World Journal of Pharmaceutical Science and Research
www.wjpsronline.com
Review Article
ISSN: 2583-6579
SJIF Impact Factor: 5.111
Year - 2025
Volume: 4; Issue: 1
Page: 206-219

RESVERATROL: A VERSATILE NEUTRACEUTICAL COMPOUND

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Article Received: 30 November 2024 | | Article Revised: 21 December 2024 | | Article Accepted: 13 January 2025

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How to cite this Article: Aher Kalyani Nandkishor, Aher Mansi Dinkar, Aher Parina Nitin, Ahir Komal Kishanlal, Dr. Shital J. Patil (2025). RESVERATROL: A VERSATILE NEUTRACEUTICAL COMPOUND. World Journal of Pharmaceutical Science and Research, 4(1), 206-219. https://doi.org/10.5281/zenodo.14785106

ABSTRACT

One of the most prevalent and plentiful classes of plant metabolites are polyphenols, which include anthocyanins, flavonoids, and stilbenes. These metabolites are essential to a person's diet. Some plants naturally manufacture resveratrol (3, 5, 4'-trihydroxystilbene) as a self-defence polyphenol, which possesses antifungal properties. This antitoxin found in herbal remedies, grapes, red wine, peanuts and strawberries, etc. It is a natural polyphenol and it occurs in many fruits and vegetables, resveratrol is employed as a curative and cancer preventive agent to treat wide range of diseases. Resveratrol has antioxidant, anti-inflammatory, anti-diabetic, anti-viral and various other uses. Resveratrol can be recognized as a best neutraceutical. This natural Table top food has a lower bioavailability with lower aqueous solubility. From this review we can conclude that resveratrol is a unique complex having various properties with lots of other benefits.

KEYWORDS: Resveratrol, Stillbenoid, Oxidative stress, Anti-oxidant, Phytoalexines Anti- Inflammatory, Eicosanoids.

1. INTRODUCTION

Although phytoalexin molecules have a very wide range of chemical properties, those from the families *Vitaceae*, *Fabaceae*, and *Pinaceae* appear to belong to a very small group of compounds in the stilbene family, which is made up of two aromatic rings joined by a methylene bridge. Resveratrol compound (3, 5, 4'-trihydroxystilbene) found in the *Fabaceae* and *Vitaceae*, or pinosylvin (trans-3, 5-dihydroxystilbene) found in the *Pinaceae*, is the basis of stilbenes.

There are two forms of resveratrol, which are produced by different plant species: cis-resveratrol and trans-resveratrol. The Trans isomer, with excessive biological effect due to the appearance of 4'-hydroxystyryl group, was discovered in 1940 in the roots of white hellebore (*veratrum grandiflorum*).[1]

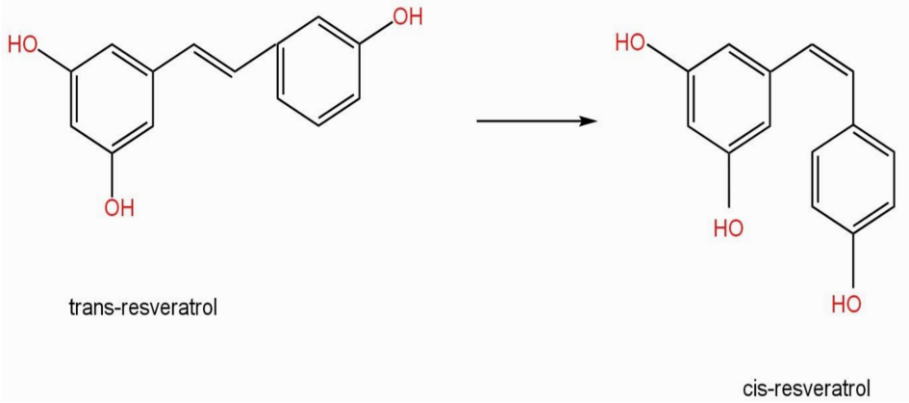

Fig. 1: Isomeric forms of Resveratrol.

Resveratrol has been recognised in nearly 72 plant species, spread across 31 genera and 12 families. These families include *Myrtaceae, Vitaceae, Cyperaceae, Dipterocarpaceae, Pinaceae, Gnetaceae, Fabaceae, Moraceae, Liliaceae, and Fagaceae*, all belonging to the division of spermatophytes. Resveratrol was first discovered by a Japanese scientist from the roots of *Veratrum grandiflorum*, and then it was extracted from and it was later isolated from the roots of *Polygonumcuspidatum*. *Polygonum cuspidatum* is a perennial herb from the Polygonaceae family, native to both Asia and North America. In Japan and Korea, it is used as folk medicine. The roots, stems, leaves, flowers, fruits and seeds are commonly used for extraction.[2]

