Beneficial Effects of Collagen Hydrolysate: A Review on Recent Developments

Article · July 2017

CITATIONS
11

READS
11,718

2 authors:

Hongdong Song
University of Shanghai for Science and Technology
9 PUBLICATIONS **63** CITATIONS
SEE PROFILE

Bo Li
China Agricultural University
54 PUBLICATIONS **1,553** CITATIONS
SEE PROFILE

DOI: 10.26717/BJSTR.2017.01.000217

Bo Li. Biomed J Sci & Tech Res

ISSN: 2574-1241

Research Article Open Access

Beneficial Effects of Collagen Hydrolysate: A Review on Recent Developments

Hongdong Song[1] and Bo Li[1,2*]

[1]*Beijing Advanced Innovation Center for Food Nutrition and Human Health, China Agricultural University, China*

[2]*Beijing Higher Institution Engineering Research Center of Animal Product, China*

Received: July 15, 2017; **Published:** July 24, 2017

***Corresponding author:** Bo Li, Beijing Higher Institution Engineering Research Center of Animal Product, Beijing Advanced Innovation Center for Food Nutrition and Human Health, 17, Qinghua East Road, Haidian District, Beijing 100083, China, Tel: + 86 10 6273 7669; Email: libo@cau.edu.cn

Abstract

Collagen hydrolysate (CH) has received increasing attention in recent decades. This review mainly summarizes the recent developments (year 2010-2017) regarding the beneficial effects of CH in animal experiments and clinical trials. These beneficial effects include antioxidant, anti aging, anti osteoporotic and anti osteoarthritis, anti-inflammatory, anti tumor, wound healing, anti hypertensive and anti atherosclerotic, anti obesity and hypoglycemic effects. We also make comments on the current researches and give suggestions for future studies in this review. Considering the wide availability of CH in the field of pharmaceuticals and foods, the study of the potential beneficial effects of CH provides guidance to develop CH-based health care supplements for disease prevention and/or treatment.

Keywords: Collagen Hydrolysate; Beneficial Effect; Animal Experiment; Clinical Trial

Introduction

Collagen is the main structural protein of the different connective tissues, such as skin, bone, cartilage and tendons, and comprises about one-third of total proteins in mammals. Collagen extracted from collagen-rich materials with hot water is known as gelatin. The common materials used for extracting gelatin include pig skin (46%), bovine hide (29.4%), bones (23.1%) and other sources (1.5%) [1]. However, fish gelatin has received great attention in recent years due to the religions, cultures and health concerns. The further enzymatic hydrolysis of gelatin results in collagen hydrolysate (CH). CH has long been used in pharmaceuticals and foods in many countries and regions, such as United States, Europe, China and Japan. Approved as Generally Recognized As Safe (GRAS), the safety of CH has been affirmed by the Food and Drug Administration (FDA) Center for Food Safety and Nutrition. The bioavailability and absorption of CH have also been widely studied. It has been reported that CH is more easily absorbed and has higher bioavailability than gelatin [2,3]. Besides free amino acids, small peptides especially dipeptide and tripeptide are also absorbed into body by peptide transporter 1 (PepT1) [4]. To date, more than30 peptides (mainly dipeptides and tripeptides) have been identified in blood after gelatin and CH intake, and Pro-Hyp is the most abundant collagen-derived peptide [5-7]. These peptides may exert various beneficial effects on body health as previous studies reported [8-9]. In this paper, we will mainly focus on the recent findings (year 2010-2017) regarding the beneficial effects of CH in animal experiments and clinical trials (Figure 1). The possible mechanisms underlying CH will also be briefly discussed.

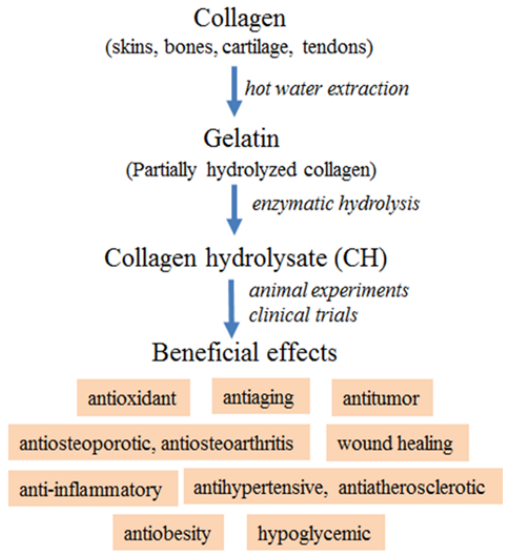

Figure 1: The beneficial effects of CH in animal experiments and clinical trials.

