preclinical and clinical studies, **De-Stress Peptides™** (αS1-CH) is consistently associated with:

- Modulation of GABA receptors
- Attenuation of stress-induced autonomic responses
- Improvements in sleep-related outcomes
- Reduced cortisol responses to stress
- Enhanced cardiovascular and digestive stress tolerance
- Support for emotional and cognitive function under stress

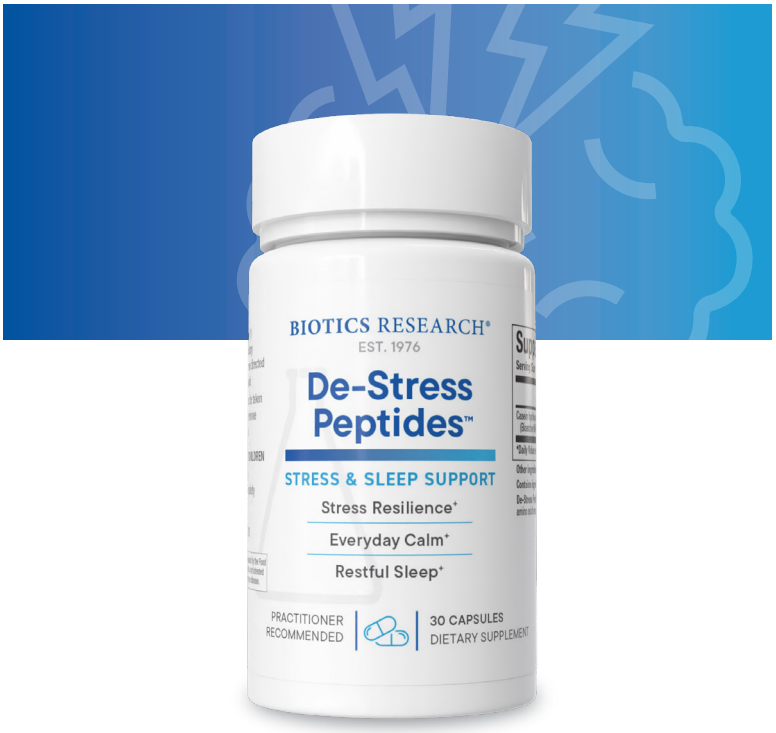
These findings support the concept of functional stress resilience—the body's capacity to return toward homeostasis following stress exposure. Emerging evidence also suggests downstream effects on autonomic balance, immune signaling, and stress-related skin manifestations.

Supporting Homeostasis Across Systems

The evidence indicates that **De-Stress Peptides™** may help the body adapt to stress across multiple systems. By modulating GABAergic signaling, influencing HPA axis activity, and reducing stress-mediated inflammatory responses, αS1-CH shows potential to support:

- Emotional regulation
- Sleep quality
- Cardiovascular stress responses
- Digestive function
- Cognitive performance
- Skin health

These effects highlight the interconnections among neuroendocrine, immune, and dermatologic systems, demonstrating how stress manifests throughout the body—and how targeted peptide support may promote systemic resilience.



Supplement Facts

Serving Size: 1 Capsule

	Amount Per Serving	% Daily Value
Casein hydrolysate (Bioactive Milk Peptides)(Lactium®)	150 mg	*

***Daily Value not established**

Other ingredients: Capsule shell (gelatin and water).

Contains ingredients derived from milk.

De-Stress Peptides™ supplies a decapeptide, as determined by its amino acid sequence, having anxiolytic activity.+

Patent # 5,846,939

This product is gluten free.

Recommended Usage: One (1) capsule each day as a dietary supplement or as otherwise directed by a healthcare professional. **De-Stress Peptides™** can be taken during the day at time of intense stress or before bedtime.

Key Clinical Benefits

- ✓ Supports healthy stress response and balanced cortisol levels*
- ✓ Promotes calm, emotional balance, and mental clarity*
- ✓ Helps ease tension and encourage relaxation*
- ✓ Supports restful, high-quality sleep throughout the night*
- ✓ Promotes healthy cognitive function under stress*
- ✓ Supports digestive comfort during stressful periods*
- ✓ Encourages the body's natural adaptation to stress*
- ✓ Helps maintain a positive mood and overall well-being*
- ✓ Non-habit forming and well-tolerated*

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