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ORIGINAL ARTICLES

Development of Novel Glucose Sensing Fluids with Potential Application to Microelectromechanical Systems-Based Continuous Glucose Monitoring

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Abstract

Background:

We have previously presented a microelectromechanical systems (MEMS) viscometric sensor for continuous glucose monitoring. The sensing fluid used therein was based on protein concanavalin A, which is known to have significant drawbacks, such as immunotoxicity and instability. To address this issue, a stable, biocompatible polymeric sensing fluid has been developed.

Methods:

In the polymeric sensing system, glucose reversibly formed strong ester bonds with the phenylboronic acid moiety on the poly(acrylamide-*ran*-3-acrylamidophenylboronic acid) (PAA-*ran*-PAAPBA) polymer backbone, resulting in cross-linking of the copolymers and an increase in the solution viscosity. The copolymers were synthesized via classic free radical copolymerization processes. The viscosity of the PAA-*ran*-PAAPBA, dissolved in phosphate-buffered saline buffer and in the presence of glucose at physiologically relevant concentrations, was measured by an Ubbelodhe viscometer and a prototype MEMS viscometric device.

Results:

Experimental results showed that the polymer molecular weight and composition depended on the solvent quantity, while the sensing fluid viscosity was determined by the polymer molecular weight and percentage composition of PAAPBA. The study of the temperature effect on viscosity showed that the polymer sensed glucose effectively under physiological conditions, although the high temperature lowered its sensitivity. Through proper adjustment of these parameters, a distinctive viscosity increase was observed when the glucose concentration increased from 0 to 450 mg/dl, which was detectable by our prototype MEMS device.

Conclusions:

We have successfully developed a stable, biocompatible polymeric system for the sensitive detection of glucose. MEMS experiments demonstrated that the sensing fluid was able to sense glucose at different concentrations. This sensing system can potentially enable highly reliable, continuous monitoring of glucose in interstitial fluid from subcutaneous tissue.

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Abbreviations: (AAPBA) *N*-3-acrylamidophenylboronic acid, (AIBN) 2,2′-azodiisobutyronitrile, (CGM) continuous glucose monitoring, (^{13}C NMR) carbon nuclear magnetic resonance, (Con A) concanavalin A, (DMSO) dimethyl sulfoxide, (^{1}H NMR) proton nuclear magnetic resonance, (ISF) interstitial fluid, (MEMS) microelectromechanical systems, (M_w) molecular weights, (NPAA) *N*-phenylacrylamide, (PAA-*ran*-PAAPBA) poly(acrylamide-*ran*-3-acrylamidophenylboronic acid), (PAA-*ran*-PNPAA) poly(acrylamide-*ran*-*N*-phenylacrylamide), (PBA) 3-aminophenylboronic acid, (PBS) phosphate-buffered saline

Keywords: affinity biosensors, boronic acid, copolymer, glucose sensing, MEMS

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