Int J Nutr Sci 2026;11(1):1-13

International Journal of Nutrition Sciences

Journal Home Page: ijns.sums.ac.ir

Review Article

Key Phytochemicals with Anti-Aging Effects: A Narrative Review

Ali Sattarian[1], Minoo Akbarzadeh Morshedi[2*]

1. School of Medicine, Kashan University of Medical Sciences, Kashan, Iran
2. Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Science, Kashan University of Medical Sciences, Ravand, Kashan, Iran

ARTICLE INFO

Keywords:
Phytochemicals
Aging
Resveratrol
Curcumin
Quercetin

**Corresponding author:*
Minoo Akbarzadeh Morshedi, BSc;
Research Center for Biochemistry and Nutrition in Metabolic Diseases, Institute for Basic Science, Kashan University of Medical Sciences, Ravand, Kashan, Iran
Tel: +98-9392772650
Email: Mi.akbarzadeh213@gmail.com

Received: November 1, 2025
Revised: January 25, 2026
Accepted: February 2, 2026

ABSTRACT

Aging is a multifaceted biological process characterized by a decline in physiological function and increased susceptibility to age-related diseases. This narrative review explored the potential anti-aging effects of phytochemicals-bioactive compounds derived from plants by examining their mechanisms of action and health benefits. Phytochemicals exhibit significant antioxidant and anti-inflammatory properties that may mitigate oxidative stress and chronic inflammation, both of which are pivotal contributors to aging. We conducted a comprehensive search across major medical and scientific databases, including PubMed, Google Scholar, Web of Science, Scopus, and Embase, to identify reviews, meta-analyses, original articles, randomized clinical trials, and case series related to the anti-aging effects of phytochemicals. The search strategy utilized the keywords of phytochemicals, bioactive compounds, antioxidants, nutraceuticals, aging, oxidative stress, cellular senescence, and inflammation. Studies published between 2000 and 2025 were included, with an emphasis on the most recent and high-quality research addressing the role of phytochemicals in the aging process. Key phytochemicals such as resveratrol and curcumin can activate longevity-associated pathways, including sirtuins, to promote cellular health and longevity. Furthermore, phytochemicals can modulate cellular signaling pathways related to senescence and metabolic regulation. The integration of these compounds into dietary strategies presents a promising approach to enhance health. By elucidating the protective effects of phytochemicals against age-related decline, this article aimed to inform future research directions and dietary recommendations for aging populations, ultimately contributing to improved health outcomes and quality of life in older adults.

Please cite this article as: Sattarian A, Akbarzadeh Morshedi M. Key Phytochemicals with Anti-Aging Effects: A Narrative Review. Int J Nutr Sci. 2026;11(1):1-13. doi: 10.30476/ijns.2026.107333.1491.

Introduction

Aging is a complex biological process characterized by a gradual decline in physiological functions, increased vulnerability to diseases, and a reduction in overall health (1). As the global population age increases, there is a growing interest in understanding the mechanisms underlying aging and identifying potential interventions to promote

longevity and enhance quality of life (2). Among these interventions, phytochemicals as bioactive compounds derived from plants have garnered significant attention due to their diverse therapeutic properties and potential role in mitigating age-related decline (3). Phytochemicals encompass a wide range of substances, including flavonoids, polyphenols, terpenoids, and alkaloids, which are known for their antioxidant, anti-inflammatory, and neuroprotective effects (4). These compounds can modulate various biological pathways associated with aging, such as oxidative stress, inflammation, and cellular senescence (5). Oxidative stress, resulting from an imbalance between Reactive Oxygen Species (ROS) production and antioxidant defenses, is a key contributor to age-related cellular damage (6). Phytochemicals possess the ability to scavenge free radicals and enhance endogenous antioxidant mechanisms, thereby potentially reducing oxidative damage and promoting cellular health (7).

Inflammation is another critical factor in the aging process. Chronic low-grade inflammation, often referred to as "inflammaging", has been implicated in the development of age-related diseases such as cardiovascular disorders, neurodegenerative diseases, and metabolic syndromes (8). Many phytochemicals exhibit anti-inflammatory properties by inhibiting pro-inflammatory cytokines and signaling pathways, suggesting their utility in combating age-associated inflammation (9). Moreover, phytochemicals have been shown to influence cellular signaling pathways that regulate longevity (10). For instance, compounds like resveratrol and curcumin have been identified as activators of sirtuins, a family of proteins associated with longevity and metabolic regulation (11, 12). By modulating these pathways, phytochemicals may contribute to improved health span as the period of life spent in good health beyond merely extending lifespan (13).

This narrative review aimed to consolidate current knowledge regarding the anti-aging effects of various phytochemicals. By examining the existing literature on their mechanisms of action, potential health benefits, and implications for aging populations, we searched to provide a comprehensive overview that could highlight the relevance of these natural compounds in promoting healthy aging. Ultimately, understanding the role of phytochemicals in the aging process could pave the way for novel dietary strategies and therapeutic approaches aimed at enhancing longevity and improving quality of life for older adults.

Materials and Methods

A narrative literature review was conducted from May 2000 to May 2025, encompassing all available literature from the following databases undertaken including ISI Web of Science, MEDLINE (PubMed), Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Google Scholar, Science Direct, and Scopus. The search strategy enrolled both Medical Subject Headings (MeSH) and non-MeSH keywords: ((“Phytochemicals” OR “Bioactive Compounds” OR “Antioxidants” OR “Flavonoids” OR “Polyphenols” OR “Terpenoids” OR “Glucosinolates” OR “Phytosterols” OR “Secondary Metabolites” OR “Nutraceuticals” OR “Plant-Derived Compounds”) AND (“Aging” OR “Senescence” OR “Cellular Senescence” OR “Telomeres” OR “Cellular Aging” OR “Oxidative Stress” OR “Gerontology” OR “Longevity” OR “Age-related Diseases” OR “Epigenetics” OR “Mitochondrial Dysfunction” OR “Inflammation”)). These search terms were tailored to the specific databases and comprised a blend of free-text searches.

The selection of articles was restricted to studies published in English, with no limitations on the year of publication; however, the most significant articles were those published after 2020. Ultimately, a total of 109 articles were chosen for inclusion in the review. The following data regarding study characteristics were extracted from the included records as type of study, type of phytochemical agent, and the conclusions drawn by each study. The authors reviewed both the titles and abstracts. If the abstracts indicated the use of diaries containing narrative elements, the full texts were examined, and those meeting the pre-established eligibility criteria were incorporated into the review. A narrative approach, featuring summary tables and graphs, would aid in synthesizing the included studies.

Aging and Related Mechanisms

Aging is a complex process involving the gradual decline of cellular function, linked to mechanisms like telomere attrition, DNA damage, and mitochondrial dysfunction (Table 1) (14). Cellular senescence, a state of permanent cell cycle arrest, is triggered by stresses such as oxidative damage, radiation, or oncogenic activation (15). This process is mediated by pathways like p53/p21 (16) and p16INK4a/pRB (17), which halt proliferation to prevent potential cancer, but also contribute to aging by releasing the Senescence-Associated Secretory Phenotype (SASP), including inflammatory cytokines and proteases (18). Senescence is induced by telomere shortening, activating the DNA Damage Response (DDR) and engaging p53 and p16INK4a to enforce cell cycle arrest (19, 20). Oncogene-Induced Senescence (OIS) occurs via the ARF-p53-p21 pathway, acting as a tumor suppressor (21).

Table 1: A summary of key mechanisms and pathways in aging.

Mechanism	Key pathways/Regulators	Associated features
Telomere Attrition	DDR, p53, p16INK4a	Cell cycle arrest, DNA damage
Oncogene-induced senescence (OIS)	ARF-p53-p21	Tumor suppression, proliferation halt
Mitochondrial dysfunction	Increased ROS production	DNA/protein damage, reinforced senescence
Epigenetic changes	Histone modifications, SAHF formation	Stable repression of proliferation genes
SASP and inflammation	cGAS-STING, NF-κB	Chronic inflammation, tissue dysfunction

DDR: DNA Damage response; ARF: Alternative reading frame; ROS: Reactive oxygen species; SAHF: Senescence-associated heterochromatic foci; SASP: Senescence-associated secretory phenotype; NF-κB: Nuclear factor κB.

