International Journal of Zoology and Applied Biosciences ISSN: 2455-9571
Volume 10, Issue 4, pp: 122-127, 2025
https://doi.org/10.55126/ijzab.2025.v10.i04.010 http://www.ijzab.com

Case Study Report

COMPREHENSIVE ANALYSIS OF RESVERATROL'S HEALTH BENEFITS, MECHANISMS OF ACTION, AND POTENTIAL THERAPEUTIC APPLICATIONS IN CHRONIC DISEASES

[1*]Vijay Kant Pandey, [2]Mousumi Ghatak, [3]Debolina Sinha and [4]Santosh Kumar Singh

[1*]Department of Life Science, Netaji Subhas University, Jamshedpur
[2]Department of Zoology, Netaji Subhas University, Jamshedpur
[3]Department of Agriculture, Netaji Subhas University, Jamshedpur
[4]Department of Biotechnology, Arka Jain University, Jamshedpur

Article History: Received 19th May 2025; Accepted 27th June 2025; Published 31st July 2025

ABSTRACT

Resveratrol, a plant-derived polyphenol found in grapes, berries, and peanuts, among others, has gained much attention in recent years due to its potential multiple health benefits and its therapeutic application. In this review, the current body of knowledge regarding the health benefits and mechanisms of action of resveratrol in the management and treatment of chronic diseases will be discussed. The review will also take into account its antioxidant, anti-inflammatory, and anti-ageing activities and its influence on cardiovascular health, metabolic disease, neurodegeneration, and cancer. Finally, this review will address possible restraints of clinical applications of resveratrol.

Keywords: Resveratrol, Antioxidant, Anti-inflammatory, Anti-aging properties.

INTRODUCTION

Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is a naturally occurring polyphenolic compound found in many plants, including the skins of red grapes, peanuts, and berries (Baur *et al.,* 2006). Resveratrol has been the subject of extensive research as a function of its associations with several health benefits and inhibitory potential. Resveratrol was isolated for the first time in 1940 from the roots of white hellebore (*Veratrum grandiflorum*), and in the 1990s, following recognition of the "French Paradox", high interest grew in resveratrol because of the apparent ability of Red Wine, which contains resveratrol, to provide decreased incidence of coronary heart disease even in populations with a diet high in saturated fats (Renaud *et al.,* 1992). Resveratrol is an example of stilbene, the class of compounds known for their anti-oxidant capabilities. This natural stilbene has attracted much scientific interest due to its surprising pleiotropic biological effects and potential therapeutic benefits in various chronic diseases (Yu *et al.,* 2024). The heightened interest in resveratrol stems from information which has grown to suggest that there are potential health-promoting effects which are simply beyond just a cardiovascular process. The passage of time has resulted in research directing its focus onto the health-promoting effect of resveratrol as it relates to chronic diseases such as cancer, diabetes and neurodegenerative disorders, which has piqued an interest in its mechanisms, activity, and dosaging formula for clinical health efficacy. Many researchers have investigated resveratrol in varying degrees, with an impressive range of health functions potentially attributed to it. The broad spectrum of effects is particularly wide which include antioxidant, cardioprotective, neuroprotective, anti-cancer and anti-inflammatory functions (Catalgol *et al.,* 2012). Resveratrol has been demonstrated to mimic various aspects of caloric restriction, have anti-inflammatory and anti-oxidative effects, and have many influences on the initiation and development of many diseases through various mechanisms (Godos *et al.,* 2024). This review seeks to encapsulate the health-promoting function of resveratrol, the mechanisms attributed to its health-promoting actions, its potential therapeutic effect administered for the treatment of chronic disease disorders.

*Corresponding Author: Dr. Vijay Kant Pandey, Associate Professor, Department of Life Science,
Netaji Subhas University, Jamshedpur, Email: pandeyvijay00@gmail.com

CHEMICAL STRUCTURE AND BIOSYNTHESIS

Chemical Structure

Resveratrol is a stilbenoid (a natural phenol). Structurally, resveratrol consists of two phenol rings connected by a double styrene bond. Resveratrol naturally occurs in two isomers, Trans-resveratrol, and Cis-resveratrol. The trans-isomer is more stable and bioactive than the cis-isomer (Gambini *et al.,* 2015).

