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How oral collagen intake can be useful in dermatology

Collagen is the main component of dermis. It represents as much as 75 % of dry skin weight. With aging, collagen content decreases in the skin, because of a reduced production by the fibroblasts and higher metabolism rate. This leads to the common signs of skin aging, i. e. loss of elasticity of the skin, fine lines and wrinkles. Therefore, there is a need for bringing extra collagen to the skin. This cannot be made by topical creams, as the molecular size of the molecule does not permit its absorption through the skin. On the contrary, oral collagen hydrolytes, are easily absorbed by the gut, and reach the skin in abundance, where they remain for a certain time. Many studies, which are reviewed in this article, show the benefits of oral intake of collagen hydrolyte not only on the skin, but also on the nails, on hair growth and even on cellulite.

Key words

Collagen, oral intake, absorption, sources, skin, aging, hair, nails, cellulite.

The extracellular matrix of connective tissues represents a complex blend of variable members of diverse protein families defining structural integrity and various physiological functions. The supramolecular arrangement of fibrillar elements, microfibrillar networks as well as soluble proteins, glycoproteins and a wide range of other molecules define the biophysical characteristics. Composition and structure vary considerably among different types of connective tissues. Tissue-specific expression and synthesis of structural proteins and glycoprotein components result in the unique functional and biological characteristics at distinct locations [1].

The most abundant proteins in the extracellular matrix are members of the collagen family. Collagens were once considered to be a group of proteins with a characteristic molecular structure with their fibrillar structures contributing to the extracellular scaffolding. Thus, collagens are the major structural element of all connective tissues, especially the skin, and are also found in the interstitial tissue of virtually all parenchymal organs, where they contribute to the stability of tissues and organs and maintain their structural integrity [1].

1. Structure of collagens

The name «collagen» is used as a generic term for proteins forming a characteristic triple helix of three polypeptide chains and all members of the collagen family form these supramolecular structures in the extracellular matrix although their size, function and tissue distribution vary considerably. So far, 26 genetically distinct collagen types have been described [1]. Based on their structure and supramolecular organization, they can be grouped into fibril-forming collagens, fibril-associated collagens (FACIT), network-forming collagens, anchoring fibrils, transmembrane collagens, basement membrane collagens and others with unique functions. The most abundant and widespread family of collagens with about 90 % of total collagen is represented by the fibril-forming collagens. Type I collagen is the major structural component of the skin. Despite their structural diversity, all members of the collagen family have several characteristic features in common:

- A right-handed triple helix composed of three a-chains. These might be formed by three identical chains (homotrimers) as in collagens II, III, VII, VIII, X and others or by two or more different chains (heterotrimers) as in collagen types I, IV, V, VI, IX and XI.
- Each of the three a-chains within the molecule forms an extended left-handed helix with a pitch of 18 amino acids per turn [2].
- The three chains, staggered by one residue relative to each other, are supercoiled around a central axis in a right-handed manner to form the triple helix [3].
- A structural prerequisite for the assembly into a triple helix is a glycine residue, the smallest

amino acid, in every third position of the polypeptide chains resulting in a (Gly-X-Y)n repeat structure which characterizes the «collagenous» domains of all collagens.

2. Collagen in the skin

Collagen and elastic connective tissues are the main types of fibrous connective tissues in dermis. The mechanical properties of dermis depend on the properties of the matrix molecules per se and on its supramolecular organization in fibrous elements, its assembling and integration in a cross-linked structure. Other no-fibrous molecules of connective tissue include glycoproteins in fine filaments and proteoglycans and glycosaminoglycans of the basal matrix.

Collagen is the main component of the dermis [4]. It constitutes approximately 75 % of dry skin weight and conveys resistance to traction and elasticity. Interstitial collagens with periodic stripes (types I, III and V) are responsible for the major proportion of collagen in the dermis by adults. Around 80—90 % of collagen is type I and 8—12 % type III. Type V collagen, in spite of representing less than 5 %, is co-distributed and assembled in fibrils with types I and III collagens, and it is supposed that it helps in regulating the diameter of fibrils [5]. A great numbers of factors such as physical and chemical properties of the collagen molecules and their interaction with proteoglycans (PG) and other proteins (including other collagens) in the extracellular space influence the assembling of the molecules to constitute fibrils [5]. Recent studies suggest that in vivo the collagen fibrils are constituted by various types of collagen and other macromolecules, such as PG. Collagen fibrils in dermis are hybrids of type I and III collagens [6].

3. Collagen in skin aging

As a result of cellular senescence, non-dividing aged dermal fibroblasts accumulate in the dermal connective tissue and the synthesis of various extracellular matrix proteins by senescent fibroblasts is undoubtedly reduced. It is well known that the synthesis of fibrillar collagen, which is the major extracellular matrix protein and provides a supportive extracellular framework, is reduced in aged skin [7]. In a study of collagen production in chronologically aged skin, the content of type I collagen, the major collagen in the skin and a marker of collagen synthesis, is deceased by 68 % in old skin versus young skin, and cultured young fibroblasts synthesize more type I collagen than old cells [8]. The main reason for decreased production of collagen was found to be due to decreased synthesis of mRNA for type I collagen, and there was a threefold reduction in the steady-state level of type I collagen mRNA in senescent fibroblasts [9]. More fundamental mechanisms for age-related collagen synthesis involve the transforming growth factor-β (TGF-β)-induced signalling pathway of collagen synthesis. The ability of TGF-β to stimulate the synthesis of extracelluar matrix components in cultured fibroblasts is well-documented [10—12]. TGF-β-induced Smad2 phosphorylation is an initial molecular event mediated by TGF-β receptor I kinase. Phosphorylated Smad2 dissociates from the receptor and then forms a complex with Smad4. The Smad complex translocates to the nucleus where it activates the transcription of target genes including COL1A2, a gene for type I procollagen. In the early step of this process, Smad2 phosphorylation may also occur as the result of activation of a kinase located downstream of MEK-1 and upstream of the MAPK/ERK pathway [13]. Other intermediate factors may be involved in this signalling pathway; one protein that induces the gene expression of extracellular matrix protein is the connective tissue growth factor (CTGF), a cysteine-rich peptide [14].

CTGF is secreted by fibroblast cells after activation by TGF-β and acts as a downstream mediator of TGF-β-induced collagen synthesis [15]. It has been recently reported that CTGF is potently induced by TGF-β and stimulates type I procollagen expression through COL1A2 promotor activation [16, 17].

