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Review Article

RESVERATROL: A MULTIFACETED NATURAL COMPOUND WITH THERAPEUTIC POTENTIAL

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ABSTRACT

Resveratrol, a plant-derived polyphenol abundant in grapes, berries, peanuts, and red wine, has been the subject of intense scientific exploration for more than three decades. First associated with the French Paradox, it is now widely studied for its ability to influence multiple biological pathways that underlie chronic disease and aging. Experimental evidence shows that resveratrol reduces oxidative stress, modulates inflammatory cascades, improves mitochondrial function, and regulates cell survival and metabolism. Through these actions, it exerts antioxidant, anti-inflammatory, cardioprotective, anticancer, neuroprotective, antidiabetic, hepatoprotective, antimicrobial, and anti-aging effects. While laboratory and animal studies provide compelling support, outcomes from human trials remain variable, reflecting challenges such as poor bioavailability, rapid metabolism, and differences in study design. Recent innovations including nanoparticle based carriers, synthetic analogs, and synergistic formulations are being developed to enhance its stability and clinical utility. Resveratrol is not a miracle cure, but rather a promising candidate for adjunct therapy, underscoring the potential of natural compounds to complement conventional medicine pending further clinical validation. Its journey underscores the need for rigorous, long-term, and well controlled clinical studies to establish effective doses, safety profiles, and therapeutic applications. By bridging traditional phytotherapy and modern translational science, resveratrol continues to inspire both researchers and clinicians in the search for holistic approaches to health and disease management.

Keywords: Resveratrol, Polyphenol, Antioxidant, Cardioprotection, Neuroprotection, Anticancer, Anti-inflammatory, Anti-aging, Bioavailability

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INTRODUCTION

Resveratrol (3,5,4′-trihydroxy-trans-stilbene) is a naturally occurring phytoalexin from the stilbene family of polyphenols. Plants synthesize it as a protective response to environmental stressors such as ultraviolet (UV) radiation, microbial infection, or physical injury. The compound was first identified in the 1940s from *Veratrum grandiflorum* and later from the roots of *Polygonum cuspidatum*, a plant still widely used as a commercial source [1]. Resveratrol entered the scientific spotlight in the early 1990s when its presence in red wine was linked to the French paradox in which the observation that French populations had relatively low rates of cardiovascular disease despite diets rich in saturated fat [2]. Since then, it has become a central point of research, extending far beyond heart health to potential benefits in cancer prevention, neuroprotection, metabolic regulation, and healthy aging.

From a chemical perspective, resveratrol occurs in two structural forms-trans and cis isomers, with the trans-form being both more stable and biologically active [3]. This compound is remarkably versatile, interacting with a broad range of molecular targets that include signaling cascades and transcription factors [4]. Through these interactions, resveratrol influences key cellular processes such as oxidative stress regulation, inflammatory signaling, mitochondrial biogenesis, cell proliferation, and programmed cell death [5–8]. Because of this pleiotropic activity, resveratrol has attracted interest as a potential therapeutic agent for several chronic conditions, including cardiovascular disease, diabetes, cancer, neurodegenerative disorders, osteoporosis, and hepatic and renal dysfunction.

Despite the wealth of promising preclinical data, translating resveratrol's benefits into clinical practice has proven difficult. One of the major barriers is its pharmacokinetic profile: resveratrol has poor water solubility, undergoes rapid metabolism, and shows very low systemic bioavailability following oral administration [9–11]. These limitations significantly reduce its therapeutic effectiveness in humans. To overcome these hurdles, researchers have been actively exploring advanced delivery strategies, including nanoparticle-based carriers, liposomal formulations, and synthetic analogs designed to improve stability, absorption, and tissue targeting [12–14].

