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Review ARTICLE

Resveratrol and Trans-Resveratrol in Respiratory Diseases: Immunobiological Mechanisms and Public Health Implications

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Abstract:

Chronic respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD), represent a significant global public health burden due to their high prevalence, morbidity, and socioeconomic impact. Persistent airway inflammation, oxidative stress, and immune dysregulation are central mechanisms underlying disease progression and exacerbations. Resveratrol and its biologically active isomer, trans-resveratrol, are naturally occurring polyphenols widely investigated for their antioxidant, anti-inflammatory, and immunomodulatory properties. This mini-review summarizes current evidence on the biological effects of resveratrol and trans-resveratrol in the respiratory system, focusing on their molecular targets, signaling pathways, and immunobiological actions relevant to asthma and COPD. Special emphasis is placed on their potential role as preventive and adjuvant strategies from a public health perspective. The available data support resveratrol as a context-dependent immunomodulator capable of attenuating chronic airway inflammation while preserving essential host defense mechanisms.

Key words: resveratrol; trans-resveratrol; asthma; copd; respiratory inflammation; public health; immunomodulation

Introduction:

Asthma and chronic obstructive pulmonary disease (COPD) are among the most prevalent chronic respiratory diseases worldwide and constitute major public health challenges due to their long-term morbidity, healthcare costs, and impact on quality of life [1,2]. Both conditions are characterized by chronic airway inflammation, immune imbalance, oxidative stress, and progressive structural changes in the respiratory tract [3]. Although current pharmacological therapies are effective in symptom control, they often fail to fully address the underlying inflammatory mechanisms or prevent disease progression, particularly in severe or treatment-resistant cases [4].

In this context, naturally derived bioactive compounds have gained attention as complementary strategies aimed at modulating inflammatory and oxidative pathways. Resveratrol (3,5,4′-trihydroxystilbene), particularly its trans-isomer, has been extensively studied due to its pleiotropic biological effects and favorable safety profile [5].

Resveratrol and Trans-Resveratrol: Biological Characteristics:

Resveratrol is a polyphenolic stilbene produced by several plant species as a phytoalexin in response to environmental stressors, including ultraviolet radiation and pathogen exposure [6]. Among its isomeric forms, trans-resveratrol is considered the most biologically stable and active, exhibiting higher bioactivity in experimental models [7].

After oral administration, resveratrol undergoes rapid metabolism, resulting in low systemic bioavailability; however, both parent compounds and metabolites retain biological activity, particularly at the tissue level [8]. These characteristics are relevant for respiratory diseases, where local pulmonary effects may be achieved even at low circulating concentrations.

Immunobiological Mechanisms in the Respiratory Tract:

Modulation of Inflammatory Signaling Pathways:

Resveratrol and trans-resveratrol exert anti-inflammatory effects through the modulation of key intracellular signaling pathways implicated in airway inflammation. Inhibition of nuclear factor-κB (NF-κB) and mitogen-activated protein kinases (MAPKs), including p38 and ERK, leads to reduced transcription of pro-inflammatory cytokines and chemokines [9,10].

Additionally, activation of sirtuin-1 (SIRT1) and AMP-activated protein kinase (AMPK) contributes to the regulation of inflammatory gene expression and cellular metabolism, reinforcing their role as immunomodulators rather than broad immunosuppressive agents [11].

Effects on Oxidative Stress and Antioxidant Defense:

Oxidative stress plays a central role in the pathophysiology of asthma and COPD, promoting epithelial damage and amplifying inflammatory responses [12]. Resveratrol activates the nuclear factor erythroid 2-related factor 2 (Nrf2)/heme oxygenase-1 (HO-1) axis, enhancing endogenous antioxidant defenses and reducing reactive oxygen species production in airway cells [13].

Regulation of Immune Cell Responses:

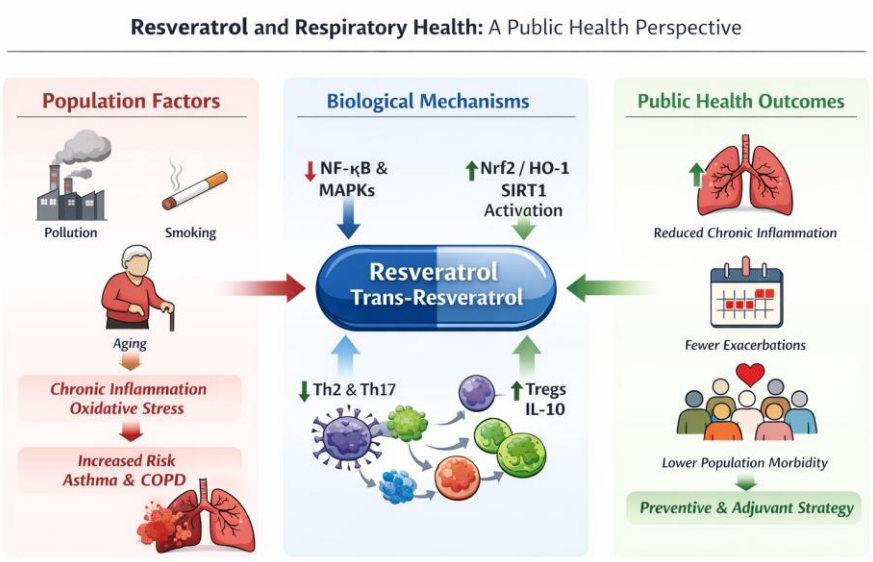
In experimental models, resveratrol modulates adaptive immune responses by attenuating excessive Th2 and Th17 polarization, which are associated with allergic inflammation and neutrophilic airway disease, respectively [14]. At the same time, it promotes regulatory T cell (Treg) function and interleukin-10 (IL-10) production, contributing to immune homeostasis without compromising protective immunity [15].

Implications for Asthma and COPD:

In asthma, resveratrol has been shown to reduce eosinophilic inflammation, mucus hypersecretion, and airway hyperresponsiveness through downregulation of Th2-associated cytokines such as IL-4 and IL-13 [16]. In COPD, its effects are primarily linked to suppression of neutrophilic inflammation, inhibition of NF-κB-dependent pathways, and attenuation of oxidative stress, mechanisms that are particularly relevant in smoking-related lung injury [17].

Public Health Perspective:

From a public health standpoint, the high prevalence of chronic respiratory diseases underscores the importance of preventive and adjunctive strategies aimed at reducing inflammation and disease progression. Resveratrol and trans-resveratrol, due to their immunomodulatory and antioxidant properties, represent promising candidates for complementary approaches in populations at risk, particularly when integrated with lifestyle and environmental interventions [18]. While clinical evidence is still emerging, the strong mechanistic rationale supports further investigation in well-designed translational and population-based studies.



Conceptual framework of resveratrol's role in mitigating chronic respiratory diseases.

Conclusion:

Resveratrol and trans-resveratrol exhibit multifaceted immunobiological actions in the respiratory system, targeting key inflammatory and oxidative pathways involved in asthma and COPD. Rather than inducing generalized immunosuppression, these compounds act as context-dependent modulators that restore immune balance and reduce chronic airway inflammation. Their favorable safety profile and biological plausibility support their potential role as preventive or adjuvant strategies in respiratory health from a public health perspective.

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