Table 2: key phytochemicals and the related mechanisms affecting aging.

Phytochemical	Mechanisms affecting aging	Specific effects and numbers
Resveratrol	Reduces oxidative stress, activates AMPK/SIRT1, inhibits IGF-1, anti-inflammatory, induces autophagy	Extends lifespan by 70% in yeast, 26-25% in high-fat diet mice, improves insulin resistance, reduces ROS; 0.01-0.04% dietary dose
Curcumin	Anti-inflammatory, antioxidant, induces autophagy, increases SOD, extends lifespan	Extends Drosophila lifespan, 0.2% tetrahydrocurcumin increases mouse survival, 32% increase in SOD activity at 2 mg/g in Drosophila
Quercetin	Scavenges ROS (6x antioxidant capacity of trolox/vitamin C), anti-inflammatory, activates proteasome, extends lifespan via age-1/daf-2	Extends *Caenorhabditis elegans* lifespan by 20% at 200 mM, rejuvenates senescent fibroblasts; inhibits IL-1α, TNF-α production
Epigallocatechin Gallate (EGCG)	Reduces oxidative stress, activates SIRT1, anti-inflammatory, induces autophagy	Extends *Caenorhabditis elegans* lifespan, increases mouse lifespan from 801 to 852 days at 80 mg/L (18% EGCG), diminishes mid-life deaths in female mice
Epicatechin gallate (ECG)	Reduces oxidative stress, increases SOD/GSH, activates AMPK, lowers IGF-1, anti-inflammatory, induces autophagy	Promotes survival (8.4% mortality vs. 50% in controls after 15 weeks in diabetic mice), 0.25% in drinking water; increases hepatic SOD

AMPK: AMP-activated protein kinase; SIRT1: Sirtuin 1; IGF-1: Insulin-like growth factor 1; ROS: Reactive oxygen species; SOD: Superoxide dismutase; GSH: Glutathione.

Mitochondrial dysfunction increases ROS, damaging DNA and proteins, reinforcing senescence (22). Epigenetic changes, such as histone modifications and the formation of Senescence-Associated Heterochromatin Foci (SAHF), stabilize this state (23); while the cGAS-STING pathway links DNA damage to inflammation and amplifies SASP effects (24). In aging, senescent cells accumulate, resisting apoptosis and promoting chronic inflammation via SASP, linked to "inflammaging," which exacerbates tissue dysfunction and age-related diseases (25). This accumulation alters tissue homeostasis and stem cell function and accelerates aging (26). A recent research explored senotherapeutics, like senolytics to eliminate senescent cells and senomorphics to modulate SASP, offering potential to extend health span and improve quality of life, though challenges remain in targeting specific cell types (27).

Cellular Aging and Key Phytochemicals

Phytochemicals, which are natural compounds found in plants, can help slow down aging by fighting oxidative stress and inflammation (Table 2) (28). These agents like resveratrol (found in grapes) and quercetin (in onions) act like antioxidants, neutralizing these harmful molecules and boosting our body's own defenses, such as enzymes that protect cells (29). For example, it was shown that quercetin is more effective than vitamin E at fighting oxidation (30). They also reduce inflammation, which is like a low-level fire in the body that can speed up aging, by calming down pathways that cause it, such as one called Nuclear Factor κB (NF-κB). This can help lower the risk of diseases like heart problems or arthritis (31-33).

Phytochemicals also seem to help by influencing how the cells age and clean themselves. As the human get older, cells can enter a state called senescence, where they stop dividing and start releasing chemicals that can harm nearby cells, speeding up aging (34). Compounds like resveratrol can delay this by activating proteins called sirtuins, which help cells

handle stress better (35). Another way is by boosting autophagy, which is like a cleanup process where cells remove damaged parts (36). For instance, curcumin (from turmeric) and Epigallocatechin Gallate (EGCG; from green tea) can trigger this process, helping cells stay healthy (37, 38). In simple organisms like worms, it was shown that these compounds can extend life, suggesting they might do the same for us by keeping cells functioning well (39).

Finally, phytochemicals might affect how the genes work, which is key to aging. In the aging process, the tips of chromosomes, called telomeres, shorten, and the gene activity can get out of balance due to changes in how genes are turned on or off, known as epigenetic changes (40, 41). While there are no much direct evidences yet, and some phytochemicals like resveratrol may help by activating sirtuins, which can tweak gene activity to support longevity (42). They can also change the gut bacteria, leading to substances that influence how genes are expressed, potentially keeping cells younger. This area is still being studied, but it suggests phytochemicals could help maintain our genetic health as we age (43).

Resveratrol

The anti-aging effects of resveratrol are mediated through multiple pathways. It activates SIRT1, which regulates proteins like p53 and FOXO transcription factors, crucial for cellular senescence (44). This activation mimics caloric restriction, extending lifespan in yeast, worms, and flies (45). Resveratrol reduces oxidative stress by scavenging ROS and enhancing antioxidant enzyme activity, protecting against DNA damage and mitochondrial dysfunction (46). It also exhibits anti-inflammatory effects by inhibiting NF-κB and reducing proinflammatory cytokines like IL-6 and TNF-α, mitigating inflammaging (47). Resveratrol modulates cellular senescence by influencing cell cycle arrest pathways, such as p53 and p16INK4a, and inducing autophagy, which enhances cellular cleanup and delays senescence (48). A preclinical study suggested resveratrol to influence telomere length by activating telomerase, the enzyme maintaining telomeres, with animal studies showing an increased telomere length and telomerase activity in rats treated with resveratrol. However, these effects are less studied in humans (49).

Some Randomized Clinical Trials (RCTs) have explored the efficacy of resveratrol on aging-related markers, with mixed results. A systematic review and meta-analysis of 17 RCTs, including 736 subjects, found that resveratrol supplementation did not significantly affect circulating inflammatory markers such as IL-6, TNF-α, and hs-CRP, with weighted mean differences calculated using fixed-effects or random-effects models, suggesting limited anti-inflammatory benefits (50). Another systematic review of 10 RCTs concluded that resveratrol supplements, at doses ranging from 8 mg/day to 1500 mg/day for 2-12 months, did not improve cardiovascular risk markers, including C-reactive protein (CRP), cholesterol level, blood pressure, and blood glucose, indicating no significant cardioprotective effects in healthy individuals. These findings highlight the gap between preclinical promise and human translational outcomes, with subgroup and sensitivity analyses showing heterogeneity in study results (51).

While some RCTs have focused on specific age-related diseases, such as Alzheimer's disease, showing that resveratrol can alter AD biomarkers and preserve blood-brain barrier integrity (52). A review over 110 clinical trials on resveratrol focused on cardiovascular functions with conflicting results on energy metabolism in humans suggested variability in efficacy for resveratrol (53). Notably, there is a lack of large-scale human RCTs specifically examining resveratrol's effect on telomere length suggesting potential but with no definitive human evidence to call for future observational and large-scale clinical trials to confirm these effects. (54).

The potential efficacy of resveratrol to influence telomere length is supported by an *in vitro* study illustrating delayed senescence in endothelial progenitor cells through telomerase activation (55), and animal studies demonstrated an increased telomere length in rats (56). However, translating these findings to humans requires further research, given the complexity of aging mechanisms and the variability in RCT outcomes. Therapeutic implications include potential dietary interventions using resveratrol-rich foods, but challenges include determining clinically relevant doses and understanding long-term effects. Future researches should focus on human intervention trials, particularly on telomere length and other direct aging biomarkers, to bridge the gap between preclinical and clinical evidence (57).

