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Review Article

The Role of Anti-Inflammatory Diets and Gut Microbiome Modulation in Clinical Management of Depression and Anxiety: A Narrative Review

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ABSTRACT

This narrative review investigated the current evidences on anti-inflammatory diets and gut microbiome modulation for depression and anxiety management. Comprehensive literature search identified 127 relevant publications through PubMed, Scopus, and Web of Science until March 31, 2024. The evidences suggested Mediterranean and anti-inflammatory diets to be associated with reduced depression risk (33-42% in observational studies) and symptom improvement in randomized trials. Probiotics demonstrated strain-specific benefits, though heterogeneity in formulations complicated the recommendations. Prebiotics showed promising but limited evidences. Proposed mechanisms were presented as gut-brain axis modulation, inflammatory pathway regulation, and microbial metabolite production. Current evidences supported nutritional interventions as adjunctive approaches, though methodological limitations and inconsistent outcome measures necessitated cautious interpretation. Future researches should prioritize standardized interventions, longer follow-up, and personalized nutrition approaches.

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Introduction

Depression and anxiety disorders represent significant global health challenges, with conventional treatments demonstrating limited efficacy for substantial patient populations (1, 2). Emerging researches highlighted the potential role of nutritional factors and gut-brain axis interactions in mood disorder pathophysiology (3, 4). While previous reviews have examined dietary patterns or microbiome interventions separately, few have integrated these approaches while critically assessing methodological limitations (5). The inflammatory hypothesis of depression has gained substantial support, with documented elevations in pro-inflammatory cytokines among affected individuals (6). Concurrently, gut microbiome alterations have been consistently reported in mood disorders (7). Dietary interventions represent promising modifiable factors that may simultaneously address inflammatory processes and microbial dysbiosis (8-10).

Recent evidences from 2023 to 2024 has expanded our understanding of specific microbial metabolites and their neuroactive properties (11, 12). However, considerable heterogeneity in study methodologies and inconsistent findings

complicated clinical translation. This narrative review aimed to synthesize current evidenced while critically examining methodological limitations and identifying priorities for future research.

Materials and Methods

Search Strategy and Selection Criteria

A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science from inception through March 31, 2024. The search strategy employed Boolean operators: ("depression" OR "anxiety" OR "mood disorders") AND ("anti-inflammatory diet" OR "Mediterranean diet" OR "nutrition") AND ("gut microbiome" OR "microbiota" OR "probiotics" OR "prebiotics") AND ("inflammation" OR "cytokines") AND ("clinical trial" OR "observational study"). Inclusion criteria encompassed: (i) human studies; (ii) English-language publications; (iii) original research or systematic reviews; (iv) investigation of dietary patterns, probiotics, or prebiotics; and (v) measurement of depression/anxiety outcomes. Exclusion criteria included: (a) animal studies; (b) non-English publications; (c) studies without validated outcome measures; and (d) case reports with n<10 participants (Table 1).

Data Extraction and Quality Assessment

Two independent reviewers extracted data using standardized forms,with discrepancies resolved through consensus. The Newcastle-Ottawa Scale assessed observational study quality, while the Cochrane Risk of Bias Tool evaluated randomized trials. AMSTAR-2 guided assessment of systematic reviews.

Data Synthesis and Analysis

Giventhenarrativereviewmethodology,qualitative synthesis focused on identifying consistent patterns, methodological limitations, and evidence gaps. Effect sizes with 95% confidence intervals were reported where available. Heterogeneity was assessed through examination of study designs, populations, and outcome measures.

Observational Evidence: Dietary Patterns and Mood Disorders

Prospective cohorts consistently demonstrated inverse associations between anti-inflammatory dietary patterns and depression incidence.The SUN cohort (n=15,980) reported 33% reduced depression risk with high Mediterranean diet adherence (HR=0.67, 95% CI: 0.55-0.82) (13). The AIDI study found 42% risk reduction with anti-inflammatory diets (OR=0.58, 95% CI: 0.44-0.77) (14). Recent evidences confirmed these associations (15). Limitations include residual confounding and self-reported dietary data (Table 2).

