Application of Nanoparticles Used for Gastric Ulcer Therapy: *In vitro and In vivo* Studies (1/3)

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Abstract

Helicobacter pylori, a gastric pathogen that colonized the human gastric mucosa, is strongly associated with several gastric diseases and gastric cancer. The most widely recommended regimen in treating *H. pylori* infection includes a triple therapy, over a period of two weeks, which combines some antibiotics and a proton pump inhibitor. But the antibiotic is not stable in the gastric acid and poor permeation across the mucus layer, which is the *H. pylori* survival situation. To overcome the above–mentioned problems, our study was to develop amoxicillin–loaded nanoparticles that could protect encapsulated amoxicillin in the environment of gastric acid and interact locally with *H. pylori* infection sites. However, the amoxicillin has low molecular weight and hydrophilic characteristics, thus the amoxicillin is difficult to load in the prepared nanoparticles. Therefore, in this study, by water-in-oil emulsification method, the chitosan/heparin nanoparticles containing the amoxicillin were successfully obtained and the particle size of nanoparticles was 200–300 nm, with positive surface charge. The transmission electron microscopy also showed the prepared nanoparticles were stable at pH 1.2–2.5 environment, allowing protecting the incorporated drug from destructive gastric acid. The prepared nanoparticles showed high encapsulation capability of amoxicillin and provided great drug release ability at different pH values (pH 1.2–7.0, simulating gastric acid, gastric mucosa and the *H. pylori* survival situation). In addition, the cell viability evaluation by the MTT assay had proved that the prepared nanoparticles by using the emulsion method had no any signification toxicity to human gastric mucosal AGS cell line (human gastric adenocarcinoma cell line). The confocal microscopy analysis that the amoxicillin-loaded chitosan/heparin nanoemulsion particles localized specifically to intercellular spaces or the cell cytoplasm, the site of *H. pylori* infection, and significantly increased *H. pylori* growth inhibition compared with amoxicillin alone. Results of *in vivo* clearance assays indicated that amoxicillin-loaded chitosan/heparin nanoemulsion particles had a more complete *H. pylori* clearance effect on induced gastric *H. pylori* infection mice compared with amoxicillin alone.

Keywords: emulsification, nanoparticles, amoxicillin, *Helicobacter pylori*