



COLLAGEN AS A BIOMATERIAL IN DENTISTRY

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ABSTRACT

Collagen is the most abundant protein that holds the whole body together in humans. It is found in the skin, bones, muscles and tendons and provides a scaffold to give strength and structure. These are proteins of unique structure and function with wide distribution throughout the animal kingdom ranging from insects to man. They are the major fibrous protein of the connective tissue which constitute about 1/3rd of the total protein in the body. Collagen is a highly versatile material and extensively used in the field of medicine for the management of severe burns, non-healing ulcers, traumatic, surgical wounds and various cosmetic procedures. In dentistry collagen is found to have a good scope of improvement, as materials which are biocompatible and easily absorbed by the tissues are more acceptable than synthetic one's. It has a proven rate of success in the field of dentistry as GTR membrane, Root conditioning agent, Haemostatic agent and wound dressing agent. This paper aims to present an overview of collagen, its structure, biocompatibility and also focuses on the applications in the field of dentistry.

Keywords: Collagen, Collagen fibril, Tropocollagen

INTRODUCTION

In nature, collagen is found exclusively in the connective tissues and flesh of animals. It has more tensile strength and is found as the component of fascia, ligaments, tendons, cartilage, skin and bone. It is needed for skin elasticity and strength, as degradation of it leads to wrinkles that accompany ageing. It also plays a role in tissue development by strengthening the blood vessels. ¹It is derived from Greek word 'Kolla' (glue) and a French word 'Collagene' designates glue producing constituent. ²

TYPES

So far 29 types of Collagen has been identified even though it occurs in many parts of the body and of which 90% is type I, II, III, and IV Collagen. ¹

- Collagen One: Skin, Tendon, Vascular, Ligature, Bone and Organs
- Collagen Two: Cartilage
- Collagen Three: Reticulate

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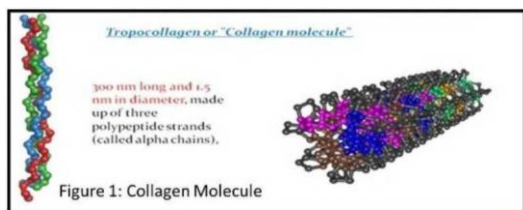
- Collagen Four: forms bases of cell basement membrane
- Collagen Five: Cells surfaces, hair and placenta

Ryan H. Fitzgerald, John S Steinberg (2009) ³demonstrated that Collagens make up the largest fibrous element of the extracellular matrix (ECM) in the dermal matrix. The ECM is the largest component of the dermal skin layer and is composed of water, polysaccharides and collagen proteins. The ECM provides a significant role in regulating and providing a framework for the processes of healing.

STRUCTURE OF COLLAGEN

Molecular structure:

In the mid 1930, a regular structure at the molecular level was confirmed, till that time many scholars like Nobel laureates Crick, Yonath, Brodsky, Pauling, Rich, Berman and Ramachandran concentrated on the conformation of the collagen monomer. While dealing with the confirmation of each individual peptide chain, several competing models correctly gave a way to the triple-helical "Madras" model which provided an essentially correct model of the molecule's quaternary structure even then this model still needed some refinement. (Figure 1)



Courtesy: <https://en.wikipedia.org/wiki/Collagen>

Figure 1 : Collagen molecule

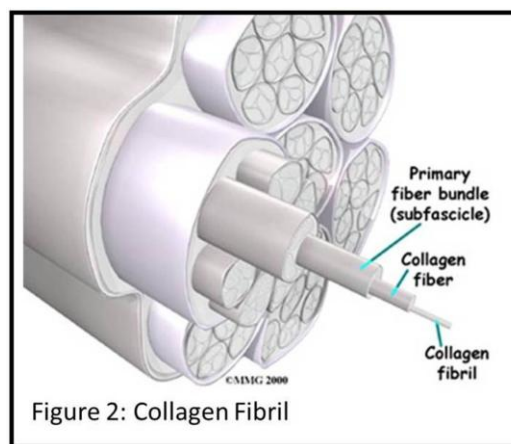
The "Tropocollagen" or "Collagen molecule" is a subunit and constitutes the larger collagen aggregates such as fibrils. It is 1.5 nm in diameter and 300 nm long approximately and made up of three polypeptide strands known as alpha chains, each of which possess the conformation of a left-handed helix. These three left-handed helices are twisted together into a right-handed coiled coil, a triple helix or super helix, a quaternary structure stabilized by numerous hydrogen bonds. Each triple-helix associates into a right-handed super-coil that is referred to as the collagen micro fibril. Each micro fibril is then inter digitized with its neighboring micro fibrils to a point that might suggest that they are individually unstable though within collagen fibrils they are so well ordered as to be crystalline.

