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RESVERATROL IN TREATMENT OF CANCER: MACHANISM, EFFICACY AND FUTURE DIRECTION

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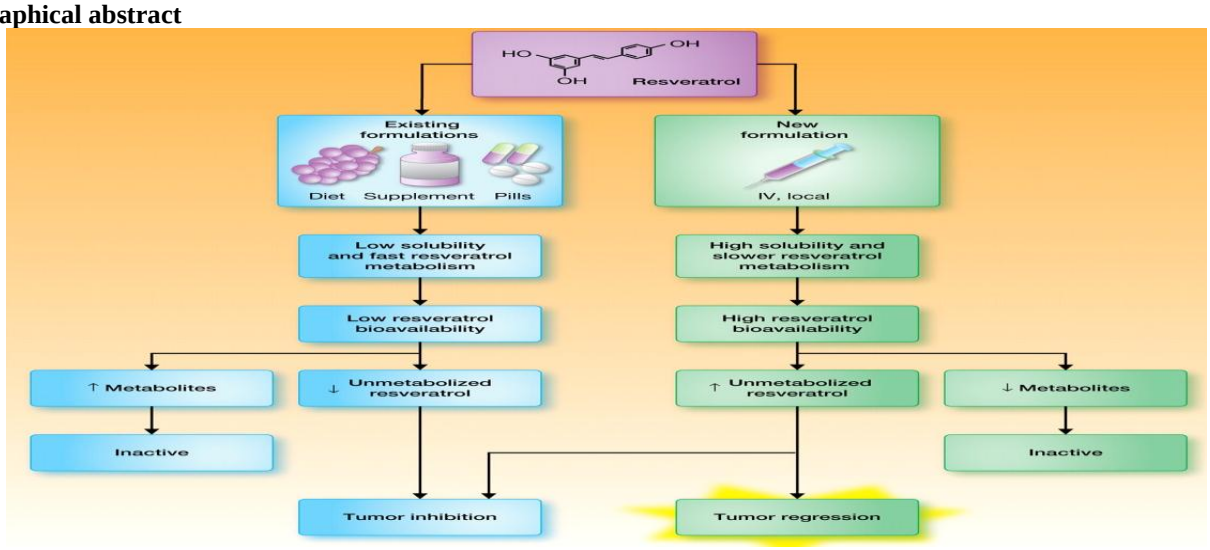
ABSTRACT

Resveratrol a polyphenolic compound primarily find in grapes, berries, and peanuts, has emerged as a promising agent in cancer research due to its potential anticancer properties. Pathway in a process similar to that of flavonoids. Resveratrol comes in both cis and trans isomeric forms, with trans-resveratrol seemingly being the more prevalent and stable natural form. It has two phenol rings (Monophenol and diphenol) joined by a double styrene link. Three hydroxyl groups in this molecule are engaged in metal chelation and free radical scavenging. Additionally, hydroxyl groups make it easier to interact with macro molecules. This article looks into the several ways resveratrol works to prevent cancer, such as by preventing the growth of cancer cells, causing them to die, and altering important signaling pathways such the PI3K/Akt and MAPK pathways. Preclinical research has state that resveratrol is effective against a number of cancer types, such as colorectal, prostate, and breast cancers, suggesting that used as an adjuvant treatment in addition to traditional therapy. Moreover, resveratrol has shown the ability to enhance the result of chemotherapeutic agents while reducing their associated side effects, indicating its dual role in improving therapeutic outcomes. Its impact on the tumor microenvironment, suppression of angiogenesis, and reduction of metastatic spread further accentuates its therapeutic promise. However, challenges such as low bioavailability and limited clinical data hinder its widespread application in oncology. This review emphasizes the need for rigorous clinical trials to assess the efficacy and safety of resveratrol in cancer treatment. By synthesizing current findings and identifying research gaps, this paper aims to provide a comprehensive overview of resveratrol's role as an anticancer agent. Ultimately, the insights gained could contribute to the increasing of innovative cancer treatment strategies, potentially improving patient outcomes and advancing the term of oncological pharmacotherapy.

KEYWORD:- Natural compounds cancer therapy**,** Resveratrol experimental trials cancer, Resveratrol clinical trials cancer, chemo preventive, Polyphenols compound, cancer therapy.