Curcumin

Curcumin, found in turmeric, might help treatment of many diseases (58-60). Curcumin can slow down aging by fighting damage from harmful molecules and reducing inflammation, which can speed up aging (61). Curcumin reduces oxidative stress by scavenging ROS and enhancing antioxidant enzyme activity, such as superoxide dismutase (SOD), with a 32% increase in SOD activity observed at 2 mg/g in Drosophila (62, 63). It also

exhibits anti-inflammatory effects by inhibiting NF-κB and reducing proinflammatory cytokines like IL-6, TNF-α, and CRP, with significant reductions observed in seven of ten meta-analyses of RCTs (64, 65). Curcumin modulates cellular senescence by influencing cell cycle arrest pathways, such as p53 and p16INK4a, and inducing autophagy, which enhances cellular cleanup and delays senescence (66). A preclinical study suggested curcumin to influence telomere length by reducing shortening, with animal studies showing extended lifespan in model organisms like *C. elegans* and *D. melanogaster* (67).

Curcumin also impacts muscle function and physical performance, critical for aging populations (68). A RCT has shown improvements in handgrip strength (1.43% increase), weightlifting strength (6.08% increase), and walking speed (5.51 m improvement) in healthy elderly individuals, as well as enhancing physical performance in frail elderly, with large effect sizes in short physical performance battery (d=0.75), knee extension (d=0.69), and flexion peak torque (d=0.82) (69). For cognitive health, curcumin reduces amyloid-beta level and improves cognitive scores in neurodegenerative diseases, with mixed results in RCTs, particularly in Alzheimer's disease (70, 71).

A systematic review included 15 RCTs, focusing on conditions like sarcopenia, frailty, Parkinson's disease, dementia, Alzheimer's disease, and cognition, with detailed outcomes. For sarcopenia, a study with 30 participants (69.8±5 years, 13 male, 17 female) found curcumin (500 mg/day Cureit) to improve handgrip strength by 1.43%, weightlifting strength by 6.08%, and walking speed by 5.51 m over three months, with no adverse events (72). For frailty, another RCT with 17 participants (66–94 years, 8 males, 9 females) showed curcumin (1000 mg/day Curcumin) enhanced physical performance, with large effect sizes (d=0.75 for short physical performance battery, d=0.69 for knee extension, d=0.82 for flexion peak torque), also with no adverse events (73).

In neurodegenerative diseases, RCTs demonstrated mixed results. For Parkinson's disease, curcumin improved motor function and quality of life (74), while in Alzheimer's disease, it reduced amyloid-beta level and improved cognitive function, but not consistently (75). A meta-analysis of RCTs illustrated that curcumin could significantly lower malondialdehyde (MDA) level in five of six meta-analyses, and reduced CRP, IL-6, and tumor necrosis factor alpha (TNF-α) in multiple studies, indicating its role in reducing oxidative stress and inflammation as key aging markers (76). Another RCT with 60 overweight and obese adolescent girls found curcumin (500 mg/day) to significantly reduce IL-6, hs-CRP, and MDA, and increased total antioxidant capacity (TAC), after controlling for confounders, suggesting benefits for inflammation and oxidative stress markers relevant to aging (77).

The effect of curcumin on telomere length is supported by preclinical studies, but human RCTs specifically on telomere length are limited, with most evidences from animal models showing extended lifespan. The variability in RCT outcomes, particularly for cognitive function, suggests challenges in bioavailability and dosage, with clinical practice noting low solubility and rapid degradation under physiological conditions (78, 79). Therapeutic implications include dietary interventions using curcumin-rich foods, but challenges include determining clinically relevant doses and understanding long-term effects. Future researches should focus on human intervention trials, particularly on telomere length and other direct aging biomarkers, to bridge the gap between preclinical and clinical evidence (80).

Quercetin

Quercetin, a flavonoid found in foods like onions, apples, and berries, exhibits anti-aging potential through the antioxidant, anti-inflammatory, and senomorphic properties (81-83). This phytochemical reduces oxidative stress by scavenging ROS and enhances antioxidant enzymes like SOD via the Nuclear factor erythroid 2-related factor 2 (Nrf2) pathway (84). It also mitigates inflammation by inhibiting NF-κB and reducing cytokines like IL-6 and TNF-α (85). Quercetin also delays senescence by modulating p53/p21 and p16INK4a pathways, inducing autophagy, and acting as a senolytic, selectively clearing senescent cells (86). In *Caenorhabditis elegans*, quercetin extended lifespan, suggesting longevity potential, though human translation remains understudied (87).

Human RCTs evaluating the effects of quercetin on aging-related cellular and biochemical markers are limited but provide insights into its potential. A meta-analysis found that quercetin supplementation (500–1000 mg/day, 8–12 weeks) significantly reduced inflammatory markers like CRP and IL-6 in patients with chronic conditions such as metabolic syndrome and osteoarthritis (88). Another RCT on sarcopenic elderly participants showed that quercetin (500 mg/day for 12 weeks) improved physical function and improvement in walking speed, suggesting benefits for age-related muscle decline (89). However, a review of RCTs noted inconsistent effects on oxidative stress markers like MDA, and no significant impact on TAC in most trials (85). No RCTs directly assessed quercetin's impact on telomere length or senescence-

specific markers like p16INK4a in humans, though preclinical studies suggest it rejuvenates senescent fibroblasts (90). The lack of consistent human RCT data on cellular senescence markers, coupled with challenges in bioavailability, highlights the need for larger, well-designed trials to confirm the anti-aging effects. Future researches must focus on telomere dynamics and senescence biomarkers to bridge the gap between preclinical promise and clinical efficacy (91).

Epigallocatechin-3-gallate (EGCG)

EGCG, found in green tea, might help slow down aging by fighting damage from harmful molecules and reducing inflammation, which can speed up how cells age (92). It reduces oxidative stress by scavenging ROS and enhancing antioxidant enzyme activity, such as SOD (93). It also exhibits anti-inflammatory effects by inhibiting NF-κB and reducing proinflammatory cytokines like IL-6 and TNF-α (94). EGCG modulates cellular senescence by influencing cell cycle arrest pathways, such as p53 and p16INK4a, and inducing autophagy, which enhances cellular cleanup and delays senescence (95). Preclinical studies suggest EGCG can act as a senolytic, selectively eliminating senescent cells, further supporting its anti-aging potential (96). Additionally, EGCG has shown neuroprotective effects, reducing amyloid-beta levels and improving cognitive scores in neurodegenerative diseases, as seen in reviews on Alzheimer's disease (97).

Human RCTs evaluating EGCG on aging cellular and biochemical markers are limited but provide insights into its potential. A notable RCT investigated a diet and lifestyle intervention that included green tea (a source of EGCG) and reported a significant decrease in DNA methylation age (DNAmAge), a biochemical marker of biological aging, in the treatment group compared to controls. Specifically, the treatment group showed a 3.23-year decrease in DNA age compared to controls (p=0.018), with an average 1.96-year decrease within the group (p=0.066) (98). Additionally, RCTs have explored EGCG's impact on cognitive function in populations at risk for accelerated aging, such as individuals with Down syndrome (99). Researchers found that EGCG combined with cognitive training may improve memory, executive function, and attention in young adults with Down syndrome, though amyloid biomarkers were not reported due to technical issues (100). RCTs in healthy adults showed mixed results, with single doses of EGCG having little influence on cognition but potentially increasing calmness and reducing stress, with increased brain waves associated with relaxation and focused attention. However, no RCTs directly assessed EGCG impact on telomere length or other specific aging markers like oxidative stress or inflammation. The lack of consistent human RCT data on cellular senescence markers, underscores the need for larger, well-designed trials to confirm EGCG's anti-aging effects (101).

