zgłoszono 12.09.2025 – zaakceptowano 23.09.2025

The gerobiotic concept: lactic acid bacteria as modulators of cellular aging

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Abstract

According to the World Health Organization, the global population over 60 years of age will nearly double by 2050, reaching 2.1 billion. This demographic shift has intensified efforts to identify strategies that modulate aging and extend healthspan. Once viewed as inevitable, aging is increasingly recognized as a process shaped by cellular senescence, mitochondrial dysfunction, and gut microbiota imbalance - pathways that may be amenable to intervention. Senotherapeutics, including senolytics and senomorphics, target these mechanisms, while the emerging category of gerobiotics - probiotics, prebiotics, and postbiotics designed for older adults offers a complementary approach. Lactic acid bacteria, abundant in fermented foods, show promise in promoting healthy aging by enhancing mitochondrial function, regulating immune responses, restoring microbial balance, and reducing inflammation and oxidative stress. Although clinical evidence remains limited, preliminary findings support gerobiotics as potential tools for improving metabolic, immune, and cognitive functions, underscoring their value in science-based strategies for healthy longevity. (Gerontol Pol 2025; 33; 228-233) doi: 10.53139/GP.20253323

Keywords: *lactic acid bacteria, gerobiotics, cellular senescence, senotherapeutics, healthy aging, gut microbiota*

Introduction

By 2050, the number of people aged 60 years and older is projected to double to nearly 2.1 billion, according to the World Health Organization [1]. This profound demographic shift has intensified the search for interventions that can slow or modulate the aging process. Increasingly, aging and its associated diseases are being recognized as pathological conditions rather than inevitable outcomes, a perspective that has catalyzed the development of anti-aging therapies, innovative dietary supplements, and strategies promoting healthy longevity [2]. Central to these efforts is the study of cellular senescence, a process in which cells permanently exit the cell cycle in response to telomere attrition, DNA damage, oxidative stress, or other insults. Although senescent cells cease to divide, they remain metabolically active and release a pro-inflammatory secretome known as the senescence-associated secretory phenotype (SASP), which disrupts tissue homeostasis and drives chronic inflammation [3,4]. Accumulation of senescent cells disrupts tissue homeostasis and contributes to age-related diseases, including cardiovascular disease, diabetes, neurodegeneration, and cancer. These insights have catalyzed the emergence of senotherapeutics, a class of interventions designed to eliminate senescent cells or suppress their harmful secretions [5-10]. In parallel, growing evidence implicates the gut microbiome in shaping immune function, metabolism, cognitive health, and systemic inflammation during aging [11-14]. This recognition has given rise to the concept of gerobiotics - probiotics, prebiotics, and postbiotics specifically selected to target fundamental aging processes and support healthy longevity [15,16].

Senotherapeutics

Senotherapeutics can be broadly classified into two categories:

– Senolytics: agents that selectively eliminate senescent cells. These include chemotherapeutics such as dasatinib and navitoclax; flavonoids such as fisetin and quercetin; and emerging immunotherapies, including senolytic vaccines, antibody–drug conjugates, and CAR-T cells [6-9],
– Senomorphics (or senostatics): agents that suppress SASP factors without killing senescent cells. Examples include rapamycin, resveratrol, kaempferol, apigenin, and metformin [5,7,8].

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Preclinical studies have shown that senotherapeutics can restore tissue function, extend healthspan, and reduce disease burden in animal models. Early clinical studies demonstrate feasibility, but key challenges remain: defining biomarkers of efficacy, standardizing treatment regimens, ensuring safety in multimorbid older adults, and identifying optimal drug combinations [10]. In addition to pharmacological approaches, natural compounds and microbiome-modulating strategies have been proposed as indirect senotherapeutics. Evidence suggests that phytochemicals and probiotics can attenuate SASP-driven inflammation, reduce oxidative stress, and improve mitochondrial function mechanisms that overlap with those of canonical senomorphics [16-18].

Gerobiotics: framework and rationale

The term gerobiotics was introduced to describe microbiome-based interventions probiotics, prebiotics, postbiotics, and synbiotics, specifically designed to promote healthy aging [17]. Unlike conventional probiotics, gerobiotics are defined by their ability to beneficially affect fundamental aging processes. Tsai et al. (2021) proposed a translational framework for their development, consisting of: (i) high-throughput screening in invertebrate models such as *Caenorhabditis elegans* and *Drosophila melanogaster*; (ii) validation in mammalian aging models, particularly mice, and (iii) well-designed human clinical trials with standardized aging biomarkers [17]. Recent perspectives emphasize that strain specificity, host–diet interactions, and baseline microbiota composition are critical determinants of gerobiotic efficacy. Mahamud et al. (2025) argue that gerobiotics should be evaluated through the lens of the hallmarks of aging, including mitochondrial dysfunction, deregulated nutrient sensing, and chronic inflammation, while acknowledging the regulatory, methodological, and ethical challenges of conducting long-term trials in elderly populations [16].