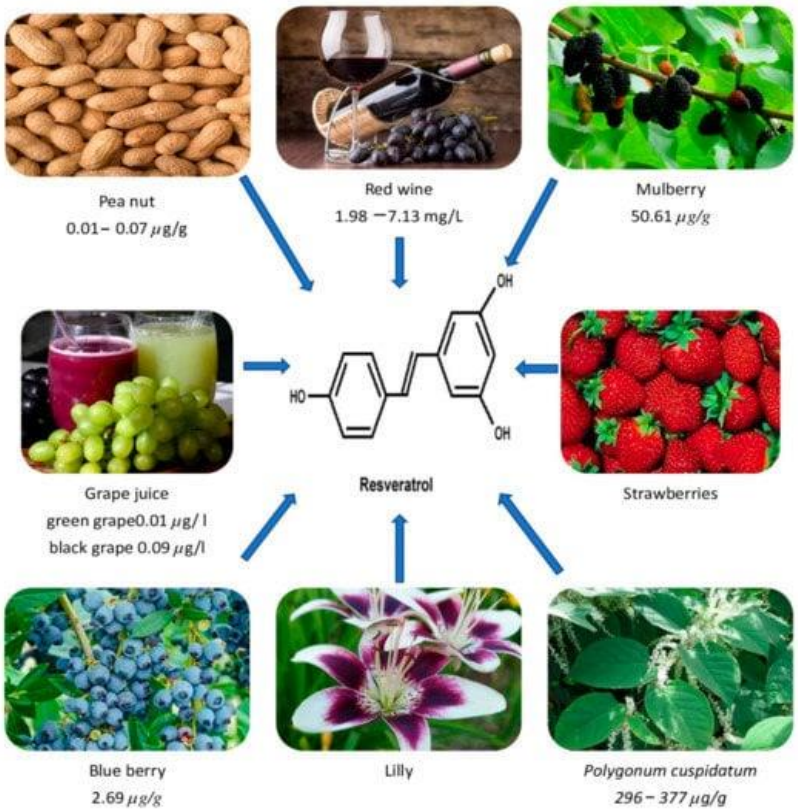

Fig. 2: Sources of Resveratrol.

The high concentration of resveratrol has occurred in grapes, peanuts, berries, soybeans, red wine and hence they are used in resveratrol supplements. In grapes 0.16-3.54mg/gm. of RV, dry grapes skin contains about 24mg/gm. of RV, cranberry juice carries about 0.2 mg/l of RV, in red wine concentration of RV ranges from 0.1-14mg/l. At the same moment, white wine contains only 0.1-2.1mg/l of RV.

Resveratrol is classified as a phytoalexin, a type of compound plants produce under environmental stress, such as unfavorable weather or threats from insects, animals, or pathogens. This production process in plants is facilitated by the enzyme resveratrol synthase. Widespread interest in resveratrol only emerged in 1992 when its presence in wine was linked to the probable cardioprotective benefits of moderate wine consumption.[3]

Resveratrol is gaining attention in field of nutrition and medicine for its probable health advantages .Resveratrol shows that trans-resveratrol shows powerful anti-oxidant ,inhibiting lipid peroxidation of LDL(low density lipoprotein).it also safeguard cells from oxidative harm, reduces the cytotoxic effects of oxidized LDL, and lowers the tumor promotion activity by inhibiting cyclooxygenase -1(COX-1)and platelet aggregation. These properties suggest a promising role of resveratrol in cardiac diseases health and cancer prevention.[4]

2. THE PHYSICAL PROPERTIES OF RESVERATROL

Table 1: Physical properties of resveratrol.

Molecular Formula	$C_{14}H_{12}O_3$
Synthetic Name	5-[(E)-2-(4-hydroxyphenyl)-ethyl]benzene-1,3-diol
Other Names	Trans-resveratrol Trans-3,5,4'-trihydroxystilbene (E)-5-(P-hydroxystyryl)resorcinol 3,5,4'-trihydroxy-cis-stilbene 3,5,4'-trihydroxy-trans-stilbene
Molecular Weight	228.25 g/mol
Boiling Point	253-255 ^{0}C
Physical Structure	White-solid
Solubility	methanol, soluble in water and acetone

3. SYNTHESIS, OCCURRENCE AND CONTENT OF RESVERATROL IN WINE AND PLANTS

Resveratrol is a phytoalexin which harmonized in plants and can be produce by microbial infection, ultra-violet radiation (UV), and revelation to ozone (O_3). Resveratrol is manufactured in leaf epidermis and skin of grape berries but not in beef. The polyphenol concentration in grape species ranges from 50-100 microgram/g fresh weight of leaves. The factors like grape variety, environmental factor in the wine yard, juice extraction, wine processing technique, etc. affect the amount of this compound in various type of grape juice and wine.[5]

Resveratrol is a secondary metabolite which is harmonised as a protective compound against numerous external factors and found most generously in the product obtained by the drying of the roots of "*polygonum cuspidatum*" it is a plant traditionally used in Japan and China.

Resveratrol is formed by the combination of 3 molecules of CoA and 1molecule of 4-cuamoryl CoA. It is main aspect that the enzyme require for the formation of resveratrol is not normally active and activated when the plant faced with a stress factor.

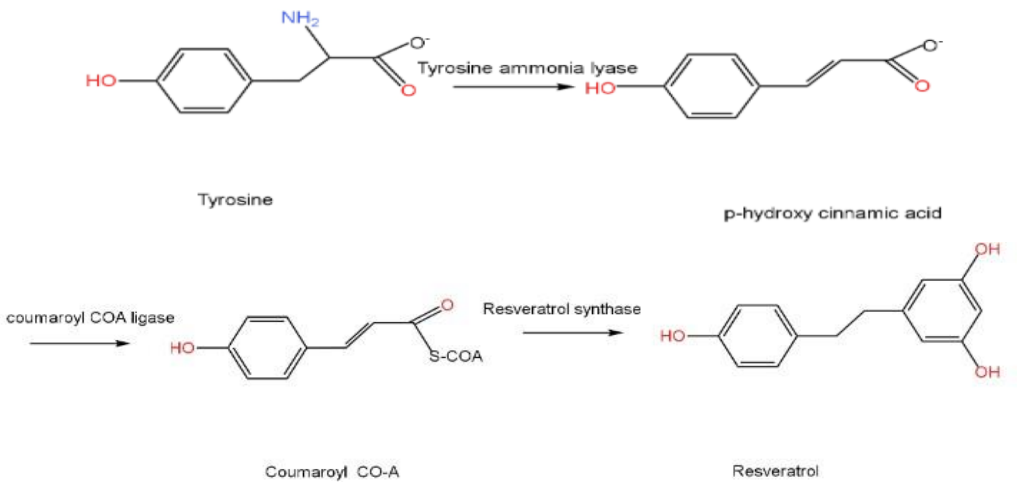

Fig. 3: Resveratrol biosynthesis from Tyrosine.

