Delivery of Human Growth Hormone via DSM’s Polyesteramide

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Introduction

The sustained release of therapeutic biologics provide unique opportunities for the treatment of various pathologies. However, the development of efficacious drug delivery systems for biologics remains a prototypical challenge, due in part to the sensitivity of these therapeutics to their local environment.

Epithelial renewal involves reorganization, migration and proliferation of epithelial cells, and has been shown to be stimulated by a number of topically applied growth factors including epidermal growth factor and fibrillar growth factor. Recombinant human growth hormone (rHGH, 22 kDa) is approved by the FDA for the treatment of numerous indications (e.g., growth hormone deficiency) and is available via prescription in a variety of formulations (i.e., liquid or solid). rHGH has also been shown to increase rate of re-epithelialization of skin graft donor sites, speeding the wound healing process.

Purpose

Fibrillar, degradable polymer-based constructs for the local, sustained delivery of recombinant human growth hormone (rhGH) were generated. The safety, tolerability and possible efficacy of subconjunctivally placed devices (Figure 1) was evaluated in a rabbit dermabration model. rhGH was selected based upon its ability to up-regulate and modulate various growth factors (e.g., insulin growth factor, epidermal growth factor) that have been shown to be involved in corneal re-epithelialization.

Polyester amide

DSM’s versatile amino acid-based polyester amide (PEA) material (Figure 2) platform provides distinct advantages in the formulation of degradable devices for controlled release.

- Natural building blocks
- Control over polymer structure
- Control over material hydrophilic/hydrophobic balance
- Tunable material degradation rate
- Predictable degradation products
- Maintains neutral microenvironment during degradation

Figure 2: Structure of Polyester amide. The chemical structure of PEAIII and the constitutive amino acid, diol, and diacid building blocks.

Figure 1: Placement of the Drug Delivery System. A thin protein-loaded PEA fiber is to be implanted into the subconjunctival space, facilitating the local delivery of rHGH.

Conclusions

PEA fibers show excellent biocompatibility in the ocular setting. rHGH was successfully incorporated into PEA matrices through use of an innovative film formation and assembly procedure (Figure 3). Constructs were subsequently shaped into fibers with dimensions that facilitate passage through a 27 gauge needle (Figure 4).

Figure 3: Schematic representation of the lamination-based solvent extraction method used to generate high-loaded PEA films and fibers

Figure 4: Images of high-loaded PEA fiber. A. The fiber has injectable dimensions of 3 mm length and diameter < 0.2mm. B. SEM fiber cross-section; individual layers of the construct as well as homogenous solid protein dispersion is visible.

Figure 5: Cumulative release of rHGH from multi-layer PEA devices. The conc. of rHGH in the release medium was determined by IEC-HPLC. The release is expressed in percentage of theoretical rHGH load. In multi-layer construct design reveal the potential to sustain the release of rHGH for multiple weeks.

References