Structural Hierarchy in Collagen and Factors Affecting the Collagen Structure

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Introduction

The fibrous proteins are divided into three classes according to their structures, α-keratin, collagen, and silk fibroin. Collagen is a fibrous protein made of polypeptide chains that are arranged in long strands or sheets that are most abundantly found in mammals that give support to skin, cartilage, ligaments, tendons, teeth, and bones. It is also found in the cornea of the eye in crystalline form. Collagen exhibits high tensile strength and elasticity. Degradation of the protein in skin results in wrinkles that go along with skin ageing. There are also different types of collagen, type I- XXVII. This report will discuss the structure of collagen with the first 13 types of collagen being defined, however, more emphasis will be placed on types I, II, III, V, and XI, because these conformations are able to interact with each other to form fibrillar structures.

Types of Collagen [1]

Because collagen is the most abundant protein found in vertebrate and mammalian species, each area of the body where collagen is found corresponds to a different type of collagen. Type I collagen is the most abundant collagen of the human body. It is present in scar tissue. It is also found in tendons and the organic matrix of the bone. Type II collagen is articular cartilage. Type III collagen is present in the body as granulation tissue, and is produced quickly by young fibroblasts before the tougher type I collagen is synthesized. Type IV collagen is found primarily in the basal lamina and the eye lens. Type V and VI collagen are associated with type I, with only type V being found in the placenta. Type VII collagen is found in epithelia. Type VIII collagen is

found in some endothelial cells. Type IX collagen cartilage is associated with type II. Type X collagen is a type of mineralizing cartilage. Type XI collagen is found in many types of cartilage. Type XII collagen is able to interact with types I and III. Finally, type XIII collagen interacts with types I and II.

Composition and Structure

Collagen has an unusual, but unique supramolecular structure where the molecules within collagen are able to interact within the protein to produce other structures with various functions, which is why there are 27 different types of collagen found in many areas of the body that all have different forms. It has three chains where each chain is over 1000 amino acid residues long that all twist around each other to form a triple helix.

In primary structures of collagen, some combinations make up 10 polypeptide chains, named α1(I), α2(I), a1(II), α1(III), α1(V), α2(V), α3(V), a1(XI), α2(XI) and α3(XI) [2]. The amino acid sequence is a set of five or six peptide repeating units of Gly-X-Pro or Gly-X-HyPro, or Gly-X-Y with X representing any amino acid residue [3]. The derivative of proline, hydroxyproline facilitates in collagen stability. All α- chains in fibrillar compounds consist of 300 uninterrupted Gly-X-Y residues that are surrounded by shorter terminals of a different type of structure [2].

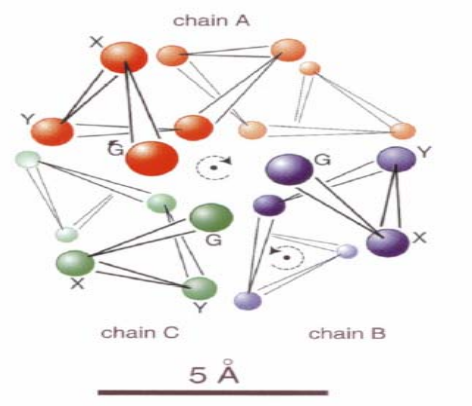


Figure 1. Tripeptide structure of Gly-X-Y repeating chains [4]

The polypeptide chains form a right- handed α –helix with a residue- to- residue angular separation of approximately 108^{o}. This type of position results in coiling that is due to steric repulsion between X positioned Proline residues, and Y positioned 4-hydroxyprolines [2]. Glycine must occupy every third residue, and the side chain is made up of single, Glycine hydrogen atoms. This arrangement gives the appearance of "clear" lines following a slightly left- handed helix [2].

Located on the ends of the α-chains are C-telopeptides and N-telopeptides. The C-terminal extension peptides form disulphide crosslinks, and the triple helix forms a long, rod-like, but flexible bond giving procollagen [5].

Figure 2: Structure of collagen with C and N telopeptide terminals [6].

These bonds are stabilized by the hydrogen bonding of one chain of Glycine and Proline of another chain [7]. Depending on the type of collagen, these triple helices can

be either homotrimers (collagen types II and III) or heterotrimers (commonly type I, type V, and type XI) [2].