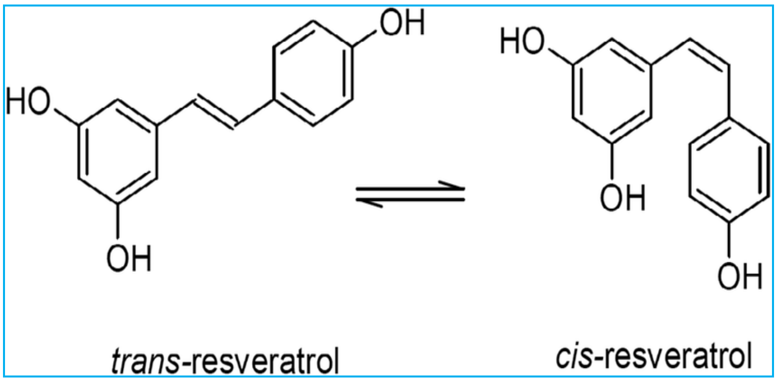

Figure 1. Structural formula of trans-resveratrol and cis-resveratrol.

Biosynthesis

The biosynthesis of resveratrol in plants occurs via the phenylpropanoid pathway with phenylalanine serving as the starting substrate. The first committed step is catalyzed by phenylalanine ammonia-lyase (PAL), which acts to deaminate phenylalanine to generate trans-cinnamic acid that is subsequently converted to 4-coumaric acid by the enzyme cinnamate 4-hydroxylase (C4H). The 4-coumaric acid is modified to 4-coumaroyl-CoA by the enzyme 4-coumarate: CoA ligase (4CL), which provides an immediate substrate for the formation of stilbenes (Chong *et al*., 2009). The final and most significant reaction involves stilbene synthase (STS) which converts one molecule of 4-coumaroyl-CoA with three molecules of malonyl-CoA into resveratrol. This reaction is remarkably similar to the reaction catalyzed by chalcone synthase in the flavonoid biosynthetic pathway (Watts *et al*., 2006).

Regulation of the biosynthesis of resveratrol is very intricate and comprises several levels of control, including transcriptional, post-transcriptional, and post-translational regulation. Environmental stresses like UV light, pathogen infection, and abiotic stresses dramatically affect the expression of genes encoding biosynthetic enzymes, especially STS (Langcake & Pryce, 1976). Transcription factors from the MYB, bHLH, and WD40 families combine to create regulatory complexes that regulate phenylpropanoid pathway gene expression, while particular stilbene-associated transcription factors regulate resveratrol synthesis in reaction to environmental stimuli (Hichri *et al*., 2011). New developments in molecular biology and metabolic engineering have shed further light on the tissue-specific and developmental regulation of resveratrol biosynthesis. In grapevines, resveratrol is most abundant in berry skin and seed, and concentrations differ greatly among cultivars and as an effect of environmental factors (Flamini *et al*., 2013). The temporal and spatial STS gene expression profiles indicate a complex regulatory system allowing for maximum resveratrol production at times and places where it is most needed to protect the plant.

Bioavailability and Metabolism

Although resveratrol has many health benefits, its bioavailability is very low. After oral consumption, resveratrol is swiftly absorbed in the intestine, though it is heavily metabolized in the liver, with low plasma concentrations of the free form (Walle and Thomas, 2011). Major metabolites of resveratrol are glucuronides and sulfates, which are more water-soluble but biologically inactive compared to the parent compound (Wenzel *et al.,* 2005). Methods for improving resveratrol's bioavailability, such as nanoformulations and synergizing with other compounds, are a focus of investigation (Smoliga *et al.,* 2011).

