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Research Article

Tea Polyphenol Liposomes Overcome Gastric Mucus to Treat Helicobacter Pylori Infection and Enhance the Intestinal Microenvironment

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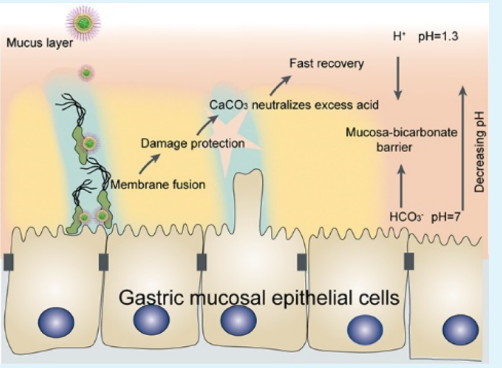
ABSTRACT: Infection with *Helicobacter pylori* (*Hp*) is one of the leading causes of stomach cancer. The ability to treat *Hp* infection is hampered by a lack of stomach gastric acid environment. This work introduces a nanoliposome that can rapidly adjust the gastric acid environment to ensure a drug's optimal efficacy. We introduce $CaCO_3$@Fe−TP@EggPC nanoliposomes (CTE NLs) that are composed of Fe^{3+} and tea polyphenols (TPs) forming complexes on the surface of internal $CaCO_3$ and then with lecithin producing a phospholipid bilayer on the polyphenols' outer surface. Through the action of iron−TP chelate, the phospholipid layer can fuse with the bacterial membrane to eliminate *Hp*. Furthermore, $CaCO_3$ can promptly consume the excessive gastric acid, ensuring an ideal operating environment for the chelate. TPs, on the other hand, can improve the inflammation and gut microbes in the body. The experimental results show that CTE NLs can quickly consume protons in the stomach and reduce the bacterial burden by 1.2 orders of magnitude while reducing the inflammatory factors in the body. The biosafety evaluation revealed that nanoliposomes have good biocompatibility and provide a new strategy for treating *Hp* infection.



KEYWORDS: *Hp infection, nanoliposomes, tea polyphenols, neutralize stomach acid, reduce inflammatory factors*

INTRODUCTION

Helicobacter pylori (*Hp*) is a Gram-negative bacterial pathogen that colonizes about 50% of the world's population and is a risk factor for developing gastric/duodenal ulcers and gastric cancer.[1] The urease produced by *Hp* can hydrolyze urea, creating a protective layer of ammonia cloud around the bacteria to resist the adverse effects of gastric acid on *Hp*.[2,3] In addition, *HP's* acid resistance and ability to neutralize acids making it resilient in acidic environments,[4] which is also considered to be a critical factor in destroying gastric mucosal cells. The injury of the gastric mucosa destroys the mucus−bicarbonate barrier and intensifies the erosion of gastric acid and pepsin on the mucosa, forming a vicious circle. Furthermore, *Hp* infection increases inflammatory factors and causes gastric tissue lesions (Scheme 1).

Due to the rising resistance to current antibiotics, the demand for new therapeutic agents that can prevent the occurrence and development of diseases has not been satisfied. The current clinical trials of *Hp* rely on at least two antibiotics (clarithromycin, amoxicillin, or metronidazole, etc.) and proton pump inhibitors (PPIs).[5,6] Unfortunately, the *Hp* mutation has evolved into resistance to clarithromycin and other macrolide medications, resulting in a high proportion of treatment failures. Therefore, the *Hp* eradication rate with a standard triple therapy has dropped significantly. On the other hand, long-term treatment is associated with adverse effects such as antibiotic resistance, reinfection, high cost, gastrointestinal side effects, and poor patient compliance.[7,8] Currently, alternative drugs and treatments for the drug resistance are being actively studied. Therefore, there is an urgent need for new methods to overcome these limitations.

Since ancient times, tea has been recognized as a traditional Chinese medicine that can improve or prevent various diseases.[9] Recent research has revealed that tea polyphenols (TPs), including epigallocatechin (EGC), epicatechin gallate (ECG), epigallocatechin gallate (EGCG), and tannic acid (TA), have antibacterial and anticancer properties.[10,11] Natural polyphenols have recently received widespread attention due to their surface adaptability and interfacial adhesion, as well as

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