Sturgeon-Derived Peptide LLLE Reduced Colitis by Regulating Gut Microbiota and Metabolites

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Introduction

Inflammatory Bowel Disease (IBD), including ulcerative colitis (UC) and Crohn's disease, is a chronic disorder characterized by persistent inflammation of the gastrointestinal tract. The pathogenesis of IBD involves genetic predisposition, dysbiosis of the gut microbiome, and immune dysregulation. Recent studies highlight the potential therapeutic benefits of bioactive peptides in modulating gut microbiota and reducing intestinal inflammation. This study investigates the efficacy of the sturgeon-derived peptide LLLE (Leu-Leu-Leu-Glu) in alleviating colitis through its impact on gut microbiota composition and fecal metabolites in a dextran sulfate sodium (DSS)-induced colitis mouse model.

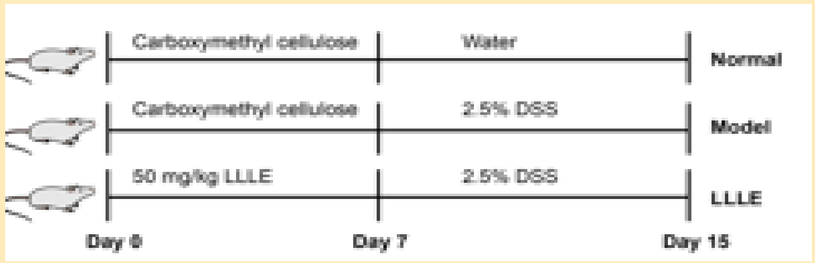
Methods

Animal Model and Treatment:

Seven-week-old male BALB/c mice were acclimated and divided into three groups (n=8 each): Control, DSS-induced colitis (Model), and LLLE-treated (50 mg/kg/day). Colitis was induced with 2.5% DSS in drinking water for seven days, while the LLLE group received the peptide treatment.

Assessments:

- Disease Activity Index (DAI): Monitored daily, incorporating weight loss, stool consistency, and fecal blood.
- Histopathology: Colon tissues were sectioned and stained with hematoxylin and eosin (H&E) to assess tissue damage.
- Cytokine Analysis: Serum levels of interleukin-6 (IL-6) were quantified using enzyme-linked immunosorbent assay (ELISA).
- Gut Microbiota Analysis: 16S rRNA sequencing was performed on fecal samples to evaluate microbial composition.
- Metabolomics: Fecal metabolites were analyzed using LC-MS to identify metabolic alterations.



Results

- Clinical Improvement: LLLE-treated mice showed significantly reduced weight loss and lower DAI scores than the DSS model group.
- Histological Analysis: LLLE administration mitigated DSS-induced colon shortening and mucosal damage, with reduced inflammatory cell infiltration.
- Inflammatory Markers: IL-6 levels were significantly reduced in LLLE-treated mice, indicating an anti-inflammatory effect.
- Gut Microbiota Modulation: DSS-induced colitis increased Bacteroidetes abundance, while LLLE treatment partially restored microbial balance, particularly reducing the prevalence of pro-inflammatory taxa.
- Metabolomic Changes: LLLE intervention increased fecal levels of indole-3-propionic acid, a metabolite known for its anti-inflammatory properties.

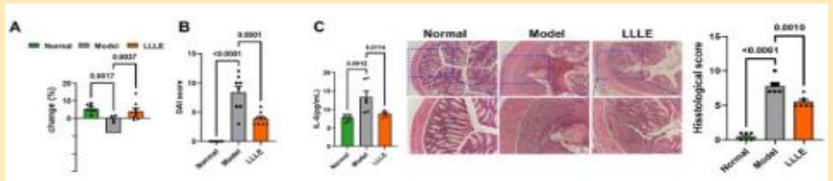


Figure 1. LLLE alleviated DSS-induced colitis in mice. (A) Colon length. (B) Disease activity index. (C) Serum IL6 levels.

Figure 2. LLLE mitigates colon tissue damage and inflammation in colitis mice.

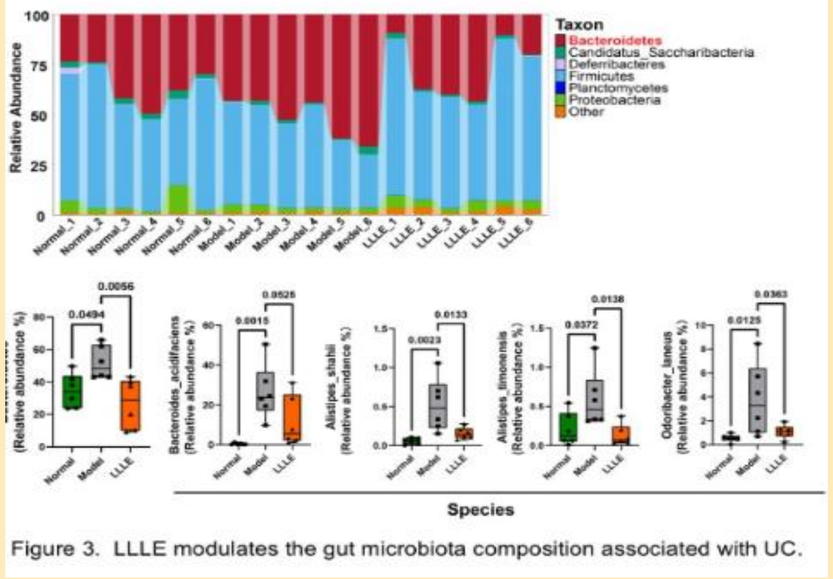


Figure 3. LLLE modulates the gut microbiota composition associated with UC.

Results (Cont.)

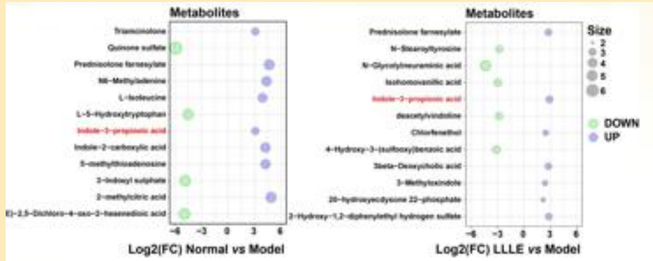


Figure 4. LLLE altered the composition of indole derivatives in feces

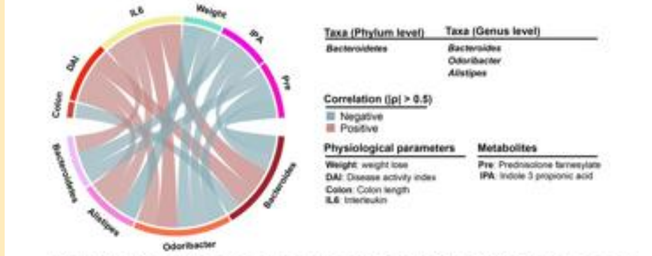


Figure 5. Correlation analysis among the significant difference genera ($P < 0.05$), crucial metabolites, and physiological parameters ($|\rho| > 0.5$, $P < 0.05$).

Conclusion

This study demonstrates that the sturgeon-derived peptide LLLE effectively alleviates DSS-induced colitis by modulating gut microbiota composition and restoring beneficial metabolites. The reduction in inflammatory markers and histological damage suggests that LLLE has potential as a therapeutic agent for IBD management. Future research should explore the molecular mechanisms underlying its protective effects and evaluate its efficacy in human models.

References