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REVIEW

Comprehensive review of collagen types: sources, structure, and human health applications

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Summary

Collagen is a protein that helps maintain the structural integrity and functionality of connective tissue. Collagen hydrolysate, which has recently gained popularity due to its high bioavailability, has attracted attention due to its reported benefits, such as improving skin health, relieving joint pain, and reducing signs of ageing. This review aims to compile and categorize 28 well-researched and well-known, as well as less popular, types of collagens, and investigate their relationship with physiological processes and diseases. It also examines how collagen affects ageing and its potential impact on various health conditions. Collagen hydrolysate is a food ingredient known for its support of collagen synthesis and a wide range of health benefits, such as antioxidant, anti-inflammatory, and antihypertensive effects. Types I, II, and III collagen constitute 80–90 % of the human body. Collagen Types I through VII are most commonly associated with skin health, with other collagen types also playing a variety of roles in health and disease. Dietary supplements containing collagen hydrolysate have been shown to have positive effects, including reducing signs of ageing, maintaining skin health, reducing symptoms of joint disorders, and improving overall quality of life.

Keywords

collagen types; collagen hydrolysate; skin; ageing

The origin of the word collagen is derived from the Greek words ‘colla’ meaning glue and ‘gen’ meaning to produce. The term collagen was first used in history to describe connective tissue. Collagen is a structural protein found in high amounts in all animals [1]. Collagen, which has become a popular ingredient for an active and healthy lifestyle, is the most important of the structural proteins that make up the extracellular matrix. It is a long and fibrous protein synthesized by the human body and found in many organs of our body, consisting of about 30 % of the total protein mass of the body and 75 % of our skin.

While collagen is produced by the body at a young age, collagen production in the body decreases with increasing age. It has been reported that the collagen in our body is lost by 1 % every year after the age of 20. In its deficiency, skin wrinkles, ageing, bone and joint problems, bone resorption, serious health problems have been reported. Some clinical studies in specific populations, such as older adults with joint pain or athletes, have used daily doses of collagen hydrolysate such as 1.2 g or 10 g per day. However, these studies do not establish a general intake recommendation for the overall adult population [2]. Collagen hydrolysate, which is a functional ingredient, has recently started to be used as a food supplement and added to foods and other products to provide functional properties; it has become a popular ingredient used in food, cosmetics, biomedical, nutraceutical and phar-

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maceutical fields. The global market for collagen has been propelled by increasing awareness of the health benefits of collagen hydrolysates. The use of collagen hydrolysates has gained importance due to their reported health effects in order to eliminate the deficiencies and negativities that occur in our body as a result of the decrease in collagen synthesis and decreased quality with age. Collagen hydrolysate is supported as GRAS for its intended conditions of use based on FDA GRAS Notices for specific collagen-derived preparations (e.g., GRN No. 713); additionally, peptones (a broad group of hydrolysed animal proteins) are affirmed as GRAS with the qualification that current good manufacturing practice (cGMP) must be upheld [3]. In addition, collagen hydrolysate, which is generally considered to have a low allergen risk, is suitable for use in foods according to the Turkish Food Codex (TFC) Communiqué on Supplementary Foods [4]. In spite of extremely low allergenic risk regarding the ingestion of collagen hydrolysates, certain caution is still appropriate, because rare cases of anaphylaxis can occur under some circumstances, as illustrated by Fujimoto et al. [5].

Collagen has been utilised in various fields, including wound recovery, surface coating of medical devices and supplementation for skin health. Collagen supplements are an important component in the fight against the effects of the ageing process, having the ability to heal skin damage and restore the rejuvenated and healthy appearance sought in the quest for beauty. This review article has been written to compile all types of collagens that have been well researched or are less popular and their relationship with physiological processes and diseases, especially ageing.

Molecular and chemical structure of collagen

The collagen triple helix was named 'Madras Helix' in 1954 by Kartha and Ramachandran based on fibre diffraction data. In 1955, Crick, North, Rich et al. organised this structure and presented the currently accepted triple helix structure [6]. The triple helical structure is comprised of three parallel left-handed polyproline II-type helices, characterised by a repeating amino acid sequence generally written as (Gly-X-Y), where glycine (Gly) appears in every third position. The X and Y positions can often be proline and hydroxyproline amino acids. At the X and Y positions, any of the other 16 amino acids encoded by DNA can be present except tryptophan (TRP) and cysteine (CYS). Collagen contains approximately 35 % glycine, 11 % alanine, 21 % proline (PRO), and 12 % hydroxyproline (HYP). Collagen is differentiated from other proteins by its proportional PRO and HYP content. The total PRO and HYP ratio of collagen may vary based on the source from which the collagen is obtained [7]. Gly allows for the close contact necessary for stability. Hydroxylation of proline and lysine residues is important for maintaining the structural integrity of the triple helix by hydrogen bonding. In addition, covalent cross-linking between collagen molecules further enhances its stability, making collagen essential for tissue strength [8].

Different collagen types and structure

In vertebrates, 28 different types of collagens, consisting of at least 46 different polypeptide chains, have been identified [9]. The classification of collagen depends on its three-dimensional organisation and structure, which includes network-forming collagens, fibril-forming collagens, FACIT collagens (Fibril-Associated Collagens with Interrupted Triple Helices), transmembrane collagens, anchoring fibrils, basement membrane collagens, multiplexin collagens, and microfibrillar collagens. All groups of collagens and their distribution in the body were summarised in Tab. 1. As is known, 80–90 % of the collagens in the body are Type I, Type II and Type III collagen. Different collagen types are found in very low amounts in specific organs such as the cornea, lung, heart muscle, basement membrane, intestinal mucosa [8].

Collagen biosynthesis and dietary source of collagen

Collagen biosynthesis is considered to be an important process consisting of many stages, complex and involving many modifications. Collagen molecules are secreted from fibroblast cells and transformed into characteristic strands that provide the functional integrity of skin, bone, joints and tendons. During collagen biosynthesis, procollagen, a biosynthetic starting material, is first formed in the human body. Procollagen is degraded by special enzymes to form collagen [10].

In order to regulate and increase collagen synthesis, various active substances and delivery systems that support skin self-renewal and the improvement of skin problems have been identified in experimental and clinical studies. The most investigated of these are vitamin C (ascorbic acid), vitamin A, oestrogens, retinoids, asiaticoside-rich extracts, β-glucans, glycolic acids, liposomal systems and matrix metalloproteinase (MMP) inhibitors. In addition, in vitro fibroblast culture studies have examined several biological regulators, including growth factors (such as transforming growth factor-β) and peptide complexes (such

Tab. 1. Types of collagens in different structures and their distribution.

Groups of collagen	Type	Location in cells
Fibril-forming collagens	I	Skin, tendons, ligaments, bone structure
	II	Cartilage structure, nucleus pulposus, vitreous body
	III	Skin, reticular fibers
	IV	Hair, lung, cornea, placenta
	XI	Articular cartilage, vitreous body
Network-forming collagens	VIII	Endothelial cells
	X	Cartilage structure
FACIT collagens	IX	Cornea, cartilage structure, vitreous body
	XII	Tendons, perichondrium, ligaments
	XIV	Skin, tendons, placenta, lung
	XIX	Rhabdomyosarcoma cells
	XX	Embryonic skin, sternal cartilage, tendons
	XXI	Blood vessel wall
Transmembrane collagens	XIII	Skin, hair, endomysium
	XVII	Dermal - epidermal junctions
Anchoring fibrils	VII	Oral mucosa, skin
Basement membrane collagens	IV	Basement membrane
Microfibrillar collagens	VI	Skin, intervertebral disc, cartilage, placenta
Multiplexin collagens	XV	Kidney, fibroblasts, muscle cells
	XVI	Fibroblasts, amniotic fluid, keratinocytes
	XVIII	Lung, liver

as copper tripeptide complexes), which can modulate collagen synthesis [11]. However, a number of other experimental agents reported in the literature are not suitable for clinical or cosmetic use due to safety or toxicity concerns and are therefore beyond the scope of this review.

Dietary sources of collagen mostly come from animal-derived foods such as bone broth, chicken skin, fish, and specific cuts of meat rich in connective tissues, like tendons and skin. These foods contain gelatine as a form of collagen, which is derived from hydrolysis during cooking [9, 12]. Marine sources are considered a valuable collagen source because of their bioavailability and high levels of Type I collagen, which is particularly beneficial for skin health [1]. Additionally, some plant-based foods are not rich in collagen but are rich in nutrients such as vitamin C that support collagen synthesis [13].

Commercial collagen sources and extraction methods

The most commonly used raw materials in commercial collagen extraction are cattle, pigs, fish, chickens and their skin, cartilage, bone and tendons. The hydrolysis of different collagen sources is summarised in Fig. 1. Due to the emergence of diseases that pose a threat to humans, such as foot-and-mouth disease (FMD), transmissible spongiform encephalopathy (TSE) and

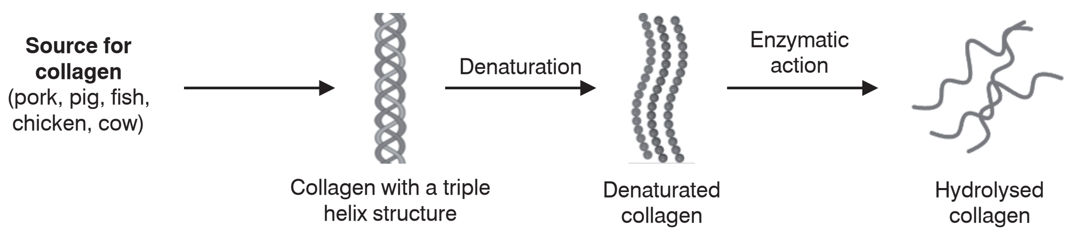

Fig. 1. Hydrolysis of different collagen sources.

mad cow disease (BSE), and religious restrictions, researchers are looking for more reliable alternative sources of collagen.