Beneficial Effects

Enhancing Antioxidant Capacity

CH itself has good antioxidant activity as demonstrated by in vitro assays [10,11]. CH intake also increases the activities of antioxidant enzymes in body, including SOD, GSH-Px and CAT [3,12]. Nuclear factor E2-related factor 2 (Nrf2)-antioxidant response element (ARE) pathway plays a central role in regulating antioxidant enzymes. Therefore, we speculate that CH exerts it antioxidant effect in a direct and/or indirect manner. More work is needed to investigate the effect of CH on Nrf2-AREsignaling.

Anti aging effect

Anti aging effect of CH has been widely investigated in several animal models, including photo aged model, chronologically aged model and acetone-induced dry skin model [3,12-15]. General beneficial effects, including increasing skin hydration, decreasing the formation of deep wrinkles and improving skin elasticity, are also observed in clinical trials after taking 10g of CH once a day for more than 6 weeks [16]. It should be noted that anti aging effect of CH is more obvious on women aged more than 30 years. Mechanisms underlying the beneficial effects may be involved in the dual effects of CH on skin collagen synthesis and degradation, as previous study reported [13].

Preventing and treating osteoporosis and osteoarthritis

Anti osteoporotic and anti osteoarthritis effects of CH have been reviewed by Daneault et al. [17] and Porfírio et al. [18]. Daily doses equivalent to 12g of CH significantly promotes an improvement in the symptoms of osteoarthritis and osteoporosis [18]. Combined CH with other nutritional ingredients has received much interest. It has been reported that combined oral administration of CH with calcium and vitamin D has better effects on bone health than alone administration of CH or calcium and vitamin D [19-21]. Future studies are needed to determine the optimal form and optimal dose of CH.

Enhancing wound healing

Oral administration of marine CH is reported to enhance cutaneous wound healing and angiogenesis in rats [22-23]. In addition to elevated VEGF and FGF-2 expression, the effect of CH on fibroblast may be one of the mechanisms underlying enhanced wound healing, as previous study reported that Pro-Hyp, a collagen-derived dipeptide, exerts a chemotactic action on fibroblast and stimulates fibroblast proliferation [8].

Anti-inflammatory effect

Glycine is one of the major structural units of collagen, accounting for one-third of the amino acids.CH has the ability to reduce inflammatory responses [24,25]. This effect may be constituted by inhibiting the production of pro-inflammatory cytokine via glycine-gated chloride channels (GlyR).

Antitumor effect

Liang et al. reported CH intake inhibited spontaneous tumor incidence and increase life spanin sprague-dawley (SD) rats [26]. Our previous study found that CH intake inhibited platelet release and down regulated proangiogenic factors in blood [27]. Considering angiogenesis is of key importance in the process of tumorprogression. Our results provide a possible mechanism underlying antitumor effect of CH.

Reducing the risk of cardiovascular diseases

Antihypertensive effect of CH has been reported in animal experiments and clinical trials [28,29]. Oral administration of collagen derived Gly-Leu-Prosignificantly decreases systolic blood pressure by inhibiting angiotensin I converting enzyme (ACE) [28]. Tang et al. [30]found that oral administration of collagen tripeptide had an inhibitory effect on atherosclerosis development in hypercholesterol emic rabbits [30]. Platelets are involved in the patho physiology of atherosclerosis and thrombosis.CH has an inhibitory activity on platelet release and platelet aggregation, which may justify potential application of CH as a health care supplement to prevent and/or treat atherosclerosis and thrombosis-related cardiovascular diseases [27].

Other effects

CH intake has an effect on the absorption and metabolism of lipid and glucose.CH significantly reduces high fat diet-induced body weight gain and down regulates serum levels of total cholesterol, triglyceride and low-density lipoprotein [31]. Further, CH could alter lipid metabolism-related gene expression and the unfolded protein response in mouse liver [32]. The hypoglycemic effects of CH have also been reported [33,34]. It has been reported that CHcan improve glucose tolerance by inhibiting intestinal glucose uptake and enhancing insulin secretion [34], suggesting the anti diabetic property of CH.

Conclusion and Perspective

Increasing evidence demonstrates that CH has various beneficial effects on body health. Those effects make CH new and potential healthcare supplement for disease prevention and/or treatment in pharmaceuticals and foods. However, several issues should be noted and need to be further explored. First, many in vitro studies only focus on the biological activities of CH, neglecting its tolerance in gastrointestinal tract. Certain collagen peptides isolated in in vitro studies may be hydrolyzed by gastrointestinal enzymes and exert no biological activity in body as expected in in vitro studies. In vitro simulated GI digestion and Caco-2 mono layers have been widely used and allow the prediction of oral compounds digestion and absorption in humans. Second, although many beneficial effects of CH have been reported, what is the peptide sequence responsible for certain beneficial effect? The study on structure-activity relationship will guide the application of CH. Third, the biological activities of protein hydrolysates are highly affected by their molecular structure and weight, which are greatly impacted by their processing conditions. Therefore, processing conditions are needed to be optimized for obtaining CH with certain beneficial effect.