Resveratrol can be synthesized from tyrosine through a series of enzymatic reaction that use following genes: Tyrosine ammonia lyase, 4-coumarate: COA ligase, Resveratrol synthase.[6]

4. PHARMACOKINETIC PROPERTIES OF RESVERATROL

Even at high doses (like 1000–1500 mg per day), resveratrol is safe for mammals. Generally, taking 100–1000 mg per day is considered safe, according to both animal studies and human trials. While doses up to 5 grams are usually non-toxic, some people may experience mild stomach issues or diarrhoea at dosage of 2 grams taken twice a day.

Micronized resveratrol (a form that is not difficult for the body to absorb) tends to be better tolerated. People absorb about 70% of resveratrol taken by mouth or through an IV. It gets processed in the liver and intestines by specific enzymes that create different forms of resveratrol. At low amounts, the main form is glucuronides, while at higher amounts, sulfates become more common.

Gut bacteria also help produce other forms of resveratrol. In the bloodstream, proteins like low-density lipoprotein and albumin carry resveratrol and its processed forms. It can enter cells easily but might form complexes with other molecules that make it harder for cells to use it.

After taking 25 mg, levels of resveratrol in the blood showed that the processed forms are much more available than the original compound. Even at high doses of 2–5 grams, the total amount in the blood doesn't go above 10 µMicronized resveratrol (5 g per day) showed significantly higher absorption in patients with colorectal cancer compared to regular resveratrol. It resulted in a threefold increase in peak levels in the blood.

Resveratrol is mostly removed from the body through urine in its processed forms. Interestingly, factors like age and gender can affect how resveratrol is metabolized. Studies suggest that taking resveratrol with substances like piperine or quercetin may increase its absorption.[7]

5. PROPERTIES OF RESVERATROL

5.1. Anti-oxidant properties of resveratrol

The term "oxidative stress" describes a state in which there is an imbalance between the generation of free radicals and the anti-oxidant defence mechanism, which increases oxygen radical and damages tissue. Oxidative damage can lead to

ageing, diabetes mellitus, coronary heart disease, rheumatoid arthritis, and other conditions Antioxidant substances or the controlled production of antioxidant enzymes, however, can reverse this effect. Finding a material with antioxidant qualities should be the main goal in order to stop the growth of the disease, even though it is unknown how the oxidative stress response causes the illness.[8]

Free radicals, arising from endogenous and exogenous sources, are pivotal in the pathogenesis of diseases associated with oxidative stress. These reactive species play crucial roles in biochemical processes essential for aerobic life and metabolism. Phenolic compounds, recognized for their natural antioxidant properties, effectively neutralize or scavenge free radicals, chelate metal ions, and inhibit lipid peroxidation.

Resveratrol is well-known for its potent antioxidant properties, primarily attributed to its functional group arrangement. The arrangement, replacement, and number of hydroxyl groups significantly influence its mechanisms of action, including antioxidant and metal ion chelation. Studies indicate that while the hydroxyl group in the 4′ position is important, the 3- and 5-OH groups also play critical roles in its antioxidant activity.

Furthermore, resveratrol has demonstrated protective effects against oxidative stress in cells, particularly against hydrogen peroxide and UV-induced damage. Its cellular defense mechanisms involve direct antioxidant action and the induction of various cellular antioxidant pathways, helping to maintain cellular redox balance.[9]

The dual role of resveratrol as both an antioxidant and a prooxidant has been highlighted, indicating that its effects can vary significantly based on concentration and cellular context. For instance, research by Dudley et al. demonstrated that low doses (5 mM–10 mM) of resveratrol offered cardio protective benefits by acting as an antioxidant, whereas higher doses resulted in a prooxidant effect, contributing to myocardial damage and increased cardiomyocyte apoptosis. This underscores the importance of considering both the dose and the specific cell type when evaluating the therapeutic potential of resveratrol in cardiac health. Further investigations into these dynamics could help optimize resveratrol's applications in clinical settings.[10]

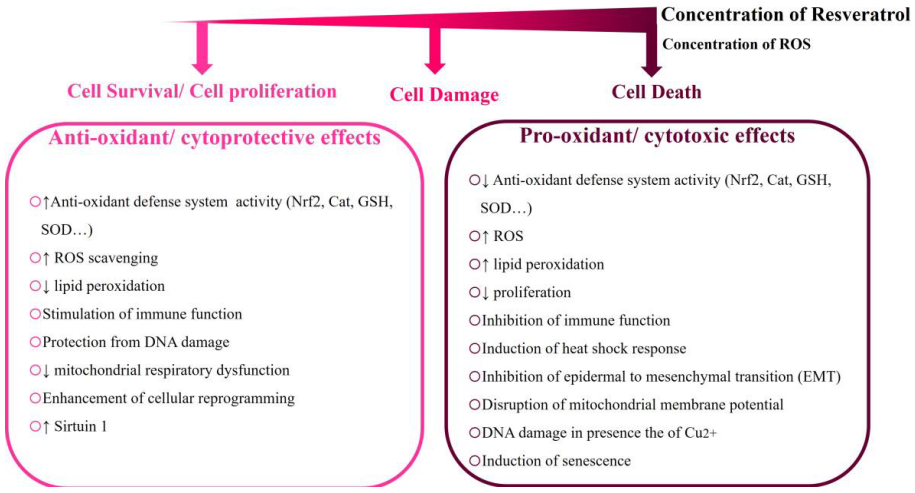

Fig. 4: Biphasic hermetic dose-dependent effects of resveratrol (RE).