The SMILES trial (n=67) demonstrated significant improvement in depressive symptoms with Mediterranean diet intervention (MADRS difference: -7.1 points, 95%CI: -10.2 to -4.0) (16). The HELFIMED study (n=152) showed enhanced effects with combined Mediterranean diet and omega-3 supplementation (17). However, recent replication attempts have yielded mixed results, highlighting intervention fidelity challenges and participant adherence issues.

Probiotic Interventions: Strain-Specific Effects

Meta-analyses indicate strain-dependent effects,with specific combinations showing significant benefits (SMD: -0.34, 95% CI: -0.61 to -0.07) (18). Recent high-quality trials demonstrated concurrent inflammatory marker reduction and mood improvement (19). Substantial heterogeneity exists in formulations (10^8-10^{11} CFU/day), durations (4-12 weeks), and outcome measures.

Prebiotics and Dietary Fiber

Limited evidences support prebiotic interventions,with inulin supplementation

Table 1: Literature search and selection.

Database	Search results	After duplicate removal	Full-text reviewed	Included
PubMed	245	198	85	47
Scopus	189	167	72	42
Web of Science	156	134	58	38
Total	590	499	215	127

Table 2: Key observational studies.

Reference	Design	Population	Follow-up	Main findings	Quality score
(13)	Prospective	15,980 Spanish	10 years	33% ↓ depression risk	8.9
(14)	Cross-sectional	6,807 Australian	N/A	42% ↓ depression risk	6.9
(15)	Prospective	24,685 Italians	8.2 years	Linear inverse trend	7.9

Randomized controlled trials: Dietary interventions.

demonstrating increased Bifidobacterium abundance and mood improvement (20). High-fiber diets were associated with reduced anxiety symptoms (OR=0.58, 95% CI: 0.45-0.75) (21). Most studies featured small samples and short durations.

Methodological Limitations and Heterogeneity

Significant heterogeneity stems from:(i) diverse outcome measures; (ii) variable intervention protocols; (iii) participant characteristics; and (iv) cultural dietary patterns. Publication bias remains a concern, with Egger's test indicating small-study effects in probiotic research (p=0.03).

Discussion

Comparison with Existing Literature

Our findings align with previous systematic reviews regarding Mediterranean diet benefits (22, 23), though effect sizes appeared more modest in recent replication studies. The strain-specific effects of probiotics corroborated earlier meta-analyses (24), while highlighting the need for standardization.

Mechanistic Considerations

The gut-brain axis mediates diet-mental health relationships through multiple pathways including (i) microbial metabolite production (SCFAs); (ii) inflammatory modulation; and (iii) neuroendocrine regulation (25-27). Recent human studies using multi-omics approaches have identified specific microbial signatures associated with treatment response (28).

Clinical Implications and Implementation Challenges

Nutritional interventions should be considered adjunctive rather than standalone treatments. Implementation requires consideration of (i) cultural and economic factors affecting dietary adherence (29); (ii) Individual microbiome variability influencing treatment response; and (iii) Practical challenges in maintaining long-term dietary interventions (30).

Limitations of Current Evidence

Methodological limitations were mentioned as (a) small sample sizes in most RCTs; (b) short follow-up durations; (c) heterogeneous outcome measures; (d) limited diversity in study populations; and (e) potential conflicts of interest in industry-funded probiotic research.

Future Research Directions

Priority areas were described as (1) large-scale RCTs with standardized interventions; (2) longer follow-up periods (>12 months); (3) biomarker development for personalized approaches; (4) economic evaluations of nutritional interventions; and (5) cultural adaptation of dietary recommendations.

Conclusion

Current evidences suggest anti-inflammatory diets and microbiome modulation may provide benefits as adjunctive interventions for depression and anxiety. However, methodological limitations and inconsistent findings necessitate cautious interpretation. Clinical implementation should consider individual preferences, cultural factors, and practical constraints. Future researches should address current methodological limitations; while exploring personalized nutrition approaches based on individual microbiome characteristics and inflammatory profiles. Nutritional psychiatry holds promise; but requires more rigorous evidences to inform clinical practice.

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Authors' Contribution

MMT: Conceptualization, writing, original draft, investigation, and methodology. MG: Writing, review and editing, methodology, validation, and formal analysis. All authors read and approved the final manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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