Epicatechin

Epicatechin gallate (ECG), found in green tea, might help slow down aging by fighting damage from harmful molecules and reducing inflammation (102). The anti-aging effects of ECG are inferred from antioxidant properties, which may reduce oxidative stress, a primary driver of cellular senescence (103). ECG, like other catechins, can scavenge ROS, potentially protecting against these damages, as suggested by studies on tea polyphenols (104). It may also exhibit anti-inflammatory effects by inhibiting NF-κB and reducing proinflammatory cytokines. However, specific studies on ECG-related pathways such as p53/p21 or p16INK4a, are limited, with most evidence derived from EGCG, which shows delay in senescence by inducing autophagy and acting as a senolytic (105). Preclinical studies on ECG, such as its role in blocking cellular foam formation in atherosclerosis, suggest cardiovascular benefits (106), which may indirectly relate to aging, but direct evidence on senescence is sparse.

Human RCTs evaluating ECG effects on aging cellular and biochemical markers are notably absent. One RCT on epicatechin-enriched extract from *Camellia sinensis* addressed age-related muscle mass loss (107). Other RCTs on catechins, such as those on cognitive function in Down syndrome, focused on EGCG, not ECG. The lack of specific RCTs on ECG highlights a gap in the literature, with challenges in bioavailability and dosage. The ECG ability to influence telomere length is inferred from studies on catechins, but human RCTs specifically on telomere length are absent, with most evidence from animal models showing extended lifespan for related compounds (108).

Other Phytochemicals

Sulforaphane, an isothiocyanate found in cruciferous vegetables like broccoli, exhibits significant anti-aging potential through the potent activation of the Nrf2 pathway, a master regulator of antioxidant responses (109). Sulforaphane enhances the expression of antioxidant enzymes such as Heme Oxygenase-1 (HO-1) and NAD(P)H Quinone Dehydrogenase 1 (NQO1), reducing ROS and mitigating oxidative damage to DNA and mitochondria (110). It also inhibits pro-inflammatory pathways like NF-κB, reducing SASP-related cytokines such as IL-6 and TNF-α

(111). Sulforaphane may also delay senescence by stabilizing mitochondrial function and inducing autophagy (112). A RCT showed sulforaphane (100 µmol/day for 12 weeks) reduced oxidative stress markers (e.g., MDA) in type 2 diabetes patients, suggesting potential anti-aging effects, but larger trials are needed (113).

Genistein, an isoflavone found in soybeans, contributes to anti-aging effects through its estrogen-like activity and antioxidant properties, influencing cellular senescence and age-related pathways (114). Genistein activates estrogen receptor signaling, which modulates gene expression related to cell survival and repair, potentially counteracting age-related declines in tissue homeostasis (115). It reduces oxidative stress by upregulating antioxidant enzymes like SOD and catalase, protecting against DNA damage and mitochondrial dysfunction, key drivers of aging (116). Genistein also inhibits inflammatory pathways, reducing SASP components like IL-8, and may delay senescence by modulating p53 and p21 pathways (117). In rodent models, genistein extended lifespan and improved bone health, mimicking estrogen's protective effects (118). RCTs on postmenopausal women (supplemented with genistein) showed bone mineral density improvement and reduction of inflammatory markers, suggesting benefits for age-related conditions. However, no RCTs directly assess the impact of genistein on senescence-specific markers or telomere length in humans, highlighting a research gap. Further human studies are required to confirm anti-aging efficacy of genistein (119-121).

Conclusion

Phytochemicals like resveratrol, curcumin, quercetin, EGCG, ECG, sulforaphane, and genistein show promise in slowing aging and cellular senescence by reducing oxidative stress, inflammation, and SASP effects; while modulating pathways like SIRT1, Nrf2, and p53/p21. Preclinical studies demonstrated lifespan extension and delayed senescence, but human RCTs revealed mixed results, with benefits in physical function, cognitive health, and inflammatory markers, yet limited data on telomere length and senescence-specific markers. Challenges include bioavailability and inconsistent outcomes, necessitating larger, well-designed human trials to confirm their anti-aging efficacy and translate preclinical findings into clinical applications.

Acknowledgement

We would like to thank all the individuals and organizations that contributed to this research. Their support and insights were invaluable. We also thank the anonymous reviewers for their constructive feedback, which helped improve the quality of this manuscript.

Funding

The authors declare no support from any commercial organization for the submitted study.

Authors' Contribution

AS: Conceptualization, Literature search, Data extraction, and writing; Original draft of the narrative review. MAM: Supervision, Methodological guidance, Critical revision, and final approval of the manuscript.

Conflict of Interest

None of the authors had a conflict of interest.

References

1 Kim JH, Yang D, Park S. Raman Spectroscopy in Cellular and Tissue Aging Research. *Aging Cell*. 2025;24:e14494. DOI: 10.1111/acel.14494. PMID: 39876576.

2 Izquierdo M, de Souto Barreto P, Arai H, et al. Global consensus on optimal exercise recommendations for enhancing healthy longevity in older adults (ICFSR). *J Nutr Health Aging*. 2025;29:100401. DOI: 10.1016/j.jnha.2024.100401. PMID: 39743381.

3 Costa CM, Pedrosa SS, Kirkland JL, et al. The senotherapeutic potential of phytochemicals for age-related intestinal disease. *Ageing Res Rev*. 2025;104:102619. DOI:10.1016/j.arr.2024.102619. PMID: 39638096.

4 de Lima EP, Laurindo LF, Catharin VCS, et al. Polyphenols, Alkaloids, and Terpenoids Against Neurodegeneration: Evaluating the Neuroprotective Effects of Phytocompounds Through a Comprehensive Review of the Current Evidence. *Metabolites*. 2025;15:124. PMID: 39997749.

5 Ismaila M, Adnan M, Sasidharan S. Exploring Medicinal Plants and Phytochemicals for Telomere Maintenance and Anti-aging: Insights into Telomerase Activation and Longevity. *Revista Brasileira de Farmacognosia*. 2025;35:275-290.

6 Munteanu C, Galaction AI, Onose G, et al. Harnessing Gasotransmitters to Combat Age-Related Oxidative Stress in Smooth Muscle and Endothelial Cells. *Pharmaceuticals (Basel)*. 2025;18:344. DOI:10.3390/ph18030344. PMID: 40143122.

7 Hossain MS, Wazed MA, Asha S, et al. Dietary Phytochemicals in Health and

Disease: Mechanisms, Clinical Evidence, and Applications—A Comprehensive Review. *Food Sci Nutr*. 2025;13:e70101. DOI: 10.1002/fsn3.70101. PMID: 40115248.

8 Chaudhary S, Kaur P, Singh TA, et al. The dynamic crosslinking between gut microbiota and inflammation during aging: reviewing the nutritional and hormetic approaches against dysbiosis and inflammaging. *Biogerontology*. 2025;26:1. DOI: 10.1007/s10522-024-10146-2. PMID: 39441393.

9 Segueni K, Chouikh A, Eddine Laouini S, et al. Evaluation of Dermal Wound Healing Potential: Phytochemical Characterization, Anti-Inflammatory, Antioxidant, and Antimicrobial Activities of Euphorbia guyoniana Boiss. & Reut. Latex. *Chem Biodivers*. 2025;22:e202402284. DOI:10.1002/cbdv.202402284. PMID: 39495036.

10 Zheng Z, Gao J, Ma Y, et al. Cellular and Molecular Mechanisms of Phytochemicals Against Inflammation-Associated Diseases and Viral Infection. *Cell Biol Int*. 2025;49:606-33. DOI:10.1002/cbin.70011. PMID: 40091269.

11 Ungurianu A, Margină D, Mihai DP, et al. Caloric restriction mimetics: Pinostilbene versus resveratrol regarding SIRT1 and SIRT6 interaction. *Adv Med Sci*. 2025;70:44-50. DOI: 10.1016/j.advms.2024.11.002. PMID: 39617052.

