



Enteric coated spheres produced by extrusion/spheronization provide effective gastric protection and efficient release of live therapeutic bacteria

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<https://doi.org/10.1016/j.ijpharm.2015.06.051>

Abstract

We present a novel but simple enteric coated sphere formulation containing probiotic bacteria (*Lactobacillus casei*). Oral delivery of live bacterial cells (LBC) requires live cells to survive firstly manufacturing processes and secondly GI microbicidal defenses including gastric acid. We incorporated live *L. casei* directly in the granulation liquid, followed by granulation, extrusion, spheronization, drying and spray coating to produce dried live probiotic spheres. A blend of MCC, calcium-crosslinked alginate, and lactose was developed that gave improved live cell survival during manufacturing, and gave excellent protection from gastric acid plus rapid release in intestinal conditions. No significant loss of viability was observed in all steps except drying, which resulted in approximately 1 log loss of viable cells. Eudragit coating was used to protect dried live cells from acid, and microcrystalline cellulose (MCC) was combined with sodium alginate to achieve efficient sphere disintegration leading to rapid and complete bacterial cell release in intestinal conditions. Viability and release of *L. casei* was evaluated *in vitro* in simulated GI conditions. Uncoated spheres gave partial acid protection, but enteric coated spheres effectively protected dried probiotic LBC from acid for 2 h, and subsequently released all viable cells within 1 h of transfer into simulated intestinal fluid.

Graphical abstract

