COLONIC CAPSULES FOR AQUEOUS BACTERIAL SUSPENSION

Fatma Abdi[1], Marina Green Buzhor[1], Jean-Christophe Leroux[1]

[1] *Institute of Pharmaceutical Sciences, ETH Zurich, 8093, Zurich*

Objectives: Many studies have underlined the important contribution of the human microbiome in modulating many metabolic functions that are beneficial for human health preservation. However, harnessing the microbiome properties is, among others, limited by the inefficient delivery of living bacteria to the distal part of the gastrointestinal (GI) tract. Indeed, most manufacturing processes of bacterial oral formulations involve steps such as drying that may lead to a substantial loss of bacterial survival. This often results in the administration of high doses to compensate for this loss or in using impractical delivery modes (e.g. enema). The objective of this work was to engineer capsules capable of delivering aqueous suspensions of live bacteria to the ileum/colon.

Methods: The capsules consisted of a thin hydrophobic double-layered coating whose resistance to pressure decreases as the capsule moves along the GI tract. Hydroxypropyl methyl cellulose commercial capsules were modified with hydrophobic cellulose derivatives and methacrylic acid copolymers using the dip-coating method. The capsules were characterized for various physicochemical properties and their opening assessed in Beagle dogs.

Results: Thicknesses of the coatings ranged from 7.5 µm to 15 µm. Their hydrophobic nature allowed the capsules to encapsulate aqueous media and to withstand external aqueous fluids. These capsules prevented to some extent the diffusion of oxygen and the acidification of the encapsulated aqueous content when exposed to simulated gastric fluids. Disintegration tests showed that the capsules maintained their integrity under simulated GI conditions, while breaking at pressures and conditions encountered in the ileum. Surface dissolution testing confirmed that the enteric coating dissolved at the average pH encountered in the ileum, thus facilitating their subsequent rupture. *In vivo,* the capsules opened between 3-4 h after intake, which in dogs, is indicative of an opening near the ileum/colon.

Conclusion: Colonic capsules suitable for the aqueous delivery of live bacteria were developed. This simple up-scalable delivery system may allow in the future, studying the effect of microbiota supplementation with minimum hurdles while providing higher amounts of live bacteria to the distal part of the GI tract. The Swiss National Science Foundation (grant 315230_197644/1) financially supported this work.
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