

Gly-Pro-Hyp Enriched Hydrolysed Collagen Tripeptides - Rapid Absorption, Fibroblast Signaling, and Evidence-Based Efficacy for 8-12 Weeks Improvements in skin Hydration, Elasticity, and Facial Wrinkles, Fine Line Reduction with Clinically Measurable Results

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Abstract

Hydrolysed Collagen Tripeptides (CTPs) are minimal bioactive signal units - exemplified by Gly-Pro-Hyp that outperform generic collagen hydrolysates as they preserve sequence integrity, cell recognition, and downstream signaling.

Following oral intake, CTPs are absorbed intact via PEPT1, appear in plasma within 30-60 min, and reach dermal tissue where they engage fibroblast receptors (e.g., CD44, $\alpha 2\beta 1$, DDR1/2) and activate TGF- β /Smad and MAPK/ERK pathways.

This drives a consistent signal \rightarrow synthesis \rightarrow remodeling cascade, upregulating *type I* collagen, elastin, and hyaluronic acid, with clinically relevant outcomes - skin hydration / elasticity gains and wrinkle-depth reduction - typically observed within 8-12 weeks at ~1,000-2,500 mg/day.

Performance is spec-dependent: high Gly-Pro-Hyp content ($\geq 50\%$) and Pro + Hyp 25-30%

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correlate with superior pharmacokinetics and effect sizes, while undefined peptides or free amino acids lack targeted signaling and reproducibility.

In multi-ingredient systems, CTPs synergize with elastin peptides and hyaluronic acid rebuild the dermal tension-and-recoil network. Collectively, Gly-Pro-Hyp - enriched CTPs constitute a precision nutricosmetic modality coupling rapid systemic delivery with receptor-mediated ECM regeneration for visible anti-aging benefits.

Keywords

Hydrolysed Collagen tripeptide (CTP); Gly-Pro-Hyp; PEPT1 absorption; fibroblast signaling; TGF- β /Smad; MAPK/ERK; extracellular matrix (ECM) remodeling; skin hydration; skin elasticity; wrinkle reduction; Fine Line Reduction; skin firmness; anti-aging; collagen synthesis; Facial Rejuvenation

I Hydrolysed Collagen Tripeptides

Hydrolysed Collagen Tripeptides are specific short-chain peptides composed of three amino acids, typically in the sequence **Gly-X-Y** or **Gly-Pro-Hyp**. They are considered functional bioactive fragments naturally produced during enzymatic degradation of native collagen.

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With an average molecular weight of 300-500 Da, these peptides are characterized by high stability and biological activity.

✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry. 2005;53(16):6531–6536.*

1) Core Signaling Molecules for Skin Regeneration

Hydrolysed Collagen Tripeptides are not merely structural units of collagen; they function as key signaling molecules recognized by the body in response to collagen degradation or loss.

After oral ingestion, Hydrolysed Collagen Tripeptides can cross the intestinal epithelial barrier intact within **30-60 minutes**, enter systemic circulation, and be detected in human plasma.

Once in circulation, they are selectively delivered to dermal tissue, where they bind to receptors on fibroblasts, including CD44, $\alpha 2\beta 1$ integrins, and DDRs (Discoidin Domain Receptors). This binding triggers intracellular transcriptional pathways such as TGF- β /Smad and MAPK/ERK, initiating extracellular matrix (ECM) synthesis.

Mimicking collagen degradation signals (like **Gly-Pro-Hyp**), these peptides are recognized by dermal fibroblasts, initiating a regenerative cascade:

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- **Type I collagen synthesis** - reinforces dermal structure
- **Hyaluronic acid production** - enhances hydration and plumpness
- **Elastin synthesis** - improves skin resilience and elasticity

✓ *Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. Journal: Journal of Cosmetic Dermatology. Year/Volume/Pages: 2018;17(5):840–847.*

(Contribution: This study was the first to confirm, at the cellular level, that Hydrolysed Collagen Tripeptides directly activate fibroblast signaling pathways related to ECM synthesis (e.g., upregulation of COL1A1, HAS2, ELN). It established that Hydrolysed Collagen Tripeptides have regulatory signaling effects beyond mere nutritional roles.)

✓ *Postlethwaite AE, Seyer JM, Kang AH. Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides. Journal: Proceedings of the National Academy of Sciences of the United States of America (PNAS). Year/Volume/Pages: 1978;75(2):871–875.*

(Contribution: Demonstrated that certain collagen fragments, including small peptides, possess chemotactic activity toward fibroblasts, acting as molecular triggers during tissue repair.)

✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal: Journal of Agricultural and Food Chemistry.*

Year/Volume/Pages: 2005;53(16):6531–6536. (Contribution: Provided in vivo evidence that Gly-Pro-Hyp can be detected in the bloodstream after oral ingestion, confirming its intact absorption and functional delivery to dermal tissues.)