5.2. Anti-aging properties of resveratrol

Attractiveness and beauty hold significant value in contemporary society, with facial attractiveness often associated with youthful, smooth, and evenly pigmented skin. These characteristics, however, are significantly influenced by the

aging process. External factors like UV exposure and environmental pollution accelerate skin aging by increasing the production of free radicals—highly reactive oxygen species that can damage living cells. Typically, the skin counters these external threats with a natural defense system involving various enzymes and vitamins to combat oxidative stress. However, prolonged exposure to pollutants can overwhelm this protective mechanism, compromising the skin's resilience.[11]

The anti-aging effects of resveratrol are attributed to its ability to inhibit the phosphorylation of survivin—a protein that prevents cellular apoptosis—along with its mRNA. Resveratrol also blocks the activity of various cellular components, including Cyclin-dependent kinases 2, 4, and 6, nuclear factor kappa B, cyclins D1 and D2, matrix metalloproteinases, IκB kinase Rα, MAPKK, and MAPK. This polyphenol further diminishes skin edema and inflammation by inhibiting the migration of white blood cells in response to UV-B radiation. The isobutyrate and butyrate forms of resveratrol are considered as productive for skin, as they significantly reduce inflammatory cytokines (e.g., interleukin 6 and interleukin 8), increase levels of collagen A1, tissue inhibitors of matrix metalloproteinase 1, and fibrillin 1 (levels unaffected by pure resveratrol), and decrease matrix metalloproteinase 9 through gene modulation. Additionally, resveratrol influences aging biomarkers, including nerve growth factor, calcium-binding proteins A8, A9, and S100, proliferating cell nuclear antigen, and 5α-reductase. The polyphenol also slows skin aging by exhibiting antioxidant properties that inhibit Bcl-2 phosphorylation, and reduce cell adhesion kinase, hydroperoxide, in addition to B and C protein kinase activity.[12]

Polyphenol also plays a role in speeding up wound healing and regeneration, minimizing scarring, and reducing scar size. This effect is due to an increase in endothelial growth factors, which in turn helps to bring the wound edges closer together. Aging is influenced by various factors affecting the body, with key features including the buildup of oxidative stress, chronic low-grade inflammation, and cell apoptosis. Furthermore, growing research highlights the function of mitochondrial abnormility and an imbalance in gut microbiota in driving oxidative damage and influencing cellular longevity.[15]

5.3. Anti-cancer properties of resveratrol

In many literature reports the anticancer effects of RSV has shown.In fact RSV shows its anticancer effects through various mechanisms of action. Its ability to function on multiple targets has contributed to its usefulness as an anticancer agent; in combination with other therapies (chemotherapeutics and radiotherapy).

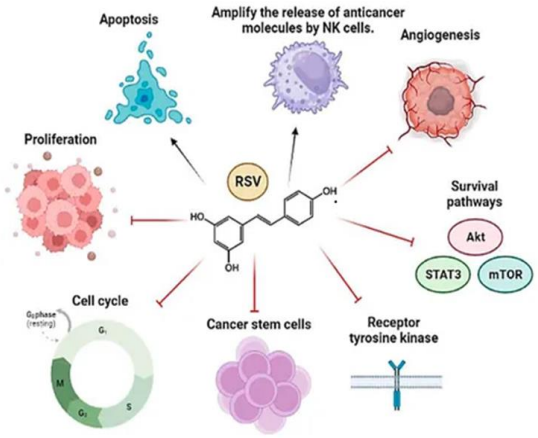

Fig. 5: Effects of Resveratrol in Cancer.

In addition, it has been seen that RSV protects healthy cells from the unfavourable effects of conventional agents. Therefore, its ability as an anticancer agent is quite attractive. RSV targets in carcinogenesis are shown in Figure 3.[14]