Literature search strategy

To ensure a comprehensive and unbiased overview, a thorough search of the scientific literature was conducted using the PubMed, Scopus, and Web of Science databases. The search spanned the years 2000 to 2025 and combined key terms such as "resveratrol," "NAD^+ metabolism," "SIRT1," "oxidative stress," "inflammation," "clinical trials," "pharmacokinetics," and *"disease* prevention." This review article focused on peer-reviewed research articles, reviews, and clinical studies published in English, giving preference to recent work that offered clear mechanistic or translational insight. Additional relevant sources were identified by manually cross-checking references from key publications. This approach ensured that the review reflects the most current and balanced understanding of resveratrol's biological and clinical potential.

Natural sources of resveratrol

Resveratrol is found in a variety of foods and medicinal plants, though its levels vary widely depending on species, cultivation, and processing. Grapes and red wine are the best-known sources, with higher concentrations in grape skins, seeds, and stems. Berries such as blueberries, cranberries, and mulberries, along with peanuts and peanut products, also contribute to dietary intake, with boiling shown to enhance resveratrol levels in peanuts. Among medicinal plants, *Polygonum cuspidatum* (Japanese knotweed) is the richest natural source and is widely used for supplement production [15–18]. Environmental factors such as UV exposure, pathogen attack, and post-harvest storage further influence resveratrol content, highlighting the variability of its dietary availability [19].

Safety and tolerable dose

The safety profile of resveratrol in humans has been assessed in a limited number of clinical trials, and while findings are encouraging, long-term tolerability data remain scarce. In a 29 d randomized study involving 44 healthy volunteers, participants received escalating doses of 500, 1000, 2500, and 5000 mg/d of RES. Mild gastrointestinal disturbances, including nausea, diarrhea, and abdominal discomfort, were reported primarily at doses exceeding 1000 mg/d [31]. Similarly, another trial administering 1000 mg/d of

RES to healthy adults found the compound to be generally safe, with only mild and transient adverse effects [32].

Evidence from longer-term supplementation is limited but noteworthy. In a one-year study, daily intake of grape-derived RES at a relatively low dose of 8 mg/d was associated with improved cardiovascular risk profiles, without significant adverse events [33]. Overall, available data suggest that resveratrol is well tolerated at low to moderate doses, with gastrointestinal discomfort being the most frequent side effect at higher intakes. However, no official safe upper limit or Tolerable Upper Intake Level (UL) has been established by major regulatory agencies such as the U. S. Food and Drug Administration (FDA) or the European Food Safety Authority (EFSA). However, more comprehensive and long-term clinical trials are necessary to fully establish itssafety profile across diverse populations.

Table 1: Natural sources of resveratrol and approximate content

Source	Plant part/Sample type	Total resveratrol content (µg/g)	Notes	Reference
Red Grape	Skin	0.03-29.5	Found mainly as trans-resveratrol; varies by cultivar and season (highest in Pinot Noir, Feteasca Neagra, lowest in Mamaia)	[20]
Red wine	Fermented beverage	0.3-7.0*	It depends on the cultivar of the grape from which red wine is derived. Lowest from Cabernet Sauvignon and highest from Pinot Noir	[20, 21]
Grape Resin	Dried skin	1-80	Highest in Black Bordeaux (red grape), lowest in Torontel (white grape) cultivar	[22]
Dark chocolate	Processed product	0.3-0.5	The concentration of resveratrol is influenced by the cocoa content.	[23]
Tomato	Whole fruit	1-100	Transgenic tomato developed by inserting grapevine stilbene synthase gene produced high amount of resveratrol than that of wild variety. The tomato lineLoxS produced lowest resveratrol and 35SS produced highest concentration of resveratrol at ripening stage.	[24]
Apples	Skin	0.67	The lowest concentration reported in the Golden Delicious variety (green apple), while the highest concentration is found in the Bravo de Esmolfe variety (red apple). The resveratrol content is influenced by postharvest stress and pigmentation levels.	[25–28]
Mulberry	Whole fruit	50.61		[29]
Java plum (*Syzygiumcumini*) seed	Seed	34.87	Detected via HPLC; mostly trans-resveratrol form.	[29]
Japanese knotweed (*Polygonum cuspidatum*) root extract	Root extract	0.23–3,140	Concentration of total resveratrol depends on plant part, geographical region and season. Stem of *Polygonum cuspidatum* from Kagami region of Japan contains lowest resveratrol, whereas during summer season it contains highest resveratrol (3140 µg/g)	[15]
Itadori tea (*Polygonum cuspidatum*)	Stem	0.46*	Sunlight, rainfall, and insect damage influence resveratrol levels.	[30]

