Collagen: Role in Oral Tissues: A Review

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Abstract: ***Collagen constitutes the most abundant proteins found in the body. The collagen family consists of at least 30 different genes, which produce 19 known types of collagen. All collagens contain greater or lesser stretches of triple helix. The purpose of this article is to review the available literature on collagen with special emphasis on its role in development and maintenance of oral tissues.***

Keywords: Collagen, Oral tissues, Gingiva, Periodontium

1. Introduction

Collagen is the most abundant protein in mammals, constituting a quarter of their total weight (1). Possessing a great tensile strength, it provides an extracellular framework for all metazoan animals and exists in virtually every animal tissue. About 19 distinct types of collagen made up of about 30 distinct polypeptide chains (encoded by the same number of collagen genes) have been identified in human tissues. Although several of these are present in only in small proportions, they may play important role in determining the physical properties of the tissues (2). The word 'collagen' comes from the Greek, means "glue producing". Fibrous in nature, it connects and supports other body tissues, such as skin, bone, tendons, muscles, and cartilage. It also supports the internal organs and is even present in teeth.

1.1 Types of collagen

Collagen occurs virtually, in almost all parts of body. Table 1 describes the various types of collagen described in literature (3). The structure of collagen eluded scientists for decades. Many prominent scholars, including nobel laureates like Watson and Crick and Linus Pauling were known to have been working on collagen structure when it was finally discovered. Table 2 classifies the collagen, based on their structure that they form.

The triple helical structure that is known to be correct in the essentials was proposed by **G. N. Ramachandran** and **Gopinath Kartha** in the year 1954. This proposed structure came to be known as "Madras helix".

1.2 Uses of collagen

- It is the main component of fascia, cartilage, ligaments, tendons, bone and teeth. It is responsible for skin strength and elasticity, and its degradation leads to wrinkles that accompany ageing.
- It strengthens blood vessels and plays a role in tissue development and nutrition.
- It is present in the cornea and lens of the eye in crystalline form

1.2.1 Medical Uses

1. Collagen has been widely used in cosmetic surgery, as a healing aid for burn patients, for reconstruction of bone and a wide variety of dental, orthopedic and surgical purposes.
2. Collagen sponge is also used in filling bone defects.
3. It is also used as a haemostatic agent and as a wound dressing. Eg. Collatape, collacote, and collaplug.
4. It is used as a slow drug delivery system. For eg. Phosphorylated collagen used in delivery of epidermal growth factor and DNA- infused gel of modified collagen for the delivery of cytokines.
5. Injectable collagen has been used in an attempt to correct distensible acne scars, atrophy from disease or trauma, postrhinoplasty irregularities, glabellar frown lines, nasolabial folds and variety of other surface depressions and abnormalities.
6. It is also used to treat shoulder instability.
7. Collagen is also used as a GTR membrane
8. It is also sold commercially as a joint mobility supplement [4].

2. Role of collagen in Oral Tissues

2.1 Alveolar Bone

Alveolar bone contains both organic and inorganic material. The dominant collagen is type I, although small amounts of type III collagen may be present, particularly in immature or healing bone. Most of this collagen can be regarded as intrinsic collagen secreted by osteoblasts. However, collagen inserted as Sharpey's fibers can be considered as extrinsic collagen formed by adjacent fibroblasts. Mutation in the genes encoding the constituent peptides of the collagen type I triple helix may give rise to inherited conditions of Osteogenesis Imperfecta & Dentinogenesis Imperfecta (5). Collagen of bone occurs as fibers arranged at an angle to each other so as to resist mechanical shear from any direction (6). Woven bone is characterized by interwined collagen fibrils oriented in many directions, showing wide interfibrillar spaces. However, in case of lamellar bone, collagen fibrils are generally thicker nd arranged in ordered sheets consisting of aligned and closely packed fibrils (7).

