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Oral Use of Collagen Supplements in Dermatology

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ABSTRACT: Collagen is a crucial protein found in bones, muscles, skin, and tendons that provides strength and elasticity to tissues. It is obtained from sources such as marine organisms, cows, pigs, and chickens and is widely used in medicine and cosmetics. Hydrolyzed collagen peptides in the form of powder or liquid are typically used in food supplements. Marine collagen, produced from fish skin, is considered a high-quality source of collagen in food supplements. Research suggests that supplementation of hydrolyzed collagen improves skin hydration, elasticity, and collagen content. UV radiation, aging, and environmental toxins lead to the breakdown of collagen, causing wrinkles, dryness, and reduced elasticity. Excessive sun exposure should be avoided to boost collagen production. However, collagen supplementation has potential risks, including allergies and product quality. Oral supplements based on hydrolyzed collagen show promising results for the health and well-being of the skin, especially when sourced from marine collagen.

KEYWORDS: collagen, hydrolyzed collagen, skin aging, food supplements

INTRODUCTION

Collagen is a pivotal protein with a profound influence on our body's structural, mechanical, and tissue-building aspects. It is present in skin, bones, cartilage, smooth muscles, and the basal lamina, and makes up almost 30% of our body weight (1).

With 28 types identified so far, each one has a distinct role based on its chemical composition, morphology, distribution, and function.

The methods used in protein hydrolysis significantly impact the composition of the peptides in the final product, affecting molecular weight, amino acid composition, solubility, and functionality: Fibril-forming collagens; Fibril-associated collagens with interrupted tripled helices; Collagens forming networks; Transmembrane collagens; Multiplexins; Anchor fibers; and Beaded filament-forming collagens (1,2).

Extracted from industrial by-products such as bones, cartilage, tendons, and the skin of various animals including cattle, pigs, chickens, fish, and other marine organisms, collagen undergoes a hydrolysis process to yield bioactive peptides (3). The variables and methods employed in protein hydrolysis play a crucial role in shaping the composition of the peptides in the final product, impacting molecular weight, amino acid composition, and the solubility and functionality of the end product (4,5).

Structure and biosynthesis of collagen

Collagen is a protein that has several unique features, including a right-oriented triple helix composed of three α-chains, which contributes to its rigidity. The main amino acids that contribute to collagen's rigidity are glycine (33.5%), proline (12%), and hydroxyproline (10%) (2,6).

The structural levels of collagen include primary structure (amino acid triplet), secondary structure (α-helix), tertiary structure (triple helix), and quaternary structure (fibers). Based on the structures they form, collagens can be classified into different groups, such as fibril-forming collagens, network-forming collagens, FACIT collagens, MACIT collagens, and MULTIPLEXIN collagens (3,7).

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Collagen biosynthesis involves various cells, including fibroblasts, chondroblasts, osteoblasts, and odontoblasts, and is a complex process that starts with gene transcription in the cell nucleus.

Collagen is initially synthesized as a larger precursor, pro-protein, and is then synthesized as a large precursor polypeptide called procollagen. Biosynthesis starts with gene transcription in the cell nucleus, and individual polypeptide α-chains are synthesized on the rough endoplasmic reticulum. The propeptide is removed upon entering the endoplasmic reticulum, and prolyl and lysyl residues undergo hydroxylation and glycosylation. Procollagen molecules are then packaged into secretory vesicles in the Golgi apparatus and secreted into the extracellular space. Procollagen peptidases remove registration peptides outside the cell, and tropocollagen is formed by the association of molecules. Tropocollagen molecules are linked by lysyl oxidase to form collagen fibrils, which are further connected to form collagen fibers (3,5,8).

