International Journal of Research in Medical Sciences
Córdova JG et al. Int J Res Med Sci. 2025 Oct;13(10):4465-4469
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20253209

Review Article

Effects of probiotics on neurodegenerative diseases

Juan G. Córdova*, Edison H. Freile, Prisca del P. Acosta, Paolo T. Cañarte, José N. Castillo, Ma A. Núñez, Melpisa P. Andrade

Ministry of Public Health, Quito, Ecuador

Received: 17 August 2025
Accepted: 18 September 2025

***Correspondence:**
Dr. Juan G. Córdova,
E-mail: carlosachangor@gmail.com

ABSTRACT

Neurodegenerative diseases, including Alzheimer's disease, Parkinson's disease, and multiple sclerosis, represent a growing public health challenge due to their high prevalence and the lack of curative therapies. In this context, research on the gut–brain axis has highlighted the crucial role of the intestinal microbiota in modulating neurological processes and in the pathophysiology of these disorders. Probiotics, defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host, have shown potential neuroprotective effects. Preclinical and clinical studies have demonstrated that probiotics may modulate neuroinflammation, reduce oxidative stress, improve blood–brain barrier integrity, and regulate the production of neurotransmitters such as serotonin, GABA, and dopamine. In Parkinson's disease, the administration of Lactobacillus and Bifidobacterium strains has been associated with improvements in gastrointestinal symptoms and reductions in systemic inflammatory markers. In Alzheimer's disease, probiotic supplementation has been linked to benefits in cognitive parameters and decreases in inflammatory biomarkers. Likewise, in multiple sclerosis models, probiotics appear to modulate immune responses by promoting an anti-inflammatory profile. Although current findings are promising, the heterogeneity of probiotic strains, variability in study designs, and the limited number of controlled clinical trials highlight the need for further research to establish standardized protocols. Incorporating probiotic-based therapies may represent a complementary approach in the prevention and management of neurodegenerative diseases within the framework of personalized and interdisciplinary medicine.

Keywords: Probiotics, Gut–brain axis, Intestinal microbiota, Neuroinflammation, Alzheimer's disease, Parkinson's disease, Multiple sclerosis, Neuroprotection

INTRODUCTION

Neurodegenerative diseases, such as Alzheimer's disease, Parkinson's disease, and multiple sclerosis, are among the leading causes of disability and mortality worldwide. Characterized by progressive neuronal loss and chronic neuroinflammation, these disorders currently lack curative treatments, with available therapies largely limited to symptomatic management.[1] This growing clinical and social burden has stimulated interest in exploring novel therapeutic strategies that target modifiable risk factors and biological pathways beyond the central nervous system.[2]

In recent years, the gut–brain axis has emerged as a key area of research linking intestinal microbiota composition with neurological health.[3] Accumulating evidence suggests that dysbiosis, defined as an imbalance in microbial populations, contributes to systemic inflammation, altered neurotransmitter production, oxidative stress, and impaired blood–brain barrier function—all mechanisms implicated in neurodegenerative disease progression. Within this framework, probiotics have gained particular attention as potential modulators of both gut homeostasis and brain function.[4]

Probiotics, mainly belonging to the genera Lactobacillus and Bifidobacterium, have demonstrated the ability to regulate host immune responses, enhance intestinal barrier integrity, and influence the synthesis of neuroactive compounds such as gamma-aminobutyric acid (GABA), serotonin, and dopamine.[5] Preliminary findings from animal models and early-phase clinical trials indicate that probiotic supplementation may alleviate cognitive decline, improve gastrointestinal dysfunction, and attenuate inflammatory processes in patients with neurodegenerative disorders.[6]

Despite these promising results, the evidence remains heterogeneous and strain-specific, with significant gaps in our understanding of the optimal dosage, duration, and combination of probiotic therapies. Nevertheless, the integration of probiotics into preventive and therapeutic strategies represents a promising frontier in neurology and translational medicine. Investigating their role in neurodegenerative diseases not only broadens our knowledge of the gut–brain axis but also opens the door to innovative interventions within the scope of personalized medicine.

METHODS

It is a descriptive-exploratory study type of bibliographic review. The literature search period is from 2018 to 2024 in electronic databases such as PubMed, Elsevier, and Web of Science. The keywords used in the MesH search were: probiotics; gut–brain axis; intestinal microbiota; neuroinflammation; Alzheimer's disease; Parkinson's disease; multiple sclerosis; and neuroprotection.

Inclusion criteria

Search terms, level of evidence, summaries and keywords were included.