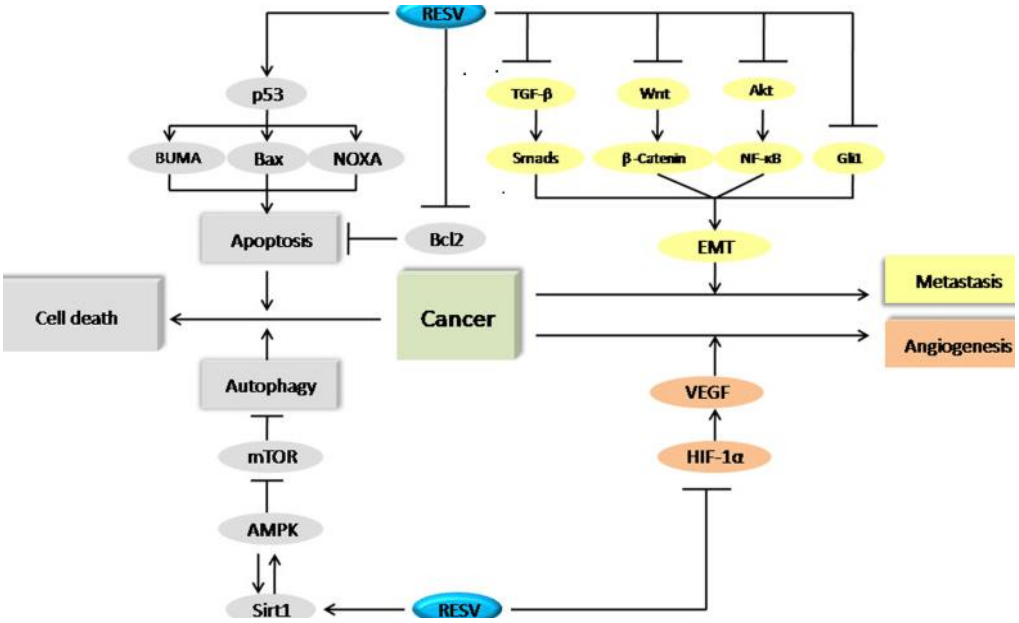

Fig. 6: Common mechanism of resveratrol in management of cancer.

Cancer is one of the root cause of death in globe. Radiotherapy and chemotherapy are standard first –line treatments for cancer patients, despite their huge side effects most cancer cells become resistant to both radiotherapy and chemotherapy. This took researchers to look for more different alternatives with less side effects. Due to its ample biological effects, RSV, a naturally occurring polyphenolic phytoalexin, has gained a lot of observance. Several mechanisms contribute to the therapeutic action of RSV, they are:[13]

1. Resveratrol induces autophagy
2. Resveratrol induces apoptosis
3. Resveratrol inhibits metastasis
4. Resveratrol inhibits angiogenesis

5.4. Anti-inflammatory properties of resveratrol

Resveratrol is gaining attention in field of nutrition and medicine for its probable health benefits. Resveratrol shows that trans-resveratrol shows powerful anti-oxidant ,inhibiting lipid peroxidation of LDL(low density lipoprotein).it also makes cells safe from oxidative damage, reduces the cytotoxic effects of oxidized LDL, and lowers the tumour promotion activity by inhibiting cyclooxygenase -1(COX-1)and platelet aggregation. These properties suggest a promising role of resveratrol in cardiac health and cancer prevention.[16]

Many studies have indicated that the development of diseases such as cancers, neurodegenerative, respiratory and heart diseases are caused by the chronic yet low-grade inflammation of cells. These studies have discovered the cellular and microscopic level mechanisms of underlying inflammation, but to date, no therapeutic therapies have been discussed. Interaction with multiple targets and alteration of the deregulation inflammatory pathways as well as mediators of phytochemicals suggested a potential for the expansion of an affordable, novel and safe drugs to treat inflammation underlying chronic disease. Resveratrol, is a polyphenol that has gained interest purported to protect inflamed cells by

directly and indirectly modulate major signalling pathways. Preclinical studies have shown some positive results, although there is small clinical evidence that demonstrates its effective therapeutic effect in humans considering resveratrol has poor water solubility and bioavailability. Nevertheless, resveratrol 'favorable in ameliorating inflammation in patients with chronic diseases should not be denied and should be confirmed in in-depth scientific investigations and large-scale clinical trials.[17]

Resveratrol's protective effects may be attributed to its ability to reduce inflammation by suppressing the production and liberation of provocating molecules. This is achieved through various mechanisms, including: Inhibiting the synthesis of pro-inflammatory mediators Modifying eicosanoid synthesis Suppressing the activity of immune cells Inhibiting enzymes such as COX-1 and COX-2, which are involved in the generation of provocating mediators Interfering with transcription factors like NFκB and AP-1, which regulate the formation of inflammatory genes Despite its limited bioavailability and rapid clearance from the bloodstream, resveratrol has shown promise as a probable substitute to anti-inflammatory drugs. This review aims to provide evidence of resveratrol's anti-inflammatory effcts and explore the underlying mechanisms that contribute to its cardioprotective effects. While the cardioprotective effects of RSV are probably linked to its anti-inflammation properties, this review will focus on the mechanisms that drive its anti-inflammatory activity, which in turn contributes to its cardioprotective effects.[18]

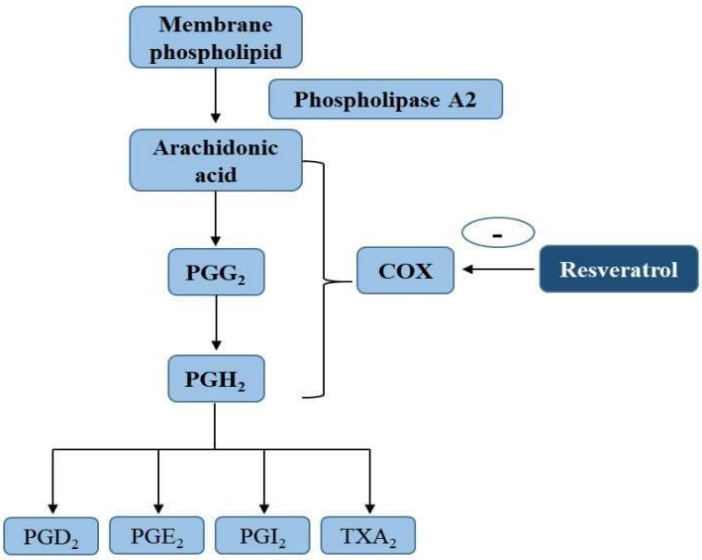

Fig.7: Inhibition of arachidonic acid metabolic pathway by resveratrol.

