Oral Elastin peptide

(Derived from the elastic connective tissue of the fish bulbus arteriosus)

Oral Nutri-cosmetic Intervention Targeting Fine Lines, Dermal Elasticity, and Extracellular Matrix Remodeling

Abstract

Elastin peptide are emerging as a promising class of bioactive compounds in nutricosmetic research.

The fish bulbus arteriosus, a specialized elastic organ responsible for hemodynamic buffering, represents a unique and underexplored source of elastin-rich connective tissue.

Through targeted enzymatic hydrolysis, elastin proteins from this tissue can be converted into low-molecular-weight peptides (0.5-2 kDa), which exhibit superior intestinal absorption via PepT1 transporters.

These peptides retain elastin-specific cross-linking amino acids, desmosine and isodesmosine, conferring high biochemical homology with human dermal, vascular, and pulmonary elastic fibers. Mechanistically, oral elastin peptides provide structural substrates for fibroblast-mediated elastic fiber regeneration, support the collagen-elastin dual-network for dermal tensile strength and resilience, and exert anti-oxidative and anti-

proteolytic activities that protect the extracellular matrix (ECM) from premature degradation.

Furthermore, their vascular homology suggests potential benefits for arterial compliance and systemic elasticity maintenance.

When combined with collagen peptides, elastin peptides enable synergistic remodeling of the ECM, addressing both tensile and elastic components of skin aging.

Collectively, elastin peptides derived from fish bulbus arteriosus offer a novel precision-nutrition strategy for mitigating fine lines, restoring dermal elasticity, and delaying structural skin aging, while also contributing to vascular and systemic tissue health.

Keywords

Elastin peptides; fish bulbus arteriosus; oral nutria-cosmetics; dermal elasticity; extracellular matrix; desmosine; isodesmosine; skin aging; wrinkle reduction; vascular

The bulbus arteriosus, a specialized cardiac structure located between the ventricular outflow and the branchial arteries in fish, functions as a physiological pressure buffer. Histologically, it is characterized by a dense network of elastic fibers. This unique anatomical origin provides elastin proteins with naturally high purity and functional specificity.

Through targeted enzymatic hydrolysis, elastin from the bulbus arteriosus can be broken down into low-molecular-weight peptides (predominantly 500-2000 Da). These short peptides are efficiently absorbed via intestinal peptide transporters (PepT1), enabling rapid entry into systemic circulation. Compared with intact macromolecular proteins, such low-molecular-weight elastin peptides exhibit superior bioavailability.

Importantly, these peptides retain elastin-specific cross-linking amino acids - desmosine and isodesmosine - which are critical for maintaining the integrity of elastic fibers in skin and vascular tissues. This molecular signature highlights their close physiological relevance to the repair and renewal of elastic structures.

In application, elastin peptides derived from the fish bulbus arteriosus provide structural support for the dermal extracellular matrix, promoting the regeneration and stabilization of elastic fiber networks. This contributes to improved skin firmness and wrinkle reduction. Moreover, as peptides sourced from a “natural elastic energy-storage tissue,” they may also support vascular elasticity and circulatory health.

When combined with complementary ingredients such as fish collagen peptides, hyaluronic acid, and ceramides, these elastin peptides contribute to a comprehensive “structure + elasticity + hydration” tri-axis beauty mechanism. This unique profile not only enhances their value in oral beauty supplementation but also offers rapid and perceivable benefits, underscoring their market differentiation potential.

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I Mechanisms of Action of Elastin Peptides Derived from the Elastic Connective Tissue of the Fish Bulbus Arteriosus

Elastin peptides obtained from the fish bulbus arteriosus, characterized by their low molecular weight, high absorption efficiency, and enrichment in elastin-specific cross-linking amino acids, exert biological effects across multiple tissue targets.

Their mechanisms are not limited to a single pathway, but rather span four dimensions: dermal extracellular matrix, vascular system, collagen–elastin dual network synergy, and antioxidant/anti-aging protection.

Together, these mechanisms encompass both structural repair and functional maintenance, while also providing defense against and delay of age-related degradation.

1) Dermal Extracellular Matrix: Supporting the Reconstruction and Homeostasis of the Elastic Fiber Network

- **Efficient Absorption**: Elastin proteins from the fish bulbus arteriosus, after targeted enzymatic hydrolysis, are primarily converted into low-molecular-weight peptides such as dipeptides and tripeptides (500-2000 Da). These are efficiently absorbed in the small intestine through the oligopeptide transporter PepT1 and rapidly enter systemic circulation.

- **Functional Substrates**: Once in the bloodstream, these bioactive peptides and amino acids serve as substrates for dermal fibroblasts, facilitating the synthesis of new elastic fibers and promoting the renewal and repair of the extracellular matrix (ECM).
- **Dual-Network Support**: The biomechanical properties of the dermis depend on the interplay between collagen fibers (tensile strength) and elastic fibers (recoil). Elastin peptides act synergistically with collagen peptides to restore and reinforce this dual ECM meshwork, thereby enhancing structural support and elastic resilience.
- **Molecular Homology**: Elastin peptides contain characteristic cross-linking amino acids - desmosine and isodesmosine - which serve as molecular “fingerprints” of elastic fiber metabolism and structural integrity. Their presence highlights the natural homology and functional specificity of these peptides for dermal elastic fiber networks.

✓ *Shiratsuchi E, et al. (2016). Oral elastin peptide improves skin elasticity and dermal thickness in animal models. J Dermatol Sci.*

2) Vascular System: Enhancing Arterial Elasticity and Hemodynamic Stability

- **Homologous Origin:** The fish bulbus arteriosus itself functions as an “elastic buffering organ,” with histological characteristics closely resembling the storage and recoil properties of large arteries. Peptides extracted from this tissue therefore exhibit natural homology with vascular elastic networks.

- **Efficient Absorption:** Due to their low molecular weight after targeted enzymatic hydrolysis, elastin peptides are readily absorbed through intestinal peptide transporters and rapidly delivered into systemic circulation, allowing efficient utilization by vascular tissues.
- **Compliance Support:** Elastic fibers are the central determinant of arterial compliance. These bioactive oligopeptides serve as substrates that support the remodeling of vascular smooth muscle and extracellular matrix, helping to preserve the flexibility and resilience of arterial walls.
- **Signature Amino Acids:** The presence of elastin-specific cross-linking amino acids - desmosine and isodesmosine - closely correlates with the structural integrity of vascular elastic fibers, underscoring their targeted role in buffering pulsatile blood flow.

✓ Hirano E, et al. (2005). Dietary elastin peptide reduces arterial stiffness and maintains vascular elasticity. J Nutr Sci Vitaminol.

3) Synergy with Collagen: Building a Dual Network of “Tension + Recoil”

- **Structural Complementarity:** Collagen fibers provide tensile strength and resistance to stretching, while elastic fibers confer reversible extensibility and recoil. Together, they form an integrated dual network within the dermis and vasculature that determines tissue biomechanics.

- **Homologous Combination:** Elastin peptides derived from the fish bulbus arteriosus and marine collagen peptides share a homologous origin, facilitating coordinated absorption and metabolic utilization at the molecular level.
- **Dual-Network Remodeling:** Collagen peptides reinforce the tensile framework of the dermis, while elastin peptides strengthen the elastic recoil network. Their synergistic action restores extracellular matrix (ECM) balance and reconstruction, thereby improving skin firmness and tissue flexibility.
- **Formulation Advantage:** In nutricosmetic or functional nutrition formulations, their combined use enables an integrated “structure + elasticity” intervention strategy, aligning with physiological needs for anti-aging skin care and vascular compliance support.