Exclusion criteria

Anything not related to the topic, outside the year limit, and not available studies were excluded.

They will be classified by year, type of study and level of evidence. For eligibility, a critical reading is carried out, level of evidence, documents available for analysis and according to the topic. A total of 30 sources were obtained for analysis and synthesis.

RESULTS

Efficacy of probiotics in Parkinson's disease

A randomized, double-blind, placebo-controlled study (12 weeks, 60 patients) found that probiotic supplementation significantly reduced the Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) (PD severity scale) score, decreased high-sensitivity C-reactive protein and malondialdehyde levels, and increased glutathione levels. It also improved metabolic profiles related to insulin and insulin resistance. The gut microbiota plays an essential role in controlling the immune system. Variations in microbiota composition can influence the immune system's response, promoting autoimmune processes that could lead to the development of thyroid disorders, such as autoimmune thyroiditis, which could be linked to the appearance of thyroid nodules.[7]

A high-evidence (class I) trial evaluated the effect on constipation in 72 patients with PD. The probiotic-treated group showed a significant increase in spontaneous bowel movements per week (+1.0 versus -0.3 in placebo; $p<0.001$), improved bowel consistency, and greater patient satisfaction. There were no significant differences in fecal inflammatory markers (calprotectin).[8]

Another meta-analysis (9 RCTs, N=663) showed improvements in motor symptoms (UPDRS-III), constipation, bowel quality of life, anxiety, and depression. Reduced laxative use and increased serum glutathione levels were also observed. However, the certainty of the evidence was rated as "very low" or "low" for many outcomes.[9]

An additional meta-analysis concluded that probiotics improve motor and non-motor symptoms, and even depression. Improvement in gastrointestinal motility was greater when probiotics were administered in capsule form rather than fermented dairy products, and there were more lasting effects with longer follow-up.[10]

A recent clinical study (12 weeks) evaluated the impact on motor (UPDRS III) and non-motor (NMSS) symptoms, as well as immunological markers. The probiotic-treated group showed improvement in both types of symptoms, reduction of IL-6, decrease of IFN-γ and increase of TGF-β, indicating an immunomodulatory effect.[11]

Preclinical and animal model studies

In animal models (MitoPark mice, mice exposed to MPTP/rotenone, or 6-OHDA), supplementation with Lactobacillus and Bifidobacterium mixtures improved motor function, preserved dopaminergic neurons, increased neurotrophic factors (BDNF, GDNF), reduced neuroinflammation and oxidative stress, and stimulated butyrate production.[12] In invertebrate and cellular models, Bacillus subtilis was shown to reduce α-synuclein aggregation, and certain strains inhibited the production of proinflammatory cytokines and reactive oxygen species in cells from PD patients.[13]

Efficacy of probiotics in multiple sclerosis

Interest in the role of probiotics in multiple sclerosis (MS) has grown significantly as evidence points to the role of intestinal dysbiosis in disease pathogenesis and progression. Early clinical studies and recent systematic

reviews suggest that modulating the microbiota with probiotics could attenuate inflammatory processes, improve immunological parameters, and offer symptomatic benefits, although the available evidence remains heterogeneous and strain-dependent.

Clinical and mental health parameters

In another 12-week RCT, probiotic supplementation improved clinical scores (disability), depression/anxiety/ stress and biomarkers (NO, MDA), and impacted metabolic profiles, relative to placebo.[14] Clinical and mental health parameters: In another 12-week RCT, probiotic supplementation improved clinical scores (disability), depression/anxiety/ stress and biomarkers (NO, MDA), and impacted metabolic profiles, relative to placebo.[15]

Recent RCTs report good short-term tolerance and adherence; no serious adverse events attributable to the probiotic were observed in these pilot studies. However, long-term safety data and data on interactions with disease-modifying therapies are lacking.[16]

Immunological and metabolic effects

A randomized clinical trial (12 weeks, 60 patients with relapsing-remitting MS) showed that administration of a multistrain probiotic (*Lactobacillus acidophilus*, *L. casei*, *L. fermentum*, *Bifidobacterium bifidum*) significantly reduced ultrasensitive C-reactive protein (hs-CRP), malondialdehyde (MDA) and serum nitric oxide, while improving the total antioxidant profile and clinical parameters such as disability (EDSS), fatigue and mood compared to placebo.[17]

Symptoms and quality of life

Another 12-week study of probiotics in patients with relapsing-remitting MS reported significant improvements in depression, anxiety, and perceived stress, suggesting a positive impact on psychoneurological outcomes as well as immune function.[18]