5.5. Mechanism of resveratrol on cardiovascular diseases

Cardiovascular diseases can lead to heart failure, a condition where the heart muscle weakens and loses its ability to function properly, ultimately causing the heart to fail to meet the body's energy and metabolic needs. Research has explored the potential of RSV to reduce inflammation in heart failure using animal models. Heart failure can be caused by acute myocardial ischemia/reperfusion injury, and resveratrol (RSV) has demonstrated to have anti-inflammatory effects on this type of injury. A recent study found that RSV decreased coronary infarction areas and inflammation in a mockup of heart attack, and that these effects were dependent on the nitric oxide and cyclic guanosine monophosphate pathways. Additionally, RSV was found to reduce the formation of inflammatory genes, including NF-κB and TLR4, which are involved in innate immune responses. These findings are consistent with previous research manifest that resveratrol safeguards cardiac muscle cells in opposition to anoxia/reoxygenation wound through the TLR4/NF-kappa

B signaling pathway. Furthermore, hypertension is a risk factor for heart failure, and RSV administration has been demonstrated to reduce inflammation in spontaneously hypertensive rats. However, RSV did not lower blood pressure in these animals. These results advised that combination of resveratrol with antihypertensive agents may be an effective plan for overturn cardiac problems in high blood pressure victims.

Causes of Atherosclerosis

I. Arterial inflammation
II. Lipid accumulation in vessel walls
III. Plaque formation
IV. Thrombosis
V. Late complications: myocardial infarction and ischemic stroke
VI. Importance of Anti-Inflammatory Treatments

Given the crucial character of inflammation in fat deposition, anti-inflammatory treatments like RSV may offer a promising approach to controlling the disease.[19]

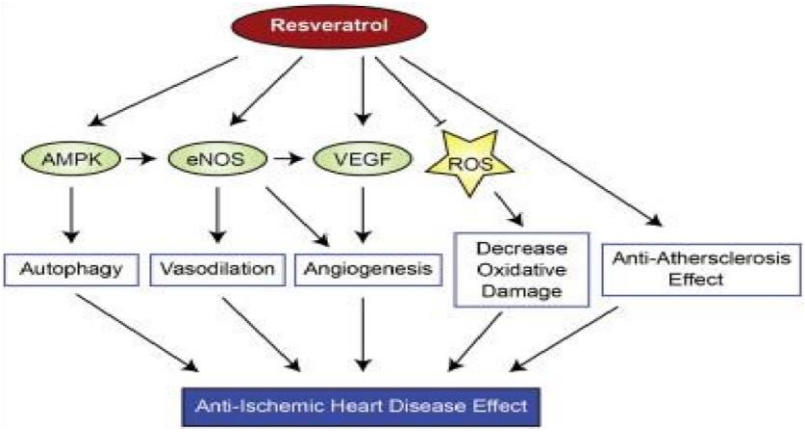

Fig. 8: Mechanism of resveratrol on cardiovascular diseases.

5.6. Mechanism of resveratrol in respiratory diseases

Apoptosis, or programmed cell death, plays a key role in various respiratory diseases, including asthma, airway inflammation, acute lung injury, and lung cancer. Free radical, a natural byproduct of cellular metabolism, can induce cell death when present in excess. However, SIRT1, an enzyme, can reduce ROS levels and promote cell activity. Resveratrol, a polyphenol, has been displayed to upregulate SIRT1, reducing ROS production, maintaining cell membrane potential, and inhibiting apoptosis in alveolar epithelial cells. This leads to a reduction in hyperoxia-associated lung injury. . The antiapoptotic effects of resveratrol have been demonstrated in various studies, including: Reducing lung injury and apoptosis in mice with paraquat-induced acute lung injury by inhibiting NF-κB p65 translocation and cytokine production.

Exhibiting protective effects in a rat model of chronic bronchitis by reducing endoplasmic reticulum stress-induced apoptosis in alveolar epithelial cells. Preventing mitochondrial dysfunction and upregulating MFN2 in human bronchial epithelial cells, thereby reducing apoptosis. Improving mitochondrial function and inhibiting apoptosis in the lung, both in vitro and in vivo, when used as a dimer (Vam3).

Reducing sodium arsenite-induced oxidative and genetic damage, also apoptosis, by regulating glutathione homeostasis in human bronchial epithelial cells.

Protecting lung function by inhibiting apoptosis in rats with severe acute pancreatitis. Attenuating apoptosis in pulmonary microvascular endothelial cells (HPMEC) activated by high tangential stress with proinflammatory factors, by activating the SIRT1 signaling pathway and inhibiting oxidative-stress-dependent phenotypical shift. Overall, RSV has representated to have ant apoptotic effects in various respiratory diseases, making it a potential therapeutic agent for the healing of these conditions.[20]

5.7. Mechanism of resveratrol on microglia-mediated neuroinflammation

Research has shown that neuroinflammation plays a key role in the development of various neurological disorders, including traumatic injuries, stroke, depression, and neurodegenerative diseases. The key indicator of neuroinflammation is the activation of microglia, the immune cells that serve as the first line of defence in the nervous system (NS). Under normal conditions, microglia maintain homeostasis in the CNS by removing toxins and dead cells. However, when activated, microglia undergo changes in shape and function, leading to the release of pro-inflammatory factors that can damage neurons. These factors include prostaglandins, chemokines, cytokines, and reactive oxygen species. Inhibiting microglial activation may be a promising approach to treating neurological disorders related to inflammation.[21]

5.7.1. Suppression of mapk pathways in mammalian innate immunity

The mammalian innate immune system recognizes bacterial components, such as lipopolysaccharides (LPS), through specific Toll-like receptors (TLRs). This recognition enhancing the activation of the MAPK and NF-κB cascade signalling pathways. The MAPK pathway, particularly ERK1/2, p38, and c-Jun-N-terminal kinase (JNK), plays a crucial role in the signal transduction cascades responsible for increased TNFα and inducible nitric oxide synthase (iNOS) expression in glial cells.

