

Studies which show anti skin cancer preventative properties of Resveratrol

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Chemoprevention of skin cancer by grape constituent resveratrol: relevance to human disease?

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According to the *World Cancer Report*, skin cancer constitutes ~30% of all newly diagnosed cancers in the world, and solar ultraviolet (UV) radiation (particularly, its UVB component; 290-320 nm) is an established cause of ~90% of skin cancers. The available options have proven to be inadequate for the management of skin cancers. Therefore, there is an urgent need to develop mechanism-based novel approaches for prevention/therapy of skin cancer. In this study, we evaluated the chemopreventive effects of resveratrol against UVB radiation-mediated skin tumorigenesis in the SKH-1 hairless mouse model. For our studies, we used a UVB initiation-promotion protocol in which the control mice were subjected to chronic UVB exposure (180 mJ/cm², twice weekly, for 28 weeks). The experimental animals received either a pretreatment (30 min before each UVB) or post-treatment (5 min after UVB) of resveratrol (25 or 50 micro mole/0.2 ml acetone/mouse). The mice were followed for skin tumorigenesis and were killed at 24 h after the last UVB exposure, for further studies. The topical application of skin with resveratrol (both pre- and post- treatment) resulted in a highly significant 1) inhibition in tumor incidence, and 2) delay in the onset of tumorigenesis. Interestingly, the post-treatment of resveratrol was found to impart equal protection than the pretreatment; suggesting that resveratrol-mediated responses may not be sunscreen effects. Because Survivin is a critical regulator of survival/death of cells, and its overexpression has been implicated in several cancers, we evaluated its involvement in chemoprevention of UVB-mediated skin carcinogenesis by resveratrol. Our data demonstrated a significant 1) up-regulation of Survivin (both at protein- and mRNA- levels), 2) up-regulation of phospho-Survivin protein, and 3) down-regulation of proapoptotic Smac/DIABLO protein in skin tumors; whereas treatment with resveratrol resulted in the attenuation of these responses. Our study also suggests that resveratrol enhanced apoptosis in UVB-exposure-mediated skin tumors. Our study, for the first time, demonstrated that 1) resveratrol imparts strong chemopreventive effects against UVB exposure-mediated skin carcinogenesis (relevant to human skin cancers), and 2) the chemopreventive effects of resveratrol may, at least in part, be mediated via modulations in Survivin and other associated events. **On the basis of our work, it is conceivable to design resveratrol-containing emollient or patch, as well as sunscreen and skin-care products for prevention of skin cancer and other conditions, which are believed to be caused by UV radiation.**

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Resveratrol inhibits phorbol ester-induced expression of COX-2 and activation of NF- κ B in mouse skin by blocking I κ B kinase activity

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Aberrant expression of cyclooxygenase-2 (COX-2) has been implicated in tumor promotion. **Resveratrol**, a phytoalexin present in grapes, was reported to inhibit multistage mouse **skin** carcinogenesis. In the present study, we found that topically applied **resveratrol** significantly inhibited COX-2 expression induced by the tumor promoter 12-*O*-tetradecanoylphorbol-13-acetate (TPA). **Resveratrol**-suppressed phosphorylation and subsequent degradation of I κ B α , thereby inhibiting activation of nuclear factor- κ B (NF- κ B) in TPA-stimulated mouse **skin**. Pretreatment with **resveratrol** also suppressed TPA-induced phosphorylation of extracellular signal-regulated protein kinase (ERK) and p38 mitogen-activated protein (MAP) kinase. **Resveratrol** blunted TPA-induced phosphorylation of p65 and its interaction with CBP/p300, rendering NF- κ B transcriptionally inactive. To get further insights into the molecular basis of NF- κ B inactivation by **resveratrol**, we examined the role of I κ B kinase (IKK) in mediating TPA-induced activation of NF- κ B and COX-2 expression. TPA treatment led to rapid induction of IKK activity in mouse **skin**, which was abolished either by **resveratrol** or an IKK inhibitor Bay 11-7082. Topical application of Bay 11-7082 also abrogated TPA-induced NF- κ B activation and COX-2 expression, supporting the involvement of IKK in TPA-induced COX-2 expression. Taken together, the above findings suggest that **resveratrol** targets IKK in blocking TPA-induced NF- κ B activation and COX-2 expression in mouse **skin in vivo**.

[Resveratrol kills germs, fungus and viruses on the skin](#)

Antimicrobial effect of resveratrol on dermatophytes and bacterial pathogens of the skin*¹

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Abstract

The phytoalexin resveratrol is commonly found in food and drinks, including red wine, grapes, and peanuts. Many studies have shown that this compound has anti-inflammatory properties, and it has been ascribed as having health benefits that help to prevent cancer and coronary heart disease. **As a treatment that combines antimicrobial and anti-inflammatory actions resveratrol may be desirable for alleviating many skin conditions that range in severity.** Therefore, we evaluated the antimicrobial activity of resveratrol against bacteria and dermatophytes that are major etiologic agents of human

skin infections. Using the broth microdilution protocol of the National Committee for Clinical Laboratory Standards (NCCLS) M7-A5, growth of the bacterial species *Staphylococcus aureus*, *Enterococcus faecalis*, and *Pseudomonas aeruginosa* was inhibited at 171–342 µg/mL of resveratrol in the solvent dimethyl sulfoxide. Using the NCCLS protocol M38-P, activity against the fungal species *Trichophyton mentagrophytes*, *Trichophyton tonsurans*, *Trichophyton rubrum*, *Epidermophyton floccosum*, and *Microsporum gypseum* was also tested. The growth of dermatophytes was inhibited at 25–50 µg/mL of resveratrol. Thus, this study indicates a novel application for resveratrol, a molecule of plant defense, to combat human fungal pathogens. **Resveratrol and its analogs may have wide application to skin conditions that afflict a significant portion of our population, and may also have promising clinical potentials in diabetic wounds.**