Mechanistically, gerobiotics appear to influence aging through several convergent pathways:

– Immune modulation and inflammaging control: restoring gut barrier integrity, reducing endotoxemia, and dampening NF-κB-driven cytokine cascades,
– Mitochondrial and redox homeostasis: enhancing oxidative stress resistance and supporting energy metabolism,
– Nutrient sensing and metabolic regulation: modulating AMPK and mTOR pathways, improving insulin sensitivity, and influencing IGF-1 signaling [16,17],
– Gut–brain axis effects: studies suggest gerobiotics may reduce neuroinflammation, improve neurotransmitter balance, and protect against age-related cognitive decline, including in Alzheimer's disease models [18].

Together, these mechanisms position gerobiotics as a complementary branch of senotherapeutics, with the potential to promote systemic resilience and extend healthspan by targeting both local gut processes and systemic aging pathways.

Evidence for gerobiotics in aging

Invertebrate models

Invertebrate organisms such as the nematode *Caenorhabditis elegans* and the fruit fly *Drosophila melanogaster* are widely used to evaluate the impact of microbial interventions on lifespan and aging-related pathways. These models provide cost-effective, high-throughput systems that allow rapid screening of probiotic strains and elucidation of conserved molecular mechanisms [19–21]. For example, *Ligilactobacillus murinus* CR147 increased nematode size and lifespan while reducing interleukin-8 production in intestinal epithelial cells [22]. *Ligilactobacillus salivarius* FDB89 extended nematode lifespan by nearly 12%, partly by mimicking dietary restriction mechanisms [23]. In *Drosophila melanogaster*, supplementation with Limosilactobacillus reuteri extended lifespan by modulating insulin/insulin-like growth factor-1 (IGF-1) signaling [24]. These findings suggest that gerobiotic effects on evolutionarily conserved nutrient-sensing and stress-response pathways may contribute to longevity promotion.

Rodent studies

Rodent models provide valuable insights into the systemic effects of probiotics and their role in mitigating hallmark features of aging. Accelerated aging paradigms, such as the D-galactose model, have been used extensively to test lactic acid bacteria (LAB). *Levilactobacillus brevis* OW38 alleviated inflammation in aged mice by reducing lipopolysaccharide levels and inhibiting pro-inflammatory cytokines [25]. Similarly, *Limosilactobacillus reuteri* BM36301 improved metabolic health, reduced weight gain, and enhanced skin and reproductive parameters in aging mice [26]. *Lacticaseibacillus paracasei* NCC2461 boosted antigen-specific immune responses, highlighting the immunomodulatory potential of gerobiotics [27]. Studies using D-galactose-induced oxidative stress models demonstrated that *Lactiplantibacillus plantarum* strains AR113 and AR501 enhanced antioxidant enzyme activity via nuclear factor erythroid 2–related factor 2 (Nrf2)-mediated pathways, reducing oxidative damage in hepatic tissue [28]. Similarly, *Lactiplantibacillus plantarum* CCFM10 protected against oxidative stress and gut dysbiosis [23]. These data collectively support a role for LAB in modulating oxidative stress, inflammation, mitochondrial function, and immunity four major axes of aging biology. These experimental outcomes are summarized in Table I, which highlights representative lactic acid bacteria strains and their effects across model organisms.

Human trials

Building on these preclinical findings (table I), several clinical studies have begun to evaluate LAB-based interventions in older adults. Despite promising preclinical data, clinical research on gerobiotics remains limited. Nonetheless, several human studies have reported encouraging results. In elderly nursing home residents, continuous intake of a fermented milk drink containing *Lacticaseibacillus casei* Shirota reduced fever duration and enhanced natural killer (NK) cell activity, accompanied by increased levels of the anti-inflammatory cytokine interleukin-10 [29]. A randomized, double-blind trial demonstrated that *Lactiplantibacillus plantarum* HY7714 improved skin hydration, elasticity, and reduced wrinkle depth, providing evidence for gerobiotic effects on skin aging [30]. Emerging human data also suggest that gut microbiota modulation may influence cognitive health and resilience in aging. In particular, Ağagündüz et al. (2022) highlighted the potential role of gerobiotics in Alzheimer's disease, proposing mechanisms such as reduced neuroinflammation, improved neurotransmitter metabolism, and strengthened gut–brain axis signaling [18]. Although promising, these findings underscore the need for large, placebo-controlled trials using standardized biomarkers of aging, such as markers of senescence, mitochondrial function, and systemic inflammation. Mahamud et al. (2025) emphasize that the translational success of gerobiotics will depend on rigorous clinical validation, regulatory clarity, and precise strain characterization [16].

