ISSN: 2835-7329

Case Report

Dermatology Journal of Cosmetic and Laser Therapy

The Complex Structure of Collagen in the Skin

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Submitted: 2024, Jan 31; **Accepted:** 2024, Feb 14; **Published:** 2024, Feb 29

Citation: Grosan, E. D., Butnariu, M. (2024). The Complex Structure of Collagen in the Skin. *Dearma J Cosmetic Laser Therapy, 3*(1), 01-04.

Abstract

Collagen, ubiquitous component and the most abundant protein in the human body is a biopolymer with an open internal structure, it contains a large number of binding sites available for interaction with various biologically active substances: hormones, enzymes, peptides, etc. Their accessibility to the collagen binding sites is facilitated by its extraordinary hydrophilic capacity. It is also involved, directly or indirectly, in the attachment and differentiation of cells as well as in immunological processes, so that, apart from its structural role, collagen participates in complex processes such as: development, morphogenesis and pathological processes. The variety of collagen types is not, however, the exclusive result of structural differences at the molecular level, it also appears as a result of cellular activity in the process of assembling molecules into supramolecular structures. Thanks to its moisturizing properties, collagen helps prevent and reduce wrinkles, especially the first expression wrinkles. In addition, it contributes to the reduction of pigment spots, improving blood circulation at the same time.

Keywords: Biopolymer; Collagen; Structural Protein, Collagen Structure, Skin.

1. Introduction

Collagen is a major structural protein that the body synthesizes naturally. It is one of the most abundant proteins in the body, representing a third of the body's protein composition. The name comes from the Greek word "kolla" which means glue [1]. Strong collagen fibres help make bones strong, allow skin and tendons to stretch, and help skin recover from injury. It is a major component of bones, skin, muscles, tendons and ligaments. It is also found in many other parts of the body, including the blood vessels, cornea and teeth [2]. Being the main component of the connective tissue, collagen is the most widespread protein in the human body, representing approximately 25% to 35% of the total amount of proteins [3].

2. Chemical Composition and Supramolecular Structure of Collagen

Collagen is the fibrillar, extracellular protein, made up of a triple helix, each strand of it, containing 1000 amino acid (AA) residues. The AA sequence is regular, in the sense that almost every third amino acid is represented by glycine (Gly). The sequence Gly-Pro-Hyp was repeated regularly. Collagen is a natural polymer formed by the polymerization of 20 AAs, arranged in characteristic sequences for the collagen molecule, which has a unique triple helix conformational structure. Thus, in the composition of collagen, the amino acid Gly represents approximately 33%, and the AAs proline (Pro) and hydroxyproline (Hyp) represent; about 22% [4].

The sequence of AAs of the protein is called the primary structure. This structure determines how the protein is packed: in a-helix, b-stratified or b-twisted. Each AA, with its special structure, shape and chemical functions, contributes to the type of packaging. In the last 30 years, the studies carried out on synthetic polypeptides with various sequences allowed the prediction of the structural conformation, depending on the AA sequence [3]. Thus, the complete sequence of the constituent AAs in the a chains of type I collagen was established. In this terminology, "a" denotes a collagen chain produced by a single gene [5].

The type of collagen, designated by a Roman numeral I, II, III, etc., refers to a single whole molecule with its chains of type a. It has been proposed to classify the structural ordering of proteins, in order to understand the complicated structure of collagen, as follows:

- the primary structure represents the chaining of AAs in the polypeptide chains of the collagen macromolecule;
- secondary structure – refers to a single polypeptide chain (minor helix oriented from left to right) from the triple helix of the collagen molecule;
- tertiary structure – is represented by the collagen molecule made up of three chains twisted together from right to left, around a common axis, thus creating a triple helix or the major helix;
- quaternary structure - represents the way of aggregation of collagen macromolecules to form fibrils, fibers and collagenous tissue [6].

Collagen is essentially a polytripeptide in the α-helix chain, having Gly in every third position. The analysis of the native collagen sequences highlighted the fact that the polypeptide chains can be similar to a terpolymer for which the following formula (1) is valid:

$H_2N – NC1 – (Gly – X – Y)n – NC_2 – COOH$

(1)

where: NC1 and NC2 are telopeptides, X is most often Pro; Y Hyp and n = 100 – 400.

From a compositional point of view, the main features of collagens are: the considerable proportion of Gly (30-40%) and the imino acids Pro and Hyp (25-35%); the appearance of the hydroxylated forms of Pro and lysine (Lys) -Hyp and Hyl (hydroxylysine); variable glycosylation of certain Hyl residues with glucose (Glu) and galactose (Gal) in the Hyl-Gal and Hyl-Gal-Glu variants [7]. The polypeptide chains that make up the main types of collagen have a crystalline α-helical conformation, located in the central area of the macromolecular chain. This structure with water bonds according to the arrangement/ secondary architecture, explains the role played by Hyp in the collagen structure. The water molecule can be linked through a hydrogen bond with the -OH group of Hyp. Only one of the protons of the water molecule acts as a donor for a hydrogen bond to a carbonyl oxygen, while the water oxygen is involved in a hydrogen bond with the -NH group [8]. That's why the second proton of water is free and it can bind through a hydrogen bond with an oxygen atom of Hyp. In this way, Hyp in collagen can serve as a hydrogen bond receptor, stabilizing the structure [9].