2.2 Periodontal ligament

The collagen of periodontal ligament is Type I (80%), type III (20%) with lesser amounts of Type IV, V, VI & XII also present. Type I collagen is the major protein component of most connective tissues including skin, gingiva and bone. It contains two identical α1 chains and a chemically different α2 chain. It is low in hydrolysine and glycosylated hydrolysine. It is the main collagen of the organic matrix of bone and cementum and is virtually insoluble due to crosslinks which provide the structural and mechanical stability for normal function. Type III collagen(20%) also consists of three α1 chains. It is high in hydroxyproline, low in hydroxylysine and contains cysteine. It is present in similar proportions to those found in embryonic tissues, and this probably reflects the high turnover rate within the ligament. Type III collagen is more fibrillar and extensible than type I and may be important in maintaining the integrity of the ligament during the small vertical and horizontal movements which occur during chewing. The principal fibers are composed mainly of collagen type I, whereas reticular fibers are composed of collagen type III. Collagen type III generally co-distributes with collagen type I to form mixed fibrils of infinitely varying proportions, a higher proportion of collagen type III is present in fetal tissue. Collagen type IV is a short chain molecule that has only recently been located in the periodontal ligament. It is found in the basal lamina. It is a microfibril forming collagen that ramifies the extracellular matrix, but it doesn't directly associate with the major banded collagen fibrils. The molecule may be central in retaining the integrity & elasticity of the extracellular matrix. The molecular configuration of collagen fibers provides them with a tensile strength greater than that of steel. Thus, collagen imparts a unique combination of flexibility and strength to the tissues (8). Radiographic studies with radiolucent thymidine, proline and glycine indicate a very high turnover rate of collagen in the periodontal ligament. The rate of collagen synthesis is twice as fast as that in gingiva and four times as fast in skin, as established in rat molar (9).

2.3 Cementum

Cementum is approximately 45 to 50% hydroxyappatite (inorganic) and 50% collagen and noncollagenous matrix proteins (organic). Collagen type I is the predominant collagen. It plays a key role in regulating periodontal tissues during development and regeneration. In addition, during early stages of cementogenesis, development and repair, type III collagen is present in high amounts but is decreased with maturation of this tissue. Also, type XII collagen may assist in maintaining periodontal ligament space versus continuous formation of cementum. Trace amounts of other collagens, including type V and type XIV are also found in extracts of mature cementum (10).

2.4 Dentine

Mature dentine is made up of approximately 70% inorganic material, 20% organic material and 10% water by weight, and 45%, 33% & 22% respectively by volume. The organic phase is about 30% collagen (mainly type I with small amounts of type III & V) with fractional inclusions of lipids and noncollagenous matrix proteins. Collagen type I acts as a scaffold that accommodates a large proportion (estimated at 56%) of the mineral in the holes and pores of fibrils. Most of the collagen fibers in dentine run parallel to the pulpal surface. In mineralized dentine, the collagen fibrils are of larger diameter (100nm) and are more closely packed than in predentine. Collagen fibrils in dentine are not assembled into bundles as they are in many non-mineralized connective tissues such as tendon or periodontal ligament (10).

2.5 Dental Pulp

The principle fibrous component of the dental pulp is type I collagen, although type III is also present. It is present as fibrils thinly scattered through the pulp in the young tooth. Their arrangement in pulp is irregular, except in the periphery, where they become aligned approx. parallel to forming predentine surface. During early development some of the bundles are arranged at right angles to the developing dentine, contributing to the appearance of 'Vonkorff' fibers in outer dentine. About 56% of pulpal collagen is type I and 41% is type III. Whereas overall collagen content of the pulp increase with age, the ratio between type I & type III remains stable, and the excess amount of collagen organizes into fiber bundles. 11 Small amounts of type V and type VI collagen are also present. Overall, collagen forms 3-5 % of wet weight of pulp, a low proportion in comparison with other loose connective tissue (12). The greatest concentration of collagen generally occurs in the most apical portion of the pulp (13).