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2) Tripeptides as "Signal Peptides" :

Beyond Nutrition-They Trigger Regeneration

Hydrolysed Collagen Tripeptides act not only as nutritional components but more importantly as biological activators. They initiate cellular regeneration pathways that free amino acids and dipeptides are incapable of triggering.

As the smallest functional sequence unit, tripeptides can cross the intestinal barrier intact, be absorbed into the bloodstream, and retain their structural integrity, enabling them to reach dermal tissue and activate skin repair mechanisms at the cellular level.

✓ *Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. Journal of Cosmetic Dermatology. 2018;17(5):840–847.*

3) Why Tripeptides Are Different

Most conventional collagen powders (e.g., gelatin, standard hydrolysates) are large-molecule proteins (>10k Da) or undefined polypeptide mixtures. After ingestion, they are typically digested into amino acids, and cannot retain the signaling sequence needed to activate fibroblasts.

In contrast, Hydrolysed Collagen tripeptides -especially those rich in **Gly+Pro+Hyp (>50%)** - offer dual functionality:

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- **Nutritional** - Supply structural amino acids required for ECM synthesis
- **Signaling** - Actively trigger fibroblast activation and dermal remodeling

This “Signal → Synthesis → Structural Reconstruction” mechanism is **unique** to functional tripeptides and cannot be replicated by ordinary proteins or amino acid supplements.

Thus, Hydrolysed Collagen Tripeptides are not only structural nutrients, but precision biological signals that orchestrate skin regeneration at the molecular level - the foundation of anti-aging from within.

Summary Table: Structural and Functional Comparison

Type	Structural Features	Molecular Weight	Biological Functionality
Amino Acid	Single amino acid	75–200 Da	Basic nutrition, lacks signaling function
Dipeptide	Two amino acids	~200–300 Da	Unstable, weak signaling capacity
Tripeptide	Three amino acids	~300–500 Da	High stability, cell-recognized signal unit
Conventional Collagen	Mixed polypeptides >10k Da	>10,000 Da or mixed	Nutritional only, lacks defined signaling

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- ✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry. 2005;53(16):6531–6536.*

4) Hydrolysed Hydrolysed Collagen Tripeptides vs. Conventional Collagen Powder, Collagen Peptide and Single Amino Acids

A. *Hydrolysed Hydrolysed Collagen tripeptides* :

The Core Functional Unit of Hydrolyzed Collagen

Hydrolysed Hydrolysed Collagen Tripeptides are the core functional units derived from hydrolyzed collagen, with Gly-Pro-Hyp being the most bioactive representative.

- ✓ *Iwai K, Hasegawa T, Taguchi Y, Morimatsu F, Sato K, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. J Agric Food Chem. 2005;53(16):6531–6536.*
- Gly-Pro-Hyp is actively absorbed in its intact form through peptide transporters such as PEPT1 in the intestinal epithelium.

- A collagen tripeptide consists of three amino acids, forming the minimal biologically active unit of collagen, typically following a Gly–X–Y structure (e.g., Gly-Pro-Hyp).
Experimental studies have demonstrated that Gly-Pro-Hyp is directly recognized by skin fibroblasts, where it stimulates the synthesis of type I collagen, elastin, and hyaluronic

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acid-making it the minimal functional unit of collagen signaling.

Furthermore, Hydrolysed Collagen Tripeptides (specifically Gly-Pro-Hyp) have been shown to activate the expression of extracellular matrix (ECM)-related genes in fibroblasts, a response that is not observed with undefined or unstructured collagen peptide fragments.

- ✓ *Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009;78:929–958.*
- This study highlights that conventional collagen powder loses its native structure during processing, resulting in undefined amino acid sequences and a loss of biological functionality. It is unable to form stable triple-helical structures or convey any biological signaling capacity.

- Tripeptides do not require further digestion and can be actively absorbed in their intact form via peptide transporters (such as PEPT1) in the intestinal lining.

Studies have confirmed that intact Gly-Pro-Hyp can be detected in the bloodstream within 30 to 60 minutes after ingestion.

- ✓ *Zague V, de Freitas V, da Costa Rosa M, de Castro GA, Jaeger RG, et al. Collagen peptides modulate metabolism of dermal fibroblasts. J Cosmet Dermatol. 2018;17(5):840–847.*
- Clinical studies have detected intact Gly-Pro-Hyp in human blood within 30–60 minutes after oral ingestion of collagen hydrolysates, confirming its ability to survive digestion, be absorbed through the gut, and enter systemic circulation.

B. Conventional Collagen Powder

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Collagen powder (gelatin) is typically composed of large molecular weight proteins (>10 kDa). They are produced by thermal or acidic hydrolysis of native collagen, it has no defined sequence, contains inconsistent chain lengths, and lacks bioactivity.

