Construction of Chlorogenic Acid-Functionalized Stimuli-Responsive Hydrogel and Its Promoting Effect on Diabetic Wound Healing

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Abstract

Diabetic chronic wounds are often characterized by delayed healing, dysregulated inflammation, and excessive oxidative stress, and there is still a lack of safe and effective therapeutic strategies in clinical practice. In this study, a stimuli-responsive hydrogel loaded with chlorogenic acid (CGA) was designed and constructed. Through material structure optimization and regulation of biological activities, the hydrogel was endowed with synergistic antioxidant, anti-inflammatory, and pro-healing effects targeting the wound microenvironment. Systematic characterization results showed that the hydrogel possessed a three-dimensional interconnected porous structure, good swelling properties, and mechanical stability, and enabled sustained and stable release of chlorogenic acid. In vitro cell experiments demonstrated that the hydrogel extract exhibited no significant cytotoxicity against mouse embryonic fibroblasts (L929), indicating excellent biocompatibility. In a streptozotocin-induced diabetic mouse model with full-thickness excisional wounds, CGA-functionalized hydrogel significantly accelerated wound closure, with a healing rate of ~98% at day 14 post-surgery, outperforming blank controls, blank hydrogels, and commercial wound dressings. Moreover, this hydrogel significantly reduced local reactive oxygen species (ROS) levels and the expression of inflammatory cytokines (TNF-α, IL-6) at the wound site, promoted angiogenesis and the polarization of macrophages from the M1 toward the M2 phenotype, thereby remodeling the wound immune microenvironment and accelerating tissue regeneration and repair. In summary, the chlorogenic acid-functionalized hydrogel constructed in this study possesses good biocompatibility, antioxidant and anti-inflammatory capabilities, and efficient wound healing performance. It provides a safe, simple, and effective new material and strategy for the treatment of chronic refractory diabetic wounds, showing promising clinical translation prospects in the fields of skin tissue engineering and wound repair.

Keywords

Stimuli-responsive Hydrogel, Chlorogenic Acid, Diabetic Wound, Antioxidant, Wound Healing