The bones and skin of the pig are also sources of collagen. These sources are mainly used for industrial purposes. Adult pig dermis and small intestinal mucosa are used for tendon strengthening, plastic and reconstructive surgery, skin and wound healing [14]. Porcine collagen is similar to collagen from humans, so the allergenicity is low [15]. Due to the risk of animal disease transmission and differences in beliefs, the consumption of collagen hydrolysates obtained from pigs is restricted. Bones and skins of bovine animals such as cows, oxen, buffaloes and cattle are the main sources of industrial collagen. The use of collagen hydrolysates derived from by-products of bovine sources has disadvantages due to some health problems, such as the possibility of carrying FMD, TSE or BSE, and faith-based restrictions. Another reason for not using bovine collagen is that about 3 % of the population is allergic to it [15].

In recent years, fish waste has been considered an alternative and reliable source for collagen hydrolysate extraction. Collagen extraction from animal origin is a difficult, time-consuming and expensive process. Concerns about adverse inflammatory and immunological responses and the prevalence of various diseases causing health complications in land animals have led researchers to marine sources. Significant amounts of protein are reported to be present in fish waste. Fish skin, scales and fish bone are a very good source of collagen. Inexpensive collagen hydrolysate can be provided by utilising these wastes [16]. Fish by-products are the source of Type I collagen, the most abundant protein in our body. The rate of obtaining collagen hydrolysate from fish by-products varies according to the production method, season and fish species. Fish-derived collagen hydrolysate can be used as an alternative raw material to bovine collagen hydrolysate. In this way, waste products that cannot be utilised as biowaste and which are largely encountered as environmental pollutants will be utilised, thus reducing environmental pollution [17].

Chicken, rat tail tendon, kangaroo tail, duck feet and skin, bird feet are some of the collagen sources. Chicken feet are abundant sources of collagen. Studies on collagen extraction from poultry by-products are also available in the literature.

Various extraction methods can be performed depending on the collagen sources. The method for collagen isolation consists of three steps: pretreatment, extraction and recovery. Collagen properties vary based on the raw material and extraction method. The most frequently used methods reported in the literature are acid extraction (ASC), enzymatic extraction and salt precipitation. Ultrasound-assisted extractions (UAC), deep eutectic solvent (DES) and supercritical fluid (SF) extractions, which have been developed as alternatives to traditional methods and are called environmentally friendly methods, are extraction methods developed in recent years for collagen isolation [9, 12]. The product obtained by these methods is usually referred to as hydrolysed collagen (HC).

Amino acid composition, bioavailability and bioaccessibility of collagen hydrolysates

Collagen hydrolysate or collagen peptides are the lower molecular weight, water-soluble structures formed by the breakdown of large molecular weight collagen obtained from animal by-products such as bone and skin, usually by enzymatic or acidic extraction [9, 18]. High levels of Type I collagen are obtained from by-products such as skin, tendon of fish, pig and bovine sources. The molecular weight of collagen peptides obtained from hydrolysis is quite low compared to native collagen (285–300 kDa). Low molecular weight is the factor that increases its functional properties such as antioxidant capacity, antimicrobial activity and higher bioavailability [19]. As mentioned earlier, hydrolysed collagen is obtained in the industry from by-products such as skin, bone, tendon from bovine, fish and porcine sources. Fish collagen hydrolysate has been investigated as a source of mineral-chelating peptides with promising bioactivity and bioavailability [20]. In addition, fish-derived collagen hydrolysate has been incorporated into various functional foods and beverages in the literature, reflecting its favourable technological and sensory properties compared with other sources [9, 21].

Collagen contains 19 different amino acids in its structure; it contains 8 of 9 the essential amino acids. Compared to other proteins, important amino acids such as proline and glycine are found in high amounts in collagen hydrolysate. Proline and hydroxyproline provide rigidity and strength to the collagen molecule. Hydroxyproline is the amino acid characteristic of collagen and determines the thermal stability of collagen. Hydroxyproline has many functions such as glycine synthesis, repair of connective tissue and regulation of cellular activities [1]. The amino acid composition of fish, bovine and pork collagen is given in Tab. 2 [22–24]. Considering these data, when the amino acid composition of food supplement products containing collagen hydrolysate is examined, it will be seen that the amino acid compositions of bovine, fish and chicken source collagen hydrolysates differ.

Before discussing the bioaccessibility and bioavailability of collagen hydrolysates, it is necessary to emphasise the difference between these two terms. The concept of bioaccessibility is defined as the dissolution of nutrients after digestion and making them accessible for intestinal absorption. In general, food components that are not released from the food matrix and do not show the ability to pass through the intestinal barrier are not bioaccessible. Bioavailability describes the amount of nutrients or components that are actually absorbed, distributed to tissues, metabolised and excreted by the body. Bioavailability is also expressed as the rate of absorption and participation in metabolic activities and the amount of distribution to tissues [25]. In studies on bioavailability and bioaccessibility, in vivo or in vitro methods are generally used to determine the bioaccessibility and therefore bioavailability of nutrients. These in vivo studies are ethically problematic, time-consuming, intensive, costly, complex and limited in the number of samples analysed. In vitro methods, on the other hand, allow a large number of samples to be analysed in a simple, economical, rapid and reproducible manner [26].

When collagen is consumed in the form of a natural protein, it is converted into smaller molecular weight peptides by the enzymes in the digestive tract of the stomach and small intestine to become small peptides or free amino acids. They are then absorbed by the intestine in the form of peptides, free amino acids and di- or tripeptides. Comparing collagen hydrolysate with the collagen molecule, collagen hydrolysate is easily digested by the body and has high absorption compared to the collagen molecule due to the reduction of collagen hydrolysate to low molecular weight in the enzymatic production process [27]. It has been revealed that marine collagen hydrolysate is biologically present in connective tissue 4 hours after consumption, and 90 % of it is digested. It is known from in vitro and in vivo studies that more than 90 % of collagen hydrolysates are digested and rapidly absorbed after oral intake [28]. In bioavailability studies, it is important to confirm in vitro findings with in vivo findings. In a study conducted in 2015 [29], it was observed that the hydroxyproline amino acid had the closest value in the correlation curve of the increasing amino acid amount in blood plasma against collagen content after the oral intake of collagen hydrolysate. Therefore, hydroxyproline amino acid is suitable for the evaluation of the bioaccessibility of collagen hydrolysate. In 2007, in a clinical study on five healthy male volunteers [30], the amount and structure of hydroxyproline in human blood after oral consumption of Type I gelatine hydrolysates derived from fish scale, fish skin or pork skin after 12 hours of fasting were investigated. Over a 24-hour period, the amount of hydroxyproline-containing peptides constituted approximately 30 % of the total amount of hydroxyproline detected. They concluded that the amount and structure of hydroxyproline-containing peptides in human blood after oral administration of gelatine hydrolysates vary depending on the gelatine source and that the source affects bioavailability. The amount of hydroxyproline-containing peptides varied according to the gelatine source, and proline-hydroxyproline was the main peptide in human blood plasma after oral administration of collagen hydrolysate [30]. In another study [21], 5 different ratios of collagen hydrolysate (1, 1.5, 2, 2.5 and 3 %) were added to beverages prepared from fruit juices with 4 different ingredients (100 % orange, orange-white grape, apple and apple-white grape). Enzymatically derived collagen hydrolysate from fish was used as collagen hydrolysate. The study shows that the bioaccessibility of hydrolysed collagen examined through the in vitro gastrointestinal digestion model is very high. According to the bioaccessibility results evaluated after the

Tab. 2. Amino acid composition of fish, bovine and pork collagen hydrolysates.

	Collagen hydrolysate		
	Fish [23]	Bovine [22]	Pork [24]
Amino acids [g·kg^{-1}]			
Glycine	236	225	234
Alanine	118	86	89
Proline	110	128	130
Glutamic acid + glutamine	102	70	101
Hydroxyproline	89	102	113
Arginine	79	74	79
Aspartic acid + asparagine	56	53	55
Serine	35	34	33
Threonine	33	23	17
Lysine	32	35	36
Leucine	29	30	27
Valine	24	19	23
Phenylalanine	17	20	19
Isoleucine	14	13	12
Histidine	11	6	7

in vitro digestion procedure, among the beverages to which hydrolysed collagen was added at a concentration of 2.5 %, the bioaccessibility of orange (95.4 %) and apple juice (90.7 %) beverages was higher, while the addition of grape juice reduced this value to 83.4 % and 86.3 % for orange-grape juice and apple-grape juice mixtures, respectively. The decrease in bioaccessibility is attributed to the ability of phenolic compounds in white grape juice to directly or indirectly reduce the digestibility of protein [21].

As a result, the factors affecting bioaccessibility and bioavailability include person-dependent factors, the source from which the collagen hydrolysates contained in food supplements are obtained, the production method and the processes to which they are exposed until they reach the final product, amino acid composition, low molecular weight, bioactive compounds such as multivitamins, minerals, polyphenol, probiotics added to collagen hydrolysates have a synergistic effect [31, 32].