Accordingly, the TGF-β/Smad/CTGF/procollagen axis is the main signalling pathway for collagen synthesis in dermal fibroblasts and it is also found that TGF-β, CTGF, and type I procollagen genes are all down-regulated in aged human skin in vivo [17]. In one study [18], expression levels of TGF-β, CTGF, and type I procollagen genes were reduced to 70, 50 and 75 %, respectively, in aged dermis compared to young dermis. Therefore, reduced synthesis of collagen in aged skin can be clearly explained by down-regulation of signalling proteins in TGF-β-mediated collagen synthesis. The loss of collagen synthesis is recognized as a characteristic of chronologically aged skin by the cellular senescence of fibroblasts. However, there are some reports providing evidence that collagen synthesis is decreased by UV irradiation, the major factor for extrinsic skin aging [19, 20]. The mechanism of reduced collagen production by UV irradiation is also related to the TGF-β/Smad pathway. In human skin, UV irradiation impairs the TGF-β/Smad pathway by down-regulating TGF-β type II receptor, and leads to reduced TGF-β responsiveness and repression of TGF-β target genes including type I procollagen [21, 22]. UV irradiation can also reduce collagen production in dermal fibro-

blasts by a different mechanism associated with mechanical tension. According to previous studies, fibroblasts in healthy cells have normal mechanical tension by attaching to intact collagen fibrils and containing abundant actin in their cytoplasm [23, 24]. In contrast, cells in photo-aged skin are in a mechanically relaxed state from contacting fragmented or amorphous collagen and having lower amounts of actin. With reduced mechanical tension, signalling through MAPK or TGF-β is not effectively transduced to the nucleus and subsequent transcription of collagens genes is inhibited [25, 26]. Another key condition of skin aging associated with atrophy of the dermal connective tissue is the destruction of extracellular matrix (ECM) components, in particular collagen fibres.

4. Absorption of collagen taken orally

Native collagen is very resistant and regarded as indigestible; the average molecular weight of collagen is about 300 000 and it is difficult to grasp how it could be absorbed and transported to the different organs [27]. To increase solubility of collagen, some enzymatic hydrolysates of collagen have been prepared. Hydrolysed collagen, or collagen hydrolysates (CH) feature a heterogeneous mixture of polypeptides; hydrolysed collagen is easily attacked by proteolytic enzymes resulting in a product called gelatines hydrolysate and which contains peptides with a mean MW of 3—6 kD [28]. Before speculating about the therapeutic mechanism, effectiveness of hydrolysed collagen and its mechanism of action, the question must be clarified as to whether hydrolysed collagen can be absorbed from the intestine and furthermore in what form and quantity. The first response to this question was brought by a study [28] in which absorption of ^{14}C labelled gelatine hydrolysate was compared to control mice administered ^{14}C labelled proline following intra-gastric application. More than 90 % of the administered radioactivity was removed from the gastrointestinal tract within the first 6 hours subsequent to oral administration of gelatine hydrolysate, showing its high and rapid digestibility. Further, 95 % of internally applied gelatine hydrolysate was absorbed within the first 12 h. In this study the distribution of labelled gelatine in the various tissues under study was similar to that of labelled proline with the exception of cartilage, where a pronounced and long-lasting accumulation of gelatine hydrolysate was observed. The absorption of gelatine hydrolysate in its high molecular form, with peptides of 2,5—15 kD was detected following intestinal passage, demonstrating intestinal absorption and tissue accumulation of gelatine hydrolysate following its oral intake. Several studies have observed a transient increase in collagen-derived peptides, especially of Pro-Hyp [28, 29] in the blood [28, 30, 31] and skin [32] after ingestion of collagen hydrolysate. Some Hyp-containing peptides were also detected in human blood after ingestion of hydrolysate from fish scales [27]. The major constituents of Hyp-containing peptides that remained in the blood were identified as Ala-Hyp, Pro-Hyp, Ala-Hyp-Gly, Ser-Hyp-Gly, Phe-Hyp, Pro-Hyp-Gly, Gly-Pro-Hyp, Ile-Hyp and Leu-Hyp. Hence they were featuring a combination of dipeptides and tripeptides. However, no quantitative analysis of peptides had been reported in an earlier human absorption study until Ichikawa's work in 2010 [29]. By far the major constituent of food-derived collagen peptides remaining in blood was confirmed to be Pro-Hyp (201.17 nmol/ml), while the minor components were Ala-Hyp-Gly, Ser-Hyp-Gly, Ala-Hyp, Phe-Hyp, Leu-Hyp, Ile-Hyp, Gly-Pro-Hyp, and Pro-Hyp-Gly (from 37.72 to 1.49 h nmol/ml). This result indicated that Pro-Hyp was the major Hyp-containing peptide in plasma after oral ingestion of fish-scale gelatine hydrolysate, as reported earlier by Ohara [27]. In this study, Pro-Hyp reached its maximum concentration in plasma 2 h after oral ingestion of fish-scale gelatine hydrolysate, while Ala-Hyp and Ala-Hyp-Gly reached their maximum concentrations 1 h after ingestion of the hydrolysate [29]. This suggests that oral ingestion of collagen can result in biological activities that depend on food-derived Hyp-containing peptides.

5. Orally-absorbed collagen effectively reaches the skin

This is a wrong question, as collagen by itself only reaches the gut, where it is dissociated in bioactive dipeptides and tripeptides, as previously shown. The right question would be «Do bioactive peptides issued from oral administration of collagen hydrolysates reach the skin»?

Previously, the time course of gelatine hydrolysate absorption and its subsequent distribution in various tissues in mice (C57/BL) were investigated [28]. Following to oral administration of ^{14}C labelled gelatine hydrolysate, a rapid increase of radioactivity was observed in plasma, reaching a maximal concentration 6 h after the beginning of the observation period. This peak was followed by a marked decrease of radioactivity. After beginning of the experiment (24 h) more than 85 % of radioactivity in plasma disappeared. Radioactivity in skin attained its peak values 12 h after the administration of ^{14}C labelled gelatine hydrolysate and in contrast to plasma, ^{14}C-activity remained relatively high up to 96 h. At the end of the observation

period (192 h), measured radioactivity declined to 58 % of the peak value [28]. Further, in the same manner, it was demonstrated that when administered to Wistar rats with either [^{14}C] proline or glycyl-[^{14}C] prolyl-hydroxyproline, low molecular weight collagen hydrolysate (LMW-CH) rapidly increased plasma radioactivity. LMW-CH was absorbed into the blood of Wistar rats in the peptide form [33]. In skin, radioactivity was detected as soon as 1 h after intake of LMW-CH and at 14 days after administration, radioactivity mostly disappeared from all the organs, except for the skin, for which radioactivity persisted at a level 70 % of that observed after 6 h [33].