*For liquids like wine and tea, concentrations are reported as µg/ml; conversion to µg/g is approximate for comparison only. Assuming the density of wine and tea is close to water (1 g/ml), I have convert mg/l to µg/g using: 1 mg/l=1 µg/g

Table 2: Biological activities of resveratrol: mechanisms and representative references

Biological activity	Primary mechanisms/targets	Typical readouts/models	References
Antioxidant	Direct ROS/RNS scavenging; metal chelation; activation of Nrf2 leads to upregulation of HO-1, NQO1, SOD, GPx; mitochondrial ROS lowering via SIRT1/AMPK–PGC-1α axis.	Lowers MDA, promotes GSH, SOD, catalase, GPx activity; improved mitochondrial respiration	[6, 36–39]
Anti-inflammatory	Inhibition of NF-κB, STAT3, COX-2, iNOS; lowers IL-6, TNF-α	Lowers CRP and cytokines in cell, animal, and clinical models	[33, 40–42]
Cardioprotective	Promotes eNOS/NO bioavailability; lowers LDL oxidation; lowers platelet aggregation; improved mitochondrial efficiency via SIRT1/AMPK	Improved endothelial function, BP, lipid profile, infarct reduction	[43–46]
Anticancer	Cell cycle arrest, apoptosis (p53/caspases); inhibition of NF-κB, PI3K/Akt, Wnt/β-catenin, MAPK; suppression of EMT/MMP; autophagy/dormancy induction	Lowers tumor growth, invasion, metastasis; promotes apoptosis; lowers proliferation in multiple cancer models	[47–51]
Metabolic/Antidiabetic	AMPK/SIRT1 activation; improved insulin signaling; anti-inflammatory adipokine modulation	Improved glucose tolerance, lowers HOMA-IR, lipid profile changes	[34, 51–54]
Hepatoprotective (NAFLD/NASH)	Antioxidant and anti-inflammatory actions; lipid handling; mitochondrial regulation	Lowers ALT/AST, lowers hepatic fat, improved histology.	[55–58]
Neuroprotective/Anti-aging	SIRT1/AMPK–PGC-1α activation; antioxidant (Nrf2); anti-amyloid/tau aggregation; improved cerebral blood flow	Promotes Memory/cognition; lowers Aβ/tau pathology; promotes CBF in human studies	[59–62]
Bone/Osteoprotective	Promotes osteoblast activity; lowers osteoclastogenesis; anti-inflammatory via NF-κB inhibition	Promotes bone mineral density; improved biomechanics	[63, 64]
Antimicrobial/Antiviral	Interference with quorum sensing, bacterial membranes, viral replication inhibition	Lowers bacterial growth and viral replication (HSV, influenza)	[65, 66]
Dermatologic/Photoprotection	Antioxidant and anti-inflammatory; MMP inhibition	Lowers UV-induced skin damage, lowers MMP-1	[67, 68]
Renal/Organ protection	Anti-oxidative and anti-fibrotic effects; SIRT1-mediated mitochondrial protection	Lowers AKI, CKD progression, lowers fibrosis markers	[69]

Clinical applications and challenges

Though laboratory studies consistently demonstrate the strong therapeutic promise of resveratrol, results from human clinical trials have been far less consistent [34]. One of the main challenges lies in its pharmacokinetics, resveratrol is poorly absorbed, rapidly metabolized, and achieves only low circulating levels after ingestion [9]. To address these limitations, researchers are actively exploring innovative strategies, including nanoparticle based delivery systems, the development of more stable structural analogs, and synergistic formulations with other bioactive compounds. These approaches aim to improve bioavailability and, ultimately, enhance the clinical efficacy of resveratrol [35].

