**Microfluidic fabrication of thiolated hyaluronic acid-alginate microsphere with** **dual adhesion function for colon-targeted co-delivery probiotics and postbiotics**

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The health benefits of oral probiotics are significantly hindered by their low survival rate in harsh stomach conditions and short retention time in intestine. Herein, we developed a novel microsphere with dual adhesion to bacterial and intestinal mucosa using thiolated hyaluronic acid (HA-SH) and sodium alginate (SA) for colonic targeted delivery of probiotics. This dual-network microsphere was prepared in microfluidics platform through an ingenious combination of photoinduced disulfide crosslinking and ionic crosslinking, achieving uniform particle size (257 ± 20.5 μm) and high encapsulation efficiency (82.1%). Owing to the protective effects of the microsphere, the embedded probiotics exhibited high survival rates (8.69 log CFU/mL) in simulated gastric fluid and a high release rate (80.2%) in the intestine. Moreover, the adhesion tests demonstrated that the grafting of thiol groups into the microspheres significantly enhanced both bacterial adhesion rate (53.9%) and mucosal adhesion rate (74.33%). In DSS-induced colitis mice, the microsphere embedded with probiotics and postbiotics demonstrated superior therapeutic efficacy by downregulating proinflammatory cytokines, repairing the intestinal barrier, and remodelling the gut microbiome. Overall, this microsphere offers a promising strategy to enhance the vitality, colonization, and health benefits of oral probiotics.

An oral presentation will eventually be the presented for this work.