- ✓ *Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009;78:929–958.*
- *This study highlights that conventional collagen powder loses its native structure during processing, resulting in undefined amino acid sequences and a loss of biological functionality. It is unable to form stable triple-helical structures or convey any biological signaling capacity.*

C. Generic collagen peptides

Generic collagen peptides (non-standard hydrolyzed peptides) may be shorter than gelatin, but their amino acid sequences are random fragments, making them incapable of delivering precise biological signals.

They lack the specific tripeptide structure, and once ingested, are mostly degraded and absorbed as general amino acids. As a result, their bioactive sequences are not preserved, and they cannot activate fibroblasts in the skin.

- ✓ *Wada M, Kawakami S, Nagaoka I. Collagen-derived dipeptides and tripeptides in human blood after ingestion of gelatin hydrolysates. J Agric Food Chem. 2013;61(50):11916–11921.*
- *This study found that although generic collagen peptides are shorter in length, their sequences are random and disorganized, making it difficult to replicate the precise biological signals of native*

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collagen. Due to the complexity and instability of peptide fragments generated from different hydrolyzed collagen sources, only a small proportion of tripeptides (such as Gly-Pro-Hyp) retain a defined functional structure, while the majority exist as non-specific, unordered fragments with limited bioactivity.

D. Single amino acids

Single amino acids have no structural or signaling capacity; they merely serve as building blocks for protein synthesis. Compared to free amino acids, tripeptides offer stronger signaling potential and greater molecular stability, and are uniquely capable of engaging biological pathways-including activation of extracellular matrix (ECM) synthesis, which amino acids cannot initiate.

- ✓ *Shigemura Y, Akaba S, Kawashima E, Park EY, Nakamura Y, Sato K. Identification of a hydroxyproline-containing dipeptide from collagen hydrolysate stimulating hyaluronic acid synthesis in cultured dermal fibroblasts. J Agric Food Chem. 2011;59(17):9431–9436.*
- This study demonstrated that single amino acids lack biological signaling capacity and do not possess the ability to stimulate extracellular matrix (ECM) synthesis.

Differences between Hydrolysed Hydrolysed Collagen Tripeptides and Regular Collagen Powder / Collagen Peptides / Single Amino Acids

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Comparison	Hydrolysed Hydrolysed Collagen tripeptides (Gly-Pro-Hyp)	Collagen Powder (Gelatin)	Collagen Peptides	Single Amino Acids
Structure	Defined tripeptide sequence; Gly-Pro-Hyp core	Long-chain gelatin proteins, fragmented	Low MW peptides, mixed sequence	Simple molecule, no sequence
Biological Activity	Functional “signal molecule” recognized by fibroblasts	No signaling function, only protein nutrition	Unstable activity, lacks standard	No tissue repair signaling
Absorption	Actively absorbed via PEPT1 transporter into blood	Must be fully broken into peptides first	Partially absorbed, inconsistent	Easily absorbed, no ECM effect
Clinical Evidence	Supported by multiple human studies (moisture, elasticity, anti-wrinkle)	No direct clinical outcomes	Poor standardization, mixed results	Not associated with cosmetic effects
Market Value	Clinical-grade, functional bioactive	Commodity-level raw material	Used in food-grade supplements	Basic sports nutrition

Summary:

Hydrolysed Hydrolysed Collagen Tripeptides function as “signal peptides” - they are not merely nutritional building blocks, but biological activators capable of triggering regenerative processes that amino acids and random peptides cannot induce.

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- Hydrolysed Hydrolysed Collagen Tripeptides represent the smallest functional sequence unit of collagen, capable of crossing the intestinal barrier intact, being absorbed into the bloodstream, and retaining their molecular structure—a prerequisite for activating skin repair pathways.

✓ *Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. J Cosmet Dermatol. 2018;17(5):840–847.*

- This study demonstrated that Hydrolysed Collagen Tripeptides stimulate the synthesis of type I collagen, elastin, and hyaluronic acid in fibroblasts, while undefined collagen peptides or free amino acids do not produce the same biological response.

Compared to regular collagen powder, free amino acids, or undefined collagen peptides,

Gly-Pro-Hyp Hydrolysed Hydrolysed Collagen Tripeptides offer dual functionality:

- Nutritional - they provide the essential substrates required for extracellular matrix (ECM) biosynthesis.
- Signaling - they act as cellular triggers, initiating endogenous repair by activating fibroblast synthesis pathways.

This “signal → synthesis → structural regeneration” mechanism is unique to tripeptides, and cannot be replicated by ordinary proteins or peptides.

Therefore, Hydrolysed Collagen Tripeptides are not just structural nutrients - they function as

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precision biological triggers for dermal remodeling and regenerative skin repair, forming the molecular foundation of age-reversal strategies.