6. Mechanism of action of oral collagen

Once more, it must be emphasized on that the biological activity is not due to collagen itself, but to so called «collagen hydrolysate», «hydrolyzed collagen» or sometimes «collagen peptides», all being products of hydrolyzation of native collagen, and used in food supplements [34]. As early as 1978, it was demonstrated in human dermal fibroblasts in culture that human type I, II and III collagens but also synthetic tri- and dipeptides containing hydroxyproline, isolated α chains, and smaller peptides derived from degradation of collagen are also chemotactic for fibroblasts. These means that these compounds are able to attract fibroblasts and increase their activity [35]. As we know, orally ingested collagen undergoes degradation to small di- or tripeptides. Their influence on dermal extracellular matrix components and cell proliferation was studied using cultured human dermal fibroblasts [36]. Of the various collagenous peptides tested here, the dipeptide proline-hydroxyproline (Pro-Hyp) enhanced cell proliferation (1.5-fold) and hyaluronic acid synthesis (3.8-fold) at a dose of 200 nmol/mL. This was concomitant with a 2.3-fold elevation of hyaluronan synthase 2 (HAS2) mRNA levels. These results suggest that Pro-Hyp stimulates both cell mitotic activity and hyaluronic acid synthesis, which is mediated by activation of HAS2 transcription [36]. On the other hand, Wistar rats were fed a modified AIN-93 diet containing 12 % casein as the reference group or CH as the treatment group. A control group was established in which animals were fed a non-protein-modified AIN-93 diet. The relative amount of type I and IV collagens was significantly increased after CH intake compared with the reference diet group (casein). Moreover, CH uptake significantly decreased both pro-enzyme and active forms of MMP2 compared to casein and control groups, which constitute another mechanism of action of CH at skin level [37].

7. Different sources of oral collagen

There are different sources of collagen, but all collagens are not the same. The most abundant sources of gelatine are pig skin (46 %), bovine hide (29.4 %) and pork and cattle bones (23.1 %). Fish gelatine accounted for less than 1.5 % of total gelatine production in 2007, but this percentage was double that of the market data for 2002, indicating that gelatine production from alternative non-mammalian species had grown in importance [38]. Apart from the well-known socio-cultural and sanitary aspects, the rising interest in putting by-products from the fish industry to good use is one of the reasons why exploring different species and optimizing the extraction of fish gelatine has attracted the attention of researchers in the last decade. The main drawback of fish gelatines is that gels based on them tend to be less stable and have worse rheological properties than gelatines from land mammals, and this may limit their field of application, especially in the food industry. The classical food, photographic, cosmetic and pharmaceutical application of gelatine is based mainly on its gel-forming and viscoelastic properties. Recently, and especially in the food industry, an increasing number of new applications have been found for gelatine in products such as emulsifiers, foaming agents, colloid stabilizers, fining agents, biodegradable packaging materials and micro-encapsulating agents, in line with the growing trend to replace synthetic agents with more natural ones. Moreover, in many cases, these studies are dedicated to using collagens and gelatines from alternative sources to land-based animals [39]. On the other hand, enzyme hydrolysed collagen plays an increasingly important role in various products and applications. Its different properties and functionalities benefit the end consumer now in ways which were not present ten years ago. Over the past decade, a large number of studies have investigated enzymatic hydrolysis of collagen or gelatine for the production of bioactive peptides. Besides exploring diverse types of bioactivity, studies focused on the effect of oral intake in both animal and human models have revealed the excellent absorption and metabolism of Hyp-containing peptides [39]. The most common raw materials for collagen and gelatine extraction are skins or hides, bones, tendons and cartilages from pork and bovines. Although less versatile than gelatine, fish collagen has received considerable attention for its potential use as an ingredient in processed functional food manufacturing, as well as for cosmetic, biomedical and pharmaceutical applications. Besides the skin, scales constitute another important fish industry residue and may account for around 5 % of the mate-

rial contained in fish collagenous waste. Although mammalian gelatines are widely used in the field of nutraceuticals, the use of gelatines from marine-discarded sources for preparing protein hydrolysates is nowadays increasing, as they are not associated with the risk of outbreaks of bovine spongiform encephalopathy and also meet certain religious requirements of Jewish and Muslim markets [40]. Frequently, it may be necessary to differentiate between gelatines from different sources not only for safety and religious reasons, but because it has been reported that most gelatine-allergic patients develop allergic reactions to bovine and porcine gelatine, but do not react to fish gelatine [41]. A study [27] compared the quantity and structure of hydroxyproline-containing peptides in human blood after oral ingestion of gelatine hydrolysates from three different sources: fish scale, fish skin and porcine skin. In the same manner as in previous reports, healthy human volunteers ingested hydrolysates of these three types of collagen hydrolysates after 12 h of fasting. Amounts of free form hydroxyproline and hydroxyproline-containing peptide were measured over a 24-h period. The amount of free form hydroxyproline was found to be significantly higher in the fish scale group than in the porcine skin and fish skin groups 2 and 7 h after administration. The amount of hydroxyproline-containing peptide in the fish scale group was also significantly higher than in both the fish skin and porcine skin groups 1, 2 and 4 h after intake. The total areas under the concentration time curves were compared. The fish scale value was approximately 1,5-fold higher than the skin value. Proline-Hydroxyproline was a major constituent of hydroxyproline-containing peptides. Demonstration was made that the quantity and structure of hydroxyproline-containing peptides in human blood after oral administration of gelatine hydrolysate depends on the gelatine source [27].

Taken together, these data confirm that fish-scale collagen hydrolysates constitute to date the highest-standard CH existing on the market, in terms of efficacy as well as in terms of safety.

8. Activity of oral collagen

8.1. *In vitro studies*

The aim of a first study was to analyse the chemotactic response of human dermal fibroblasts to type I, II and III human collagens and collagen derived peptides by an in vitro assay [35]. All three native human collagens and constituent α-chains serve as in vitro chemo-attractants for fibroblasts. In addition, also di- and tri-peptides containing hydroxyproline resulted chemotactic for fibroblasts. The authors suggested that both collagen and collagen derived peptides might function as chemotactic stimuli for fibroblasts in vivo and attract these cells for the repair of damaged tissues [35]. A further study investigated the influence of collagen peptides on migration and growth of mouse skin fibroblasts [42]. The authors report that the number of cells migrating from the explanted skin increased significantly after treatment with Proline-hydroxyproline peptide. However, they also found contrasting results and finally concluded that Pro-Hyp has a minor effect on fibroblasts' motility. On the other hand, they showed that Pro-Hyp increases significantly fibroblasts growth [42]. In an attempt to study the effect of different concentrations of hydrolysed collagen from fish on fibroblasts and keratinocytes, both proliferation and collagen secretion and/or the expression of mRNA type I collagen were investigated [43]. A concentration of collagen ranging between 48~97 μg/mL resulted in an increase in proliferation percentage of 191 %. Also the highest keratinocytes proliferation was achieved with a collagen concentration between 0.76~1.53 μg/mL and induced an increase in proliferation percentage of 242 %. Finally the authors reported an increase in the expression of collagen I mRNA from fibroblasts [43]. To support the function of collagen peptides in stimulating dermal fibroblasts proliferation and synthesis of hyaluronic acid, eight different collagen derived peptides, containing Hyp, were analysed [55]. Positive effect on the proliferation was observed for Ala-Hyp, Ala-Hyp-Gly and Pro-Hyp. Pro-Hyp induced the maximal stimulation of cell proliferation of ~ 1.5-fold. Further investigation was performed on the effect of different concentrations of Pro-Hyp. In addition, the same eight peptides were tested to study their effect on hyaluronic acid synthesis. The results were consistent with the proliferation study as Pro-Hyp showed highest efficacy, where 200 nmol/mL induced a 3.8-fold increase in hyaluronic acid synthesis. In addition, the authors suggest that hyaluronic acid increases hydration of the extracellular space that aids fibroblast proliferation [27]. In skin explants used to study extracellular matrix components in the presence of collagen peptides *ex vivo*, it was shown that oral collagen peptide supplementation significantly increased skin hydration after 8 weeks of intake [44]. The collagen density in the dermis significantly increased and the fragmentation of the dermal collagen network significantly decreased already after 4 weeks of supplementation. Both effects persisted after 12 weeks. Ex vivo experiments demonstrated that collagen peptides induce collagen as well as glycosaminoglycan production, offering a mechanistic explanation for the observed clinical effects [44].

