Review Article

Collagen: An Overview from Past to Future Applications

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Abstract

Collagen, a structural protein, prevalent in animals, especially in skin, bones, and joints, responsible for providing fundamental structural support, is being used extensively in cosmetics. Mammalian and fish skin are the most common sources of collagen. Collagen's unique qualities, such as its role as a natural humectant and moisturizer for the skin, have piqued the curiosity of both academics and the cosmetic industry. In this review study, collagen biosynthesis, collagen sources used in the cosmetic industry, and collagen's function in cosmetics are discussed along with future aspects of collagen-based materials in cosmetics.

Keywords: *Animal source, Collagen, Cosmetics, Cosmetic industry, Synthetic source*

Introduction

From the moment a newborn is born, beauty has been a defining characteristic of society and its problems concerning physical qualities (Sionkowska et al., 2020). One set of standards that illustrates this is the one known as various types of aesthetic marks, such as tattooed symbols; considered to have glowing skin and origins from Colombia, western civilizations are known for their curvaceous, slim forms. However, in the modern era, beauty ideals have adapted to the desire of the customer; demanding younger and healthier skin (Avila Rodríguez et al., 2018; Ressini, 2015). A customer is faced with various beauty products and methods such as skin peelings, facial creams, galvanic current, and oral supplements containing hydrolysate biomolecules that can improve skin conditions (Ganceviciene et al., 2012). All of which aim to enhance and or replace collagen production of the skin.

Collagen, one of the most abundant proteins in human, forms a supportive net over cellular structures to stabilize and strengthen the body tissues. However, over time fiber deteriorates resulting in the development of unfavorable wrinkles (León-López et al., 2019; Ricard-Blum, 2011). According to studies, impaired fibers can be replaced by the consumption of hydrolyzed proteins (Bhagwat & Dandge, 2016; León-López et al., 2019). In another study, it was determined that these proteins were also responsible to amplify the appearance of tissues. Thus, the cosmetic industry has been involved in producing numerous products with these biomolecules. For an injured skin, the antihypertensive and lipid-lowering activity, antioxidant characteristics, and reparative capabilities of collagen hydrolysate has already been established (Avila Rodríguez et al., 2018; Deng et al., 2020; Ding et al., 2019; Du et al., 2021). Collagen hydrolysate has a dual function; firstly, producing elastin and collagen and secondly, it acts as a binding receptor for fibroblasts which results in hyaluronic acid production (Fan et al., 2013; Sibilla et al., 2015). Different studies conducted to authenticate the most suitable form of collagen for cosmetic use, are summarized in this review (Gopalakrishnan et al., 2021; Kumar et al., 2014; Park & Lakes, 2007).

Biology of Collagen

Collagen, a family of most prevalent human structural proteins, include all the proteins with a triple-helix polypeptide chain structure (Figure 1), out of which there have been 26 diversities so far (Bailey & Paul, 1998; Ricard-Blum, 2011). The three polypeptide fibrils can range in size from 10-500 nm in diameter, 285 kDa or less in molecular weight, and 1400 amino acids in length, with glycine as their distinctive amino acid every three residues.

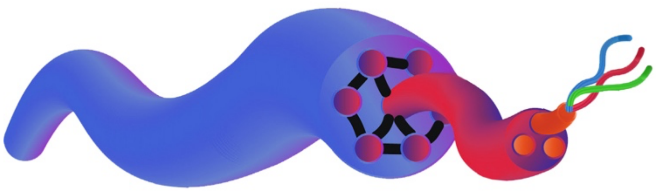

Figure 1: The structure of collagen with its triple helix polypeptides. This is able to give the collagen its tensile and elastic nature; with each of the triple helix having a varying width or diameter.

In tissues, collagen fibers, frequently white and opaque have high tensile strength and made of low extensibility viscoelastic material. Mammalian fibrils have shrinkage temperature (Ts) ranging from 62°C to 65°C whereas in fishes this range is 38°C to 54°C. The isoelectric point (PI) of collagen is approximately pH 5.8. The denaturation temperature (Tm), however, is between 25°C and 30°C.

