

# Investigation of the Potential of Nebivolol Hydrochloride-Loaded Chitosomal Systems for Tissue Regeneration: In Vitro Characterization and In Vivo Assessment

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## Abstract

In this study, we evaluated the synergistic effect of nebivolol hydrochloride (NVH), a third-generation beta-blocker and NO donor drug, and chitosan on the tissue regeneration. Ionic gelation method was selected for the preparation of NVH-loaded chitosomes using chitosan lactate and sodium tripolyphosphate. The effect of different formulation variables was studied using a full factorial design, and NVH entrapment efficiency percentages and particle size were selected as the responses. The chosen system demonstrated high entrapment efficiency (73.68%±3.61%), small particle size (404.05±11.2 nm), and good zeta potential value (35.6±0.25 mV). The best-achieved formula demonstrated spherical morphology in transmission electron microscopy and amorphization of the crystalline drug in differential scanning calorimetry and X-ray diffraction. Cell culture studies revealed a significantly higher proliferation of the fibroblasts in comparison with the drug suspensions and the blank formula. An in vivo study was conducted to compare the efficacy of the proposed formula on wound healing. The histopathological examination showed the superiority of NVH-loaded chitosomes on the wound proliferation and the non-significant difference in the collagen deposition after 15 days of the injury to that of intact skin. In conclusion, NVH-loaded chitosomes exhibited promising results in enhancing skin healing and tissue regeneration.

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