8.2. *In vivo studies*

Examining, in the dermis of pig, the effects related to collagen peptide ingestion (0.2 g/kg body weight, for 62 days) on fibroblasts and on the extracellular matrix, the authors found a significant increase in collagen fibres density and diameter along with an increase in fibroblasts density [45]. The diameter of collagen fibrils didn't change significantly between the control and animals that ingested the lactalbumin containing diet. Instead, the diameter and density of collagen fibrils increased significantly when collagen peptide was administered, and this was associated with an increase of the density of fibroblasts. This implies that the effect mediated by hydrolysed collagen was protein specific and not dependant on amino-acid intake [45]. To investigate the effects of the treatment with collagen peptides together with vitamin C in age-related skin pathology, study was done in hairless Sod1–/– double mutant mice and the authors showed that co-treatment with these compounds corrected age-related skin thinning by attenuating oxidative damage [46]. A study was organized to examine the effect of daily ingestion of collagen peptides on skin after damage induced by repeated UV-B irradiation [47]. The length of the study was 6 weeks and it was conducted on hairless mice divided in three groups: 1) mice not exposed to UV-B; 2) mice exposed to UV-B; 3) mice exposed to UV-B but fed with collagen peptides 0.2 g/kg body weight daily. After the 6 weeks period skin samples were taken and analysed. On mice exposed to UV-B irradiation a decrease was observed in the hydration of skin, hyperplasia of the epidermis occurred and there was a reduction in collagen I levels. On the other hand, ingestion of collagen peptides improved significantly skin condition and collagen levels. The authors suggested that collagen peptides, as a dietary supplement, are beneficial to suppress UV-B induced skin damage and photo-ageing [47]. In order to investigate the effect of marine collagen peptides on wound healing and angiogenesis in rats, 96 animals were randomly treated with vehicle or with 2 g/kg marine collagen peptides [48]. Wound closure and tensile strength were calculated. Angiogenesis was assessed by immuno-histological methods. The rats treated with marine collagen peptides showed quicker wound closure and better tissue regeneration at the wound site. Moreover, marine collagen peptides treatment improved angiogenesis and contributed in forming a thicker and better organised collagen fibre deposition when compared to vehicle-treated group [48]. The aim of another study [49] was to investigate the long-term effects of Salmon skin marine collagen hydrolysate on the anomalous collagen matrix homeostasis in chronological aged skin. 4 weeks old rats were supplemented with oral intake of marine collagen hydrolysate (diet concentrations of 2.25 % and 4.5 %) for 24 months. The histological and biochemical analysis revealed that marine collagen hydrolysate inhibited the collagen loss and collagen fragmentation in chronological aged skin. Based on immuno-histochemistry and western blot analysis, collagen type I and III protein expression levels significantly increased in marine collagen hydrolysate-treated groups when compared with the aged control group. Moreover, marine collagen hydrolysate could alleviate the oxidative stress in chronological aged skin due to its influence on collagen matrix homeostasis [49]. To investigate the effect of daily ingestion of collagen hydrolysate (CH) on skin extracellular matrix proteins, four-week-old male Wistar rats were fed a modified AIN-93 diet containing 12 % casein as the reference group or CH as the treatment group. A control group was established in which animals were fed a non-protein-modified AIN-93 diet. The diets were administered continuously for 4 weeks when six fresh skin samples from each group were assembled and subjected to extraction of protein [50]. The relative amount of type I and IV collagens was significantly ($p < 0.05$) increased after CH intake compared with the reference diet group (casein). Moreover, CH uptake significantly decreased both pro-enzyme and active forms of MMP2 compared with casein and control groups ($p < 0.05$). In contrast, CH ingestion did not influence on MMP9 activity. These results suggest that CH may reduce aging-related changes of the extracellular matrix by stimulating anabolic processes in skin tissue [50]. In another similar study, 2.5, 5 and 10 g of fish collagen peptide were administered and compared to the placebo. The skin stratum corneum hydration was measured at baseline and after 4 weeks. When all subjects were included in the analysis no significant difference between the treated groups (2.5/5/10 g) and the placebo was observed. However, when only the subjects older than 30 years were considered, there was a significant difference ($p < 0.05$) between the treated group (5 and 10 g) and the placebo.

8.3. *Clinical studies*

Skin. The aim of a study was to evaluate the effect of daily ingestion of hydrolysed collagen (10 g) on skin hydration of 20 healthy Japanese women and compare this to placebo group (19 volunteers) [51]. Through 60 days, a gradual improvement in water absorption capacity was observed in volunteers who ingested collagen peptides (when compared to placebo group). However, this improvement was