Collagen has low immunogenicity, where the only region to activate an immune response is the helical area and the telopeptide region. This decreases the probability that any foreign body will not abide by it. Despite the minimal antigenicity of this molecule, it can be altered to block the specific immune response. Alternatively, the banded structure can be denatured via heat or chemical treatment, with the nonhelical region being degraded by proteinases or cross-linked.

Applications and variations of collagen

Based on the structure, chain bonding and location in the body, 26 different kinds of collagen proteins are grouped in eight (Song et al., 2019). The basement membrane, microfibrillar, anchoring fibrils, hexagonal network-forming, fibril-associated collagens with interrupted triple helix [FACIT], transmembrane, and multiplexins are among these classifications (Bailey & Paul, 1998; Ricard-Blum, 2011; Song et al., 2019). The applications and used of collagens are summarized in Table 1.

Collagen based compounds have been used in multiple applications, such as glass and bead anchors for cell culture cells, (Bax et al., 2019; Ramshaw et al., 2001), as a biomaterial for vascular prosthesis, (Ramshaw et al., 2001; Stang et al., 2009), as subcutaneous injection microparticles, (Sorushanova et al., 2019), for tissue scaffold regeneration, (Rodrigues et al., 2021; Silvipriya et al., 2015; Tian et al., 2022), as a feedstock for gelatin, glues, and cosmetics, (Avila Rodríguez et al., 2018; Sionkowska et al., 2020), and as for the creation of oral administration hydrolysates,(León-López et al., 2019). The most common use of collagen for remedial purpose is Fibril-forming types. Collagen serves as a preferred feedstock for cosmetics businesses, this is because of its wide accessibility, biocompatibility, and biodegradability (Gopalakrishnan et al., 2021; Prockop et al., 1976). Aging affects the dermis which constitutes types I and II collagen, making up 90% of the layer. Targeting these collagens is an ideal approach for anti-aging products. Collagens used for medical applications will not be covered because the current review's focus is on aesthetic uses of collagen, rather than the medicinal benefits or impacts. (Samad & Sikarwar, 2016; Sorushanova et al., 2019)-

Table 1: Applications and uses of different kinds of collagens.

Family	Collagen Type	Application	Reference
Basement membrane	IV	Diabetic nephropathy	(Dehdashtian et al., 2020; Miner, 2020)
Microfibrils	VI	Hemostats	(Kong et al., 2021)
Anchoring fibrils	VII	Dystrophic epidermolysis bullosa	(Uitto, 2019)
FACIT	IX	Co-distributes in cartilage	(Blease, 2021)
	XIV	Fibril diameter regulator	(Sadri et al., 2022)
	XX	Function is unknown	[N/A]
	XXI	Matrix assembly of vascular network	(Papanicolaou et al., 2022)
Transmembrane	XVII	Adhesion of epithelial cell and teeth formation	(Fischer et al., 2022; Ikeda et al., 2022)
Multiplexins	XV	Form a bridge in fibrils containing collagen I & III	(Bretaud et al., 2020)
	XVIII	Closure of neural tube and retinal structure	(Bretaud et al., 2020; Schroeder et al., 2020)

Natural sources

Collagen is mostly acquired from bovine, porcine, human collagen, scales, and skin of fish; however, animal and vegetable sources are both used to obtain collagen as well (Figure 2) (Jridi et al., 2015; Wei et al., 2019). To treat extra-oral wounds on burn victims, bovine collagen is the regular choice, due to its biocompatibility. Whereas porcine collagen matrices are best suited for soft tissue transplanting. Animal sources on land include chicken, kangaroo tail, equine tendon, alligator skin, rat tail tendons, duck feet, bird's feet, frog skin, sheepskin, and feet. Types I and II are derived from horse skin, flexors, and cartilage. Collagen types I through V are derived from the chicken neck. The sternal cartilage of chicken embryos contains type IX, as do types I, III and IV from muscle tissue and skin. (Silvipriya et al., 2015; Sorushanova et al., 2019).