Feasibility study with prebiotics versus probiotics

A crossover study compared the administration of a multi-strain probiotic (Visbiome®, with 8 strains of Lactobacillus and Bifidobacterium) versus a prebiotic (enriched inulin) for 6 weeks in patients with MS. Both were well tolerated and showed signs of symptomatic and microbial benefit, confirming the feasibility of microbiota-modulating interventions in this group.[19]

Evidence on probiotics in Alzheimer's disease

Several randomized, double-blind clinical trials have evaluated supplementation with Lactobacillus and Bifidobacterium strains (and multi-strain mixtures) in patients with Alzheimer's disease or mild cognitive impairment (MCI). Some 8–12-week RCTs reported modest and transient improvements in cognitive scales (MMSE, ADAS-Cog, or other cognitive tests), in addition to favorable effects on inflammatory and oxidative stress markers (e.g., ↑ TAC, ↓ MDA, ↓ hs-CRP). These studies are promising but generally have small sample sizes and short duration.[20]

Quantitative syntheses published between 2020 and 2024 show heterogeneous results: several meta-analyses report a statistically significant overall improvement in cognitive function following probiotic supplementation in MCI/AD populations, although the effect varies by study and heterogeneity (I^2) is often high. The reviews conclude that the effects could be mediated by reduced inflammation, improved oxidative profile, and improved insulin sensitivity, but caution about the low or moderate quality of the evidence and the need for more robust RCTs.[21]

Published clinical trials generally report good tolerability: mild adverse effects (bloating, gas, GI discomfort) and no serious related events. However, long-term data (years) and data in vulnerable subgroups (immunocompromised, very frail patients) are lacking.[22]

DISCUSSION

Accumulating evidence suggests that modulation of the gut microbiota by probiotics may favorably influence parameters relevant to Alzheimer's disease (AD), although the strength and consistency of the effects remain limited. Short-term (usually 8–12 weeks) randomized, double-blind clinical trials have reported modest improvements in cognitive scores (e.g., MMSE, ADAS-Cog) and in systemic markers associated with neurodegeneration—such as reduced inflammatory markers and oxidative stress and increased total antioxidant capacity—providing preliminary evidence of clinical-biological benefit in populations with AD or mild cognitive impairment. However, these studies are often small and heterogeneous in design and probiotic formulation.[23]

Plausible biological mechanisms

Several translational mechanisms explain the plausibility of the observed effects. First, the reduction in systemic inflammation (↓ IL-6, ↓ TNF-α, ↓ hs-CRP) following probiotic supplementation may translate into less microglial activation and neuroinflammation, central processes in AD.[24] Second, the attenuation of oxidative stress (↓ MDA; ↑ antioxidant markers) protects vulnerable neuronal structures in the hippocampus and cortex. Third, the restoration of intestinal barrier integrity and the decrease in lipopolysaccharide (LPS) translocation may reduce peripheral proinflammatory stimuli that fuel neuroinflammation.[24] Finally, the production of beneficial microbial metabolites (SCFAs such as butyrate) and the modulation of tryptophan/AHR pathways may influence synaptic plasticity and microglial function. These mechanisms are supported by preclinical studies in

transgenic models of AD where probiotic mixtures improved memory and reduced neuropathological markers.[25]

Clinical relevance and practical interpretations

The clinical findings suggest that probiotics could play an adjuvant role in the early stages of cognitive impairment or as part of integrated strategies (diet + probiotic + vascular/metabolic approach). The benefits observed in metabolic parameters (e.g., insulin sensitivity) and inflammatory markers could be particularly relevant in patients with metabolic comorbidity, where the synergy between metabolism and neurodegeneration is evident. However, the magnitude of the cognitive improvement reported in current trials is generally small and of limited duration, so their true clinical impact remains uncertain.[26]

Critical limitations of the evidence

The literature presents important methodological limitations that restrict firm conclusions: heterogeneity of probiotic strains (different species of Lactobacillus, Bifidobacterium, and multi-strain mixtures), doses, and administration matrices; small sample sizes and short follow-up periods (≤12 weeks in most), insufficient to assess sustained clinical progression; variability in cognitive outcomes and limited use of direct brain biomarkers (CSF, PET/amyloid, volume/atrophy MRI); and risk of bias and possible selective publication in some meta-analyses. These limitations require caution when interpreting the results and proposing universal clinical recommendations.[27,28]

Safety and tolerability profile

Published clinical studies report good tolerability of probiotic formulations in populations with AD or MCI: adverse effects are generally mild and gastrointestinal (bloating, flatulence), and no serious events attributed to probiotics have been documented in the available trials. However, long-term data and studies in vulnerable subgroups (very frail, immunosuppressed patients) are lacking, so recommendations for chronic use require further evidence.[29,30]