Graphical abstract



1. INTRODUCTION

Resveratrol (3,5,4-trans-trihydroxystilbene) is a phyalexin with polyphenolic properties that belongs to the stilbene family. This natural compound is predominantly found in grape skins and seeds, but it also used in wines and a of other plant foods, particularly in peanuts, berries, and tea. Over 70 plant species produce resveratrol in answer to conditions such as infection, stress, injury, bacterial or fungal attacks, and UV exposure. The creation of this compound in plants is driven by the enzyme resveratrol synthase within the phenylpropanoid way, a process akin to the production of flavonoids. Resveratrol features two phenolic rings (a monophenol and a diphenol) connected by a double bond, current in both cis and trans isomer forms, with trans-resveratrol being more prevalent in nature. This molecule contains trio hydroxyl groups, contributing to its capability to scavenge free radicals and chelate metals. Additionally, the hydroxyl groups enhance its interaction with macromolecules.[1]

At first, resveratrol was described as a phytoalexin, an antibacterial compound that plants produce in reaction to infection. Resveratrol was the subject of several groundbreaking studies, one of which examined how it inhibited the breakdown of arachidonate by interfering with the leukocytes' cyclooxygenase (COX) and 5-lipoxygenase pathways.6) But until 1992, when it was hypothesized to reason for one of the cardioprotective benefits of wine, resveratrol garnered little attention.[2] Since then, Several investigations have shown that resveratrol can improve stress resistance, lengthen longevity, and prevent or reduce progression of a number of disorders, such as cancer cardiovascular diseases, and ischemia injuries (8–12).[3] Numerous direct targets of resveratrol have been identified as a result of nearly universally successful attempts to show positive effects in vitro. The effects of resveratrol on endothelial nitric oxide synthase (e NOS), peroxisome proliferator activated receptor (PPAR), and COX are covered in this article.[4]

1.1 Introduction and Basic Concepts of Cancer

Generally speaking, cancer is a wide category of illnesses that can impact any organ in body. With a projected 14.1 million cases also 8.2 million losses in 2012, it is major causes of illness and mortality worldwide.[1,5] cancer would increase by almost 70% concluded the next 20 years (WHO, 2017). It's interesting to note that the occurrence of cancer varies greatly throughout the world. The results displayed that cancer incidence rates are generally lower in the least developed regions and higher in middle-income countries (around 200 cases × 10-5 persons). According to global figures from 2012, colorectal cancer (0.7 million), stomach cancer (0.6 million), liver cancer (0.5 million), lung cancer (1.2 million), and prostate cancer (1 million) were the most common cancers in men. Aimed at women, the following cancers are prevalent: stomach cancer (0.3 million), lung cancer (0.6 million), colorectal cancer (0.6 million), cervical cancer (0.5 million), besides breast cancer (1.6 million). While breast, colorectal, lung, and endometrial cancers are common in low-income countries, prostate, liver, esophagus, and lung cancers are normal men and breast, cervical, ovarian, and esophageal cancers are common in women. In very-high-income countries, prostate, lung, colorectal, and bladder cancers are common in men.[6]

2. Types

A. Carcinoma

About 80–90% of all cancer cases are arcinoma, or malignancies of epithelial tissues, which typically affect organs or glands that can secrete, including the breast, lung, colon, prostate, bladder, etc. It could be either adenocarcinoma.[2,7]

B. Sarcoma

Sarcoma is another type of cancer who originates in connective and supporting tissues, including bone, tendons, cartilage, muscle, and fat. Sarcomas include osteosarcoma, chondrosarcoma, leiomyosarcoma, and others.[7]

C. Myeloma

Myeloma is related with the overproduction of immature white blood cells and starts in bone marrow plasma cells. For instance, lymphatic, lymphocytic, lymphoblastic, granulocytic, or myelogenous leukemia, among others.

D. Lymphoma

Often stated to as "solid cancers," lymphomas arise in the lymphatic system's glands or nodes that are complex in the creation of lymphocytes and the purification of body fluids.[6]

3. Global burden of cancer

The most recent period for which prevalence and humanity data are accessible is two to four times behind schedule the current period due to the time essential for data collecting, gathering, compilation, and dissemination. In order to quantify the current cancer burden, we use two-step statistical modeling, as detailed elsewhere, to anticipate the number of new cancer cases and deaths in the United States in 2023. Different SDI regions had distinct changes in etabolic variables. In 2019, the ASDRs were 14.42, 12.23, 9.38, 6.23, and 5.14 per 100,000 persons, respectively, sum of cancer deaths from metabolic variables ranging from high to low SDI regions was 0.28, 0.25, 0.23, 0.08, and 0.02 million (numbers 2B, C). The death problem is easily advanced in advanced SDI regions than in lower SDI regions. Nonetheless, lower SDI regions have seen a more notable growth trend over the last 30 years. The AAPCs of the ASDR were 0.42, 0.58, 1.51, 2.36, and 1.96, independently, while the shift in mortality rates from high to low SDI regions was 108.72, 135.7, 288.26, 375.34, and 288.32.[8]