HEALTH BENEFITS AND MECHANISMS OF ACTION

Antioxidant Properties

As a strong antioxidant, resveratrol is able to scavenge free radicals and reduce oxidative stress (de la Lastra *et al.,* 2005). Its capacity to reduce oxidative stress occurs through more than one mechanism: Direct scavenging of reactive oxygen species (ROS), Upregulating antioxidant enzymes, including superoxide dismutase and glutathione peroxidase, inhibiting lipid peroxidation, Chelating metal ions that generate free radicals (Xia *et al.,* 2017). The antioxidant property of resveratrol adds to its protective effect against many diseases associated with oxidative stress.

Anti-inflammatory Effects

Chronic inflammation contributes to the pathology of many diseases. Resveratrol has strong anti-inflammatory effects through several pathways including: Inhibition of pro-inflammatory mediators (COX-2 and inducible nitric oxide synthase (iNOS)), Inhibition of nuclear factor-κB (NF-κB) activation, Modulation of inflammatory cytokines, Inhibition of adhesion and migration of leukocytes (Švajger, *et al .,* 2012). These promising effects suggest that resveratrol may be an effective agent for management of inflammatory diseases such as arthritis and inflammatory bowel disease.

Cardiovascular Protection

Resveratrol possesses well-documented cardioprotective effects, including: an improvement of endothelial function through enhanced nitric oxide production; a reduction in platelet aggregation; modulation of lipid metabolism and a decrease in atherosclerosis; protection from ischemia-reperfusion injury; and anti-hypertensive effects. Collectively, these effects are due to its influence on many pathways, including the activation of sirtuin 1 (SIRT1), AMP-activated protein kinase (AMPK), and endothelial nitric oxide synthase (eNOS).

Metabolic Effects

Resveratrol has shown promise regarding metabolic health and weight, especially in diabetes and obesity: Improvement of insulin sensitivity and glucose uptake, Activation of AMPK and increased fatty acid oxidation, Mitochondrial biogenesis and improved energy metabolism, Reduction of adipogenesis and stimulation of lipolysis (Andrade *et al.,* 2014); these effects may have implications for metabolic syndrome, type 2 diabetes and obesity.

Neuroprotective Effects

Neuroprotection properties of resveratrol have been shown in multiple neurodegenerative disease models: reducing β-amyloid aggregation in Alzheimer's disease models, protecting against oxidative stress and mitochondrial dysfunction in Parkinson's disease, anti-inflammatory effects in multiple sclerosis, and improving cognitive function and neuroplasticity (Sawda *et al.,* 2017). The neuroprotective properties of resveratrol are believed to be due to its antioxidant and anti-inflammatory properties, as well as its ability to increase SIRT1 and mitochondrial function (Bastianetto *et al.,* 2000).

Anti-cancer Properties

Resveratrol has demonstrated anti-cancer effects in various cancers, including breast, prostate, colon and lung cancer. Mechanisms for anti-cancer effects include:Inhibition of cell proliferation and apoptosis, Modulation of cell cycle regulators, Anti-angiogenic effects, Inhibition of metastasis and Epigenetic changes by affecting DNA methyltransferases and histone deacetylases (Rauf *et al.,* 2018). Although most data are from in vitro and animal studies, clinical research is current ongoing exploring resveratrol's potential as an adjunct therapy in cancer treatment.

Potential Therapeutic Applications in Chronic Diseases

Resveratrol, a polyphenol compound in many plants, has received notable interest in the study of chronic disease management. The wide range of biological activities exhibited by resveratrol suggested that it could have a pharmacological benefit in preventing and treating several chronic conditions including cardiovascular diseases, cancer, neurodegeneration, and diabetes (Figure 2).

