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The effect of oral synbiotics on the gut microbiota and inflammatory biomarkers in healthy adults: a systematic review and meta-analysis

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Despite extensive research showing clinical benefits of probiotic supplementation in humans, studies have failed to indicate a significant consistent and beneficial effect on the gut microbiota.[1] Synbiotics, the combination of a probiotic and prebiotic, have been explored in specific clinical populations for their gut-modulating properties and clinical benefits.[2–4] However, the body of evidence related to the effect of synbiotics on gut health in healthy adult populations has not been reviewed to date. A systematic literature review was undertaken to summarise the available evidence on the effect of synbiotics on the gut microbiota and inflammatory markers in healthy adults and those with conditions that do not directly affect the gut microbiota. A systematic literature search was conducted according to the Cochrane handbook [5] using the Scopus, PubMed, Web of Science, ScienceDirect, MEDLINE, CINAHL and Cochrane Library databases, following PRISMA reporting guidelines.[6] Randomised controlled trials examining the primary outcome of gut microbiota profile or intestinal permeability after synbiotic supplementation in healthy adults were included. Secondary outcomes included short-chain fatty acids (SCFAs), inflammatory biomarkers and measures of gut microbial diversity. Risk of bias was assessed using the Cochrane RoB 2.0 tool,[7] and quality of evidence assessed using the GRADE framework.[8] Weighted or standardised mean difference outcome data were pooled in restricted maximum likelihood models using random effects. Twenty-eight articles met the eligibility criteria and included data from 27 studies and 1288 adults. Population characteristics included healthy, elderly and overweight adults, and adults with type 2 diabetes, asthma or migraines. The most common prebiotics were inulin, fructooligosaccharide and galactooligosaccharide, with the probiotics commonly containing one or more species of *Lactobacillus* or *Bifidobacterium*. Meta-analyses of 17 studies showed significant increase in Lactobacillus cell count (SMD 0.74; $p = 0.01$) and Propionate concentration (SMD 0.22; $p = 0.03$). A non-significant increase in Bifidobacterium relative abundance (WMD 0.97; $p = 0.10$) and cell count (SMD 0.82; $p = 0.06$) was seen. No significant difference in other SCFA measures, zonulin, IL-6, CRP or endotoxins were seen. Narrative synthesis of synbiotic use showed 18 included studies reported increased *Lactobacillus* and/or *Bifidobacterium* across all population groups after supplementation. Across various adult populations, synbiotics modulate the gut microbiota by increasing *Bifidobacterium* and *Lactobacillus* populations and may result in increased SCFA production, specifically propionate. Further human clinical trials replicating existing synbiotic combinations are necessary to confirm their effectiveness and investigate wider changes to the gut microbiota. This synthesis suggests the need for tailored approaches in researching microbiota-modulating agents in specific health and disease states, including more standardised outcome measures and reporting guidelines to reduce heterogeneity. Significant variations in synbiotic type, dose and duration should be considered as limitations when considering application to clinical practice.

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