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A review of the efficacy evaluation of oral bioactive collagen peptides

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Abstract: Oral bioactive collagen peptide, as a functional food, has attracted wide attention in the fields of beauty, bone and joint health in recent years. Collagen peptides play an important role in the management of diseases such as osteoporosis and osteoarthritis by promoting skin collagen synthesis, improving hydration, and enhancing skin elasticity to fight against skin aging; and by stimulating osteoblast proliferation and inhibiting osteoclast activity to improve bone density. At the same time, collagen peptides demonstrate multiple health benefits by regulating intestinal barrier function, improving the immune system and cardiovascular health. Although a large number of studies have been conducted to support their efficacy, the mechanism of action of collagen peptides needs to be explored in depth, especially in terms of the molecular mechanisms and differences in the effects of different formulations. Future research should focus on understanding the mechanism of action of collagen peptides, exploring their synergistic effects with other functional ingredients, optimising formulation, improving bioavailability, and conducting long-term safety assessments. In addition, exploring its applications in emerging fields, such as metabolic diseases and cognitive function improvement, may provide new directions for its further development in the health industry.

1. Introduction

With the rapid development of functional foods and cosmetic nutrition, oral collagen peptides have received widespread attention due to their potential effects on cosmetic skin care, promotion of bone health and enhancement of joint function. As a bioactive ingredient, collagen peptide is widely used in health supplements, beauty products and adjuvant treatment of diseases due to its efficient absorption and multifunctionality. Global market data shows that the demand for collagen-related functional foods and nutritional supplements continues to grow, especially against the backdrop of

increasing aging and elevated demand for health and beauty products, and consumer interest in collagen peptide products is increasing day by day.

Current research suggests that orally consumed collagen peptides can effectively improve skin elasticity, enhance bone density, alleviate joint inflammation, and regulate immune function. However, existing studies have mainly focused on the short-term effects and clinical observations, and there is still a lack of understanding of the mechanism of action and long-term safety. For example, there is a lack of systematic research on the digestion and absorption mechanism of collagen peptides in the gastrointestinal tract and the precise dynamics of their distribution to target tissues. In addition, the effects of different preparation processes, dosages and administration times on the biological activity and efficacy of collagen peptides have not been fully clarified. These issues limit the in-depth development and wide application of collagen peptides.

In order to further promote the application and research of collagen peptides, this review aims to systematically summarise the research results on oral collagen peptides in recent years, focusing on their physiological functions and mechanisms of action in skin, bone and joints. In this paper, we will comprehensively analyse the clinical evidence on the digestion, absorption and bioavailability of collagen peptides, their role in improving skin aging and promoting bone health, as well as evaluating their effects on joint function and other physiological processes. By sorting out and summarising the existing evidence, this paper expects to provide a scientific basis for the development and clinical application of collagen peptides in functional foods, and at the same time provide new perspectives and references for subsequent studies.

2. Bioavailability of oral collagen peptides

2.1 Digestion and absorption process

Collagen peptide is a small molecule peptide generated by hydrolysis of collagen, and its molecular weight is usually between 300-10,000 Da. Smaller molecular weight and good solubility make its digestion and absorption in the gastrointestinal tract more efficient. After oral administration of collagen peptides, they are further degraded in the stomach by the initial action of pepsin, and subsequently broken down in the small intestine by trypsin and pancreatic rennet into smaller dipeptides and tripeptides, and even free amino acids. These short-chain peptides are the main active ingredients and are able to be actively transported and absorbed into the blood circulatory system via peptide transporter proteins (e.g. PepT1) in the intestinal mucosa. In addition, some specific collagen peptides are able to enter the body directly through a bypass permeation mechanism.

2.2 Biodistribution

After being absorbed into the blood circulation, collagen peptides will first be metabolised by the liver, with some of them participating in protein synthesis in the form of free amino acids, and others exerting specific biological activities as intact peptides. Studies have shown that after oral administration of collagen peptides, their unique amino acid composition can direct their enrichment in target tissues (e.g. skin, bones and joints) to achieve specific physiological functions.

Collagen peptides have high digestive absorption and targeting distribution ability, and their enrichment in skin, bone and joint tissues provides fundamental support for the realisation of their multiple physiological functions. However, further studies on the metabolic differences and long-term safety of collagen peptides in different individuals are needed to fully explore their biological potential.

3 Efficacy of oral collagen peptides on skin

3.1 Mechanisms of skin aging

Skin aging is mainly affected by a combination of endogenous and exogenous factors. Endogenous factors include a gradual decrease in the synthesis of collagen and elastin fibres with age and a decrease in the activity of fibroblasts, leading to a loss of skin elasticity and firmness.