Antioxidant activity

Resveratrol protects against oxidative stress through both direct and indirect mechanisms. It directly scavenges reactive oxygen/nitrogen species and chelates transition metals, thereby reducing lipid peroxidation and even influencing iron-dependent cell death pathways such as ferroptosis [70–72]. More importantly, it enhances endogenous defenses by activating Nrf2 signaling**,** leading to upregulation of antioxidant enzymes including superoxide dismutase (SOD), catalase, glutathione peroxidase, and phase II detoxifying enzymes like HO-1 and NQO1 [37, 73]. In parallel, resveratrol modulates mitochondrial function through the SIRT1/AMPK–PGC-1α pathway**,** improving oxidative phosphorylation and reducing mitochondrial ROS production [74–76]. These mechanisms collectively place resveratrol as a key regulator of redox homeostasis across different experimental models.

Evidence from animal and cell studies is strong, but human trials show more variable outcomes**.** Meta-analyses suggest modest improvements in oxidative stress and inflammatory biomarkers such as TNF-α and high-sensitivity C-reactive protein (hs-CRP), although results vary by dose, formulation, duration and study population [53, 77]. Poor bioavailability and rapid metabolism are major barriers, fueling research into advanced delivery strategies such as nanoparticle formulations, structural analogs, and hybrid molecules with enhanced stability and metal-chelating properties [78, 79].

Notably, resveratrol can act as a pro-oxidant under certain conditions, particularly at high concentrations or in metal-rich environments [72]. The pro-oxidant activity of resveratrol is notably amplified in the presence of transition metals. Copper-resveratrol interactions generate ROS through Fenton-like reactions. The mechanism involves resveratrol reducing Cu^{2+} to Cu^{+}, which leads to the generation of ROS. This is similar to a Fenton-like reaction, although the article doesn't use that exact term [80]. In another study, plasmid DNA (pBR322) used as a model system, the researchers observed that resveratrol, in combination with Cu^{2+}, caused significant DNA strand breaks and mutagenic lesions, as evidenced by electrophoretic mobility shifts. The underlying mechanism was attributed to the reduction of Cu^{2+} to Cu^{+} by resveratrol, leading to the generation of reactive oxygen species (ROS) such as hydroxyl radicals, which attack DNA bases and the sugar-phosphate backbone [81]. This paradoxical activity may contribute to its chemopreventive potential, as moderate ROS generation can trigger selective apoptosis in premalignant or cancerous cells [82]. However, these same mechanisms also highlight the importance of dose control, since excessive or chronic oxidative stress may lead to cellular toxicity. Overall, although resveratrol is not a universal antioxidant remedy, its dual antioxidant and pro-oxidant capacities when properly contextualized make it a promising adjunct for redox modulation and cancer prevention, provided dosing and biological context are carefully managed.

Cardioprotective activity

Resveratrol is increasingly appreciated for its cardioprotective effects, which arise from its ability to counter oxidative stress, dampen inflammation, and support healthy vascular function. A key mechanism involves the stimulation of endothelial nitric oxide synthase (eNOS), leading to greater nitric oxide (NO) availability. This not only promotes vascular relaxation and improved blood flow but also contributes to the regulation of blood pressure and protection against hypertension [43, 83]. Through the activation of the SIRT1/AMPK signaling pathways, resveratrol enhances mitochondrial efficiency, curbs oxidative stress, and supports stable cardiac energy metabolism. By sustaining mitochondrial health, it helps the heart adapt to metabolic stress and maintain optimal function under both physiological and pathological conditions [76, 84]. Resveratrol also counters vascular inflammation by suppressing NF-κB signaling and downregulating the expression of adhesion molecules. This action reduces endothelial activation and leukocyte recruitment, thereby limiting the initiation and progression of atherosclerotic lesions [85]. Experimental evidence also highlights resveratrol's ability to lower LDL oxidation, inhibit platelet aggregation, and preserve endothelial progenitor cell function, mechanisms that work together to maintain vascular integrity and reduce the risk of cardiovascular events.

