COLLAGEN SOLUTIONS
MATERIALS FOR LIFE

Collagen for Drug Delivery

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Drug delivery is a valuable therapeutic approach to treat a wide variety of diseases. Administration of pharmacological agents can be localized and the release time can be controlled to selectively target virtually any area of the body, making delivery less likely to produce the unwanted side effects that may normally arise from systemic treatment.

As the scientific community has gained a greater understanding of its structure and chemistry, collagen has increasingly been used as a material for drug delivery. Because collagen is a natural biopolymer found abundantly in humans and animals, it is non-toxic and has low immunogenicity (Ramshaw, Werkmeister and Glattauer, 1996). Additionally, collagen is biodegradable, biocompatible, and possesses an excellent safety profile when compared to other natural biopolymers (Lee, Singla and Lee, 2001). For these reasons, collagen has a long history of use in a number of clinically approved devices and therapies, and as such, collagen has become a molecule of interest in various drug delivery applications.

One attribute of collagen that makes it well-suited for drug delivery is that it can be molded into a variety of shapes and sizes, then modified to control the release rate of various molecules upon implantation. A common limitation of current ocular delivery systems is inadequate retention time of the drug at the delivery site. To achieve prolonged retention time in the eye, Miyaya et al. created a soluble collagen mixture with dexamethasone, which was gelled and air-dried into ovoid shapes for ocular delivery (US Patent No. 4,164,559, 1979). Using this method, a therapeutic delivery rate and complete solubility was achieved in the eye. Such membranes would be an appropriate alternative to eye drops and ointments that would normally need to be reapplied constantly and risk being washed out by natural tear production. In another example where a scaffold structure was designed to control the release of a molecule, Jeckle et al. constructed a multilayer collagen sheet from sponges and, by changing the processing conditions of each layer and the number of sponges, varying release profiles of gentamicin were achieved (WO Patent No. 2001066162, 2001). Another study by Ipsen et al. showed that collagen sponges were superior to poly-methacrylate (PMMA) beads when assessing antibiotic release and safety in the treatment of chronic osteomyelitis (Ipsen, Jorgensen, Damholt, and Torholm, 1991). It has also been shown that liposomes coated with collagen membranes are stable carriers for drugs targeting the liver (Fonseca, Alsina and Reig, 1996). In this study, collagen-coated liposomes exhibited a selective accumulation in the liver and a much higher stability in mice than their uncoated counterparts.

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To control the varying pore size of collagen, chemical and physical cross-linking is often employed. Common chemical cross-linkers include glutaraldehyde, formaldehyde, and chromium tanning. Collagen can also be physically cross-linked with UV-light and dehydrothermal treatment. The open network of fibrillar collagen results in large pore sizes, which are usually not ideal for the prolonged, sustained release rates that are often sought. However, a study found that changing the charge distribution of these matrices could prolong the release of electrostatically bound gentamicin molecules (Singh, Stefko, Lumpkin and Rosenblatt, 1995). After 2.5 days, 50-90% of the loaded gentamicin was released from the collagen gels, depending on the modifications that were made.

Collagen is a versatile material that has been proven to be effective in controlled release and localized drug delivery. As researchers achieve a greater understanding of the mechanisms in which collagen can be modified and combined with other natural and synthetic biopolymers, the types of drugs that can be administered and the types of disease states that can be treated will surely increase at an accelerated rate.

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