Phenylboronic Acid-based Composite Hydrogel Microneedles for Multifunctional Glucose-responsive Transdermal Insulin Delivery

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Abstract

Poor compliance with conventional insulin injection therapy has driven interest in microneedle-mediated transdermal delivery, which combines the advantages of percutaneous and injectable administration. However, long-term application of microneedles can induce localized tissue damage, including infection, oxidative stress, and inflammation. To address these challenges, this study integrates skin-repair biomaterials with glucose-responsive microneedle technology. A phenylboronic acid-based composite glucose-sensitive microneedle system was developed by blending phenylboronic acid-modified quaternized chitosan (QCS-FPBA) with polyvinylpyrrolidone (PVP), polyvinyl alcohol (PVA), epigallocatechin gallate (EGCG), and insulin (INS). This integrated system simultaneously confers antibacterial, antioxidant, anti-inflammatory, and skin-regenerative functionalities. The hydrogel microneedles were comprehensively evaluated through systematic physicochemical characterization, *in vitro* biological assays, and *in vivo* pharmacodynamic studies to assess their morphology, biological effects, and glucose-responsive performance. Experimental results demonstrated that the three composite hydrogels constructed with QCS-FPBA as the core component all formed dynamic and reversible crosslinked networks. Notably, the QCS-FPBA-25-PVP-PVA-EGCG hydrogel exhibited optimal glucose sensitivity, and the fabricated microneedles exhibited uniform morphology and robust mechanical strength. The synergistic antioxidant, anti-inflammatory, and antibacterial efficacy of the system, arising from the cooperative action of boronate ester bonds, quaternized chitosan, and EGCG, was validated through DPPH radical scavenging assays, fluorescent probe analysis, ELISA, and antimicrobial testing. Preliminary biocompatibility was established *via* CCK-8 cytotoxicity assays, hemolysis tests, and histological staining. *In vivo* pharmacodynamic studies demonstrated that the microneedles enabled sustained and dynamic glycemic regulation under the "three-meal-per-day" mode. Collectively, this phenylboronic acid-based composite glucose-sensitive hydrogel microneedle system integrates exceptional glucose-responsive drug release with robust antioxidant, anti-inflammatory, and antibacterial functionalities, effectively mitigating localized adverse reactions associated with long-term transdermal microneedle application, and holds substantial promise for intelligent transdermal drug delivery in diabetes management.

Keywords

Glucose-sensitive Microneedles, Phenylboronic Acid Hydrogel, Intelligent Insulin Delivery, Antioxidant, Anti-inflammatory