not statistically significant between the treated group and the placebo. This could be addressed to the low number of volunteers included in the trials [51]. In another trial with a similar aim, the authors found an improvement of the skin condition of women volunteers after ingestion of fish collagen peptide for 6 weeks. The percentage of positive response between the subjects was very high, however the study did not have a placebo control [52]. In another similar study 2.5, 5 and 10 g of fish collagen peptide were administered and compared to the placebo. The skin stratum corneum hydration was measured at baseline and after 4 weeks. When all subjects were included in the analysis no significant difference between the treated groups (2.5/5/10 g) and the placebo was observed. However, when only the subjects older than 30 years were considered, there was a significant difference ($p < 0.05$) between the treated group (5 and 10 g) and the placebo [53]. Other authors demonstrated that women after ingestion of 5 or 10 g of pig skin collagen perceived improvement of their skin already after 3 weeks and at the end of the treatment after 7 weeks [54]. To investigate the effects of collagen hydrolysate on skin biophysical parameters related to cutaneous ageing: skin elasticity, skin moisture, trans-epidermal water loss and skin roughness, 69 women (35—55 years old) were randomized to receive collagen hydrolysate (2.5 g or 5.0 g) or placebo once a day for 8 weeks [55]. At the end of the study, skin elasticity in both collagen hydrolysate dosage groups showed a statistically significant improvement when compared to placebo. In terms of skin moisture and skin evaporation, a positive influence of collagen hydrolysate treatment could be observed in a subgroup analysis, but data were not significant [55]. In an attempt to investigate the effect of a dietary supplement, containing hydrolysed collagen type II, hyaluronic acid and chondroitin sulphate, in 26 healthy females with signs of natural photo-ageing in the face [56], daily supplementation with 1 g of hydrolysed collagen for 12 weeks brought to a significant reduction ($p < 0.05$) of skin dryness/scaling and global lines/wrinkles. Moreover, a significant increase in haemoglobin and collagen content of the skin dermis was observed after 6 weeks of supplementation. At the end of the study, the haemoglobin increase remained significant, while the increase in collagen content was maintained, although the difference from baseline was not significant. The authors suggested that dietary supplementation with hydrolysed collagen can physiologically counteract natural and photo-ageing processes. A placebo-controlled study is necessary to confirm these observations [56]. A. Béguin et al. intended to test the efficacy and safety in skin ageing of a micronutrient supplement, containing marine collagen proteins, through a 4 month randomized double-blind controlled clinical study [57]. The trial included 40 subjects. The supplement was tested against placebo for a period of 3 months followed by 1 month without supplementation to assess lasting effects. Efficacy measurements were: skin surface evaluation, ultrasound measurement of sun-exposed skin and protected areas and photographic assessment. When compared to placebo, all investigated parameters showed a continuous and significant improvement in the group taking the supplement during the 3 months of trial ($p < 0.01$). Photographs showed visible improvement of the overall skin appearance and a reduction of fine lines. In the active group, ultrasound measurements showed an increase in dermis density of up to 78 %. The final assessment, after 1 month without supplementation, showed no further improvements and there was a slight decrease in most improved parameters. No treatment-related side effects were reported. The study demonstrated that the supplement may be effective to protect the skin and support its repair process [57]. In a randomized trial [58], to evaluate the effect of daily collagen peptide supplementation on skin properties, 32 healthy volunteers received for 12 weeks either 1/no supplement, 2/collagen peptide 3 g, 3/collagen peptide 3 g and vitamin C 500 mg or 4/vitamin C 500 mg. Skin properties such as hydration, transepidermal water loss and elasticity were evaluated. The data showed that daily collagen peptide supplementation improved skin hydration and elasticity ($p < 0.05$), but the association with low-dose vitamin C intake did not enhance the effect of collagen peptide on skin properties [58]. A double-blind, randomized, placebo controlled clinical trial was conducted on healthy subjects to assess whether an oral supplement containing hydrolyzed collagen, hyaluronic acid, and essential vitamins and minerals, could improve certain specific skin properties of post-menopausal women, namely depth of facial wrinkles, skin elasticity and hydration [59]. This study proved that the combination of specific ingredients present in this nutritional drink acts to significantly reduce the depth of facial wrinkles and increase skin elasticity and hydration [59]. To assess the anti-aging potential of three type I fish collagen hydrolysates on skin aging signs for three different body sites of mature women, a double-blind, randomized and placebo-controlled clinical study was designed [60]. Sixty women aged 46—69 years having skin aging signs on the face. Intervention: Participants were randomized to receive a once daily 5 g dose of one

of the CHs or Placebo for 8 weeks. Skin biomechanics indicated a significant improvement of skin firmness for the three CHs compared to Placebo, in particular for CH_2. An increase of overall skin elasticity for CH_3 ($p = 0.017$) and CH_2 ($p = 0.044$) on the abdomen was also observed. This was corroborated by the significant decrease of the crow's-feet wrinkle score at week 8 for both CH_3 and CH_2 ($p = 0.023$ and $p = 0.014$, respectively). In conclusion, the tested type I fish collagen hydrolysates have beneficial effects on skin quality. In particular, CH_2 demonstrated the greatest range of these effects including improvement of skin biomechanics, decrease of wrinkles, good subject satisfaction and no related adverse events [60].

Nails. T.T. Tyson [61] reported in 1950 that oral ingetion of 7.0 g of gelatine per day for three months returned fragile finger nails to practically normal appearance and texture. T.H. McGavack [62] obtained a similar finding in three to twelve weeks when gelatine was administered orally at a dosage of 7.5 g per day. S. Rosenberg [62] observed improvement in 43 of 50 subjects with brittle nails after three months of ingestion of 7.0 g of gelatine per day. In earlier studies S. Rosenberg and K. Oster [63, 64] noted improvement after three months in 26 of 36 subjects receiving 7.0 g of gelatine per day. M. Schwimmer and M.G. Mulinos [65], using a dosage of 7.5 g of gelatine per day, found improvement in 14 of 17 subjects after three months. J.L. Derzavis and M.G. Mulinos [166], in a series of experiments, evaluated the improvement of fingernails during oral administration of gelatine at different dosages. These investigators used a dose of 1.8 g per day in one set of experiments and 7.0 g per day in another. They reported a 2.5 times improvement in the nails of the test subjects at the lower dosage of gelatine compared to the placebo subjects and 5 times improvement in subjects receiving 7.0 g of gelatine daily. In a recent open-label, single-center trial [67], 25 participants took 2.5 g of specific bioactive collagen peptides (BCP, VERISOL) once daily for 24 weeks followed by a 4-week off-therapy period. Nail growth rate and the frequency of cracked and/or chipped nails as well as an evaluation of symptoms and global clinical improvement score of brittle nails were assessed by a physician during treatment and 4 weeks after discontinuation. Bioactive collagen peptides treatment promoted an increase of 12 % nail growth rate and a decrease of 42 % in the frequency of broken nails. Additionally, 64 % of participants achieved a global clinical improvement in brittle nails, and 88 % of participants experienced an improvement 4 weeks post-treatment. This study demonstrated that the daily ingestion of BCP increased nail growth and improved brittle nails in conjunction with a notable decrease in the frequency of broken nails [67].

