Abstract

Human Gut Commensal-Derived Exopolysaccharide-Mediated Short-Chain Fatty Acid Production by In Vitro Gastrointestinal Digestion and Its Enzymatic Inhibitory Mechanism Targeting the Microbial Composition of Irritable Bowel Disease (IBD)

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Abstract: The intestinal microbiome is important for synthesising nutrients, breaking down polysaccharides, protecting against foreign microbes, and aiding immune system development by producing short-chain fatty acids (SCFAs). SCFAs are formed through the interaction between the gut microbiota and the diet in the gut lumen. This study aims to extract exopolysaccharide (EPS) from the gut isolate Proteus mirabilis DMTMMR-11, a probiotic species which was optimised to improvise the yield of EPS through one-factor-at-a-time (OFAT) and response surface methodology. The central composite design (CCD) increased the yield up to 2.32 ± 0.4 g/L, and characterization was performed to study the structural and functional moieties of EPS by Fourier transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR) for proton and carbon (1H and C13-NMR). The EPS was subjected to artificial simulated gastrointestinal digestion by mimicking the gut conditions of healthy humans. These data reveal the higher concentrations of SCFA derivatives such as propionate, acetate, and other bioactive metabolites. The in vitro experiments in IBD (irritable bowel syndrome) patients' gut homogenates were treated with EPS digest with SCFA, revealing that dysbiosis is reinstated, by improvising the colonisation of probiotic and gut symbionts by inhibiting the growth of pathogenic bacteria, which was studied by the metagenomic sequencing (V3–V4) region of the 16S rRNA gene. The EPS digest with SCFA was subjected to biological activities such as scavenging and reducing power, which showed 32.03 ± 0.21 and 13.04 ± 0.3 µg/mL. The anti-diabetic activity, like α-amylase, α-glucosidase and DPP-IV, was studied, expressing reduced IC50 values at (9.21 ± 0.3, 4.43 ± 0.4, 21.4 ± 0.33) µg/mL. Anti-inflammatory activity was higher up to 75%, and the anti-lipidemic inhibition property expressed inhibition up to 40% in cholesterol esterase and pancreatic lipase. These results indicate that EPS digest with SCFA is a beneficial substrate and can be administered for combinational IBD therapies.

Keywords: exopolysaccharide; short-chain fatty acids; dysbiosis; enzymatic inhibition

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