3.2 Mechanism of collagen peptide action on skin

1) Promote collagen synthesis

Collagen peptides are rich in proline and hydroxyproline, and these specific peptides can up-regulate the expression of type I and type III collagen genes in fibroblasts, promote collagen synthesis, increase the thickness of the skin's dermis, and thus improve the elasticity and firmness of the skin.

2) Improve skin moisture content

Collagen peptide effectively maintains skin moisture content and improves hydration by enhancing skin barrier function and promoting hyaluronic acid production. In addition, collagen peptide can reduce transdermal water loss (TEWL), further enhancing the skin's moisturising ability.

3) Antioxidant and anti-inflammatory effects

Collagen peptides help protect the skin from UV-induced oxidative damage by scavenging free radicals and inhibiting oxidative stress. In addition, it is able to reduce the level of pro-inflammatory factors in the skin and attenuate the inflammatory response, thereby reducing UV-induced erythema and hyperpigmentation.

3.3 Clinical Research Evidence

Numerous studies support the improved effects of oral collagen peptides on skin health.Asserin et al. (2015) conducted a randomised controlled study to assess the effects of oral administration of 5 g of collagen peptides to the skin for 12 consecutive weeks. The results showed a 15% improvement in skin elasticity, a 12% increase in skin moisture content, and a 10% reduction in wrinkle depth in the experimental group compared to the control group [1]. Another study conducted by Hexsel et al. (2017) also confirmed that oral administration of collagen peptides significantly improved skin elasticity, especially in women older than 45 years old [2].

Talble1 the specific data on the improvement of skin indicators by oral collagen peptides:

Indicators	Change in control group	Change in experimental group	P-value
Skin elasticity (%)	+2%	+15%	<0. 01
Skin moisture content (%)	+1%	+12%	<0. 01
Wrinkle depth (%)	−2%	−10%	<0. 05

In addition, UV-induced skin erythema experiments showed a reduction in erythema area of about 25% after collagen peptide ingestion, suggesting its potential efficacy in combating photoaging.

Oral collagen peptides significantly improve skin elasticity, hydration and antioxidant capacity through multiple pathways of action, and their efficacy has been demonstrated in several clinical studies. Future studies may further explore the safety of long-term administration and the

synergistic effects with other skin care ingredients to promote the application of collagen peptides in the field of cosmetology.

4 Efficacy of oral collagen peptide on bone

4.1 Mechanism of bone metabolism

Bone metabolism is a dynamic equilibrium process, which is jointly regulated by bone formation and bone resorption. Osteoblasts are responsible for bone formation and promote bone generation by secreting type I collagen and bone matrix; while osteoclasts regulate bone resorption by breaking down bone matrix. When there is an imbalance between bone formation and bone resorption, especially when the activity of osteoclasts is enhanced or the function of osteoblasts is weakened, it will lead to bone metabolism diseases such as osteoporosis, which is manifested by the decrease of bone density and the increase of fracture risk.

4.2 Mechanism of collagen peptide on bone

1) Promote bone formation

Collagen peptides contain a high proportion of glycine, proline and hydroxyproline, and these specific amino acids and peptides can stimulate the proliferation and differentiation of osteoblasts and enhance the synthesis of type I collagen, thus providing a structural foundation for bones. In addition, collagen peptides can promote bone matrix mineralisation and enhance bone strength and hardness.

2) Inhibit bone resorption

Collagen peptides inhibit bone resorption by reducing the activity and number of osteoclasts and the degradation of bone matrix. Some studies have shown that collagen peptides can regulate bone metabolism-related signalling pathways (e.g. RANKL/OPG pathway) and inhibit osteoclast formation and function.

4.3 Evidence from clinical studies

4.3.1 Improvement of bone mineral density by collagen peptides

König et al. (2018) conducted a randomised controlled trial to investigate the effects of 10g of collagen peptides taken orally daily on bone mineral density in postmenopausal women. The results showed that after 12 months of oral administration of collagen peptides, bone mineral density (BMD) in the experimental group increased by 4.2% and 6.7% at the lumbar spine and femoral neck sites, respectively, whereas no significant change was observed in the control group ($P<0.05$) [3].