3.1 Estimated Number* of Sex-Related Deaths and Novel Cancer Cases, US, 2023
Projected new cases estimated deaths
Table 1

All sites	Both sexes	Male	Female	Both sexes	Male	Female
Respiratory tract	256,290	131,150	125,140	132,330	71,170	61,160
Larynx	12,380	9,900	2,480	3,820	3,070	750
Lung & bronchus	238,340	117,550	120,790	127,070	67,160	59,910
Digestive system	348,840	194,980	153,860	172,010	99,350	72,660
Liver	41,210	27,980	13,230	29,380	19,000	10,380
Esophagus	21,560	17,030	4,530	16,120	12,920	3,200
Stomach	26,500	15,930	10,570	11,130	6,690	4404
Breast	300,590	2,800	297,790	43,700	530	43,170

1Estimated Number Cancer Death Cases and Cases by Sex, US, 2023*

4. What Percentage of People Survive Cancer?

Relative survival, which compares the life expectation of cancer cases to that of the general residents of the same age, race, and coitus, is generally used to characterize cancer survival.8. Meanwhile the early 1960s, the 5- time relative existence rate for all malice combined has significantly increased, rising from 27 to 64 for Black people and from 39 to 69 for White people. increases in survival.[9]

5. Expected number of cancer expiries

In 2023, a projected 609,820 Americans will lose their lives to cancer, or 1670 losses every day. Cancers of the lung, bone, and colorectum in women and the lung, prostate, and colorectum in males regard for the maturity of losses.10. gives the approximate number of deaths by state from these and other common malice. Lung cancer kills about 350 people per day, which is over 2.5 times further than number of expiries from colorectal cancer (CRC), the alternate most general cause of cancer-related deaths. Of the 127,070 lung cancer losses (81) that will do in 2023, nearly 103,000 will be directly related to cigarette smoking, while another 3560 will be due to secondary bank.35 If classified collectively, the remaining balance of about 20,500 lung cancer deaths that are n't related to smoking would be the seventh most simples cause of cancer deaths for both relations combined.[10]

6. Treatments and Prevention of cancer

The conventional methods of treating cancer include surgery, chemotherapy, radiotherapy, and, if applicable, immunotherapy, either separately. There are strategies to prevent the development of a tumor before receiving cancer treatment. According to reports, nutrition and diet play a key role in the expansion or reduction of cancer risk, and by taking preventative measures, 30% to 40% of cases might be averted.[11]

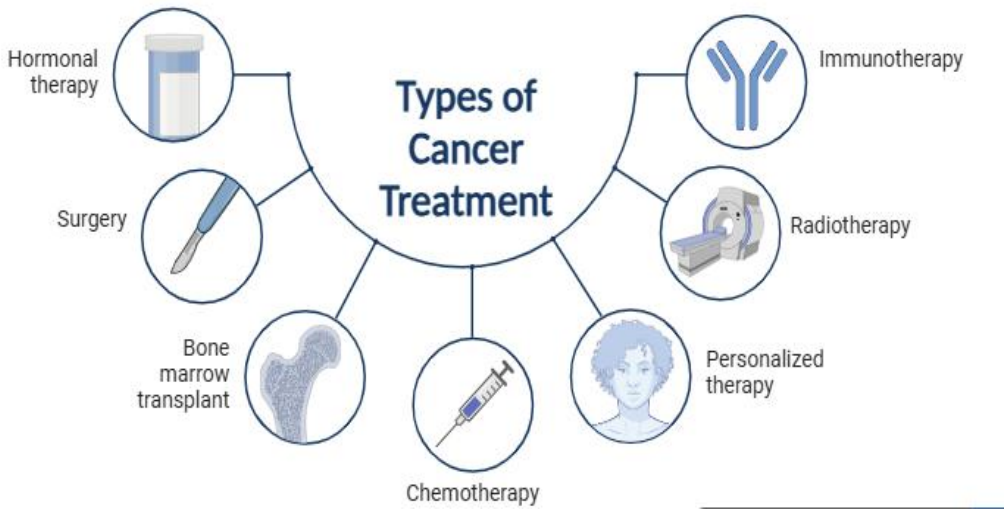


Figure 1

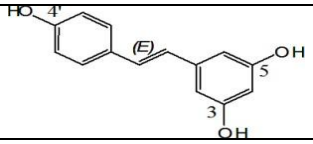
It's interesting to memo that studies in epidemiology, medicine, preclinical research, and experimentation show that diet particularly the Mediterranean diet can prevent stomach cancers. Omega-3 fatty acids, fibers, and polyphenols (including resveratrol) seem to the most protective elements.[12]

Table 1: Source of resveratrol.

