The Journal of Phytopharmacology 2025; 14(6):543-549
Online at: www.phytopharmajournal.com

The Journal of Phytopharmacology
(Pharmacognosy and phytomedicine Research)

Exploring the therapeutic potential of Resveratrol: A natural compound with multifaceted health benefits

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Review Article

ISSN 2320-480X
JPHYTO 2025; 14(6): 543-549
November- December
Received: 25-11-2025
Accepted: 12-01-2026
Published: 30-01-2026

doi: 10.31254/phyto.2025.14616

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ABSTRACT

Resveratrol is a polyphenol characterized as stilbenoids, also recognized as 3,5,4'-trihydroxy-trans-stilbene, with a chemical formula of $C_{14}H_{12}O_3$ and a molecular weight of 228.25 g/mol. Two phenol rings linked together by an ethylene bridge define the structure. Plants such as grapes, plums, apples, peanuts and blue berries produce RSV. Renowned for its vast biological effects its significance on well-being of humans is noteworthy. This review was designed to organize a broad review on the various biological effects, prospective therapeutic applications of RSV by integrating various scientific investigations. Various databases comprising Google Scholar, PubMed, Science Direct etc. with specific keywords combined with RSV were expended to assemble data and the gathered information were summarized. RSV validated strong antioxidant qualities and influences various molecular pathways such as NF-kB, MAPK, AMPK and SIRT-1. Based on the current knowledge, it is reasonable to express that RSV displays significant potential for treating cancer, cardiovascular, obesity, neurodegenerative, inflammatory and age-related diseases. It is imperative to focus on in-depth research to utilize the properties of RSV and promote the development of phytopharmaceuticals for effective therapies.

Keywords: Stilbene, Grapes, Dipterocarpaceae, Anticancer, Anti-ageing.

INTRODUCTION

Resveratrol, a polyphenolic stilbene and non-flavonoid phytoalexin is generated by plants when exposed to adverse environmental conditions [1]. Michio Takaoka, a Japanese researcher recognized RSV firstly from *Veratrum grandiflorum* in 1939 followed by Nomomura in 1963 from *Polygonum cuspidatum* [2]. RSV, the phytoalexin is widely distributed in *Vitis vinifera* skin, stem and root and its glycosylated forms are found in red currants, berries and peanuts. RSV has been related with the “French Paradox” which stated that moderate consumption of wine protects against coronary heart disease by means of reducing platelet aggregation. The existence of RSV in Spermatophyta including 31 genera, 12 families and 72 species were described [3]. Several researchers have discovered the presence of RSV in various plant families such as Vitaceae, Dipterocarpaceae, Myrtaceae, Cyperaceae, Fabaceae, Gnetaceae etc. (Table 1). RSV was also discovered in hops signifying it would also be present in beer formulations [4]. Almost 92 new RSV compounds have been identified from various plant families including 6 monomers, 39 dimers, 23 trimers, 13 tetramers, 4 pentamers, 6 hexamers, and one octamer. Amongst various families, Dipterocarpaceae is the most common producer of RSV (Table 1). The compound has been marketed as a dietary supplement owing to its pharmacological benefits like protecting cells from oxidative stress [5]. RSV (E-5-(4-hydroxystyryl) benzene-1,3-diol) is characterized by two phenol rings linked by an ethylene bridge and it exists in two isomeric forms; the cis- and trans- (Figure 1). It is the trans-RSV related with numerous bioactivities such as stimulating cellular responses as cell cycle arrest, apoptosis and anti-proliferation of cancerous cells [6,7]. Three glycosylated RSV variants: piecid, piceatannol glucoside, and resveratroloside that are powerful antibacterials have been discovered in *Polygonum cuspidatum* [8]. From *Pterocarpus santalinus*, pterostilbene an analogue of RSV was discovered which is structurally similar to RSV but differs by a methoxyl group replacing positions 3 and 5 in the A ring [9].