Use of collagen hydrolysates in nutrition

Collagen offers good biocompatibility and biodegradability; hence it is safe and effective as a biomaterial and has been used as a safe and effective biomaterial in tissue engineering and clinical practice in recent years. Biomaterials widely used in tissue engineering are mainly produced from Type I, II, III, V and XI collagen [33]. Collagen supplements have become popular as an anti-ageing functional products and their use has increased. The most prominent features of collagen hydrolysate food supplements are that they reach the deeper layers of the skin and promote skin physiology and appearance, improving hydration, elasticity, firmness and wrinkle reduction. Collagen is widely used in the cosmetic industry due to its excellent water retention, low allergic reaction and ability to repair damaged skin [34, 35].

Collagen hydrolysate, which has widespread use in the food sector, is used as an emulsifier, microencapsulation agent, stabiliser, foaming agent, and biodegradable film-forming material [36]. In recent years, it has focused on the preparation of functional foods and beverages, food supplements, meat processing, and the production of food biofilms. In food science, collagen hydrolysate plays a role in minimising or preventing damage to cells and tissues during freezer storage, so it is an option for use in foods that require low-temperature storage [37].

Supplementary foods are products with a determined daily intake dose for the purpose of supplementing normal nutrition. Supplementary foods are products prepared in capsule, tablet, liquid or powder form, alone or in the form of a mixture of concentrated or extracted forms of nutrients such as vitamins, minerals, proteins, fatty acids, carbohydrates, amino acids, or substances with nutritional and physiological effects and bioactive substances [5]. Collagen supplements in powder form, containing collagen hydrolysate with low molecular weight, are quickly assimilated by our enzymes and enter our bloodstream. Research indicates that powdered or liquid collagen that is readily absorbed and utilised by the body is the best form of collagen for collagen hydrolysates. This collagen hydrolysate form enters the bloodstream quickly after consumption, allowing the body to use it. It is the most favoured type of collagen due to its high bioavailability. Powdered collagen supplements are simpler to use, can be mixed with water, coffee, or any other liquid you want, and are easily ingested [36]. Liquid collagen supplements have similar properties to powdered collagen forms. Since it is a liquid hydrolysed collagen supplement, it is faster and easier to absorb. Most collagen supplements are available in powder or liquid form. Liquid collagen hydrolysates often contain sweeteners and flavourings [35]. Collagen supplements in tablet or capsule form take longer to break down and absorb than other forms. Collagen tablets or capsules may seem easy to use, but they can actually be misleading. You'll need to swallow a lot of these tablets or capsules to consume the daily recommended amount of collagen hydrolysate [38].

Types of collagen hydrolysates and human health

When the current literature is examined, it is seen that the majority of studies on the effects of collagen on human health focus on Types I, II and III collagen. This is related to the fact that these collagen types are the most common forms in the body and have direct functional roles in tissues such as skin, bone and cartilage [1, 9]. In contrast, data on lesser-known collagen types such as Types V, VI, VII, XII, XIV, XIX and XXI–XXVIII are limited to a limited number of animal models or in vitro studies. This prevents the physiological effects of these collagen types from being adequately understood, especially in the context of chronic diseases, tissue regeneration, oxidative stress management and their relationships with the intestinal microbiota. This imbalance in the literature offers a wide potential area for future research; it is important to address the mechanisms of action of lesser-known collagen types at the tissue level from the perspective of molecular biology, nutritional science and clinical research.

In this part, the effects of collagen hydrolysates on human health are examined in detail under the headings of skin health, digestive system, metabolic diseases, oxidative stress and ageing in line with the current literature. In particular, the current findings on the potential roles of lesser-known collagen types in these areas will be evaluated and the gaps for further research will be highlighted.

Changes in the skin with ageing and collagen

Collagen, elastin and hyaluronic acid are crucial parts of the skin and take on a role in protecting its structure and moisture. Skin collagen is produced mostly by fibroblasts. The collagen-rich extracellular matrix builds and repairs the structure of skin components; collagen is the most abundant connective tissue in the dermis and is responsible for the skin's strength and durability [39]. The loss of collagen in the body begins between the ages of 18 and 29, and after the age of 40, the human body can lose approximately 1 % of collagen per year. In an approximately 80-year-old body, collagen production may have decreased by 75% compared to younger adults. There are other factors in the body that contribute to natural ageing, such as free radicals, smoking, alcohol, poor nutrition and disease. Since ageing is a natural process that involves changes in the human body, the skin is subject to morphological, structural and functional deterioration over time; collagen decreases, and elastin fibres support the formation of lines and wrinkles [40]. Controlling skin ageing is one of the main problems in the cosmetic industry. Collagen hydrolysates have been reported to be an alternative solution to slow down the effects of ageing. Collagen is a crucial component of the wound healing process; it acts as a natural structural scaffold or substrate for new tissue growth and plays a key role in all phases of wound healing, including haemostasis, inflammation, proliferation, and remodelling. Anti-ageing agents are those that limit or prevent the progression of ageing, but the anti-ageing activity of collagen hydrolysates may be related to their antioxidant activity [37, 41].

In the literature, studies have been conducted by giving different collagen hydrolysate sources to humans at different doses in order to counteract the effects of ageing on the skin. In a randomized controlled trial, 10 g of marine collagen hydrolysate supplements were given to women between the ages of 45 and 60 for 12 weeks. The results of this study showed significant improvements in wrinkle scores on both sides of the face, cheek skin hydration, and self-reported elasticity, hydration, radiance, firmness, and wrinkle scores in the collagen hydrolysate group compared to the control group [42]. Choi et al. evaluated 11 randomized clinical trials in their systematic review and showed that oral hydrolysed collagen supplementation increased skin elasticity, hydration, and collagen density, improved wound healing, and protected the skin against ageing [35]. Barati et al. analysed 10 randomized clinical trials in their systematic review and concluded that the consumption of both intact and hydrolysed collagen improved clinical signs of skin health by increasing the synthesis of the extracellular matrix or by enhancing the interaction of regulatory T cells and type 2 macrophages in maintaining the skin immune response to endogenous collagen [43].

Research has emphasised the health effects of different collagen types. Firstly, Type I collagen's functions are to provide structural support, increasing the elasticity and hydration of the skin. In wound healing, it promotes skin regeneration. Most skin problems, such as wrinkles, loss of firmness, and other signs of ageing are related to decreased levels of Type I collagen. Research in the literature suggests that supplementation may improve wrinkle problems due to its hydration and elasticity-enhancing functions [44]. Type II collagen is mostly associated with joint problems, such as osteoarthritis, in addition to its skin improvement features [18, 45]. Type III collagen's level is associated with ageing complications similar to Type I [44, 46]. Type IV collagen preserves the unity of the skin. Due to this function, it participates in the structural integrity of the skin. Type IV collagen forms a layered structure in the basal lamina and plays roles in cellular adhesion. For these reasons, decreased levels of Type IV collagen worsen the signs of ageing [47]. Collagen Type V provides structural integrity to tissue scaffolds by interacting with matrix collagens and structural proteins. Collagen Type V acts as a regulator of collagen fibrillogenesis, assembling into heterotypic fibrils in the cornea and skin dermis. Collagen Type V deficiency is associated with loss of corneal transparency and classic Ehlers-Danlos syndrome, while collagen Type V overexpression is found in cancer, granulation tissue, inflammation, atherosclerosis and fibrosis of the lung, skin, kidney, adipose tissue and liver [48]. Scleroderma is characterised by fibrotic skin fibrosis, vasculopathy and autoimmunity. Fibrosis is associated with altered remodelling of the extracellular matrix due to unbalanced accumulation and degradation of fibrillar collagen Types I, II and V. Among these collagens, Type V is thought to play a crucial role in the pathogenesis of fibrosis in scleroderma [49]. Type VI collagen supports skin health by maintaining elasticity and hydration through positive regulation of dermal matrix assembly and fibroblast motility; it also exhibits cytoprotective properties and counteracts oxidative damage [50]. Type VII collagen is essential for skin stabilisation and integrity. It forms anchoring fibrils that fix the epidermis to the dermis and is consequently vital for wound healing and skin repair. Type VII collagen is associated with disorders such as recessive dystrophic epidermolysis bullosa (RDEB), characterised by severe skin fragility and blistering. Therapies targeting Type VII collagen have shown potential to enhance wound healing in affected patients [41]. Type IX collagen functions in skin and cartilage health by supporting the maintenance of skin moisture and elasticity. However, its specific role in reducing wrinkles and visible signs of ageing has not been clearly demonstrated; current evidence mainly comes from studies using mixed collagen preparations [45]. Type XII collagen's functions relate to maintaining skin elasticity and structural unity. Type XII collagen interacts with collagen I fibres, supporting the extracellular matrix. Altered expression of Type XII collagen has been associated with impaired tissue repair and matrix organisation, but its direct role in skin hydration and wound healing in humans remains to be clarified [51]. Type XIII collagen promotes cell adhesion and protects the skin integrity. It is concentrated in skin fibroblasts and focal adhesions and therefore may contribute to skin elasticity and hydration by supporting the extracellular matrix [52]. It supports the extracellular matrix and condenses in skin fibroblasts, aiding in healing the skin's hydration status. While oral collagen supplementation has been reported to improve skin elasticity and appearance in general [39], the specific contribution of Type XIII collagen to these effects has not yet been isolated in clinical studies. Type XIX collagen is a basement membrane-associated collagen with structural and biological roles in various tissues [53]. To date, its specific involvement in skin structure, ageing, or clinical skin outcomes has not been clearly demonstrated. While some clinical trials on hydrolysed collagen supplementation report improvements in skin elasticity and hydration [54], these studies do not isolate the effects of Type XIX collagen itself. Type XV collagen is a multiplexin that is present in several tissues, where it contributes to collagen fibril organisation and maintenance of tissue integrity. However, its specific role in skin ageing and potential anti-ageing effects on skin appearance have not yet been demonstrated in clinical studies [55]. Type XVI collagen behaves as an adaptor protein. Due to this function, it increases the integrity and stability of the extracellular matrix, which connects and organises fibrillar networks and is crucial for skin elasticity and overall skin structure [56]. The hydrolysed form of collagen supplementation has been researched for these effects, and it has shown promising effects on reducing signs of skin ageing. Type XVII collagen has critical role in protecting epidermal unity and cell adhesion. It participates in stem cell behaviour regulation, which is crucial for skin regeneration and wound healing. Finally, it is associated with health conditions such as bullous pemphigoid and junctional epidermolysis bullosa [57]. Although the findings obtained from the studies are not clear, Type XVIII collagen is effective in reducing hydration and wrinkles due to its presence in the basement membrane and role in tissue regeneration [45]. Collagen Type XXII acts as a cell adhesion ligand for skin epithelial cells and fibroblasts and contributes to the maintenance of tissue connections, elasticity and hydration of the skin. It plays an important role in the structure of the extracellular matrix. It has shown potential benefits in relieving skin ageing and other related skin conditions [58]. Collagen Type XXIII is a transmembrane collagen that shares some structural and localisation features with collagen Type XXII. Recent genetic and functional studies have shown that variants and overexpression of collagen XXIII (COL23A1) are associated with increased susceptibility to eczema herpeticum in patients with atopic dermatitis; however, its direct role in more common skin conditions, such as wrinkling or intrinsic skin ageing, has not yet been elucidated in clinical studies [59]. Collagen Types XXVI, XXVII and XXVIII have similar functions, such as maintaining skin structure, elasticity and hydration. However, their specific roles in maintaining skin structure, elasticity and hydration, or in slowing age-related skin changes, have not yet been clearly defined in clinical studies [60].