Natural Sources	Trans-RSV Concentration (µg/g)
Hops	0.50 ± 0.05
Peanuts	5.10 ± 2.85
Peanut butter	0.30 ± 0.10
Grape skin	**27.50 ± 1.30**
Itadori root (*Polygonum cuspidatum*)	523 ± 1

7. Resveratrol Polyphenols: A brief overview

Table 2: Properties of resveratrol.

Molecular Formula	$C_{14}H_{12}O_3$
Structural Formula	
Systematic Name	5-[(E)-2-(4-hidroxyphenyl)-ethenylbenzene-1,3-diol
Other Names	Trans-resveratrol Trans-3,5,4'-trihydrozystilbene 3,4',5-stilbenetriol (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℃
Physical Structure	White – Solid
Solubility	Easily dissolves in water, methanol and acetone.

Three CoA molecules and one 4-cuamoryl CoA molecule combine to make resveratrol. it's key that the enzyme required for resveratrol synthesis is not active and becomes active in replay to a stressor.[13]

A secondary metabolite that is produced as a defense against a kind of external stressors, resveratrol is most prevalent in the product made by drying the part of Polygonum cuspidatum, also known as Konjo-Kon Itadori tea or Konjo-Kon, a plant that has long been utilized in China and Japan.[14]

Studies on resveratrol and derivative stilbene compounds have revealed that it can also be create in other herbal sources, mostly in grape and grape products. In addition to fruits, resveratrol was found in high concentrations in peanuts, peanut oil painting, blueberries, and strawberries. It was also found in dark chocolate, chocolate liqueur, and hop factories used to make beer.

7.1 Synthesis of resveratrol

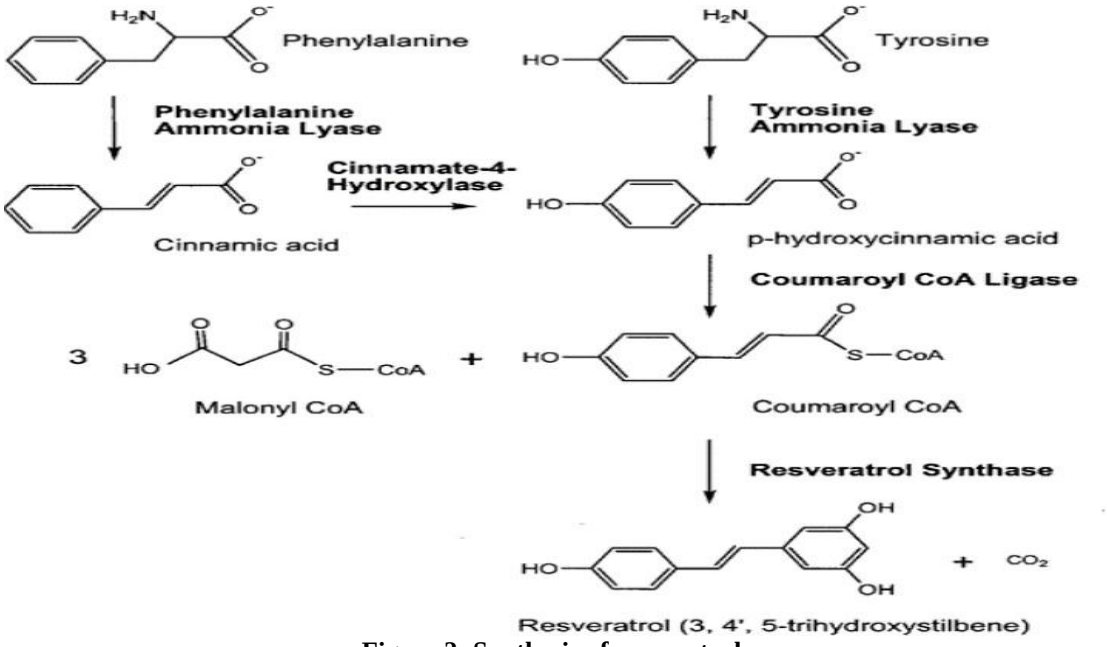


Figure 2: Synthesis of resveratrol.