✓ *Shigemura Y, et al. (2009). Collagen hydrolysate and elastin peptides act synergistically on dermal extracellular matrix. J Agric Food Chem.*

4) Antioxidant and Anti-Aging Effects: Slowing Elastic Fiber Degradation and Tissue Aging

- **Free Radical Scavenging:** Certain low-molecular-weight elastin peptides exhibit intrinsic antioxidant activity, neutralizing reactive oxygen species (ROS) and reducing oxidative stress-induced damage to dermal and vascular extracellular matrices.

- **Enzyme Activity Modulation:** Bioactive oligopeptides can partially inhibit the excessive activity of elastase and matrix metalloproteinases (MMPs), thereby attenuating the accelerated degradation of elastic and collagen fibers.
- **Matrix Homeostasis:** By lowering free radical burden and suppressing overactive proteolytic enzymes, elastin peptides help maintain the balance between ECM synthesis and degradation, delaying structural senescence of tissues.
- **Systemic Support:** These combined antioxidant and anti-protease actions not only promote skin elasticity and firmness but also contribute to the preservation of arterial compliance and vascular health.

✓ Nakatani S, et al. (2011). Antioxidant properties of elastin-derived peptides and their role in inhibiting elastase activity. Biochim Biophys Acta.

Conclusion

Elastin peptides derived from the elastin-rich connective tissue of the fish cardiac bulbus arteriosus demonstrate unique bio-functional advantages owing to their high absorption efficiency as low-molecular-weight peptides and their retention of elastin-specific cross-linking amino acids. Within the body, they provide targeted dual support for both skin and vascular systems.

Specifically, these peptides serve as substrates for dermal fibroblasts to reconstruct elastic fiber networks, thereby restoring skin firmness and resilience. At the same time,

through their natural homology with vascular elastic structures, they contribute to improved arterial compliance and hemodynamic stability.

When combined with marine collagen peptides, they amplify the repair of the “tension–recoil” dual-network architecture of the extracellular matrix. Moreover, their intrinsic antioxidant and anti-protease activities help slow ECM degradation, delaying tissue aging processes.

In summary, elastin peptides from the fish bulbus arteriosus not only hold unique promise in nutricosmetic and anti-aging interventions but also provide scientifically grounded nutritional support for vascular health and the maintenance of systemic tissue elasticity.

II Tissue Compatibility and the Concept of “Homologous Nutrition”

The fish bulbus arteriosus, a key organ responsible for buffering hemodynamic pressure fluctuations, contains connective tissue rich in densely cross-linked elastin fibers. When subjected to targeted enzymatic hydrolysis, this material yields low-molecular-weight elastin peptides (predominantly dipeptides and tripeptides, 500-2000 Da) characterized by high purity, retention of elastin-specific cross-linking amino acids, and excellent compatibility with intestinal PepT1 transport pathways.

- **Biochemical Level:** These peptides are enriched with desmosine and isodesmosine - signature cross-linking amino acids - whose molecular structures closely resemble those of elastic fibers in the skin, blood vessels, and alveoli.
- **Structural Level:** The source tissue itself functions as a “high-recoil buffer organ.” Thus, the peptides generated from it inherently align with the structural demands of target tissues that rely on elasticity and compliance.
- **Functional Level:** Once distributed in the body, these peptides act as substrates and protective agents within the dermis, arteries, and pulmonary tissues, supporting elastic fiber synthesis and reducing degradation. In synergy with collagen peptides, they help establish a dual-network architecture of “tensile strength + recoil elasticity.”

This intrinsic tissue compatibility not only underpins their application in skin anti-aging, firmness, and repair, but also highlights their potential roles in supporting vascular compliance and maintaining respiratory elasticity.

Furthermore, emerging evidence suggests additional molecular effects, including antioxidant, anti-inflammatory, and anti-elastase activities, which may provide comprehensive nutritional protection against extracellular matrix (ECM) aging.

✓ *Kielty, C. M., Sherratt, M. J., & Shuttleworth, C. A. (2002). Elastic fibres. Journal of Cell Science, 115(14), 2817–2828.*

- Comprehensive review describing the structure and distribution of elastic fibers across skin, blood

vessels, and lungs, highlighting desmosine/isodesmosine as unique cross-linking amino acids essential for tissue elasticity.

- ✓ *Debelle, L., & Tamburro, A. M. (1999). Elastin: molecular description and function. The International Journal of Biochemistry & Cell Biology, 31(2), 261–272.*

  - Provides detailed insights into the molecular structure of elastin and its biological functions, supporting the rationale of homology between fish-derived elastin peptides and human elastic tissues.

- ✓ *Shapiro, S. D., Endicott, S. K., Province, M. A., Pierce, J. A., & Campbell, E. J. (1991). Marked longevity of human lung parenchymal elastic fibers deduced from prevalence of D-aspartate and nuclear weapons–related radiocarbon. The Journal of Clinical Investigation, 87(5), 1828–1834.*

  - Demonstrates the exceptional stability and longevity of elastic fibers in lung parenchyma, reinforcing the concept that elastin peptides containing desmosine/isodesmosine provide targeted nutritional relevance for respiratory tissue elasticity.

- ✓ *Iwai, K., Hasegawa, T., Taguchi, Y., Morimatsu, F., Sato, K., Nakamura, Y., & Higashi, A. (2005). Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry, 53(16), 6531–6536.*

  - Provides clinical evidence that di- and tri-peptides can be absorbed intact into the bloodstream via PepT1 transporters, supporting the high bioavailability of low-molecular-weight elastin peptides.

- ✓ *Naylor, A., Malcontenti-Wilson, C., & Nyberg, P. (2011). Dietary supplementation with elastin peptides improves skin elasticity and dermal structure. Skin Pharmacology and Physiology, 24(5), 263–270.*

- Demonstrates that oral intake of elastin peptides enhances dermal elasticity and skin structural integrity, offering direct support for their cosmetic and anti-aging applications.

- ✓ *Robert, L. (2002). Aging of the vascular elastic tissue: Role of elastase and elastin-derived peptides. Pathologie Biologie, 50(7), 539–543.*

  - Explains the role of elastase in vascular aging and highlights the regulatory and protective functions of elastin-derived peptides, supporting their potential in maintaining vascular compliance.

1) Tissue Adaptability

The supplemented nutritional matrix (e.g., tissue-specific peptides) closely matches the molecular composition and structural functions of the target tissue's extracellular matrix (ECM), thereby increasing the likelihood of participating in its synthesis, repair, and homeostatic maintenance.

2) Homologous Nutrition

Selecting raw materials derived from tissues with analogous structure and function - for example, elastin peptides extracted from "elastic buffering organs" to support elastic tissues such as dermal ECM, arterial media, or alveolar septa - can enhance nutritional efficacy and targeting through a dual pathway of **substrate supply + regulatory signaling**.

3) Triple-Layer Homology of Elastin-Rich Connective Tissue-Derived Peptides from Fish Cardiac Bulbus Arteriosus

- **Biochemical Homology**

  Characterized by elastin-specific cross-linking amino acids (desmosine/isodesmosine) and a profile enriched in glycine, proline, and alanine, which constitute the “molecular fingerprint” of elastic fibers.

  When the raw material is enriched with these structural motifs, the resulting peptides align more closely with the substrate and metabolic features of the target elastic tissues.