It has a characteristic feature of regular arrangement of amino acids in each of the three chains of these collagen subunits. The sequence of pattern includes Glycine-Proline-X or Glycine-X-Hydroxyproline, where X may be any of various amino acid residues. Proline or Hydroxyproline constitute about 1/6 and Glycine accounts for the 1/3 of the sequence. This represents that half of the collagen sequence is not Glycine, Proline or Hydroxyproline and a fact is frequently missed due to the distraction of the unusual GX_1X_2 character of Collagen alpha-peptides. So, regular repetition and high Glycine(Gly) content is found in fibrous proteins, such as silk fibroin. Approximately 75-80% of silk is Gly-Ala-Gly-Ala with 10% serine and elastin is rich in Glycine, Alanine (Ala) and proline,, whose side group is a small and inert methyl group. Such high Glycine and regular repetitions are not found in globular proteins. Therefore, Glycine plays a unique role in fibrous structural proteins as it has smallest amino acid with no side chain.¹

Fibrillar structure:

The Tropocollagen subunits are self-assembled with regularly staggered ends into the larger arrays in the tissue extracellular spaces. The molecules in the Fibrillar collagens are staggered from each other by

about 67 nm and this unit is referred as 'D'. In each D-period there is repeat of the micro fibril and a part that contains five molecules called the "overlap" and a part that contains four molecules called the "gap" in cross-section. In cross section of both the gap and overlap regions, the triple-helices are also arranged in a hexagonal or quasi-hexagonal array. Formation of larger fibrillar bundles are done with different classes of proteins, glycoproteins and proteoglycans to form the various types of mature tissues. Collagen fibrils are semi crystalline aggregates of collagen molecules.



Courtesy: <http://loptonline.com/patient-education/injuries-conditions/foot-anatomy/>

Figure 2 : Collagen fibril

Collagen fibers are bundles of fibrils. (Figure 2) Collagen fibrils/aggregates are arranged in various combinations and concentrations in several tissues to provide different tissue properties. In bone, entire collagen triple helices lie in a parallel and staggered array. In between the ends of the tropocollagen subunits, 40 nm gaps approximately equal to the gap region serve as nucleation sites for the deposition of hard, long and fine crystals of the mineral component, which is hydroxyapatite $[Ca_{10}(PO_4)_6(OH)_2]$ with some phosphate. In this way, certain kinds of cartilage turn into bone. Type I Collagen gives bone its tensile strength.¹

BIOCOMPATIBILITY

In the present day various forms of collagen are being used successfully in the field of medicine and dentistry. Collagen is the material of choice in the management of severe burns, non healing ulcers, traumatic and surgical wounds and various cosmetic surgical procedures.⁴ Studies in dental research aim at the development of suitable biomaterials with unique functional properties. The wide use of collagen is associated to natural properties that

