International Journal of
Active & Healthy Aging

e-ISSN :3023-6045
https://ndpapublishing.com/index.php/ijaha

Microbiome-Driven Nutrition for Active Aging

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Article Info
Received: 27 August 2025
Revised: 05 November 2025
Accepted: 15 November 2025
Published:30 December 2025

Keywords
Active Aging
Gut Microbiome
Gut-Brain Axis
Precision Nutrition
Metabolic Resilience
Healthy Longevity

ABSTRACT

Advancing age is accompanied by physiological, metabolic, and cognitive changes that are closely linked to alterations in the gut microbiome. Recent evidence demonstrates that dietary phytonutrients, prebiotics, probiotics, and postbiotics can synergistically promote active aging by modulating gut microbial composition, enhancing immune regulation, and supporting neurocognitive function. This review synthesizes recent mechanistic insights into how these bioactive compounds interact with the gut-microbiota-immune-metabolic axis to sustain health and longevity. Phytonutrients such as polyphenols and carotenoids promote microbial diversity and short-chain fatty acid (SCFA) production, reducing oxidative stress and systemic inflammation. Prebiotics, including inulin and galactooligosaccharides, selectively stimulate beneficial taxa like *Bifidobacterium* and *Lactobacillus*, improving intestinal integrity and metabolic resilience. Probiotics reinforce mucosal defense, modulate cytokine networks, and contribute to mental well-being via the gut-brain axis, while postbiotics - non-viable microbial metabolites - offer safe and potent immunomodulatory and anti-inflammatory effects. Collectively, these biotic agents form a microbiome-centered nutritional strategy capable of mitigating age-related metabolic decline, cognitive impairment, and chronic inflammation. Integrative approaches combining synbiotics and phytonutrient-rich diets represent a promising avenue for extending healthspan and fostering active, independent living in older adults.

1. INTRODUCTION

Aging is an inevitable biological process characterized by a gradual decline in physiological function, immune resilience, and metabolic stability. However, the emerging concept of active aging emphasizes extending healthspan the period of life spent in good health rather than merely prolonging lifespan [1,2,3,4]. Maintaining gut microbial diversity and function has become increasingly recognized as a cornerstone of healthy aging. The gut microbiome, which regulates digestion, immunity, metabolism, and even brain function, undergoes significant compositional and functional changes with age. These shifts often lead to dysbiosis, low-grade inflammation, and increased susceptibility to chronic diseases such as metabolic syndrome, cardiovascular disorders, and neurodegeneration.

Recent research highlights that nutritional strategies targeting the microbiome particularly through phytonutrients, prebiotics, probiotics, and postbiotics offer promising tools for preserving physiological vitality and cognitive function in older adults. Phytonutrients such as polyphenols and carotenoids exert antioxidant and anti-inflammatory effects while stimulating the growth of beneficial gut microbes and promoting short-chain fatty acid (SCFA) production. Prebiotics (e.g., inulinfructooligosaccharides,galactooligosaccharides) selectively nourish commensal taxa like Bifidobacterium and Lactobacillus, enhancing gut barrier integrity and modulating immune responses [5,6]. Probiotics introduce live beneficial microorganisms that counteract pathogens, strengthen mucosal defense, and improve metabolic and neurological health via the gut-brain axis. Postbiotics nonviable microbial