Synthetic sources

Remodeling tissues and blood clotting are frequently supported by collagen. Collagen has also made its use in therapy as many therapeutic applications use natural animal-sourced collagen. However, these collagens have several side effects, from inflammation to even the potential of disease transfection (Williams, 2014). Synthetic-sourced products such as collagen mimetic peptide (KOD) brand are able to counter these immunological side effects. The KOD is a 36 amino acids synthetic protein, that is able to resemble natural protein, by self-assembling it into triple-helix nanofibers and hydrogels. Based on the amino acid sequence (P-**K**-G) (P-**O**-G) (**D**-O-G) of the synthetic peptide, it was named KOD (Kumar et al., 2014).

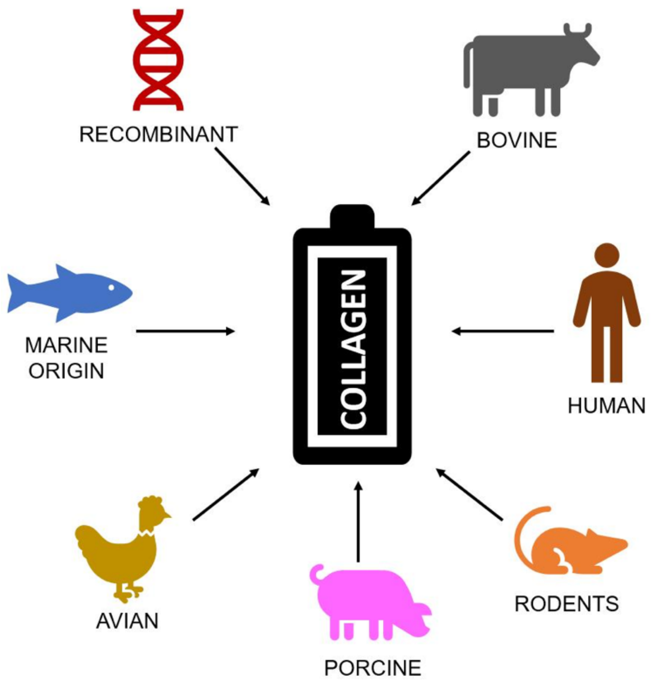

Figure 2: Common natural sources of collagen, mostly obtained from animals.

The review also enlists the hypothetical analogs for natural collagen in procoagulatory fractions, protein folding, and structures that might encourage platelet adhesion and activation (Karsdal, 2019). The use of recombinant technology to create a different artificial source of collagen that produces high-quality, animal-derived collagen-free products, has been applied. Forming these recombinant collagens, mammalian cells were cultured in various other cell cultures, which results in the formation of a clotting agent as it is able to subdue bleeding. Transgenic crop seeds, such as maize, barley and tobacco, are often applied in bone treatments and application, nonetheless, recent studies indicate that by using these transgenic crops the production of recombinant plant collagen is possible. Animal collagen may be the optimal standard in therapeutic and research scenarios, but human collagens are far more effective. The reason why human collagen is not commonly used is because there are numerous shortcomings in the technology of obtaining it.

Collagen sourced from marine animals are relatively risk-free and offer a higher absorption capability, lower molecular weight, lessened inflammatory response and much more. Several marine species are used, where specific organs and tissues of these marine lives are taken to gain the molecule. The different species and their locations on how to secure natural collagen are summarized in Table 1 (Gallo et al., 2022; Geahchan et al., 2022; Niculescu et al., 2019; Sorrentino et al., 2022). Although marine-sourced collagen output a higher yield, and is considered as the finer alternative, it falls short in thermal stability (Sorrentino et al., 2022).

Cosmetics and collagen

Due to its biological functions, collagen has a significant potential for use in cosmetics, medicine, and healthcare industry (Niculescu et al., 2019; Sorrentino et al., 2022). Collagen types I, II, and III make up the majority of tissue structural fibrils; the other remaining types of collagens are responsible for fibril interactions. The other varieties of collagen have not been developed for cosmetic purposes. Due to its high biocompatibility and fibril-forming, type I collagen is the used in cosmetic product manufacturing (Sorrentino et al., 2022).