Clinical evidence, though somewhat heterogeneous, indicates that resveratrol supplementation may lead to modest improvements in blood pressure, lipid metabolism, and vascular reactivity, particularly in individuals at elevated cardiovascular risk [44, 86]. However, the clinical outcomes remain inconsistent, largely because of variations in dosage, formulation, and the inherently low bioavailability of resveratrol, challenges that are common to many natural compounds under investigation. To overcome these barriers, researchers are exploring novel delivery approaches such as nanoparticle formulations, structural analogs, and synergistic combinations with other bioactive to enhance its cardiovascular efficacy. Taken together, the current body of evidence supports resveratrol as a promising adjunctive strategy for cardiovascular health, but its translation into routine practice will require large-scale, long-term clinical trials to confirm safety, efficacy, and optimal therapeutic protocols.

Anticancer activity

Resveratrol shows considerable promise as an anticancer agent because it can act on several hallmarks of cancer simultaneously. It helps protect the cells from key drivers of tumor initiation. At the same time, it can trigger cell cycle arrest and apoptosis through activation of tumor suppressors such as p53 and caspases, while blocking major growth and survival pathways including NF-κB, PI3K/Akt, Wnt/β-catenin, and MAPK [47, 48, 87]. Recent studies demonstrate that resveratrol can also impede tumor invasion and metastasis by blocking epithelial-to-mesenchymal transition (EMT) and downregulating matrix metalloproteinases (MMPs). Furthermore, it promotes autophagy-associated tumor dormancy, maintaining malignant cells in a quiescent, non-proliferative state and thereby slowing disease progression [88-90]. Notably, under certain conditions, particularly in the presence of transition metals such as copper-resveratrol may display controlled pro-oxidant activity, contributing to selective apoptosis in premalignant or cancerous cells, a mechanism proposed to support its chemopreventive potential [82].

Extensive preclinical studies across various cancer models, including breast, prostate, colon, lung, and oral cancers, consistently support these antitumor mechanisms. Early human trials indicate that resveratrol is well tolerated and can modulate biomarkers of tumor growth and proliferation [91, 92]. However, these biomarker changes rarely translate into measurable tumor regression or survival benefits in human subjects, underscoring the gap between preclinical promise and clinical efficacy. Limitations related to poor bioavailability, rapid metabolism, and heterogeneous dosing regimens continue to hinder therapeutic translation. To address these challenges, current research focuses on advanced formulations, including nanoparticle delivery systems, synthetic analogs, and synergistic combinations with existing chemotherapies, aimed at improving systemic exposure and clinical outcomes [93, 94].

Anti-aging activity

Resveratrol has been widely studied for its potential anti-aging properties, largely because it influences molecular pathways that regulate longevity, stress resistance, and metabolic health (table 3). One of its most well-characterized effects is the activation of sirtuin 1 (SIRT1), a key NAD^{+}-dependent deacetylase involved in DNA repair, mitochondrial biogenesis, and metabolic regulation [6, 36].

By enhancing SIRT1 activity and interacting with AMPK and PGC-1α signaling, resveratrol helps improve mitochondrial efficiency, reduce oxidative stress, and support cellular energy balance all of which are central to slowing age-related decline [76, 95].