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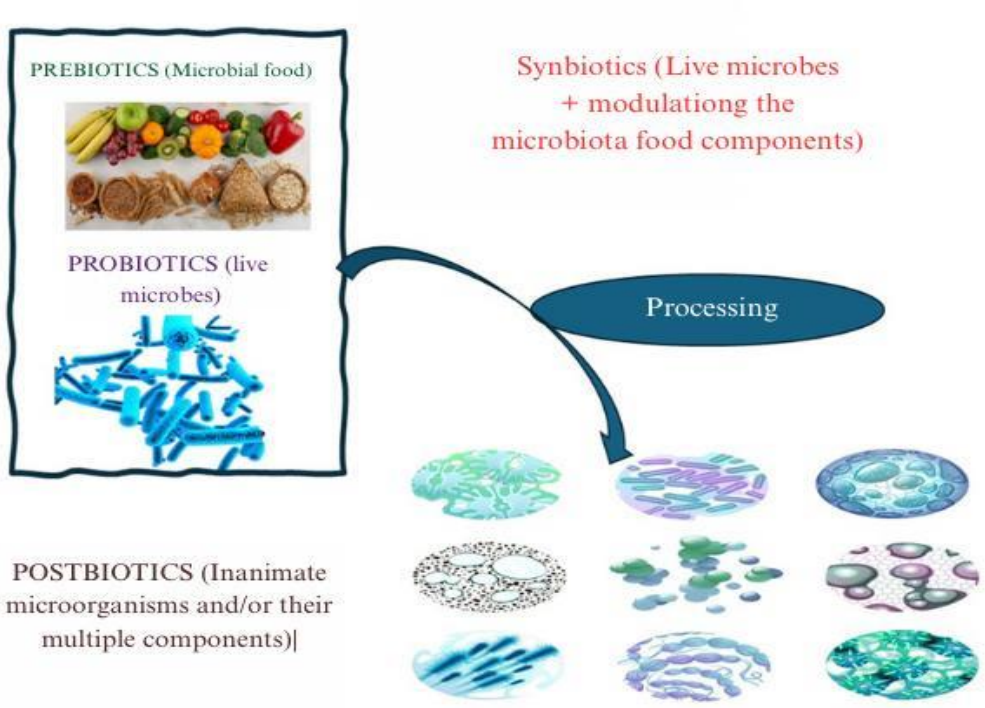
How to cite this article
Amirova, M. F. K., Musayev, K. N., Huseynova, E. E. G., Mammadova, F. I., Guliyeva, S. R. G., Baghirova, S. A. G., & Aliyev, A. N. (2025). Microbiome-Driven Nutrition for Active Aging. Int. J. Act. Health Aging, 3(2), 62-70.

Review Article/ DOI: 10.5281/zenodo.18002345

metabolites such as SCFAs, bacteriocins, and indole derivatives further regulate host signaling pathways with proven safety in older and immunocompromised populations [7]. Together, these bioactive agents form a microbiome-centered nutritional paradigm that can mitigate age-associated decline, enhance immune balance, and support neurocognitive well-being. Understanding their mechanisms and synergistic interactions provides a foundation for developing precision nutrition strategies aimed at fostering resilience, mobility, and cognitive health throughout the aging process.



Graphical Abstract

Interactions among phytonutrients, prebiotics, probiotics, and postbiotics promote active aging by maintaining gut microbial diversity, enhancing immune regulation, and supporting cognitive and metabolic health. Phytonutrients and prebiotics serve as substrates that stimulate beneficial microbes, increasing short-chain fatty acid (SCFA) production. Probiotics reinforce mucosal barrier integrity and modulate inflammatory signaling, while postbiotics act as safe bioactive metabolites that stabilize immune and metabolic pathways. Together, these biotic agents form a synergistic, microbiome-driven framework for healthy aging, reducing inflammation, improving energy metabolism, and protecting against age-related decline through the gut-microbiota-immune-brain axis.

Microbial Fermentation and Bioactive Metabolite Production in Active Aging

Central to the concept of healthy and active aging is the microbial fermentation of non-digestible dietary components, such as fibers and phytochemicals. This process produces a variety of bioactive metabolites, particularly SCFAs - acetate, propionate, and butyrate - which play a crucial role in maintaining gut and systemic health throughout the aging process [8]. Butyrate exhibits strong anti-inflammatory and antioxidant properties, reinforcing intestinal barrier function and reducing the risk of age-related disorders like colorectal cancer. Propionate contributes to balanced lipid metabolism and appetite regulation, supporting metabolic stability in older adults, while acetate serves as an essential energy source for peripheral tissues, helping sustain vitality and physical function. A decline in SCFA production has been linked to metabolic dysregulation, low-grade inflammation, and chronic diseases such as obesity, inflammatory bowel disease (IBD), and type 2 diabetes conditions that accelerate biological aging [9]. In addition to their metabolic benefits, SCFAs have dual molecular functions. They act as epigenetic regulators, inhibiting histone deacetylases (HDACs) to promote histone acetylation and gene expression patterns that support inflammation resolution, energy metabolism, and immune tolerance [10,11]. Simultaneously, SCFAs engage in receptor-mediated signaling by binding to G-protein–coupled receptors (GPR41/FFAR3, GPR43/FFAR2, GPR109A), thereby influencing energy homeostasis, immune responses, and

inflammatory pathways [12]. Through these mechanisms, SCFAs serve as vital mediators of microbiome-driven longevity, linking dietary habits to improved metabolic health, immune balance, and cognitive function - all fundamental elements of active aging.