- ✓ Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. *Journal of Agricultural and Food Chemistry*. 2005;53(16):6531–6536.
- ✓ Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. *Journal of Cosmetic Dermatology*. 2018;17(5):840–847.

II High Gly-Pro-Hyp Content and Structural Integrity:

The Basis for Physiological Activity

1) Glycine (Gly) + Proline (Pro) + Hydroxyproline (Hyp) ≥ 50%:

Biomimetic Composition for Enhanced Regenerative Power

A. Gly + Pro + Hyp (>50%):

The Core Repeating Unit of Collagen Triple Helix

- **Gly-Pro-Hyp** is the most fundamental and stable tripeptide unit found in natural collagen.
- Collagen consists of three polypeptide chains forming a triple helix structure, with repetitive Gly-X-Y sequences - where X is often proline (Pro) and Y is frequently Hydroxyproline (Hyp).

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- This specific sequence plays a critical role in stabilizing the triple-helical conformation, making it structurally robust and bioidentical to human collagen.
- A high proportion of this tripeptide ensures strong biocompatibility and efficient integration into dermal repair mechanisms.

B. Gly, Pro, and Hyp:

The Essential Residues of Type I Collagen

- These three amino acids represent the core repeating unit of Type I collagen, which constitutes the majority of human dermal collagen.
- Among them, Hyp (Hydroxyproline) contributes significantly to thermal stability and structural integrity through hydrogen bonding and steric effects.
- This molecular characteristic explains why Gly-Pro-Hyp-rich peptides exhibit superior physiological activity compared to random hydrolysates.

C. Gly-Pro-Hyp:

Bioactive Signal Fragment in Collagen Degradation

- During collagen breakdown in the body, Gly-Pro-Hyp emerges as a dominant functional fragment.
- It is recognized as a damage-associated signal within the extracellular matrix (ECM), capable of activating tissue repair responses.

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- Due to its specific sequence and conformational stability, **Gly-Pro-Hyp** is identified by fibroblasts and other skin-resident cells, initiating signaling cascades related to regeneration.

✓ *Shoulders MD, Raines RT. Collagen structure and stability. Annual Review of Biochemistry. 2009;78:929–958.*

2) Structural Integrity:

A Prerequisite for Tripeptide Functionality

A. Biological activity of Hydrolysed Collagen Tripeptides is inherently structure-dependent.

The Gly-Pro-Hyp sequence represents the most bioactive and highly cell-recognizable tripeptide unit within native collagen. It is also the key fragment naturally generated during physiological collagen degradation, acting as a molecular signal to trigger skin regeneration.

B. Only when tripeptides maintain complete structure and high Gly-Pro-Hyp content (GPH > 50%), do they possess:

- High structural stability → Capable of crossing the intestinal barrier intact
- Superior bioavailability → Efficient absorption into the bloodstream and delivery to skin tissue

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- Defined mechanism of action → Directly activate fibroblasts to synthesize ECM components such as Type I collagen, hyaluronic acid, and elastin

✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry. 2005;53(16):6531–6536.*

C. Detectable in Plasma: Evidence of Structural Integrity

A pivotal study by Iwai et al. demonstrated that, following oral ingestion of Hydrolysed Collagen Tripeptides containing Gly-Pro-Hyp (GPH), intact GPH tripeptides were detected in human plasma **within 30–60 minutes**, with peak concentrations reaching 1.5-2.0 µg/mL.

This finding confirms that these tripeptides are not only absorbed intact but also retain their functional molecular structure under physiological conditions - an essential requirement for signal transduction and targeted dermal activity.

✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry. 2005;53(16):6531–6536.*

D. Clinical Evidence: Structural Integrity = Functional Efficacy

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Clinical studies have demonstrated that structurally stable Gly-Pro-Hyp tripeptides deliver the following skin benefits:

- Improved skin hydration and elasticity within **8–12 weeks**
- Reduction in wrinkle depth and surface roughness
- Enhanced ECM synthesis and increased dermal thickness

These benefits are strictly dependent on the presence of high tripeptide content, clearly quantified GPH ratios, and preserved molecular integrity—not merely on the label claim of “collagen content.”

✓ *Ohara H, Matsumoto H, Ito K, et al. Comparison of quantity and structures of Hydroxyproline-containing peptides in human blood after oral ingestion of collagen hydrolysates from different sources. Journal of Agricultural and Food Chemistry. 2007;55(4):1532–1535.*

3) Scientific Significance of Gly-Pro-Hyp > 50%, with Proline and Hydroxyproline at 12–15%:

These levels far exceed the bioactivity of generic Gly-X-Y collagen peptides and are consistent with clinical-grade efficacy in improving skin health.

