Development of biodegradable hydrogels as epidermal growth factor carrier for chronic wound healing

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Growth factors, a promising approach to chronic wound healing, have great potential as therapeutic proteins because of the specific structure and highly selectivity. Most of the current researches related to wound healing formulations used natural and synthetic polymers as controlled drug delivery system, usually with a degradation time up to tens of days. However, it's common practice in wound care to replace the dressing and clean the wound area in a few days to ensure the effectiveness of the dressing and to prevent microbial infection. The objective of this study was to design biodegradable hydrogel systems which degrade within 1 to 7 days, and to apply the system for a topical recombinant human epidermal growth factor (rhEGF) delivery system for wound healing.

Hydrogels composed of natural, biodegradable materials were fabricated, and characterized with scanning electron microscopy and Fourier transform infrared spectroscopy. The swelling, in vitro degradation properties and drug release of the hydrogels were also investigated. The effectiveness of rhEGF-loaded hydrogels was evaluated in a full-thickness wound model in streptozotocin-induced diabetes mice. The animals were divided into six groups: (i) PBS control, (ii) rhEGF solution, (iii) once daily hydrogel, (iv) once daily rhEGF-loaded hydrogel, (v) once every-3-day hydrogel, (vi) once every-3-day rhEGF-loaded hydrogel, and treated for six days.

The results revealed that the natural-biodegradable-materials-based hydrogels have interconnected pores (20-300 μm in diameter) with good swelling properties and biodegradability. The swelling ratio and degradation rate decreased with the concentration of cross-linker content in hydrogel preparations. Release of rhEGF from hydrogels was sustained in a short term through diffusion and degradation. Overall healing effects on diabetic mouse model treated with rhEGF-loaded hydrogels was significantly superior to PBS control group (p<0.001), and once every-3-day rhEGF-loaded hydrogel significantly improved wound healing in comparison with other treatment groups (p<0.001). There was no significant difference between rhEGF solution group and PBS control group. The once every-3-day rhEGF-loaded hydrogels demonstrated promising wound healing effect and improved collagen deposition. The result suggested that the frequency of administration has a critical role in wound management and the developed hydrogels meet the needs for clinical practice, which have potential application as protein drug delivery system platform for wound healing.