

# Resveratrol and its biological activities

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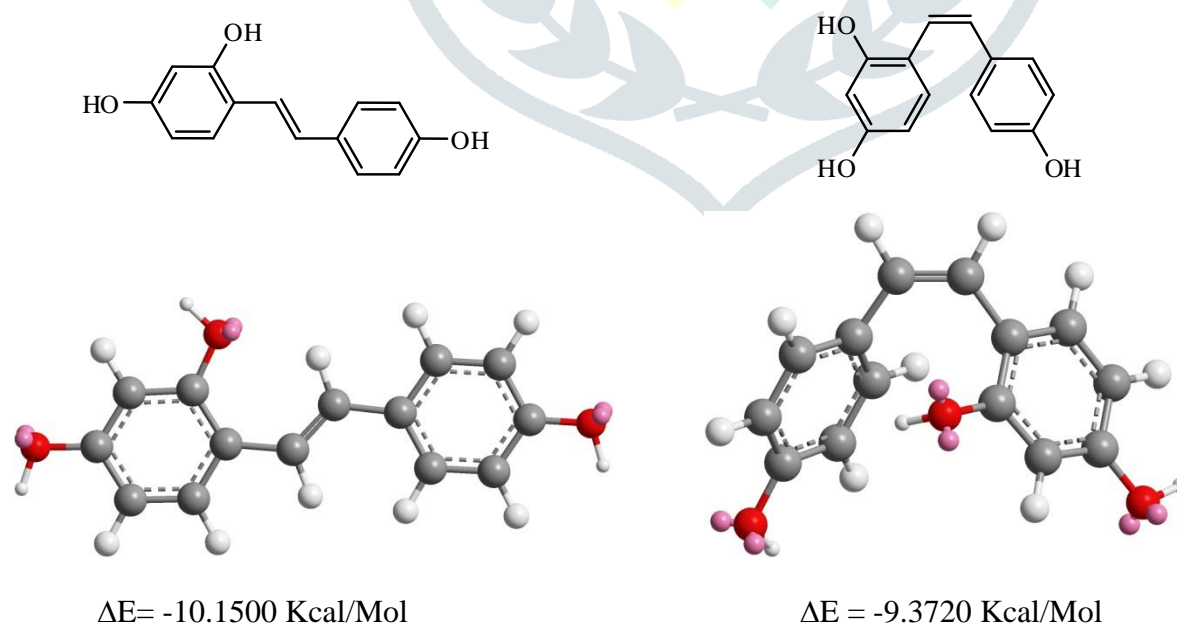
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**Abstract:** Resveratrol is an important polyphenolic phytoconstituent found in variety of plants berries, beans and other. It is known as potential agent for diverse biological activities such as antioxidant, anti-inflammatory, antimicrobial, anticancer, anti-diabetic, anti-asthmatic, anti-arthritic, cytoprotective etc. The trans isomer of resveratrol is the major contributor to the biological activities due to its higher stability than cis isomer. It acts by different mechanisms of activity ranging from free radical scavenging to targeting various enzymes and receptors. Here, we reviewed the various biological activities and mechanisms of actions of resveratrol.

**Keyword:** Resveratrol, Polyphenolic, Phytoconstituents

## 1. Introduction

Resveratrol is an important phytoconstituents belong to polyphenols and found in variety of plant products such as grapes (*Vitis vinifera*), peanuts (*Arachis hypogaea*), soybean (*Glycine max*), Japanese knotweed (*Polygonum cuspidatum*), bilberry (*Vaccinium myrtillus L.*), blueberries (*Vaccinium angustifolium Aiton*, *Vaccinium ashei Reade*, *Vaccinium corymbosum L.*), cranberries (*Vaccinium macrocarpon*), strawberry (*Fragaria ananassa*), gooseberry (*Ribes uva-crispa*) etc [1]. Chemically it is 3,5,4'-trihydroxystilbene which exists in two isomeric forms as *trans* (E)-resveratrol and *cis* (Z)-resveratrol. The trans-isomer is more stable than cis and found to be responsible for dominant biological activities of resveratrol. However, both *cis* and *trans* forms are interconvertible under effect of heat and light. The resveratrol has been shown a wide range of biological activities such as antioxidant, anti-inflammatory, antimicrobial, anticancer, anti-diabetic, anti-asthmatic, anti-arthritic, cytoprotective, cardioprotective, antiaging, melanogenesis inhibitor etc. Here, we reviewed different biological activities of resveratrol with updated underling mechanism of its action.



**Fig. 1:** Trans and Cis isomeric forms of resveratrol and their energy minimized 3D orientations.

## 2. Biological activities of resveratrol

Resveratrol has been shown diverse biological activities *in vitro* and *in vivo* with various potencies dependent on its concentration. Some of these biological activities and mechanism action of resveratrol has been discussed in the following sections.

**2.1 Anticancer:** Resveratrol has been found to be active against various cancers such as colorectal cancer (CRC). The mechanism could be inducing cell death, oxidative stress, and inhibiting the cell proliferative activity. Bioinformatic tool based target-functional protein interaction network evaluation has been identified protein kinase B1 (AKT1), interleukin 6 (IL6), tumor protein p53, vascular endothelial growth factor, and mitogen-activated protein kinase 1 as anti-CRC targets for resveratrol. By affecting above targets, resveratrol regulates different pathways such as apoptosis, immune response, cellular communication, signal transduction, nuclide metabolism etc. Further, *in vitro* evaluation study in HCT116 cells has been shown reduced intracellular levels of AKT1 and IL6 as a sign of its anti-proliferative and apoptotic activity [2]. Previous study has also been shown that resveratrol also regulates PTEN/PI3K/Akt, Wnt/ $\beta$ -catenin pathways for its biological functions [3].