include the low immune response and toxicity; achieve homeostasis; ability to promote cellular growth and attachment and the ability of collagen solutions to reconstitute in vitro into the microfibrillar structure found in natural tissues.⁵ Collagen is also frequently used in scientific research applications for studying cell behavior, cell culture and cellular interactions with the extracellular environment.¹ David Brett (2008)⁶ reviewed collagen based wound dressings and stated that they are uniquely suited to address the elevated levels of MMPs that act as a sacrificial substrate in the wound. It has also been demonstrated that breakdown collagen products are chemotactic for a variety of cell types required for the formation of granulation tissue. Further more these collagen based dressings have the ability to absorb wound exudates and maintain a moist wound environment. Doillon C J, Silver F H (1986)⁷ also revealed that collagen-based dressings produce a significant increase in the fibroblast production. It has a hydrophilic property that is important in encouraging fibroblast penetration, enhancing the deposition of organized and oriented collagen fibers by attracting fibroblasts and cause a directed migration of cells which aid in the uptake and bioavailability of fibronectin that help to preserve leukocytes, macrophages, fibroblasts and epithelial cells. These assist in the maintenance of the chemical and thermostatic microenvironment of the wound. Postlewaithe and Kang (1978) demonstrated that collagen placed topically can initiate wound healing by activating inflammatory cells and promoting increased vascularization of the healing tissue. Dunn and Ebendal (1978) have demonstrated that the physical three-dimensional collagen structure has the ability to induce fibroblastic growth, which is essential in the formation of granulation tissue.⁴

APPLICATIONS IN DENTISTRY

As GTR membrane: It allows selective repopulation of periodontal ligament cells and is chemotactic for fibroblasts and weakly immunogenic. Commercial products available are Zyderm, Biosite.

As Root conditioning agent: Recently PEPGEN-P-15 peptide is used as root conditioning agent instead of citric acid as it enhances fibroblast attachment and the migration of periodontal cells to root surfaces. It also enhances alkaline phosphates expression and increases nucleic acid and protein synthesis. P-15

with a concentration of 400ng/g can be used as root conditioning agent.

As Haemostatic agent: Microfibrillar Collagen is used. Commercial products available are Hemostat, Collastat.

As wound dressing agent: Type I medical Collagen is known to support new tissue growth during the wound repair cycle. Collatape, Collacote and Collaplug are commercially available products.²

As Pulpal Medicament: Collagen products like cross-linked collagen gel and enriched collagen solution have been reported as pulpotomy medicaments in animals. Teuta Marsan et al (2003)⁸ used collagen, bio-resorbable membrane (Bio-Gide) as a pulp capping material in mongrel dogs. After six weeks, the pulp tissue preserved the pulp vitality with a better blood supply and an increased number of blood vessels. The reparatory bridge formation was not noticed in any of the tested samples. The authors also revealed that collagen bioresorbable membrane showed preservation of the morphology of all histological structures.

On the other hand, study conducted by Fuks AB et al (1991)⁹ assessed histologically the pulp tissue reaction to a commercial collagen preparation in pulpotomized primary teeth of baboons and concluded that Zyderm (Collagen Corp. Palo Alto, CA) can't be recommended as a pulpotomy agent. Till today, no clinical studies have been reported in humans on the use of collagen as a medicament, however collagen the biomaterial known for its excellent wound healing properties, increased vascularization, pulp healing ability and biocompatibility is found to be a better material for its use as a Pulpotomy agent in human primary teeth.⁸

Based on the biocompatibility of collagen, Pranitha et al (2013)¹⁰ conducted a histological study to evaluate the pulpal responses to Collagen (Biofil AB particles) and commercial available cement (Pulpotec^R) as pulpal medicaments, as the biological effect of any pulp protection materials can be evaluated fundamentally only by the response to the pulp tissue. A total of twenty retained, non carious primary teeth were selected and a pulpotomy procedure was carried out using collagen particles and Pulpotec cement in Group I and II and extracted after 1 week, 15 days and 30 days intervals. The specimens were decalcified and histologically evaluated using a research microscope. Based on the

results obtained, both collagen and pulpotec can be considered as alternatives to the existing pulp medicaments. Increased vascularity and excellent wound healing capacity of collagen makes it a more bio-compatible material.

CONCLUSION

Apart from the field of medicine, where Collagen is used for management of severe burns, non healing ulcers, traumatic and surgical wounds, it has got its substantial role as a biocompatible material in dentistry. Today, the dental practitioners are confronted with many new materials which continue to appear in the market. Therefore collagen, the biomaterial known for its excellent wound healing properties, increased vascularization, pulp healing capacity and biocompatibility can be also be chosen as a suitable pulpal medicament as part from its usage in the dentistry.

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