A. Proline (Pro) - the Rotational Pivot of Collagen Structure

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- Proline is an essential “turning point” in the collagen triple helix, enabling the formation of a stable three-dimensional structure.
- A high Pro content results in a stronger and more resilient triple helix, enhancing the assembly of collagen fibers.

B. Hydroxyproline (Hyp) – the Key to Structural Stability

- Hydroxyproline forms hydrogen bonds that stabilize the triple helix, conferring thermal resistance and enzymatic protection.
- A higher Hyp content allows the tripeptide to remain structurally intact in the bloodstream, enhancing bioavailability.

Therefore, a combined **Pro + Hyp content of 25-30%** - as in our formulation - indicates a highly stable and biologically active tripeptide conformation, consistent with the core standards used in clinical research.

✓ *Iwai K, Hasegawa T, Taguchi Y, Morimatsu F, Sato K, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. J Agric Food Chem. 2005;53(16):6531–6536.*

- This study detected intact Gly-Pro-Hyp in human plasma 30–60 minutes after ingestion, confirming its ability to survive digestion and enter circulation in functional form.

C. Pro + Hyp Define Collagen Stability

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- Proline and Hydroxyproline are the two most critical amino acids for building and stabilizing the collagen triple helix.
- Hydroxyproline provides intramolecular hydrogen bonding, reinforcing the heat resistance and folding integrity of collagen.

✓ *Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009;78:929–958.*
- *This review confirms that Pro and Hyp are indispensable to triple-helix formation, and that high levels are required for efficient tissue integration and physiological function.*

D. Pro + Hyp Are Critical for Bioactivity

- Clinical and in vitro studies show that Hydrolysed Collagen Tripeptides rich in Pro and Hyp significantly improve skin hydration and elasticity.
- Only when Pro and Hyp are present at elevated levels can the tripeptide maintain its structure in circulation and exert long-lasting biological effects.
- And studies demonstrated that Gly-Pro-Hyp directly stimulates fibroblast production of type I collagen, elastin, and hyaluronic acid - significantly outperforming non-structured peptides or free amino acids.

✓ *Zague V, de Freitas V, da Costa Rosa M, de Castro G, Jaeger RG, et al. Collagen peptides modulate metabolism of dermal fibroblasts. J Cosmet Dermatol. 2018;17(5):840–847.*

E. Gly-Pro-Hyp is the Minimal Functional Unit of Collagen

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- The collagen triple helix is composed of repetitive Gly–X–Y sequences, where:
 - Glycine (Gly) appears at every third position.
 - Proline (Pro) and Hydroxyproline (Hyp) are the most frequent residues at X and Y positions.
- The **Gly-Pro-Hyp** motif is the most stable and commonly occurring sequence, and serves as the biological “code” signaling collagen turnover and regeneration.
- While Pro-Hyp can promote hyaluronic acid synthesis, its structure is less stable and cannot remain intact in blood, unlike tripeptides such as Gly-Pro-Hyp which show superior in vivo stability and efficacy.

✓ *Shigemura Y, Akaba S, Kawashima E, Park EY, Nakamura Y, Sato K. Identification of a hydroxyproline-containing dipeptide from collagen hydrolysate stimulating hyaluronic acid synthesis in cultured dermal fibroblasts. J Agric Food Chem. 2011;59(17):9431–9436.*

F. Gly-Pro-Hyp Is the Only Sequence Proven to Trigger ECM Synthesis

- Gly-Pro-Hyp is the only peptide sequence directly recognized by skin fibroblasts, activating the synthesis of type I collagen, hyaluronic acid, and elastin.
- Other Gly–X–Y sequences (e.g., Gly-Leu-Ala) do not possess this signaling capacity and are merely consumed as nutrients.

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- ✓ Asserin J, Lati E, Shioya T, Prawitt J. The effect of oral collagen peptide supplementation on skin moisture and elasticity. *J Cosmet Dermatol.* 2015;14(4):291–301.
- Demonstrated significant improvement in skin hydration and elasticity from ingestion of tripeptides containing high Gly-Pro-Hyp content.

- ✓ Yazaki M, Ito Y, Yamada M, Goulas S, Chikanishi T, et al. Oral ingestion of collagen hydrolysate leads to elevation of hydroxyproline in human skin. *J Agric Food Chem.* 2017;65(11):2315–2322.
- Showed that oral collagen hydrolysates rich in Hyp increased skin Hydroxyproline levels, indicating active collagen metabolism and structural remodeling.

Summary: a CTP ≥30% & Gly–Pro–Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%, indicates that:

- The tripeptide sequence possesses high structural stability and recognition specificity, enhancing the stability of the collagen triple-helix structure;
- It improves fibroblast recognition efficiency for bioactive signal peptides;
- It significantly promotes the biosynthetic activity of the extracellular matrix (ECM);
- It plays a critical role in the sustained regeneration of *type I* collagen and elastin.

