Title : Nisin-conjugated Liposomes Encapsulated with Doxorubicin as a Delivery System

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ABSTRACT

Conventional drug delivery systems continue to face major limitations, including non-specific drug distribution, toxicity to normal tissues, and inadequate control of drug release, which necessitate the use of high drug doses and increase the risk of adverse side effects. This study aims to develop a doxorubicin (dox) delivery system based on nisin-conjugated liposomes using two bioconjugation strategies, carbodiimide and thiol–maleimide methods, when nisin was selected as a ligand due to its positive charges for targeting negatively charged membrane. The physicochemical properties of non-conjugated and nisin-conjugated liposomes were compared, and the release behavior and mechanisms of dox were investigated at pH 5.5 and 7.4, using appropriate kinetic models. Liposomes were prepared by the thin-film hydration method using soybean phosphatidylcholine and cholesterol as the main components, and dox was encapsulated via a remote loading technique. The results demonstrated that liposomes prepared by both methods exhibited an encapsulation efficiency of 99%. Nisin conjugation efficiencies obtained by the carbodiimide and thiol–maleimide methods were approximately 86% and 53–54%, respectively. Dynamic light scattering analysis revealed that the liposomes had an average particle size of approximately 120 nm with a narrow size distribution. Drug release studies were conducted using a dialysis method in a sodium phosphate buffer at pH 5.5 and 7.4 at 37°C for 8 days, and the release mechanisms were analyzed using the Korsmeyer–Peppas kinetic model. The results indicate that liposomes conjugated via the thiol–maleimide method exhibited slower and more controlled drug release profile, particularly under acidic condition that simulated the cancer microenvironment. These findings highlight the potential of nisin-conjugated liposomes as a controlled dox delivery system. Further studies at the cellular and animal levels would help to validate the efficacy and safety of the developed system and support its future medical application.

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