LPS and oxidative stress activate MAPKs, leading to increased TNFα and iNOS expression in glial cells. subcellular free radicle induce the activation of MAPK cascades and the NF-κB pathway in activated microglia. The ROS-scavenging enzyme catalase and the inhibitor of NADPH oxidase prevent the activation of MAPK and NF-κB pathways.

5.7.2. NFκB and sirt1 pathways

NF-κB is a transcription factor that regulates the generation of pro-inflammation factors, including NO, TNFα, and interleukin-1β (IL-1β). In response to inflammatory stimuli, NF-κB is released from its inhibitors, IκBs, and translocate to the nucleus, balancing the formation of target genes.

Resveratrol decreases the stimulation of the NF-kappa B pathway in Lipopolysaccharide-activated microglia by diminishing the acetylation and destruction of kappa Bα. Resveratrol reduces the formation of subsequent genes, including TNFα, iNOS, IL-1β, and IL-6Resveratrol exhibits neuroprotection through the activation of Sirtulin 1, which protects against oxidative stress and microglia-dependent Aβ toxicity.

5.7.3. Reduction of pro-inflammatory factors

Activated microglia release a more amount of pro-inflammatory factors, including TNFα, IL-1β, and NO, which can not only affect the immune system but also harm neurons. Inhibiting Pro-inflammatory factors can help combat inflammation-related neurological disorders. Research has shown that resveratrol can inhibit the production of pro-inflammatory factors such as NO, TNFα, PGE2, and IL-1β in microglia activated by LPS. Additionally, studies have found that resveratrol can reduce the overexpression of TNFα, IL-1β, IL-6, COX-2, and iNOS in primary midbrain neuron-glia cultures Resveratrol inhibits the generation of provocative factors in microglia. Resveratrol reduces the overexpression of pro-inflammatory genes in neuron-glia cultures. Resveratrol's Neuroprotective effects are mediated by: Attenuating reactive oxygen species production. Suppressing MAPK and NF-κB cascade signalling pathways. Inducing Sirt1.[22]

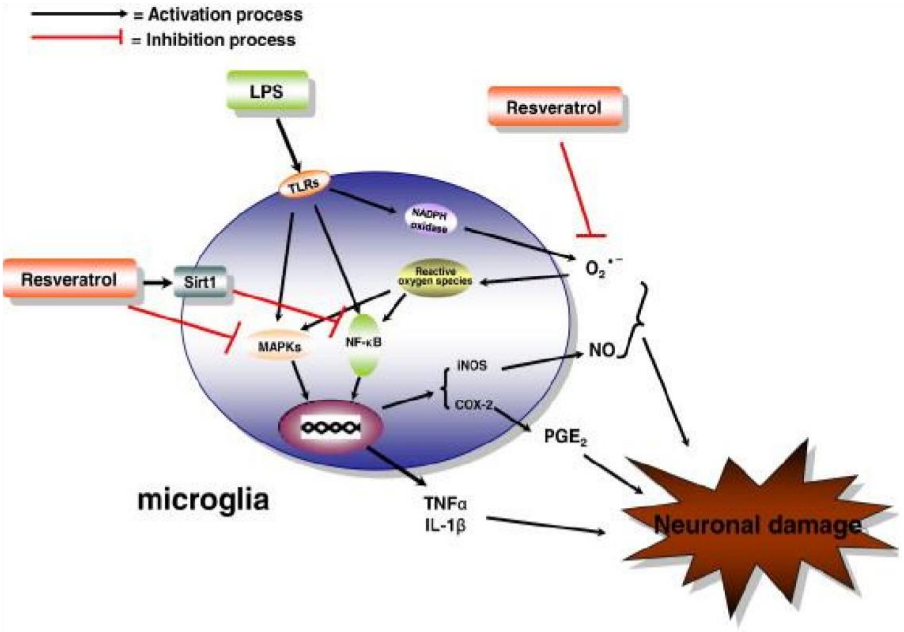

Fig. 9: Anti-inflammatory effect of resveratrol on LPS-induced microglia activation.