Red grapes and red wine are widely recognized as opulent sources of RSV [10]. However, RSV has been detected in diverse array of plants, including Japanese knotweed, *Polygonum cuspidatum* [11], peanuts [12], and various species of *Vaccinium* (such as blueberry, bilberry, and cranberry) [13], *Reynoutria japonica* and Scots pine (Figure 2; Table 1). Additional plant sources of RSV include grapevines, mulberry, lilies, legumes, rhubarb, eucalyptus, spruce, pine, grasses, clover, beech trees, peonies, *Artocarpus*, *Gnetum*, *Pleuropterus ciliinervis*, *Bauhinia racemosa*, *Scilla nervosa*, and *Tetrastigma hypoglaucum*. Isorhapontigenin, extracted from *Belamcanda chinensis*, has a similar structure to RSV and shows strong antioxidant capabilities (Table 1). Compounds structurally related to RSV, found in numerous plant species, may harbor similar biological effects. Red grapes are the chief sources of RSV extracts, with fresh grape skins containing approximately 5-10 × 10^{-2} g kg^{-1} of RSV. Normally, red wine has RSV levels between 1.5 to 3 mg L^{-1}, however, some research indicated it could be as high as 4-20 mg L^{-1}. Elevated levels have been noticed in particular white and rose wines as well [14].

RSV is a powerful antioxidant fighting against disease-inducing free radicals in the body and protects the cells from oxidative stress and damage. It possesses anti-inflammatory and cardioprotective potentials and enhances cardiovascular health, reduces blood pressure and monitors cholesterol levels. It was also reported to defense against neurodegenerative diseases like Alzheimer's and Parkinson's through minimization of inflammation and oxidative stress in the brain. In various forms of cancer RSV inhibited cancer cell proliferation and encouraged apoptosis. Anti-aging qualities of RSV is due to its ability to stimulate precise genes that are related to long life and enhancing cell repair mechanisms. RSV aids in reducing blood sugar levels, manages weightiness and promotes metabolic health. Besides, it also exhibits antimicrobial potential combatting against several fungal and bacterial pathogens as evident from various researches. The unique exploration spotlighting the distinct medicinal properties of RSV underscores its importance as a polyphenolic compound discovered in various plant sources.

METHODOLOGY

Data were composed precisely from various sources viz., Scopus, PubMed, Science Direct, Web of Science, Scientific Electronic Library Online, Google Scholar, EMBASE, PubChem, JSTOR, Springer Link, Oxford University Press, MDPI and Taylor and Francis online. The data gathered consists of primary studies and evaluations printed in peer-reviewed periodicals, books, theses, dissertations, case studies, and other reports encompassing the chemistry, synthesis, and medicinal possibilities of RSV. Specific keywords, search terms, and inclusion/exclusion criteria were employed to identify pertinent studies and information. Comprehensive full-text data were gathered, stored, and meticulously analyzed.

BIOACTIVITIES OF RESVERATROL

Anticancer activity

Despite the defense of novel chemotherapeutic agents, cancer is one of the world's notable reasons for death, and patients habitually have serious side effects. Because of this, scientists are investigating for safer and less risky cancer treatments. Because RSV may affect cell death, inhibit cell development, and lessen inflammation, it is supposed to be a feasible agent for the battle against cancer. In particular, a reduction in caspase levels during carcinogenesis is associated with apoptosis inhibition. Rats treated with RSV had considerably greater caspase levels than the DMH (1,2-Dimethylhydrazine) carcinogen control group after a 30-week experiment, according to research. Increased apoptosis incidents have been linked to elevated caspase levels [15]. Cancer cells have been displayed to have Heat Shock Proteins - HSP-70 and HSP-27, which inhibit cell death. Rats treated with both the carcinogen and RSV showed significantly lower levels of HSP-70 and HSP-27 than rats injected with the carcinogen alone. Rats given RSV had lower levels of HSP-70 and HSP-27, which may have contributed to cell death. The reciprocal relationship between RSV and HSP highlights the potential of RSV as an apoptosis-promoting cancer treatment.