2. MATERIALS AND METHODS

This review employed a systematic and integrative approach to collect and analyze current research on phytonutrients, probiotics, prebiotics, and postbiotics in relation to active aging. Literature was retrieved from major scientific databases, including PubMed, Scopus, Web of Science, and Google Scholar, covering studies published between January 2010 and May 2025, with priority given to works from the last five years. Search terms included combinations of: phytonutrients, polyphenols, probiotics, prebiotics, postbiotics, SCFAs, gut microbiota, aging, cognitive health, metabolic regulation, immune modulation, AMPK pathway, and PPAR-γ [5]. Inclusion criteria comprised peer-reviewed original research, clinical trials, and high-quality reviews focusing on mechanistic insights or health outcomes relevant to aging. Non-peer-reviewed papers, conference abstracts, and studies lacking methodological rigor were excluded. Selected studies were evaluated for scientific quality, relevance, and reproducibility. Data on bioactive compounds, microbial strains, SCFA production, immune and metabolic pathways, and their effects on age-related disorders (e.g., metabolic syndrome, cognitive decline, inflammaging) were extracted and synthesized. Preference was given to studies supported by in vitro, in vivo, or clinical evidence, emphasizing reproducibility and translational potential for promoting healthy and active aging.

3. RESULTS AND DISCUSSION

3.1. Epigenetic and Metabolic Impact of Phytonutrients on Microbiome-Related Aging

Recent studies highlight the intricate mechanisms linking microbial metabolites to the biological processes of aging. A 2025 review emphasized that host genetic and epigenetic variability in receptors such as GPR41 significantly affects individual responses to diet-driven SCFA modulation, underscoring the potential for personalized nutritional strategies in older adults [13, 14]. A 2023 *Nature Immunology* study further demonstrated the immunoregulatory role of SCFAs in controlling autoimmune and inflammatory responses through receptor-specific signaling and histone deacetylase (HDAC) inhibition [15]. These findings reveal how microbial metabolites help maintain immune tolerance and inflammatory balance, both of which are crucial in delaying age-associated immune decline. Moreover, recent systems biology analyses integrating microbiome and metabolome data provide a comprehensive view of how coordinated microbial metabolism sustains SCFA synthesis and correlates with host markers of metabolic health, cognitive resilience, and longevity. This integrative approach establishes SCFAs as central mediators connecting microbial activity with metabolic efficiency, immune stability, and neuroprotection - key determinants of active aging [1,16].

3.2. Enhancing SCFA-Producing Gut Microbes for Healthy Aging

Plant-derived bioactives such a**s polyphenols, flavonoids, and carotenoids,** along with dietary fibers, serve as primary substrates for SCFA-producing bacteria including *Faecalibacterium*, *Roseburia*, and *Bacteroides* [5, 17]. These interactions are fundamental to maintaining metabolic and cognitive vitality during aging. Polyphenols and flavonoids are metabolized by gut microbes into phenolic acids that modulate inflammatory pathways, enhance intestinal integrity, and support the gut–brain axis [18]. They also promote the growth of beneficial taxa such as *Bifidobacterium* and *Lactobacillus*, thereby sustaining SCFA synthesis essential for immune and metabolic regulation in older adults. Although polyphenols are poorly absorbed in the upper gastrointestinal tract, they reach the colon intact, where microbial fermentation transforms them into bioactive metabolites that reinforce gut health and longevity. Similarly, carotenoids such as lycopene and β-carotene exhibit improved bioavailability when combined with prebiotics or advanced delivery systems, amplifying their antioxidant and anti-inflammatory effects.

Prebiotics, including inulin, fructooligosaccharides, galactooligosaccharides, resistant starch, and pectin, act as fermentable substrates that selectively nourish beneficial microbial populations [19]. This fermentation enhances SCFA production, stabilizes intestinal ecosystems, and contributes to metabolic balance and immune resilience, both critical for sustaining functional independence and healthy aging (Table 1).