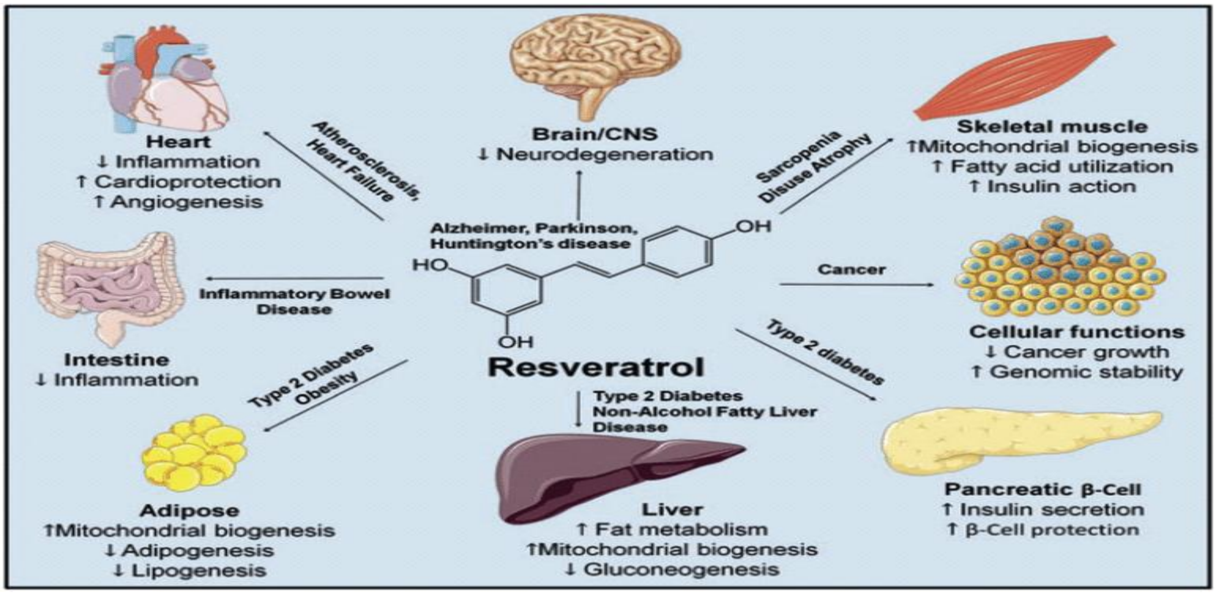

Figure 2. Resveratrol therapeutic effects on different tissues and systems of the human body (Arora and Jaglan, 2017).

Cancer

Resveratrol (RES) is a natural polyphenolic compound that holds great promise for targeting breast cancer through various cellular mechanisms. RES promotes both autophagy and apoptosis, which are the primary pathways for eliminating cancer cells. In regard to autophagy, RES induces autophagy through the AMPK/mTOR signaling pathway, while in regard to apoptosis (Behroozaghdam *et al.,* 2022) (Figure 3), RES promotes apoptosis through the upregulation of pro-apoptotic proteins, such as Bax, while downregulating Bcl-2, an anti-apoptotic protein. RES also inhibits the epithelial-mesenchymal transition (EMT), an important process for cancer metastasis, by inhibiting transcription factors responsible for driving EMT, such as Snail, Slug, and Twist to reduce the migration and invasion of cancer cells. In addition to these pathways, RES also disrupts the redox homeostasis of cancer cells, causing oxidative stress, which leads to cancer cell death and adds to the effects of RES to suppress breast tumor growth and spread. While various in vitro or in vivo studies have suggested RES has a therapeutic role in breast cancer, the clinical translational potential of RES is limited by its low bioavailability and rapid metabolism.