An alternative pathway that hampers cancer cell proliferation involves the upregulation of MIC-1, which diminishes cancer growth upon activation. RSV was demonstrated to be effective in this process by hindering COX. Through COX inhibition, RSV activates MIC-1, leading to reduced proliferation. Purified RSV exhibited potential for preventing cancer in three main stages of tumor development. It acted as an antioxidant and antimutagen, boosted phase II drug-metabolizing enzymes, and displayed anti-initiation properties. Additionally, it revealed anti-inflammatory properties by inhibiting the functions of COX and hydroperoxidase, exhibiting anti-promotion effects [16]. RSV defends against initial DNA damage through two distinct mechanisms: initially, it functions as an antimutagen by activating Phase II enzymes like quinine reductase, which eliminate carcinogens by inhibiting COX and cytochrome P450; secondly, it acts as an antioxidant, stopping DNA damage caused by ROS [17].

Cardiovascular activity

Cardiovascular diseases (CVDs) are the primary reasons for sickness and mortality in developed nations, with a projected worldwide total surpassing 23.6 million deaths by 2030 [18]. According to WHO, CVDs includes several health conditions influencing the heart and blood vessels such as high blood pressure, coronary artery disease, stroke, peripheral artery disease, heart muscle diseases, and heart failure. Atherosclerosis, caused by chronic inflammation of the arterial wall is the reason for many CVD's. However, complex exchanges between metabolic and molecular modifications, such as oxidative stress, inflammation, lipid metabolism, and dysfunction in endothelial and myocardial functions, lead to the development of various heart problems, including heart failure [19]. The main ways that RSV helps the heart are by reducing oxidative stress, controlling inflammation, and having a beneficial effect on cardiovascular risk factors. Atherosclerosis pathogenesis is commonly associated with dysregulation in cholesterol and lipoprotein metabolism. LDL (low density lipoprotein) exposed to macrophages within atherosclerotic lesions undergo oxidation, resulting in oxidized LDL particles (LDL-ox) that harm endothelial cells, promoting atherosclerotic lesion advancement. Several preclinical studies indicated that RSV can affect this pathway by reducing triglycerides and LDL-cholesterol levels in blood while increasing HDL (high density lipoprotein) - cholesterol.

Various animal studies conducted have shown that including RSV can lower triglyceride, total cholesterol, and LDL-C levels by increasing bile acid production and release, while also diminishing oxidative stress and inflammation [20]. RSV assists in managing diabetes-related complications and regulating glucose levels by modulating pathways like SIRT1/AMPK/NF-kB and p38-MAPK/TGF-beta1, preventing mitochondrial division by Drp1, and halting ER stress-triggered NLRP3 inflammasome activation [21]. RSV showed potential in improving the autonomic function of heart and blood vessels, as well as safeguarding red blood cells by interacting with hemoglobin, leading to a decrease in heme-iron oxidation [22].

Neuroprotective activity

Gradual loss of neurons at specific sites of the central nervous system causes neurodegenerative disorders. Several researches have demonstrated that chronic inflammation plays a vital role in development of Parkinson's disease [23]. The continuous inflammation in the brain are caused by the microglia that are overactive and neurons that are not working. This unhealthy circle results in the slow and continuous degeneration of the brain diseases. Increase of microglial activity in rats is attributed to the rise of inflammatory agents such as cytokines, nitric oxide and prostaglandins [24]. 6-OHDA stimulates microglia, resulting in the release of pro-inflammatory chemicals that eventually disrupt the ongoing inflammation cycle in substantia nigra neurons [25]. RSV is expected to prevent microglia formation by 6-OHDA and, as a result, slows the progression of chronic inflammation. RSV demonstrated capability in down-regulating the manufacture of the proinflammatory mediators, including COX-2 and TNF, which were boosted by 6-OHDA [26].