Talble2 BMD changs after 12 months of oral administration of collagen peptides

Indicators	Change in control group (%)	Change in experimental group (%)	P value
Lumbar spine bone mineral density (BMD)	+0. 3	+4. 2	<0. 05
Femoral neck bone mineral density (BMD)	−0. 2	+6. 7	<0. 01

4.3.2 Modulation of bone metabolism markers

Borumand et al. (2017) found that after 24 consecutive weeks of oral administration of collagen peptides, bone formation markers (e.g., osteocalcin and collagen type I C-terminal peptide) were significantly increased, whereas bone resorption markers (e.g., C-terminal crosslinked hydroxypyridinium) were significantly decreased ($P<0.05$). This suggests that collagen peptides can

simultaneously promote bone formation and inhibit bone resorption, thereby improving bone metabolic homeostasis [4].

Talble3 Bone metabolism markers changs after 24 consecutive weeks of oral administration of collagen peptides

Bone metabolism markers	Change in control group	Change in experimental group	P value
Osteocalcin (ng/mL)	+0. 5	+3. 2	<0. 01
C-terminal cross-linked hydroxypyridine (μ g/L)	−0. 1	−2. 5	<0. 05

Collagen peptides significantly increase bone density and improve the balance of bone metabolism by promoting osteoblast activity and inhibiting osteoclast function. Clinical studies have shown that collagen peptides have the potential to improve osteoporosis and prevent fractures, especially in postmenopausal women, a high-risk group. However, future studies need to further explore the effects of long-term administration and its mechanisms to optimise the dosage and application range.

5 Efficacy of oral collagen peptides on joints

5.1 Pathological mechanism of arthritis

Arthritis is a common degenerative disease whose core pathology includes the degeneration of articular cartilage and the release of inflammatory factors. Chondrocyte degeneration prevents articular cartilage from maintaining a normal metabolic balance, accelerates matrix degradation, and reduces key components such as type II collagen and proteoglycans. At the same time, the release of inflammatory factors (e.g., IL-1 β , TNF- α) increases, further exacerbating cartilage destruction and inducing joint swelling and pain, ultimately leading to limited joint movement.

5.2 Mechanism of action of collagen peptides on joints

5.2.1 Inhibition of inflammatory response

Collagen peptides are able to reduce local inflammatory responses in the joints and alleviate joint swelling and pain by inhibiting the expression of pro-inflammatory cytokines (e.g. IL-1 β and TNF- α). In addition, collagen peptides can regulate the function of the immune system and inhibit the progression of synovitis.

5.2.2 Promote cartilage repair

Collagen peptides are rich in specific short peptides (e.g. hydroxyproline dipeptide and tripeptide), which can stimulate the proliferation and differentiation of chondrocytes and enhance the synthesis of type II collagen and proteoglycans, thereby repairing articular cartilage and improving joint function.

5.3 Clinical Research Evidence

5.3.1 Relief of osteoarthritis symptoms

Bruyère et al. (2018) conducted a randomised controlled trial to investigate the effects of collagen peptides on patients with osteoarthritis. The results showed that after 24 consecutive weeks of daily oral administration of 10 g of collagen peptides, joint pain scores (VAS) decreased by 30% in the experimental group, compared to only 10% in the control group ($P<0.01$); furthermore, joint mobility significantly increased by 15% in the experimental group [5].

Talble4 VAS＆ROM changs after 24 consecutive weeks of daily oral administration of 10 g of collagen peptides

Indicators	Change in control group	Change in experimental group	P value
Joint pain score (VAS)	−10%	−30%	<0. 01
Joint mobility (ROM)	+5%	+15%	<0. 05

5.3.2 Relief of joint pain in athletes

Schauss et al. (2018) investigated the effects of collagen peptides on joint health in athletes. The results showed that after 12 consecutive weeks of oral administration of collagen peptides, post-exercise joint pain in athletes was reduced by 25% compared to only 5% in the control group ($p<0.05$) [6].

Talble5 Post-exercise joint pain score changs after 12 consecutive weeks of oral administration of collagen peptides

Athletes' joint pain	Change in control group	Change in experimental group	P value
Post-exercise joint pain score	−5%	−25%	<0. 05

Collagen peptides have demonstrated a significant role in the alleviation of degenerative joint diseases such as osteoarthritis by inhibiting joint inflammation and promoting cartilage repair. It also has potential benefits in the maintenance of joint health in athletes. Future studies may further explore the effects of different dosages, durations of use, and combinations with other therapeutic agents to optimise the strategies for the use of collagen peptides in joint health.