The collagen molecule is the conformational element that builds the superstructure of the different genetic types of collagen in the connective tissue, through the process of extracellular aggregation. Triple helix domains vary in size from 300 to 1000 AA residues. The longest triple helices, containing 1000 AAs on each α-helix, form the isotypes of fibrillar collagen, by their lateral aggregation and offset by a quarter of their length. This alignment of the collagen molecules gives fibrillar collagen a unique axial periodicity of 67 nm, observed under the electron microscope. The length of the fibrillar collagen molecule is 4.4 times the length of the axial periodicity (approx. 300 nm), indicating an overlap of the molecules at the ends of 25 nm. At both ends of the molecule are extensions of non-helical peptides: NH2 - terminal and COOH – terminal [10]. The formation and growth of collagen fibrils remains one of the most important biological problems related to collagen, with implications in the connective tissue formation processes.

3. Properties of Collagen

Collagen in all its characteristic forms is presented as a polymer that is individualized by accentuated hydrophilicity, variable ionic character and diverse functionality, being able to be involved in a large number of interaction systems with other micro or macromolecular components [11].The stability of the collagen structure is ensured by the multitude of stable bonds: covalent, electrovalent, hydrogen bonds and hydrophobic bonds. In its natural state, the skin contains 75-80% water, this separating the structural elements, mainly through reversible hydrogen bonds formed at the level of the a-helix and triple helix (intra and intermolecular). The hydrogen bond of the H•••OH type formed by a water molecule with another water molecule or directly to the reactive groups in the polypeptide chain stabilizes the structure of the collagen molecule, and at the level of fibrils and tissue fibers it mediates reversible reactions in the "aqueous" environment biological".

The mechanical, physico-chemical and chemical behavior of collagen is due to the duality of its structure, crystalline and amorphous, presenting both the properties of crystals and gels. The relative stability of collagen (dimensional, biological, chemical, etc.) is attributed to its crystalline properties, and the classical ones of flexibility, reactivity, etc. properties of polar amorphous particles. Due to the coexistence of both structures, animal skin can be tanned and a wide range of finished leather varieties can be obtained. The properties of fibrillar colloid collagen and its specific histological structure compete with the specific characteristics of tanned skin.

Therefore, collagen can exist both in the gel state and in the soil state. In a dissolved state, it does not diffuse through semipermeable membranes, because the particles are smaller than 1 mm, so they have the dimensions of the colloidal state. Colloidal particles can be formed from macromolecules or collagen molecular aggregates, the initial phase in the formation of insoluble collagen.

The colloidal state of collagen in solution gives it all the physico-chemical properties characteristic of colloidal systems: low osmotic pressure, low diffusion capacity, tensioactivity, etc. [12]. There is an uneven distribution of diffusible ions at the moment of equilibrium. The insoluble collagen, fulfilling the role of the non-diffusible ion, also constitutes a semi-permeable membrane which, in the acidic environment, is positively charged, and the acid ions are diffusible. In the presence of neutral salts, the membrane potential decreases; the decrease is accentuated as the salt concentration increases [13].

The physio-chemical transformations that take place in the skin during the process of obtaining finished skins are conditioned by the semi-crystalline structure of collagen and its colloidal and polyelectrolyte properties. The physio-chemical properties of fibrillar collagen, especially the insolubility and high tensile strength, are directly related to the arrangement of the polymerized molecules, joined by intra- and intermolecular bonds. In order to transform raw leather into finished leather in the rejuvenation process, new intermolecular reticulations are introduced by means of inorganic (chromium salts, zirconium) and organic (aldehydes, polyphenols) tanning substances. Collagen is synthesized intracellularly (intrafibroblastic), in the form of large, soluble precursor molecules, called procollagens, in which each chain presents additional extension peptides-propeptides in the terminal regions [14]. After the secretion of procollagens in the extracellular space, the propeptides are removed by the action of some procollagen metalloproteinases. The resulting molecules spontaneously self-assemble in the immediate vicinity of the fibroblasts to form fibrils. At higher levels, the fibrils can be organized into fibers, which can be arranged in extremely complex shapes.

4. Collagen and Skin

The dermis is mostly made up of collagen and elastin fibers. Thick collagen fibers support the skin. Collagen is the main component of the dermis, the one that gives elasticity and flexibility. With benefits in maintaining the qualitative structure and elasticity of the skin, but also with an active role in toning it, collagen has moisturizing properties and prevents the appearance of wrinkles or even diminishes the existing ones, prevents cellulite and stretch marks and helps the rapid healing of injuries from dermis level. Collagen is a biopolymer that in vivo has a structural function based precisely on the interactions that are created to maintain the cells in the tissues, available for interaction with various biologically active substances: hormones, enzymes, peptides, etc. [2]. Their accessibility to the collagen binding sites is facilitated by its extraordinary hydrophilic capacity. At neutral pH it can adsorb water at a level of 100% of its dry weight and up to 500% at extreme, very acidic or very basic pH values [15].