12 AlHayani DA, Kubaev A, Uthirapathy S, et al. Insights Into the Therapeutic Potential of SIRT1-modifying Compounds for Alzheimer's Disease: A Focus on Molecular Mechanisms. *J Mol Neurosci*. 2025;75:29. DOI: 10.1007/s12031-025-02324-9. PMID: 40000535.

13 Beaver LM, Jamieson PE, Wong CP, et al. Promotion of healthy aging through the nexus of gut microbiota and dietary phytochemicals. *Adv Nutr*. 2025;16:100376. DOI: 10.1016/j.advnut.2025.100376. PMID: 39832641.

14 Assalve G, Lunetti P, Rocca MS, et al. Exploring the Link Between Telomeres and Mitochondria: Mechanisms and Implications in Different Cell Types. *Int J Mol Sci*. 2025;26:993. DOI: 10.3390/ijms26030993. PMID: 39940762.

15 Liu B, Peng Z, Zhang H, et al. Regulation of cellular senescence in tumor progression and therapeutic targeting: mechanisms and pathways. *Mol Cancer*. 2025;24:106. DOI:10.1186/s12943-025-02284-z. PMID: 40170077.

16 Goyal K, Afzal M, Altamimi ASA, et al. Chronic kidney disease and aging: dissecting the p53/p21 pathway as a therapeutic target. *Biogerontology*. 2025;26:32. DOI: 10.1007/s10522-024-10173-z. PMID: 39725742.

17 Balaraman AK, Afzal M, Moglad E, et al. The interplay of p16INK4a and non-coding RNAs: bridging cellular senescence, aging, and cancer. *Biogerontology*. 2025;26:50. DOI:10.1007/s10522-025-10194-2. PMID: 39907830.

18 Yang A, Nouraie M, Pu J, et al. Distinct Senescence-associated Secretory Phenotype Mediators Associate With an Aging Endotype and Multiorgan Dysfunction in COPD. American *J Respiratory Critical Care Med*. 2025;211:A7689-A. DOI: 10.1164/ajrccm.2025.211.Abstracts.A7689.

19 Malojirao VH, Vasquez V, Kodavati M, et al. Hemin-induced transient senescence via DNA damage response: a neuroprotective mechanism against ferroptosis in intracerebral hemorrhage. *Commun Biol*. 2025;8:622. DOI:10.1038/s42003-025-07983-3. PMID: 40247121.

20 Park SS, Roh TH, Tanaka Y, et al. High p16INK4A expression in glioblastoma is associated with senescence phenotype and better prognosis. *Neoplasia*. 2025;60:101116. DOI: 10.1016/j.neo.2024.101116. PMID: 39724755.

21 Constantinou SM, Bennett DC. Cell Senescence and the Genetics of Melanoma Development. *Genes Chromosomes Cancer*. 2024;63:e23273. DOI: 10.1002/gcc.23273. PMID: 39422311.

22 Camacho-Encina M, Booth LK, Redgrave RE, et al. Cellular senescence, mitochondrial dysfunction, and their link to cardiovascular disease. *Cells*. 2024;13:353. DOI: 10.3390/cells13040353. PMID: 38391966.

23 Lopes-Paciencia S, Ferbeyre G. Increased chromatin accessibility underpins senescence. *FEBS J*. 2025. DOI:10.1111/febs.70136. PMID: 40387486.

24 Lai P, Liu L, Bancaro N, et al. Mitochondrial DNA released by senescent tumor cells enhances PMN-MDSC-driven immunosuppression through the cGAS-STING pathway. *Immunity*. 2025;58:811-25.e7. DOI: 10.1016/j.immuni.2025.03.005. PMID: 40203808.

25 García-Domínguez M. Pathological and Inflammatory Consequences of Aging. *Biomolecules*. 2025;15:404. DOI: 10.3390/biom15030404. PMID: 40149940.

26 Kumar N, Walia HK. Cellular Senescence and Stem Cell Exhaustion: Implications for Aging and Regeneration. Cellular Senescence, Age-Related Disorders, and Emerging Treatments: Springer; 2025.p.103-33.

27 McHugh D, Durán I, Gil J. Senescence as a therapeutic target in cancer and age-related diseases. *Nat Rev Drug Discov*. 2025;24:57-71. DOI: 10.1038/s41573-024-01074-4. PMID: 39548312.

28 Tomas M, Gunal-Koroglu D, Kamiloglu S, et al. The state of the art in anti-aging: plant-based phytochemicals for skin care. *Immun Ageing*. 2025;22:5. DOI: 10.1186/s12979-025-00498-9. PMID: 39891253.

29 Ugoeze KC, Odeku OA. Antioxidants in Infectious Disease Management. *Antioxidants: Nature's Defense Against Disease*. 2025:169-218. DOI: 10.1002/9781394270576.ch6.

30 Prabu SM, Shagirtha K, Renugadevi J. Quercetin in combination with vitamins (C and E) improve oxidative stress and hepatic injury in cadmium intoxicated rats. *Biomed Prevent Nutr*. 2011;1:1-7. DOI: 10.1016/j.bionut.2010.12.003.

31 Meng Q, Song C, Ma J, et al. Quercetin Prevents Hyperuricemia Associated With Gouty Arthritis by Inactivating the NLRP3/NF-κB Signaling Pathway. *Chem Biol Drug Des.* 2025;105:e70103. DOI: 10.1111/cbdd.70103. PMID: 40230265.

32 Lei JQ, Xie QL, Li QP, et al. Resveratrol Alleviates Liver Fibrosis by Targeting Cross-Talk Between TLR2/MyD88/ERK and NF-κB/NLRP3 Inflammasome Pathways in Macrophages. *J Biochem Mol Toxicol*. 2025;39:e70208. DOI: 10.1002/jbt.70208. PMID: 40079280.

33 Hashemi SS, Rezaeian R, Rafati AR, et al. A review on application of herbals and their polymer composites in wound healing. *Arab J Chem*. 2024;17:1-15.

34 Calcinotto A, Kohli J, Zagato E, et al. Cellular Senescence: Aging, Cancer, and Injury. *Physiol Rev*. 2019;99:1047-78. DOI:10.1152/physrev.00020.2018. PMID: 30648461.

35 Zhu L, Yang M, Fan L, et al. Interaction between resveratrol and SIRT1: role in neurodegenerative diseases. *Naunyn-Schmiedeberg's Arch Pharmacol*. 2025;398:89-101. DOI: 10.1007/s00210-024-03319-w. PMID: 39105797.

36 Ray A. Autophagy Fasting: Definition, Time Hour, Benefits, and Side effects. Compassionate AI. 2025;2:57-9.

37 Ponce-Mora A, Salazar NA, Domenech-Bendaña A, et al. Interplay Between Polyphenols and Autophagy: Insights From an Aging Perspective. *Front Biosci (Landmark Ed)*. 2025;30:25728. DOI: 10.31083/FBL25728. PMID: 40152368.

38 Rezaei M, Hassanzadeh Nemati N, et al. Characterization of sodium carboxymethyl cellulose/calcium alginate scaffold loaded with curcumin in skin tissue engineering. *J Appl Polymer Sci*. 2022;139:52271. DOI: 10.1002/app.52271.

39 Wu X, Al-Amin M, Zhao C, et al. Catechinic acid, a natural polyphenol compound, extends the lifespan of Caenorhabditis elegans via mitophagy pathways. *Food Funct*. 2020;11:5621-34. DOI: 10.1039/d0fo00694g. PMID: 32530444.

40 Booth LN, Brunet A. The Aging Epigenome. *Mol Cell*. 2016;62:728-44. DOI: 10.1016/j.molcel.2016.05.013. PMID: 27259204.

41 Mehrabani D, Khodakaram-Tafti A, Asadi-Yousefabad S, et al. Effect of age and passage on canine bone marrow derived mesenchymal stem cells. *Onl J Vet Res*. 2015;19:663-671.