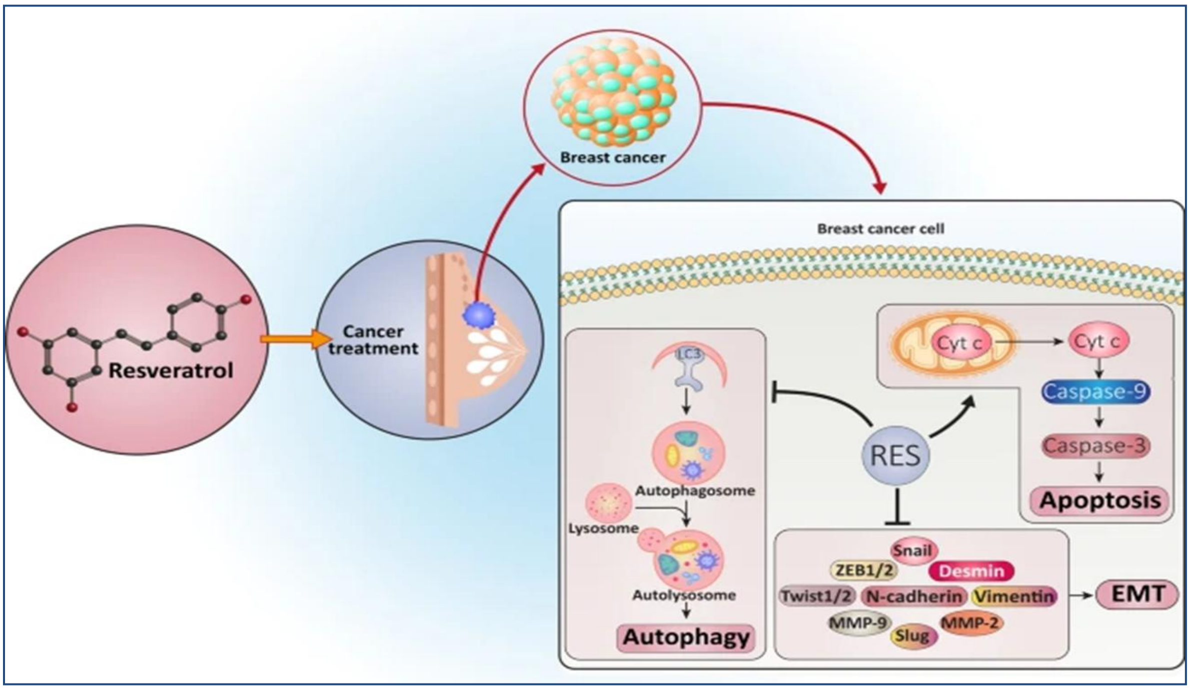

Figure 3. RES promotes both autophagy and apoptosis, help for eliminating cancer cells (Behroozaghdam *et al.,* 2022).

Although resveratrol's anti-cancer effects have been well documented in the preclinical setting, its clinical use as an anti-cancer agent is not completely clear. The current research, however, is focused on the potential of it being a chemoprevention agent and alongside existing oncological therapies (Singh *et al*., 2015).

Cardiovascular Diseases

Resveratrol has potential in the prevention and treatment of cardiovascular disease because of its cardioprotective properties. In clinical studies, patients with both coronary artery disease and hypertension have demonstrated improved endothelial function, decreased inflammatory markers, and improvements in lipid profiles (Tomé-Carneiro *et al.,* 2013).

Type 2 Diabetes and Metabolic Syndrome

The impact of resveratrol on insulin sensitivity and glucose metabolism indicates that it may be a potential treatment for type 2 diabetes and metabolic syndrome. Clinical trials have reported improvements in glycemic control, increased insulin sensitivity and reductions in oxidative stress markers in diabetes patients (Szkudelski *et al*., 2011).

Neurodegenerative Diseases

With the neuroprotective implications of resveratrol, it is conceivable that there may be a potential use of resveratrol in neurodegenerative illnesses like Alzheimer's disease and Parkinson's disease. Despite limited clinical studies investigating the result of resveratrol infusion on cognitive impairment, and ongoing clinical trials to measure resveratrol's effect on these diseases (Turner *et al.,* 2015).

Inflammatory Disorders

Resveratrol has anti-inflammatory effects that may provide uses in chronic inflammatory diseases like rheumatoid arthritis and inflammatory bowel disease. Early clinical studies have yielded favorable results, but large clinical trials are necessary to establish efficacy (Oliveira *et al* ., 2017).

CONCLUSION

Resveratrol is a versatile natural product that has many possible health benefits for humans. Resveratrol has antioxidant, anti-inflammatory, and metabolic effects which make it a potential therapeutic agent for many chronic diseases. However, important challenges need to be addressed, including low bioavailability and limited clinical evidence. Future research should address these limitations and explore the full potential of resveratrol as a therapeutic agent. New and radical therapeutic approaches for chronic diseases may be developed as we learn more about the mechanisms of action of resveratrol.