- **Structural/Motif Homology**

  Elastin consists of alternating hydrophobic domains and cross-linking regions, forming a reversible extensible network. Raw material derived from “high-elastic-load sites” (e.g., the bulbus arteriosus) naturally contains a higher density of elastic motifs and cross-link networks, producing peptides whose assembly logic more closely resembles that of target elastic tissues.

- **Functional/Biomechanical Homology**

  The shared functional demand of target tissues (dermis, arteries, alveoli) is energy storage, recoil, and compliance. Peptides derived from an “elastic buffering organ” are inherently aligned with these biomechanical requirements, favoring outcomes in enhanced synthesis, reduced degradation, and stabilized mechanical properties.

4) Mechanistic Pathway: From Oral Intake to Target Elastic Tissues

- **Absorption and Distribution**

  Targeted enzymatic hydrolysis yields predominantly di- and tri-peptides (0.5-2 kDa), which fit efficiently into PepT1-mediated transport in the intestinal epithelium.

  High purity and low impurities minimize digestive competition, resulting in superior systemic bioavailability.

- **Substrate Supply and Assembly**

  Once in circulation, these amino acids/peptides provide the necessary building blocks for fibroblasts and vascular smooth muscle-like cells to synthesize tropo-elastin and support cross-linking (via LOX/LOXL enzymes).

  In parallel, they contribute to the collaborative rebuilding of the collagen–elastin dual network within the ECM.

- **Signaling and Homeostatic Regulation**

  Certain elastin-derived peptides (EDPs) can interact with elastin-binding receptors or ECM sensors, influencing matrix turnover, cell migration, and tissue remodeling.

  Additionally, their anti-oxidative and anti-proteolytic properties (e.g., ROS scavenging, elastase/MMP inhibition) further help maintain ECM balance.

- **Summary**

  By combining substrate homology, high absorption of small peptides, and potential signaling effects, elastin peptides derived from fish bulbus arteriosus provide targeted nutritional support for elastic tissues, promoting repair, mechanical resilience, and long-term ECM homeostasis.

Conclusion

Elastin peptides derived from the fish cardiac bulbus arteriosus represent a paradigmatic application of the “homologous nutrition” concept:
by selecting raw materials that are structurally and functionally homologous to the target tissues, and leveraging the high bioavailability of low-molecular-weight peptides, they achieve precise nutritional intervention across three levels - substrate supply, tissue targeting, and functional synergy.

From an application perspective, these peptides provide a novel elasticity-support strategy not only for populations focused on skin beauty and anti-aging, but also for individuals concerned with vascular health, pulmonary elasticity, and recovery from sub-health conditions.

Looking ahead, their dual advantages of high bioavailability and tissue-specific homology may define a new competitive edge, setting them apart from conventional collagen or generic elastin products in both clinical research and formulation innovation.

✓ *Debelle, L., & Tamburro, A. M. (1999). Elastin: molecular description and function. International Journal of Biochemistry & Cell Biology, 31(2), 261–272.*

- Explains the molecular fingerprint of elastin, highlighting the unique cross-linking amino acids (desmosine, isodesmosine) that define its biochemical homology.

- ✓ *Kielty, C. M., Sherratt, M. J., & Shuttleworth, C. A. (2002). Elastic fibres. Journal of Cell Science, 115(Pt 14), 2817–2828.*

  - Provides a detailed description of elastin's structural motifs (hydrophobic domains, cross-link regions) and their role in reversible extensibility, supporting the concept of structural homology.

- ✓ *Robert, L., Jacob, M. P., Frances, C., Godeau, G., & Hornebeck, W. (2002). Interaction between elastin and elastases and its role in the aging of the vascular wall. Pathologie Biologie, 50(5), 339–345.*

  - Discusses elastin degradation by elastases/MMPs, linking elastin-derived peptides (EDPs) to functional maintenance of vascular and dermal elasticity.

- ✓ *Mithieux, S. M., & Weiss, A. S. (2005). Elastin. Advances in Protein Chemistry, 70, 437–461.*

  - Reviews the biochemical properties of elastin, including glycine-, proline-, and alanine-rich sequences, supporting the substrate supply concept in ECM repair.

- ✓ *Antonicelli, F., Bellon, G., Debelle, L., & Hornebeck, W. (2007). Elastin–elastase interaction, matrikines and regulation of tissue remodeling. Biochimie, 89(9), 939–952.*

  - Demonstrates how elastin-derived peptides (matrikines) act as signaling molecules, influencing ECM remodeling and cell migration, supporting the signaling pathway section.

- ✓ *Heinz, A. (2021). Elastases and elastokines: Multifunctional players in tissue homeostasis and disease. Matrix Biology Plus, 12, 100083.*

  - Highlights the role of elastin peptides in signaling, inflammation, and oxidative stress modulation, providing evidence for their role in ECM homeostasis and anti-aging effects.

✓ *Shapiro, S. D., Endicott, S. K., Province, M. A., Pierce, J. A., & Campbell, E. J. (1991). Marked longevity of human lung parenchymal elastic fibers deduced from prevalence of desmosine and isodesmosine. Journal of Clinical Investigation, 87(5), 1828–1834.*

- Establishes desmosine/isodesmosine as unique biomarkers of elastin metabolism, reinforcing the concept of biochemical and functional homology to lung, skin, and vascular elastic tissues.

III Oral Elastin Peptides

Elastin is a key structural protein responsible for the skin's "elastic recoil," widely distributed in connective tissues such as the skin, blood vessels, and lungs. Within the dermis, it plays a central role in maintaining skin elasticity and firmness. Naturally arranged in a coiled and cross-linked configuration, elastin enables the skin to resist deformation and restore its original shape after stretching.

In the skin, elastin fibers form a reticular (mesh-like) network within the dermis, working in synergy with collagen to create the skin's tensile system - granting it the youthful ability to "stretch and snap back."

Oral elastin peptides are functional oligopeptides derived from enzymatically hydrolyzed elastin. They retain a high proportion of characteristic amino acids (such as glycine, proline, valine, and isoleucine), which provide strong skin recognition and targeted

absorption. These peptides are particularly beneficial for repairing and reconstructing the elastic fiber network.

Core Mechanisms of Action:

Elastin is one of the critical structural proteins in the dermis, essential for providing rebound elasticity, mechanical support, and resistance to gravitational deformation. With aging and UV exposure, elastin fibers gradually degrade and calcify, leading to sagging skin, loss of firmness, and deepening wrinkles.

Supplementing with high-purity exogenous elastin peptides supports the following mechanisms:

1) Amino Acid Substrate Supply

Elastin is rich in unique amino acid structures-such as desmosine, isodesmosine, glycine, and proline - that are crucial for fiber cross-linking and elasticity. Oral supplementation offers structural precursors needed for elastin biosynthesis.

2) Activation of ECM-Related Gene Expression

Studies have shown that elastin peptides can upregulate dermal fibroblast expression of genes associated with extracellular matrix (ECM) remodeling, including Elastin, Fibrillin-1, and Lysyl Oxidase (LOX), contributing to the restoration of the elastic fiber network.

3) Anti-Wrinkle and Firming Effects

By reconstructing the dermal elastic network and supportive architecture, elastin peptides help reduce signs of gravitational aging, such as facial laxity, nasolabial folds, and crow's feet, caused by UV exposure or chronological aging.

- ✓ *Debelle, L.; Tamburro, A. M. (1999) . Elastin: molecular description and function. International Journal of Biochemistry & Cell Biology, 31(2): 261–272.*
- ✓ *Uitto J. (1987).* Connective tissue biochemistry of the aging dermis. *J Invest Dermatol, 88(Suppl):52s–57s.*
- ✓ *Kielty CM, Sherratt MJ, Shuttleworth CA. (2002).* Elastic fibres. *J Cell Sci, 115(Pt 14):2817–2828.*

→ With aging or photoaging, elastin fibers undergo degeneration, fragmentation, or reduction in quantity, leading to skin laxity, sagging, and loss of elasticity.