CONCLUSION

Overall, the available evidence supports the biological plausibility that probiotics can modulate pathogenic processes implicated in AD and produce modest benefits in cognitive function and inflammatory-oxidative markers. However, methodological heterogeneity, small trial sizes, and the short duration of most studies limit the robustness of clinical recommendations. Probiotics are currently emerging as a promising adjuvant intervention that warrants larger, standardized trials with extended follow-up before their routine adoption in clinical practice for Alzheimer's disease.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Taghizadeh Ghassab F, Shamlou Mahmoudi F, Taheri Tinjani R, Emami Meibodi A, Zali MR, Yadegar A. Probiotics and the microbiota-gut-brain axis in neurodegeneration: beneficial effects and mechanistic insights. Life Sci. 2024;350:122748.
2. Gitler AD, Dhillon P, Shorter J. Neurodegenerative disease: models, mechanisms, and a new hope. Dis Model Mech. 2017;10(5):499-502.
3. Wyss-Coray T. Ageing, neurodegeneration and brain rejuvenation. Nature. 2016;539(7628):180-6.
4. Kritsilis M, Rizou S, Koutsoudaki PN, Evangelou K, Gorgoulis VG, Papadopoulos D. Ageing, Cellular Senescence and Neurodegenerative Disease. Int J Mol Sci. 2018;19(10).
5. Gammon K. Neurodegenerative disease: brain windfall. Nature. 2014;515(7526):299-300.
6. Wilson DM, Cookson MR, Van Den Bosch L, Zetterberg H, Holtzman DM, Dewachter I. Hallmarks of neurodegenerative diseases. Cell. 2023;186(4):693-714.
7. Tamtaji OR, Taghizadeh M, Daneshvar Kakhaki R, Kouchaki E, Bahmani F, Borzabadi S, et al. Clinical and metabolic response to probiotic administration in people with Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Clin Nutr. 2019;38(3):1031-5.
8. Tan AH, Lim SY, Chong KK, A Manap MAA, Hor JW, Lim JL, et al. Probiotics for Constipation in Parkinson Disease: A Randomized Placebo-Controlled Study. Neurology. 2021;96(5):e772-82.
9. Chu C, Yu L, Li Y, Guo H, Zhai Q, Chen W, Tian F. Meta-analysis of randomized controlled trials of the effects of probiotics in Parkinson's disease. Food Funct. 2023;14(8):3406-22.
10. Park JM, Lee SC, Ham C, Kim YW. Effect of probiotic supplementation on gastrointestinal motility, inflammation, motor, non-motor symptoms and mental health in Parkinson's disease: a meta-analysis of randomized controlled trials. Gut Pathog. 2023;15(1):9.
11. Magistrelli L, Contaldi E, Visciglia A, Deusebio G, Pane M, Amoruso A. The Impact of Probiotics on Clinical Symptoms and Peripheral Cytokines Levels in Parkinson's Disease: Preliminary In Vivo Data. Brain Sci. 2024;14(11):1147.
12. Pandey S, Das S, Bamola VD, Kochhar KP. Long-term Probiotics Intervention Facilitates Recovery of Motor and Non-motor Functions by Regulating Inflammation and Modulating Gut-brain Axis in 6-OHDA Rat Model of Parkinson's Disease. Ann Neurosci. 2025;09727531251335746.
13. Jia X, Chen Q, Zhang Y, Asakawa T. Multidirectional associations between the gut microbiota and Parkinson's disease, updated information from the

