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Preparation of mucoadhesive methacrylated chitosan nanoparticles for delivery of ciprofloxacin

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ABSTRACT

Mucoadhesive polymers and their nanoparticles have attracted a lot of attention in pharmaceutical applications, especially transmucosal drug delivery (TDD). Mucoadhesive polysaccharide-based nanoparticles, particularly chitosan, and its derivatives, are widely used for TDD owing to their outstanding features such as biocompatibility, mucoadhesive, and absorption-enhancing properties. Herein, this study aimed to design potential mucoadhesive nanoparticles for the delivery of ciprofloxacin based on methacrylated chitosan (MeCHI) using the ionic gelation method in the presence of sodium tripolyphosphate (TPP) and compared them with the unmodified chitosan nanoparticles. In this study, different experimental conditions including the polymer to TPP mass ratios, NaCl, and TPP concentration were changed to achieve unmodified and MeCHI nanoparticles with the smallest particle size and lowest polydispersity index. At 4:1 polymer /TPP mass ratio, both chitosan and MeCHI nanoparticles had the smallest size (133 ± 5 nm and 206 ± 9 nm, respectively). MeCHI nanoparticles were generally larger and slightly more polydisperse than the unmodified chitosan nanoparticles. Ciprofloxacin-loaded MeCHI nanoparticles had the highest encapsulation efficiency (69 ± 13 %) at 4:1 MeCHI /TPP mass ratio and 0.5 mg/mL TPP, but similar encapsulation efficiency to that of their chitosan counterpart at 1 mg/mL TPP. They also provided a more sustained and slower drug release compared to their chitosan counterpart. Additionally, the mucoadhesion (retention) study on sheep abomasum mucosa showed that ciprofloxacin-loaded MeCHI nanoparticles with optimized TPP concentration had better retention than the unmodified chitosan counterpart. The percentage of the remained ciprofloxacin-loaded MeCHI and chitosan nanoparticles on the mucosal surface was 96 % and 88 %, respectively. Therefore, MeCHI nanoparticles have an excellent potential for applications in drug delivery.

1. Introduction

Mucoadhesive drug delivery systems are the drug carriers which have the ability to adhere to the mucus layer covering the mucosal membranes. The mucoadhesion of the drug delivery systems increases the residence time of the drug at the site of application and/or absorption and may enhance the absorption of the drug through mucosal membranes [1–3]. Increasing the residence time of the drug achieved by mucoadhesive drug delivery systems can significantly decrease the frequency of drug administration and therefore improve the patients' compliance. These systems can also be used for targeting a drug to a specific region of the body for extended periods of time, resulting in decreased systemic drug exposure and minimizing the side effects of the drugs [2,4].

Mucoadhesive drug delivery systems include different formulations such as tablets [5], patches [6], suppositories [7,8], gels [9], liposomes [10,11], microparticles [12], and nanoparticles [13–16]. Among these, the mucoadhesive nanoparticles have attracted the attention of researchers owing to their small size, better distribution throughout the mucosal tissues, better physical stability [17,18], high drug loading [19], and feasibility for applications via different routes of administration, including oral [20,21], rectal [22], vaginal [23], nasal [24], ocular

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