7.2 The belongings of resveratrol on health

Chemical complexes with one or further unmatched electrons in their external orbitals are known as free revolutionaries.[15] Even though oxidation or reduction reactions in organisms produce reactive chemical compounds, extrinsic sources like radiation, UV light, air pollution, fossil fuel combustion products, some insecticides, herbicides, viruses, diseases, and medications can also produce them. Free radicals induce aging and pathological diseases they are not removed from an organism. Antioxidants change the structures of free radicals and/or lessen their possessions on the body and food, which considerably slows down or delays oxidation reactions. The Heart protective, antithrombotic, antioxidant, anti-inflammatory, blood sugar-lowering, and anticancer properties of resveratrol have been highlighted in a number of research.[16] There are two distinct isomeric forms seen in nature, although investigations have that the trans form is more significant and permanent. Trans resveratrol more potent cardioprotective and antioxidant benefits, and it possesses distinct biological characteristics. Sufficient levels of antioxidant enzymatic activity can stop the body from developing cancer.[14]

7.3 Absorption and bioavailability

Oral dosages of 25 mg,3,4—equivalent to a moderate quantity of red wine—were used in two of the earliest human studies on the absorption besides of resveratrol. Finding unmetabolized resveratrol in the circulating plasma was challenging, despite the use of highly sensitive and molecularly specific analytical techniques. It was expected that peak levels of fewer than 10 ng/mL would appear 0.5–2 hours after the oral dose.[17] Resveratrol's oral bioavailability was very low, as evidenced by estimates of resveratrol-plus-total-metabolite plasma concentrations that were significantly higher, at 400–500 ng/mL (≈2 μM), 3, 4. In the ongoing study of the absorption and bioavailability of dietary resveratrol, the two studies' strong agreement highlighted the use of radioactive doses and liquid chromatography (LC), unlabeled doses and liquid chromatography/mass spectrometry (LC/MS), or gas chromatography mass spectrometry (GC)/MS as the preferred techniques.[18]

8. Cancer: Complex disease

Cancer can under stood as a strong procedure that is inherent to human growth, while being a chronic degenerative disease. Since cancer is thought to be hereditary disease, traditional research has concentrated on identifying the genetic abnormalities that cause it.[17,19] Because it ignores the many processes involved in determining phenotypes from a particular gene, this genocentric approach has inherent limitations. It has proved in systems biology that the dynamics of a complex gene regulatory network (GRN) underlie cell lineage commitment and differentiation.[20]

8.1 Hallmark of cancer or their molecular mechanisms

The vital reasons of mortality globally, cancer claimed 7.6 million lives in 2008, or 13% of all fatalities.45 For case, the lifetime risk of getting cancer in the U.S is approximately 44% for males and 38% for women. Exact roots of cancer are unknown, well-known risky factors include radiation, infections, obesity, alcohol and tobacco misuse, and a sedentary lifestyle.[21] Despite being a diverse gathering of illnesses, "cancer" is considered by the growth of aberrant cells that proliferate beyond their normal limits. The six features of tumor that Hanahan Weinberg and Hanahan outlined in 2000 collectively constitute the basic idea behind this malignant change.47 Normal cells gradually proceed to the neoplastic stage because tumor formation is a multi-step process, and during this time, they develop specific abilities that make them carcinogenic. These fundamental, unique, and supplemental signature abilities include: (1) maintaining proliferative signaling; (2) avoiding growth suppressors; (3) permitting replicative immortality; (4) initiating attack and metastasis; (5) promoting angiogenesis and (6) avoiding cell death. Significant advancements in cancer research over the past ten years have improved our comprehension of these distinctive qualities while also causing changes and, eventually, extensions of the original idea.[22]

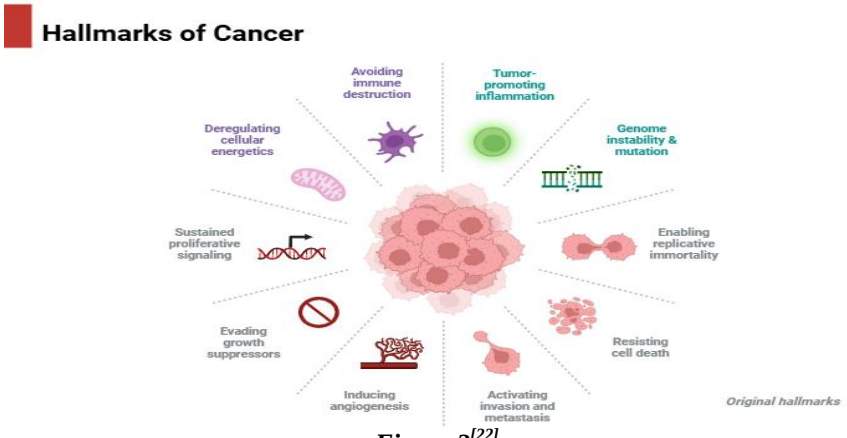


Figure 3[22]