5.8. Anti-viral effect of resveratrol

In vitro, resveratrol appears to boost the effectiveness of certain antiretroviral medications against HIV. Nuclear Factor ÎºB (NF-ÎºB) is a cell protein that is typically activated by herpes simplex virus infection. In Vero cells, a study conducted by North-eastern Ohio Universities College of Medicine discovered that resveratrol inhibits the activation of this protein linked to transcription and apoptosis. The study also discovered a decrease in the generation of viral DNA and a reduction in or full blockage of certain viral protein products.[23]

5.9. Anti-diabetes effect of resveratrol

Diabetes is a long-term medical illness characterized by high blood sugar levels that is caused by either insufficient insulin synthesis or inefficient insulin utilization by the body. By stimulating the development of pancreatic β-cells and increasing insulin production, resveratrol lowers elevated blood sugar levels. In order to restore and maintain glucose balance, the enhanced insulin release enables either the storage of surplus glucose as glycogen or its use by tissues.[24]

5.10. Antibacterial properties of resveratrol

Another feature of resveratrol is that it prevents harmful Gram-positive and Gram-negative bacteria and fungi from becoming planktonic. Research shows that resveratrol efficiently stops Candida albicans from growing. Dimethoxy resveratrol derivatives have antifungal action against eleven distinct species of Candida and a minimum bactericidal concentration (MBC) of 29 to 37 μg/ml against Candida albicans.[25]

5.11. Anti-obesity effect of resveratrol

By lowering metabolic rate, triggering AMPK in muscle, and raising SIRT1 and peroxisome proliferator-activated receptor gamma coactivator 1 alpha protein levels, RV replicated the reaction of calorie limitation. Along with lowering the liver's fat content, circulating dextrose, triglycerides, AAT, and other indicators of inflammation, RV also boosted citrate synthase activity. Following the intervention, the equilibrium model assessment index also improved. Obese or plump patients received supplements of RV and epigallocatechin-3-gallate (0.08 and 0.28 gm/day, resp.) throughout the course of 12 weeks in order to examine the longer-term impact of certain polyphenols on the digestion profile. Along with improved skeletal muscle oxidative capability, there was also an improvement in mitochondrial capacity and fat oxidation stimulation. Triacylglycerol concentration did not alter during RV treatment, in contrast to the placebo group, due to the preservation of fasting and postprandial fat oxidation; however, auxiliary, liver, or adipose tissue insulin resistance did not improve.[26]

5.12. Intestinal effects of resveratrol

Reduced occludin and zonula occluden (ZO-1) expression and phosphorylation, as well as enhanced decompose in Caco-2 cells and the duodenal epithelium, are linked to intestinal hyper permeability. Regarding this, Wang et al.'s research has shown that resveratrol administration raises occludin and ZO-1 phosphorylation and epithelial expression in a concentration-vulnarable manner. Resveratrol has also been shown to increase the generation levels of superoxide dismutase and heme oxygenase-1 (HO-1), decrease the levels of malondialdehyde and intracellular reactive oxygen species, and protect Caco-2 cells from oxidative harm caused by H2O2. 151 It can also prevent p38 phosphorylation and H2O2-induced protein kinase C activity. Additionally, other researchers discovered that 20 μM of resveratrol substantially increases NO production in endothelial EA. hy926 and Caco-2 cells, and dramatically reduces intercellular adhesion molecule-1 (ICAM-1), VEGF, ROS, and IL-8 in TNF-α-activated endothelial cells.[27]

6. RESVERATROL INTERACTIONS

6.1. Interaction with cytochrome p450

Patients on generic medications frequently consume natural items, increasing their chance of coming into contact with both pharmaceuticals and natural products. A number of medications can interact with resveratrol. When consumed in high dosages, it may cause interactions with other cytochromes P450 (CYP). This polyphenol can also be advantageous or detrimental because it has demonstrated to have strong interactions with phase I and II enzymes both in vitro and in vivo. It is now well acknowledged that the transport function is transformed in addition to digesting enzymes. P-glycoprotein (P-gp), multidrug-resistant protein (MRP2), and organic anion transporter 1/3 (OAT1/OAT3) have indicated to be significantly inhibited by resveratrol. Nevertheless, resveratrol's interaction with carriers is still somewhat evident. Furthermore, a number of clinical investigations were carried out to identify the resveratrol-drug interaction. However, it is also thought that large resveratrol dosages engage with other polyphenols of transporters, decreasing their detection as well as any possible confounding effects. Furthermore, as necessary for the prediction of

resveratrol-drug interactions, the human absorption, distribution, kidney elimination, and/or liver elimination of active resveratrol compounds have not been sufficiently assessed. Consequently, the impact of resveratrol reuptake on transporter-drug interactions validates additional research.

6.2. Interaction with antiplatelet and anticoagulant drugs

In vitro, resveratrol has represented to prevent human platelet aggregation. Given that taking supplements containing high levels of resveratrol can raise the risk of bleeding and damage when combined with anticoagulant, antiplatelet, and even non-inflammatory medicines (NSAIDs) such aceclofenac and diclofenac.[28]

7. CONCLUSION

In conclusion, Small and affordable, resveratrol is simple to get and functionalise. It can be employed for commercial reasons due to its low toxicity and various biological activity. This study examines research on the latest developments in resveratrol, emphasising its plant sources, production techniques, stability, modification, and possible medicinal uses.

Due to their low cost and little side effects, natural products and the compounds obtained from them are currently gaining enormous popularity worldwide in place of conventional and modern pharmaceuticals for the cure of numerous ailments. These phytonutrients have been shown in numerous experiments to be effecacious in treating a wide range of pathological conditions and diseases, such as diabetes, cognitive impairments, depression, anxiety, inflammation, hypertension, hepatic disorders, asthma, pain, cancer, and skin diseases. Resveratrol is a stilbene-class polyphenol that is not a flavonoid. Its beneficial effects, particularly on cardiovascular illnesses, cancer, type 2 diabetes, and neurological disorders, have been demonstrated by recent studies. Numerous research investigations on resveratrol will persist as our comprehension of its advantageous impacts on health expands.

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