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COLLAGEN SHIELDS- A NOVEL DRUG DELIVERY SYSTEM

Soji S.*[1], Prothibha Das[1], Minnu George[1] and Anjali C. S.[1]

Malik Deenar College of Pharmacy, Kasaragod, Kerala.

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***Corresponding Author**
Soji S.
Malik Deenar College of Pharmacy, Kasaragod, Kerala.

ABSTRACT

Collagen shield basically consist of cross linked collagen, fabricated with foetal calf skin tissue and developed as a corneal bandage to enhance wound healing. They topically applied antibiotic conjugated with delivery. They determined the influence of size, molecular weight and number of amine, carboxylate and hydroxyl surface groups in several series of dendrimers. The residence time was longer for the solutions containing dendrimers with carboxylic and hydroxyl surface groups. The objective of this review article is to summarize information available on collagen dosage forms for drug delivery as well as to communicate an outline regarding current preparation of collagen available in market includes - collagen sponges for burns/wounds, mini-pellets and tablets, gel preparations in combination with liposomes for sustained delivery of drug, formulations for transdermal drug delivery, and nanospheres for gene delivery, collagen matrices for cell culture.

KEYWORDS: Collagen; Drug delivery system; Opthalmology.

INTRODUCTION

Collagen shields is also known as collagen corneal shield, they are newly developed, potentially versatile ophthalmic lens, which is made up of collagen, since collagen is a natural, commonly available protein involved in the support and protection of vital structures, many researchers have tried to use peripheral collagen to protect the surface of the eye. Generally collagen shields are manufactured from bovine or type l collagen. They are act as a short term bandage and allow sufficient oxygen transmission for essential metabolism occurring in eye cornea.[1]

The collagen shield was originally designed for bandage contact lenses, which are gradually dissolved in cornea. The idea of using a shield or a hydrogel lens as a delivery device has led to the development of various drug delivery systems for ophthalmic applications. One of the merits of the collagen-based drug delivery systems is the ease with which the formulation can be applied to the ocular surface and its potential for self-administration. The mechanical properties of the shield protect the healing corneal epithelium from the blinking action of the eyelids.[2]

Drug delivery by collagen shields depends on loading and a subsequent release of medication by the shield. The collagen matrix acts as a reservoir and the drugs are entrapped in the interstices of the collagen matrix. As tears flush through the shield and the shield dissolves, it provides a layer of biologically compatible collagen solution that seems to lubricate the surface of the eye, minimize rubbing of the lids on the cornea, increase the contact time between the drug and the cornea, and faster epithelial healing. A bolus release of drug from the lenses was attributable to the enhanced drug effect.[3]

Therefore, this system allows the higher corneal concentrations of drug, and the more sustained drug delivery into the cornea and the aqueous humor. Delivery of drugs through the collagen shield was more comfortable and reliable than frequent application of other conventional treatments, such as drops, ointment or daily subconjunctive injection. Modifications of collagen were made to simplify the application, to meet the highest compliance, to reduce blurring of vision, and to enhance the drug concentration and bioavailability of drugs in the cornea and aqueous humor. Collagen shields as a drug carrier for topical agents have many advantages. Experimental and clinical studies showed that the speed of epithelial healing is faster and more complete with the use of the collagen shield than conventional formulations. There was less stromal edema at the wound sites in collagen-treated corneas. The application of collagen shields for drug delivery is limited by several disadvantages, such as reducing visual activity, causing slight discomfort, and a short duration at the inserted site.[4]

1. Collagen

Basically collagen is a naturally existing protein present in the animal body, fibrous in nature, and especially found in the connective tissue and flesh of mammals. Approximately 25%-35% of total body protein is comprised of collagen, in the form of elongated fibrils; collagen is abundantly present in fibrous tissue like bone, cartilage, tendons, blood vessels, ligament, skin, cornea, inter-vertebral disc and the gut. The synthesis of collagen in the body is made by fibroblast cells. Collagens possess good tensile strength, and found both outside and inside the body cells. In combination with elastic, collagen provides support to body tissues and organs, basically collagen offers firmness and strength and elastic provides flexibility to body tissues. In fact gelatin which is used in food and pharmaceutical industries is collagen that has been hydrolyzed irreversibly.[5]

2. Structure of collagen

Basically collagen possesses a triple helix structure, which generally made up of two homologous chains (α-1) and one supplementary chain that varies slightly in its chemical composition (α-2). These chains are polypeptide in nature and coiled around one another in a cable form. Each has a distinct turn in the reverse direction, these chains are connected together chiefly by hydrogen bonds between nearby CO and NH groups.[6] The weight of collagen molecule is 300 k da[7] and its structure is rope shaped and having a length of 300 NM and a width of 1.5 NM. The major content of glycine and amino acid residue is affecting the helix formation.[8]

3. Characteristics possessed by collagen

- Stretch-ability under stress condition collagen stretch rather than break;
- Strength;
- Biochemical compatibility;
- These three amino acid monomers are strongly fused and they look like single monomer;
- Several hydrogen bonds are present in collagen, on applying stress they canbe wrecked and re-joined after removal of pressure;
- Collagen is biodegradable;
- Collagen show good absorption in-vivo;
- Collagen possesses weak antigenicity;

4. Fabrication methods for Collagen nanoparticles

There are basically four type of methods for the manufacturing the protein based nanoparticles namely-

- Emulsification
- Desolvation
- Coacervation
- Spray drying

Emulsification

In this process, A collagen aqueous phase containing a hydrophilic surfactant and water, and an organic phase containing a lipophilic surfactant, oil and water miscible solvent is mixed with rapid agitation by a mechanical homogenizer at room temperature to form a homogeneous emulsion. Then the above emulsion will be mixed in preheated oil (120) drop by drop resulting formation of collagen nanoparticles.

Desolvation

The process of Desolvation includes the addition of alcohol or natural salt as desolvation factor to the collagen solution, which alters the tertiary structure of collagen, when the critical level of desolvation attained the formation of collagen mass, starts lastly glutaraldehyde will be added as a cross-linking material, and then nanoparticles is formed. This process was firstly employed by Marty and coworkers.

Coacervation

This method is similar to desolvation method, the difference is only in various parameters liketemperature, molar ratio of organic solvent and protein, rate of solvent addition, concentration of cross-linker used, pH, speed of homogenizer etc.

Spray drying

Basically spherical collagen nanoparticle is fabricated by this process. This process include the spraying of dilute solution of collagen leads to the formation of hollow spheres using elevated temperature; increased temperature can lead denaturation of collagen triple –helical structure. So collagen solution is sprayed into liquid nitrogen to prevent denaturation. After that the fabricated nanospheres are successively frozen, tempered, lyophilized, cross-linked, and sterilized.[9,10]

5. Marketed preparation of collagen shields

- Biocora®
- ProshieldO®
- MediLenso®
- Irvine®
- Chiron®

CONCLUSION

Collagen has various advantages as a biomaterial and is widely used as carrier systems for delivery of drug, protein and gene. The examples described in this paper signify selected applications of collagen in the biomedical field. The effective demonstration of usefulness of human skin substitutes made of collagen has leads to the development of bioengineering tissues, such as blood vessels and ligaments. Although many applications of collagen as a drug vehicle discussed in the paper, it should be noted the information regarding collagen is very less as compare to synthetic polymers in literature because, the pure type-1 collagen is very costly, variability in different forms, complex handling processes, and risk of Bovine spongiform encephalopathy (BSE).

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