Prior researches showed that RSV inhibits inflammatory cytokines comprising TNF-α and also COX-2 inflammatory enzymes used in prostaglandin formation [27]. Development of Parkinson's disease is significantly influenced by the rise in TNF-α and COX-2 mRNA intensities. After receiving RSV therapy, the rats modelled for Parkinson's disease showed reduced levels of TNF-α and COX-2 mRNA and protein. Thus, it is hypothesized that the reduction in COX-2 and TNF-α mRNA and protein levels may account for the protective effects of RSV on Parkinson's disease-caused rats after 6-OHDA exposure. Previous research has demonstrated that incorporating polyphenols sourced from grape skin and seeds into one's diet can lower oxidative harm from chronic alcohol intake on brain synaptic membranes [28]. Although grapes and berries have many polyphenols, RSV is particularly notable for its significant role in improving overall health. While other antioxidants have been demonstrated to offer protection against alcohol-induced brain damage, RSV has been discovered to offer precise neuroprotective benefits against oxidative stress and spatial learning impairments caused by alcohol consumption.

Anti-aging activity

Getting older is often seen as a normal and complex progression marked by deteriorating changes leading to a decrease in bodily functions. These changes and harm related to age ultimately hinder the function of cells and tissues. Growing older increases the likelihood of developing various non-infectious chronic diseases such as diabetes, cardiovascular illness, cancer, and neurological disorders [29]. In last twenty years, ample researches have indicated that foods containing polyphenols might offer defense against age-related illnesses. New studies suggest that polyphenols and antioxidant supplements such as RSV have potential as anti-aging substances by impacting the key factors of aging, like oxidative stress, inflammation, telomere shortening, and cellular aging. There is a lot of evidence backing the theory that antioxidant supplements, such as RSV, can effectively delay the aging process [30]. RSV triggers the AMPK-FOXO3 pathway to shield against senescence and dysfunction triggered by oxidative stress. It aids in preserving the levels of antioxidants such as SOD, catalase, glutathione reductase, and GSH-Px in cells, safeguarding tissues against the harmful impacts of ROS in biological systems.

Furthermore, RSV has been observed to lessen oxidative damage in endothelial cells by regulating mtROS levels through enhancing the expression of IDH2, GSH-Px, and MnSOD. When combined with exercise, RSV has been proven to delay the effects of aging and preserve elevated levels of glutathione, GSH-Px, and glutathione transferase activities [31]. Additionally, grapes contain RSV, which is a natural source that helps in anti-aging by maintaining mitochondrial balance through controlling fusion and fission processes, resulting in mitophagy. AMPK, a critical nutrient detector, functions downstream in pro-longevity strategies like dietary restriction (DR), regulating cellular and physiological functions tied to aging [32]. Growing evidence suggested the advantageous impacts of RSV on anti-aging are associated with AMPK activation. Getting older signifies a slow decrease in the balance of body tissues, resulting in their decay and negative health effects. Age-related alterations frequently include declined ability to repair DNA after being damaged by oxidative stress [33]. As a result, many research studies have investigated novel treatment strategies to delay age-related alterations by incorporating compounds that have antioxidant and anti-inflammatory characteristics.

Antimicrobial activity

Researches have been conducted on the potential interactions between RSV and traditional antibiotics. In *E. coli*, adding RSV at 0.5X MIC appears to counteract the killing effects of ciprofloxacin, kanamycin, oxolinic acid, and moxifloxacin, but does not influence the lethality of oxacillin [34]. In *S. aureus*, RSV counteracts the toxic action of daptomycin, moxifloxacin, oxacillin and levofloxacin [34,35]. Since ROS generation has been linked to the lethality of bactericidal antibiotics, RSV's scavenging of ROS may diminish the bactericidal effects of the mentioned antibiotics [34]. RSV, at 0.5X MIC, significantly enhanced the effectiveness of aminoglycosides against *S. aureus* by approximately 16-fold, and to a slighter degree against other gram-positive pathogens like *Staphylococcus epidermidis*, *Enterococcus faecium*, and *Enterococcus faecalis* [36]. The suggested method underlying this enhancement involves the inhibition of ATP synthase by RSV [36], as evidenced by studies showing that inactivation of genes encoding ATP synthase in *S. aureus* also heightens the susceptibility of this pathogen to aminoglycosides [37]. Additionally, RSV augments the activity of aminoglycosides against biofilms produced by *Pseudomonas aeruginosa*.

