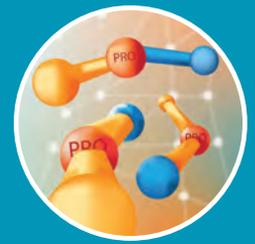


SUMMARY

- Collagen tri- and dipeptides have been identified as bioactive components of collagen food supplements, mediating beneficial health effects e.g. in joints, muscle, bone, and skin
- Low molecular weight (LMW) collagen contains a high amount of bioactive peptides that are quickly absorbed, highly bioavailable, stable, and actively transported to the skin
- *COLLinstant ultra active*⁺ (< 1000 Da) is a clinically proven, ultra low molecular weight collagen
- *COLLinstant active*[®] (< 2500 Da) is a clinically proven, low molecular weight collagen



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LMW COLLAGEN – THE FUTURE OF COLLAGEN HYDROLYSATE

Data support superior bioavailability and improved efficacy profile of LMW collagen peptides

As part of an active lifestyle, many consumers choose collagen-enriched diets to support healthy aging, skin beauty or overall mobility and fitness. While beneficial effects of standard molecular weight (SMW) collagen hydrolysate food supplements have long been supported by scientific data, recent studies on its mode of action reveal a central role of small bioactive collagen di- or tripeptides. Highly efficient low molecular weight (LMW) collagen hydrolysate with a favorable peptide profile, quick uptake, and high bioavailability appears to be the next generation food supplement.

Collagen hydrolysates are produced from animal tissues in a multi-step process that involves gelatinization and subsequent enzymatic hydrolysis of native collagen, yielding peptides with an average molecular weight of approximately 3 kDa (SMW).

Tailored enzymatic digestion with collagenase during this process preserves the collagen-specific sequence Gly-Pro-Hyp (GPH) and yields a LMW hydrolysate enriched with this bioactive tripeptide, that exerts beneficial effects in various tissues, including skin, muscles, joints or bones.^{1,2,3}

This short review provides a brief overview of recent findings regarding uptake, bioavailability, mode-of-action, and efficacy profile of bioactive peptides in LMW collagen hydrolysates.

UPTAKE & BIOAVAILABILITY

A study on rats with radioactively marked Carbon (¹⁴C) as tracer could map LMW collagen in muscles, joints, bones and cartilage where it remains while

disappearing in plasma and organs.⁴ Radioactivity is retained at a high level in the skin until 14 days after administration (70% of the level observed at 6 h). Human trials focussing on GPH have found that after ingestion, the tripeptide is very efficiently absorbed, rapidly transported into the blood and detectable in a dose-dependent manner in plasma and skin.^{2,5} In the skin GPH is further hydrolyzed to the bioactive dipeptide Pro-Hyp (PH).

While SMW collagen is degraded in the gastrointestinal tract but not readily cleaved into bioactive peptides, GPH and PH enriched in LMW collagen easily cross the intestinal barrier into the blood stream via the peptide transporter PEPT1 and remain intact over the entire gastrointestinal pathway.^{1,4,5}

The method of collagen hydrolysate preparation apparently influences the peptide profile in the blood stream.^{2,5}



Collagen tri- and dipeptides are stable, quickly absorbed and bioactively available at target organs, such as skin, muscles, joints and bones.

KEYWORDS

Collagen hydrolysate, low molecular weight collagen, collagen peptides, collagen tripeptides, collagen food supplement, nutraceutical, nutricosmetic, cosmeceutical, skin health.



TARGET TISSUES & MODE OF ACTION

Several physiological activities of metabolized collagen di- and tripeptides have been described:

#Cardiovascular system: *In vivo* studies found that collagen tripeptides inhibit thrombosis, decrease the number of macrophages in atherosclerotic plaques and can reduce blood pressure.^{6,7,8}

#Joints & Bones: One of the most established benefits of collagen hydrolysate is the promotion of joint and bone health and regeneration (reviewed by Moskowitz).⁹ The specific effect of bioactive collagen peptides has been shown, e.g. by Watanabe-Kamiyama et al. who demonstrated that an oral administration for 20 weeks improves bone composition with an increase in organic substance.⁴ Collagen tripeptides have also been shown to reduce inflammation and stimulate cartilage formation and bone healing.^{10,11,12}

#Skin: The support of skin health by collagen food supplementation is well documented in the literature (reviewed by Sibilla et al.).¹³ Regarding bioactive collagen di- and tripeptides there appears to be a triple mode of action:

1. Induction of collagen expression via the p38 MAPK pathway,¹⁴
2. providing free amino acids as building blocks for the formation of collagen and elastin fibers, and
3. acting as ligands for fibroblast receptors, stimulating growth, the production of new collagen and hyaluronic acid synthesis.^{2,15,16,17,18}

In clinical studies, collagen tripeptides could improve skin elasticity and hydration and were effective in wrinkle reduction and the promotion of wound healing (reviewed by Choi).¹⁸ The efficacy of a collagen hydrolysate appears to be proportional to its concentration of bioactive peptides.

Conclusion: SMW collagen hydrolysate is an evidence-based oral health food supplement. The current body of literature supports that its beneficial effects are mostly mediated by metabolized bioactive collagen tri- or dipeptides, in particular GPH or PH. LMW collagen hydrolysate with a high concentration of these characteristic peptides has major advantages over SMW products, including quicker and more efficient peptide uptake, higher bioavailability, as well as enhanced stability and efficacy, especially in the skin.

FINAL REMARKS

Until now, all manufacturers of hydrolyzed collagen have focused on optimizing the organoleptic characteristics of the supplement, achieving the best smell and taste in standard molecular weights.

With *COLLInstant ultra active* +[®] (MW of < 1000 Da) and *COLLInstant active*[®] (MW of < 2.5 kDa), Viscofan has developed two collagen hydrolysates according to latest scientific insights as food ingredients or supplements. In a clinical study, a daily intake of only 2.5 g *COLLInstant ultra active* +[®] for 6 weeks was sufficient to elucidate beneficial effects on skin health: The ultra low molecular weight collagen led to a significant reduction of wrinkles, a considerable increase in skin hydration as well as to modest improvements in skin elasticity.¹⁹

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