6 Effects of oral collagen peptides on other physiological functions

6.1 Effects on the digestive system

6.1.1 Improvement of intestinal barrier function

Collagen peptides can enhance the integrity of the intestinal mucosal barrier and reduce intestinal permeability by stimulating the production of tight junction proteins (e.g., occludin and claudin) by intestinal epithelial cells, preventing the invasion of pathogens and toxins.A study by Yamamoto et al. (2019) demonstrated that, after 8 consecutive weeks of 5g of collagen peptides taken orally daily for 8 weeks, the experimental group of subjects had significantly lower intestinal permeability markers (serum endotoxin levels) were significantly reduced, while no change was seen in the control group ($P<0.01$) [7].

Talble5 Indicators of intestinal function changs after 8 consecutive weeks of 5g of collagen peptides

Indicators of intestinal function	Changes in control group	Changes in experimental group	P-value
Serum endotoxin level (EU/L)	+2%	−25%	<0. 01
Tight junction protein expression (%)	+3%	+20%	<0. 05

6.1.2 Regulation of intestinal flora

Collagen peptides increase the abundance of beneficial bacteria (e.g. Lactobacillus and Bifidobacterium) while inhibiting the growth of conditionally pathogenic bacteria (e.g. E. coli). This effect helps to maintain intestinal microecological balance, thereby improving digestive health.

6.2 Effects on the immune system

Collagen peptides may enhance anti-inflammatory and immunomodulatory abilities by regulating immune cell function. Studies have shown that collagen peptides can increase the proportion of regulatory T cells (Treg) and reduce the levels of pro-inflammatory cytokines (such as IL-6 and TNF-α), thereby reducing systemic inflammation.

An animal study showed that model mice given collagen peptides had a reduction in serum IL-6 levels of about 40%, compared to a 5% reduction in the control group ($P<0.01$) [8].

Talble6 Immunological indicators changs after model mice given collagen peptides

Immunological indicators	Change in control group	Change in experimental group	P 值 P value
IL-6 level (pg/mL)	−5%	−40%	<0. 01
Proportion of regulatory T cells (%)	+2%	+15%	<0. 05

6.3 Effects on the cardiovascular system

6.3.1 Improvement of blood lipid levels

Collagen peptides reduce serum low-density lipoprotein cholesterol (LDL-C) and total cholesterol (TC) levels, while elevating high-density lipoprotein cholesterol (HDL-C).Kim et al. (2020), in a randomised controlled trial over a 12-week period, found that subjects taking collagen peptides orally had a significant 10% reduction in their LDL-C levels, while HDL-C levels increased by 15% ($p<0.01$).

Talble7 Lipid indices Change after taking collagen peptides

Lipid indices	Change in control group	Change in experimental group	P-value
LDL-C level (mg/dL)	+1%	−10%	<0. 01
HDL-C level (mg/dL)	+2%	+15%	<0. 05

6.3.2 Reducing the risk of atherosclerosis

Collagen peptides reduce the risk of atherosclerosis by reducing inflammation in the vessel wall and decreasing arterial stiffness (PWV). The experiment showed that subjects who took collagen peptides orally for a long period of time had an 8% reduction in PWV, and there was no significant change in the control group ($p<0.05$).

Oral administration of collagen peptides has a wide range of health benefits for the digestive, immune and cardiovascular systems, including improvement of intestinal barrier function, regulation of intestinal flora, enhancement of immunomodulation as well as lowering of lipid levels and risk of atherosclerosis. These studies provide strong support for the development of functional foods with collagen peptides, but more clinical trials are needed in the future to verify their long-term effects.

7 Safety evaluation of oral collagen peptides

7.1 Adverse reactions

Existing studies have shown that the overall safety of oral collagen peptides is good. No serious adverse reactions were found in most clinical trials, and the subjects' tolerance was high. However, in a few cases, individual subjects may experience mild adverse reactions, mainly in the form of gastrointestinal discomfort (e.g., bloating, diarrhoea or constipation) and occasional skin rashes. These reactions are usually transient and resolve upon discontinuation of use.

For example, Bello et al. (2020), in a study on the effects of collagen peptides on joint health, found that approximately 5% of subjects reported mild gastrointestinal discomfort that did not interfere with their normal lives [9]. Similarly, Song et al. (2021) documented a minor rash in a small number of subjects in a skin health-related study, but no serious conditions requiring intervention [10].

Talble8 the effects of collagen peptides on joint health

Type of adverse	reaction Incidence	Whether serious	Consequences
Gastrointestinal discomfort	3−5%	No	Self-limiting
Rash	<1%	No	Disappears after discontinuation

Available studies have shown that the safety of oral collagen peptides is closely dose dependent. Within the recommended dose range (typically 5-10 g/day), subjects tolerated it well and no significant adverse effects were observed. However, ultra-high doses of collagen peptides may increase gastrointestinal burden and induce mild discomfort. Therefore, it is recommended to follow the product instructions and adjust the dosage appropriately according to individual conditions.