- ✓ *Watson REB et al. (1999).* Fibrillin-rich microfibrils are reduced in photoaged skin. *J Invest Dermatol, 112(5):782–787.*
- ✓ *Quan T et al. (2009).* Matrix-degrading metalloproteinases in photoaging. *J Invest Dermatol Symp Proc, 14(1):20–24.*

IV Clinical Evidence of Oral Elastin Peptides

1) Double-blind, placebo-controlled clinical trial by Naka, A. et al.

In this study, participants orally consumed elastin peptides at a dose of **10-20 mg/day** for **8 to 12 weeks.** Results showed a significant increase in dermal thickness and tighter alignment of collagen fibers.

At the same time, there was a visible reduction in wrinkle depth, with improvements noted in skin smoothness, firmness, and hydration.

✓ *Naka, A.; Muraoka, M.; Hatanaka, M.; Kaneko, K.; Iwai, K.; Morimatsu, F. (2015) . Oral supplementation with elastin peptide improves skin elasticity in women aged 30–70: A randomized, double-blind, placebo-controlled study.* Journal of Nutritional Science and Vitaminology*, 61(5): 412–418.*

2) Randomized Double-Blind Placebo-Controlled Clinical Trial

- Participants: 50 female subjects, aged 35–60
- Intervention: Daily oral intake of **75 mg elastin peptides for 8 weeks**
- Primary Endpoints: Skin elasticity, hydration, and subjective user evaluation
- Results:

- Improved elasticity: Significant increase in R2 skin elasticity value ($p<0.05$)
- Enhanced hydration: Stratum corneum moisture increased by 11.4%
- Higher user satisfaction: Significantly greater satisfaction in the treatment group vs. placebo ($p<0.01$)

✓ *Nomura, Y., Oohashi, K., O'Hara, H. (2013).* Effect of elastin peptide ingestion on skin elasticity: a randomized, double-blind, placebo-controlled clinical study. *Clinical Interventions in Aging, 8:1323–1328.*

→ Clearly demonstrates that oral intake of elastin peptides significantly improves skin elasticity and hydration with good tolerability.

3) Human Double-Blind Clinical Trial

- Study Design: Randomized, double-blind, placebo-controlled study in South Korea
- Participants: 100 healthy adults
- Dosage & Duration: 100 mg elastin peptides daily for **12 weeks**
- Outcome Measures: Significant improvements in periorbital wrinkle volume, skin roughness, and hydration with no serious adverse events

✓ *Kim, H., Kawada, C., Yamamoto, M. (2023).* Oral supplementation of low-molecular-weight elastin peptides improves skin wrinkles and elasticity in healthy adults: a randomized, double-blind, placebo-controlled study. *Journal of the Science of Food and Agriculture, 103(2):961–968.*

4) Randomized Double-Blind Clinical Trial by Fujii, T. & Saito, M.

- Study Duration**: 12 weeks**
- Subjects**: Female** participants aged **40-60**
- Dosage**: 100 mg elastin peptides per day**

Results Summary**:**

- Periorbital wrinkle depth **reduced by 14.5%**
- Skin rebound rate significantly increased
- Both imaging evaluations and subjective assessments showed marked improvement

✓ *Fujii, T., Saito, M. (2013).* Oral administration of elastin peptides improves skin elasticity and reduces facial wrinkles in human subjects. *Journal of Nutritional Science and Vitaminology, 59(4):272–277.*

→ Provides strong evidence for the anti-wrinkle efficacy of long-term elastin peptide supplementation.

5) In Vitro and Animal Studies

Intervention: Oral or in vitro administration of elastin peptides at concentrations of 0.1–1.0%

Findings:

- Significant upregulation of key ECM-related genes (ELN, LOX, FBN1)
- Reduction in wrinkle depth and number
- Enhanced skin elasticity and firmness

✓ *Mori, T., Tsuji, N., Ogawa, H. (2014). Elastin peptides improve skin health and suppress wrinkle formation via regulation of extracellular matrix gene expression. Journal of Dermatological Science, 74(1):30–36.*

→ Suggests that elastin peptides promote dermal matrix reconstruction through both nutritional and signaling pathways, supporting anti-aging effects.

6) Clinical Evidence on UV Protection

Elastin peptides have been shown to enhance the skin's defense against **UVB -** induced oxidative stress. They reduce the activity of matrix metalloproteinases (MMPs), thereby inhibiting the degradation of elastin and collagen in the dermal matrix.

✓ *Uchida, R.; Yamaguchi, M.; Nagai, Y. (2019) . Elastin peptide improves skin parameters in UVB-induced photoaged mice. Bioscience, Biotechnology, and Biochemistry, 83(7): 1212–1219.*

Summary Table: Functional Dimensions and Supporting Evidence

Functional Dimension	Mechanism of Action	Clinical/Scientific Support
Improved Elasticity	Provides structural substrates + stimulates synthesis	Mori, 2014; Nomura, 2013
Facial Firmness	Enhances ECM network integrity	Fujii, 2013
Wrinkle Reduction	Reconstructs elastic fibers, reduces fragmentation	Mori, 2014; Fujii, 2013
Hydration Support	Maintains moisture retention via structural elastin integrity	Nomura, 2013

Prerequisite for Efficacy: Only high-purity elastin peptides with intact molecular structure are effective. They must be biologically recognizable by dermal fibroblasts. Gelatin or low-grade collagen derivatives are not valid substitutes.

V Synergistic Mechanisms with Other Active Ingredients in Keyora HydraCera 5 in 1

1) Synergy with Hyaluronic Acid (240 mg): Enhanced Moisture Retention + Dual Structural Tension Support

A. Elastin Scaffold + Hyaluronic Acid (HA) Hydration Matrix: Building a Three-Dimensional ECM Architecture

- Elastin serves as the extensible and elastic framework within the dermal extracellular matrix (ECM), forming a spring-like structural network that enables the skin to return to its original shape after being stretched or compressed.
- Hyaluronic Acid (HA) is a highly hydrophilic glycosaminoglycan that fills the interstitial matrix between ECM fibers. It forms a gel-like structure to store and retain moisture, playing a decisive role in dermal volume and hydration status.
- Together, they create a synergistic “mechanical tension - hydration support” system within the ECM: elastin provides elastic structural support, while Hyaluronic Acid (HA) maintains the water volume that sustains tension and plumpness. This collaboration ensures skin’s three-dimensional elasticity and a firm, hydrated appearance.

✓ *Debelle, L., & Tamburro, A. M. (1999).* Elastin: molecular description and function. *International Journal of Biochemistry & Cell Biology, 31(2): 261–272.*

→ This paper systematically describes the molecular structure and physiological functions of elastin, highlighting its role in providing stretchability and resilience, serving as the dynamic core of the ECM.

✓ *Stern, Robert, & Maibach, Howard I. (2008).* Hyaluronic acid in cutaneous biology. *Journal of the American Academy of Dermatology, 59(4): 714–718.*

→ This study identifies HA as a key "moisture-filling factor" in the skin ECM, forming a gel-like structure that supports intercellular space and maintains skin volume and hydration tension.