Hair. The effect of daily gelatine ingestion on human scalp hair was studied in a normal adult population [68]. The most dramatic effect of supplementing the normal diet with 14 grams of gelatine daily was an increase in hair diameter averaging 9.3 % in the first study and 11.3 % in the second study. Approximately seventy percent of the subjects in both studies showed increases in hair diameter ranging from 5 to 45 %. It is postulated that this increase constitutes an improvement in the mechanical properties of the hair. Further, it was shown that the increase in hair diameter was generally inversely proportional to the initial, predosing value. Within 6 months after cessation of gelatine dosing, hair diameter reversed back its original level. The increase was therefore directly attributable to gelatine ingestion. Yield point and yield extension increased with increases in hair diameter. Furthermore, yield stress values indicated that strength changes in the hair fibres were due mainly to increases in diameter and not to changes in hair structure. Gelatine ingestion did not affect linear hair growth. Increases in hair diameter was not affected by age of subjects or diet quality. Generally, male subjects exhibited smaller increases than females, possibly as a consequence of greater initial hair thickness [68].

Cellulite. In a double-blind, placebo-controlled clinical study, the efficacy of specific bioactive collagen peptides (BCP) was investigated on the cellulite treatment of normal and overweight women [69]. In total, 105 women aged 24—50 years with moderate cellulite were randomized to orally receive a daily dosage of 2.5 g BCP or a placebo over 6 months. The degree of cellulite was evaluated before starting the treatment and after 3 and 6 months of intake. In addition, skin waviness, dermal density, and the length of subcutaneous borderline were assessed. BCP treatment led to a statistically significant decrease in the degree of cellulite and a reduced skin waviness on thighs ($p < 0.05$) in normal weight women. Moreover, dermal density was significantly improved ($p < 0.05$) compared to placebo. The subcutaneous borderline showed a significant shortening after BCP intake compared to the beginning of the study, indicating cellulite improvement. The efficacy of BCP treatment was also confirmed in overweight women, although the impact was less pronounced in comparison with women of normal body weight [59].

9. Conclusion

Collagen, the major constituent of the skin, is slowly, but importantly decreasing with age, which leads to the common signs of skin aging such as loss of elasticity, skin dryness, skin thinning, but also fine lines and wrinkles. It was demonstrated that collagen hydrolysates are absorbable at the level of the gut and reach the dermis. This review also highlights the beneficial effects of oral intake of collagen hydrolysates on skin, nails, hair and cellulite.

Given the high tolerability of oral collagen, whose oral intake is recognized as safe by both USFDA and European Food Agencies, this food supplement can usefully integrate the recommendations to our patients worried about the signs of skin aging, hair loss, nail brittleness and even cellulite.

References

1. Gelse K., Pöschl E., Aigner T. Collagens-structure, function, and biosynthesis // Advanced Drug Delivery Reviews. 2003.— Vol. 55.— P. 1531—1546.
2. Hofmann H., Fietzek P.P., Kuhn K. The role of polar and hydrophobic interactions for the molecular packing of type I collagen: a three-dimensional evaluation of the amino acid sequence // J. Mol. Biol.—1978.— Vol. 125.— P. 137—165.
3. Fraser R.D., MacRae T.P., Suzuki E. Chain conformation in the collagen molecule // J. Mol. Biol.— 1979.— Vol. 129.— P. 463—481.
4. Burgeson R.E. Genetic heterogeneity of collagen // J. Invest. Dermatol.— 1982.— Vol. 79.— 25 s.
5. Kadler K.E. et al. Collagen fibril formation // Biochem. J.— 1996.— Vol. 316.— P. 1—11.
6. Fleischmajer R. et al. Type I and type III collagen interactions during fibrillogenesis // Ann. NY Acad. Sci.— 1990.— Vol. 580.— P. 161—175.
7. Uitto J., Fazio M.J., Olsen D.R. Molecular mechanisms of cutaneous aging. Age-associated connective tissue alterations in the dermis // J. Am. Acad. Dermatol.— 1989.— Vol. 21 (3Pt. 2).— P. 614—622.
8. Varani J., Dame M.K., Rittie L. et al. Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation // Am. J. Pathol.— 2006.— Vol. 168 (6).— P. 1861—1868.
9. Furth J.J. The steady-state levels of type I collagen mRNA are reduced in senescent fibroblasts // J. Gerontol.— 1991.— Vol. 46 (3).— B122—124.
10. Ignotz R.A., Massague J. Transforming growth factor-beta stimulates the expression of fibronectin and collagen and their incorporation into the extracellular matrix // J. Biol. Chem.— 1986.— Vol. 261 (9).— P. 4337—4345.
11. Raghow R., Postlethwaite A.E., Keski-Oja J. et al. Transforming growth factor-beta increases steady state levels of type I procollagen and fibronectin messenger RNAs posttranscriptionally in cultured human dermal fibroblasts // J. Clin. Invest.— 1987.— Vol. 79 (4).— P. 1285—1288.
12. Bitzer M., von Gersdorff G., Liang D. et al. A mechanism of suppression of TGF-beta/SMAD signaling by NF-kappa B/RelA // Genes. Dev.— 2000.— Vol. 14 (2).— P. 187—197.
13. Brown J.D., DiChiara M.R., Anderson K.R. et al. MEKK-1, a component of the stress (stressactivated protein kinase/c-Jun N-terminal kinase) pathway, can selectively activate Smad2-mediated transcriptional activation in endothelial cells // J. Biol Chem.— 1999.— Vol. 274 (13).— P. 8797—8805.
14. Grotendorst G.R. Connective tissue growth factor: a mediator of TGF-beta action on fibroblasts // Cytokine Growth Factor Rev.— 1997.— Vol. 8 (3).— P. 171—179.
15. Duncan M.R., Frazier K.S., Abramson S. et al. Connective tissue growth factor mediates transforming growth factor beta-induced collagen synthesis: down-regulation by cAMP // FASEB J.— 1999.— Vol. 13 (13).— P. 1774—1786.
16. Holmes A., Abraham D.J., Sa S. et al. CTGF and SMADs, maintenance of scleroderma phenotype is independent of SMAD signaling // J. Biol. Chem.— 2001.— Vol. 276 (14).— P. 10594—10601.
17. Gore-Hyer E., Shegogue D., Markiewicz M. et al. TGF-beta and CTGF have overlapping and distinct fibrogenic effects on human renal cells // Am. J. Physiol. Renal. Physiol.— 2002.— Vol. 283 (4).— F707—716.
18. Quan T., Shao Y., He T. et al. Reduced expression of connective tissue growth factor (CTGF/CCN2) mediates collagen loss in chronologically aged human skin // J. Invest. Dermatol.— 2010.— Vol. 130 (2).— P. 415—424.
19. Hwang K.A., Yi B.R., Choi K.C. Molecular mechanisms and in vivo mouse models of skin aging associated with dermal matrix alterations // Lab. Anim. Res.— 2011.— P. 27 (1).— P. 1—8.
20. Fisher G.J., Datta S., Wang Z. et al. c-Jun-dependent inhibition of cutaneous procollagen transcription following ultraviolet irradiation is reversed by all-trans retinoic acid // J. Clin. Invest.— 2000.— Vol. 106 (5).— P. 663—670.
21. Quan T., He T., Kang S. et al. Solar ultraviolet irradiation reduces collagen in photoaged human skin by blocking transforming growth factor-beta type II receptor/Smad signaling // Am. J. Pathol.— 2004.— Vol. 165 (3).— P. 741—751.
22. Quan T., He T., Shao Y et al. Elevated cysteine-rich 61 mediates aberrant collagen homeostasis in chronologically aged and photoaged human skin // Am. J. Pathol.— 2006.— Vol. 169 (2).— P. 482—490.
23. Grinnell F. Fibroblast-collagen-matrix contraction: growth-factor signalling and mechanical loading // Trends Cell Biol.— 2000.— Vol. 10 (9).— P. 362—365.
24. Grinnell F. Fibroblast biology in three-dimensional collagen matrices // Trends Cell Biol.— 2003.— Vol. 13 (5).— P. 264—269.
25. Grinnell F., Zhu M., Carlson M.A., Abrams J.M. Release of mechanical tension triggers apoptosis of human fibroblasts in a model of regressing granulation tissue // Exp. Cell Res.— 1999.— Vol. 248 (2).— P. 608—619.
26. Varani J., Schuger L., Dame M.K. et al. Reduced fibroblast interaction with intact collagen as a mechanism for depressed collagen synthesis in photodamaged skin // J. Invest. Dermatol.— 2004.— Vol. 122 (6).— P. 1471—1479.
27. Ohara H., Matsumoto H., Ito K. et al. Comparison of quantity and structures of hydroxyproline-containing peptides in human blood after oral ingestion of gelatine hydrolysates from different sources // J. Agric. Food Chem.— 2007.— Vol. 55 (4).— P. 1532—1536.
28. Oesser S., Adam M., Babel W., Seifert J. Oral administration of ^{14}C labelled gelatine hydrolysate leads to an accumulation of radioactivity in cartilage of mice (C57/BL) // J. Nutr.— 1999.— Vol. 129 (10).— P. 1891—1895.
29. Ichikawa S., Morifuji M., Ohara H. et al. Hydroxyproline-containing dipeptides and tripeptides quantified at high concentration in human blood after oral administration of gelatine hydrolysate // Int. J. Food Sci. Nutr.— 2010.— Vol. 61.— P. 52—60.
30. Kawaguchi T., Nanbu P.N., Kurokawa M. Distribution of prolylhydroxyproline and its metabolites after oral administration in rats // Biol. Pharm. Bull.— 2012.— Vol. 35.— P. 422—427.
31. Wang L., Wang Q., Liang Q. et al. Determination of bioavailability and identification of collagen peptide in blood after oral ingestion of gelatine // J. Sci. Food Agric.— 2015.— Vol. 95.— P. 2712—2717.