2.6 Temporomandibular Joint

The most superficial layers of the articulating surface is made of collagen. Even the intra-articular disc is composed of dense collagenous fibrous tissue. In the thinner, central region of disc, the collagen fibers run mainly in anteroposterior direction. At the periphery of the disc, collagen fiber bundles are arranged circumferentially. When viewed in polarized light, the collagen fibers show alternatively dark and light bands indicating that they are wavy or crimped (which can be visualized directly using specialized interference microscopy). The periodicity of the crimping is of the order of 15-20 µm. Crimping in the intra-articular disc is indicative of tensional loads. The fibers within intra-articular disc are principally composed of type I collagen and comprise about 80% (dry weight) of the disc. Small amounts of type III collagen is also present throughout the disc. The apparent presence of localized areas of fibrocartilage indicate presence of type II collagen (12).

2.7 Gingiva

The connective tissue of the gingiva is known as lamina propria. Normal gingival tissue contains type I and type III collagens at a ratio of 5:1, which account for 99% of the collagen, type IV, which is associated with basal lamina accounts for remaining 1%. In granulation tissue, type III collagen predominates initially, and as it matures, decreases gradually to approximately 20% of the total collagen. The ratio of type V to type I collagen is increased at extraction sites in the early healing stages and gradually diminishes to usual levels, as does the ratio of type III to type I. the increase is probably related to angiogenesis, in which type V collagen may facilitate the migration of endothelial cells. The tensile strength of the wound augments as the content of type I collagen increases [14]. Type IV collagen (argyrophilic reticulum fiber) branches between collagen type I bundles and is continuous with fibers of the basement membrane and blood vessel walls. Increasing age results in coarser and denser gingival connective tissue (14).

2.8 Basal Lamina

Type IV and VII are the principle collagen of the basal lamina [14]. The lamina lucida consists of a glycoprotein called Laminin, which cements non-fibrillar type IV collagen in the lamina densa to the epithelial cells. The lamina densa consists of type IV collagen coated on each side by a Glycosaminoglycan(GAG) – Heparan Sulfate. Thick collagen fibrils attach onto the lamina densa with finer fibrils running through these to link the whole complex mechanically to the connective tissue (12).

3. Conclusion

Collagen is the most important protein, not only for humans, but for all vertebrates. As we know that how important blood is to an organism, but few of us are aware that as an organism, we are literally swimming in collagen. Collagen is also an essential component of various oral tissues like alveolar bone, dentine, periodontal ligament, dental pulp and gingiva.

References

1. Hulmes, D. J. (2002). "Building collagen molecules, fibrils, and suprafibrillar structures". J Struct Biol **137** (1–2): 2–10.
2. Murray RK, Granner DK, Mayes PA, Rodwell VW. Harper's biochemistry, 25th edition, pp 695.
3. Traub, W,Yonath A., Segal DM.. "On the molecular structure of collagen". Nature 1969 **221** (5184): 914–917.
4. Vandana KL, Savitha B: Collagen-Microscopy to Macroscopy!, JISP 2005; 9:100-103.
5. Berkovitz BKB, Holland GR, Moxham BJ. Oral anatomy, histology and embryology, 3rd edition pp 385.
6. Champe PC, Harvey RA, Ferrier DR. Biochemistry,3rd edition, pp 43-45.
7. Nanci A. Tencate's oral histology, 6th edition, page-111.
8. Okuyama K. Okuyama K. "Crystal and molecular structure of a collagen-like polypeptide (Pro-Pro-Gly)$_{10}$". J Mol Biol 1981 **152** (2): 427–443.
9. Bella, J, Eaton, M, Brodsky B, Berman, HM. "Crystal and molecular structure of a collagen-like peptide at 1.9 A resolution". Science 1994; **266** (5182): 75–81.
10. Hingorani D, Mehta DS. Matrix metalloproteinases and their role in periodontal destruction, repair and remodeling, JISP 2002;5:55-60
11. Fraser, R. D. B., MacRae, T. P. "Unit cell and molecular connectivity in tendon collagen". Int. J. Biol. Macromol. 1981 **3** (3): 193–200.
12. Fraser, R. D, MacRae T. P, MillerA. "Molecular packing in type I collagen fibrils". J Mol Biol 1987;**193** (1): 115–125.
13. Wess, TJ, Hammersley, AP. "Molecular packing of type I collagen in tendon". J Mol Biol 2001; **275** (2): 255–267.
14. Raspanti, M; Ottani, V; Ruggeri A. "Subfibrillar architecture and functional properties of collagen: a comparative study in rat tendons". J Anat. 1990' **172**: 157–164. PMC 1257211

