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Enhancement of curcumin wound healing ability by complexation with 2-hydroxypropyl-γ-cyclodextrin in sacran hydrogel film

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ABSTRACT

Curcumin is one of promising agents to accelerate the wound-healing process. However, the efficacy of curcumin is limited due to its poor water solubility and stability. To enhance the properties of curcumin, 2-hydroxypropyl-γ-cyclodextrin (HP-γ-CyD) can be used through complexation. Recently, we revealed that sacran has the potential to form a hydrogel film (HGF) as a wound dressing material. Therefore, in the present study, we investigated the wound healing ability of curcumin/HP-γ-CyD (Cur/HP-γ-CyD) complex in sacran-based HGF (Sac-HGF). We prepared the Cur/HP-γ-CyD complex in Sac-HGF without surface roughness. Additionally, the amorphous form in the Cur/HP-γ-CyD complex in Sac-HGF were observed. In contrast, the curcumin in Sac-HGF and curcumin/HP-γ-CyD physical mixture in Sac-HGF formed inhomogeneous films due to crystallization of curcumin. Furthermore, HP-γ-CyD played an important role to increase the elastic modulus of the Sac-HGF with high re-swelling ability. The Cur/HP-γ-CyD complex in Sac-HGF maintained antioxidant properties of curcumin. Curcumin was gradually released from the HP-γ-CyD complex in Sac-HGF. Notably, the Cur/HP-γ-CyD complex in Sac-HGF provided the highest wound healing ability in hairless mice. These results suggest that the Cur/HP-γ-CyD complex in Sac-HGF has the potential for use as a new transdermal therapeutic system to promote the wound-healing process.

1. Introduction

Wound healing is a series of complex and sophisticate physiological responses consisting of the four different phases, although some of the phases are partially overlying. The first coagulation phase begins immediately after wound injury by releasing clotting factors, platelet-derived growth factor and transforming growth factor-β, to initiate the repair process. Then, the second inflammation phase is initiated by neutrophils for wound cleansing and developed under the influence of macrophages that release proinflammatory cytokines. In the third proliferative phase, fibroblasts proliferate and synthesize extracellular matrix (ECM) components in the presence of newly formed blood vessels. The final remodeling phase includes formation of cellular connective tissue and establishment of newly shaped epithelium [1–3]. However, an impaired healing process occurs in chronic wounds with a persistent inflammation, an insufficient ECM synthesis and neovascularization. An exceed fabrication of oxygen free radicals and other reactive oxygen species (ROS) as secondary products of pro-inflammatory mediators causes an impairment of wound healing [4]. Therefore, several drugs with specific delivery system have been extensively investigated to manage a balance by reducing the ROS levels at wound site.

Curcumin, a main curcuminoid present in rhizome of *Curcuma longa* L., has several biological activities such as antioxidant, anti-inflammatory, anticoagulant and anti-infection effects [5]. In addition, curcumin exhibits the scavenging action against the peroxy radicals, and inhibits hydrogen peroxide (H_2O_2)-induced damage to keratinocytes and fibroblasts [6,7]. However, the therapeutic efficacy of curcumin is limited due to its poor water solubility, photosensitivity, poor bioavailability, and extensive first pass metabolism [8,9]. Therefore, an improvement in solubility and stability of curcumin is required.

Cyclodextrins (CyDs), cyclic (α-1,4)-linked oligosaccharides of α-D-glucopyranose, have hydrophilic cavity exteriors and

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