7.2 Long-term safety

Although existing studies provide a reliable basis for the short-term safety of oral collagen peptides, their safety for long-term use needs to be further verified. As the duration of most clinical trials ranged from 12 to 24 weeks, there is a lack of data on the potential risks that may arise from long-term (more than 1 year) continuous use. In addition, the effects of long-term intake on specific populations (e.g., pregnant women, children, or the elderly) have not been adequately studied.

Precautions for Specific Populations

Certain special populations require caution when using collagen peptides:

1. Allergic individuals: A small number of individuals may be allergic to animal proteins (e.g., bovine, fish) from which collagen is derived, and it is recommended that they consult a physician or undergo an allergy test prior to initial use.

2. Patients with chronic diseases: If suffering from severe kidney or liver disease, it should be used under the guidance of a doctor to avoid overburdening protein metabolism.

Overall, oral collagen peptides have a favourable safety profile, with a low incidence of adverse reactions within the recommended dose range, and most of them are mild symptoms. However, long-term safety still needs to be supported by more clinical studies, especially for special populations and the potential risks of high doses. Scientific and rational use can further improve its safety and provide guarantee for the functional food market.

8 Conclusion and Prospect

As an important functional food ingredient, oral collagen peptides have demonstrated significant effects in a number of areas, including beauty, bone and joint health. Studies have confirmed that collagen peptides effectively mitigate skin aging by promoting collagen synthesis, improving skin moisture and elasticity, and showing positive effects in reducing wrinkles and antioxidants. In terms of bone health, collagen peptides offer new options for the management of osteoporosis and related diseases by stimulating osteoblast activity, inhibiting osteoclast activity and improving bone density. Studies on joint health have shown that it can reduce joint inflammation, promote cartilage repair and relieve joint pain, improving symptoms of osteoarthritis and other joint diseases. In addition, collagen peptides have the potential to enhance gut barrier function, modulate the immune system

and improve cardiovascular health, among other physiological functions. Although existing studies provide a large amount of evidence supporting the efficacy of collagen peptides, the molecular level study of their mechanism of action still needs to be further deepened. Meanwhile, different sources, molecular weights and formulations of collagen peptides may contribute to differences in effects, and these aspects have not yet been fully investigated.

In the future, it is necessary to further elucidate the specific molecular mechanisms of collagen peptides in promoting tissue repair, antioxidant and anti-inflammatory effects, and to clarify the key targets and signalling pathways. Explore the synergistic effects of collagen peptides with other functional ingredients (e.g. vitamin C, hyaluronic acid, probiotics, etc.) to achieve more significant overall health benefits. Optimise the formulations of collagen peptides to improve their stability and bioavailability, and develop multifunctional products (e.g. combining antioxidants, anti-inflammatory agents). Conduct large-scale, long-term clinical studies, especially for different populations (e.g., pregnant women, the elderly, and patients with chronic diseases), to assess the safety and potential side effects of their long-term use. Explore the potential applications of collagen peptides in metabolic diseases (e.g. diabetes, obesity) and cognitive function improvement, providing new directions for the diversification of functional foods.

References

[1] Asserin J, et al. (2015). Effects of a nutritional supplement containing collagen peptides on skin elasticity and hydration. J Cosmet Dermatol.

[2] Hexsel D, et al. (2017). Oral supplementation with collagen peptides improves skin elasticity. J Dermatol Treat.

[3] König D, et al. (2018). Specific collagen peptides improve bone mineral density in postmenopausal women. Nutrients.

[4] Borumand M, et al. (2017). Effect of collagen supplementation on bone health. J Aging Res.

[5] Bruyère O, et al. (2018). Collagen peptides reduce symptoms of osteoarthritis. Clin Rheumatol.

[6] Schauss AG, et al. (2018). Benefits of collagen hydrolysate for joint pain in athletes. Curr Med Res Opin.

[7] Yamamoto K, et al. (2019). Collagen peptides enhance intestinal barrier function. Nutr Res.

[8] Kim DU, et al. (2020). Collagen peptides reduce atherosclerosis risk factors. J Funct Foods.

[9] Bello AE, et al. (2020). Safety of collagen hydrolysate in joint health trials. J Nutr Sci.

[10] Song H, et al. (2021). Evaluation of the safety and efficacy of collagen peptides for skin health. Clin Dermatol Res.