Collagen Peptides – Source, Properties and Benefits

Address correspondence to: Dr. Ilka Czech, Seagarden AS - R&D Department, Husoyvegen 278, 4262 Avaldsnes, Norway e-mail address: info@seagarden.no

Collagen peptides, oral ingested and topical administered, have positive effects on human health and beauty. These effects of supplemented collagen peptides are based on their impact on human collagen, naturally found as one of the most abundant proteins in the body. Human collagen is vital for the elasticity, flexibility and strength in skin, tendons and ligaments, but also in the cornea, cartilage, bones, blood vessels, gut and more. Today, collagen peptides are increasingly used as dietary supplement or active ingredient in nutraceuticals, functional foods and cosmetics. Collagen peptides are the building blocks of the versatile high protein ingredient gelatin.

Gelatin is a natural animal derived food ingredient and traditionally used in human nutrition for hundreds of years. Collagen peptides, also called hydrolysed gelatin or collagen hydrolysate, are soluble in water and show better bioavailability in the human body than gelatin. The diversity of possible applications and innovations increased the interest in a wider variation of collagen peptides with diverse properties. Fish derived collagen peptides received more attention in the recent past due to their favourable characteristics and less consumer reservations compared to mammal-derived ingredients.

Since the 1950s, various studies report beneficial health and beauty effects of gelatin and collagen peptides. In the following review, we will give some background information and summarize recent studies on the positive effects of oral and topical administered collagen peptides on human health and beauty.

Collagen, gelatin and collagen peptides

Collagen is found in all connective tissue and accounts for 25-35 % of the whole-body protein content. Cooked collagen is the well-known foodstuff gelatin. Gelatin is industrially extracted from collagen rich sources like animal bones and skin. In that process, the structure of the insoluble collagen is partly denatured by thermal hydrolysis. Additional chemical or biochemical treatment with acid, base or enzymes can be carried out to modify the amino acid composition and functional properties of the extracted gelatin (Schrieber & Gareis, 2007).

Beside the traditional bovine and porcine sources became marine sources, especially fish a valuable raw material for gelatin extraction (Silva et al., 2014). Fish gelatin is available in high values from fish by-products (Arnesen & Gildberg, 2006; Wasswa et al., 2007). Compared to mammal gelatins it has slightly different physical and chemical characteristics and is not in conflict with religious restrictions (Karim et al., 2009). The amino acid composition in all gelatins is very specific and the primary structure (Gly-X-Y) is highly conserved (Kadler et al., 2007).

The amino acid composition in fish gelatin shows a wider variety in amino acids and differs in the amount of amino acids. These small modifications in the fish gelatin composition might be the reason for the lower melting point and weaker gel strength (Avena-Bustillos, 2006; Karim, 2009). Gelatin is widely utilized i.e. as gelling or binding agent, stabilizer, emulsifier and foam former in food, cosmetic applications and other fields. Furthermore, it is an important protein source and contains eight out of the nine essential amino acids.

Collagen peptides are the building blocks of gelatin and can be produced by enzymatic hydrolysis of gelatin, using proteases. The specific properties of collagen peptides make them available for utilization as ingredient and food supplement in the form of drinks, tablets or powders, but also in liquid cosmetic applications, crèmes, sprays and mousses (Thorkelsson et al., 2009). Hydrolysed collagen peptides have usually a molecular weight between 0.3 and 8 kDa, depending on the extraction methodology and processing. They are water-soluble, highly digestible, easily absorbed and can be distributed in the human body (Sibilla et. al, 2015). An even higher solubility show fish derived collagen peptides because of the low melting point especially of cold water fish collagens. This characteristic make the cold water fish collagen peptides attractive for use in certain applications like fluids. In oral administered applications this property might e.g. make chewing much more comfortable. Fish collagens also have been shown to be a capable ingredient in topical administered cosmetic applications (Chai et al, 2010; Wang et al., 2008).

Food safety

Gelatin and collagen peptides, used in human nutrition and cosmetics, are generally regarded as safe. In 1975 gave the FDA GRAS status to gelatin, due to the fact that gelatin is hydrolysed collagen, an ingredient naturally occurring in all animal derived foodstuff. Based on international research results, both the World Health Organization and European Commission for Health and Consumer Protection have confirmed that collagen peptides are safe.

Collagen peptide supplementation – Effect on health and beauty

Today's consumers care more about the nutritional value of food products than before. They became demanding regarding food quality and nutritional value of their consumed foodstuff. A modern customer not only expect food to fill up, it should add value to the customer's well-being. Nutraceuticals and so-called functional foods, claiming health and beauty effects, were shown to have obvious benefits for the consumer. The market for functional foods has significantly increased in the recent past (Leatherhead, 2013). Collagen peptides are ideally suitable as dietary supplement and ingredient in modern nutrition. Various beneficial health and beauty effects have been reported (Zague, 2008; Wu, 2004).

