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 (SCFA). SCFAs are formed through the interaction between the gut microbiota and the diet in the gut lumen. The study aims to extract exopolysaccharide (EPS) from the gut isolate *Bacillus spizizenni* DMTMMR-17 a probiotic species which was optimised to improvise the yield of EPS through One factor at a time (OFAT) and Response surface methodology- central composite design (CCD) increased the yield up to

2.32 ± 0.4 g/l, characterization was done to study the structural and functional moieties of EPS by Fourier transform infrared spectroscopy (FTIR) and Nuclear magnetic resonance (NMR) for proton and carbon (^{1}H and C^{13}-NMR). The EPS was subjected to artificial simulated gastrointestinal digestion by mimicking the gut conditions of healthy humans. The simulated digestion was carried out for 90 min, the digest was purified by reverse-phase high-performance liquid chromatography (RP-HPLC), and SCFA was identified by gas chromatography-mass spectrometry (GC-MS/MS). These data reveals 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 of SCFA, revealing that dysbiosis is reinstated, by improvising the colonisation of probiotic and gut symbionts by inhibiting the growth of pathogenic bacteria was studied by metagenomic sequencing (V_3-V_4) region of 16S rRNA gene. The EPS digest with SCFA was subjected to biological activities such as scavenging and reducing power was 32.03 ± 0.21, 13.04 ± 0.3 µg/ml, the anti-diabetic activity like α-amylase, α-glucosidase and DPP-IV were studied expressing reduced IC_{50} values at (9.21 ± 0.3, 4.43 ± 0.4, 21.4 ± 0.33) µg/ml. Anti-inflammatory activity was higher up to 60-75%, and anti-lipidemic inhibition property expressed inhibition up to 40 % in cholesterol esterase and pancreatic lipase. This confirms the enzymatic inhibition responsible for various gut diseases. These results indicate that EPS digest with SCFA is a beneficial substrate and can be administered for combinational IBD therapies.