RSV has antibacterial effects on important foodborne bacteria like *Escherichia coli*, *Staphylococcus aureus*, *Vibrio cholerae*, *Campylobacter jejuni*, and *Listeria monocytogenes*, potentially by promoting DNA breakage. Additionally, RSV decreases cellular function associated with harm to the membrane and serves as a blockade to cell replication. It has shown strong efficiency in fighting numerous foodborne pathogens, suggesting its potential as an alternative to ensure the creation of top-notch, advantageous products for consumers [38]. Clinical trials have been conducted on RSV as a medicine, and it has been found that 5 g/day dose are safe and can be tolerated well for a month. Following oral administration in humans, RSV is easily absorbed. Research has confirmed that RSV is effective in preventing the growth of *Candida albicans*. Dimethoxy RSV derivatives showed antifungal activity against 11 different Candida species with MIC varying between 29-37 µg/ml, particularly against *Candida albicans* [39]. However, the effectiveness of RSV as an antifungal agent remains contentious.

CONCLUSION

The popularity of using natural products and their derived compounds is increasing significantly around the globe, as opposed to traditional/modern medicines, because of their cost-effectiveness and lower levels of toxicity, especially in the treatment of different disorders. Resveratrol is a polyphenol that is categorized as a non-flavonoid stilbene and has been revealed in different studies to be effective in treating a range of medical conditions. Supplementing with resveratrol has been shown to help prevent and handle a diversity of diseases with several underlying mechanisms. RSV can interact with a range of molecular targets and has demonstrated no adverse effects. Kinases, growth factors, enzymes, apoptotic proteins, receptors, and pro- and anti-inflammatory cytokines are all regulated by it. Additionally, it influences NF-kB, Nrf-2, and the signalling pathways linked to them in a variety of clinical settings. Because of its cardioprotective, immunomodulatory, anticancer, anti-aging, neuroprotective, and antioxidant properties, RSV has a broad range of therapeutic potential, as the extensive review of the literature makes clear. Although the exact dosage and how RSV treats many diseases are still unknown, this paper aims to encourage researchers worldwide to investigate RSV as a medicinal alternative for addressing significant health concerns.

Abbreviations

RSV – Resveratrol; MIC-1 – Macrophage-Inhibitory Cytokine-1; COX – Cyclooxygenase; ROS – Reactive oxygen species; SOD – Superoxide dismutase; NF-kB - Nuclear factor kappa B; MAPK - Mitogen-activated protein kinase; SIRT1 – Sirtuins; AMPK - Adenosine monophosphate-activated protein kinase; TGF - Transforming growth factor; Drp1 - Dynamin-related protein 1; NLRP3 - Nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3; 6-OHDA – 6-hydroxydopamine; TNF – Tumor Necrosis Factor; FOXO3 – Fork head box O3A protein; MnSOD – Manganese superoxide dismutase; mtROS – Mitochondrial reactive oxygen species; IDH2 – Isocitrate dehydrogenase 2; GSH-Px – Glutathione peroxidase; Nrf-2 – Nuclear factor (erythroid 2 -related factor)-2.