Future perspectives and challenges

Although gerobiotics represent a promising frontier in aging research, their advancement from concept to clinical application faces several obstacles.

1. Clinical trial design

Most studies to date rely on invertebrate and rodent models, while human trials remain sparse, small in scale, and often focused on general health outcomes rather than validated biomarkers of aging. Placebo-controlled, longitudinal trials in elderly populations are particularly challenging because of frailty, comorbidities, and polypharmacy, which can confound results. Mahamud et al. (2025) stress the importance of integrating standardized biomarkers such as senescence-associated proteins, mitochondrial function markers, and systemic inflammation indices to reliably assess gerobiotic efficacy [16].

Table I. Modulation of Cellular Aging by Lactic Acid Bacteria (examples)

Strain	Action	Model organism	Reference
Ligilactobacillus murinus CR147	Reduced interleukin-8 production in Caco-2 cells; increased lifespan and body size	*Caenorhabditis elegans*	(22)
Ligilactobacillus salivarius FDB89	Increased lifespan by 11.9%, mimicking dietary restriction		(23)
Limosilactobacillus reuteri	Lifespan extension; downregulation of insulin/IGF-1	*Drosophila melanogaster*	(24)
Levilactobacillus brevis OW38	Anti-inflammatory effects; reduced lipopolysaccharide and cytokine expression	Aging mice	(25)
Limosilactobacillus reuteri BM36301	Reduced weight gain; increased testosterone in males; improved skin in females		(26)
Lacticaseibacillus paracasei NCC2461	Enhanced antigen-specific adaptive immunity		(27)
Lactiplantibacillus plantarum AR113 and AR501	Improved antioxidant defense via Nrf2 activation; reduced oxidative liver damage	D-galactose-induced aging mice	(28)
Lactiplantibacillus plantarum CCFM 10	Protected against oxidative damage and gut dysbiosis		(23)
Lacticaseibacillus casei Shirota	Enhanced NK cell activity, increased IL-10, reduced fever days	Older adults	(29)
Lactiplantiobacillus plantarum HY771	Reduced wrinkle depth, improved skin tone, elasticity, and hydration	Volunteers	(30)

2. Strain specificity and host context

The effects of lactic acid bacteria and other probiotics are highly strain-dependent. Benefits observed in one strain cannot be generalized to others within the same species. Moreover, efficacy is influenced by host factors such as diet, genetics, baseline microbiota composition, and overall health status. This complexity demands precise strain characterization and an understanding of host–microbe interactions to ensure reproducible outcomes [16,17].

3. Regulatory and manufacturing considerations

Gerobiotics occupy a gray zone between dietary supplements, functional foods, and therapeutic agents. Regulatory frameworks differ across regions, and current standards may not adequately address strain-level claims or aging-specific indications. Manufacturing challenges include maintaining viability and stability of live strains, ensuring reproducibility, and developing delivery systems that preserve functionality in elderly individuals with altered gut physiology [16].

4. Mechanistic clarity

Although multiple pathways have been proposed including modulation of nuclear factor κB (NF-κB), mechanistic target of rapamycin (mTOR), AMP-activated protein kinase (AMPK), and the gut-brain axis definitive mechanistic links remain to be established in humans. Integrating multi-omics approaches, such as metabolomics, transcriptomics, and microbiome sequencing, will be critical to uncover how gerobiotics influence aging biology at the molecular level. Ağagündüz et al. (2022) emphasize that understanding gut–brain signaling and neuroinflammation is particularly important in the context of Alzheimer's disease and cognitive aging [18].

5. Ethical and practical issues

Long-term gerobiotic supplementation in elderly populations raises ethical and logistical concerns. These include informed consent in frail participants, safety in multimorbid patients, and the risk of over-commercialization of products before sufficient scientific validation. The dietary supplement market already capitalizes on health trends, and premature claims may undermine scientific credibility [31].