ACKNOWLEDGMENT

The authors express sincere thanks to the head of the Department of Life Science, Netaji Subhas University, Jamshedpur for the facilities provided to carry out this research work.

CONFLICT OF INTERESTS

The authors declare no conflict of interest

ETHICS APPROVAL

Not applicable

FUNDING

This study received no specific funding from public, commercial, or not-for-profit funding agencies.

AI TOOL DECLARATION

The authors declares that no AI and related tools are used to write the scientific content of this manuscript.

DATA AVAILABILITY

Data will be available on request

REFERENCES

Andrade, J. M. O., Paraíso, A. C., de Oliveira, M. V. M., Martins, A. E. M., Neto, J. F., Guimarães, A. L. S., de Paula, M. M., Quesada, M., & de Paula, A. M. B. (2014). Resveratrol increases brown adipose tissue thermogenesis markers by increasing SIRT1 and energy expenditure and decreasing fat accumulation in adipose tissue of mice fed a standard diet. *European Journal of Nutrition, 53*(7), 1503–1510.

Bastianetto, S., Zheng, W.H., & Quirion, R. (2000). Neuroprotective abilities of resveratrol and other red wine constituents against nitric oxide-related toxicity in cultured hippocampal neurons. *British Journal of Pharmacology, 131*(4), 711–720.

Baur, J. A., & Sinclair, D. A. (2006). Therapeutic potential of resveratrol: the in vivo evidence. *Nature Reviews Drug Discovery, 5*(6), 493–506.

Behroozaghdam, M., Dehghani, M., Zabolian, A. *et al.* (2022). Resveratrol in breast cancer treatment: from cellular effects to molecular mechanisms of action. *Cell. Molecular Life Science,* (79) , 539.

Berman, A. Y., Motechin, R. A., Wiesenfeld, M. Y., & Holz, M. K. (2017). The therapeutic potential of resveratrol: a review of clinical trials. *NPJ Precision Oncology, 1*(1), 35.

Catalgol, B., Batirel, S., Taga, Y., & Kartal Ozer, N. (2012). Resveratrol: French paradox revisited. *Frontiers in Pharmacology, 3*, 141.

Chong, J., Poutaraud, A., & Hugueney, P. (2009). Metabolism and roles of stilbenes in plants. *Plant Science, 177*(3), 143–155.

de la Lastra, C. A., & Villegas, I. (2005). Resveratrol as an anti-inflammatory and anti-aging agent: Mechanisms and clinical implications. *Molecular Nutrition & Food Research, 49*(5), 405–430.

Flamini, R., Mattivi, F., De Rosso, M., Arapitsas, P., & Bavaresco, L. (2013). Advanced knowledge of three important classes of grape phenolics: anthocyanins, stilbenes and flavonols. *International Journal of Molecular Sciences, 14*(10), 19651–19669.

Gambini, J., Inglés, M., Olaso, G., Lopez-Grueso, R., Bonet-Costa, V., Gimeno-Mallench, L., Mas-Bargues, C., Abdelaziz, K. M., Gomez-Cabrera, M. C., Vina, J., & Borras, C. (2015). Properties of resveratrol: in vitro and in vivo studies about metabolism, bioavailability, and biological effects in animal models and humans. *Oxidative Medicine and Cellular Longevity, 2015*, Article ID 837042.

Godos J, Romano GL, Gozzo L, Laudani S, Paladino N, Dominguez Azpíroz I, Martínez López NM, Giampieri F, Quiles JL, Battino M, Galvano F, Drago F and Grosso G (2024) Resveratrol and vascular health: evidence from clinical studies and mechanisms of actions related to its metabolites produced by gut microbiota. *Front. Pharmacol.* 15:1368949.

Hichri, I., Barrieu, F., Bogs, J., Kappel, C., Delrot, S., & Lauvergeat, V. (2011). Recent advances in the transcriptional regulation of the flavonoid biosynthetic pathway. *Journal of Experimental Botany, 62*(8), 2465–2483.

