Supramolecular Layer-by-Layer Engineered Probiotics for Inflammatory Bowel Disease Therapy

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The global incidence of Inflammatory Bowel Disease (IBD) is on a continuous rise. Probiotic therapy has emerged as a research hotspot due to its synergistic advantages in "regulating intestinal flora and inhibiting inflammation". However, the oral delivery of live probiotics is hampered by destructive gastric acid and oxidative stress in the inflamed gut. In this study, we constructed a novel probiotic delivery system using the model probiotic Escherichia coli Nissle 1917 (EcN). A foundational layer-by-layer (LbL) shell of chitosan (CS) and hyaluronic acid (HA) for electrostatic physical protection, topped with a supramolecular network formed by Beta-cyclodextrin-azobenzene (CD-AZO) host-guest crosslinking for enhanced robustness. Successful assembly was verified by sequential zeta potential reversal of probiotic surface, scanning electron microscopy (SEM), confocal microscopy, and flow cytometry. The engineered EcN maintained a proliferation rate equivalent to bare EcN, indicating no adverse effects on viability. Crucially, the multilayer coating alone significantly enhanced bacterial stress resistance, with the 3-layer coated EcN showing a 5-fold higher survival rate after 4-hour exposure to simulated gastric fluid (pH 2.0) compared to free EcN. Thus, the combination of electrostatic layering and host-guest crosslinking provided synergistic protection. The developed system effectively shields probiotics from gastrointestinal insults while enabling targeted release at inflammatory sites, thereby overcoming key bottlenecks in the oral delivery of probiotics for IBD treatment.

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