Antibacterial Activity and Wound Healing Effect of Nitric Oxide (NO)-Releasing Chitosan Film

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Purpose
Since nitric oxide (NO) is known to have antibacterial activity and promote wound healing, NO is a promising therapeutic agent for treating wound. Due to its gaseous property and a very short half-life, however, specific topical formulations that store and release NO in a controlled manner is required. In this study, we have developed NO-releasing chitosan (CS/NO) films that can be applied on wounds. The CS/NO films were composed of chitosan as a film-forming polymer and S-nitrosoglutathione (GSNO) as a NO donor.

Methods
The films were prepared by blending chitosan and glycerol with GSNO (CS/NO films) or without GSNO. The surface morphology of the films was examined by scanning electron microscopy (SEM). Thermal properties of the pure GSNO and the films were analyzed using differential scanning calorimetry (DSC). Tensile strength and percentage elongation at break were measured using a tensile test machine to characterize mechanical properties of the films. GSNO stability in the films was studied under various storage conditions. The NO released from the GSNO was measured by the Griess method. Antibiofilm activities were tested against Pseudomonas aeruginosa and Staphylococcus aureus. Wound healing activity was determined in rats using excision wounds models.

Results
SEM images showed that the CS/NO film had homogenous and smooth surface morphology. In DSC study demonstrated a molecular dispersion of GSNO in the films. NO was released from the CS/NO film following the first-order kinetic pattern for 48 hrs. GSNO in the films were stable at 4°C for 30 days. In antibiofilm study, the CS/NO film notably decreased the number of bacteria compared with films without GSNO. The CS/NO film enhanced wound healing rate and accelerated the epithelialization rates. Furthermore, histopathological studies showed that the CS/NO films favorably aid the re-epithelization and reconstruction of skin.

Conclusion
The results confirmed that the NO-releasing films have antibacterial and wound healing activities. Therefore, the CS/NO film is a promising formulation for treating full-thickness wounds.