Acknowledgement

This study was supported by the grants from China Agriculture Research System (CARS-46) and National Natural Science Foundation of China (NSFC,No. 31271846).

References

1. Ali ME, Sultana S, Hamid SBA, Hossain MM, YehyaWA, et al. (2016) Gelatin Controversies in Food, Pharmaceuticals and Personal Care Products: Authentication Methods, Current Status and Future Challenges. Crit Rev Food SciNutr 29: 1-7.
2. Oesser S, Adam M, Babel W, Seifert J (1999) Oral administration of 14C labeled gelatin hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL). J Nutr 129(10): 1891-1895.
3. Song H, Meng M, Cheng X, Li B, Wang C (2017) The effect of collagen hydrolysates from silver carp (Hypophthalmichthys molitrix) skin on UV-induced photo aging in mice: molecular weight affects skin repair. Food Funct 8(4): 1538-1546.
4. Brandsch M (2013) Drug transport via the intestinal peptide transporter PepT1. Curr Opin Pharmacol 13(6): 881-887.
5. Wang L, Wang Q, Liang Q, He Y, Wang Z, et al. (2015) Determination of bioavailability and identification of collagen peptide in blood after oral ingestion of gelatin. J Sci Food Agric 95(13): 2712-2717.
6. Taga Y, Kusubata M, Ogawa-Goto K, Hattori S (2016) Efficient absorption of X-hydroxyproline (Hyp)-Gly after oral administration of a novel gelatin hydrolysate prepared using ginger protease. J Agric Food Chem 64(14): 2962-2970.
7. Yazaki M, ItoY, Yamada M, Goulas S, Teramoto S, et al. (2017) Oral Ingestion of Collagen Hydrolysate Leads to the Transportation of Highly Concentrated Gly-Pro-Hyp and Its Hydrolyzed Form of Pro-Hyp into the Bloodstream and Skin. J Agric Food Chem 65: 2315-2322.
8. Ohara H, Ichikawa S, Matsumoto H, Akiyama M, Fujimoto N, et al. (2010) Collagen-derived dipeptide, proline-hydroxyproline, stimulates cell proliferation and hyaluronic acid synthesis in cultured human dermal fibroblasts. J Dermatol 37(4): 330-338.
9. Hatanaka T, Kawakami K, Uraji M (2014) Inhibitory effect ofcollagen-derived tripeptides on dipeptidylpeptidase-IV activity. JEnzyme InhibMedChem 29(6): 823-828.
10. Alemán A, Giménez B, Pérez-Santin E, Gómez-Guillén MC, Montero P (2011) Contribution of Leu and Hyp residues to antioxidant and ACE-inhibitory activities of peptide sequences isolated from squid gelatin hydrolysate. Food Chem 125: 334-341.
11. Nakchum L, Kim SM (2016) Preparation of squid skin collagen hydrolysate as an antihyaluronidase, antityrosinase, and antioxidant agent. Prep BiochemBiotechnol 46(2): 123-130.
12. Wang Z, Wang Q, Wang L, Xu W, He Y, et al. (2017) Improvement of skin condition by oral administration of collagen hydrolysates in chronologically aged mice. J Sci Food Agric 97(3): 2721-2726.
13. Liang J, Pei X, Zhang Z, Wang N, Wang J, et al. (2010) The Protective Effects of Long-Term Oral Administration of Marine Collagen Hydrolysate from Chum Salmon on Collagen Matrix Homeostasis in the Chronological Aged Skin of Sprague-Dawley Male Rats. J Food Sci 75(8): 230-238.
14. Fan J, Zhuang Y, Li B (2013) Effects of collagen and collagen hydrolysate from jellyfish umbrella on histological and immunity changes of mice photoaging. Nutrients 5: 223-233.
15. Okawa T, Yamaguchi Y, Takada S, Sakai Y, Numata N, et al. (2012) Oral administration of collagen tripeptide improves drynessand pruritus in the acetone-induced dry skin model. J DermatolSci 66(2): 136-143.
16. Sibilla S, Godfrey M, Brewer S, Budh-Raja A,Genovese L (2015) An overview of the beneficial effects of hydrolysed collagen as a nutraceutical on skin properties: Scientific background and clinical studies. Open Nutraceuticals J 8: 29-42.
17. Daneault A, Prawitt J, Fabien Soulé V, Coxam V, Wittrant Y (2017) Biological effect of hydrolyzed collagen on bone metabolism. Crit Rev Food Sci Nutr 57(9): 1922-1937.