Langcake, P., & Pryce, R. J. (1976). The production of resveratrol by *Vitis vinifera* and other members of the *Vitaceae* as a response to infection or injury. *Physiological Plant Pathology, 9*(1), 77–86.

Li, H., Xia, N., & Förstermann, U. (2012). Cardiovascular effects and molecular targets of resveratrol. *Nitric Oxide, 26*(2), 102–110.

Oliveira, A. L. B., Monteiro, G. F., Saraiva, K., Oliveira, J. T., Andrade, L. E. C., Silva, N. P., & Trevisani, V. F. M. (2017). Resveratrol role in autoimmune disease—a mini-review. *Nutrients, 9*(12), 1306.

Rauf, A., Imran, M., Iahtisham-Ul-Haq, Ullah, N. A., Akram, M., Mubarak, M. S., & Patel, S. (2018). Resveratrol as an anti-cancer agent: A review. *Critical Reviews in Food Science and Nutrition, 58*(9), 1428–1447.

Renaud, S., & de Lorgeril, M. (1992). Wine, alcohol, platelets, and the French paradox for coronary heart disease. *The Lancet, 339*(8808), 1523–1526.

Sawda, C., Moussa, C., & Turner, R. S. (2017). Resveratrol for Alzheimer's disease. *Annals of the New York Academy of Sciences, 1403*(1), 142–149.

Singh, C. K., Ndiaye, M. A., & Ahmad, N. (2015). Resveratrol and cancer: Challenges for clinical translation. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, 1852*(6), 1178–1185.

Smoliga, J. M., Baur, J. A., & Hausenblas, H. A. (2011). Resveratrol and health–a comprehensive review of human clinical trials. *Molecular Nutrition & Food Research, 55*(8), 1129–1141.

Švajger, U., & Jeras, M. (2012). Anti-inflammatory effects of resveratrol and its potential use in therapy of immune-mediated diseases. *International Reviews of Immunology, 31*(3), 202–222.

Szkudelski, T., & Szkudelska, K. (2011). Anti-diabetic effects of resveratrol. *Annals of the New York Academy of Sciences, 1215*, 34–39.

Tomé-Carneiro, J., Larrosa, M., González-Sarrías, A., Tomás-Barberán, F. A., García-Conesa, M. T., & Espín, J. C. (2013). Resveratrol and clinical trials: the crossroad from in vitro studies to human evidence. *Current Pharmaceutical Design, 19*(34), 6064–6093.

Turner, R. S., Thomas, R. G., Craft, S., van Dyck, C. H., Mintzer, J., Reynolds, B. A., Brewer, J. B., Rissman, R. A., Raman, R., & Aisen, P. S. (2015). A randomized, double-blind, placebo-controlled trial of resveratrol for Alzheimer disease. *Neurology, 85*(16), 1383–1391.

Walle, T. (2011). Bioavailability of resveratrol. *Annals of the New York Academy of Sciences, 1215*, 9–15.

Watts, K. T., Lee, P. C., & Schmidt-Dannert, C. (2006). Biosynthesis of plant-specific stilbene polyketides in metabolically engineered *Escherichia coli*. *BMC Biotechnology, 6*(1), 22.

Wenzel, E., & Somoza, V. (2005). Metabolism and bioavailability of trans-resveratrol. *Molecular Nutrition & Food Research, 49*(5), 472–481.

Xia, N., Daiber, A., Daiber, A., Förstermann, U., & Li, H. (2017). Antioxidant effects of resveratrol in the cardiovascular system. *British Journal of Pharmacology, 174*(12), 1633–1646.

Yu X, Jia Y and Ren F (2024) Multidimensional biological activities of resveratrol and its prospects and challenges in the health field. *Front. Nutrition. 11*, 1408651.

Arora, D., Jaglan, S. (2017). Nanocarriers for Resveratrol Delivery. In: Ranjan, S., Dasgupta, N., Lichtfouse, E. (eds) *Nanoscience in Food and Agriculture 5. Sustainable Agriculture Reviews, vol 26*. Springer, Cham.