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ORIGINAL ARTICLES

"Smart Tattoo" Glucose Biosensors and Effect of Coencapsulated Anti-Inflammatory Agents

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Abstract

Background:

Minimally invasive glucose biosensors with increased functional longevity form one of the most promising techniques for continuous glucose monitoring. In the present study, we developed a novel nanoengineered microsphere formulation comprising alginate microsphere glucose sensors and anti-inflammatory-drug-loaded alginate microspheres.

Methods:

The formulation was prepared and characterized for size, shape, *in vitro* drug release, biocompatibility, and *in vivo* acceptability. Glucose oxidase (GOx)- and Apo-GOx-based glucose sensors were prepared and characterized. Sensing was performed both in distilled water and simulated interstitial body fluid. Layer-by-layer self-assembly techniques were used for preventing drug and sensing chemistry release. Finally, *in vivo* studies, involving histopathologic examination of subcutaneous tissue surrounding the implanted sensors using Sprague–Dawley rats, were performed to test the suppression of inflammation and fibrosis associated with glucose sensor implantation.

Results:

The drug formulation showed 100% drug release with in 30 days with zero-order release kinetics. The GOx-based sensors showed good enzyme retention and enzyme activity over a period of 1 month. Apo-GOx-based visible and near-infrared sensors showed good sensitivity and analytical response range of 0–50 mM glucose, with linear range up to 12 mM glucose concentration. *In vitro* cell line studies proved biocompatibility of the material used. Finally, both anti-inflammatory drugs were successful in controlling the implant–tissue interface by suppressing inflammation at the implant site.

Conclusion:

The incorporation of anti-inflammatory drug with glucose biosensors shows promise in improving sensor biocompatibility, thereby suggesting potential application of alginate microspheres as "smart tattoo" glucose sensors with increased functional longevity.

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Abbreviations: (CB) competitive binding, (DI) distilled, (FITC) fluorescein isothiocyanate, (FITCD) fluorescein isothiocyanate dextran, (FRET) fluorescence resonance energy transfer, (GOx) glucose oxidase, (LbL) layer-by-layer, (MW) molecular weight, (NIR) near-infrared, (PAH) poly(allylamine hydrochloride), (PBS) phosphate buffered saline, (PSS) sodium poly(styrene sulfonate), (Ru(dpp)) ruthenium-tris(4,7-diphenyl-1,10-phenanthroline) dichloride, (SIF) simulated interstitial fluid, (TRITC) tetramethyl rhodamine isothiocyanate, (TRM) tissue response modifier, (w/v) weight in volume

Keywords: alginate, anti-inflammatory drugs, controlled release, glucose sensing, layer-by-layer self-assembly

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