Table 1. Prebiotics as gut microbiota modulators for healthy aging

Prebiotic Class	Abbreviatio/ Examples	Gut Target & Mechanism	Health Outcomes Relevant to Aging
Fructans	FOS, inulin	Stimulate Bifidobacterium and Lactobacillus; fermentation enhances SCFA generation	Supports digestive regularity, improves lipid metabolism, and contributes to metabolic balance in older adults
Galacto-oligosaccharides	GOS	Promote selective Bifidobacterium growth; enhance mucosal immunity	Strengthen gut barrier, boost IgA response, and sustain immune resilience during aging
Resistant starch & fibers	Resistant starch, pectin	Drive butyrate and propionate production through microbial fermentation	Nourish colonocytes, reduce inflammation, and protect against age-related intestinal dysfunction
Polyphenol-based prebiotics	Berries, tea, cocoa	Enhance SCFA-producing bacteria; suppress pathogenic species	Support metabolic and cardiovascular health, modulate inflammation, and lower chronic disease risk in aging populations

[13, 20, 21, 22, 23]

Regular consumption of prebiotic-rich foods such as onions, garlic, bananas, chicory root, and oats has been shown to stimulate the growth of SCFA-producing microbes, elevate fecal butyrate concentrations, enhance intestinal barrier integrity, and improve glucose metabolism [24]. These effects collectively contribute to maintaining gut health and metabolic stability during aging.

Recent findings indicate that polyphenols and prebiotic fibers act synergistically in shaping the gut microbiome. While prebiotic fibers serve as fermentable substrates that directly nourish beneficial bacteria, polyphenols influence microbial diversity and suppress harmful species [25]. This combined action optimizes the microbial ecosystem, promoting higher SCFA output and improved host-microbe interactions. Diets abundant in plant-based diversity - such as the Mediterranean diet naturally support this synergy, fostering greater microbial richness and lowering the incidence of chronic age-related diseases. Furthermore, phytonutrients including flavonoids, phenolic acids, stilbenes, and carotenoids undergo extensive microbial biotransformation in the gut, resulting in smaller metabolites with enhanced bioactivity and bioavailability [26]. These metabolites exhibit hormetic behavior, meaning they stimulate adaptive cellular defense mechanisms at low concentrations while exerting inhibitory effects at higher doses. They modulate crucial redox-sensitive pathways such as Nrf2/ARE, NF-κB, and MAPK, which are central to antioxidative, anti-inflammatory, and anti-proliferative responses - mechanisms vital for healthy aging and disease prevention [27,28]. Prebiotics also create a favorable environment for commensal taxa like *Bifidobacterium* and *Lactobacillus*, facilitating the establishment and metabolic activity of probiotic species [19,29]. In parallel, probiotics, when administered in sufficient quantities, promote host health by outcompeting pathogens, enhancing the expression of tight junction proteins (e.g., claudins and occludin), and modulating immune balance through dendritic cell signaling and Treg/Th17 regulation. Together, these mechanisms reinforce gut integrity, reduce systemic inflammation, and support the metabolic and immune resilience essential for healthy aging [30, 31].

3.1. Probiotics for healthy aging

According to the Food and Agriculture Organization (FAO) and the World Health Organization (WHO), probiotics are defined as live microorganisms that, when administered in adequate amounts, confer health benefits to the host. The predominant genera include *Lactobacillus*, *Bifidobacterium*, and *Saccharomyces*, along with emerging psychobiotic strains that influence the gut brain axis and emotional well-being [19]. Probiotics enhance intestinal barrier integrity and generate beneficial metabolites, including SCFAs, which act as postbiotics and mediate immune and metabolic signaling. Their mechanisms of action encompass colonization resistance through modulation of the local microbiota, immune regulation via increased production of regulatory T cells (Tregs), stimulation of immunoglobulin A (IgA) and antimicrobial peptides, and cholesterol lowering effects through bile salt deconjugation [9, 13, 20, 32, 33, 34]. Furthermore, probiotics strengthen tight junctions by upregulating proteins such as claudins and occludin, supporting barrier function and reducing systemic inflammation. Collectively, these actions promote gut health, improve

metabolic balance, and support cognitive and emotional stability, all of which are essential for healthy aging.

3.2. Healthy aging with postbiotics consumption

Postbiotics are defined as non-viable microbial components or metabolites that provide health benefits to the host. These include SCFAs, bacteriocins, enzymes, peptides, and cell wall fragments. Unlike live probiotics, postbiotics offer safety and stability advantages, making them particularly relevant for aging populations with compromised immunity. Their biological activities involve immune modulation through the regulation of Toll like receptors (TLRs), which maintain immune tolerance and balance. Postbiotics also enhance gut barrier function by stimulating the synthesis of tight junction proteins, and they exhibit anti-inflammatory and metabolic benefits, contributing to improved outcomes in chronic diseases, diabetes, and metabolic syndrome [35,13]. By providing microbial derived signaling without the risks associated with live organisms, postbiotics serve as potent modulators of host homeostasis and play a key role in promoting resilience and longevity in aging individuals.