18. Porfírio E, Fanaro GB (2016) Collagen supplementation as a complementary therapy for the prevention and treatment of osteoporosis and osteoarthritis: a systematic review. RevistaBrasileira de Geriatria e Gerontologia 19: 153-164.
19. Liu J, Wang Y, Song S, Wang X, QinY, et al. (2015) Combined oral administration of bovine collagen peptides with calcium citrate inhibits bone loss in ovariectomized rats. PloS one 10(10): e0135019.
20. Elam ML, Johnson SA, Hooshmand S, Feresin RG, Payton ME, et al. (2015) A calcium-collagen chelate dietary supplement attenuates bone loss in postmenopausal women with osteopenia: a randomized controlled trial. J Med Food 18(3): 324-331.
21. Hooshmand S, Elam ML, Browne J, Campbell SC, Payton ME (2013) Evidence for bone reversal properties of a calcium-collagen chelate, a novel dietary supplement. J Food NutrDisor 2: 1.
22. Zhang Z, Wang J, Ding Y, Dai X, Li Y (2011) Oral administration of marine collagen peptides from Chum Salmon skin enhances cutaneous wound healing and angiogenesis in rats. J Sci Food Agric 91(12): 2173-2179.
23. Wang J, Xu M, Liang R, Zhao M, Zhang Z, et al. (2015) Oral administration of marine collagen peptides prepared from chum salmon (Oncorhynchus keta) improves wound healing following cesarean section in rats. Food Nutr Res 59: 26411.
24. Hartog A, Cozijnsen M, de Vrij G, Garssen J (2013) Collagen hydrolysate inhibits zymosan-induced inflammation. ExpBiol Med 238(7): 798-802.
25. Zhang Y, Kouguchi T, Shimizu K, Sato M, Takahata Y, et al. (2010) Chicken collagen hydrolysate reduces proinflammatory cytokine production in C57BL/6.KOR-ApoEshl mice. J NutrSciVitaminol 56(3): 208-210.
26. Liang J, Pei XR, Wang N, Zhang ZF, Wang JB, et al. (2010) Marine collagen peptides prepared from chum salmon (Oncorhynchus keta) skin extend the life span and inhibit spontaneous tumor incidence in sprague-dawley rats. J Med Food 13(4): 757-770.
27. Song H, Zhang L, Luo Y, Zhang S, Li B (2017) Effects of Collagen Peptides Intake on Skin Aging and Platelet Release in Chronologically Aged Mice Revealed by Cytokine Array Analysis.
28. Lee JK, Jeon JK, Byun HG (2014) Antihypertensive effect of novel angiotensin I converting enzyme inhibitory peptide from chum salmon (Oncorhynchus keta) skin in spontaneously hypertensive rats. J Funct Foods 27: 381-389.
29. Kouguchi T, Ohmori T, Shimizu M, Takahata Y, Maeyama Y, et al. (2013) Effects of a chicken collagen hydrolysate on the circulation system in subjects with mild hypertension or high-normal blood pressure. BiosciBiotechnolBiochem 77 (4): 691-696.
30. Tang L, Sakai Y, Ueda Y, Katsuda S (2015) Effects of oral administration of tripeptides derived from type I collagen (collagen tripeptide) on atherosclerosis development in hypercholesterolemic rabbits. J BiosciBioeng 119(5): 558-563.
31. Lee EJ, Hur J, Ham SA, Jo Y, Lee S, et al. (2017) Fish collagen peptide inhibits the adipogenic differentiation of preadipocytes and ameliorates obesity in high fat diet-fed mice. Int J BiolMacromol 104: 281-286.
32. Tometsuka C, Koyama YI, Ishijima T, Toyoda T, Teranishi M, et al. (2017) Collagen peptide ingestion alters lipid metabolism-related gene expression and the unfolded protein response in mouse liver. Br J Nutr 117(1): 1-11.
33. Zhang R, ChenJ, Jiang X, Yin L, Zhang X (2016) Antioxidant and hypoglycaemic effects of tilapia skin collagen peptide in mice. Int J Food Sci 51(10): 2157-2163.
34. Iba Y, Yokoi K, Eitoku I, Goto M, Koizumi S, et al. (2016) Oral Administration of Collagen Hydrolysates Improves Glucose Tolerance in Normal Mice Through GLP-1-Dependent and GLP-1-Independent Mechanisms. J Med Food 19: 836-843.