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Gut Microbiome Modulation through Probiotics and Prebiotics for Metabolic Health: A Narrative Review

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ABSTRACT

Background: The gut microbiome plays a central role in host energy harvest, glucose homeostasis, and inflammation, and its disruption (dysbiosis) is implicated in obesity, type 2 diabetes mellitus (T2DM), and related cardiometabolic disorders. Probiotics and prebiotics have been investigated as accessible dietary strategies to modulate the microbiome and improve metabolic outcomes. This narrative review synthesizes evidence on mechanisms linking gut microbiota to metabolic health and evaluates the clinical efficacy of probiotic and prebiotic interventions in obesity and T2DM.
Methods: A non-systematic search was performed in PubMed, Web of Science, and the Cochrane Library for systematic reviews, meta-analyses of randomized controlled trials (RCTs), and key mechanistic studies published within the last ten years, using terms related to gut microbiota, probiotics, prebiotics, synbiotics, short-chain fatty acids, and metabolic disease.
Results: Dysbiosis is characterized by reduced microbial diversity, diminished short-chain fatty acid production, impaired intestinal barrier integrity, and metabolic endotoxemia, collectively promoting low-grade inflammation and insulin resistance. Multiple meta-analyses of RCTs show that probiotic and synbiotic supplementation modestly but significantly reduces fasting glucose, HbA1c, and insulin resistance in T2DM, with more consistent effects for multi-strain, capsule-based formulations than fermented dairy vehicles. Emerging evidence on next-generation probiotics, particularly pasteurized Akkermansia muciniphila, shows improved insulin sensitivity and lipid profile in overweight and obese adults.
Conclusion: Probiotic and prebiotic interventions offer a biologically plausible, low-risk adjunct for metabolic disease management, though effect sizes remain modest and strain-, dose-, and duration-dependent, warranting cautious interpretation and further long-term trials.

Keywords: gut microbiota; insulin resistance; metabolic syndrome; prebiotics; probiotics

A. BACKGROUND

The human gastrointestinal tract harbours trillions of microorganisms that collectively form the gut microbiome, a dynamic ecosystem that influences nutrient absorption, immune function, and host energy metabolism[1]. Advances in culture-independent sequencing technologies over the past two decades have revealed that the composition and functional capacity of this microbial community differ markedly between lean and obese individuals, and between healthy individuals and those with type 2 diabetes mellitus (T2DM), suggesting a mechanistic link between gut microbiota and cardiometabolic disease[1,2]. Dysbiosis, broadly defined as an imbalance in the diversity, composition, or function of the gut microbiota, has been associated with impaired intestinal barrier integrity, metabolic endotoxemia, chronic low-grade inflammation, and dysregulated short-chain fatty acid (SCFA) production, all of which are implicated in the pathophysiology of obesity, insulin resistance, and related metabolic disorders[1,3].

Given the modifiable nature of gut microbiota composition, considerable research attention has focused on dietary strategies capable of restoring microbial balance. Probiotics are defined as live microorganisms that, when administered in adequate amounts, confer a health benefit on the host, while prebiotics are selectively fermented substrates, typically non-digestible carbohydrates such as inulin and fructo-oligosaccharides, that promote the growth and activity of beneficial gut bacteria[1,4]. Synbiotics combine both components, and postbiotics refer to non-viable microbial products or metabolites, such as SCFAs and bacterial cell-wall fragments, that confer benefits without requiring live organisms[4]. These interventions are widely available, generally well tolerated, and increasingly marketed for metabolic health, yet the magnitude and consistency of their clinical benefit remain subjects of ongoing investigation and debate.

This narrative review aims to: (1) summarize the mechanistic pathways linking gut microbiota composition to obesity and T2DM; (2) evaluate clinical trial evidence on the efficacy of probiotic, prebiotic, and synbiotic supplementation for glycaemic and metabolic outcomes; (3) examine emerging next-generation probiotic candidates, particularly Akkermansia muciniphila; and (4) discuss clinical and public health implications, including considerations relevant to dietary and fermented food practices in Indonesia and the broader Asian context.