Although there are many studies on the effects of collagen hydrolysates on skin ageing, the generalizability of these data is limited. Most of the existing studies have been conducted with small samples, short-term, and usually with female participants of a certain age group. In addition, many studies have used collagen in combination with other components such as vitamin C or hyaluronic acid, which makes it difficult to clearly assess the effect of collagen alone. The lack of consistency among collagen sources, doses, and forms limits the comparability of the results. Therefore, larger sample sizes, long-term, and well-designed clinical studies are needed to establish the anti-ageing effects of collagen types with stronger evidence. In addition, mechanistic studies explaining the tissue-specific effects of different collagen types are still lacking.

Collagen types in obesity

The most studied collagen types in relation to obesity are Types I, III, IV, and VI, due to their roles in extracellular matrix remodelling, fibrosis, inflammation, and metabolic dysfunction. Less-investigated collagens (Types V–XXVIII) have also attracted attention for their potential roles in obesity through participation in extracellular matrix organisation. According to the results of an animal study, Type I collagen was found to decrease in the myocardium of obese rats, coinciding with increased leptin expression and metalloproteinase-2 activity [61]. This finding suggests that obesity can induce extracellular matrix changes in cardiac tissue, potentially via enhanced collagen degradation.

Recent studies have explored the potential of collagen in obesity management using technologically modified collagen with high water-retention capacity. In a randomised controlled trial, daily consumption of 20 g of a collagen-based supplement for 12 weeks led to significant reductions in body weight, body mass index (BMI), waist circumference, total fat mass, fatty liver index, and systolic blood pressure, accompanied by increased satiety and decreased hunger-suggesting an appetite-regulating effect [62]. However, because the study did not record detailed food intake, it remains unclear whether the observed benefits were due solely to the collagen supplementation or to indirect effects. This uncertainty highlights the need to investigate possible mechanisms of action, such as the influence of bioactive collagen peptides, postprandial glucose responses, or gut microbiota modulation, in order to fully understand how collagen supplementation may aid in weight management.

One line of inquiry into collagen's mechanism involves its interaction with the gut microbiota. It has been reported that certain collagen peptides derived from fish skin can positively modulate the intestinal microbiota and ameliorate obesity-related symptoms in high-fat diet-induced obese mice. In this model, collagen peptide supplementation helped restore microbial balance by reducing the *Firmicutes*/*Bacteroidetes* ratio and increasing beneficial bacteria (such as *Clostridium, Faecalibaculum*, and *Bacteroides*). These microbiota changes activated metabolic pathways involved in carbohydrate degradation and amino acid synthesis, resulting in significant improvements in outcomes like excessive fat accumulation, hyperglycaemia, and weight gain [63]. These findings suggest that marine-derived collagen peptides have potential for a microbiota-mediated complementary therapy in obesity, though further clinical studies are required to confirm similar effects in humans.

Obesity is also associated with alterations in collagen turnover and extracellular matrix composition within adipose tissue. For instance, collagen VI deposition is markedly elevated in the subcutaneous fat of obese individuals, and this excess collagen VI has been implicated in adipose tissue inflammation and dysfunction [64]. Additionally, some other collagens (e.g. certain basement membrane and fibrillar collagens) may be upregulated during adipose tissue expansion, contributing to matrix reorganisation and metabolic consequences. When considering lesser-known collagen types, the FACIT collagens (e.g. Types XII, XIV, XVI) are known to interact with fibril-forming collagens (Types I–III) to regulate matrix assembly during adipose tissue expansion. Similarly, non-fibrillar collagens such as Type XVIII contribute to basement membrane integrity, although to date there are no specific studies detailing the role of collagen XVIII in obesity. In summary, collagen is an important structural protein in the pathophysiology of obesity, and further research is needed to clarify the contributions of both well-known and less-studied collagen types in obesity-related metabolic dysfunction.

In the pathophysiology of obesity, collagen represents an important structural component of the extracellular matrix, particularly through mechanisms involving matrix remodelling, inflammation, and metabolic dysfunction. Although reductions in body weight, fat mass and hunger perception have been reported following collagen supplementation, the physiological pathways underlying these effects remain insufficiently defined. Future research should incorporate not only anthropometric outcomes but also mechanistic biomarkers such as appetite-regulating hormones (ghrelin, GLP-1, PYY), postprandial glucose responses, and gut microbiota composition to better elucidate these effects. In addition, placebo-controlled, double-blind, longer-term randomised clinical trials that include quantitative dietary assessments (e.g., weighed food records or multi-day food diaries) are required to distinguish the direct effects of collagen peptides from indirect behavioural or dietary adaptations. Such approaches will clarify whether collagen-based interventions provide a meaningful contribution to obesity management and through which biological pathways they exert their effects.

Collagen types' roles in diabetes management

Studies on the relationship between collagen types and diabetes have focused on many hypotheses, including the management of diabetes complications. However, some changes occur in collagen metabolism in diabetes. An example of these changes is that the synthesis of some types of collagen (Type IV) increases, which leads to thickening of the renal basement membrane and advances nephropathy [32]. Types I and III collagen play a role in tissue fibrosis, a common complication of diabetes. Their accumulation in tissues such as the kidney and skin contributes to structural abnormalities. In diabetic nephropathy, signalling pathways such as Notch, Wnt/β-catenin, mechanistic target of rapamycin (mTOR) and Toll-like receptors (TLRs) regulate gene expressions related to collagen metabolism. These pathways have the potential to regulate metabolism and therapeutic interventions [31, 32]. When examining the therapeutic effects of collagen types in diabetes, collagen peptides, especially those obtained from seafood, have been reported to have anti-diabetic effects in both animal models and clinical studies. They show their anti-diabetic effects by increasing insulin sensitivity, reducing fasting blood sugar and reducing glycated haemoglobin (HbA1c) [65, 66]. In addition, there is another mechanism to improve diabetes prognosis, and this mechanism involves inhibition of dipeptidyl peptidase-IV (DPP-IV), which increases incretin hormone activity and promotes insulin secretion [66]. One of the complications of diabetes is the late healing of wounds in the body. In a clinical study conducted on this subject, collagen peptides obtained from sources such as squid cartilage (Type II collagen) have been shown to support wound healing by increasing the expression of growth factors such as insulin-like growth factor 1 (IGF-1) and Irisin [65]. Moreover, a study in which individuals with type 2 diabetes were given 13 g of collagen peptides daily for 3 months showed a decrease in fasting glucose, triglyceride and free fatty acid levels, and an increase in insulin sensitivity. Improvement in kidney function was also reported. In the same study, it was reported that the therapeutic effect was more pronounced in individuals with diabetes who were not hypertensive [67]. These results suggest that marine collagen peptides may have positive effects on metabolic control.

Although there are studies that provide meaningful results, most of the data in this area are based on short-term clinical observations. Long-term, controlled human studies, particularly those comparing the efficacy of collagen peptides depending on the source, dose, and duration of administration, are limited. While studies on Types I–IV collagen are relatively abundant, the role of less studied collagen types (e.g. Types V, XVIII) in diabetic microvascular complications remains largely unclear. This represents an important gap in both basic science and clinical research.

