Accepted Manuscript

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Zi-Wei Jing, Yi-Yang Jia, Ning Wan, Min Luo, Meng-Lei Huan, Tai-Bin Kang, Si-Yuan Zhou, Bang-Le Zhang

PII: S0142-9612(16)00059-4

DOI: 10.1016/j.biomaterials.2016.01.045

Reference: JBMT 17321

To appear in: *Biomaterials*

Received Date: 17 October 2015

Revised Date: 17 January 2016

Accepted Date: 21 January 2016

Please cite this article as: Jing Z-W, Jia Y-Y, Wan N, Luo M, Huan M-L, Kang T-B, Zhou S-Y, Zhang B-L, Design and evaluation of novel pH-sensitive ureido-conjugated chitosan/TPP nanoparticles targeted to *Helicobacter pylori*, *Biomaterials* (2016), doi: 10.1016/j.biomaterials.2016.01.045.

Design and evaluation of novel pH-sensitive ureido-conjugated chitosan/TPP nanoparticles targeted to *Helicobacter pylori*

Zi-Wei Jing [1], Yi-Yang Jia [1], Ning Wan, Min Luo, Meng-Lei Huan, Tai-Bin Kang, Si-Yuan Zhou, Bang-Le Zhang *

Department of Pharmaceutics, School of Pharmacy, Fourth Military Medical University, Xi'an, 710032, China

ABSTRACT

The covalently modified ureido-conjugated chitosan/TPP multifunctional nanoparticles have been developed as targeted nanomedicine delivery system for eradication of *Helicobacter pylori*. *H. pylori* can specifically express the urea transport protein on its membrane to transport urea into cytoplasm for urease to produce ammonia, which protects the bacterium in the acid milieu of stomach. The clinical applicability of topical antimicrobial agent is needed to eradicate *H. pylori* in the infected fundal area. In this study, we designed and synthesized two ureido-conjugated chitosan derivatives UCCs-1 and UCCs-2 for preparation of multifunctional nanoparticles. The process was optimized in order to prepare UCCs/TPP nanoparticles for encapsulation of amoxicillin. The results showed that the amoxicillin-UCCs/TPP nanoparticles exhibited favorable pH-sensitive characteristics, which could procrastinate the release of amoxicillin at gastric acids and enable the drug to deliver and target to *H. pylori* at its survival region effectively. Compared with unmodified amoxicillin-chitosan/TPP nanoparticles, a more specific and effective *H. pylori* growth inhibition was observed for amoxicillin-UCCs/TPP nanoparticles. Drug uptake analysis tested by flow cytometry and confocal laser scanning microscopy verified that the uptake of FITC-UCCs-2/TPP nanoparticles was associated with urea transport protein on the membrane of *H. pylori* and reduced with the addition of urea as competitive transport substrate. These findings suggest that the multifunctional amoxicillin-loaded nanoparticles have great potential for effective therapy of *H. pylori* infection. They may also serve as pharmacologically effective nanocarriers for oral targeted delivery of other therapeutic drugs to treat *H. pylori*.

Keywords*: Helicobacter pylori*; chitosan; multifunctional nanoparticles; pH-sensitive; targeted delivery

[1] These two authors contributed equally to this work.

*Corresponding author. Tel.: +86 2984776813; fax: +86 2984776813.

E-mail address: blezhang@fmmu.edu.cn (B.-L. Zhang).