B. METHODS

This article was prepared as a narrative literature review. A search was conducted in PubMed/MEDLINE, Web of Science, and the Cochrane Library for articles published between 2016 and 2026, using combinations of the keywords “gut microbiota,” “gut microbiome,” “probiotics,” “prebiotics,” “synbiotics,” “postbiotics,” “short-chain fatty acids,” “Akkermansia muciniphila,” “type 2 diabetes,” “obesity,” and “metabolic syndrome.” Priority was given to systematic reviews and meta-analyses of randomized controlled trials, key mechanistic studies, and landmark proof-of-concept human trials. Studies published only as conference abstracts, non-peer-reviewed commentaries, or without available full text were excluded. Findings were thematically synthesized around mechanisms of host–microbiome interaction, clinical outcomes by intervention type, emerging probiotic candidates, and translational and regional considerations, consistent with the scope of a literature-based review article.

C. RESULT AND DISCUSSION

1. Gut Dysbiosis and Mechanistic Pathways to Metabolic Disease

Several converging mechanisms have been proposed to explain how alterations in gut microbiota composition contribute to obesity and insulin resistance. First, the gut microbiota ferments non-digestible dietary fibres in the colon to produce SCFAs, principally acetate, propionate, and butyrate, which serve as energy substrates for colonocytes and as signalling molecules acting through G protein-coupled receptors and histone deacetylase inhibition to regulate appetite, glucose homeostasis, and immune function[5,6]. Reduced SCFA production, particularly of butyrate, has been associated with weakened tight-junction-dependent intestinal barrier function, increased gut permeability, and translocation of bacterial lipopolysaccharide (LPS) into systemic circulation, a phenomenon termed metabolic endotoxemia[5,6]. Circulating LPS activates Toll-like receptor 4 signalling in adipose tissue, liver, and skeletal muscle, triggering chronic low-grade inflammation and impairing insulin signalling pathways central to the development of insulin resistance[6,7].

Second, certain bacterial taxa appear to directly influence host energy balance. Dysbiotic microbiota associated with obesity often show an altered Firmicutes-to-Bacteroidetes ratio and reduced microbial diversity, which has been linked experimentally to enhanced energy harvest from the diet[1,7]. Third, specific commensal species, most notably Akkermansia muciniphila, a mucin-degrading bacterium that resides in the protective mucus layer of the gut, have been consistently and inversely correlated with adiposity, insulin resistance, and untreated T2DM across human observational studies[8]. Mechanistically, A. muciniphila and its outer-membrane

protein Amuc_1100 have been shown to reinforce gut barrier integrity, reduce circulating LPS, and modulate host energy metabolism, providing biological plausibility for its candidacy as a next-generation probiotic[8,9].

2. Clinical Evidence: Probiotics, Prebiotics, and Synbiotics in Type 2 Diabetes and Obesity

Multiple systematic reviews and meta-analyses of randomized controlled trials (RCTs) have evaluated the metabolic effects of probiotic supplementation in individuals with T2DM. An early meta-analysis of seven RCTs reported that probiotic consumption significantly reduced fasting plasma glucose (FPG) by 15.92 mg/dL and glycated haemoglobin (HbA1c) by 0.54 percentage points compared with control groups, with larger reductions observed when multiple probiotic species were used and when the intervention duration was at least eight weeks[10]. A subsequent updated meta-analysis of 14 RCTs similarly found significant reductions in HbA1c, fasting insulin, and homeostasis model assessment of insulin resistance (HOMA-IR), and notably found that probiotic supplements produced significant glycaemic improvements while probiotic foods such as yoghurt did not reach statistical significance, suggesting that delivery format and probiotic dose may influence clinical efficacy[11].

A more recent and comprehensive meta-analysis of 41 RCTs involving nearly 3,000 participants with diabetes confirmed statistically significant, though modest, improvements in HbA1c, FPG, and insulin levels following probiotic or synbiotic supplementation, with multispecies strains showing particularly favourable effects on HbA1c[12]. Complementary meta-analyses focusing specifically on fermented dairy vehicles, however, have produced more equivocal results: a meta-analysis of nine RCTs evaluating probiotic yoghurt found no significant benefit over conventional yoghurt for glycaemic markers in either T2DM or obesity, underscoring that delivery vehicle, baseline diet, and probiotic strain selection are important determinants of clinical effect[13]. Within special populations, probiotic supplementation in pregnant women, including those with gestational diabetes mellitus, has been associated with significant reductions in fasting glucose, fasting insulin, and insulin resistance, although effects on HbA1c and post-prandial glucose excursions have generally been non-significant[14]. Taken together, the cumulative trial evidence supports a real but modest glucose-lowering and insulin-sensitizing effect of probiotic and synbiotic supplementation, with the magnitude of benefit dependent on strain composition, dose, duration of at least eight weeks, and delivery format. Across these meta-analyses, effect sizes are generally more favourable for multi-strain formulations and supplement-based delivery than for fermented food vehicles, although trial heterogeneity in strain, dose, formulation, and outcome measurement complicates direct