Table 1: The Collagens

Type	*Gene*	*Tissue distribution*	*Major function*
Fibrillar collagens			
I	COL1A1 COL1A2	Abundant in skin, bone, dentin, cementum, tendons, ligaments and most connective tissue	Provides strength to connective tissue
II	COL2A1	Cartilage, vitreous humor, and intervertebral disk	Provides strength to connective tissue
III	COL3A1	Embryonic connective tissue, pulp, skin, blood vessels, and lymphoid tissue (reticular fibers)	Provides strength to connective tissue
V	COL5A1 COL5A2 COL5A3	Basement membrane, blood vessels, ligaments, skin, dentine, and periodontal tissues	Forms core of type I fibrils; provides tensile strength
XI	COL11A1 COL11A2	Cartilage and vitreous humor	Forms core of type I fibrils; provides tensile strength
Basement membrane collagens			
IV	COL4A1 COL4A2 COL4A3 COL4A4 COL4A5 COL4A6	Basement membranes (basal lamina)	Structural network of basement membranes
Fibril associated collagens with interrupted triple helices (FACIT)			
IX	COL9A1 COL9A2 COL9A3	Cartilage and vitreous humor	Attaches functional groups to surface of type II fibrils
XII	COL12A1	Widespread in many connective tissues	Modulated fibril interactions
XIV	COL14A1	Widespread in many connective tissues	Modulated fibril interactions
Meshwork-forming collagens			
VIII	COL8A1 COL8A2	Cornea (Descemet's membrane) and endothelium	Tissue support and porous meshwork
X	COL10A1	Hypertrophic zone of cartilage growth plate	Calcium binding
Anchoring-fibril collagen			
VII	COL7A1	Epithelium (skin and mucosa)	Strengthens epithelial – connective junction
Microfibril-forming collagens			
VI	COL6A1 COL6A2 COL6A3	Ligaments, skin and cartilage	Bridging between cells and matrix
Transmembrane collagens			
XIII	COL13A1	Cell surfaces, focal adhesions, and intercalated disks	Cell matrix and cell-cell adhesion
XVII	COL17A1	Hemidesmosomes	Cell attachment to matrix
Endostatin-forming collagens			
XV	COL15A1	Endothelial basement membranes	Proteolytic release of antiangiogenic factor
XVIII	COL18A1	Endothelial basement membranes	Proteolytic release of antiangiogenic factor
Other collagens			
XVI	COL16A1	Endothelial, perineural, muscle, and some	Unknown

		endothelial basement membranes	
XIX	COL19A1	Endothelial, perineural, muscle, and some endothelial basement membranes	Unknown

Table 2: Classification of collagens, based primarily on the structure that they form

Class	*Type*
Fibril forming	I, II, III, V and XI
Network like	IV, VIII, X
FACITs*	IX, XII, XIV, XVI, XIX
Beaded filaments	VI
Anchoring fibrils	VII
Transmembrane domain	XIII, XVII
Others	XV, XVIII

*Facits = fibril associated collagens with interrupted triple helices