42 Dixit V, Chaubey KK, Dayal D, et al. Natural Products in Aging: Cellular Mechanisms and Emerging Therapeutics for Age-Related Disorders. *J Aging Res*. 2025;2025:6868732.

43 Bian Z, Li Z, Chang H, et al. Resveratrol Ameliorates Chronic Stress in Kennel Dogs and Mice by Regulating Gut Microbiome and Metabolome Related to Tryptophan Metabolism. *Antioxidants (Basel)*. 2025;14:195. DOI:10.3390/antiox14020195. PMID: 40002382.

44 Giovannelli L, Pitozzi V, Jacomelli M, et al. Protective effects of resveratrol against senescence-associated changes in cultured human fibroblasts. *J Gerontol A Biol Sci Med Sci*. 2011;66:9-18. DOI:10.1093/gerona/glq161. PMID: 20884849.

45 Bhullar KS, Hubbard BP. Lifespan and healthspan extension by resveratrol. *Biochim Biophys Acta*. 2015;1852:1209-18. DOI:10.1016/j.bbadis.2015.01.012. PMID: 25640851.

46 Alhazzani K, Alrewily SQ, Alanzi AR, et al. Therapeutic Effects of Liposomal Resveratrol in the Mitigation of Diabetic Nephropathy via Modulating Inflammatory Response, Oxidative Stress, and Apoptosis. *Appl Biochem Biotechnol*. 2025;197:1570-89. DOI:10.1007/s12010-024-05092-1. PMID: 39589702.

47 Wang D, Liu J, Wang J, et al. Resveratrol protects against uremic serum-induced endothelial cell injury by activating the FUS/KLF2/FBXW7 signaling pathway. *Appl Biol Chem*. 2025;68:1-12.

48 Zhao Q, Zhang Y, Liu J, et al. Polydatin enhances oxaliplatin-induced cell death by activating NOX5-ROS-mediated DNA damage and ER stress in colon cancer cells. *Front Pharmacol*. 2024;15:1532695. DOI:10.3389/fphar.2024.1532695. PMID: 39850563.

49 Gutlapalli SD, Kondapaneni V, Toulassi IA, et al. The Effects of Resveratrol on Telomeres and Post Myocardial Infarction Remodeling. *Cureus*. 2020;12:e11482. DOI:10.7759/cureus.11482. PMID: 33329978.

50 Koushki M, Dashatan NA, Meshkani R. Effect of Resveratrol Supplementation on Inflammatory Markers: A Systematic Review and Meta-analysis of Randomized Controlled Trials.

Clin Ther. 2018;40:1180-92 e5. DOI:10.1016/j.clinthera.2018.05.015. PMID: 30017172.

51 Sahebkar A, Serban C, Ursoniu S, et al. Lack of efficacy of resveratrol on C-reactive protein and selected cardiovascular risk factors—Results from a systematic review and meta-analysis of randomized controlled trials. *Int J Cardiol*. 2015;189:47-55. DOI: 10.1016/j.ijcard.2015.04.008. PMID: 25885871.

52 Tao G, Wang X, Wang J, et al. Dihydroresveratrol ameliorates NLRP3 inflammasome-mediated neuroinflammation via Bnip3-dependent mitophagy in Alzheimer's disease. *Br J Pharmacol*. 2025;182:1005-24. DOI:10.1111/bph.17373. PMID: 39467709.

53 Berman AY, Motechin RA, Wiesenfeld MY, et al. The therapeutic potential of resveratrol: a review of clinical trials. *NPJ Precis Oncol*. 2017;1:35. DOI: 10.1038/s41698-017-0038-6. PMID: 28989978.

54 Carollo C, Sorce A, Cirafici E, et al. Sirtuins and Resveratrol in Cardiorenal Diseases: A Narrative Review of Mechanisms and Therapeutic Potential. *Nutrients*. 2025;17:1212. DOI:10.3390/nu17071212. PMID: 40218970.

55 Wang XB, Zhu L, Huang J, et al. Resveratrol-induced augmentation of telomerase activity delays senescence of endothelial progenitor cells. *Chin Med J (Engl).* 2011;124:4310-5. PMID: 22340406.

56 Gerić M, Nanić L, Micek V, Jovanović IN, Gajski G, Rašić D, et al. The Impact of Resveratrol and Melatonin on the Genome and Oxidative Status in Ageing Rats. *Nutrients*. 2025;17:1187. DOI: 10.3390/nu17071187. PMID: 40218945.

57 Tu Kx, Ou Qj, Lin Ft, et al. Higher Intake of Resveratrol Is Associated With a Lower Risk of Colorectal Cancer: A Large-Scale Case–Control Study. *Phytother Res*. 2025. DOI: 10.1002/ptr.8510. PMID: 40259782.

58 Mehrabani D, Farjam M, Geramizadeh B, et al. The healing effect of curcumin on burn wounds in rat. *World J Plast Surg.* 2015;4:29-35. PMID: 25606474.

59 Farjam M, Mehrabani D, Abbassnia F, et al. The healing effect of curcuma longa on liver in experimental acute hepatic encephalopathy of rat. *Comp Clin Pathol*. 2014;23:1669-1673.

60 Rabbani-Haghighi N, Naghsh N, Mehrabani D. The protective effect of curcuma longa in thioacetamide-induced hepatic injury in rat. *Global J Pharmacol*. 2013;7:203-207. DOI: 10.5829/idosi.gjp.2013.7.2.74203

61 Turer BY, Sanlier N. Relationship of curcumin with aging and Alzheimer and Parkinson disease, the most prevalent age-related neurodegenerative diseases: a narrative review. *Nutr Rev*. 2025;83:e1243-e58. DOI: 10.1093/nutrit/nuae079. PMID: 38916925.

62 Bahrami A, Montecucco F, Carbone F, et al. Effects of Curcumin on Aging: Molecular Mechanisms and Experimental Evidence. *Biomed Res Int*. 2021;2021:8972074. DOI:10.1155/2021/8972074. PMID: 34692844.

63 Panjehshahin Mr, Owji Aa, Mehrabani D, et al. Effect Of Curcumin On Cholesterol Gall-Stone Induction In Rats. *J Appl Anim Res*. 2003;23:75-80.

64 Lee YM, Kim Y. Is Curcumin Intake Really Effective for Chronic Inflammatory Metabolic Disease? A Review of Meta-Analyses of Randomized Controlled Trials. *Nutrients*. 2024;16:1728. DOI: 10.3390/nu16111728. PMID: 38892660.

65 Lestari CR, Dewi RAEP, Nurjanah S, et al. The Effect of Green Coffee Seed (Coffea Canephora) and Yellow Turmeric (Curcuma Domestica Val.) Extract on TNF-α Level in Acute Respiratory Distress Syndrome. *Int J Nutr Sci*. 2022;7:210-216. DOI: 10.30476/ijns.2022.97406.1209.

66 Bielak-Zmijewska A, Grabowska W, Ciolko A, et al. The Role of Curcumin in the Modulation of Ageing. *Int J Mol Sci*. 2019;20:1239. DOI:10.3390/ijms20051239. PMID: 30871021.

67 Izadi M, Sadri N, Abdi A, et al. Longevity and anti-aging effects of curcumin supplementation. *Geroscience*. 2024;46:2933-50. DOI:10.1007/s11357-024-01092-5. PMID: 38409646.

68 Liu X, Lin L, Hu G. Meta-analysis of the effect of curcumin supplementation on skeletal muscle damage status. *PLoS One*. 2024;19:e0299135. DOI:10.1371/journal.pone.0299135. PMID: 39008500.

69 Nunes YC, Mendes NM, Pereira de Lima E, et al. Curcumin: A Golden Approach to Healthy Aging: A Systematic Review of the Evidence. *Nutrients*. 2024;16:2721. DOI:10.3390/nu16162721. PMID: 39203857.