comparison and contributes to inconsistent findings, particularly for probiotic yoghurt[13]. Many included trials are also limited by small sample sizes, short follow-up periods, and variable risk of bias, and most have enrolled adults already diagnosed with T2DM or established obesity rather than populations at earlier stages of metabolic risk, limiting inference regarding primary prevention[11,12]. The field further lacks consensus on optimal strain selection and dosing, and on the relative contribution of live organisms versus their metabolic by-products (postbiotics); commercially available over-the-counter probiotics are accordingly not currently recommended as a substitute for established first-line management of obesity or diabetes.

3. Akkermansia muciniphila and Next-Generation Probiotics

Building on consistent observational associations between A. muciniphila abundance and favourable metabolic profiles, a randomized, double-blind, placebo-controlled pilot trial administered live or pasteurized A. muciniphila daily for three months to overweight and obese insulin-resistant adults[9]. Compared with placebo, pasteurized A. muciniphila supplementation significantly improved insulin sensitivity by 28.6%, reduced fasting insulin by 34.1%, and lowered plasma total cholesterol by 8.7%, alongside modest reductions in body weight and fat mass, with the intervention found to be safe and well tolerated[9]. These findings represented the first human evidence supporting A. muciniphila as a viable next-generation probiotic candidate and have since stimulated further controlled trials examining its role in long-term weight maintenance following dietary weight loss, illustrating the translational potential of mechanistic microbiome research. While promising, regulatory approval, large-scale manufacturing, and longer-term safety data for pasteurized A. muciniphila remain in earlier stages relative to conventional Lactobacillus- and Bifidobacterium-based probiotics, and dietary strategies that naturally promote A. muciniphila abundance, such as polyphenol-rich and fibre-rich diets, have also been proposed as complementary approaches[8].

4. Regional and Translational Considerations

Within Indonesia and the broader Asian region, traditionally fermented foods such as tempeh, fermented cassava products, and various lactic-acid-fermented vegetables and dairy preparations represent naturally occurring sources of live microorganisms and microbial metabolites that may confer comparable benefits to commercially formulated probiotics, although rigorous clinical trial data specific to these traditional foods remain comparatively limited relative to the global literature on standardized probiotic strains[4,8]. Given the generally lower cost and broader accessibility of fermented traditional foods compared with imported or commercially branded probiotic supplements, locally generated clinical trial evidence

evaluating their metabolic efficacy would meaningfully strengthen the translational relevance of gut-microbiome-targeted interventions for the Indonesian population, particularly amid the country's rising prevalence of obesity and type 2 diabetes. From a public health perspective, probiotic and prebiotic strategies should be regarded as a low-risk adjunct to, rather than a replacement for, established dietary, physical activity, and pharmacological management of metabolic disease. In the Indonesian context, where fermented traditional foods are widely consumed and culturally embedded, there is a clear opportunity to generate locally relevant clinical evidence that could both validate traditional dietary practices and inform culturally appropriate, cost-effective public health recommendations for metabolic disease prevention. Future research priorities should include longer-duration RCTs with standardized strain reporting, head-to-head comparisons of delivery formats, mechanistic studies clarifying the relative contribution of live bacteria versus postbiotic metabolites, and locally generated trials evaluating traditional fermented foods within Indonesian and regional Asian populations.

D. CONCLUSION

Current evidence supports a mechanistically plausible and clinically modest role for gut microbiota modulation, through probiotic, prebiotic, and synbiotic supplementation, in improving glycaemic control, insulin sensitivity, and lipid profile in individuals with obesity and type 2 diabetes mellitus. Effects are strongest for multi-strain supplements administered for at least eight weeks, while evidence for fermented food vehicles remains more inconsistent. Emerging next-generation probiotics such as pasteurized Akkermansia muciniphila show particular promise but require further large-scale and longer-term validation. Given Indonesia's rich tradition of fermented foods and its growing burden of metabolic disease, locally generated clinical research evaluating both standardized probiotic strains and traditional fermented foods represents a valuable and underexplored avenue for context-specific public health intervention.

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