

Oral Delivery of Engineered Bacterial Membrane Vesicles to Ameliorate Inflammatory Bowel Diseases

Beibei Wu, Jinhan He

West China School of Pharmacy, Sichuan University, Chengdu, China.



1. Introduction

Gut probiotics (e.g., *Akkermansia muciniphila*, *Bifidobacterium*) have been reported to ameliorate gut disorders in both mice and humans. However, the use of live bacteria raises safety concerns, including the potential for infection and immune interference. Here, we introduce a **cell-free, gut-targeted** strategy based on probiotic-derived outer membrane vesicles (OMVs).

2. Methodology

OMV isolation: Ultracentrifugation from the supernatant of probiotic cultures.

POT formulation: tannic acid biomineralization of OMVs.

POTA formulation: POT encapsulated in pH-responsive alginate microbeads (Fig. 1A).

Antioxidant effect: evaluated by measuring DPPH• scavenging activity.

Anti-inflammatory effect: assessed by examining the gene expression levels of inflammatory factors in RAW264.7 cells.

Intestinal targeted release: investigated through stability tests in simulated gastrointestinal fluids and in vivo distribution experiments.

Therapeutic efficacy: evaluated by Dextran sulfate sodium (DSS)-induced IBD mice models.

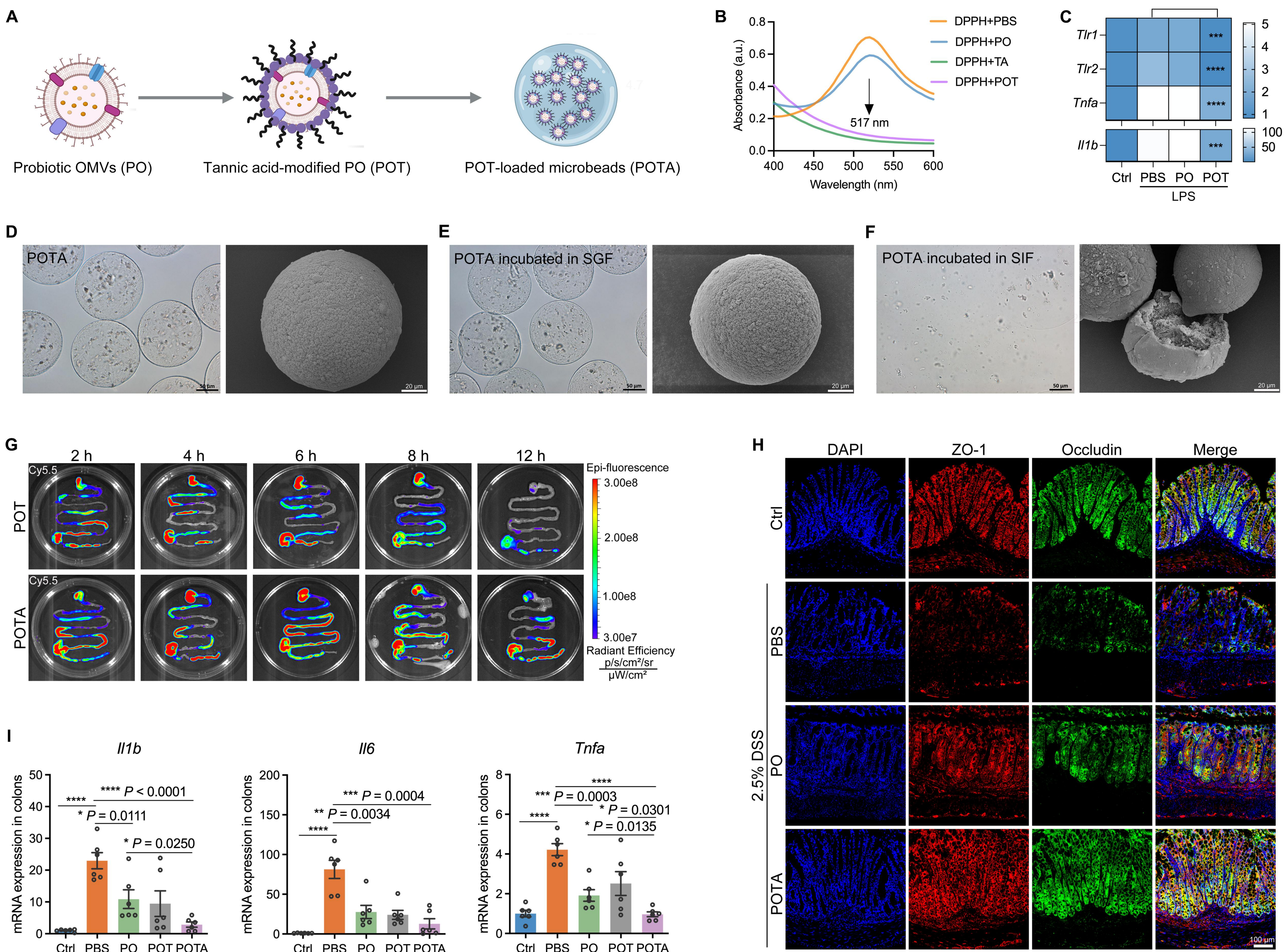
3. Key results

(1) Biomineralization with tannic acid significantly enhances the antioxidant and anti-inflammatory properties of PO (Fig. 1B,C).

(2) POT-loaded microbeads exhibit great stability under acidic conditions (e.g., simulated gastric fluid, SGF) to protect the payload and swell in alkaline environments (e.g., simulated intestinal fluid, SIF) to facilitate content release (Fig. 1D-F).

(3) The intestinal fluorescence signal of Cy5.5-labelled POTA was significantly higher than that of POT post administration (Fig. 1G).

(4) In mouse models of IBD, POTA restores intestinal barrier integrity (Fig. 1H) and suppresses inflammation (Fig. 1I).



4. Conclusion

This work establishes engineered bacterial vesicles as a safe and effective modality for treating IBD and reveals a translatable framework for microbiome-based therapeutics beyond live bacteria.