Beyond cellular metabolism, resveratrol combats chronic low-grade inflammation by downregulating NF-κB activity and reducing the production of pro-inflammatory cytokines [40]. It also activates Nrf2-dependent antioxidant defenses, thereby protecting cells from oxidative damage, one of the primary drivers of aging [96]. Animal studies show that resveratrol can extend lifespan in lower organisms and improve health span markers in mammals, including vascular function, glucose metabolism, and cognitive performance [6, 97]. Human trials are more limited and heterogeneous but suggest modest benefits for metabolic health, vascular function, and inflammatory biomarkers, especially in older or at-risk populations [55, 98, 99]. While not a miracle 'longevity pill,' resveratrol remains one of the most promising natural compounds for supporting healthy aging, with ongoing research into optimized formulations to improve its bioavailability and clinical efficacy.

Table 3: Anti-aging mechanisms and evidence of resveratrol

Mechanism	Preclinical evidence	Human evidence	References
SIRT1 activation and AMPK–PGC-1α signaling	Extends lifespan in yeast, worms, and flies; improves mitochondrial biogenesis and energy metabolism in rodents.	Improved mitochondrial function and insulin sensitivity in obese humans.	[6, 36, 99]
Antioxidant defense via Nrf2 pathway	Upregulates HO-1, SOD, and catalase; reduces ROS and oxidative DNA damage in aging models.	Limited but suggests reduced oxidative biomarkers in at-risk groups.	[37, 100]
Anti-inflammatory effects (lowers NF-κB, cytokines)	Suppresses pro-inflammatory cytokines (IL-6, TNF-α); delays vascular aging in rodents.	Modest reductions in CRP and inflammatory markers in clinical trials.	[40, 76, 101]
Metabolic health	Improves glucose tolerance, lipid profile, and insulin signaling in rodents.	Improved metabolic profile in obese adults, but no effect in NAFLD patients.	[55, 97, 98]
Neuroprotection and cognitive aging	Enhances synaptic plasticity, memory, and protects against neurodegeneration in animal models.	Early studies show improved cerebral blood flow and memory in older adults.	[6, 97, 102]

Neuroprotective potential

Resveratrol has attracted considerable interest for its ability to cross the blood–brain barrier and modulate stress-response pathways relevant to neurodegenerative disorders. Mechanistically, resveratrol activates SIRT1 and AMPK, enhancing mitochondrial biogenesis and redox homeostasis via PGC-1α/NRF1/NRF2 signaling [103]. It exerts potent antioxidant and anti-inflammatory effects, lowering reactive oxygen species, upregulating endogenous enzymes such as superoxide dismutase and catalase, and suppressing NF-κB–mediated cytokine release and microglial activation, thereby preserving neuronal function and blood–brain barrier integrity [104, 105].

Resveratrol also promotes autophagy and proteostasis, facilitating the clearance of amyloid-β, tau, and α-synuclein aggregates and damaged mitochondria, while modulating PI3K/Akt/mTOR and Wnt signaling to limit apoptosis [106, 107]. Preclinical models of Alzheimer's disease and Parkinson's disease consistently demonstrate reduced protein aggregation, preserved dopaminergic neurons, and improvements in cognitive and motor outcomes [107, 108].

Clinical translation, however, remains challenging. In a Phase II randomized, double-blind, placebo-controlled trial involving patients with mild-to-moderate Alzheimer's disease, resveratrol (1 g twice daily for 52 w) was well tolerated and demonstrated biomarker engagement, including reduced CSF MMP9 levels and attenuated brain volume loss. However, the study failed to meet its primary cognitive endpoints, indicating that while resveratrol modulated molecular and imaging biomarkers, these effects did not translate into measurable clinical improvement [102]. In ischemic stroke models, resveratrol attenuates excitotoxicity, apoptosis, and blood–brain barrier disruption, resulting in smaller infarct size and better functional outcomes, largely via SIRT1/NRF2 activation [104, 105]. However, its low bioavailability and rapid metabolism remain major translational barriers, prompting exploration of nano formulations, liposomes, and prodrugs to enhance clinical efficacy [103]. Overall, while resveratrol exhibits promising neuroprotective mechanisms, clinical benefits have not yet been demonstrated, underscoring the need for large, well-controlled trials to bridge the gap between biomarker modulation and meaningful neurological improvement.