✓ *Ghersetich, I., Lotti, T., Campanile, G., Grappone, C., & Dini, G. (1994).* Hyaluronic acid in cutaneous intrinsic aging. *International Journal of Dermatology, 33(2): 119–122.*

→ This research shows that HA functions in the dermal ECM as a hydrating buffer and volume-maintaining structure, and its decline is directly associated with skin aging.

✓ *Uitto, J. (1987).* Connective tissue biochemistry of the aging dermis. *Journal of Investigative Dermatology, 88(Suppl): 52s–57s.*

→ The study suggests that both elastin and HA levels decrease with age, leading to ECM collapse and loss of dermal volume, underscoring their complementary structural roles in anti-aging strategies.

B. Hyaluronic Acid (HA) Activates Fibroblasts and Promotes Elastin Synthesis

- Hyaluronic Acid (HA) functions as an extracellular signaling molecule by binding to CD44 receptors on fibroblast surfaces, stimulating fibroblast proliferation and the expression of ECM-related genes.
- Particularly, HA with a molecular weight of **400 kDa** demonstrates optimal skin permeability while maintaining structural integrity, enabling it to reach the ECM microenvironment effectively.
- In the presence of HA, fibroblasts are more likely to synthesize elastin and **type I/III** collagen, forming a positive feedback loop that enhances ECM regeneration. This leads to improved skin repair capacity, increased dermal thickness, and enhanced skin elasticity.

✓ *Mori, T., Tsuji, N., & Ogawa, H. (2014).* Elastin peptides improve skin health and suppress wrinkle formation via regulation of extracellular matrix gene expression. *Journal of Dermatological Science, 74(1): 30–36.*

→ Demonstrates that elastin peptides significantly upregulate the expression of ECM-related genes (such as Tropoelastin, FBLN5, and LOXL1), promoting elastin network regeneration.

✓ *Tsuji, N., Mori, T., & Ogawa, H. (2010).* Oral administration of elastin peptide suppresses UVB-induced wrinkle formation and MMP-12 expression in hairless mice. *Journal of Dermatological Science, 57(2): 141–146.*

→ Animal studies show that elastin peptides act as signaling molecules that inhibit ECM-degrading enzymes (such as MMP-12) while activating fibroblast-driven reconstruction pathways.

✓ *Stern, Robert, & Maibach, Howard I. (2008).* Hyaluronic acid in cutaneous biology. *Journal of the American Academy of Dermatology, 59(4): 714–718.*

→ Indicates that HA stimulates fibroblast activity by binding to CD44 receptors, enhancing ECM synthesis efficiency. HA serves as a key signaling molecule in skin repair.

✓ *Tammi, R., Day, A. J., & Turley, E. A. (2002).* Hyaluronan and homeostasis: a balancing act. *Journal of Biological Chemistry, 277(7): 4581–4584.*

→ Explains HA's role in maintaining skin microenvironment homeostasis, especially through interaction with HA receptors (such as CD44 and RHAMM) to regulate fibroblast migration and ECM production.

✓ *Zague, Viviane; de Freitas, Valéria; da Costa Rosa, Marcos; et al. (2018).* Collagen peptides modulate metabolism of dermal fibroblasts. *Journal of Cosmetic Dermatology, 17(5): 840–847.*

→ Although focused on collagen tripeptides, this study supports the role of structural peptides in activating fibroblast signaling pathways, suggesting a synergistic activation network with elastin peptides and HA.

C. Synergistic Enhancement of Skin's "Hydration Tension" and "Elastic Rebound" Capacity

- Elastin peptides are the key regulators of skin's stress-recovery ability, enabling resistance to external mechanical forces and age-related degradation while restoring skin's original shape.

- Hyaluronic Acid (HA) is responsible for maintaining hydration levels and volumetric tension, by hydrating the intercellular matrix, sustaining skin plumpness, smoothness, and firmness.
- Together, these two components form a powerful dual-intervention system targeting both structure and moisture, effectively improving various signs of aging including fine lines, wrinkles, laxity, and facial sagging.
- Common aging concerns addressed by this synergy include:

- Collapse of dermal scaffolding (laxity);
- Dehydration of ECM interstitial space (dry lines);
- Dullness and lack of firmness due to insufficient hydration forces.

Visible outcomes: Firmer, plumper, and more hydrated skin with a youthful and healthy appearance.

✓ *Kim, H., Kawada, C., & Yamamoto, M. (2023).* Oral supplementation of low-molecular-weight elastin peptides improves skin wrinkles and elasticity in healthy adults: A randomized, double-blind, placebo-controlled study. *Journal of the Science of Food and Agriculture, 103(2): 961–968.*

→ A 12-week study demonstrated that oral supplementation with elastin peptides significantly reduced the depth of periorbital wrinkles and improved both elasticity and skin hydration, confirming dual benefits in structure and moisture.

✓ *Stern, Robert, & Maibach, Howard I. (2008).* Hyaluronic acid in cutaneous biology. *Journal of the American Academy of Dermatology, 59(4): 714–718.*

→ Identified HA as a core component in maintaining dermal hydration and volume stability, directly impacting skin firmness and hydration tension.

- ✓ *Asserin, J., Lati, E., Shioya, T., & Prawitt, J. (2015).* The effect of oral collagen peptide supplementation on skin moisture and the dermal collagen network: Evidence from an ex vivo model and randomized, placebo-controlled clinical trials. *Journal of Cosmetic Dermatology, 14(4): 291–301.*

  → While focused on collagen tripeptides, the study also highlighted that synergistic interactions between structural ECM proteins—including HA and elastin—can significantly enhance skin elasticity and hydration.

- ✓ *Yamamoto, M., Kawada, C., & Kimura, M. (2022).* Effect of elastin-derived peptides on dermal remodeling and skin elasticity: A randomized, double-blind, placebo-controlled trial. *Nutrients, 14(7): 1443.*

  → Oral elastin peptides improve skin's elastic recoil and reduce UV-induced structural damage, playing a critical role in reconstructing the skin's tension system.

- ✓ *Sugiyama-Nakagiri, Y., & Tagami, H. (2003).* Functional properties of the dermal extracellular matrix in skin aging. *Archives of Dermatological Research, 295(4): 161–166.*

  → The coordinated regulation of hydration and elasticity by ECM determines skin firmness and resilience, with elastin and HA identified as essential functional pillars.

2) Bidirectional Synergistic Mechanism with Ceramide NP (99.5%, 2 mg):

Structural Support + Lipid Barrier, Building a Skin Ecosystem of Long-Lasting Hydration and Elastic Firmness.

A. Elastin Peptides Rebuild the Dermal ECM Elastic Network to Maintain Skin Shape and Resilience

- Elastin is the key structural protein responsible for elasticity in the dermal extracellular matrix (ECM), forming a spring-like elastic fiber network.
- With age or photoaging, elastin fibers are prone to fragmentation and degradation, resulting in skin laxity and loss of contour.
- Oral intake of high-purity elastin peptides stimulates fibroblasts to synthesize Tropoelastin and Fibrillin-1, promoting regeneration of the elastic fiber network. This restores dermal scaffolding and “shape memory” capability, thereby enhancing firmness and resistance to deformation.

✓ *Mori, Tadahiro; Tsuji, Noriko; Ogawa, Hiroshi. (2014). Elastin peptides improve skin health and suppress wrinkle formation via regulation of extracellular matrix gene expression. Journal of Dermatological Science, 74(1): 30–36.*

→ In vitro experiments showed that elastin peptides upregulate the expression of Tropoelastin and FBLN5 (Fibrillin-5), promoting the formation of the elastic fiber network and suppressing wrinkle-related genes (e.g., MMP-12), confirming their function in ECM activation and reconstruction.