Studies reveal, collagen forming fibrils are often used in many biomaterials that are necessary for tissue engineering. Type I collagen is also common in ophthalmology, dental composites, collagen shields and other applications. Studies have also shown how the molecule is able to synthesize enzymes and function as a solid support microcarrier, all of which are known for non-cosmetic purposes. Researchers and developers alike are working on alternative sources of collagen as bovine collagen causes protein misfolding and potential allergenicity. Marine collagen, as mentioned above, is a great source, since it is economically reasonable and avoids bovine spongiform encephalopathy (BSE) (Stang et al., 2009). Given its low immunogenicity, it has made a lot of progress in the medical field to treat skin grafts and wound dressings (Parenteau-Bareil et al., 2010; Sionkowska, 2021; Sionkowska et al., 2017).

Moreover, it is able to prevent trans-epidermal water loss and protect the skin from corrosive factors (Heath et al., 2022; Sharma et al., 2022). The peptide occlusion prevents skin damage brought due to physical stress (Heath et al., 2022). Another study showed that tissue regeneration and healing wounds are enhanced and boosted by collagen (Geahchan et al., 2022). The cosmetic potential of collagen is shown in Figure 3. even though bovine collagen may lead to BSE, it is more common in the industries.

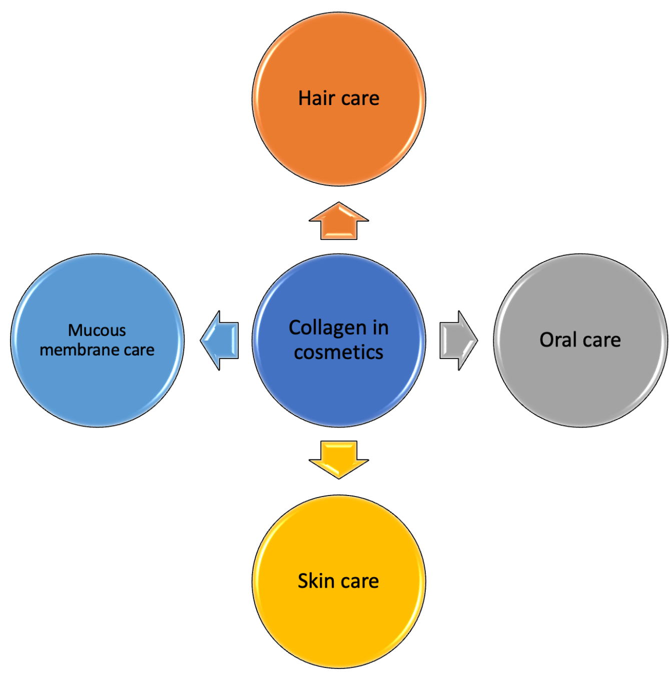

Figure 3: How collagen is made used in the cosmetic industry with its varying degree of applications in different areas of cosmetics alone.

Conclusions and future perspectives

The most abundantly present protein in animals is collagen, with different varieties, with varying functions and locations in the human body, collagens are distinguishable by their structural features. Collagens are widely used in regenerative methods and biological techniques such as tissue engineering, due to their low immunogenicity and high biocompatibility.

However, infections can be caused by the protein, and therefore, numerous studies are being carried out to investigate the cause. There still remain many different protein sources that remain unexamined which may serve to be crucial in the near future. Recently, an analysis asserted that the global collagen peaked a USD 3.71 billion which is expected to increase in the following years, the study predicts that by 2025 the value will increase to USD 6.63 billion. This price rise is due to the customer demand for goods, which is highly related to the growing population. The global tissue-engineered collagen biomaterial market is anticipated to expand at a healthy CAGR (compound annual growth rate) of 10.4% by 2025.

The use of collagen has become quite popular and common in a multitude of different areas, however with so many types of collagens it is important to be noted, the products using collagen, and which type is constituted in that product. Collagen is an integral part of human biochemistry, another issue that arises is how was this molecule obtained. Collagen is sourced from various natural sources as well as synthetic collagens, which has affected the global collagen market. We expect collagen research and novel discoveries will increase as will its uses in cosmetic and other industries will.

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Author Contributions

FZ and MW designed the study. FZ supervised and wrote the article. MW analyzed the data and draw figures. AMS also participated in the article write-up and revised the manuscript. All authors reviewed the article and approved the final version.

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