ANTIBACTERIAL WOUND HEALING GELS FROM OLIGOCHITOSAN SALTS

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Abstract

Background: Wound healing process is a complex series of events that starts after injuries. The natural wound healing process could be retarded if the wound becomes infected. A number of wound healing materials have been developed to protect wounds from bacterial infection and provide a moist and healing environment. Chitosan is a versatile biopolymer. Its intriguing biological properties, e.g., antimicrobial activity, ability to promote wound healing, biodegradability and biocompatibility, have drawn a great deal of attention for its uses in wound healing applications. It was previously reported that the positive charge of chitosan ammonium salt could interact with the bacterial membrane, resulting in cell death.

Objectives: The objectives of this study were to develop and evaluate the in vitro and in vivo biologicalproperties of oligochitosan salts-based antibacterial wound healing gels.

Methods: Oligochitosan (OCS), Mn ≈ 4.5 kDa (determined by GPC) and deacetylation of 95.5% (determined by 1H-NMR), was directly prepared from chitosan according to the method described in the literature [4]. L-glutamic acid (Glu), L-aspartic acid (Asp) and malic acid (Mli) were purchased from Fluka, whereas malonic acid (Mlo) and succinic acid (Suc) were purchased from Acros. Guar gum (GG) was purchased from Behn Meyer Chemical. All reagent-grade chemicals, including acetic acid (Ac) and hydrochloric acid (HCl), were used as received. Intrasite, a commercial gel product of Smith & Nephew, was also used as received.

Results: The OCHAsp and OCHHCl salts were then selected and used in the preparation of two different antibacterial wound gels by mixing with crosslinked guar gum (GG): the first gel composed of OCHAsp was denoted as GG(OCHAsp), while the other one composed of OCHHCl was denoted as GG(OCHHCl). After S. epidermidis was in contact with each of the wound gels for 24 h, all the bacteria were destroyed completely. GG(OCHHCl) could also absolutely kill E. Coli, when GG(OCHAsp) could markedly kill E. Coli more than 99% of the initial bacterial population. The positive charges of the OCS salts in the gel instantaneously interacted with negatively charged molecules at the bacterial cell surface, resulting in the cell death. At the early stage of wound healing, all wounds became swollen; the % remaining wound areas appeared greater than 100% at day 5. During these five days, the wounds were essentially in the inflammatory phase. At prolonged healing time, the wounds were healed more progressively; the % remaining wound areas decreased significantly.

GG(OCHHCl) healed the wounds more slowly than GG(OCHAsp), but more quickly than Intrasite. All the wounds were closed within 14 days with the treatment of the wound gels, while the wounds treated with Intrasite were still incompletely closed within 17 days. About 2.1% wound area still remained in the wounds treated with Intrasite. These findings strongly suggested that, compared with Intrasite, the OCS salt-based wound gels could promote the wound healing more effectively.

Conclusions: The prepared OCS salts demonstrated different MIC values, in the range of 16-256 µg/mL. They appeared non-cytotoxic to the fibroblasts. Among all of the salts, OCHAsp and OCHHCl could stimulate the production of IL-8 by the fibroblasts. The two prepared antibacterial wound healing gels, i.e., GG (OCHAsp) and GG(OCHHCl), could also effectively inhibit the growth of S. epidermidis and E. Coli. Moreover, they promoted the proliferation of the fibroblasts and stimulated the production of IL-8 by the fibroblasts in the 3-D collagen gels. In the animal model, the full thickness excisional wounds in the Wistar rats were completely closed when treated with each wound gel within 14 days, when more than 17 treating days were required for the wound closure with the use of Intrasite.

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