Table 1: List of plants producing resveratrol

S. No.	Vernacular Name	Botanical Name	Family	Plant Parts producing RSV
1	Peanut	*Arachis hypogaea* L.	Fabaceae	Hull, skin, and kernel
2	Jackfruit	*Artocarpus heterophyllus* Lam.	Moraceae	Fruits
3	Bidi leaf tree	*Bauhinia racemosa* Lam.	Caesalpiniaceae	Heartwood
4	Blackberry lily	*Belamcanda chinensis* (L.) DC	Iridaceae	Rhizome
5	Peruvian legume	*Cassia quinquangulata* Rich.	Leguminosae	Plant extract
6	keruing ropol	*Dipterocarpus hasseltii* Blume	Dipterocarpaceae	Bark
7	Camphor tree	*Dryobalanops aromatica* C.F. Gaertn.	Dipterocarpaceae	Stem bark
8	Mugga ironbark	*Eucalyptus sideroxylon* A.Cunn. ex Woolls	Myrtaceae	Heartwood
9	Tall Fescue	*Festuca arundinacea* Schreb.	Poaceae	Seed, Forage
10	Texas Fescue	*Festuca versuta* Beal	Poaceae	Seed
11	Melinjo	Gnetum gnemon L.	Gnetaceae	Seed
12	Kampakam	*Hopea gregaria* Slooten	Dipterocarpaceae	Stem bark
13	Malabar Ironwood	*Hopea parviflora* Bedd.	Dipterocarpaceae	Stem
14	Ponga	*Hopea ponga* (Dennst.) Mabb.	Dipterocarpaceae	Stem bark
15	Grass	*Hordeum bogdani* Wilensky	Poaceae	Seed, Forage
16	Wild Barley	*Hordeum brevisubulatum* (Trin.) Link	Poaceae	Seed, Forage
17	Annual Ryegrass	*Lolium multiflorum* Lam.	Poaceae	Seed
18	Perennial Ryegrass	*Lolium perenne* L.	Poaceae	Seed
19	Persian Ryegrass	*Lolium persicum* Boiss. & Hohen	Poaceae	Seed
20	Annual Ryegrass	*Lolium rigidum* Gaud.	Poaceae	Seed
21	Darnel Ryegrass	*Lolium temulentum* L.	Poaceae	Seed
22	Red Mulberry	*Morus rubra* L.	Moraceae	Fruits
23	Chengal	*Neobalanocarpus heimii* (King) P.S. Ashton	Dipterocarpaceae	heartwood
24	Red Beech	*Nothofagus fusca* (Hook.f.) Oerst.	Nothofagaceae	Heartwood
25	Common garden Peony	*Paeonia lactiflora* Pall.	Paeoniaceae	Seeds
26	Norway Spruce	*Picea abies* (L.) H. Karst.	Pinaceae	Bark
27	Chir Pine	*Pinus roxburghii* Sarg.	Pinaceae	Stem and Needle
28	Scots pine	*Pinus sylvestris* L.	Pinaceae	Woods
29	Reynoturia	*Pleuropterus ciliinervis* syn. *Reynoturia ciliinervis* (Nakai) Moldenke	Polygonaceae	Roots
30	Grove blue grass	*Poa alsodes* A. Gray	Poaceae	Seed, Forage
31	Japanese Knotweed	*Polygonum cuspidatum* Sieb. et Zucc.	Polygonaceae	Roots
32	Indian kino	*Pterocarpus marsupium* Roxburgh	Fabaceae	Heartwood
33	Red sanders	*Pterocarpus santalinus* L.	Fabaceae	Wood
34	Indian redwing	*Pterolobium hexapetallum* (Roth) Santapau &Wagh	Fabaceae	Stems
35	Asiatic knotweed	*Reynoutria japonica* Houtt.	Polygonaceae	Rhizome
36	Rhubarb	*Rheum rhaponticum* L.	Polygonaceae	Root
37	Red Currant	*Ribes rubrum* L.	Grossulariaceae	Berries
38	Sand lily	*Scilla nervosa* (Burch.) J.P. Jessop	Hyacinthaceae	Bulbs
39	Yellow Meranti	*Shorea accuminatissima* Symington	Dipterocarpaceae	Stem bark
40	Red lauan	*Shorea acuminata* Dyer	Dipterocarpaceae	Stem bark
41	Meranti	*Shorea brunnescens* P.S. Ashton	Dipterocarpaceae	Stem bark
42	Meranti Daun Besar	*Shorea hemsleyana* (King) King ex Foxw.	Dipterocarpaceae	Stem bark
43	Balau wood	*Shorea maxwelliana* King	Dipterocarpaceae	Stem bark
44	Taloora Lac Tree	*Shorea roxburghii* G. Don.	Dipterocarpaceae	Bark
45	Dark red meranti	*Shorea rugosa* F. Heim.	Dipterocarpaceae	Stem bark