Antioxidant potential of some collagen types

In the human body, reactive oxygen and nitrogen species are formed both during the realisation of biological functions and due to exogenous factors. These compounds are generally free radicals or have the property of easily forming free radicals. These reactive molecules support body functions at low or medium concentrations. However, high concentrations of oxidative compounds can disrupt normal cellular signalling mechanisms by causing lipid, protein and DNA damage. Antioxidants play a vital role in defence mechanisms, and in general, antioxidant defence consists of different mechanisms [68]. The antioxidant effects of collagen differ between collagen types and forms, such as Type I and marine-derived collagen peptides. Studies have shown that Type I collagen in hydrolysed peptide form exhibits strong antioxidant properties. The possible mechanism is its ability to scavenge free radicals and inhibit lipid peroxidation. The antioxidant effect of these peptides is thought to be due to specific amino acid sequences and hydrophobic residues within the peptides [69]. In a study on the antioxidant activity of Type II collagen, it was reported that Type II collagen treatment improved antioxidant defence mechanisms by increasing glutathione (GSH) levels in the spleen and thymus in rats with adjuvant-induced arthritis. Moreover, nitric oxide-mediated signalling has been shown to induce Type IV collagen expression and promote angiogenesis in endothelial cells, although direct evidence linking this pathway to antioxidant enzyme activation is lacking [70]. Type V collagen is a regulatory fibril-forming collagen that interacts with other matrix collagens and structural proteins, thereby contributing to extracellular matrix organisation, tissue integrity and fibrotic remodelling in several organs [46]. In addition, peptides derived from Type V collagen have shown antioxidant activity in vitro, for example, in studies using hydrolysates from pearl oyster mantle collagen [71]. Considering the antioxidant effect potential of Type VI collagen, it has been shown to resist apoptosis and oxidative damage in various tissues and cells, including myofibrils, neurons and fibroblasts. The mechanisms of its cell protective role include minimising oxidative stress formation by maintaining cellular homeostasis and promoting autophagy [72]. The type of collagen predominantly expressed during arterial remodelling and in atherosclerotic lesions is Type VIII. Although its direct antioxidant effects have not been established, Type VIII collagen has mainly been implicated in extracellular matrix remodelling and plaque structure rather than in the regulation of oxidative stress. Finally, with regard to Type XI collagen, it has been shown to regulate the assembly and organisation of collagen fibrils in tendon and cartilage, thereby contributing to the biomechanical properties of these tissues [73]. Recent studies have shown that some collagen types, especially those obtained from seafood, have significant antioxidant potential. For example, it has been reported that collagen peptides obtained from cod skin reduce oxidative stress indicators, suppress reactive oxygen species (ROS), and increase antioxidant enzyme levels (SOD, GSH-Px) in RAW264.7 macrophage cells activated with lipopolysaccharide (LPS). At the same time, the decrease in malondialdehyde (MDA) levels indicates that oxidative damage at the cellular level is reduced [74]. These findings indicate that collagen peptides may also be functional in the management of oxidative stress accompanying inflammation. However, most of these studies are limited to in vitro models, and human clinical data are quite limited. The differences in parameters such as doses, bioavailability levels, and peptide chain lengths used make it difficult to generalise the results. In addition, the fact that the antioxidant effect mechanisms have not been fully explained at the level of intracellular signalling pathways continues to raise questions about the effective and generally safe use of these ingredients in functional foods. Therefore, future studies need to produce stronger evidence with human-based randomised controlled designs, tissue-specific mechanisms of action, and dose-response analyses.

Collagen types' roles on the digestive system

Types I, III, IV and V collagens have a direct role in maintaining the integrity of the digestive tract through their structural role in the extracellular matrix, improvement of barrier function, and repair mechanisms during inflammation or injury. However, research on the lesser-known and investigated collagen types is limited. This type of collagen is thought to improve intestinal health by interacting with the extracellular matrix and increasing the strength of the fibrils. Type I collagen improves intestinal health by playing a role in maintaining and improving the structural integrity of connective tissue in the intestinal wall. In a study, hydrolysed Type I collagen was found to reduce intestinal permeability by improving the intestinal barrier in leaky gut syndrome [38]. Type III collagen is plentiful in the intestinal wall's composition and is related to the elasticity and strength of the intestinal walls. Therefore, it has a critical role in a healthy digestive system. It has been reported that it plays a key role in supporting the lamina propria, a layer of connective tissue necessary for a healthy intestinal structure, adequate blood flow and immune function [75]. One of the most important components of intestinal basement membranes is Type IV collagen. It provides structural support to intestinal epithelial cells and contributes to nutrient absorption and the barrier function of the intestines. In a clinical study, it was concluded that collagen supplementation reduces the entry of toxins into the body through the intestine by protecting the tight connections between epithelial cells [76]. In addition, Type XVII collagen (COL17) is a transmembrane protein located in the epidermal basement membrane region and plays an important structural role, particularly in maintaining skin integrity. COL17 is critical for both cell-cell and cell-matrix interactions, enabling keratinocyte adhesion and supporting the stability of the epidermal-stromal junction [77]. However, knowledge of this collagen type has generally been concentrated in the context of dermatological disorders and skin physiology [57]. The potential effects of COL17 in broader pathophysiological areas such as metabolic diseases, intestinal health, or systemic inflammation remain largely unclear. Moreover, most data have been obtained from animal models or cell culture systems, limiting their direct applicability to human physiology. Therefore, translational research and clinical studies are needed to gain a more comprehensive understanding of the systemic functions of COL17. In particular, the evaluation of this collagen type in the context of epithelial barrier function, microbiota interactions and immune response may enable the development of new therapeutic strategies.

Eye health and collagen types

Although Type I collagen is the main component of the cornea and sclera, it is important for eye health together with Type II and III collagen. They play a critical role in maintaining the transparency and structure of the cornea. Studies show that Type I collagen degradation in the sclera and cornea with age plays a role in vision loss [78]. In addition, Type II collagen is an important component of vitreous humour and supports light transmission to the retina. In one study, Type II

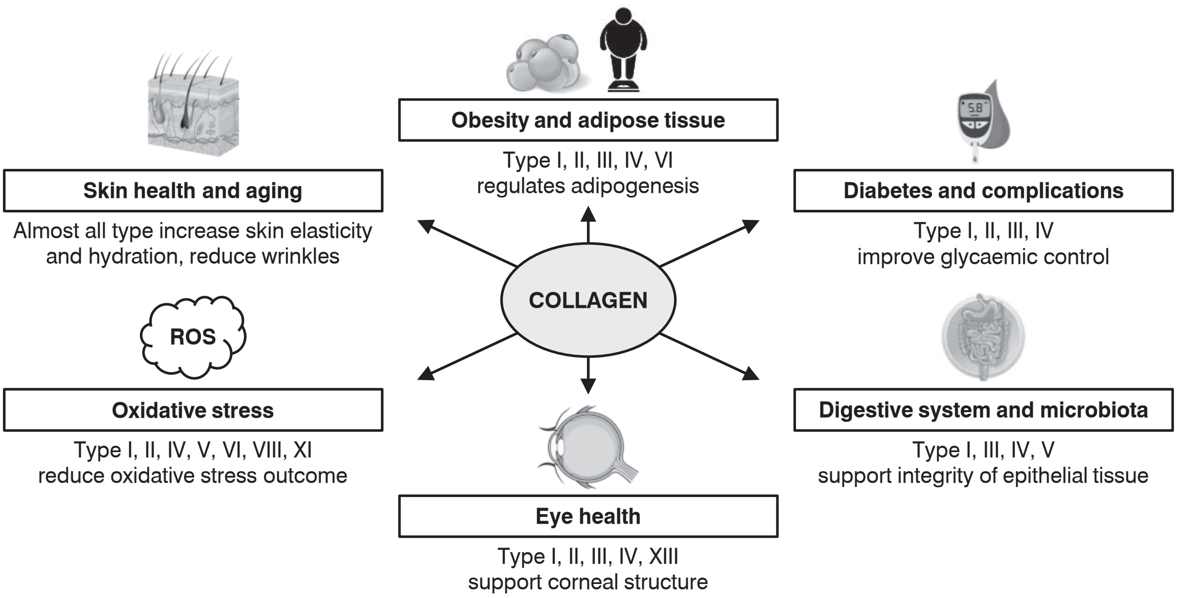

Fig. 2. Collagen types and health.

collagen was found to increase tear volume and reduce ocular inflammation [1, 78]. Type IV collagen is one of the main components of the cornea, lens and retina and supports epithelial cells. In this way, it contributes to the ocular tissue integrity with Type V collagen. Type XIII, one of the lesser-known collagen types, is widely expressed in the optic nerve and neural retina. It regulates the extracellular matrix in the regions where it is expressed [79]. As emphasised earlier, FACIT collagens interact with other collagens to regulate the extracellular matrix. Although there is no specific research, they are critical for retinal integrity. However, direct evidence on the functions of collagens, especially Type XIII and FACIT, in the retina and optic nerve is limited. In this context, advanced molecular and clinical studies are needed to reveal the effects of these collagens at the cellular level in order to understand the pathophysiology of age-related visual impairment and to develop new therapeutic targets.

The picture showing the relationship between collagen hydrolysates and health is in Fig. 2.

CONCLUSION

Collagen is one of the most basic proteins that provide the body's structural integrity and is widely found in body parts. The amount of collagen naturally produced by the body decreases with age, and this decrease paves the way for wrinkles, joint and bone problems on the skin. Collagen hydrolysate is a food ingredient known for its support of collagen synthesis and a wide range of health benefits such as antioxidant, anti-inflammatory and antihypertensive properties. In recent years, food supplements containing collagen hydrolysate have been shown to have positive effects such as alleviating the signs of ageing, protecting skin health and reducing the symptoms of joint disorders, supporting the ocular health and reducing body weight and blood glucose levels.

