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Microcontainers for oral delivery of probiotics

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Learning objectives:

1. Describe the key challenges in oral delivery of probiotics
2. Explain the ideas behind the use of microcontainers
3. Evaluate coating efficiency and survival of probiotics after release from microcontainers

INTRODUCTION: Probiotics are administered to affect the human gut microbiota, and are typically delivered orally, as freeze or spray dried bacteria. However, challenges remain, including delivery to the large intestine and colonization in the mucus layer. Micrometer sized cylindrical microcontainers have been developed for oral drug delivery. The role of the microcontainers is to protect the compound and later provide unidirectional release when desired (1). Studies have shown that microcontainers are engulfed by the intestinal mucus (2), which makes them a promising tool for targeted delivery of probiotics. The aim of the project was to spray dry *Lactobacillus rhamnosus* GG (LGG) and investigate survival and release from microcontainers in physiologically relevant buffers as a proof-of-concept study.

METHODS:

LGG was spray dried with trehalose and reconstituted skim milk powder (both 10 % (w/w)) as protectants, using a Mini Spray Dryer with an outlet temperature of 60°C. The water content in the spray dried powder was determined with a Thermogravimetric Analyzer. Afterwards, the LGG powder was loaded into microcontainers and the cavity was enteric-coated with Eudragit® L100. The release and survival rate of LGG was investigated in gastric and intestinal pH values. Firstly, the microcontainers were immersed into a solution of pH 2.5 for 30 min and then the medium was changed to a phosphate buffer with pH 7.4 for 1 h. As controls, the survival of the LGG powder (without microcontainers) was investigated in pH 1 (15 min), 2.5 (30 min) and 7.4 (1 h), respectively. Samples were serially diluted and plated on MRS agar plates to count colony-forming units (CFU).

RESULTS:

The spray drying of LGG resulted in a fine powder with a water content of 5.4 %, which was loaded into microcontainers (Fig 1A). Subsequently, a uniform coating of Eudragit® L100 was applied as a lid (Fig 1B). The controls showed survival of LGG in pH 2.5 and pH 7.4, but no visible growth in pH 1 after 15 min (Fig. 2). After 30 min in pH 2.5, a small release of LGG from the enteric-resistant microcontainers was observed (0.3 % compared to the control in pH 7.4), and LGG showed promising release and survival after additionally 1 h in pH 7.4 (128 % compared to the control in pH 7.4).

CONCLUSIONS:

LGG showed a good survival rate and release from microcontainers coated with Eudragit® L100. The current work illustrates the potential of microcontainer-based delivery of probiotics.

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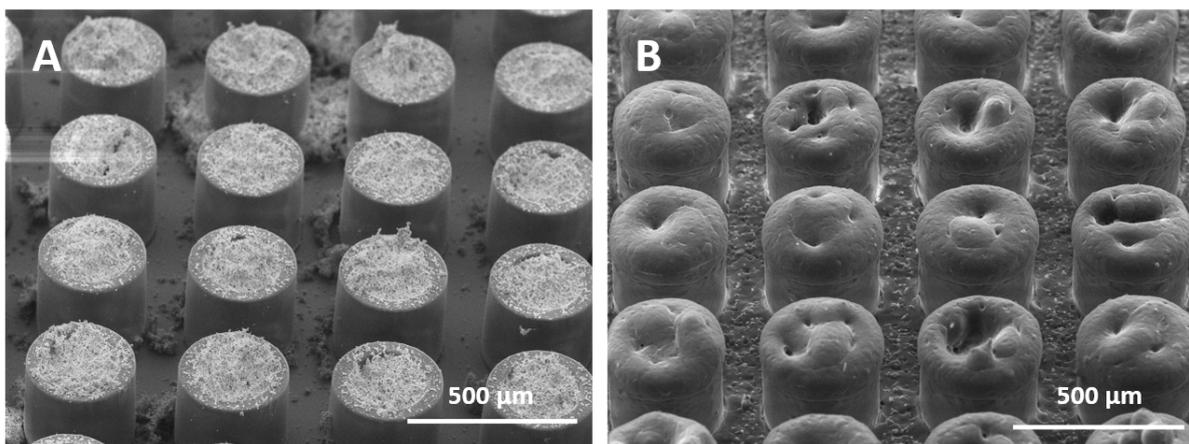


Fig. 1. SEM images of **A:** microcontainers loaded with LGG and **B:** loaded microcontainers coated with Eudragit® L100.

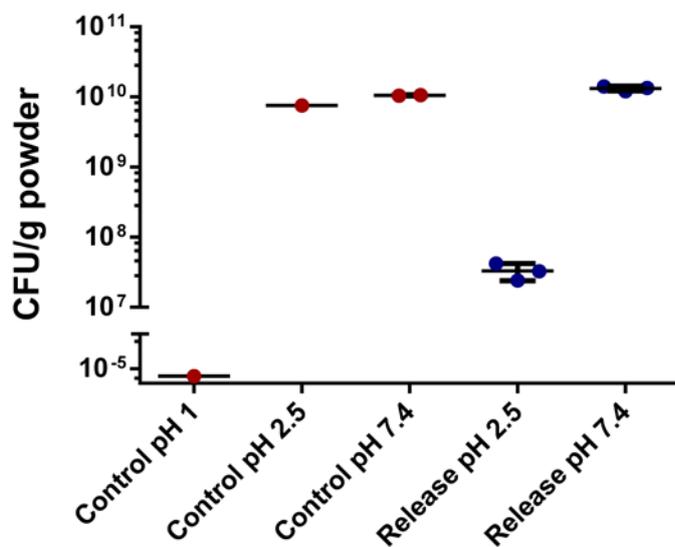


Fig. 2: Survival of LGG in powder controls and after release from microcontainers. Data shown as CFU/g powder.