



# Modulation of Inflammatory Markers in Type 2 Diabetes Mellitus through Gut Microbiome-Targeted Interventions: An Umbrella Review on Meta-Analyses

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## ABSTRACT

**Introduction:** Type 2 diabetes mellitus (T2DM) poses a significant global health challenge due to various lifestyle factors contributing to its prevalence and associated complications. Chronic low-grade inflammation, characterized by elevated levels of inflammatory markers such as C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF- $\alpha$ ), plays a pivotal role in the pathogenesis of T2DM. Modulation of the gut microbiota through microbiome-targeted therapy (MTT), including probiotics, prebiotics, and synbiotics, has emerged as a potential strategy to mitigate inflammation and improve metabolic outcomes in T2DM.

**Methods and Materials:** A systematic review and meta-analysis were conducted following PRISMA guidelines to evaluate the impact of MTT on inflammatory markers in patients with T2DM. Searches were performed in PubMed, Scopus, and Web of Science databases up to December 2023, with inclusion criteria limited to English-language meta-analyses of randomized controlled trials (RCTs) assessing the effects of probiotics, prebiotics or synbiotics on inflammatory markers in T2DM patients.

**Results:** Ten meta-analyses met the inclusion criteria, comprising studies investigating the effects of various MTT interventions on CRP, IL-6, and TNF- $\alpha$  levels in T2DM patients. Meta-analysis results indicated significant reductions in CRP (SMD: -0.070; 95% CI: -0.119 to -0.020) and TNF- $\alpha$  (SMD: -0.370; 95% CI: -0.554 to -0.186) levels following MTT, while IL-6 reductions (SMD: -0.070; 95% CI: -0.269 to 0.129) did not reach statistical significance. However, heterogeneity in study quality, intervention protocols, and participant demographics posed challenges in interpretation.

**Conclusion and Discussion:** Despite observed improvements in inflammatory markers with MTT, limitations, including heterogeneity in study quality and intervention protocols, underscore the need for further research to confirm efficacy and elucidate mechanisms. Future studies addressing these limitations, including diversity in dosage, supplement types, and bacterial strains, are essential for enhancing the reliability and applicability of MTT in T2DM management.

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