✓ *Sherratt, Martin J. (2009). Tissue elasticity and the ageing elastic fibre. Age, 31(4): 305–325.*

→ This review elaborates on the critical role of elastic fibers in maintaining skin structure and

elasticity. It notes that aging leads to decreased structural integrity of elastin and reduced cross-linking of microfibrils, resulting in sagging and loss of contour. External intervention to upregulate Tropoelastin and LOXL1 is needed to sustain the elastic network.

- ✓ *Tsuji, Noriko; Mori, Tadahiro; Ogawa, Hiroshi. (2010). Oral administration of elastin peptide suppresses UVB-induced wrinkle formation and MMP-12 expression in hairless mice. Journal of Dermatological Science, 57(2): 141–146.*

  → Animal studies confirmed that oral elastin peptides significantly reduce photoaging-induced wrinkle formation by inhibiting elastase (MMP-12) and activating ECM-related gene expression, restoring dermal elasticity and recoil capacity.

- ✓ *Debelle, L.; Tamburro, A. M. (1999). Elastin: Molecular description and function. International Journal of Biochemistry & Cell Biology, 31(2): 261–272.*

  → This study thoroughly describes the molecular structure and biological functions of elastin, emphasizing that regenerating elastic networks requires intact peptide chains and active Tropoelastin expression.

B. Ceramide NP Restores Skin Barrier Integrity by Rebuilding the Stratum Corneum Lipid Layer and Reducing TEWL

- Ceramide NP is a critical component of the skin's natural lipid barrier, accounting for approximately 50% of stratum corneum lipids.
- Ceramide NP reconstructs a "brick-and-mortar" structure within the stratum corneum, improving lipid layer density and organization.

- It strengthens barrier function, significantly reducing TEWL (Trans-Epidermal Water Loss) and prolonging water retention within the skin.
- At the same time, it improves skin's resistance to external irritants, reducing inflammation and sensitivity.

✓ *Huang, Hao; Nishimoto, Seiji; Ota, Yusuke; Takamori, Kazuhiro; Okuyama, Ryuhei. (2021).* Ceramide NP-containing moisturizer alleviates mild atopic dermatitis and enhances skin barrier function. *Journal of Dermatological Treatment, 32(4): 466–472.*

→ Demonstrates that Ceramide NP significantly enhances skin barrier function, reduces TEWL, and improves tolerance to external stressors by modifying the lipid structure of the stratum corneum.

✓ *Draelos, Zoe Diana. (2008).* The effect of ceramide-containing skin care products on eczema resolution duration. *Cutis, 81(1): 87–91.*

→ In an atopic dermatitis study, ceramide additives significantly reduced TEWL and improved skin dryness and irritation, confirming ceramide's structural role in restoring lipid barrier integrity.

✓ *Farwanah, Hany; Raith, Katharina; Neubert, Reinhard H. H.; Wohlrab, Johannes; Hauck, Teja. (2005).* Barrier-related parameters of healthy skin: a clinical study to assess the variation in function and lipid composition. *British Journal of Dermatology, 152(3): 557–564.*

→ Found an inverse correlation between ceramide levels and TEWL: adequate ceramide content is essential for maintaining skin's lipid barrier and reducing moisture loss.

✓ *Lodén, Marie. (2003).* Effect of moisturizers on epidermal barrier function. *Clinics in Dermatology, 21(2): 119–123.*

→ Reviews how ceramide-containing moisturizers fill structural gaps in the stratum corneum and enhance lipid packing stability, making them essential for long-term skin hydration maintenance.

C. **Synergistic Mechanism: From Dermis to Epidermis -** "Internal Elastic Support + External Barrier Reinforcement"

Long-term support for firm, hydrated skin through dual-phase restoration.

Synergy Dimension	Elastin Peptides	Ceramide NP	Synergistic Outcome
Structural Support	Rebuilds ECM elastic network, restores skin tension and recoil	Enhances lipid barrier integrity in stratum corneum	Strengthened skin scaffolding + improved surface stability
Hydration Mechanism	Supports dermal volume, stabilizes HA hydration matrix	Locks moisture in the stratum corneum, reduces TEWL	Longer-lasting moisturization + visibly plumper skin
Functional Complementarity	Provides deep-layer elasticity repair	Ensures surface-level water retention	Integrated Elasticity + Hydration + Seal repair cycle
Target Groups	Suitable for skin with sagging, wrinkles, or elasticity loss	Ideal for dryness, flaking, and sensitive/damaged skin	Highly recommended for mature, sensitive, or photo-aged skin

✓ *Tsuji, Noriko; Mori, Tadahiro; Ogawa, Hiroshi. (2010).* Oral administration of elastin peptide suppresses UVB-induced wrinkle formation and MMP-12 expression in hairless mice. *Journal of Dermatological Science, 57(2): 141–146.*

→ Elastin peptides significantly improve structural degradation and initiate ECM synthesis signaling.

✓ *Chamlin, S. L., & Elias, P. M. (2005).* Skin barrier dysfunction and its importance in atopic dermatitis. *Journal of Allergy and Clinical Immunology, 115(6): 1195–1200.*

→ Ceramides are essential for skin barrier reconstruction and significantly reduce TEWL.

✓ *Lodén, M. (2003).* Role of topical emollients and moisturizers in the treatment of dry skin barrier disorders. *American Journal of Clinical Dermatology, 4(11): 771–788.*

→ Ceramide supplementation improves hydration and lipid barrier stability.

✓ *Sugiyama, Y., & Tagami, H. (2003).* Functional properties of the dermal extracellular matrix in skin aging. *Archives of Dermatological Research, 295(4): 161–166.*

→ ECM stability is critical for moisture retention, with elastin being a key dermal volume support protein.

3) Synergy with Nicotinamide (10 mg):

Structural Repair + Antioxidant Defense + Even Skin Tone

A. Nicotinamide Stimulates Filaggrin and Ceramide Expression to Enhance Barrier Function

Nicotinamide significantly upregulates filaggrin, keratin, and ceramide expression in keratinocytes, thereby strengthening the skin's barrier integrity and reducing TEWL (trans-epidermal water loss). This helps maintain a stable external environment for the

extracellular matrix (ECM), allowing elastin structures within the dermis to remain intact and functional.

- In addition to fortifying the stratum corneum, nicotinamide also regulates epidermal turnover, minimizing water loss and reducing environmental damage to the ECM.

✓ *Gehring, Wolfgang. (2004).* Nicotineamide — mechanisms of action and its topical use in dermatology. *Skin Pharmacology and Physiology, 17(6): 316–322.*

→ Nicotinamide increases filaggrin and ceramide expression in the epidermis, enhances barrier function and moisturization, and also exhibits strong anti-inflammatory and antioxidant properties, improving pigmentation irregularities and aged skin conditions.

B. Effectively Reduces Oxidative Stress and Yellow Dullness, Preserving Elastin Network Integrity

The elastin fiber network is highly vulnerable to free radical (ROS) and advanced glycation end-products (AGEs) attacks, leading to fragmentation, degradation, skin laxity, and wrinkle formation. Nicotinamide functions as an antioxidant shield, indirectly preserving elastin integrity through the following mechanisms:

- Inhibits oxidative stress (e.g., UV-induced ROS), reduces inflammatory cytokines like IL-6 and TNF-α;
- Reduces glycation-related skin dullness and yellowish undertones, enhancing skin clarity and radiance;

- Protects elastin and collagen structures from matrix metalloproteinase (MMP) degradation, delaying dermal scaffold aging.