To trust the positive effects of orally administered collagen peptides, it has to make evidence that bioactive collagen peptides can pass the body's natural barrier and reach the targeted tissue. Different scientific studies show evidence for the bioavailability of collagen peptides after oral intake.

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no

Specific accumulation of labeled collagen peptides in cartilage after oral administration was proven in a scientific study already in the late 90's (Oesser et. al, 1999). Other studies suggest that bioactive collagen peptides and amino acids reach the blood stream and can further be distributed throughout the body (Iwai et al., 2005; Ohara et al., 2007). These findings provide strong support for the research showing beneficial effects of ingested collagen peptides in the human body.

Positive impact on human prettiness

The use of functional foods and nutraceuticals to maintain and restore skin beauty has increased significantly in the last 10 years. Promising results in preclinical and bioavailability studies that investigated the effect of collagen peptides on skin health promoted an increased utilization of those peptides in functional foods (Zague, 2008). This trend led to even more studies and accurate research in that field.

Collagen is the main component of the human skin. Type I collagen, together with minor amounts of type III and other collagens, are produced and organized in dermal fibroblasts, the connective tissue cells in the dermis. The collagen fibers provide structural support, elasticity and help the skin to resist stretching (Sibilla et al., 2015; Flaschmajer et al., 1990). Thicker collagen fibrils in fibroblasts are considered as mechanically stronger than fibrils with smaller diameter. Very early studies showed that collagen biosynthesis can be activated by fibroblast activation with food-derived collagen peptides in human blood. (Postlethwaite et al., 1978; Parry et al., 1978).

Collagen hydrolysate treated test subjects showed a larger diameter and higher density of collagen fibrils and a higher fibroblast density, compared to a water and a lactalbumin treated reference group. A collagen specific effect is indicated since the alternative protein diet with lactalbumin showed no significant changes in collagen fibrils and fibroblasts (Matsuda et al., 2006). A collagen specific effect on skin aging factors was shown in another study. Skin aging results from degradation of structural components, like collagen and elastin, and moisture loss in the skin. The production of matrix metalloproteinases, a group of enzymes that is capable of degrading structural components of the extracellular matrix including collagen and elastin, is inhibited after 4 weeks of a collagen peptide diet. The results suggest that collagen hydrolysate can stimulate anabolic processes and reduce aging-related processes in the skin (Zague et al., 2011). The reduction of wrinkles after 8 weeks of oral intake of collagen peptides was investigated in a study with 114 healthy female test subjects. The intake of the bioactive collagen peptides promoted a significant reduction of eye wrinkle volume in the test group compared to the placebo group (Proksch et al., 2013).

A comprehensive study on the effect of oral collagen peptide supplementation on skin aging included clinical trials with Japanese and Caucasian women. The test subjects took fish collagen peptides in the range from 2 to 5 kDa over a period of 8 or 12 weeks. The fish collagen peptides were shown to increase the skin moisture level by 12 % in a period of 8 weeks. A consistent increase in the skin collagen density over 12 weeks of fish collagen peptide ingestion was indicated by increased dermal echogenicity. The test subjects were simultaneously investigated for changes in the quality of their dermal collagen network. Visual confocal microscopy analysis showed larger collagen fragments in the epidermis of the fish collagen treated test group compared to the

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no

placebo group. *Ex vivo* studies support the results of the clinical trials and showed an increased amount of water-binding glucosaminoglucans and collagen content in human skin explants incubated with fish collagen peptides (Asserin et al., 2015).

Collagen peptides protect skin and hair

The more conventional way to apply active compounds to skin and hair is the topical administration. Manufacturers in the cosmetic industry accumulated extensive knowledge in the formulation of beauty products like creams, mousses and sprays, containing active ingredients (Zague, 2008). Collagen peptides are compatible in these formulations and research demonstrates a positive impact on skin and hair properties. (Gelita, 2016).

Collagen peptides in the range of 0.6-12 kDa can adsorb onto keratin structures like skin and hair. Larger molecules bind stronger to those structures, but the water solubility decreases with increasing size. Adsorbed collagen peptides remain active on the skin surface for hours and longer. This collagen peptide layer was shown to bind moisture and contribute to an improved skin feel (Schrieber & Gareis, 2007). Low molecular weight fragments were shown to penetrate the upper layer of the dermis and support the natural protective barrier in the skin (Gelita, 2016). In a study with 62 human test subjects were fish derived collagen peptides shown to have a positive effect on the skin moisture content. The same study documented the transdermal penetration ability of those collagen peptides and show increased abilities for fish collagen peptides in the range of 3.5-4.5 kDa (Chai et al., 2010).