perspectives of humoral pathway, cellular immune pathway and neuronal pathway. Front Cell Infect Microbiol. 2023;13:1296713.
14. Asghari KM, Dolatkhah N, Ayromlou H, Mirnasiri F, Dadfar T, Hashemian M. The effect of probiotic supplementation on the clinical and para-clinical findings of multiple sclerosis: a randomized clinical trial. Sci Rep. 2023;13(1):18577.
15. Straus Farber R, Walker EL, Diallo F, Onomichi K, Riley C, Zhang L, et al. A randomized cross-over trial of prebiotics and probiotics in multiple sclerosis: Trial feasibility, supplement tolerability and symptom abatement. Mult Scler Relat Disord. 2024;89:105762.
16. Straus Farber R, Walker EL, Diallo F, Onomichi K, Riley C, Zhang L, et al. A randomized cross-over trial of prebiotics and probiotics in multiple sclerosis: Trial feasibility, supplement tolerability and symptom abatement. Mult Scler Relat Disord. 2024;89:105762.
17. Tamtaji OR, Taghizadeh M, Daneshvar Kakhaki R, Kouchaki E, Bahmani F, Borzabadi S, et al. Clinical and metabolic response to probiotic administration in people with Parkinson's disease: A randomized, double-blind, placebo-controlled trial. Clin Nutr. 2019;38(3):1031-5.
18. Chu C, Yu L, Li Y, Guo H, Zhai Q, Chen W, et al. Meta-analysis of randomized controlled trials of the effects of probiotics in Parkinson's disease. Food Funct. 2023;14(8):3406-22.
19. Yin S, Zhu F. Probiotics for constipation in Parkinson's: a systematic review and meta-analysis of randomized controlled trials. Front Cell Infect Microbiol. 2022;12:1038928.
20. Hsu YC, Huang YY, Tsai SY, Kuo YW, Lin JH, Ho HH, et al. Efficacy of Probiotic Supplements on Brain-Derived Neurotrophic Factor, Inflammatory Biomarkers, Oxidative Stress and Cognitive Function in Patients with Alzheimer's Dementia: A 12-Week Randomized, Double-Blind Active-Controlled Study. Nutrients. 2023;16(1):16.
21. Liu N, Yang D, Sun J, Li Y. Probiotic supplements are effective in people with cognitive impairment: a meta-analysis of randomized controlled trials. Nutri Rev. 2023;81(9):1091-104.
22. Hsu YC, Huang YY, Tsai SY, Kuo YW, Lin JH, Ho HH, et al. Efficacy of Probiotic Supplements on Brain-Derived Neurotrophic Factor, Inflammatory Biomarkers, Oxidative Stress and Cognitive Function in Patients with Alzheimer's Dementia: A 12-Week Randomized, Double-Blind Active-Controlled Study. Nutrients. 2023;16(1):16.
23. Akbari E, Asemi Z, Daneshvar Kakhaki R, Bahmani F, Kouchaki E, Tamtaji OR, et al. Effect of probiotic supplementation on cognitive function and metabolic status in Alzheimer's disease: A randomized, double-blind and controlled trial. Front Aging Neurosci. 2016;8:256.
24. Tamtaji OR, Heidari-Soureshjani R, Mirhosseini N, Kouchaki E, Bahmani F, Aghadavod E, et al. Probiotic and selenium co-supplementation, and the effects on mental health parameters and metabolic status in Alzheimer's disease: A randomized, double-blind, controlled trial. Clin Nutr. 2019;38(6):2569-75.
25. Yang X, Yu D, Xue L, Li H, Du J, Yu X, et al. Probiotics modulate the microbiota–gut–brain axis and improve memory deficits in a transgenic mouse model of Alzheimer's disease. Front Aging Neurosci. 2020;12:80.
26. Markowiak P, Śliżewska K. Effects of probiotics, prebiotics, and synbiotics on human health. Nutrients. 2017;9(9):1021.
27. Akhgarjand C, Vahabi Z, Shab-Bidar S, Anoushirvani A, Djafarian K. The effects of probiotic supplements on oxidative stress and inflammation in subjects with mild and moderate Alzheimer's disease: a randomized, double-blind, placebo-controlled study. Inflammopharmacology. 2024;32(2):1413-20.
28. Tamtaji OR, Heidari-Soureshjani R, Mirhosseini N, Kouchaki E, Bahmani F, Aghadavod E, et al. Probiotic and selenium co-supplementation, and the effects on mental health parameters and metabolic status in Alzheimer's disease: A randomized, double-blind, controlled trial. Clin Nutr. 2019;38(6):2569-75.
29. Moravejolahkami AR, Chitsaz A, Hassanzadeh A, Paknahad Z. Effects of anti-Inflammatory-antioxidant-rich diet and co-supplemented synbiotics intervention in patients with progressive forms of multiple sclerosis: a single-center, single-blind randomized clinical trial. Nutr Neurosci. 2023;26(11):1078-89.
30. Barichella M, Pacchetti C, Bolliri C, Cassani E, Iorio L, Pusani C, et al. Probiotics and prebiotic fiber for constipation associated with Parkinson disease: An RCT. Neurology. 2016;87(12):1274-80.

Cite this article as: Córdova JG, Freile HE, Acosta PP, Cañarte PT, Castillo JN, Núñez MN, et al. Effects of Probiotics on Neurodegenerative Disease. Int J Res Med Sci 2025;13:4465-9.