Overall, while preclinical findings are encouraging, translating gerobiotics into validated clinical interventions will require carefully designed studies, regulatory clarity, and mechanistic insights. Addressing these challenges will determine whether gerobiotics can transition from a theoretical construct to an evidence-based component of healthy aging strategies.

Conclusion

Aging, once regarded as an inevitable decline, is now recognized as a modifiable biological process shaped by conserved cellular and molecular mechanisms. Interventions targeting cellular senescence senotherapeutics have opened new opportunities for delaying age-related diseases and extending healthspan. Parallel advances in microbiome research have given rise to the concept of gerobiotics, defined as probiotics, prebiotics, and postbiotics selected for their ability to modulate hallmarks of aging.

Evidence from invertebrate and rodent models, as well as early clinical trials, suggests that specific strains of lactic acid bacteria can influence critical pathways of aging, including inflammation, oxidative stress, mitochondrial function, nutrient sensing, and gut–brain signaling. Emerging data also point to their potential role in protecting against cognitive decline and supporting immune function in older adults.

Despite these promising findings, gerobiotics remain an emerging field. Translational progress is limited by strain specificity, methodological variability, regulatory uncertainties, and the lack of standardized aging biomarkers in human studies. Addressing these challenges will be crucial to establish gerobiotics as validated, evidence-based interventions.

In conclusion, gerobiotics represent a promising addition to the toolbox of geroscience. With rigorous mechanistic studies and carefully designed clinical trials, they have the potential to complement pharmacological senotherapeutics and contribute to the promotion of healthy longevity.

Funding
This work was supported by ongoing institutional funding. No additional grants to carry out or direct this particular research were obtained.

Conflict of interest
None

References

1. Rudnicka E, Napierała P, Podfigurna A, et al. The World Health Organization (WHO) approach to healthy ageing. Maturitas. 2020 Sept;139:6-11.
2. Tsai YC, Cheng LH, Liu YW, et al. Gerobiotics: probiotics targeting fundamental aging processes. Bioscience of Microbiota, Food and Health. 2021;40(1):1-11.
3. Ogrodnik M. Cellular aging beyond cellular senescence: Markers of senescence prior to cell cycle arrest in vitro and in vivo. Aging Cell. 2021 Apr;20(4):e13338.
4. Wang AS, Dreesen O. Biomarkers of Cellular Senescence and Skin Aging. Front Genet. 2018 Aug 23;9:247.
5. Dobrzański Z, Witkiewicz W, Kowalczyk A, Rogowska-Sobota K. Długowieczność człowieka – aktualny stan badań przeciw procesom starzenia [Internet]. 3rd ed. PL: Wydawnictwo Akademia Medycyny; 2024 [cited 2025 May 12]. 8 p. (Gerontologia Polska). Available from: https://doi.org/10.53139/GP.20243222
6. Kang C. Senolytics and Senostatics: A Two-Pronged Approach to Target Cellular Senescence for Delaying Aging and Age-Related Diseases. Mol Cells. 2019 Dec 31;42(12):821-7.
7. Kim EC, Kim JR. Senotherapeutics: emerging strategy for healthy aging and age-related disease. BMB Rep. 2019 Jan 31;52(1):47-55.
8. Lagoumtzi SM, Chondrogianni N. Senolytics and senomorphics: Natural and synthetic therapeutics in the treatment of aging and chronic diseases. Free Radical Biology and Medicine. 2021 Aug;171:169-90.
9. Lelarge V, Capelle R, Oger F, et al. Senolytics: from pharmacological inhibitors to immunotherapies, a promising future for patients' treatment. npj Aging. 2024 Feb 6;10(1):12.
10. Raffaele M, Vinciguerra M. The costs and benefits of senotherapeutics for human health. The Lancet Healthy Longevity. 2022 Jan;3(1):e67-77.
11. Xu C, Zhu H, Qiu P. Aging progression of human gut microbiota. BMC Microbiol. 2019 Dec;19(1):236.
12. Ling Z, Liu X, Cheng Y, Yan X, Wu S. Gut microbiota and aging. Critical Reviews in Food Science and Nutrition. 2022 May 3;62(13):3509-34.
13. Liu R, Sun B. Lactic Acid Bacteria and Aging: Unraveling the Interplay for Healthy Longevity. Aging Dis. 2023 Oct 10;15(4):1487-98.
14. Kim S, Jazwinski SM. The Gut Microbiota and Healthy Aging: A Mini-Review. Gerontology. 2018;64(6):513-20.
15. Tsai YC, Cheng LH, Liu YW, et al. Gerobiotics: probiotics targeting fundamental aging processes. Bioscience of Microbiota, Food and Health. 2021;40(1):1-11.
16. Mahamud AGMSU, Tanvir IA, Kabir MdE, Samonty I, Chowdhury MAH, Rahman MdA. Gerobiotics: Exploring the Potential and Limitations of Repurposing Probiotics in Addressing Aging Hallmarks and Chronic Diseases. Probiotics & Antimicro Prot [Internet]. 2025 Mar 3 [cited 2025 May 16]; Available from: https://link.springer.com/10.1007/s12602-025-10501-w.
17. Tsai YC, Cheng LH, Liu YW, et al. Gerobiotics: probiotics targeting fundamental aging processes. Bioscience of Microbiota, Food and Health. 2021;40(1):1-11.
18. Ağagündüz D, Kocaadam-Bozkurt B, Bozkurt O, et al. Microbiota alteration and modulation in Alzheimer's disease by gerobiotics: The gut-health axis for a good mind. Biomedicine & Pharmacotherapy. 2022 Sept;153:113430.
19. Son HG, Altintas O, Kim EJE, et al. Age-dependent changes and biomarkers of aging in Caenorhabditis elegans. Aging Cell. 2019 Apr;18(2):e12853.
20. Shen P, Yue Y, Zheng J, Park Y. Caenorhabditis elegans: A Convenient In Vivo Model for Assessing the Impact of Food Bioactive Compounds on Obesity, Aging, and Alzheimer's Disease. Annu Rev Food Sci Technol. 2018 Mar 25;9(1):1-22.
21. Kietz C, Pollari V, Meinander A. Generating Germ-Free Drosophila to Study Gut-Microbe Interactions: Protocol to Rear Drosophila Under Axenic Conditions. CP Toxicology. 2018 Aug;77(1):e52.
22. Pan F, Zhang L, Li M, Hu Y, Zeng B, Yuan H, et al. Predominant gut Lactobacillus murinus strain mediates anti-inflammaging effects in calorie-restricted mice. Microbiome. 2018 Dec;6(1):54.
23. Zhao Y, Zhao L, Zheng X, et al. Lactobacillus salivarius strain FDB89 induced longevity in Caenorhabditis elegans by dietary restriction. J Microbiol. 2013 Apr;51(2):183-8.
24. Lee HY, Lee JH, Kim SH, et al. Probiotic Limosilactobacillus Reuteri (Lactobacillus Reuteri) Extends the Lifespan of Drosophila Melanogaster through Insulin/IGF-1 Signaling. Aging and disease. 2023;0.