On hair, the collagen peptides also diffuse into the fibrous hair cells. Used in hair styling and dying applications, they protect against chemical damage (Schrieber & Gareis, 2007). High molecular weight, but also smaller collagen peptide fragments in a range from 1-3 kD were shown to bind stronger especially on bleached or waved hair structures (Mintz et al., 1991).

Added value for the musculoskeletal system

Products containing active collagen peptides have long been marketed on the US and European pharmaceutical and food markets. In Asia, mainly Japan, are collagen and collagen peptides sold as active ingredient in diverse functional food products. These products are used for treatment, improvement or maintenance of the musculoskeletal system (Wu et al., 2004). Many scientific and preclinical studies show various positive effects on tendon flexibility, ligaments stability, muscle and bone integrity and bone metabolism.

The extracellular matrix of tendons and ligaments contains predominantly fibrous collagen (70-80%). The highly ordered collagen fibrils, fibers and fascicles are responsible for the mechanical properties in the tendons and ligaments. A higher collagen content was shown to give more flexibility and stability to these components of the musculoskeletal system (Rumian et al., 2007). Specific collagen peptides, that can be oral administered, were shown to induce significantly increased collagen type I and III expression in fibroblasts from human ligaments and tendons. The same study conclude that therefore collagen peptides can be an option to treat and prevent pathological changes in the ligaments and tendons (Schunck and Oesser, 2013). The

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no

effect of collagen peptide supplementation on muscle mass and strength was investigated in a double blind randomized study with elderly people with class I or II sarcopenia. The data demonstrate that collagen peptide supplementation after resistance training led to an increased muscle strength and loss of fat mass. Collagen peptide supplementation was also shown to perform superior compared to supplementation with other protein sources (Zdzieblik et al., 2015).

Type I collagen plays also an important role in bone tissue. It provides not only elasticity and structure to the bones, it is also related to key processes in bone mineralization and metabolism (Marcus, 1996). The ability of collagen peptides, orally administered in high doses, to increase bone mass density and bone mineralization, was considered in an animal model. The study showed beneficial effects on bone integrity without undesirable side effects in the matured test subjects (Wu et al., 2004). Another study investigated the effect of specific fish derived collagen peptides on collagen expression, post-translational modification and mineralization in an osteoblastic cell culture. Fish collagen peptides were shown to upregulate the gene expression of collagen modifying enzymes, this effect led to an increased collagen synthesis and positive effects on collagen quality and matrix mineralization in the osteoblasts (Yamada et al., 2013).

Summary

Collagen peptides used in human nutrition and cosmetics received increasingly attention, after preclinical assays and bioavailability studies indicated positive health and beauty effects. They are regarded as safe and are applicable for topical and oral administered applications, such as body, skin and hair care products, dietary supplements, nutraceuticals and functional foods. Collagen peptides were shown to pass the intestine, enter the blood stream and be distributed to the targeted tissue in the body. They form a protective layer on skin and hair, where they prevent damage and moisture loss. The current trend in the food market leads us to expect an even greater interest in the collagen peptide field and even more future research on the different benefits. Recent research focusses much on the relative novel and unexplored collagen peptides from fish. Fish collagens have a slightly different amino acid composition with a wider variety of amino acids. That causes distinct properties and promise additional beneficial effects. Further areas of applications can be expected.

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no

References

Arnesen, JA.**,** Gildberg, A. (2006) Extraction of muscle proteins and gelatine from cod head. Process Biochemistry 41(3), 697-700.

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.

Avena-Bustillos, RJ., Olsen, CW., Olson, DA., Chiou, B., Yee, J., Bechtel, PJ., McHugh, TH. (2006) Water Vapor Permeability of Mammalian and Fish Gelatin Films. Journal of Food Science 71(4), E202-207

Chai, HJ., Li, JH., Huang, HN., Li, TL., Chan YL., Shiau, CY., Wu, CJ. (2010) Effects of size and conformations of fish-scale collagen peptides on facial skin qualities and transdermal penetration efficiency. Journal of Biomedicine and Biotechnology 2010, 1-8.

Flaschmajer, R., MacDonald, ED., Perlish, JS., Brugeson, RE., Fisher, LW. (1990) Dermal collagen fibrils are hybrids of type I and type III collagen molecules. Journal of Structural Biology 105(1-3), 162–169.

Gelita (2016), http://www.gelita.com/products/sol-c

Kadler, KE., Baldock, C., Bella, J., Boot-Handford, R.P. (2007) Collagens at a glance. Journal of Cell Science 120, 1955-1958.

Karim, AA., Bhat, R. (2009) Fish gelatin: properties, challenges, and prospects as an alternative to mammalian gelatins. Food Hydrocolloids 23(30), 563-576

Leatherhead Food Research (2013) www.leatherhead.com

Marcus, R., Feldman, D., Kelsey, J. (eds) (1996) Osteoporosis. Academic, New York

Matsuda, N., Koyama, Y., Hosaka, Y., Ueda, H., Watanabe, T., Araya, T., Irie, S., Takehana, K. (2006) Effects of ingestion of collagen peptid eon collagen fibrils and glycosaminoglycans in the dermis. Journal of Nutritional Science and Vitaminology 52(3), 211-215.