The high swelling capacity of collagen ensures an optimal hydrodynamic regime of its interaction with an enzyme, by reducing the internal transport resistance in the diffusion of the substrate and the resulting products. The protein nature of collagen contributes through polar and non-polar AA residues to strong, noncovalent interactions with biological molecules. Collagen is the main structural protein found in the extracellular space in various animal connective tissues. The biochemical structure of collagen is achieved by the interweaving of three helical polypeptide chains, which form elongated fibrils. Collagen consists of a triple helix, which generally contains two identical strands (α1) and an additional strand that differs slightly in chemical composition (α2) [2]. The composition of AAs in collagen is atypical of proteins, which is noted by the increased content of Hyp. There are many repeating AA sequences, the most common being: Gly-Pro-X and Gly-X-Hyp, where X is an AA (but not Gly, Pro, or Hyp) [16].

Collagen is the main structural protein of the skin, which gives it resistance and ensures its suppleness and hydration. Due to age and environmental factors, the level of endogenous collagen (naturally produced by the body) decreases, causing the skin to lose its brightness, elasticity and resilience. Collagen is the main structural protein of the body, composed of three protein chains wound together in a tight triple helix. This unique structure gives collagen greater tensile strength than steel. Approximately 33% of the protein in the body is collagen [8]. This protein supports tissues and organs and connects these structures to bones. In fact, bones are also composed of collagen combined with certain minerals such as calcium and phosphorus. Collagen plays a key role in providing structural 'scaffolding' around cells and thus contributes to supporting cell shape and differentiation. This is similar to how steel rods give strength to a concrete block. The collagen network, like a mesh with many meshes, holds cells together and provides the framework or supportive environment in which cells grow and function and tissues and bones heal [17].

Collagen represents 75% of the skin. Thus, the smooth and plump appearance of young, healthy skin is largely due to the presence of optimal collagen levels. The breakdown of healthy collagen and the decline in collagen production leads to the development of unwanted wrinkles and the appearance of aging skin. For this reason, beauty enthusiasts around the world are looking for new ways to support and increase collagen levels and repair collagen damage. Some people are willing to go so far as to inject collagen protein into their skin to fill in wrinkles and add volume to their lips. Collagen is created by fibroblasts, which are specialized skin cells located in the dermis [2]. Fibroblasts also produce other structural proteins of the skin, such as elastin (a protein that gives the skin its ability to retract) and glucosaminoglycans (GAGs). The GAGs make up the basic substance that keeps the dermis hydrated. To signal or activate the production of structural skin proteins, fibroblast cells have specially formed receptors on their outer membranes that act as binding points, to which signal molecules with the appropriate shape can fit [16]. When the receptors are bound by the right combination of signal molecules (called fibroblast growth factors, or FGFs), the fibroblast begins collagen production. Fibroblasts initially produce short subunits of collagen called procollagen. These are transported from the fibroblast cells and later join together to form the complete collagen molecule. Vitamin C acts as a cofactor during many steps of the process. Without a sufficient level of vitamin C, collagen formation is, quite simply, disrupted [18].

This disruption leads to a variety of disorders such as scurvy – a disease in which the body cannot produce collagen and as a result essentially “falls apart” as these support structures (collagen) deteriorate. Collagen synthesis occurs continuously throughout our lives to repair and replace damaged collagen tissue or to build new cellular structures. The degradation and recycling of old or damaged collagen is a natural process, used to create protein fragments needed to build new cellular structures, such as the healing process.

5. Conclusions and Recommendations

Collagen biomolecules help support various aspects of skin health. Collagen represents a large part of the proteins found in the body and comprises about 80% of the dry weight of the skin. Over time, the skin begins to lose its ability to maintain collagen production at the same level it produced in youth. This is due to both external and internal factors and can lead to typical signs of skin aging such as fine lines and wrinkles, uneven texture and loss of radiance. Collagen is responsible for maintaining moisture, elasticity and flexibility of the skin, reduces the depth of wrinkles and increases the elastin and procollagen content of the skin. At the same time, collagen favors the rapid healing of skin lesions, having a beneficial effect on skin affected by acne, edema and erythema. Due to the complexity of this protein and the complexity of the human body, we have several important processes such as: maintaining the elastic structure of the skin, keeping the epidermis in normal parameters, protecting internal organs, reducing facial wrinkles, reducing the risk of tissue dehydration, strengthening the bone skeleton, mitigating joint inflammations such as rheumatoid arthritis, gout, osteoarthritis, hair and nail strengthening and muscle recovery after physical exertion.

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