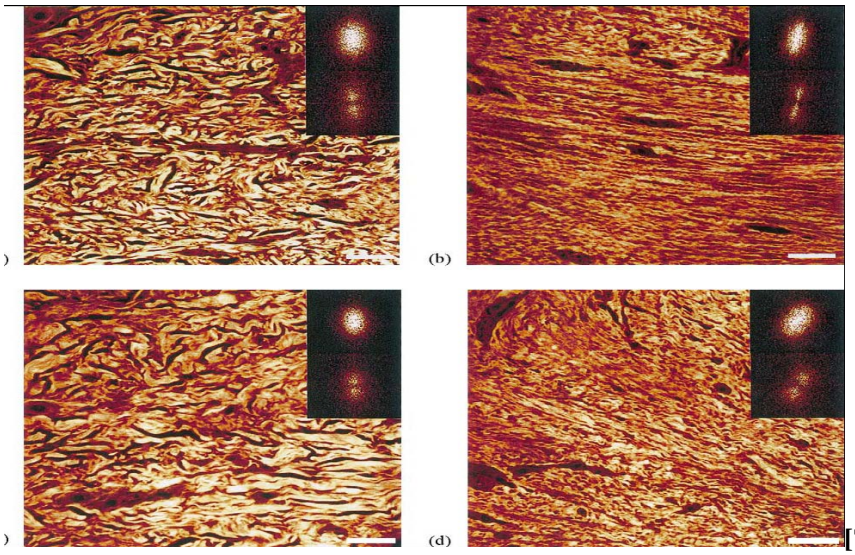
The newly formed collagen is now a very reactive molecule that is able to undergo fibrillogenesis to create larger supramolecular structures. This type of structure is only stabilized by polar, hydrophobic, and other non- covalent interactions, and depending in the stage of formation, it can also be stabilized by covalent crosslinks [2]. Some factors that affect fibrillogenesis are interactions with other molecules, temperature, and ionic strength, which lead to cylindrical fibrils. However, even when these factors interfere with the fibrillogenesis process, the molecules are still able to reassemble themselves into the proper triple-helical form. It could be noted that this triple- helix has the role of sharing the encoded information for the intermolecular interactions to occur, and the telopeptides have the responsibility for the formation of crosslinks [2]. This type of crosslinking that occurs in fibrillogenesis is what leads to the formation from molecules to microfibrils. Microfibril formation is the result of various segments crosslinking an aldehyde group of lysine and allysine telopeptides [5].

Factors affecting the formation of collagen

Effect of the orientation of collagen bundles due to skin burns

Collagen is known to be a very tough structure, however, many factors affect the properties of it. For example, when skin is burned, depending on the severity of the burn and skin type, it is often noticed that the skin does not grow back in the same condition in which it was prior to the burn. Research has found that when skin is burned, scars form that are hypertrofic, firm, and shows slightly reduced tensile strength, which relates to

poor quality of collagen networks [8]. There are a couple of differences that have been observed to describe why this is so. It has been noticed in normal skin that collagen bundles that have been formed, show a "basket-weave-like" pattern [8], whereas the scar tissue contains a smaller, more parallel form [9]. Some research has even suggested that the orientation of collagen bundles is the major factor determining the tension in collagen [9, 10]. However, more research was performed and it was determined that mechanical tension in scars could result from fibroblasts and myofibroblasts, the cells that make collagen [8]. The next figure shows a knee that is normal and a knee of the same patient that was burned using microscopy analysis.



[7]

Figure 3. Images of normal and scarred tissue imaged using confocal scanning microscopy and Fourier analysis

The first and third (normal knee) structures were those imaged with confocal scanning microscopy and the second and last (scarred knee) images were obtained via Fourier analysis. Through these micrographs, it is noticed that the normal skin in the first and third photos are aligned in a more slightly random structure. It was also observed that the packing of collagen bundles differed between scar tissue and normal skin. Because the

skin is able to endure a great amount of shearing and pulling, the skin is able to resist these forces, resulting in the structure of superficial tissue that is oriented parallel to the surface [8]. This is not the case with the deeper layers of collagen. This requires that the structure of intercepting forces lie both parallel and perpendicular to the surface area, because deeper layers are able to transfer those forces via bundles running perpendicularly to the underlying tissues [8].

Is collagen gene expression affected with photoageing?

Prolonged sun exposure has been proven to lead to age spots, skin cancer, and skin wrinkles or ageing. Since these conditions lead to a loss of skin elasticity and proper recoil, researched has been performed to study the expression of collagen genes that have undergone photoageing [10] to determine if the collagen expression is affected when introduced to significant amounts of sun exposure. It has been proposed that photoageing leads to reductions in collagen types I, III, and VII, and an increase in elastotic material in the reticular dermis and a reduction in fibrillin. However, it has been concluded that although photoageing can lead to many alterations in the extracellular matrix, it has been observed to cause little or no effect in the modification of the collagen gene and on the abundance levels of expression type VI collagen in human skin [10].

Unlike other proteins, collagen has one of the most unique structures that are found most abundantly in mammalian and vertebrate species. It is found in many parts of the body, even in crystalline forms. It starts off like other proteins with the primary, secondary, and tertiary forms, but, it differs from the fact that these molecules are able to interact with each other within the triple-helical structure to from microfibrils and fibrils. Further interaction can take place with the different types of collagen to form another

type of collagen. In summary, all of the previously mentioned steps have been discussed, lead to the tough and firm structure of collagen. Through many experimental observations, it was observed that even after damage to certain body parts due to burns, sun exposure, cuts, and surgical wounds, collagen still remains strong, and intact with very little or no alterations in the gene expression.

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