8.2 The part of environmental factors and lifestyle in cancer growth

a. Environmental Factors and Cancer

Giving a immediate of how environmental exposures affect the risk of tumor and the significance of researching these factors.[23] Air contamination and cancer: a. Ambient air contamination: investigating the relationship between exposure to volatile organic compounds, nitrogen dioxide, and particulate material with the risk of developing lung cancer and other cancers.[24] b. Indoor Air Pollution: Talking about how indoor pollutants like radon, asbestos, tobacco smoke, and volatile organic compounds can cause cancer. Cancer and Occupational Hazards: a. Carcinogenic Substances in the Workplace: Investigating how different cancer types are affected by workplace exposures to substances such formaldehyde, asbestos, benzene, and heavy metals.[25]

Cancer

- **a. Ionizing radiation:** Exploring the properties of ionizing radiation, such as medical radiation, nuclear accidents, and occupational exposures, on cancer risk, including leukemia, thyroid cancer, and solid tumors.
- **b. Workplace hazards:** Discussing the part of physical agents, including ionizing radiation, ultraviolet radiation, and shift work, in increasing the cancer risk. Radiation and Cancer.
- **c. Non-ionizing radiation:** Discussing the potential carcinogenic effects of non-ionizing radiation from bases such as electromagnetic fields (EMFs) and radiofrequency radiation.

8.3 Lifestyle Issues and Tumor

- **a. Tobacco smoking:** Examining the strong association between smoking and various tumor types, including lung, bladder, pancreatic cancer.
- **b. Diet and nutrition:** Discussing the influence of food choices, including consumption of processed foods, red and processed meat, and inadequate fruit and vegetable intake, on cancer risk.
- **c. Physical Inactivity and Obesity:** Exploring the connection between sedentary lifestyles, obesity, and improved risk of several cancers, including breast, colorectal, and endometrial cancer.[25]

9. The anticancer latent of resveratrol polyphenols

The "miracle" nutraceutical resveratrol (3,4',5-trihydroxy-trans-stilbene) has the latent to treat cancer and signal advances in cancer treatment.[26]

Resveratrol mechanisms in cancer deterrence

The reasons resveratrol has drawn so much attention as a multipurpose anti-cancer agent is its capacity to directly modify number of significant cellular pathways associated to the growth of tumors.[28] A number of studies revealed the chemo preventive upshot of resveratrol in various experimentally induced tumor models, such as lung, colon, liver, pancreas, gastric, prostate, bladder, breast, ovarian, esophagus, thyroid, skin etc. In canine oral mucosal melanoma cells, resveratrol treatment triggered differentiation, boosting the mRNA expression of melanoma differentiation markers such MIF, a transcription factor associated with microphthalmia, and improving the cells' susceptibility to cisplatin. This differentiation impact was believed to be triggered by resveratrol's suppression of JNK signaling, as evidenced by inhibitor tests and a reduction in JNK activity. 17β-estradiol increased neuroglobin levels in estrogen receptor α-positive breast tumor cells, which helped the cells survive. Resveratrol may be able to block this route, but its effectiveness was hampered by its quick metabolism. As a result, conjugating resveratrol with gold nanoparticles may increase its bioactivity and open the door to targeted breast cancer treatments. By targeting the β1integrin/HIF-1α signaling pathway and changing the tumor microenvironment, resveratrol made colorectal cancer cells more sensitive to 5-fluorouracil through β1-integrin receptors. Attempts to overcome 5-fluorouracil resistance in advanced colorectal cancer therapy may depend on this link. In addition to inhibiting tumor cell proliferation, inflammation, redox signaling, and angiogenesis, resveratrol can influence a wide range of events in tumor cells, including hormone signaling, transcription, apoptosis, and cell growth.[27]

Figure 4: Machanism.