Degradation and loss of collagen

Collagen degradation is a natural process that occurs over time as we age, but it can also be accelerated by various external and internal factors. These factors include UV radiation, pollution, alcohol consumption, smoking, poor diet, stress, genetic inheritance, and hormonal changes (9). The main cause of collagen fragmentation is the increased expression matrix metalloproteinases (MMP). MMPs belong to the family of zinc-dependent endopeptidases. The main sources of MMPs in human skin are epidermal keratinocytes and dermal fibroblasts, although endothelial cells and immunocytes can also produce MMPs under physiological conditions (10,15). MMP is created in the skin as a normal product of physiological processes, but also as a result of environmental factors such as ultraviolet radiation and reactive oxygen species (ROS) (11).

ROS is a common name for a group of very reactive compounds which include oxygen radicals superoxide anion (O_2^-) and the hydroxyl radical (OH^-) and other reactive oxygen compounds such as hydrogen peroxide (H_2O_2), reactive singlet oxygen (O_2), hypochlorous acid (HOCl) and ozone (O_3) which can also cause oxidative damage of biological molecules such as collagen and leads to accelerated aging. ROS are created in the organism during physiological and pathological processes, while exogenous are radicals part of the toxic substances that we introduce into the body (cigarette smoke, xenobiotics, alcohol, air pollution), both of which have a negative effect on collagen in terms of degradation (9,11).

As collagen ages, it becomes fragmented and unevenly distributed, leading to a decrease in its overall quantity (9,13). Also with aging, fibroblasts lose their elasticity and mechanical tension. Mechanical tension of fibroblasts plays a crucial role in collagen synthesis, and a reduction in mechanical tension of fibroblasts shifts the balance towards collagen degradation (14,16).

Sources of collagen

Collagen can be derived from various sources, including animals and marine organisms. Common sources of collagen are cows, pigs, chickens, fish, and marine animals (17). Each source has its unique composition and characteristics.

For example, bovine collagen is derived from the skin, bones, and connective tissues of cows and is rich in type I and type III collagen (18,19, 20).

Porcine collagen is obtained from pig tissues and is similar in composition to bovine collagen, containing mostly type I collagen (21).

Chicken collagen is derived from chicken sternums or cartilage and is often used for its type II collagen content, which is specific to cartilage (22).

Fish collagen is extracted from fish skin and scales, has a smaller particle size and absorption rates. Marine collagen includes collagen from fish as well as other marine sources, and it may contain type I collagen. It is often promoted for its potential bioavailability and sustainability (23,24). It is essential to select collagen supplements from reputable sources, considering factors such as purity, quality, and ethical practices in sourcing (21).

Characteristics and production of hydrolyzed collagen

Collagen proteins, in their natural form, are poorly soluble in water due to their large molecular size, approximately 300 kDa. Hydrolysis breaks down collagen molecules into low-molecular-weight segments. Hydrolyzed collagen is obtained through extraction from various sources using salts, acids, and enzymes that cause protein denaturation and peptide hydrolysis. The best results were observed when hydrolyzed collagen was obtained after four hours of enzymatic hydrolysis with an average molecular weight of 5 kDa (25). Hydrolyzed collagen has several advantages over natural collagen, such as good digestibility, improved absorption and distribution rates after oral intake, lower viscosity, neutral odor, colorlessness, and transparency (25,26).

Hydrolyzed collagen is a small peptide with low molecular weight (0.3-8 kDa), enabling easier absorption in

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the intestines and greater tissue availability. It is rich in amino acids such as glycine and proline, leading to a better effect on the synthesis of type I collagen mRNA. Fibroblasts use amino acids from hydrolyzed collagen to renew existing collagen, while the specific sequence of amino acids in these peptides is responsible for stimulating receptors on the surface of fibroblasts, resulting in increased synthesis of new collagen fibers.

Several studies indicate that hydrolyzed collagen, when taken orally, exhibits chemotactic properties toward fibroblasts, aiding in skin regeneration. Compared to natural collagen, hydrolyzed collagen has improved absorption and distribution rates after oral intake, better digestibility, and antioxidant properties (25).