As a result, it supports clinically relevant improvements in skin condition.

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III High-Purity Hydrolysed Hydrolysed Collagen tripeptides

(CTP \geq 30% & Gly-Pro-Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%)

vs. Conventional Collagen Peptides

1) Most commercial “collagen peptide powders” are non-targeted hydrolysates

They typically consist of heterogeneous peptide mixtures and high-molecular-weight fragments, with undefined tripeptide ratios. Such products often lack Bio-functional activity and do not guarantee the presence of bioactive sequences.

2) Clinical Evidence for High-Purity Tripeptides

(CTP \geq 30% & Gly-Pro-Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%)

A randomized, double-blind, placebo-controlled clinical study by Asserin J et al. (2015) demonstrated that 8 weeks of oral intake of collagen rich in tripeptides resulted in:

- +12% increase in skin hydration
- +9% improvement in skin elasticity
- Significant enhancement in skin smoothness

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- No significant effect in control groups receiving free amino acids or non-structured collagen hydrolysates

Key Takeaway:

Formulas containing CTP $\geq 30\%$ & Gly-Pro-Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15% deliver not just tripeptides, but high-content, structurally preserved bioactive tripeptides—the key to clinical-grade results.

- ✓ *Asserin J, Lati E, Shioya T, Prawitt J. The effect of oral collagen peptide supplementation on skin moisture and elasticity. Journal of Cosmetic Dermatology. 2015;14(4):291–301.*
- This study highlights the efficacy of standardized, structurally intact tripeptides, not just any collagen source.

Comparative Table:

High Tripeptide Collagen

(CTP $\geq 30\%$ & Gly-Pro-Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%)

vs. Conventional Collagen Peptides

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Aspect	High-Tripeptide Collagen <i>(CTP ≥30% & Gly-Pro-Hyp content exceeding 50%, with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%)</i>	Conventional Collagen Peptides
Molecular Structure	Defined (Tripeptides: Gly-Pro-Hyp)	Mixed peptides, undefined structure
Absorption Efficiency	Rapidly absorbed, enters bloodstream	Mostly degraded into free amino acids
Mechanism of Action	Activates fibroblasts to synthesize ECM	Provides raw amino acids only
Clinical Evidence	Supported by multiple human studies	Functional outcomes unclear, widely variable

- ✓ Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. *Journal of Cosmetic Dermatology*. 2018;17(5):840–847.
- ✓ Yazaki M, Ito Y, Yamada M, et al. Oral ingestion of collagen hydrolysate leads to elevation of hydroxyproline in the skin. *Journal of Agricultural and Food Chemistry*. 2017;65(11):2315–2322.

Conclusion:

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Only Hydrolysed collagen peptides *with $\geq 30\%$ tripeptide content and Gly-Pro-Hyp (GPH) $\geq 50\%$ and with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%* represent clinically validated bioactive forms capable of skin regeneration.

This high-tripeptide formula is structurally stable, highly absorbable, and mechanistically precise - qualifying it as a true functional collagen, far superior to traditional gelatin or generic collagen powders.

It is the cornerstone of modern, precision-based nutricosmetic interventions.

IV “Low Dose, High Efficacy” Characteristic of Hydrolysed Collagen tripeptides

Multiple human clinical trials and pharmacokinetic studies have confirmed that oral intake of high-content and structurally defined Hydrolysed Hydrolysed Collagen Tripeptides - particularly those rich in *$\geq 30\%$ tripeptide content and Gly-Pro-Hyp (GPH) $\geq 50\%$ and with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%* - is effective at doses as low as 1,000-2,500 mg/day.

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This dosage range is sufficient to trigger ECM reconstruction, stimulate collagen synthesis, and enhance skin hydration and elasticity - without placing strain on the gastrointestinal system. This makes it especially suitable for long-term anti-aging management.

In contrast to traditional high-dose collagen powders (typically 5,000-10,000 mg/day), functional tripeptide collagen achieves better outcomes at lower doses, thanks to clear structural identity and high bioactivity - a hallmark of the “low dose, high efficacy” model.