Mintz, GR., Reinhart, GM., Lent, B. (1991) Relationship between collagen hydrolysate molecular weight and peptide substantivity to hair. Journal of the Society of Cosmetic Chemists 42, 35-44.

Ohara, H., Matsumoto, H., Ito, K., Iwai, K., Sato, K. (2007) Comparison of quantity and structures of hydroxyproline-containing peptides in human blood after oral ingestion of gelatin hydrolysates from different sources. Journal of Agricultural and Food Chemistry 55 (4), 1532-1535.

Parry, DAD., Craig, AS., Barnes, GRG. (1978). Tendon and ligament from the horse: an ultrastructural study of collagen fibrils and elastic fibres as a function of age. Proceedings of the Royal Society B 203(1152), 293-303.

Postlethwaite, A. E., Seyer, J. M., & Kang, A. H. (1978). Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides. Proceedings of the National Academy of Sciences of the United States of America, 75(2), 871–875.

Proksch, E., Schunck, M., Zague, V., Degwert, J., Oesser, S. (2014). Oral intake of specific bioactive collagen peptides reduces skin wrinkles and increases dermal matrix synthesis. Skin Pharmacology and Physiology 27(3), 113-119.

Rumian, AP., Wallace, AL., Birch, HL. (2007). Tendons and ligaments are anatomically distinct but overlap in molecular and morphological features--a comparative study in an ovine model. Journal of Orthopedic Research 25(4), 458-464.

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no

Schrieber, R., Gareis, H. (2007) Gelatine Handbook: Theory and Industrial Practice. Wiley-VCH, Weinheim, 347 pp.
Schunck, M., & Oesser, S. (2013). Specific collagen peptides benefit the biosynthesis of matrix molecules of tendons and ligaments. Journal of the International Society of Sports Nutrition, 10(Suppl 1), P23.
Sibilla, S., Godfrey, M., Brewer, S., Budh-Raja, A., Genovese, L. (2015). An overview of the beneficial effects of hydrolysed collagen as a neutraceutical on skin properties: scientific background and clinical studies. The Open Nutraceutical Journal 8, 29-42.
Silva, TH., Moreira-Silva, J., Marques, ALP., Domingues, A., Bayon Y., Reis, RL. (2014) Marine Origin Collagens and Its Potential Applications. Marine Drugs 12, 5881-5901.
Thorkelsson, G., Slizyte, R., Gildberg, A., Kristinsson, HG. (2009) Fish proteins and peptide products: processing methods, quality and functional properties, Marine Functional Food, EditorJ.B.Luten, Wageningen Academic Publishers, 115-140.
Wang, L., An, X., Yang, F., Xin, Z., Zhao, L., Hu, Q. (2008). Isolation and characterization of collagens from the skin, scale and bone of deep-sea redfish (*Sebastes mentella*). Food Chemistry 108(2), 616-623.
Wasswa, J., Tang, J., Gu, X. (2007) Utilization of fish processing by-products in the gelatin industry. Food Reviews International 23(2), 159-174.
Wu, J., Fujioka, M., Sugimoto, K., Mu, G., Ishimi, Y. (2004) Assessment of effectiveness of oral administration of collagen peptide on bone metabolism in growing and mature rats. Journal of Bone and Mineral Metabolism 22(6), 547-553.**Yamada,** S., Nagaoka, H., Terajima, M., Tsuda, N., Hayashi, Y., & Yamauchi, M. (2013). Effects of fish collagen peptides on collagen post-translational modifications and mineralization in an osteoblastic cell culture system. Dental Materials Journal, 32(1), 88–95.
Zague, V. (2008), A new view concerning the effects of collagen hydrolysate intake on skin properties. Archives of Dermatological Ressearch 300 (9), 479-483.
Zague, V., Freitas, V., Costa Rosa, M., Alvares de Castro, G., Jaeger, R., Machado-Santelli, GM. (2011) Collagen hydrolysate intake increases skin collagen expression and suppresses matrix metalloproteinase 2 activity. Journal of Medical Food 14(6), 618-624.
Zdzieblik, D., Oesser, S., Baumstark, M. W., Gollhofer, A., & König, D. (2015). Collagen peptide supplementation in combination with resistance training improves body composition and increaincreases muscle strength in elderly sarcopenic men: a randomised controlled trial. The British Journal of Nutrition, 114(8), 1237–1245

Seagarden AS
Husøyvegen 278
4262 Avaldsnes
Norway
Phone: +47 52 85 94 80
www.seagarden.no