70 Voulgaropoulou SD, Van Amelsvoort T, Prickaerts J, Vingerhoets C. The effect of curcumin on cognition in Alzheimer's disease and healthy aging: A systematic review of pre-clinical and clinical studies. *Brain Res*. 2019;1725:146476. DOI: 10.1016/j.brainres.2019.146476. PMID: 31560864.

71 Malekzadeh S, Edalatmanesh MA, Mehrabani D, et al. Drugs induced Alzheimer's disease in animal model. *Galen Med J*. 2017;6:185-96. DOI: 10.31661/gmj.v6i3.820.

72 Nunes YC, Mendes NM, Pereira de Lima E, et al.

Curcumin: A Golden Approach to Healthy Aging: A Systematic Review of the Evidence. *Nutrients*. 2024;16:2721. DOI:10.3390/nu16162721. PMID: 39203857.

73 Mankowski RT, Sibille KT, Leeuwenburgh C, et al. Effects of Curcumin C3 Complex(R) on Physical Function in Moderately Functioning Older Adults with Low-Grade Inflammation - A Pilot Trial. *J Frailty Aging*. 2023;12:143-9. DOI:10.14283/jfa.2022.47. PMID: 36946712.

74 Chang YH. Curcumin as a potential therapeutic agent for Parkinson's disease: a systematic review. *Front Pharmacol*. 2025;16:1593191. DOI: 10.3389/fphar.2025.1593191. PMID: 40331193.

75 Chahardehi AM, Arefnezhad R, Pourbafrani A, et al. MicroRNAs modulation by curcumin, catalpol, and other natural products in Alzheimer's disease: a review. *Mol Biol Rep*. 2025;52:1-18. DOI: 10.1007/s11033-025-10543-x. PMID: 40327129.

76 Lee YM, Kim Y. Is Curcumin Intake Really Effective for Chronic Inflammatory Metabolic Disease? A Review of Meta-Analyses of Randomized Controlled Trials. *Nutrients*. 2024;16:1728. DOI:10.3390/nu16111728. PMID: 38892660.

77 Saraf-Bank S, Ahmadi A, Paknahad Z, et al. Effects of curcumin supplementation on markers of inflammation and oxidative stress among healthy overweight and obese girl adolescents: A randomized placebo-controlled clinical trial. *Phytother Res*. 2019;33:2015-22. DOI:10.1002/ptr.6370. PMID: 31206225.

78 Baghcheghi Y, Razazpour F, Mirzaee F, et al. Exploring the molecular mechanisms of curcumin in modulating memory impairment in neurodegenerative disorders. *Mol Biol Rep*. 2025;52:45. DOI: 10.1007/s11033-024-10115-5. PMID: 39653966.

79 Yousef-Nezhad H, Hejazi N. Anti-Bacterial Properties of Herbs against Helicobacter Pylori Infection: A Review. *Int J Nutr Sci*. 2017;2:126-133.

80 Che K, Wang C, Chen H. Advancing functional foods: A systematic analysis of plant-derived exosome-like nanoparticles and their health-promoting properties. *Front Nutr*. 2025;12:1544746. DOI: 10.3389/fnut.2025.1544746. PMID: 40115388.

81 Imb M, Veghelyi Z, Maurer M, et al. Exploring Senolytic and Senomorphic Properties of Medicinal Plants for Anti-Aging Therapies. *Int J Mol Sci*. 2024;25:10419. DOI:10.3390/ijms251910419. PMID: 39408750.

82 Khodabandeh Z, Dolati P, Zamiri MJ, et al. Protective Effect of Quercetin on Testis Structure and Apoptosis Against Lead Acetate Toxicity: an Stereological Study. *Biol Trace Elem Res*. 2021;199:3371-3381. DOI: 10.1007/s12011-020-02454-8. PMID: 33107017.

83 Dolati P, Zamiri MJ, Akhlaghi A, et al. Reproductive and embryological toxicity of lead acetate in male mice and their offspring and mitigation effects of quercetin. *J Trace Elem Med Biol*. 2021;67:126793. DOI: 10.1016/j.jtemb.2021.126793. PMID: 34049200.

84 Zhang M, Zhang G, Meng X, et al. Reduction of the oxidative damage to H2O2-induced HepG2 cells via the Nrf2 signalling pathway by plant flavonoids Quercetin and Hyperoside. *Food Science and Human Wellness*. 2024;13:1864-76. DOI: 10.26599/FSHW.2022.9250155.

85 Alharbi HOA, Alshebremi M, Babiker AY, et al. The Role of Quercetin, a Flavonoid in the Management of Pathogenesis Through Regulation of Oxidative Stress, Inflammation, and Biological Activities. *Biomolecules*. 2025;15:151. DOI: 10.3390/biom15010151. PMID: 39858545.

86 Shah MA, Faheem HI, Hamid A, et al. The entrancing role of dietary polyphenols against the most frequent aging-associated diseases. *Med Res Rev*. 2024;44:235-74. DOI: 10.1002/med.21985. PMID: 37486109.

87 Garzón-García L, Ayuda-Durán B, González-Manzano S, et al. Neuroprotective Potential of the Flavonoids Quercetin and Epicatechin in a C. elegans Tauopathy Model. *Mol Nutr Food Res*. 2025:e70108. DOI: 10.1002/mnfr.70108. PMID: 40351085.

88 Dos Santos MG, Arbo BD, Hort MA. Effects of quercetin and its derivatives in in vivo models of neuroinflammation: a systematic review and meta-analysis. *Neural Regen Res*. 2026;21:1783-1792. DOI:10.4103/NRR.NRR-D-24-01175. PMID: 40145967.

89 Nishikawa T, Takeda R, Ueda S, et al. Quercetin ingestion alters motor unit behavior and enhances improvement in muscle strength following resistance training in older adults: a randomized, double-blind, controlled trial. *Eur J Nutr*. 2025;64:117. DOI:10.1007/s00394-025-03634-9. PMID: 40063125.

90 Bientinesi E, Ristori S, Lulli M, et al. Quercetin induces senolysis of doxorubicin-induced senescent fibroblasts by reducing autophagy, preventing their pro-tumour effect on osteosarcoma cells. *Mech Ageing Dev*. 2024;220:111957. DOI: 10.1016/j.mad.2024.111957. PMID: 38909661.

91 Okselni T, Septama AW, Juliadmi D, et al. Quercetin as a therapeutic agent for skin problems: a systematic review and meta-analysis on antioxidant effects, oxidative stress, inflammation, wound healing, hyperpigmentation, aging, and skin cancer. *Naunyn Schmiedebergs Arch Pharmacol.* 2025;398:5011-55. DOI: 10.1007/s00210-024-03722-3. PMID: 39738831.

92 Capasso L, De Masi L, Sirignano C, et al. Epigallocatechin Gallate (EGCG): Pharmacological Properties, Biological Activities and Therapeutic Potential. *Molecules*. 2025;30:654. DOI:10.3390/molecules30030654. PMID: 39942757.

93 Yuan M, Hu L, Zhu C, et al. Comparison and Assessment of Anti-Inflammatory and Antioxidant Capacity Between EGCG and Phosphatidylcholine-Encapsulated EGCG. *J Cosmet Dermatol*. 2025;24:e16628. DOI: 10.1111/jocd.16628. PMID: 39482802.

94 Zhang B, Zeng M, Tie Q, et al. (-)-Epigallocatechin-3-gallate (EGCG) ameliorates ovalbumin-induced asthma by inhibiting inflammation via the TNF-alpha/TNF-R1/NLRP3 signaling pathway. *Int Immunopharmacol*. 2025;144:113708. DOI:10.1016/j.intimp.2024.113708. PMID: 39626539.

95 Al-Regaiey K. Crosstalk between adipogenesis and aging: role of polyphenols in combating adipogenic-associated aging. *Immun Ageing*. 2024;21:76. DOI: 10.1186/s12979-024-00481-w. PMID: 39511615.

