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THERAPY

High-tech linolenic acid kills *Helicobacter pylori*

"*Helicobacter pylori* ... colonizes the stomachs of about half of the world's population and is a major public health concern," remarks Liangfang Zhang, a co-investigator of research innovating linolenic acid delivery to treat *H. pylori* infection. Zhang and Marygorret Obonyo's groups with expertise in nanoengineering and *H. pylori*, respectively, have teamed up and substantially improved the bactericidal activity of linolenic acid.

Zhang points out that the emergence of antibiotic-resistant strains of *H. pylori* is an alarming development and is causing a decline in rates of eradication to unacceptably low levels. The potential of linolenic acid as a safe and natural bactericide is already known; however, it has so far fallen short of its potential as a treatment option largely because it is insoluble in water, which reduces its efficacy. The researchers have overcome this hurdle by packaging linolenic acid into liposomes (LipoLLA). Liposomes loaded with linolenic acid (~100 nm) fuse with the bacterium, which incorporates the free fatty acid into the membrane, disrupts membrane integrity and kills the bacterium.

To assess LipoLLA as a potential treatment, the investigators measured its retention and distribution in the stomachs of mice. LipoLLA was detected 4 h and, to a lesser degree, 24 h after oral administration, indicating an adequate duration of retention for effective treatment. Sectioning and immunofluorescence staining of stomach tissue revealed that the free fatty acid is delivered to areas where *H. pylori* reside, namely the mucus layer and near the gastric epithelium.

To compare this formulation of linolenic acid with other treatments, mice infected with *H. pylori* were given: saline; bare liposome; triple therapy (the current antibiotic standard of care); linolenic acid (not bound in a liposome); and LipoLLA. Efficacy was determined by bacterial counts in the stomach after treatment. As expected, the negative controls (saline and bare liposome) had the highest bacterial counts compared with positive controls (linolenic acid, triple therapy and LipoLLA). The reduction in bacteria was not statistically significant with linolenic acid treatment, but was statistically significant in both the triple therapy and LipoLLA groups, compared with negative controls. Interestingly, LipoLLA treatment led to a bigger decrease in number of bacteria than triple therapy (~2.5 versus ~1.4 order of magnitude, respectively). As well as good antibacterial properties, treatment with LipoLLA reduced the mRNA expression of proinflammatory cytokines known to be upregulated by *H. pylori* infection. LipoLLA treatment did not promote abnormal histology or increase rates of apoptosis in mouse stomachs.

Creating smarter liposomes to enhance stability and drug targeting are the groups' future aims. "Combining nanotechnology and biomedicine will lead to progress in winning the war against bacterial infections," concludes Zhang.

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