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## *The Role of Probiotics in Improving Alzheimer's Disease*

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Alzheimer's disease is the most common form of age-related dementia and is one of the most rapidly increasing diseases worldwide (Agahi *et al.*, 2018, Azm *et al.*, 2017). There are over 50 million people worldwide living with Alzheimer's disease. The prevalence of Alzheimer's disease is predicted to more than 100 million in 2050 (Cui *et al.*, 2020).

This disease is a gradual and progressive neurological disorder of the central nervous system characterized by profound impairment of cognitive function and memory (Den *et al.*, 2020). In addition, it involves a number of inflammatory processes with increased expression of acute phase proteins, interleukin-6. Serum levels of interleukins 1, 4, and 10 and interferon-gamma have been shown to change with the severity of Alzheimer's disease (Ansari *et al.*, 2020).

The main causes of this disease are hyperphosphorylation of tau proteins, formation of intracellular neurofibrillary tangles and formation of beta-amyloid plaques in the extracellular space,

which often includes a peptide consisting of 40 or 42 amino acids (Kaur *et al.*, 2020). Oxidative stress seems to play a major role in this pathogenesis. Beta-amyloid protein is deposited within and between neurons and reduces inflammation, memory, and neurodegeneration in the hippocampus, cortex, synaptic flexibility, and neurological dysfunction by causing inflammation and oxidative stress reactions (Khoury and Grossberg, 2020).

There are 10<sup>14</sup> microorganisms living in the human digestive tract. There is ample evidence that these gut microbial communities can greatly affect all aspects of physiology, including brain-gut communication, brain function, and even behavior. The term brain-gut-microbiota axis has been introduced to reflect interventions between intestinal and central nervous system microbes. Microbiota affects brain function and the brain affects the composition of the microbiota by affecting digestion (Shamsipour *et al.*, 2021).

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Some metabolic diseases, including hyperglycemia, hyperlipidemia, insulin resistance, obesity, and autoimmune diseases have been shown to be associated with Alzheimer's disease (Asl *et al.*, 2019).

Three cholinesterase inhibitors (donepezil, rivastigmine, and galantamine) are used to treat mild to severe Alzheimer's, and N-methyl receptor antagonists in aspartate (memantine) are used for moderate to severe Alzheimer's disease (Abraham *et al.*, 2019). Given the disappointing results of current treatments for cognitive disorders in Alzheimer's patients, finding better and more effective drugs in this area seems necessary (Ansari *et al.*, 2020, Wong *et al.*, 2018).

The gastrointestinal tract and central nervous system are connected by the vagus nerve, which is an important part of the autonomic nervous system that controls involuntary activities, such as breathing, swallowing, and digestion. The connection between these two organs reflects the vital role of the brain-gut axis in mental health and diseases, such as depression, anxiety, Alzheimer's, autism, and even diseases, such as irritable bowel syndrome (Shamsipour *et al.*, 2021).

Probiotics are living microorganisms that, if taken adequately, can improve host health. Different combinations of bacterial species can be used to improve the effect of probiotics. The most common of which is a mixture of Lactobacillus and Bifidobacteria. Probiotics have a wide range of effects in human and animal studies, for example, administration of Bifid and Bacterium in mice exposed to forced swimming test caused neurochemical changes and reduced inflammatory reactions, demonstrating the prescribed antidepressant ability of probiotics. Probiotics also inhibit oxidative stress by reducing inflammatory damage and increasing levels of antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase.

#### Authors' contributions

Marzban A, Rahmanian V conceived the original idea and designed the project. Marzban AR, Ramezani- Siakhulak F collected the data

and wrote the draft of manuscript. All authors read and approved the final version of manuscript.

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