Bioavailability of hydrolyzed collagen

For hydrolyzed collagen to be active in deeper skin layers, it must pass through the intestinal barrier and enter the bloodstream. Proteases, such as pancreatic proteases and peptidases, break down hydrolyzed collagen into dipeptides, tripeptides, or free amino acids. Recent research has shown that peptides can also avoid hydrolysis in the digestive tract and be absorbed intact through the Pept1 transporter (27,28).

Hydrolyzed collagen has long been used in nutritional supplements because there are clinical studies that show satisfactory oral bioavailability, rapid absorption, and passage into the bloodstream in the form of small peptides and accumulation in the skin 96 hours after ingestion (28).

Efficacy of oral collagen supplementation

Research on the efficacy of oral collagen supplementation in improving skin health, reducing signs of aging, and promoting overall well-being has gained significant attention. While individual responses may vary, several studies have reported positive outcomes.

Oral collagen supplementation has been associated with increased skin elasticity and hydration, helping in reducing the appearance of fine lines and wrinkles (30,31). Collagen is also a structural component of nails and hair. Some individuals report improvements in nail and hair health, including increased strength and growth, with oral collagen supplementation (32,33).

It's essential to note that the efficacy of oral collagen supplementation can be influenced by factors such as the type of collagen used, dosage, duration of supplementation, and individual variations (31).

It has been found that marine collagen is more readily absorbed by the body than collagen obtained from land animal sources, due to its low molecular weight. Additionally, marine collagen contains fewer toxins, and peptides derived from marine fish proteins have higher antioxidant properties (36).

There have been eleven studies conducted, involving a total of 805 patients, to review the effectiveness of collagen supplements. Eight of these studies administered collagen hydrolysate ranging from 2.5g/d to 10g/d over 8 to 24 weeks, targeting conditions such as pressure ulcers, xerosis, skin aging, and cellulite. Two studies explored collagen tripeptide, administering 3g/d for 4 to 12 weeks, and found significant improvements in skin elasticity and hydration.

Overall, the preliminary findings suggest that oral collagen supplements can be effective in wound healing and addressing skin aging concerns, both in the short and long term. These supplements can also enhance skin elasticity, hydration, and dermal collagen density. Importantly, collagen supplementation appears to be generally safe, with no reported adverse events. However, more research is needed to establish conclusive evidence and determine optimal regimens for specific outcomes (34,35).

Potential considerations and risks

While collagen supplementation is generally considered safe for most people, there are some potential considerations and risks.

Factors such as collagen intolerance and excessive intake can lead to mild reactions. These reactions vary from person to person and can affect different parts of the body, including the skin, liver, kidneys, stomach, and heart.

Symptoms such as rashes, liver fibrosis, kidney stones, digestive problems, and abnormal heart rhythm are associated with excessive and long-term intake of collagen, but further studies and clinical research are needed to confirm this assumption.

Individuals with known allergies to specific sources of collagen, such as bovine or fish, should avoid supplements derived from those sources.

Some individuals may experience digestive symptoms, such as bloating or gastrointestinal discomfort, with collagen supplements.

Choosing hydrolyzed collagen may help alleviate these issues. Ensuring the purity and safety of collagen supplements is crucial. Contaminants or impurities in low-quality supplements may pose risks. Individuals taking medications or with pre-existing

medical conditions should consult with a healthcare professional before starting collagen supplementation to avoid potential interactions (21).

CONCLUSION

In summary, collagen is a vital protein in the human body, contributing to the structure and function of various tissues. Collagen supplementation, particularly in the form of hydrolyzed collagen, has gained popularity for its potential benefits in promoting skin health and joint function. While research supports some positive outcomes, individual responses may vary, and more studies are needed to establish definitive conclusions. As with any supplement, it's advisable to consult with a healthcare professional before starting collagen supplementation, especially for individuals with allergies, digestive sensitivities, or underlying health conditions. Additionally, choosing high-quality collagen supplements from reputable sources is essential for safety and efficacy.

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