Formulation and Evaluation of Amoxicillin-Loaded Nanoemulsions Using for *Helicobacter pylori* Eradication

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Introduction

For effective *H. pylori* eradication, the standard treatment in the case is a combination of drugs, including antibiotics and a proton pump inhibitor[1)]. The failure of antibiotic therapies could be attributable to the poor stability in the gastric acid, and the poor permeation of antibiotic across the mucus layer, where sufficient drug must diffuse to the bacteria[2)]. We prepared nanoemulsion particles could encapsulate amoxicillin and infiltrate into the mucus layer, subsequently, amoxicillin release from amoxicillin-loaded nanoemulsion particles, then directly acts locally on *H. pylori* at a bactericidal concentration (Figure 1a). We investigated amoxicillin release characteristics from the nanoemulsion particles and examined the inhibition of *H. pylori* growth. The effect of the nanoemulsion particles and their mechanism of interaction with *H. pylori* were investigated in the human gastric adenocarcinoma cell line with confocal laser scanning microscopy. We also assessed the *in vivo* clearance effect of amoxicillin-loaded chitosan/heparin nanoemulsion particles in *H. pylori* infected mice.

Results and Discussion

H. pylori colonizes the human gastric mucus layer and adheres to surface epithelial cells, it produces a vacuolating cytotoxin with the ability to modulate the integrity of the epithelium. *H. pylori* may preferentially adhere not only to the gastric epithelium surface, but also close to the tight junctions of gastric mucous cells[3)]. The ideal antibiotic dose for *H. pylori* eradication must not only localize in the stomach, but must also interact locally with the bacterium.

In our study of the relationship between amoxicillin-loaded chitosan/heparin nanoemulsion particles and *H. pylori* (Figure 1b), we used CLSM to show that prepared fluorescent FA-amoxicillin loaded in Cy3-chitosan/heparin nanoemulsion particles (Cy3-chitosan: red spot, FA-amoxicillin: green spot) co-localized and interacted locally at sites of *H. pylori* infection. To improve the efficacy of anti-*H. pylori* agents, antibiotics need to localize at the *H. pylori* infection site in the gastric epithelium. As shown Campylobacter-like organism test in Figure 1c, the clearance of *H. pylori in vivo* was observed with doses amoxicillin in amoxicillin–loaded chitosan/heparin nanoemulsion particles; the clearance rate showed a more complete *H. pylori* clearance effect than with amoxicillin alone.

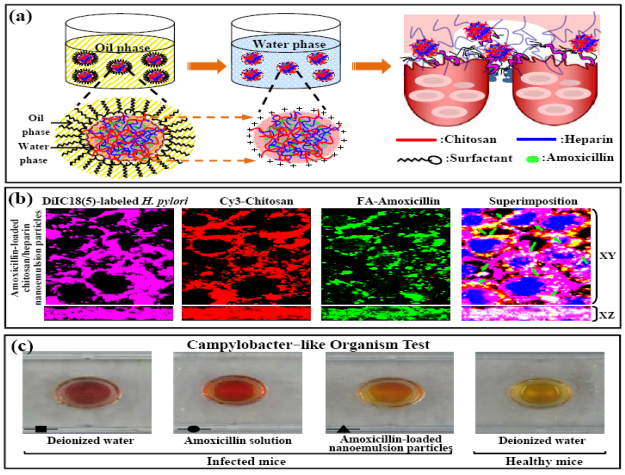

Figure 1. (a)A representation for particles for eradicating *H. pylori*. (b)Fluorescent images of AGS cell infected with fluorescent *H. pylori* and nanoemulsion particles. (c)Effects of amoxicillin-nanoemulsion particles in *H. pylori*-induced gastric infection mouse model.

Reference

1) van der Hulst, RW. et al. Helicobacter. **1996**, *1*, 6.
2) Endo, H. et al. J Antimicr. Chem. **2001**, *48*, 923.
3) Patel, JK. et al. Curr. Drug. Deliv. **2007**, *4*, 41.