Sustainable Self-Healing Pectin-Based Hydrogels for Controlled Release of Curcumin-Loaded Zein Nanoparticles for Antioxidant Wound Treatment

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Introduction

Oxidative stress is a major barrier to effective tissue regeneration, making antioxidant therapies a promising approach for wound healing. Curcumin, a natural antioxidant, has shown significant potential in reducing oxidative stress across various clinical applications. However, its poor water solubility limits its therapeutic effectiveness, necessitating its encapsulation within drug delivery systems (DDS) to enhance bioavailability. A hybrid approach combining nanoparticles (NPs) with hydrogels has emerged as an innovative strategy to optimize drug delivery [1]. In this context, zein NPs, derived from corn agricultural waste, act as biodegradable carriers for curcumin, while pectin hydrogels, sourced from citrus peels, serve as a sustainable drug delivery matrix. This work aims to develop sustainable hybrid NP-hydrogel DDS based on injectable pectin-based hydrogels for the delivery of antioxidant zein NPs for enhanced wound healing.

Materials and Methods

Curcumin-loaded zein NPs (CurZNPs) were produced via nanoprecipitation and characterized for their physicochemical properties, release kinetics and antioxidant activity [2]. To develop injectable pectin-based hydrogels, oxidized pectin (PDA) was synthesized at two oxidation levels (PDA_2.5 and PDA_5) to introduce reactive aldehyde groups and was then blended with modified gelatin (G-m) to create chemically crosslinked hydrogels [3]. These PDA/G-m hydrogels were optimized by analyzing rheological properties, stability and cytocompatibility, as well as their injectability and self-healing behavior. CurZNPs were subsequently incorporated into PDA/G-m hydrogels and their release kinetics were evaluated to determine the optimal system. Finally, the therapeutic efficacy of CurZNP-loaded PDA/G-m hydrogels was assessed for wound healing applications.

Results

CurZNPs showed high encapsulation efficiency (85%), a sustained release profile and strong antioxidant activity (SC50 of 7 µg/mL). The oxidation levels of pectin (PDA_2.5 and PDA_5) were confirmed using a colorimetric assay, yielding oxidation degrees of 2.3% and 4.5%, respectively. Rheological characterizations, degradation studies and biocompatibility tests guided the selection of optimal PDA/G-m hydrogel compositions, identifying PDA_2.5/G-m (70:30) and PDA_5/G-m (50:50) as the most promising candidates due to their injectability and self-healing properties. When CurZNPs were embedded within PDA/G-m hydrogels, PDA_2.5/G-m (70:30) exhibited the most sustained release, maintaining curcumin availability for up to 28 days. The therapeutic efficacy of the formulation was validated through HFF-1 cell viability assays, where pre-treatment with CurZNP-loaded PDA_2.5/G-m (70:30) hydrogels successfully mitigated induced oxidative stress effects after 7 days.

Discussion

This study aimed to develop a sustainable hybrid NP-hydrogel DDS capable of safe, effective, and controlled drug release for local therapeutic applications.

Zein and pectin were selected as green biomaterials for nanoparticle and hydrogel fabrication, respectively. CurZNPs were formulated using nanoprecipitation, minimizing the use of organic solvents, and demonstrating high encapsulation efficiency and antioxidant activity. Oxidized pectin (PDA) was combined with modified gelatin (G-m) to produce chemically crosslinked injectable hydrogels, with two compositions—PDA_2.5/G-m (70:30) and PDA_5/G-m (50:50)—selected for their tunable mechanical properties, injectability, and biocompatibility. Incorporating CurZNPs into these hydrogels enabled prolonged curcumin release, particularly with PDA_2.5/G-m (70:30). The final NP-hydrogel DDS successfully restored HFF-1 viability after oxidative stress, demonstrating superior therapeutic efficacy compared to free CurZNPs.

Conclusions

The results confirm that PDA/G-m hydrogels are a promising platform for in situ delivery of CurZNPs in wound healing applications. Future research will focus on expanding the potential of this antioxidant DDS for various clinical applications, paving the way for innovative and sustainable drug delivery systems designed for antioxidant and anti-inflammatory therapies.

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