46	Sleepy grass	*Stipa robusta* (Vasey) Barkworth	Poaceae	Forage
47	Jamun	*Syzygium cumini* (L.) Skeels	Myrtaceae	Seed, Pulp, skin
48	San ye Qing	*Tetrastigma hemsleyanum* Diels & Gilg	Vitaceae	Roots
49	Hop trefoil	*Trifolium campestre* Schreb.	Leguminosae	Leaf
50	Suckling clover	*Trifolium dubium* Sibth.	Leguminosae	Leaf
51	Blueberry	*Vaccinium angustifolium* Aiton	Ericaceae	Fruits
52	Cranberry	*Vaccinium macrocarpon* Aiton	Ericaceae	Berries
53	Bilberry	*Vaccinium myrtillus* L.	Ericaceae	Fruits
54	Hal plant	*Vateria copallifera* (Retz.) Alston	Dipterocarpaceae	Barks
55	The White Dammar	*Vateria indica* L.	Dipterocarpaceae	Leaves
56	White Twigs	*Vatica albiramis* Slooten	Dipterocarpaceae	Stems
57	Kokoleceran	*Vatica bantamensis* (Hassk.) Benth. & Hook.f. ex Miq.	Dipterocarpaceae	Leaves
58	South-Indian Vatica	*Vatica chinensis* L.	Dipterocarpaceae	Stems
59	Resak Rawa	*Vatica pauciflora* (Korth.) Blume	Dipterocarpaceae	Stem bark
60	White Hellebore	*Veratrum grandiflorum* Loes.	Melanthiaceae	Roots
61	Wine Grape	*Vitis vinifera* L.	Vitaceae	Fruit skins, stems, roots, seeds

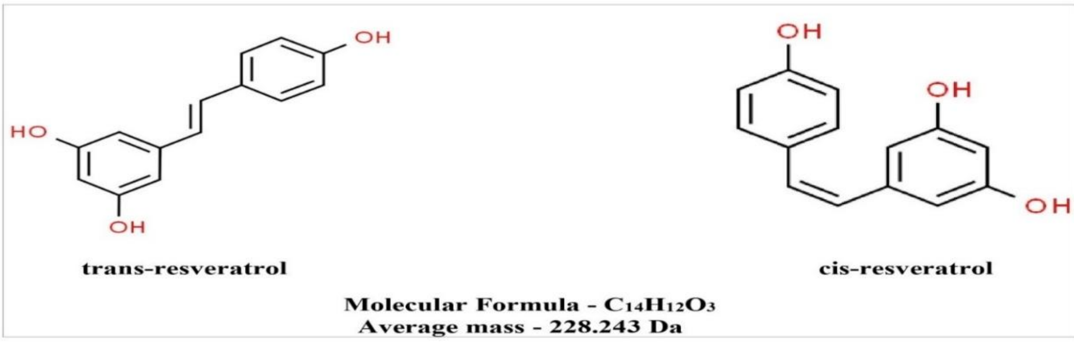

Figure 1: Structure of Resveratrol
Source: http://www.chemspider.com/Chemical-Structure.392875.html

Figure 2. Plant Sources of Resveratrol
A - *Veratrum grandiflorum* Loes.; B - *Polygonum cuspidatum* Sieb. et Zucc.; C - *Vitis vinifera* L.; D - *Arachis hypogaea* L.; E - *Ribes rubrum* L.; F - *Vaccinium macrocarpon* Aiton; G - *Vatica chinensis* L.; H - *Vateria indica* L.; I - *Shorea roxburghii* G. Don.; J - *Neobalanocarpus heimii* (King) P.S. Ashton; K - *Hopea gregaria* Slooten; L - *Dipterocarpus hasseltii* Blume; M - *Dryobalanops aromatica* C.F. Gaertn.

Acknowledgements

The author is indebted to Dr. Kavan Panneerselvam, Professor, NITT for assistance in formulating the manuscript.

Conflict of interest

The authors declared no conflict of interest.

Financial Support

None declared.

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HOW TO CITE THIS ARTICLE

Govindaraj S. Exploring the therapeutic potential of Resveratrol: A natural compound with multifaceted health benefits. J Phytopharmacol 2025; 14(6):543-549. doi: 10.31254/phyto.2025.14616