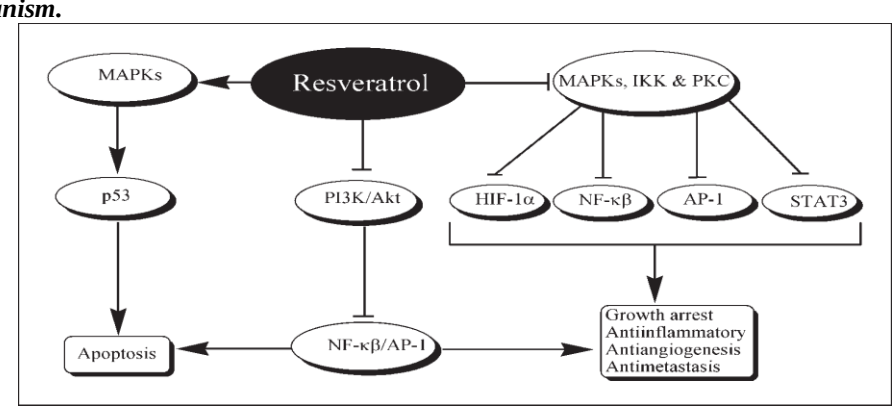


Figure 5: Mechanism.

9.1 Mechanism of resveratrol's antioxidant action

A few closely linked features of resveratrol's action should be booked into thought while considering its antioxidant qualities. Reactive oxygen (ROS) and nitrogen (RNS) species same to secondary organic radicals produced when biomolecules react with ROS and RNS, are all effectively scavenged by resveratrol. Resveratrol promotes the development of several enzymes, including glutathione peroxidase, heme oxygenase, catalase, and superoxide dismutase (SOD), which are in charge of preserving the oxidation-reduction equilibrium in a cell. Additionally, it lowers the action of enzymes like xanthine oxidase that are key players in the generation of ROS. Like other polyphenols, it effectively chelates metal ions, which stops the creation of free radicals in processes like Fenton's reaction. Resveratrol has an exceptionally potent anti-free radical effect. This individual is linked to the presence of aromatic rings, a double bond, and three hydroxyl groups in positions 3, 4', and 5. Experiments have established that eliminating hydroxyl groups or substituting them with -OCH3 groups groups results in a reduction of antioxidant properties of the compound.

9.2 Anti-inflammatory properties

The inflammatory reply is a multi-phase process that involves mediator signals and a variety of cell types. An adaptive reaction, inflammation can brought on by a lots of deanger signals, including tissue damage or microbial invasion. The exogenous or endogenous signaling molecules are known as pathogen- related molecular designs (PAMPs) and damage-associated molecular patterns (DAMPs), respectively. Both PAMPs and DAMPs are identified by numerous pattern detection receptors (PRRs). The activation of PRR causes intracellular signaling cascades, such as kinases and transcription factors. For the enhancement of inflammation, the signaling ways described above can encourage the production of several inflammatory mediators, including cytokines.

10. Vitro and In vivo studies in vivo evidence

10.1Clinical studies

There is little clinical proof a resveratrol is a useful supplement for the inhibition and treatment of cancer. The first phase I clinical trial investigating the use of resveratrol in cancer patients was published in 2009.[10] The effects of all treatment groups combined showed that resveratrol or grape powder supplementation reduced target gene expression in normal mucosa, but they had no effect on signaling in malignant mucosa. The effects of the low-dose grape powder were the most obvious.

The authors concluded that resveratrol may be able to lower the risk of colon cancer growth by lowering Want pathway signaling when mixed with other grape combinations. Nonetheless, it might be useful in preventing colon cancer that has already formed. The clinical study phase investigated the effects of resveratrol supplementation in patients with colorectal cancer that had spread to their liver (nZ9). A resveratrol supplement (5 g daily of microionized resveratrol SRT501; nZ6) increased the expression of cleaved caspase-3 over 10–21 days.[28]

Table 3: The breast cancer.

References	Strain/species	Sex	Age	Tumor model	Resveratrol dose and administration	Effect on tumorigenesis
[29]	BALB/c mice	F	17 weeks	4T1 cells	I.p.; 1, 3, or 5 mg/kg BW; daily; 23 days started at injection.	Unchanged
[30]	Sprague–Dawley rats	F	42 days	NMU	I.g.; 10 or 100 mg/kg BW 5X/week; 7 days before initiation – 120 days afte0.001% in diet; 100 mg/rat daily; 7 days before initiation – 120 days after initiation	Positive
[31]	Nude mice	F	6–8 weeks	MDA-MB-231 (ERa(K), ERb(C)) cells	I.p.; 25 mg/kg BW; daily; for 3 weeks after tumor size reached 40 mm3	Positive
[32]	Sprague–Dawley rats	F	5 weeks	DMBA	0.001% in diet; 100 mg/rat daily; 2 weeks before initiation 24 weeks after	Positive
[26]	CID mice	F	5–6 weeks	MDA-MB-231	Gavage; 0.5, 5, or 50mg/kgBW;5/week; 7 days after injection for 108 days	Negative
[25,33]	Sprague–Dawley rats	F	45 days	DMBA	0.001% in diet; 100 mg/rat daily; 7 days before initiation – 120days after initiation	Negative

10.2In vivo effects of resveratrol on cancer Development and Growth and Their possible mechanisms

Figure 6: Possible mechanisms.