32. Hiroki Ohara S.I. Improvement of Extracellular Matrix (ECM) in the Skin by Oral Ingestion of Collagen Hydrolysate // Foods & Food Ingredients J. Jpn.— 2014.— Vol. 219.— P. 216—223.
33. Watanabe-Kamiyama M., Shimizu M., Kamiyama S. et al. Absorption and effectiveness of orally administered low molecular weight collagen hydrolysate in rats // J. Agric. Food Chem.— 2010 .— Vol. 58 (2).— P. 835—841.
34. Daneault A., Coxam V., Wittrant Y. Biological Effect of Hydrolyzed Collagen on Bone Metabolism, Critical Reviews in Food Science and Nutrition.— 2015.— doi:10.1080/10408398.2015.1038377.
35. Postlethwaite A.E., Seyer J.M., Kang A.H. Chemotactic attraction of human fibroblasts to type I, II, and III collagens and collagen-derived peptides // Proc. Natl. Acad. Sci. USA.— 1978.— Vol. 75 (2).— P. 871—875.
36. Ohara H., Ichikawa S., Matsumoto H. et al. Collagen-derived dipeptide, proline-hydroxyproline, stimulates cell proliferation and hyaluronic acid synthesis in cultured human dermal fibroblasts // J. Dermatol.— 2010.— Vol. 37 (4).— P. 330—338.
37. Zague V., de Freitas V., da Costa Rosa M. et al. Collagen hydrolysate intake increases skin collagen expression and suppresses matrix metalloproteinase 2 activity // J. Med. Food.— 2011.— Vol. 14 (6).— P. 618—624.
38. Gómez-Guillén M.C., Pérez-Mateos, M., Gómez-Estaca J. et al. Fish gelatine: a renewable material for the development of active biodegradable films // Trends in Food Science and Technology.— 2009.— Vol. 20.— P. 3e16.
39. Gómez-Guillén M.C., Giménez B., López-Caballero M.E. et al. Functional and bioactive properties of collagen and gelatine from alternative sources: A review // Food Hydrocolloids.— 2011.— Vol. 25.— P. 1813—1827.
40. Alemán A., Martinez-Alvarez O. Marine collagen as a source of bioactive molecules. A review // Nat. Prod. J.— 2013.— Vol. 3 (2).— P. 105—114.
41. Sakaguchi M., Toda M., Ebihara T. et al. IgE antibody to fish gelatine (type I collagen) in patients with fish allergy // J. Allergy Clin. Immunol.—2000.— Vol. 106 (3).— P. 579—584.
42. Shigemura Y., Iwai K., Morimatsu F. et al. Effect of Prolyl-hydroxyproline (Pro-Hyp), a food-derived collagen peptide in human blood, on growth of fibroblasts from mouse skin // J. Agric. Food Chem.— 2009.— Vol. 57 (2).— P. 444—449.
43. Chen R.H., Hsu C.N., Chung M.Y. et al. Effect of different concentrations of collagen, ceramides, n-acetyl glucosamine, or their mixture on enhancing the proliferation of keratinocytes, fibroblasts and the secretion of collagen and/or the expression of mRNA of type i collagen // J. Food Drug Anal.— 2008.— Vol. 16 (1).— P. 66—74.
44. Asserin J., Lati E., Shioya T. et al. 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 // J. Cosmet. Dermatol.— 2015.— Vol. 14 (4).— P. 291—301.
45. Matsuda N., Koyama Y., Hosaka Y. et al. Effects of ingestion of collagen peptide on collagen fibrils and glycosaminoglycans in the dermis // J. Nutr. Sci. Vitaminol. (Tokyo) 2006.— Vol. 52 (3).— P. 211—215.
46. Shibuya S., Ozawa Y., Toda T. et al. Collagen peptide and vitamin C additively attenuate age-related skin atrophy in Sod1-deficient mice // Biosci. Biotech. Biochem.— 2014.— Vol. 78.— P. 1212—1220.
47. Tanaka M., Koyama Y., Nomura Y. Effects of collagen peptide ingestion on UV-B-induced skin damage // Biosci. Biotechnol. Biochem.— 2009.— Vol. 73 (4).— P. 930—932.
48. Zhang Z., Wang J., Ding Y. et al. Oral administration of marine collagen peptides from Chum Salmon skin enhances cutaneous wound healing and angiogenesis in rats // J. Sci. Food Agric.— 2011.— Vol. 91 (12).— P. 2173—2179.
49. Liang J., Pei X., Zhang Z. at al. 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.— 2010.— Vol. 75 (8).— P. 230—238.
50. Zague V., de Freitas V., da Costa Rosa M et al. Collagen hydrolysate intake increases skin collagen expression and suppresses matrix metalloproteinase 2 activity // J. Med. Food.— 2011.— Vol. 14 (6).— P. 618—624.
51. Sumida E., Hirota A., Kuwaba K. The effect of oral ingestion of collagen peptide on skin hydration and biochemical data of blood // J. Nutr. Food.— 2004.— Vol. 7.— P. 45—52.
52. Matsumoto H., Ohara H., Ito K. et al. Clinical effect of fish type I collagen hydrolysate on skin properties // ITE Lett.— 2006.— Vol. 7.— P. 386—390.
53. Ohara H., Ito K., Iida H., Matsumoto H. Improvement in the moisture content of the stratum corneum following 4 weeks of collagen hydrolysate ingestion // Nippon Shokuhin Kogaku Kaishi.— 2009.— Vol. 56.— P. 137—45.
54. Koyama Y. Effect of collagen peptide on the skin // Shokuhinto Kaihatsu.— 2009.— Vol. 44.— P. 10—12.
55. Proksch E., Segger D., Degwert J. et al. Oral supplementation of specific collagen peptides has beneficial effects on human skin physiology: a double-blind, placebo-controlled study // Skin. Pharmacol. Physiol.— 2014.— Vol. 27 (1).— P. 47—55.
56. Schwartz S.R., Park J. Ingestion of BioCell Collagen((R)), a novel hydrolyzed chicken sternal cartilage extract; enhanced blood microcirculation and reduced facial aging signs // Clin. Interv. Aging.— 2012.— Vol. 7.— P. 267—273.
57. Beguin A. A novel micronutrient supplement in skin aging: a randomized placebo-controlled double-blind study // J. Cosmet. Dermatol.— 2005.— Vol. 4 (4).— P. 277—284.
58. Choi S.Y., Ko E.J., Lee Y.H. et al. Effects of collagen tripeptide supplement on skin properties: A prospective, randomized, controlled study // J. Cosmet. Laser Ther.— 2014.— Vol. 16 (3).— P. 132—137.
59. Borumand M., Sibilla S. Effects of a nutritional supplement containing collagen peptides on skin elasticity, hydration and wrinkles // J. Med. Nutr. Nutraceut.— 2015.— Vol. 4.— P. 47—53.
60. Duteil L., Queille-Roussel C., Maubert Y. et al. Specific natural bioactive type-1 collagen peptides oral intake reverse skin aging signs in mature women // J. Aging Res. Clin. Practice.— 2016.— Vol. 5 (2).— P. 84—92.
61. Tyson T.T. The effect of gelatin on fragile finger nails // J. Invest. Dermatol.— 1950.— Vol. 14.— P. 323—325.
62. McGavack T.H. Antibiotic Med. & Clin // Therapy.— 1957, IV.
63. Rosenberg S., Oster K., Kallos A., Burrough W. Further studies in the use of gelatin in the treatment of brittle nails // AMA Arch. Dermatol.— 1957.— Vol. 76 (3).— P. 330—335.
64. Rosenberg S., Oster K. Gelatin in the treatment of brittle nails // Conn. State Med. J.—1955.— Vol. 19 (3).— P. 171—179.
65. Schwimmear M., Mulinos M.G. Salutary Effects of Gelatin on Nail Defects in Normal Subjects // Antibiotic. Med. Clin. Ther.— 1957.— Vol. 4 (7).— P. 403—407.
66. Derzavis J.L., Mulinos M.G. The brittle nail. Its treatment and prevention with gelatin // Med. Ann. Dis. Columbia.— 1961.— Vol. 30.— P. 133—137.
67. Hexsel D., Zague V., Schunck M. et al. Oral supplementation with specific bioactive collagen peptides improves nail growth and reduces symptoms of brittle nails // J. Cosmet. Dermatol.— 2017.— P. 1—7.
68. Scala J., Hollies N.R.S., Sucher P. Effect of daily gelatine ingestion on human scalp hair // Nutrition Reports International.— 1976.— Vol. 13 (6).— P. 579—592.
69. Schunck M., Zague V., Oesser S. Dietary Supplementation with Specific Collagen Peptides Has a Body Mass Index-Dependent Beneficial Effect on Cellulite Morphology //

