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ORIGINAL ARTICLE

A Fluorescent Responsive Hybrid Nanogel for Closed-Loop Control of Glucose

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Abstract

Background:

The concept of closed-loop control of glucose, in which continuous glucose sensing is coupled to a fully automated insulin delivery device, without human input, has been an attractive idea for diabetes management. This study presents a new class of hybrid nanogels that can integrate glucose sensing and glucose-responsive insulin release into a single nano-object.

Methods:

Zinc oxide@poly[N-isopropylacrylamide (NIPAM)-acrylamide (AAm)- 2-aminomethyl-5-fluorophenylboronic acid (FPBA)] hybrid nanogels were synthesized and investigated for size, morphology, volume phase transition, photoluminescence properties, and *in vitro* insulin release under different glucose concentrations. Glucose sensing was performed both in phosphate-buffered saline (PBS) and in blood samples. The insulin release in PBS of varying glucose levels, as well as a stepwise treatment between two glucose levels (126.0 and 270.0 mg/dl), was performed to test the glucose-responsive insulin release ability of the hybrid nanogels.

Results:

Zinc oxide@poly(NIPAM-AAm-FPBA) hybrid nanogels can sensitively and selectively detect glucose in highly reproducible fluorescent signals over the clinically relevant glucose concentration range of 18–540 mg/dl. The glucose-responsive volume phase transition of the nanogels can further regulate the release of the preloaded insulin. The insulin release from the nanogels exhibits the slowest rate (~5% released in 76 h) at a normal glucose level (108.0 mg/dl) but becomes quicker and quicker as the glucose increases to higher and higher levels.

Conclusions:

The rationally designed hybrid nanogel can optically signal the glucose level with high sensitivity and selectivity and simultaneously regulate the insulin release rate in response to the glucose reading, which shows a promising concept toward the development of a miniaturized closed-loop glycemic control system.

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Abbreviations: (AA) acrylic acid, (AAm) acrylamide, (EDC) N-(3-dimethylaminopropyl)-N´-ethyl-carbodiimide hydrochloride, (FPBA) 2-aminomethyl-5-fluorophenylboronic acid, (IFG) impaired fasting glucose, (NaOH) sodium hydroxide, (NIPAM) N-isopropylacrylamide, (NP) nanoparticle, (PBS) phosphate-buffered saline, (PL) photoluminescence, (QD) quantum dot, (R_h) hydrodynamic radius, (UV-Vis) ultraviolet–visible, (ZnO) zinc oxide

Keywords: fluorescent, glucose sensor, hybrid nanogel, responsive, self-regulated insulin release

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