This article examines the structural properties, bioavailability, bioaccessibility, health effects and the use of collagen hydrolysate in nutrition in detail. It has been stated that the effects of collagen hydrolysates, such as increasing skin elasticity, reducing wrinkles, maintaining its moisturising effect, supporting joint health, improving ocular functions and playing a role in the management of non-communicable diseases such as obesity and diabetes, are supported by clinical studies. It is recommended to be consumed as a food supplement to support collagen synthesis, which decreases with ageing, and it is aimed to reach a wider consumer base with safe and biologically suitable forms of these products.

The various health benefits provided by collagen hydrolysate have made it popular in the food, cosmetics, biomedical and pharmaceutical sectors. However, the development of technological methods that will increase the bioavailability of collagen hydrolysate and more studies investigating the long-term effects of collagens obtained from different sources on health are needed. The correct amount and continuous consumption of collagen hydrolysate can alleviate the effects of age-related collagen loss and improve the quality of life of individuals.

REFERENCES

1. Rahman, A. – Rehmani, R. – Pirvu, D. G. – Huang, S. M. – Puri, S. – Arcos, M.: Unlocking the therapeutic potential of marine collagen: A scientific exploration for delaying skin aging. Marine Drugs, *22*, 2024, article 159, DOI: 10.3390/MD22040159.
2. Bruyère, O. – Zegels, B. – Leonori, L. – Rabenda, V. – Janssen, A. – Bourges, C. – Reginster, J. Y.: Effect of collagen hydrolysate in articular pain: A 6-month randomized, double-blind, placebo-controlled study. Complementary Therapies in Medicine, *20*, 2012, pp. 124–130. DOI: 10.1016/j.ctim.2011.12.007.
3. Dierckx, S. – Patrizi, M. – Merino, M. – González, S. – Mullor, J. L – Nergiz-Unal, R: Collagen peptides affect collagen synthesis and the expression of collagen, elastin, and versican genes in cultured human dermal fibroblasts. Frontiers in Medicine, *11*, 2024, article 1397517. DOI: 10.3389/fmed.2024.1397517.
4. TFC 2013/49. Turkish Food Codex Notification on food supplements. Ankara: Ministry of Agriculture and Forestry, 2013.
5. Fujimoto, W. – Fukuda, M. – Yokooji, T. – Yamamoto, T. – Tanaka, A. – Matsuo, H.: Anaphylaxis provoked by ingestion of hydrolyzed fish collagen probably induced by epicutaneous sensitization. Allergology International, *65*, 2016, pp. 474–476. DOI: 10.1016/j.alit.2016.03.012.
6. Pandav, G. – Saxena, D. – Kaur, H. – Jain, S. – Dewan, A.: Collagen: basis of life. Universal Research Journal of Dentistry, *4*, 2014, article 1. DOI: 10.4103/2249-9725.127046.
7. Cadar, E. – Pesterau, A.-M. – Prasacu, I. – Ionescu, A.-M. – Pascale, C. – Dragan, A.-M. L. – Sirbu, R. – Tomescu, C. L.: Marine antioxidants from marine collagen and collagen peptides with nutraceuticals applications: a review. Antioxidants, *13*, 2024, article 919. DOI: 10.3390/antiox13080919.
8. Brodsky, B. – Persikov, A. V.: Molecular structure of the collagen triple helix. Advances in Protein Chemistry, *70*, 2005, pp. 301–339. DOI: 10.1016/S0065-3233(05)70009-7.
9. León-López, A. – Morales-Peñaloza, A. – Martínez-Juárez, V. M. – Vargas-Torres, A. – Zeugolis, D. I. – Aguirre-Álvarez, G.: Hydrolyzed collagen – Sources and applications. Molecules, *24*, 2019, article 4031, DOI: 10.3390/molecules24224031.
10. Wu, M. – Cronin, K. – Crane, J. S.: Biochemistry, collagen synthesis. StatPearls [online]. Treasure Island : StatPearls Publishing, 2023 [cited 29 October 2024]. <https://www.ncbi.nlm.nih.gov/books/NBK507709/>
11. Yener, G. – Erdal, S.: Kolajen biyosentezini aktive eden maddeler ve etki mekanizmaları. (Collagen biosynthesis activators and their mechanism of action.) Anadolu Üniversitesi Bilim ve Teknoloji Dergisi, *6*, 2005, pp. 3–13. ISSN: 1302-3160. In Turkish.
12. Daneault, A. – Prawitt, J. – Soulé, V. F. – Coxam, V. – Wittrant, Y.: Biological effect of hydrolyzed collagen on bone metabolism. Critical Reviews in Food Science and Nutrition, *57*, 2017, pp. 1922–1937. DOI: 10.1080/10408398.2015.1038377.
13. Padayatty, S. J. – Katz, A. – Wang, Y. – Eck, P. – Kwon, O. – Lee, J. H. – Chen, S. – Corpe, C. – Dutta, A. – Dutta, S. K. – Levine, M.: Vitamin C as an antioxidant: evaluation of its role in disease prevention. Journal of the American College of Nutrition, *22*, 2003, pp. 18–35. DOI: 10.1080/07315724.2003.10719272.
14. Rosadas, M. – Silva, I. V. – Costa, J. B. – Ribeiro, V. P. – Oliveira, A. L.: Decellularized dermal matrices: unleashing the potential in tissue engineering and regenerative medicine. Frontiers in Material, *10*, 2024, article 1285948. DOI: 10.3389/fmats.2023.1285948.
15. Ahmed, M. – Verma, A. K. – Patel, R.: Collagen extraction and recent biological activities of collagen peptides derived from sea-food waste: a review. Sustainable Chemistry and Pharmacy, *18*, 2020, article 100315. DOI: 10.1016/j.scp.2020.100315.
16. Srikanya, A. – Dhanapal, K. – Sravani, K. – Madhavi, K. – Kumar, G. P.: A study on optimization of fish protein hydrolysate preparation by enzymatic hydrolysis from tilapia fish waste mince. International Journal of Current Microbiology and Applied Sciences, *6*, 2017, pp. 3220–3229. DOI: 10.20546/ijcmas.2017.612.375.
17. Arvanitoyannis, I. S. – Kassaveti, A.: Fish industry waste: treatments, environmental impacts, current and potential uses. International Journal of Food Science and Technology, *43*, 2008, pp. 726–745. DOI: 10.1111/j.1365-2621.2006.01513.x.
18. Hunter, D. J.: Pharmacologic therapy for osteoarthritis – the era of disease modification. Nature Reviews Rheumatology, *7*, 2011, pp. 13–22. DOI: 10.1038/nrrheum.2010.178.
19. Hong, H. – Fan, H. – Chalamaiah, M. – Wu, J.: Preparation of low-molecular-weight collagen hydrolysates (peptides): current progress, challenges, and future perspectives. Food Chemistry, *301*, 2019, article 125222, DOI: 10.1016/j.foodchem.2019.125222.
20. Luo, J. – Zhou, Z. – Yao, X. – Fu, Y.: Mineral-chelating peptides derived from fish collagen: Preparation, bioactivity and bioavailability, *134*, 2020, article 110209. DOI: 10.1016/j.lwt.2020.110209.
21. Bilek, S. E. – Bayram, S. K.: Fruit juice drink production containing hydrolyzed collagen. Journal of Functional Foods, *14*, 2015, pp. 562–569. DOI: 10.1016/j.jff.2015.02.024.
22. Cheng, J.-H. – Zhang, X.-Y. – Wang, Z. – Zhang, X. – Liu, S.-C. – Song, X.-Y. – Zhang, Y.-Z. – Ding, J.-M. – Chen, X.-L. – Xu, F.: Potential of thermolysin-like protease A69 in preparation of bovine collagen peptides with moisture-retention ability and antioxi-