3.3. Integrative concept of phytonutrients role in healthy aging

Recent research underscores the synergistic relationship between phytonutrients and microbial interventions - namely prebiotics, probiotics, and postbiotics in shaping a microbiome conducive to healthy aging. This integrative approach, often described as symbiotic phytonutrient synergy, enhances microbial diversity, optimizes SCFA production, and reinforces host immune and metabolic networks. Phytonutrients act as modulators of microbial gene expression and antioxidant defense, while prebiotics provide substrates for fermentation, probiotics supply live beneficial organisms, and postbiotics deliver bioactive metabolites. Together, they form a multitiered system that supports gut immune brain axis regulation, reduces chronic inflammation, and preserves physiological resilience. This convergence of microbial and phytochemical strategies represents a promising avenue for sustaining metabolic flexibility, cognitive health, and overall vitality throughout the aging process.

Table 2. Biotic categories and phytonutrients: key components and mechanisms supporting healthy aging

Type	Definition	Key Components	Mechanisms & Effects Related to Healthy Aging	Research Evidence
Prebiotics	Non-digestible dietary substrates that nourish beneficial microbes	FOS, GOS, inulin, resistant starch	Stimulate SCFA production; enhance gut barrier; modulate immune and metabolic function	Strong clinical and translational evidence
Probiotics	Live beneficial microorganisms providing host health benefits	Lactobacillus, Bifidobacterium, Saccharomyces	Compete with pathogens; enhance tight junctions; regulate cytokines and Treg balance; improve metabolic and cognitive resilience	Robust human clinical data
Synbiotics	Synergistic combination of prebiotics + probiotics	e.g., Lactobacillus rhamnosus GG + FOS	Synergistic SCFA enhancement; immune balance; reduction of inflammation; improved nutrient assimilation	Emerging evidence from human trials
Postbiotics	Inactivated microbial cells or metabolites conferring health benefits	SCFAs, bacteriocins, enzymes, cell wall fragments	Support epithelial barrier; modulate TLR signaling; reduce systemic inflammation; safe for older adults	Rapidly expanding human / animal research
Phytonutrients	Plant-derived bioactive compounds supporting host–microbiome interaction	Polyphenols, flavonoids, carotenoids, stilbenes	Promote microbial diversity; antioxidant and anti-inflammatory action; enhance SCFA-producing taxa; protect against age-related decline	Strong epidemiological and mechanistic evidence

[13, 20, 19, 23].

Central to this process is the generation of bioactive metabolites such as SCFAs, the reinforcement of gut barrier integrity, and a cascade of systemic effects including anti-inflammatory, anticancer, and metabolic benefits. Phytonutrients function in a prebiotic-like manner by supporting microbial metabolism and enhancing postbiotic formation, while synbiotics the combination of probiotics and prebiotics produce synergistic outcomes that further amplify these health effects.

Interventional research combining probiotics with their metabolic byproducts (postbiotics) has demonstrated significant improvements in metabolic health markers, including lipid regulation and insulin sensitivity, through SCFA-mediated pathways [36]. Postbiotics comprising microbial-derived peptides, exopolysaccharides, cell wall components, and metabolites such as indole-3-propionic acid (IPA) and bacteriocins - exert beneficial effects even in the absence of live microorganisms [8]. These compounds engage Toll-like receptors (TLRs) and NOD-like receptors (NLRs), fostering mucosal immune balance without the risks associated with live microbial administration, an important advantage for aging or immunocompromised individuals [37]. Together, these biofunctional agents phytonutrients, prebiotics, probiotics, and postbiotics act synergistically to remodel microbial ecosystems through selective metabolic cross-feeding and to enhance epithelial integrity via zonulin regulation and SCFA-driven trophic effects. They modulate systemic inflammation by influencing cytokine networks such as IL-10, IL-6, and TNF-α, and contribute to improved metabolic homeostasis through the AMPK and PPAR-γ signaling pathways, as well as insulin sensitivity regulation [9, 38, 40]. Additionally, this multi-modal interaction extends to the gut brain axis, where microbial metabolites - including GABA, serotonin precursors, and tryptophan derivatives affect mood, cognition, and neural health. Collectively, these mechanisms establish the integrated application of phytonutrients, pre, pro, and postbiotics as a precision nutrition approach for promoting healthy aging, capable of mitigating chronic inflammation, metabolic syndrome, colorectal cancer risk, and neurodegenerative decline. The development of synbiotic or designer-food formulations represents a promising frontier in personalized nutrition and microbiome centered therapeutic strategies for longevity and wellness.

