DEVELOPMENT OF ENTERIC POLYMER BASED MICROSPHERES BY SPRAY-DRYING FOR COLONIC DELIVERY OF *LACTOBACILLUS RHAMNOSUS GG* 

<u>Elie Akanny</u><sup>1</sup>, Sandrine Bourgeois<sup>2,3</sup>, Anne Bonhommé<sup>1</sup>, Cynthia Barratier<sup>2,3</sup>, Carine Commun<sup>4</sup>, Anne Doleans-Jordheims<sup>4,5</sup>, François Bessueille<sup>1</sup>, Claire Bordes<sup>2</sup>

<sup>1</sup>Université de Lyon, Institut des Sciences Analytiques, UMR 5280, CNRS, Université Lyon 1, ENS Lyon – 5, rue de la Doua, F-69100 Villeurbanne, France

<sup>2</sup>Univ Lyon, Université Claude Bernard Lyon 1, CNRS, LAGEPP UMR 5007, 43 boulevard du 11 novembre 1918, F-69100, VILLEURBANNE, France

<sup>3</sup>Université de Lyon, Université Lyon 1, ISPB-School of Pharmacy, F-69008 Lyon, France

<sup>4</sup>Equipe de Recherche Bactéries Pathogènes Opportunistes et Environnement, UMR CNRS 5557 Ecologie Microbienne, Université de Lyon 1 & VetAgro Sup, Villeurbanne, France

<sup>5</sup>Laboratoire de Bactériologie, Institut des Agents Infectieux, Centre de Biologie et Pathologie Nord, Hospices Civils de Lyon (HCL), Lyon, France

Contact Email: elie.kouame-akanny@univ-lyon1.fr

Probiotics are widely used in encapsulation systems in order to improve their stability and preservation against adverse environmental conditions related to oral administration (i.e. acidic pH in the stomach, bile salts in the small intestine) while ensuring their release, preferably in the colon. Various colonic delivery systems were developed using different strategies such as time-dependent, pH-dependent or bacterially triggered delivery systems. Eudragit<sup>®</sup> S100 is an anionic copolymer, based on methacrylic acid and methyl methacrylate, with enteric property and frequently used for the design of pH-dependent colonic delivery systems. However, its use as a polymer for microparticle formulation usually involves the use of organic solvents inappropriate for the encapsulation of living cells.

In this study pH-responsive Eudragit<sup>®</sup> S100 microparticles were developed for the encapsulation of *Lactobacillus rhamnosus GG* (LGG) using an aqueous-based spray-drying approach (Figure. 1), and thereby avoiding the use of organic solvents. One of the main drawbacks of the spray-drying is the thermal and dehydration stress imposed on bacteria, which are the major causes of cell inactivation. The use of thermoprotectant such as mannitol and trehalose allowed to increase the survival ratio from 3% to more than 50 %, using the selected and optimized parameters of the spray-drying process. The viability of encapsulated LGG were then determined during storage and incubation in simulated gastric conditions. Encapsulated LGG showed a great stability during storage with less than 1 log reduction after 1 month thanks to the low residual moisture content (1.5-3%) achieved in presence of the protectant (versus 9% without protectant). Concerning resistance in acidic conditions, free LGG showed a dramatic loss in viability after their incubation in acidic environment since no viable cell was detectable after 1h exposure. In contrast, only 1.5 log reduction was observed for encapsulated LGG after 2 h exposure in simulated gastric conditions.



Figure. 1 SEM image of spray-dried microparticles