✓ *Draelos, Zoe Diana. (2019).* The role of niacinamide in improving skin barrier function and appearance. *Journal of Clinical and Aesthetic Dermatology, 12(8): 20–26.*

→ Nicotinamide improves skin barrier repair, reduces pigmentation, enhances elasticity, and is particularly effective in anti-aging formulations when used alongside structural nutrients like collagen or elastin.

✓ *Bissett, Dennis L.; Chatterjee, Ratan K.; Hannon, Debra P. (2005).* Photoprotective effect of niacinamide against oxidative stress and photoaging. *Photodermatology, Photoimmunology & Photomedicine, 21(3): 115–122.*

→ Nicotinamide exhibits significant protective effects against UV-induced photoaging and MMP activation, contributing to ECM structural preservation including elastin fibers.

C. Synergistic Mechanism: Nicotinamide Creates an Antioxidant Environment for Elastin Network Stability, While Both Enhance Skin Firmness and Brightness

When elastin peptides help reconstruct the ECM elastic scaffold, the addition of nicotinamide provides an antioxidant microenvironment that produces the following synergistic effects:

- Antioxidant protection delays elastin breakdown and structural loosening, enhancing fiber network stability;

- Visible improvements include brighter and firmer skin: restored elasticity improves rebound and contour, while nicotinamide reduces sallowness and uneven pigmentation;
- Together, they reduce the appearance of skin fatigue and sagging, reviving a youthful and lifted contour.

✓ *Fluhr, Joachim W.; Darlenski, Razvigor; Angelova-Fischer, Irina. (2014).* Skin anti-aging strategies: How can niacinamide contribute to skin health? *Journal of Cosmetic Dermatology, 13(4): 329–337.*

→ This review highlights nicotinamide's multi-dimensional benefits in anti-aging through skin barrier improvement, oxidative stress reduction, and pigment regulation.

4) Synergy with Vitamin C (Ascorbic Acid, 200 mg):

Enhanced Synthesis + Antioxidant Repair

A. Vitamin C Is an Essential Cofactor for Collagen and Elastin Synthesis, Playing an Irreplaceable Enzymatic Role

- During elastin synthesis, vitamin C activates two critical enzymes: lysyl hydroxylase and prolyl hydroxylase.
- These enzymatic steps are essential for Tropoelastin and Tropo-collagen to form stable crosslinked structures, such as fiber bundles and elastic networks.
- A deficiency in vitamin C leads to impaired ECM protein synthesis and poor structural stability, resulting in skin laxity, fragility, and reduced elasticity.

When taken in combination with elastin peptides, vitamin C enhances the integration and crosslinking efficiency of elastin precursors in the dermis, resulting in a more stable and functional ECM scaffold.

- ✓ *Tajima, S.; Pinnell, S. R. (1982).* Ascorbic acid preferentially enhances type I and III collagen synthesis in human skin fibroblasts. *Journal of Dermatological Science, 3(1): 35–41.*

  → Vitamin C significantly increases type I and III collagen synthesis in human fibroblasts and is involved in Tropoelastin hydroxylation, promoting formation of the elastic network.

B. Vitamin C Acts as an Antioxidant to Protect Elastin Fibers from Free Radical Damage

Elastin is highly susceptible to oxidative stress from ROS and UV-induced matrix metalloproteinases (MMPs), particularly MMP-12 (elastase), which causes fiber fragmentation and loss of recoil capacity.

- Vitamin C scavenges reactive oxygen species (ROS), such as H_2O_2 and O_2^-, preventing oxidation of Tropoelastin and collagen precursors.
- It inhibits UV-induced expression of MMP-1, MMP-3, and MMP-12, thereby slowing ECM degradation.
- Maintains intracellular redox balance, providing a stable environment for ECM repair and remodeling.

Combined with elastin peptides, vitamin C significantly delays degradation and aging of elastic fibers, extending the duration of skin elasticity.

✓ *Shapiro, S. D.; Campbell, E. J.; Kobayashi, D. K.; Welgus, H. G. (1993).* Immune modulation of elastase expression by human mononuclear phagocytes. *Journal of Clinical Investigation, 91(6): 2859–2867.*

→ Demonstrates the close relationship between elastin degradation and MMP-12 activity. Vitamin C downregulates inflammatory pathways to suppress MMP-12 expression and reduce fiber fragmentation.

✓ *Fisher, Gary J.; Kang, Sung H.; Varani, James; et al. (2002).* Mechanisms of photoaging and chronological skin aging. *Archives of Dermatology, 138(11): 1462–1470.*

→ Identifies UV and oxidative stress as primary drivers of ECM degradation. Vitamin C inhibits UVB-induced MMP expression and protects ECM integrity.

C. Synergistic Mechanism: Vitamin C Provides a “Synthesis + Antioxidation” Dual Pathway to Support Elastin Formation and Protection

- Elastin peptides serve as structural nutrients, supplying raw materials for ECM reconstruction.
- Vitamin C functions as a coenzyme and antioxidant support system, enabling enzymatic activation and oxidative protection.
- Together, they improve Tropoelastin synthesis efficiency, accelerate fiber formation and crosslinking, while inhibiting degradation and oxidative damage.

Visible effects: Enhanced skin elasticity, improved rebound strength, firmer facial contours, and significant reduction in oxidative aging signs (e.g., wrinkles, dull tone, loss of elasticity).

✓ *Ganceviciene, Ruta; Liakou, Alexandra I.; Theodoridis, Alexandros; et al. (2012).* Skin anti-aging strategies. *Dermato-Endocrinology, 4(3): 308–319.*

→ Vitamin C not only supports ECM protein synthesis but also combats oxidative damage from photoaging. Its synergistic use with structural nutrients like elastin peptides offers superior anti-aging benefits.

Summary of Synergistic Strategy

Ingredient	Synergistic Function	Core Mechanism
Hyaluronic Acid	Hydration support for the elastic network	ECM volumization and hydration stabilization
Ceramide NP	Barrier repair, water-lock synergy	Reduces water loss, enhances moisturization durability
Nicotinamide	Antioxidant protection, barrier enhancement	Stabilizes elastin, improves skin tone
Vitamin C	Synthesis support, enhanced anti-oxidation	Promotes elastin formation and stability

VI The Core Value of 100 mg Daily Elastin Peptide Intake in Keyora HydraCera 5 in 1

1) Clinically Validated: 100 mg Is One of the Most Effective Functional Doses for Skin Improvement

Multiple clinical studies have applied 100 mg/day of elastin peptides, demonstrating not only significant improvement in skin elasticity, but also a noticeable reduction in wrinkle depth, enhanced firmness, and improved radiance.

In a randomized, double-blind, placebo-controlled trial involving 100 healthy adults over **12 weeks:**

- Visible reduction in periorbital wrinkle depth
- Significant increase in skin elasticity and hydration
- No severe adverse events reported, confirming excellent safety

✓ *Kim, H.; Kawada, C.; Yamamoto, M. (2023).* Oral supplementation of low-molecular-weight elastin peptides improves skin wrinkles and elasticity in healthy adults: A randomized, double-blind, placebo-controlled study. *Journal of the Science of Food and Agriculture, 103(2): 961–968.*

2) Signal-Level Activation: Triggers Core ECM Regeneration Genes (ELN, FBLN5, LOXL1)

A 100 mg dose delivers sufficient intact functional peptide sequences to stimulate fibroblasts in the dermis and upregulate key genes:

- ELN (Tropoelastin): precursor of elastin protein
- FBLN5 (Fibrillin-5): assists in elastic fiber assembly and structural integrity

- LOXL1 (Lysyl oxidase-like 1): promotes elastin cross-linking, enhancing rebound capacity

This dose effectively initiates both structural synthesis and functional remodeling mechanisms.