Target/effects	Mechanisms	Dose/duration	References
Skin, Reduces the number of skin tumors initiated with DMBA and promoted by TPA in female CD-1 mice	↓COX-1; ↓COX-2; ↓c-myc; ↓c-fos; ↓c-Jun; ↓TGF-β1; ↓TNF-α	1, 5, 10, 25 µmol Twice/week for For 18 week	[34]
Inhibits the development of DMBA-TPA–induced skin tumors in male Swiss albino mice Prevents UVB mediated photocarcinogenesis in female SKH-1 mice Decreases UVB-induced skin hyperplasia in female SKH-1 mice	↑Apoptosis; ↑Bax; ↑p53; ↓ Bcl-2; ↑cytochrome c release; ↑APAF-1 ↓COX; ↓ODC; ↓lipid peroxidation ↑CDK-2, CDK-4, and CDK-6; ↑ cyclin D1 and cyclin D2; ↑ MAPK; ↑ p21; ↑p53; ↓COX-2; ↓ODC; ↓ survivin mRNA and protein	50 µ mol /mouse, 3-24 week 25 µ mol /mouse 10 µ mol /mouse 7 times, alternate days	[35] [36] [37]
Breast, Suppresses DMBA induced mammary Suppresses DMBA-induced mammary Sprague-Dawley rats In combination with genistein improves the tumor inhibitory action of resveratrol in DMBA-initiated rat mammary carcinogenesis.	↓NF-κB; ↓COX-2; ↓MMP-9 ↓Proliferation; ↑apoptosis	10 ppm 127 d 100 mg/kg 25 wk 100,333 mg/kg Lifetime	[38] [5]

11. Toxic effects of resveratrol

The quantity of resveratrol taken and the length of treatment determine the frequency and intensity of toxic effects. Adverse effects from the drug are minimal or nonexistent at single doses of less than 1 g. Mild and transient adverse events such as diarrhoea nausea, vomiting, flatulence, abdominal cramps, headache, and rash.[3] Similar to RE, its metabolites can induce a various type of bioactivities and have cytotoxic effects. Generally speaking, metabolites of phenolic plant extracts can have either cytotoxic or immune-toxic effects, or they might have cytoprotective and beneficial effects.[39]

Its metabolites have a wide variety of bioactivities, just as RE. In general, metabolites of phenolic plant extracts may have favorable cytoprotective effects or cytotoxic or immune-toxic effects. RE metabolites have also demonstrated beneficial effects in vivo.[40] In mice fed a high-fat diet, piceatannol may reduce liver levels of tumor necrosis factor-alpha (TNF-α) and increase the appearance of sirtuins, which are known to be involved in cellular homeostasis. By increasing the phosphorylated forms of adenosine 5'-monophosphate-activated protein kinase (pAMPK) and acetyl-CoA carboxylase (PACC) and decreasing the protein levels of fatty acid synthase (FAS) and mice fed a ketogenic diet in terms of peroxisome proliferator-activated receptor γ (PPARγ), piceatannol may lessen the accumulation of lipids in adipocytes and the liver.[44]

12. CONCLUSION

In conclusion, resveratrol a polyphenols molecule mostly found in berries, grapes, and some plants, has attracted a many of attention as a possible cancer treatment agent. Its diverse modes of action, such as inhibition of oxidation activity, signaling pathway modulation, and cell rotation monitoring influence, are in line with the faces of cancer or present encouraging treatment options. Although preclinical research and new clinical trials recommend that resveratrol can help fight different kinds of cancer, questions about its bioavailability and the best ways to take it still need to report. Notwithstanding the promising results, the adverse effects of high resveratrol dosages, including gastrointestinal issues and possible drug interactions, highlight the essential for more study to clarify its effectiveness and safety profile in many cancer scenarios, ongoing clinical research will be important. To improve therapeutic results, future studies should also concentrate on synergistic pairings with well-established medicines. All things considered, resveratrol shows ability as an addition in tumor prevention; nonetheless, more thorough research is necessary to

confirm its therapeutic uses and make it a commonplace part of oncology practice.

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