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SYMPOSIUM

A Review of the Development of a Vehicle for Localized and Controlled Drug Delivery for Implantable Biosensors

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Abstract

A major obstacle to the development of implantable biosensors is the foreign body response (FBR) that results from tissue trauma during implantation and the continuous presence of the implant in the body. The *in vivo* stability and functionality of biosensors are compromised by damage to sensor components and decreased analyte transport to the sensor. This paper summarizes research undertaken by our group since 2001 to control the FBR toward implanted sensors. Localized and sustained delivery of the anti-inflammatory drug, dexamethasone, and the angiogenic growth factor, vascular endothelial growth factor (VEGF), was utilized to inhibit inflammation as well as fibrosis and provide a stable tissue–device interface without producing systemic adverse effects. The drug-loaded polylactic-co-glycolic acid (PLGA) microspheres were embedded in a polyvinyl alcohol (PVA) hydrogel composite to fabricate a drug-eluting, permeable external coating for implantable devices. The composites were fabricated using the freeze–thaw cycle method and had mechanical properties similar to soft body tissue. Dexamethasone-loaded microsphere/hydrogel composites were able to provide anti-inflammatory protection, preventing the FBR. Moreover, concurrent release of dexamethasone with VEGF induced neoangiogenesis in addition to providing anti-inflammatory protection. Sustained release of dexamethasone is required for the entire sensor lifetime, as a delayed inflammatory response developed after depletion of the drug from the composites. These studies have shown the potential of PLGA microsphere/PVA hydrogel-based composites as drug-eluting external coatings for implantable biosensors.

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Abbreviations: (AUC) area under the curve, (C_{max}) maximum concentration, (FBR) foreign body response, (H&E) hematoxylin and eosin, (HA) humic acid, (IV) intravenous, (MW) molecular weight, (PAA) polyacrylic acid, (PBS) phosphate-buffered saline, (PLGA) polylactic-co-glycolic acid, (PVA) polyvinyl alcohol, (RSA) rat serum albumin, (s.c.) subcutaneous, (t_{max}) time required to achieve the maximum concentration, (VEGF) vascular endothelial growth factor

Keywords: biosensor, continuous release, dexamethasone, foreign body reaction, neoangiogenesis, implants, localized delivery, microspheres

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