Recent advances underscore the growing clinical relevance of symbiotics, synbiotics, and postbiotics in supporting healthy aging and managing age-associated disorders. In gastrointestinal conditions such as irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD), these interventions help restore microbial balance, enhance mucosal integrity, and alleviate inflammation [41, 42]. In metabolic disorders including diabetes, obesity, and metabolic syndrome, their beneficial effects are mediated through SCFA driven mechanisms and regulation of metabolic hormones, leading to improved insulin sensitivity, lipid metabolism, and energy homeostasis. Moreover, emerging evidence indicates that microbiome modulation may serve as an adjunct strategy for immune resilience and antiviral defense, with promising implications observed during COVID-19 and other viral infections. In the domain of mental health, the concept of psychobiotics probiotic and postbiotic strains influencing the gut–brain axis has gained attention for its potential to improve mood, cognition, and stress resilience, providing a novel avenue for addressing anxiety, depression, and age-related cognitive decline. While probiotics are generally well tolerated, rare adverse events may occur in immunocompromised individuals. In contrast, postbiotics offer a safer alternative, as their beneficial effects do not rely on microbial viability, reducing risks related to bacterial translocation or overgrowth an important consideration for older populations.

Looking ahead future research on healthy aging should focus on improving the clinical use and precision of biotics through several key directions including mechanistic elucidation using advanced tools such as genomics metabolomics and proteomics to understand host microbe interactions and identify biomarkers that predict individual responses developing precision nutrition strategies that create personalized biotic formulations based on a person's unique microbiome metabolism and genetics applying innovative delivery systems such as nanotechnology encapsulation and bioengineering to improve the stability absorption and targeted release of phytonutrients and biotic compounds and ensuring regulatory standardization through clear definitions dosage recommendations safety frameworks and large scale clinical trials to validate the effectiveness of these interventions in promoting metabolic balance cognitive resilience immune health and overall longevity

Collectively, the integration of biotic-based strategies into therapeutic and preventive healthcare holds transformative potential for advancing personalized medicine, sustainable nutrition, and healthy aging bridging the gap between molecular insight and clinical practice.

4. Conclusion

The integration of phytonutrients, prebiotics, probiotics, and postbiotics represents a transformative approach to promoting active aging through microbiome modulation. These compounds work synergistically to restore microbial diversity, strengthen gut barrier function, and optimize immune and metabolic regulation key determinants of longevity and quality of life. By enhancing short chain fatty acid production, regulating inflammatory cytokines and supporting neuroprotective signaling through the gut brain axis, these biotic interventions contribute to the prevention of age-related disorders such as metabolic syndrome, cognitive decline, and chronic inflammation. Moreover, the cross talk between the gut microbiota and host systems underscores the potential of microbiome-targeted therapies to maintain functional independence in older adults. Diets rich in phytonutrients, combined with tailored synbiotic or postbiotic formulations, can help sustain metabolic equilibrium, preserve muscle function, and promote mental clarity hallmarks of active and healthy aging. Future research should focus on personalized microbiome based nutrition, integrating genomics, metabolomics, and clinical data to design targeted interventions for aging populations. By leveraging the power of the gut microbiome, science is moving toward a new era of preventive medicine Mone that transforms aging from a period of decline into a phase of vitality, adaptability, and sustained well-being.

Highlights

Phytonutrients, probiotics, prebiotics, and postbiotics act synergistically to promote active and healthy aging.

Phytonutrients enhance microbial diversity, reduce oxidative stress, and modulate inflammatory pathways.

Prebiotics selectively nourish beneficial gut microbes, improving SCFA production and gut barrier integrity.

Probiotics and postbiotics regulate immune balance, metabolic function, and neurocognitive health through the gut brain axis.

Integrative synbiotic and phytonutrient-based strategies support longevity, resilience, and improved quality of life in aging populations.

Conflict of Interest

No conflict of interest is declared by the authors. In addition, no financial support was received.

Author Contributions

Conception and design of the study: MFKA, KNM; Data collection: KNM, EEGH; Data analysis: EEGH, FIM; Data Interpretation: SRGG, SAGB; Drafting the article and/or its critical revision: SAGB, ANA; All authors have read and agreed to the published version of the manuscript.

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