dative activity. Marine Drugs, *19*, 2021, article 676. DOI: 10.3390/md19120676.
23. Je, H. J. – Han, Y. K. – Lee, H. G. – Bae, I. Y.: Anti-aging potential of fish collagen hydrolysates subjected to simulated gastrointestinal digestion and Caco-2 cell permeation. Journal of Applied Biological Chemistry, *62*, 2019, pp. 101–107. DOI: 10.3839/jabc.2019.015.
24. Igase, M. – Kohara, K. – Okada, Y. – Ochi, M. – Igase, K. – Inoue, N. – Kutsuna, T. – Miura, H. – Ohyagi, Y.: A double-blind, placebo-controlled, randomised clinical study of the effect of pork collagen peptide supplementation on atherosclerosis in healthy older individuals. Bioscience, Biotechnology, and Biochemistry, *82*, 2018, pp. 893–895. DOI: 10.1080/09168451.2018.1434406.
25. Rodrigues, D. B. – Marques, M. C. – Hacke, A. – Loubet Filho, P. S. – Cazarin, C. B. B. – Mariutti, L. R. B.: Trust your gut: bioavailability and bioaccessibility of dietary compounds. Current Research in Food Science, *5*, 2022, pp. 228–233. DOI: 10.1016/j.crfs.2022.01.002.
26. Dima, C. – Assadpour, E. – Dima, S. – Jafari, S. M.: Bioavailability and bioaccessibility of food bioactive compounds; overview and assessment by in vitro methods. Comprehensive Reviews in Food Science and Food Safety, *19*, 2020, pp. 2862–2884. DOI: 10.1111/1541-4337.12623.
27. Al Hajj, W. – Salla, M. – Krayem, M. – Khaled, S. – Hassan, H. F. – El Khatib, S.: Hydrolyzed collagen: Exploring its applications in the food and beverage industries and assessing its impact on human health – A comprehensive review. Heliyon, *10*, 2024, article e36433. DOI: 10.1016/j.heliyon.2024.e36433.
28. Jiang, J.-X. – Yu, S. – Huang, Q.-R. – Zhang, X.-L. – Zhang, C.-Q. – Zhou, J.-L. – Prawitt, J.: Collagen peptides improve knee osteoarthritis in elderly women: A 6-month randomized, double-blind, placebo-controlled study. Agro Food Industry Hi Tech, *25*, 2014, pp. 19–23. ISSN: 1722-6996.
29. Wang, L. – Wang, Q. – Qian, J. – Liang, Q. – Wang, Z. – Xu, J. – He, S. – Ma, H.: Bioavailability and bioavailable forms of collagen after oral administration to rats. Journal of Agricultural and Food Chemistry, *63*, 2015, pp. 3752–3756. DOI: 10.1021/jf5057502.
30. Ohara, H. – Matsumoto, H. – Ito, K. – Iwai, K. – Sato, K.: Comparison of quantity and structures of hydroxyproline-containing peptides in human blood after oral ingestion of gelatin hydrolysates from different sources. Journal of Agricultural and Food Chemistry, *55*, 2007, pp. 1532–1535. DOI: 10.1021/jf062834s.
31. Ercan, P. – El, S.: Koenzim Q10'un beslenme ve sağlık açısından önemi ve biyoyararlılığı. (Importance and bioavailability of coenzyme Q10 in terms of nutrition and health.) TÜBAV Bilim Dergisi, *3*, 2010, pp. 192–200. ISSN: 1308-4933. In Turkish.
32. Bondarenko, L. B.: Diabetes and collagen: interrelations. Avicenna Journal of Medical Biochemistry, *7*, 2019, pp. 64–71. DOI: 10.34172/ajmb.2019.12.
33. Ramadass, S. K. – Perumal, S. – Gopinath, A. – Nisal, A. – Subramanian, S. – Madhan, B.: Sol-gel assisted fabrication of collagen hydrolysate composite scaffold: A novel therapeutic alternative to the traditional collagen scaffold. ACS Applied Materials and Interfaces, *6*, 2014, pp. 15015–15025. DOI: 10.1021/am502948g.
34. Chen, L. – Shen, X. – Xia, G.: Effect of molecular weight of tilapia (*Oreochromis niloticus*) skin collagen peptide fractions on zinc-chelating capacity and bioaccessibility of the zinc-peptide fractions complexes in vitro digestion. Applied Sciences, *10*, 2020, article 2041. DOI: 10.3390/app10062041.
35. Choi, F. D. – Sung, C. T. – Juhasz, M. L. W. – Mesinkovska, N. A.: Oral collagen supplementation: A systematic review of dermatological applications. Journal of Drugs in Dermatology, *18*, 2019, pp. 9–16. ISSN: 1545-9616. <https://jddonline.com/articles/oral-collagen-supplementation-a-systematic-review-of-dermatological-applications-S1545961619P0009X/>
36. Gómez-Guillén, M. C. – Giménez, B. – López-Caballero, M. E. – Montero, M. P.: Functional and bioactive properties of collagen and gelatin from alternative sources: A review. Food Hydrocolloids, *25*, 2011, pp. 1813–1827. DOI: 10.1016/j.foodhyd.2011.02.007.
37. Wang, L. – Jiang, Y. – Wang, X. – Zhou, J. – Cui, H. – Xu, W. – He, Y. – Ma, H. – Gao, R.: Effect of oral administration of collagen hydrolysates from Nile tilapia on the chronologically aged skin. Journal of Functional Foods, *44*, 2018, pp. 112–117. DOI: 10.1016/j.jff.2018.03.005.
38. Musayeva, F. – Özcan, S. – Kaynak, M. S.: A review on collagen as a food supplement. Journal of Pharmaceutical Technology, *3*, 2022, pp. 7–29. DOI: 10.37662/jpt.2022.1012432.
39. Campos, L. D. – Santos Junior, V. A. – Pimentel, J. D. – Carregã, G. L. F. – Cazarin, C. B. B.: Collagen supplementation in skin and orthopedic diseases: A review of the literature. Heliyon, *9*, 2023, article e14961. DOI: 10.1016/j.heliyon.2023.e14961.
40. Varani, J. – Dame, M. K. – Rittie, L. – Fligiel, S. E.G. – Kang, S. – Fisher, G. J. – Voorhees, J. J.: Decreased collagen production in chronologically aged skin: roles of age-dependent alteration in fibroblast function and defective mechanical stimulation. American Journal of Pathology, *168*, 2006, pp. 1861–1868. DOI: 10.2353/ajpath.2006.051302.
41. Wang, X. – Ghasri, P. – Amir, M. – Hwang, B. – Hou, Y. – Khilili, M. – Lin, A. – Keene, D. – Uitto, J. – Woodley, D. T – Chen, M.: Topical application of recombinant Type VII collagen incorporates into the dermal-epidermal junction and promotes wound closure. Molecular Therapy, *21*, 2013, pp. 1335–1341. DOI: 10.1038/mt.2013.87.
42. Evans, M. – Lewis, E. D. – Zakaria, N. – Pelipyagina, T. – Guthrie, N.: A randomized, triple-blind, placebo-controlled, parallel study to evaluate the efficacy of a freshwater marine collagen on skin wrinkles and elasticity. Journal of Cosmetic Dermatology, *20*, 2021, pp. 825–834. DOI: 10.1111/jocd.13676.
43. Barati, M. – Jabbari, M. – Navekar, R. – Farah-

mand, F. – Zeinalian, R. – Salehi-Sahlabadi, A. – Abbaszadeh, N. – Mokari-Yamchi, A. – Davoodi, S. H.: Collagen supplementation for skin health: A mechanistic systematic review. Journal of Cosmetic Dermatology, *19*, 2020, pp. 2820–2829. DOI: 10.1111/jocd.13435.