**2.2 Anti-melanogenesis:** Resveratrol is also used to inhibit the hyper pigmentation in the skin. It acts as a tyrosine kinase inhibitor. The presence of free aromatic –OH groups as characteristics of tyrosine kinase inhibiting phenolic compounds (structural similarity with enzyme substrate, tyrosine) was found to be the preferred mechanism of enzyme inhibition by resveratrol. It is a highly potent agent for inhibiting the hyperpigmentation that other phenolic groups used to inhibit tyrosine. *In vitro* tyrosine kinase inhibition assay has been indicated its higher potency with  $IC_{50}$  value 1.8  $\mu$ M. The derivative of the resveratrol such as oxyresveratrol is even more potent than the resveratrol with  $IC_{50}$  value of 0.09  $\mu$ M). Additionally, oxyresveratrol at concentration of 1  $\mu$ M is also able to inhibit the dopamine oxidase activity in brain. Moreover, resveratrol is also inhibits the  $\alpha$ -melanocyte-stimulating hormone (MSH) which is one of the major causes of pigment formation on the skin [4].

**2.3 Anti-aging:** Resveratrol is active against various skin related complications. It is able to protect from UV radiations that is why it is mostly used in the dermatology and cosmetics. It is able to inhibit the UV induced melanocyte formation in skin site. This is the reason of using resveratrol is used in suns cream. Resveratrol can easily permeate through the skin by damaging the lipids in skin and can accumulate in the skin- so it has better and improved bioavailability as compare to the other anti-aging agents [5, 6]. Various other formulations such as nanoparticles, emulsions and other topical Formulations can be prepared for the better delivery of resveratrol. But the topical bioavailability without any specific formulation is far better than oral bioavailability [7, 8].

**2.4 Antioxidant activity:** Resveratrol have been reported to have a wide range effect on intracellular mediators. *In vitro* study has been shown that resveratrol at concentration of 30  $\mu$ g/ml inhibits peroxidation of lipids upto 89.1 % and this indicated free radical scavenging as well as anti-oxidant potential of resveratrol. It acts by scavenging of variety of free radicals such as  $DMPD^{+}$ ,  $DPPH^{\bullet}$ ,  $ABTS^{+}$ ,  $H_2O_2$  and  $O_2^{\bullet-}$  etc. [9].

**2.5 Anti-inflammatory activity:** Anti-inflammatory effect of resveratrol has been evaluated by acute pharyngitis animal model to examine its potential. The tumor necrosis factor- $\alpha$ , macrophage inflammatory protein-2, interleukin (IL)-6, caspase- 3/9 activity and cyclooxygenase- 2 levels has been measured with the help of ELISA based *in vitro* assay. The resveratrol was found to inhibit tumor necrosis factor- $\alpha$  along with maintaining the other factors mentioned above. In addition to this, resveratrol suppresses TLR4 as well as p-NF-kB. Thus, *in vivo* and *in vitro* assay data indicated anti-inflammatory effect of resveratrol in preventing acute pharyngitis [10].

**2.6 Antidiabetic effect:** It has been seen that resveratrol may show antidiabetic activity by activating SIRT1 (silent mating type information regulation 1). Due to activation, FOXO1 gene and PTP1B was being

deacetylated thereby inhibiting apoptosis of pancreatic  $\beta$ - cells. As a result, improvement has been seen in glucose level regulation along with enhanced insulin sensitivity [11]. An assay was performed in vitro for evaluating the effectiveness of resveratrol on SIRT1 activation and the results were quite significant when compared with the insulin-glucose levels of a control mice [12].

**2.7 Antiarrhythmic activity:** Studies have reported that inhibition of  $I_{Ca}$  results in shortening of the action potential for prevention of ischemic depolarization and restricts the sodium as well as calcium to flow in inward direction thereby enhancing refractory period of heart [13]. For investigating Antiarrhythmic activity, an animal model (Dawley rat) was anaesthetised so as to isolate its heart. Perfusion of resveratrol resulted in antiarrhythmic activity [14].

**2.8 Anti-obesity activity:** As the polyphenol, resveratrol acts as antiobesity agent by activating SIRT1. It induces the fat browning phenomenon which is promoted by remodelling of WAT (white adipose tissues) due to activation of thermogenesis. This process improves metabolism in an obese person [15].

**2.9 Neuroprotective activity:** Resveratrol is a well-known drug for the treatment of neurodegenerative diseases such as Alzheimer's disease. SIRT1 activation plays a key role. Growth and development of neurons are widely dependent on SIRT1's activation thereby inhibiting apoptosis of neurons via deacetylation along with suppression of p53 activity [16].

## Conclusion

Resveratrol is an important molecule of natural origin with several biological activities with higher potencies. It is available to the body from various sources such as berries and beans. Thus, routine consumption of resveratrol rich food improve the functioning and maintain the body by acting as a potential agent for activities such as anti-oxidant, anticancer, neuroprotective, anti-aging, anti-diabetic, anti-inflammatory etc.

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