Antimicrobial and antiviral activity

In bacterial systems, resveratrol and its derivatives interfere with multiple cellular functions including disruption of cell wall integrity, inhibition of DNA and RNA synthesis, and suppression of quorum sensing, which collectively reduces bacterial growth and biofilm formation. These effects have been documented against diverse pathogens such as *Staphylococcus aureus*, *Escherichia coli*, and *Helicobacter pylori*, highlighting its relevance against both Gram-positive and Gram-negative organisms [66, 109]. In fungal pathogens such as *Candida albicans* and *Aspergillus fumigatus*, resveratrol and its derivatives has been shown to inhibit hyphal development, impair mitochondrial function, and trigger apoptotic cell death, thereby weakening fungal virulence and persistence [65, 110].

Resveratrol also demonstrates remarkable antiviral activity by targeting different stages of the viral life cycle and reinforcing host immune defenses. It has been reported to inhibit replication and gene expression of herpes simplex virus, suppress the replication of influenza virus, and reduce infectivity of hepatitis C virus [111–114]. More recently, in the context of coronaviruses, resveratrol was found to block SARS-CoV-2 replication by interfering with viral RNA polymerase activity and simultaneously reducing the virus-induced pro-inflammatory cytokine response, an effect that is particularly relevant to controlling hyper inflammation in severe cases [115]. Importantly, resveratrol has been shown to act synergistically with conventional antibiotics and antiviral agents, thereby enhancing therapeutic efficacy and reducing the likelihood of resistance development [65, 109].

Antidiabetic activity

Resveratrol has emerged as a promising natural compound for the management of diabetes mellitus due to its ability to modulate glucose homeostasis, insulin sensitivity, and β-cell function. One of the central mechanisms involves activation of AMP-activated protein kinase (AMPK) and SIRT1 pathways, which enhance mitochondrial biogenesis, promote fatty acid oxidation, and improve insulin signaling [6, 116]. Resveratrol also exerts potent antioxidant and anti-inflammatory effects, reducing oxidative stress and pro-inflammatory cytokine release in pancreatic islets, thereby preserving β-cell integrity [52, 54]. In animal models of type 2 diabetes (T2DM), resveratrol improves glucose tolerance, reduces insulin resistance, and protects against diabetic complications such as nephropathy and neuropathy [54].

Dose-dependent effects of resveratrol have been reported in both clinical and preclinical studies. In human trials, resveratrol doses ≥100 mg/d produced significantly greater reductions in fasting plasma glucose compared to lower doses (<100 mg/d). Doses of

300, 1000, and 1500 mg/d demonstrated the most favorable metabolic responses, including improved insulin sensitivity and reductions in HbA1c, whereas 8 mg and 50 mg/d produced minimal or no metabolic benefit [38, 52]. Interestingly, a recent meta-analysis of animal models of diabetic nephropathy revealed a U-shaped dose-response relationship, with optimal renoprotective effects observed at either lower doses (≤15 mg/kg/d) or higher doses (100–200 mg/kg/d) [117]. This suggests that both moderate and high dose regimens may confer therapeutic benefits, depending on the target tissue and specific metabolic endpoint. Collectively, resveratrol acts on multiple metabolic pathways, making it a valuable candidate for adjunct therapy in diabetes management.

