# Resveratrol and myricetin: potential modulators of immunosenescence

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Abstract

Background and Objectives
Immunosenescence, the progressive deterioration of immune function with age, is linked to heightened vulnerability to infections, malignancies, and chronic inflammatory diseases. Dietary polyphenols, such as resveratrol and myricetin found in wine, have emerged as potential modulators of immunosenescence due to their anti-inflammatory and antioxidant properties. This review evaluates preclinical evidence on the mechanisms by which these compounds may mitigate age-related immune dysfunction and explores their translational potential as therapeutic agents.

Methods
A systematic analysis of peer-reviewed preclinical studies (2000–2025) was conducted using PubMed, Scopus, and Web of Science databases. Keywords included "immunosenescence," "resveratrol," "myricetin," "polyphenols," and "aging." Inclusion criteria focused on in vitro and in vivo studies elucidating molecular pathways, immune cell modulation, and SASP reduction. Data were synthesized to highlight mechanistic synergies and translational challenges.

Results
Resveratrol, a stilbenoid, activates sirtuins (e.g., SIRT1), enhancing autophagy and mitochondrial biogenesis while suppressing NF-κB and COX-2-mediated inflammation. Myricetin, a flavonoid, scavenges reactive oxygen species (ROS) and modulates PI3K/Akt/mTOR signaling, restoring T-cell proliferation and function. Preclinical models demonstrate that both compounds reduce SASP markers (e.g., IL-6, TNF-α) and rejuvenate aged immune cells. Resveratrol enhances thymic output and macrophage phagocytosis in aged mice, while myricetin promotes regulatory T-cell (Treg) activity, countering age-related hyperinflammation. Synergistic effects in wine polyphenols amplify these benefits, as shown in co-treatment studies. However, low oral bioavailability (<1% for resveratrol) and discrepancies between effective preclinical doses (10–100 mg/kg) and dietary intake (≤1 mg/day) limit clinical applicability.

Discussion
Resveratrol and myricetin exhibit compelling immunomodulatory effects in preclinical settings, targeting hallmarks of immunosenescence such as oxidative stress, chronic inflammation, and T-cell dysfunction. Their ability to synergize with other polyphenols underscores grape's potential. However, translational gaps persist, as human trials remain limited and heterogeneous. Bioavailability barriers necessitate novel delivery systems to achieve therapeutic concentrations. While animal data are promising, long-term safety and efficacy in aging populations require rigorous validation. Future research should prioritize clinical trials to establish dose-response relationships, assess combinatorial polyphenol effects, and evaluate real-world impacts on immune resilience. These compounds represent a promising dietary strategy to delay immunosenescence, yet bridging the bench-to-bedside divide demands interdisciplinary innovation.

Keywords: immunosenescence, resveratrol, myricetin, polyphenols, aging, inflammation.