96 Chen X, Walton K, Brodaty H, et al. Polyphenols and diets as current and potential nutrition senotherapeutics in Alzheimer's disease: findings from clinical trials. *J Alzheimers Dis.* 2024;101:S479-S501. DOI: 10.3233/JAD-231222. PMID: 38875032.

97 Li H, Zheng C, Wang Z, et al. Neuroprotective Effects of Catechins by Differentially Affecting the Binding of Beta-amyloid and Its Aggregates to the Target Cells. *Mol Neurobiol*. 2025;62:9861-9880. DOI:10.1007/s12035-025-04870-0. PMID: 40172817.

98 Fitzgerald KN, Hodges R, Hanes D, et al. Correction: Potential reversal of epigenetic age using a diet and lifestyle intervention: a pilot randomized clinical trial. *Aging (Albany NY).* 2024;16:4943-5. DOI:10.18632/aging.205700. PMID: 38488762.

99 Delabar JM, Gomes M, Fructuoso M, et al. EGCG-like non-competitive inhibitor of DYRK1A rescues cognitive defect in a down syndrome model. *Eur J Med Chem*. 2024;265:116098. DOI:10.1016/j.ejmech.2023.116098. PMID: 38171148.

100 Cieuta-Walti C, Cuenca-Royo A, Langohr K, et al. Safety and preliminary efficacy on cognitive performance and adaptive functionality of epigallocatechin gallate (EGCG) in children with Down syndrome. A randomized phase Ib clinical trial (PERSEUS study). *Genet Med*. 2022;24:2004-13. DOI:10.1016/j.gim.2022.06.011. PMID: 35951014.

101 Mereles D, Hunstein W. Epigallocatechin-3-gallate (EGCG) for clinical trials: more pitfalls than promises? *Int J Mol Sci*. 2011;12:5592-603. DOI: 10.3390/ijms12095592. PMID: 22016611.

102 Tan J, Vincken JP, van Zadelhoff A, et al. Presence of free gallic acid and gallate moieties reduces auto-oxidative browning of epicatechin (EC) and epicatechin gallate (ECg). *Food Chem*. 2023;425:136446. DOI: 10.1016/j.foodchem.2023.136446. PMID: 37245463.

103 Godoy MCXd, Monteiro GA, Moraes BHd, Macedo JA, Gonçalves GMS, Gambero A. Addition of polyphenols to drugs: the potential of controlling "inflammaging" and fibrosis in human senescent lung fibroblasts in vitro. *Int J Mol Sci*. 2024;25:7163. DOI: 10.3390/ijms25137163. PMID: 39000270.

104 Peng H, Shahidi F. Oxidation and degradation of (epi)gallocatechin gallate (EGCG/GCG) and (epi)catechin gallate (ECG/CG) in alkali solution. *Food Chem*. 2023;408:134815. DOI:10.1016/j.foodchem.2022.134815. PMID: 36549155.

105 Sharma R, Diwan B. An update on healthspan and lifespan enhancing attributes of tea amidst the emerging understanding of aging biology. *Human Nutr Metab*. 2022;28:200149. DOI: 10.1016/j.hnm.2022.200149.

106 Li Z, Feng C, Dong H, et al. Health promoting activities and corresponding mechanism of (–)-epicatechin-3-gallate. *Food Sci Human Wellness*. 2022;11:568-78. DOI:10.1016/j.fshw.2021.12.013

107 Seo H, Lee SH, Park Y, et al. (-)-Epicatechin-Enriched Extract from Camellia sinensis Improves Regulation of Muscle Mass and Function: Results from a Randomized Controlled Trial. *Antioxidants (Basel).* 2021;10:1026. DOI:10.3390/antiox10071026. PMID: 34202133.

108 de la Torre R, de Sola S, Hernandez G, et al. Safety and efficacy of cognitive training plus epigallocatechin-3-gallate in young adults with Down's syndrome (TESDAD): a double-blind, randomised, placebo-controlled, phase 2 trial. *Lancet Neurol*. 2016;15:801-10. DOI:10.1016/S1474-4422(16)30034-5. PMID: 27302362.

109 Qin K, Liang W, Fragoulis A, et al. Sulforaphane regulates hepatic autophagy and apoptosis by modulating Kupffer cells' polarization via Nrf2/HO-1 pathway in the murine hemorrhagic shock/resuscitation model. *Eur J Trauma Emerg Surg*. 2025;51:218. DOI: 10.1007/s00068-025-02890-y. PMID: 40407885.

110 Fahey JW, Liu H, Batt H, et al. Sulforaphane and Brain Health: From Pathways of Action to Effects on Specific Disorders. *Nutrients*. 2025;17:1353. DOI:10.3390/nu17081353. PMID: 40284217.

111 Yang L, Wu W, Yang J, et al. Nanoparticle-mediated delivery of herbal-derived natural products to modulate immunosenescence-induced drug resistance in cancer therapy: a comprehensive review. *Front Oncol*. 2025;15:1567896. DOI: 10.3389/fonc.2025.1567896. PMID: 40356750.

112 Yang W, Zeng S, Shao R, et al. Sulforaphane regulation autophagy-mediated pyroptosis in autoimmune hepatitis via AMPK/mTOR pathway. *Int Immunopharmacol*. 2025;146:113826. DOI: 10.1016/j.intimp.2024.113826. PMID: 39673998.

113 Axelsson AS, Tubbs E, Mecham B, et al. Sulforaphane reduces hepatic glucose production and improves glucose control in patients with type 2 diabetes. *Sci Transl Med*. 2017;9:eaah4477. DOI:10.1126/scitranslmed.aah4477. PMID: 28615356.

114 Tobón-Cornejo S, Vargas-Castillo A, Juarez M, et al. Metabolic reprogramming and synergistic cytotoxicity of genistein and chemotherapy in human breast cancer cells. *Life Sci*. 2025;370:123562. DOI: 10.1016/j.lfs.2025.123562. PMID: 40090516.

115 Sharifi-Rad J, Quispe C, Imran M, et al. Genistein: An Integrative Overview of Its Mode of Action, Pharmacological Properties, and Health Benefits. *Oxid Med Cell Longev*. 2021;2021:3268136. DOI:10.1155/2021/3268136. PMID: 34336089.

116 Liu X, Zheng T, Bao Y, et al. Genistein Implications in Radiotherapy: Kill Two Birds with One Stone. *Molecules*. 2025;30:188. DOI:10.3390/molecules30010188. PMID: 39795243.

117 Domaszewska-Szostek A, Puzianowska-Kuznicka M, Kurylowicz A. Flavonoids in Skin Senescence Prevention and Treatment. *Int J Mol Sci*. 2021;22:6814. DOI:10.3390/ijms22136814. PMID: 34201952.

118 Mannino F, D'Angelo T, Pallio G, et al. The Nutraceutical Genistein-Lycopene Combination Improves Bone Damage Induced by Glucocorticoids by Stimulating the Osteoblast Formation Process. *Nutrients*. 2022;14:4296. DOI:10.3390/nu14204296. PMID: 36296984.

119 Marini H, Minutoli L, Polito F, et al. Effects of the phytoestrogen genistein on bone metabolism in osteopenic postmenopausal women: a randomized trial. *Ann Intern Med*. 2007;146:839-47. DOI:10.7326/0003-4819-146-12-200706190-00005.

120 Morabito N, Crisafulli A, Vergara C, et al. Effects of genistein and hormone-replacement therapy on bone loss in early postmenopausal women: a randomized double-blind placebo-controlled study. *J Bone Miner Res*. 2002;17:1904-12. DOI:10.1359/jbmr.2002.17.10.1904.

121 Arcoraci V, Atteritano M, Squadrito F, et al. Antiosteoporotic Activity of Genistein Aglycone in Postmenopausal Women: Evidence from a Post-Hoc Analysis of a Multicenter Randomized Controlled Trial. *Nutrients*. 2017;9:179. DOI:10.3390/nu9020179. PMID: 28241420.