Myths and facts about resveratrol

Several misconceptions surround resveratrol, often fueled by popular media. One common belief is that drinking red wine provides sufficient resveratrol for health benefits; however, wine contains only trace amounts (table 1), and achieving therapeutic levels would require impractically high consumption [20]. Another widespread myth is that resveratrol acts as a "miracle anti-aging pill" [118]. While preclinical and animal studies suggest potential longevity and health-promoting effects, evidence in humans remains inconclusive [6, 119–121]. Similarly, it is often assumed that all resveratrol supplements are equally effective, yet differences in formulation, purity, and bioavailability lead to significant variations in their efficacy [34]. Furthermore, resveratrol is sometimes promoted as a cancer cure; although it demonstrates anticancer activity in preclinical studies, it cannot be considered a stand-alone therapy [47, 122]. In summary, resveratrol holds promise as a bioactive compound with antioxidant, anti-inflammatory, and disease-modifying properties, but its benefits are frequently overstated. More rigorous and well-controlled human studies are necessary to clarify its therapeutic potential and establish its role as a supportive rather than curative agent.

Table 4: Common myths and facts about resveratrol. Summary of prevalent misconceptions and evidence-based findings illustrating that resveratrol's biological effects are context-dependent and often overstated in popular media

Myth	Fact	Reference
Drinking red wine provides enough resveratrol for health benefits	Red wine contains only trace amounts of resveratrol. Achieving the concentration used in experimental or clinical studies would require consuming unrealistically large and unsafe volumes of wine. Therefore, wine alone cannot provide meaningful physiological levels of resveratrol.	[20, 31]
Resveratrol is a miracle anti-aging pill	Although resveratrol has been shown to extend lifespan in simple organisms such as yeast, worms, silkworms and flies, its effects in mammals are inconsistent and relatively modest. There is no conclusive evidence that resveratrol prolongs lifespan in humans. Nonetheless, it may enhance cellular defense mechanisms and stress resistance, contributing to overall metabolic health.	[6, 33, 119–121, 123]
All resveratrol supplements are equally effective	The efficacy of resveratrol supplements varies significantly depending on formulation, purity, and bioavailability. Differences in absorption and metabolic stability determine how much active compound reaches target tissues, meaning not all products deliver the same biological effects.	[34]
Resveratrol supplements are always safe	In human clinical studies, resveratrol has been shown to be generally well-tolerated at doses up to approximately 0.5–1 g per day. However, higher doses, typically in the range of 2–5 g per day may lead to mild gastrointestinal discomfort in some individuals. Preclinical investigations have also revealed that resveratrol can interact with liver enzymes, particularly the cytochrome P450 system, which plays a key role in drug metabolism. This interaction suggests the need for caution when resveratrol is taken alongside medications that are metabolized through these pathways.	[31, 99, 124–126]
Resveratrol can cure cancer	While resveratrol exhibits anticancer properties in cell-based and animal studies, such as inhibiting tumor growth and inducing apoptosis, it is not a proven or standalone cancer therapy in humans. Clinical evidence remains insufficient to support its use as an anticancer drug.	[47, 87, 122, 127]

CONCLUSION

Resveratrol stands out as a versatile natural compound with broad biological activities, including antioxidant, anti-inflammatory, cardioprotective, anticancer, neuroprotective, antimicrobial, and antidiabetic effects. Its pleiotropic mechanisms make it particularly relevant in addressing complex diseases driven by oxidative stress, inflammation, and metabolic dysfunction. While preclinical evidence is robust, human clinical outcomes remain inconsistent, largely due to its poor bioavailability and rapid metabolism. Recent advances in nanoparticle delivery, structural analogs, and synergistic formulations are promising steps toward overcoming these limitations. However, resveratrol should not be viewed as a miracle cure but rather as a valuable adjunct with potential to complement conventional therapies. Future progress will depend on well-designed, long-term clinical trials that clarify effective doses, safety, and therapeutic windows. Overall, resveratrol exemplifies the promise of natural molecules in modern medicine, serving as a bridge between traditional knowledge and translational science.

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All authors have contributed equally

CONFLICT OF INTERESTS

The author confirms that there are no conflicts of interest related to this work.

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