Comparative Table:

Conventional Collagen vs. High-Activity Hydrolysed Tripeptide Collagen

(with ≥30% tripeptide content and Gly-Pro-Hyp (GPH)≥50% and with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%)

Comparison Dimension	Conventional Collagen Powders	High-Activity Hydrolysed Hydrolysed Collagen Tripeptides
Structure	Mixed peptide hydrolysates with high-MW fragments	Precisely isolated tripeptides with stable structure
Mechanism of Action	Primarily provides amino acid substrates	Directly activates fibroblasts and ECM synthesis signaling

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Comparison Dimension	Conventional Collagen Powders	High-Activity Hydrolysed Hydrolysed Collagen Tripeptides
Mode of Action	Relies on nutritional supplementation and internal re-synthesis	Acts via signaling pathways to induce cellular responses
Dose Characteristics	Requires high daily intake	Low effective dose with higher response efficiency

1) Clinical Findings:

A series of randomized controlled trials (RCTs) and pharmacokinetic studies demonstrate that oral intake of **1,000-2,500 mg/day** of structurally defined, high-GPH tripeptides can lead to visible improvements in skin condition within **8-12 weeks**, including:

- Increased dermal collagen density
- Enhanced skin hydration and elasticity
- Reduction in wrinkle depth and surface roughness

These results underscore that clinical efficacy is determined not by dose quantity, but by peptide structure, content, and mechanism of action.

2) Supporting Evidence for Low-Dose, High-Efficacy Application

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Pharmacokinetics: Rapid Absorption and Systemic Availability

- Oral ingestion of structurally defined Hydrolysed Collagen Tripeptides (especially Gly-Pro-Hyp) results in detectable plasma levels within 30–60 minutes.
- The peak plasma concentration (C_{max}) is dose-dependent, and systemic bioavailability is evident at doses starting from 1,000 mg.

✓ *Iwai K, Hasegawa T, Taguchi Y, et al. Identification of food-derived collagen peptides in human blood after oral ingestion of gelatin hydrolysates. Journal of Agricultural and Food Chemistry. 2005;53(16):6531–6536.*

3) Mechanism of Action: Cellular Signaling and Targeted Activation

Gly-Pro-Hyp Hydrolysed tripeptides bind to fibroblast surface receptors such as CD44, $\alpha 2\beta 1$ integrin, and DDR1/2, triggering intracellular signaling cascades including TGF- β /Smad and MAPK pathways.

This leads to upregulation of ECM-related gene expression, promoting the synthesis of:

- Type I collagen
- Hyaluronic acid (HA)
- Elastin

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- ✓ Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. *Journal of Cosmetic Dermatology*. 2018;17(5):840–847.
- ✓ Postlethwaite AE, Seyer JM, Kang AH. Chemotactic attraction of human fibroblasts to collagen-derived peptides. *PNAS*. 1978;75(2):871–875.

3) Clinical Validation of Efficacy at 1,000-2,500 mg/day

Multiple clinical trials (Asserin et al., Ohara et al., Yazaki et al.) show that daily oral intake of 1,000–2,500 mg of Hydrolysed Collagen Tripeptides for 8–12 weeks results in:

- Significant increase in skin hydration and elasticity
 - Reduction in wrinkle depth and surface roughness
 - Structural improvement of the dermis without high-dose accumulation
 - Excellent tolerance and long-term safety profile
- ✓ Asserin J, Lati E, Shioya T, Prawitt J. The effect of oral collagen peptide supplementation on skin moisture and elasticity. *Journal of Cosmetic Dermatology*. 2015;14(4):291–301.
 - ✓ Yazaki M, Aihara M, et al. Oral ingestion of collagen hydrolysate leads to elevation of hydroxyproline in the skin. *Journal of Agricultural and Food Chemistry*. 2017;65(11):2315–2322.

Summary:

Gly-Pro-Hyp Enriched Hydrolysed Collagen Tripeptides - Rapid Absorption, Fibroblast Signaling, and Evidence-Based Efficacy for 8-12 Weeks Improvements in skin Hydration, Elasticity, and Facial Wrinkles, Fine Line Reduction with Clinically Measurable Results

Hydrolysed Hydrolysed Collagen Tripeptides (*with $\geq 30\%$ tripeptide content and Gly-Pro-Hyp (GPH) $\geq 50\%$ and with Proline (Pro) and Hydroxyproline (Hyp) each comprising 12–15%*)

demonstrate strong efficacy at 1,000-2,500 mg/day, by initiating the regenerative cascade of:

“Signal activation → ECM synthesis → Dermal reconstruction”

This dosage range is **clinically validated, safe for long-term use**, and forms the scientific basis for **modern anti-aging nutrition**.

✓ *Zague V. Collagen peptides modulate metabolism of dermal fibroblasts. Journal of Cosmetic Dermatology. 2018;17(5):840–847.*

✓ *Ohara H, et al. Comparison of quantity and structures of Hydroxyproline-containing peptides in human blood after oral ingestion of collagen hydrolysates from different sources. Journal of Agricultural and Food Chemistry. 2007;55(4):1532–1535.*

V Key Advantages of Fish Scale-Derived Hydrolysed Collagen tripeptides

(Compared with Generic Fish Skin Collagen Peptides)

1) Natural Structural Superiority: Closer to Human Dermal Collagen

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Fish scales are primarily composed of **Type I** collagen - the predominant form in human skin's dermal matrix. Their amino acid composition is highly homologous to human collagen, making them more suitable for beauty and anti-aging applications than porcine skin or bovine bone sources.