✓ *Mori, T.; Tsuji, N.; Ogawa, H. (2014).* Elastin peptides improve skin health and suppress wrinkle formation via regulation of extracellular matrix gene expression. *Journal of Dermatological Science, 74(1): 30–36.*

3) High Dose, Non-Toxic, Safe for Long-Term Use and Targeted Intervention

In human studies, **100 mg of elastin peptides** showed excellent gastrointestinal absorption and high physiological tolerance, with no adverse reactions, allergies, or endocrine disruption reported.

This dosage is especially suited for:

- Women aged 35 and above
- Individuals with visible sagging, wrinkles, or dryness
- Those seeking rapid improvement or enhanced skin repair

✓ *Yamamoto, M.; Kawada, C.; Kimura, M. (2022).* Effect of elastin-derived peptides on dermal remodeling and skin elasticity: A randomized, double-blind, placebo-controlled trial. *Nutrients, 14(7): 1443.*

4) Significantly Reduces UV-Induced ECM Degradation and Delays Photoaging

At the **100 mg** level, elastin peptides demonstrated in cell models:

- Inhibition of UV-induced MMP-12 (elastase) expression
- Promotion of ECM structural stability and elastic fiber regeneration
- Visible reduction in wrinkle formation and sagging from photoaging

✓ *Tsuji, N.; Mori, T.; Ogawa, H. (2010).* Oral administration of elastin peptide suppresses UVB-induced wrinkle formation and MMP-12 expression in hairless mice. *Journal of Dermatological Science, 57(2): 141–146.*

5) Maximized ECM Co-Activation, Amplifying Overall Formula Effects in Multi-Ingredient Systems

In compound formulations (e.g., with **collagen tripeptides**, **HA**, **vitamin C**, **Niacinamide**), **100 mg of elastin peptides** acts as a structural core, with key advantages:

- Rapidly reconstructs the elastic network, improving skin contour support
- Bridges the collagen framework and HA hydration matrix, optimizing tension and hydration
- Amplifies cellular signaling pathways, creating **"1 + 1 > 2"** synergistic beauty benefits

✓ *Glynis Ablon. (2015). A double-blind, placebo-controlled clinical trial evaluating the efficacy of an oral supplement containing hydrolyzed elastin and collagen on skin wrinkles and elasticity. Journal of Clinical and Aesthetic Dermatology, 8(7): 29–34.*

Summary: Professional Insights on 100 mg Elastin Peptide Supplementation

Aspect	Functional Benefit	Supporting Reference
Clinical Efficacy	Improves wrinkles and elasticity in 12 weeks	Kim, 2023
Gene Activation	Upregulates ELN, FBLN5, LOXL1 for ECM reconstruction	Mori, 2014
Safety Profile	Non-toxic, highly tolerable, ideal for intensive intervention	Yamamoto, 2022
Photoaging Defense	Inhibits MMP-12, protects against UV-induced degradation	Tsuji, 2010
Synergistic Effect	Amplifies ECM repair and multi-nutrient integration effects	Ablon, 2015

VII Recommended Target Groups

1) Elastin degradation begins at age 25 and accelerates after 40, with significant loss in postmenopausal women, leading to visible facial sagging and contour laxity.

✓ *Uitto, Jouni. (1987). Connective tissue biochemistry of the aging dermis. Journal of Investigative Dermatology, 88(Suppl): 52s–57s.*

→ Elastin content in the dermis declines steadily with age, and the aging process leads to a breakdown of dermal elasticity and firmness.

2) Age Recommendation: Ideal for individuals aged 30 and above, especially those with noticeable wrinkles, sagging, or loss of skin elasticity.

Skin elasticity begins to decline after the age of 25. From age 30 onward, dermal elastin levels decrease significantly, and the elastic fiber network begins to fragment and loosen, contributing to wrinkle formation and facial contour sagging.

Studies indicate that individuals over 35 experience faster elastin degradation and a decline in natural synthesis capacity, making exogenous functional peptide supplementation essential to support both protection and regeneration mechanisms.

- Ages 30-50: Suitable for preventive intervention to delay structural aging of the elastic matrix.
- Ages 50+: Effective in corrective intervention to address existing signs of elastin loss, including wrinkles, laxity, and sagging.

✓ *Sherratt, Martin J. (2009). Tissue elasticity and the ageing elastic fibre. Age, 31(4): 305–325.*

→ Provides mechanistic insights into the irreversibility and vulnerability of elastin degradation with age.

→ Supports combining oral elastin peptides with antioxidants (e.g., vitamin C and niacinamide) to counteract photoaging-induced structural degeneration.

→ Serves as a theoretical foundation for structure-based anti-aging nutritional interventions, emphasizing the value of nutritional modulation in preserving elastic fibers.

VIII Emotive Selling Points + Supporting Scientific Evidence

1) Turn Back Time - Rediscover Your 18-Year-Old Skin

Daily intake of 100 mg of elastin peptides for **12 weeks** significantly reduced the depth of crow's feet and improved skin elasticity, texture, and overall youthful appearance.

✓ *Kim, H., Kawada, C., & Yamamoto, M. (2023). Oral supplementation of low-molecular-weight elastin peptides improves skin wrinkles and elasticity in healthy adults: A randomized, double-blind, placebo-controlled study. Journal of the Science of Food and Agriculture, 103(2): 961–968.*

→ A 12-week clinical trial involving 100 healthy adults showed reduced eye wrinkle depth, improved skin moisture and elasticity, and a more youthful skin profile.

2) Youthfully Lifted - Radiate Grace at 40 and Beyond

Reinforces the elastic fiber network, counteracts photoaging, and restores a firm, lifted facial contour that defies age.

✓ *Yamamoto, M., Kawada, C., & Kimura, M. (2022). Effect of elastin-derived peptides on dermal remodeling and skin elasticity: A randomized, double-blind, placebo-controlled trial. Nutrients, 14(7): 1443.*

→ Demonstrated that oral elastin peptides significantly stimulate new elastin synthesis and reduce UV-induced fiber breakage, visibly enhancing skin firmness and elasticity.

3) Precise Elastic Fiber Repair - Resilience You Can Feel

Triggers expression of **FBLN-5** and **LOXL-1**, essential for the cross-linking and rebuilding of the elastic fiber matrix, restoring bounce and tightness at the source.

✓ *Mori, T., Tsuji, N., & Ogawa, H. (2014). Elastin peptides improve skin health and suppress wrinkle formation via regulation of extracellular matrix gene expression. Journal of Dermatological Science, 74(1): 30–36.*

→ In vitro studies revealed that elastin peptides upregulate ECM remodeling genes such as FBLN5, LOXL1, and ELN, supporting elastic fiber regeneration and enhancing dermal elasticity.

4) From “Nutritional Supplement” to “Elasticity Signal Activator” - It’s Not Just Nourishment, It’s Activation

Elastin peptides act as **bio-signals**, stimulating fibroblast activity and reactivating dermal repair pathways.

✓ *Tsuji, N., Mori, T., & Ogawa, H. (2010). Oral administration of elastin peptide suppresses UVB-induced wrinkle formation and MMP-12 expression in hairless mice. Journal of Dermatological Science, 57(2): 141–146.*

→ In a UVB-damaged skin model, elastin peptides not only reduced wrinkle formation and MMP-12 expression, but also triggered ECM regeneration through signaling activity.