25. Jeong JJ, Kim KA, Hwang YJ, et al. Anti-inflammaging effects of Lactobacillus brevis OW38 in aged mice. BM. 2016 Nov 30;7(5):707-18.
26. Lee J, Yang W, Hostetler A, Schultz N, et al. Characterization of the anti-inflammatory Lactobacillus reuteri BM36301 and its probiotic benefits on aged mice. BMC Microbiol. 2016 Dec;16(1):69.
27. Vidal K, Benyacoub J, Moser M, et al. Effect of Lactobacillus paracasei NCC2461 on Antigen-Specific T-Cell Mediated Immune Responses in Aged Mice. Rejuvenation Research. 2008 Oct;11(5):957-64.
28. Lin X, Xia Y, Wang G, et al. Lactobacillus plantarum AR501 Alleviates the Oxidative Stress of D-Galactose-Induced Aging Mice Liver by Upregulation of Nrf2-Mediated Antioxidant Enzyme Expression. Journal of Food Science. 2018 July;83(7):1990-8.
29. Kushiro A, Shimizu K, Takada T, et al. Decreased number of days of fever detection and duration of fever with continuous intake of a fermented milk drink: a randomized, double-blind, placebo-controlled study of elderly nursing home residents. Bioscience of Microbiota, Food and Health. 2019;38(4):151-7.
30. Lee DE, Huh CS, Ra J, et al. Clinical Evidence of Effects of Lactobacillus plantarum HY7714 on Skin Aging: A Randomized, Double Blind, Placebo-Controlled Study. Journal of Microbiology and Biotechnology. 2015 Dec 28;25(12):2160-8.
31. Djaoudene O, Romano A, Bradai YD, et al. A Global Overview of Dietary Supplements: Regulation, Market Trends, Usage during the COVID-19 Pandemic, and Health Effects. Nutrients. 2023 July 26;15(15):3320.