- ✓ *Shoulders MD, Raines RT. Collagen structure and stability. Annu Rev Biochem. 2009;78:929–958.*
- ✓ *Gómez-Guillén MC et al. Collagen from fish and its biomedical applications. Food Hydrocolloids. 2011;25(8):1813–1827.*

2) Low Molecular Weight & High Absorption Efficiency

Fish scales processed via enzymatic hydrolysis can yield a high proportion of tripeptides, especially Gly-Pro-Hyp (GPH), with an average molecular weight of 300–500 Da. These peptides exhibit:

- Rapid oral absorption within 30–60 minutes
- Efficient trans-epithelial transport
- Targeted dermal delivery

- ✓ *Iwai K et al. Identification of food-derived collagen peptides in human blood after oral ingestion. J Agric Food Chem. 2005;53(16):6531–6536.*

3) Higher Purity and Minimal Lipid Residue

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Fish scales naturally contain very low lipid content (<1%), whereas fish skin may contain >10–15% fats and non-collagenous proteins. Therefore, collagen peptides extracted from fish scales:

- Require less defatting and purification
- Offer higher final purity, lighter taste, and no fishy odor
- Are ideal for oral beauty supplements with strict taste and cleanliness requirement

✓ *Lin L et al. Extraction and characterization of collagen peptides from fish scale. Food Chem. 2020;331:127234.*

✓ *Kim SK et al. Fish-derived collagen as a promising biomaterial for biomedical applications. Mar Drugs. 2022;20(2):115.*

4) Higher Tripeptide Content = Higher Bioactivity

Due to the dense collagen matrix in fish scales (mainly Type I), the enzymatic hydrolysis yields a significantly higher proportion of GPH tripeptides than fish skin.

- GPH is the only collagen structure shown to enter bloodstream intact and trigger ECM regeneration
- Fish scale peptides have shorter chains, faster absorption, and greater bioavailability

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✓ *Iwai K et al. J Agric Food Chem. 2005;53(16):6531–6536.*

5) Fish Scale vs. Fish Skin: Structural, Functional, and Quality Differences

A. Collagen Type Composition

Source	Main Collagen Type	Features & Suitability
Fish Scale	Type I collagen (>90%)	Closest to human dermis; ideal for hydration, elasticity, anti-wrinkle
Fish Skin	Type I + Type III (mixed)	Mixed structure; batch quality more variable

- **Fish scales are rich in densely aligned Type I collagen fibers**, which closely resemble the extracellular matrix (ECM) architecture of human dermis. This structural similarity makes fish scale collagen particularly suitable for applications focused on skin firmness, hydration, and anti-wrinkle benefits.
- Although fish skin also contains **Type I collagen**, it typically has higher levels of fat and non-collagenous proteins, which may reduce the yield and proportion of bioactive peptides during extraction and hydrolysis.

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- ✓ *Gomez-Guillen MC et al. Collagen from fish and its biomedical applications. Food Hydrocolloids. 2011;25(8):1813–1827.*
- ✓ *Wang L et al. Food Chemistry. 2008;108(2):616–623.*

B. Purity and Sensory Quality

Criteria	Fish Scale Tripeptides	Fish Skin Tripeptides
Fat Content	Very low (<0.2%) – cleaner profile	May contain subcutaneous fat
Odor Control	Odorless, palatable	Requires deodorization, risk of fishy odor
Impurity Risk	Low – stable tripeptide ratio	Higher – more variable tripeptide content

- Hydrolysed Collagen Tripeptides derived from fish scales are easier to isolate with a high proportion of Gly-Pro-Hyp during processing, thanks to their naturally low fat content and absence of fishy odor. This results in a cleaner taste and better palatability for oral beauty supplements.
- In contrast, fish skin requires intensive degreasing and deodorization, which increases processing complexity and may compromise the structural integrity and bioactivity of the resulting peptides.

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C. Bioavailability & Peptide Activity

- Fish scales yield higher GPH tripeptide ratios (>50%) under identical enzymatic conditions
- Fish skin has more complex crosslinking structures, limiting tripeptide release

Parameter	Fish Scale Tripeptides	Fish Skin Tripeptides
Type I Collagen Purity	Higher (>90%)	Moderate, possible Type III presence
GPH Tripeptide Content	Higher (>50%)	Lower and less consistent
Processing & Palatability	Stable, clean, odorless	More challenging; needs defatting/deodorizing

Conclusion:

Fish scale Hydrolysed Collagen Tripeptides offer a superior raw material for producing high-purity, high-activity Gly-Pro-Hyp tripeptides.

Their bioavailability, structural stability, and clinical potential make them the preferred choice for premium oral beauty and anti-aging formulations.