44. Reilly, D. M. – Lozano, J.: Skin collagen through the lifestages: importance for skin health and beauty. Plastic and Aesthetic Research, *8*, 2021, article 2. DOI: 10.20517/2347-9264.2020.153.
45. Pu, S.-Y. – Huang, Y.-L. – Pu, C.-M. – Kang, Y.-N. – Hoang, K. D. – Chen, K.-H. – Chen, C.: Effects of oral collagen for skin anti-aging: A systematic review and meta-analysis. Nutrients, *15*, 2023, article 2080. DOI: 10.3390/nu15092080.
46. D'hondt, S. – Guillemyn, B. – Syx, D. – Symoens, S. – De Rycke, R. – Vanhoutte, L. – Toussaint, W. – Lambrecht, B. N. – De Paepe, A. – Keene, D. R. – Ishikawa, Y. – Bächinger, H. P. – Janssens, S. – Bertrand, M. J. M. – Malfait, F.: Type III collagen affects dermal and vascular collagen fibrillogenesis and tissue integrity in a mutant *Col3a1* transgenic mouse model. Matrix Biology, *70*, 2018, pp. 72–83. DOI: 10.1016/j.matbio.2018.03.008.
47. Abreu-Velez, A. M. – Howard, M. S.: Collagen IV in normal skin and in pathological processes. North American Journal of Medical Sciences, *4*, 2012, pp. 1–8. DOI: 10.4103/1947-2714.92892.
48. Mak, K. M. – Png, C. Y. M. – Lee, D. J.: Type V collagen in health, disease, and fibrosis. The Anatomical Record, *299*, 2016, pp. 613–629. DOI: 10.1002/ar.23330.
49. Martin, P. – Teodoro, W. R. – Velosa, A. P. P. – de Morais, J. – Carrasco, S. – Christmann, R. B. – Goldenstein-Schainberg, C. – Parra, E. R. – Katayama, M. L. H. – Sotto, M. N. – Capelozzi, V. L. – Yoshinari, N. H.: Abnormal collagen V deposition in dermis correlates with skin thickening and disease activity in systemic sclerosis. Autoimmunity Reviews, *11*, 2012, pp. 827–835. DOI: 10.1016/j.autrev.2012.02.017.
50. Theocharidis, G. – Drymoussi, Z. – Kao, A. P. – Barber, A. H. – Lee, D. A. – Braun, K. M. – Connelly, J. T.: Type VI collagen regulates dermal matrix assembly and fibroblast motility. Journal of Investigative Dermatology, *136*, 2016, pp. 74–83. DOI: 10.1038/jid.2015.352.
51. Schönborn, K. – Willenborg, S. – Schulz, J.-N. – Imhof, T. – Eming, S. A. – Quondamatteo, F. – Brinckmann, J. – Niehoff, A. – Paulsson, M. – Koch, M. – Eckes, B. – Krieg, T.: Role of collagen XII in skin homeostasis and repair. Matrix Biology, *94*, 2020, pp. 57–76. DOI: 10.1016/j.matbio.2020.08.002.
52. Hägg, P. – Väisänen, T. – Tuomisto, A. – Rehn, M. – Tu, H. – Huhtala, P. – Eskelinen, S. – Pihlajaniemi, T.: Type XIII collagen: a novel cell adhesion component present in a range of cell-matrix adhesions and in the intercalated discs between cardiac muscle cells. Matrix Biology, *19*, 2001, pp. 727–742. DOI: 10.1016/s0945-053x(00)00119-0.
53. Calvo, A. C. – Moreno, L. – Moreno, L. – Toivonen, J. M. – Manzano, R. – Molina, N. – de la Torre, M. – López, T. – Miana-Mena, F. J. – Muñoz, M. J. – Zaragoza, P. – Larrodé, P. – García-Redondo, A. – Osta, R.: Type XIX collagen: a promising biomarker from the basement membranes. Neural Regeneration Research, *15*, 2019, pp. 988–989. DOI: 10.4103/1673-5374.270299.
54. de Miranda, R. B. – Weimer, P. – Rossi, R. C.: Effects of hydrolyzed collagen supplementation on skin aging: a systematic review and meta-analysis. International Journal of Dermatology, *60*, 2021, pp. 1449–1461. DOI: 10.1111/ijd.15518.
55. Bretaud, S. – Guillon, E. – Karppinen, S. M. – Pihlajaniemi, T. – Ruggiero, F.: Collagen XV, a multifaceted multiplexin present across tissues and species. Matrix Biology Plus, *6–7*, 2020, article 100023. DOI: 10.1016/j.mbplus.2020.100023.
56. Grässel, S. – Bauer, R. J.: Collagen XVI in health and disease. Matrix Biology, *32*, 2013, pp. 64–73. DOI: 10.1016/j.matbio.2012.11.001.
57. Nishie, W.: Collagen XVII processing and blistering skin diseases. Acta Dermato-Venereologica, *100*, 2020, pp. 102–107. DOI: 10.2340/00015555-3399.
58. Koch, M. – Schulze, J. – Hansen, U. – Ashwodt, T. – Keene, D. R. – Brunken, W. J. – Burgeson, R. E. – Bruckner, P. – Bruckner-Tuderman, L.: A novel marker of tissue junctions, collagen XXII. Journal of Biological Chemistry, *279*, 2004, pp. 22514–22521. DOI: 10.1074/jbc.M400536200.
59. Chopra, S. – Zeitvogel, J. – Traidl, S. – Klug, I. – Rodriguez, E. – Harder, I. – Lieb, W. – Weidinger, S. – Schulz, T. F. – Sodeik, B. –Döhner, K. – Roesner, L. M. – Werfel, T.: Collagen XXIII (COL23A1): A novel risk factor for eczema herpeticum. The Journal of Allergy and Clinical Immunology, *156*, 2025, pp 1247–1259. DOI: 10.1016/j.jaci.2025.06.011.
60. Wang, H.: A review of the effects of collagen treatment in clinical studies. Polymers, *13*, 2021, article 3868. DOI: 10.3390/polym13223868.
61. da Silva-Bertani, D. C. T. – Vileigas, D. F. – Mota, G. A. F. – de Souza, S. L. B. – De Tomasi, L. C. – de Campos, D. H. S. – Deus, A. F. – Freire, P. P. – Barnabe Alves, C. A. – Padovani, C. R. – Cicogna, A. C.: A redução do colágeno Tipo I está associada ao aumento da atividade da metaloproteinase-2 e da expressão proteica de leptina no miocárdio de ratos obesos. (Decreased collagen Type I is associated with increased metalloproteinase-2 activity and leptin protein expression in the myocardium of obese rats.) Arquivos Brasileiros de Cardiologia, *115*, 2020, pp. 61–70. DOI: 10.36660/abc.20180143. In Portuguese.
62. López-Yoldi, M. – Riezu-Boj, J. I. – Abete, I. – Ibero-Baraibar, I. – Aranaz, P. – González-Salazar, I. – Izco, J. M. – Recalde, J. I. – González-Navarro, C. J. – Milagro, F. I. – Zulet, M. A.: Anti-obesity effects of a collagen with low digestibility and high swelling capacity: a human randomized control trial. Nutrients, *16*, 2024, article 3550, DOI: 10.3390/nu16203550.
63. Baek, G. H. – Yoo, K. M. – Kim, S.-Y. – Lee, D. H. – Chung, H. – Jung, S.-C. – Park, S.-K. – Kim, J.-S.:

Collagen peptide exerts an anti-obesity effect by influencing the firmicutes/bacteroidetes ratio in the gut. Nutrients, *15*, 2023, article 2610. DOI: 10.3390/nu15112610.

64. Pasarica, M. – Gowronska-Kozak, B. – Burk, D. – Remedios, I. – Hymel, D. – Gimble, J. M. – Ravussin, E. – Bray, G. A. – Smith, S. R.: Adipose tissue collagen VI in obesity. Journal of Clinical Endocrinology and Metabolism, *94*, 2009, pp. 5155–5162. DOI: 10.1210/jc.2009-0947.
65. Wong, R. P. M. – Zhou, Z. K. – Strappe, P. M.: The anti-obesogenic and anti-diabetic properties of marine collagen peptides. Frontiers in Food Science and Technology, *3*, 2024, article 1270392. DOI: 10.3389/frfst.2023.1270392.
66. Devasia, S. – Kumar, S. – Stephena, P. S. – Inoue, N. – Sugihara, F. – Suzuki, K.: Double blind, randomized clinical study to evaluate efficacy of collagen peptide as add on nutritional supplement in type 2 diabetes. Journal of Clinical Nutrition and Food Science, 1, 2018, pp. 6–11. ISSN: 2641-2292.
67. Zhu, C.F. – Li, G. – Peng, H. – Zhang, F. – Chen, Y. – Li, Y.: Treatment with marine collagen peptides modulates glucose and lipid metabolism in Chinese patients with type 2 diabetes mellitus. Applied Physiology, Nutrition, and Metabolism, *35*, 2010, pp 797–804. DOI: 10.1139/H10-075.
68. Losada-Barreiro, S. – Sezgin-Bayindir, Z. – Paiva-Martins, F. – Bravo-Díaz, C.: Biochemistry of antioxidants: mechanisms and pharmaceutical applications. Biomedicines, *10*, 2022, article 3051. DOI: 10.3390/biomedicines10123051.
69. Wang, B. – Wang, Y.-M. – Chi, C.-F. – Luo, H.-Y. – Deng, S.-G. – Ma, J.-Y.: Isolation and characterization of collagen and antioxidant collagen peptides from scales of croceine croaker (*Pseudosciaena crocea*). Marine Drugs, *11*, 2013, pp. 4641–4661. DOI: 10.3390/md11114641.
70. Stewart, J. A. – West, T. A. – Lucchesi, P. A.: Nitric oxide-induced collagen IV expression and angiogenesis: FAK or fiction? Focus on "Collagen IV contributes to nitric oxide-induced angiogenesis of lung endothelial cells". American Journal of Physiology-Cell Physiology, *300*, 2011, pp. C968–C969. DOI: 10.1152/ajpcell.00059.2011.
71. Xia, G. – Zhang, X. – Dong, Z. – Shen, X.: Comparative study on the antioxidant activity of peptides from pearl oyster (*Pinctada martensii*) mantle type V collagen and tilapia (*Oreochromis niloticus*) scale type I collagen. Journal of Ocean University of China, *16*, 2017, pp. 1175–1182. DOI: 10.1007/s11802-017-3323-7.
72. Cescon, M. – Gattazzo, F. – Chen, P. – Bonaldo, P.: Collagen VI at a glance. Journal of Cell Science, *128*, 2015, pp. 3525–3531. DOI: 10.1242/jcs.169748.
73. Sun, M. – Luo, E. Y. – Adams, S. M. – Adams, T. – Ye, Y. – Shetye, S. S. – Soslowsky, L. J. – Birk, D. E.: Collagen XI regulates the acquisition of collagen fibril structure, organization and functional properties in tendon. Matrix Biology, *94*, 2020, pp. 77–94. DOI: 10.1016/j.matbio.2020.09.001.
74. Xin, X.-Y. – Zhou, J. – Liu, G.-G. – Zhang, M.-Y. – Li, X.-Z. – Wang, Y.: Anti-inflammatory activity of collagen peptide in vitro and its effect on improving ulcerative colitis. npj Science of Food, *9*, 2025, article 1. DOI: 10.1038/s41538-024-00367-7.
75. Graham, M. F. – Drucker, D. E. M. – Diegelmann, R. F. – Elson, C. O.: Collagen synthesis by human intestinal smooth muscle cells in culture. Gastroenterology, *92*, 1987, pp. 400–405. DOI: 10.1016/0016-5085(87)90134-X.
76. Abrahams, M. – O'Grady, R. – Prawitt, J.: Effect of a daily collagen peptide supplement on digestive symptoms in healthy women: 2-phase mixed methods study. JMIR Formative Research, *6*, 2022, article e36339. DOI: 10.2196/36339.
77. Watanabe, M. – Natsuga, K. – Nishie, W. – Kobayashi, Y. – Donati, G. – Suzuki, S. – Fujimura, Y. – Tsukiyama, T. – Ujie, H. – Shinkuma, S. – Nakamura, H. – Murakami, M. – Ozaki, M. – Nagayama, M. – Watt, F. M. – Shimizu, H.: Type XVII collagen coordinates proliferation in the interfollicular epidermis. eLife, *6*, 2017, article e26635. DOI: 10.7554/eLife.26635.
78. Song, Y. – Overmass, M. – Fan, J. – Hodge, C. – Sutton, G. – Lovicu, F. J. – You, J.: Application of collagen I and IV in bioengineering transparent ocular tissues. Frontiers in Surgery, *8*, 2021, article 639500. DOI: 10.3389/fsurg.2021.639500.
79. Michelacci, Y. M.: Collagens and proteoglycans of the corneal extracellular matrix. Brazilian Journal of Medical and Biological Research, *36*, 2003, pp. 1037–1046. DOI: 10.1590/S0100-879X2003000800009.

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