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Користь перорального прийому колагену в дерматології

Колаген є основним компонентом дерми. Він складає 75 % сухої ваги шкіри. З віком вміст колагену зменшується в шкірі через зменшення продукування його фібробластами і більш високою швидкістю обміну речовин. Це призводить до загальних ознак старіння шкіри, тобто до зниження еластичності шкіри, появи тонких ліній і зморщок. Таким чином, існує потреба в додатковому колагені в шкіру. Це неможливо зробити за допомогою (місцевого нанесення) кремів, оскільки розмір молекули (колагену) не дозволяє їй абсорбуватися через шкіру. Навпаки, пероральні гідролізати колагену легко засвоюються кишечником і досягають шкіри в достатній кількості, де вони залишаються протягом певного часу. Багато досліджень, розглянутих у цій статті, показують переваги перорального прийому гідроліту колагену не тільки для шкіри, а й для нігтів, росту волосся і навіть при целюліті.

Ключові слова: колаген, прийом всередину, поглинання, джерела, шкіра, старіння, волосся, нігті, целюліт.

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Польза перорального приема коллагена в дерматологии

Коллаген является основным компонентом дермы. Он составляет 75 % сухого веса кожи. С возрастом содержание коллагена уменьшается в коже из-за уменьшения продуцирования его фибробластами и более высокой скорости обмена веществ. Это приводит к общим признакам старения кожи, то есть к снижению эластичности кожи, появлению тонких линий и морщин. Таким образом, существует потребность в добавлении дополнительного коллагена в кожу. Это невозможно сделать с помощью (местного нанесения) кремов, так как размер молекулы (коллагена) не позволяет ей абсорбироваться через кожу. Напротив, пероральные гидролизаты коллагена легко усваиваются кишечником и достигают кожи в изобилии, где они остаются в течение определенного времени. Многие исследования, рассмотренные в этой статье, показывают преимущества перорального приема гидролита коллагена не только для кожи, но и для ногтей, роста волос и даже при целлюлите.

Ключевые слова: коллаген, прием внутрь, поглощение, источники, кожа, старение, волосы, ногти, целлюлит.

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