Protection from UV sun damage effects

Prevention of short-term ultraviolet B radiation-mediated damages by resveratrol in SKH-1 hairless mice *

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Abstract

Nonmelanoma skin cancer is the most common cancer among humans and solar UV radiation, particularly its UVB component (290–320 nm), is its major cause. One way to reduce the occurrence of the cancer is via the use of substances (often antioxidants) termed “*photochemopreventive agents*”. Resveratrol (*trans*-3,4',5-trihydroxystilbene), a phytoalexin found in grapes, nuts, fruits, and red wine, is a potent antioxidant with strong anti-inflammatory and antiproliferative properties. This study was designed to examine whether resveratrol possesses the potential to ameliorate the damages caused by short-term UVB exposure to mouse skin. Single topical application of resveratrol (25 µmol/0.2 ml acetone per mouse) to SKH-1 hairless mice was found to result in significant inhibition of UVB (180 mJ/cm²)-mediated increase in bifold skin thickness and skin edema. The resveratrol treatment to mouse skin was also found to result in significant inhibition of UVB-mediated induction of cyclooxygenase and ornithine decarboxylase (ODC) enzyme activities and protein expression of ODC, which are well-established markers for tumor promotion. We also observed that resveratrol inhibits UVB-mediated increased level of lipid peroxidation, a marker of oxidative stress. Taken together, our results suggest that **resveratrol may afford substantial protection against the damages caused by UVB exposure, and these protective effects may be mediated via its antioxidant properties.**

PREVENTION OF SUN INDUCED

PHOTOCARCINOGENESIS Farrukh Afaq,

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Resveratrol

Resveratrol (trans-3,4',5-trihydroxystilbene) is a polyphenolic phytoalexin found largely in the skin and seeds of grapes, but in many other plant species including peanuts and mulberries. Resveratrol is a potent antioxidant with anti-inflammatory, antiproliferative and anti-cancer properties (93, 94). Recently, we demonstrated that topical application of resveratrol (25 mmole/0.2ml acetone/mouse) to SKH-1 hairless mice resulted in significant inhibition of UVB-induced skin edema. As evaluated by histochemistry, pre-application of resveratrol caused a significant decrease in UVB-mediated generation of hydrogen peroxide and infiltration of leukocytes. In addition, topical application of resveratrol resulted in significant inhibition of UVB-mediated induction of cyclooxygenase and ornithine decarboxylase activities and protein expression of ornithine decarboxylase (42). Ornithine decarboxylase is thought to represent a marker of tumor promotion.

[Anti Inflammatory and anti aging effects](#)

Anti-Inflammatory Responses of Resveratrol

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Abstract:

Resveratrol (trans-3,4',5-trihydroxystilbene), a natural polyphenolic, non-flavonoid antioxidant, is a phytoalexin found in many plants including grapes, nuts and berries. Recent studies have documented that resveratrol has various health benefits, such as cardiovascular and cancer preventive properties. However, the experimental basis for such health benefit is not fully understood. One of the possible mechanisms for its protective activities is by down regulation of the inflammatory responses. That includes the inhibition of synthesis and release of pro-inflammatory mediators, modifications of eicosanoid synthesis, inhibition of some activated immune cells, or inhibiting the enzymes, such as cyclooxygenase-1 (COX-1) or cyclooxygenase-2 (COX-2), which are responsible for the synthesis of pro-inflammatory mediators through the inhibitory effect of resveratrol on transcription factors like nuclear factor κ B (NF κ B) or activator protein-1 (AP-1). Being a phenolic compound, resveratrol certainly possesses a low bioavailability and most importantly, a rapid clearance from the plasma. Recent growing interest in varying protective nature of resveratrol may clinically also hold a respectable position as a better alternative for anti-inflammatory drugs. The purpose of this review is to provide evidence that resveratrol exhibits potent anti-inflammatory activity and also to explain the underlying mechanism for both resveratrol- induced cardioprotective and anti-

inflammatory properties. While it is true that the cardioprotective properties of resveratrol are likely attributable, at least in part, to its anti-inflammatory properties, the mechanisms discussed address foremost mechanisms for the anti-inflammatory activity which, in turn, is responsible for cardioprotection.

Resveratrol as an anti-inflammatory and anti-aging agent: Mechanisms and clinical implications

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Resveratrol is a phytoalexin polyphenolic compound found in various plants, including grapes, berries, and peanuts. Multiple lines of compelling evidence indicate its beneficial effects on neurological, hepatic, and cardiovascular systems. Also one of the most striking biological activities of resveratrol soundly investigated during the late years has been its cancer-chemopreventive potential. In fact, recently it has been demonstrated that this stilbene blocks the multistep process of carcinogenesis at various stages: tumor initiation, promotion, and progression. One of the possible mechanisms for its biological activities involves downregulation of the inflammatory response through inhibition of synthesis and release of pro-inflammatory mediators, modification of eicosanoid synthesis, inhibition of activated immune cells, or inhibiting such as inducible nitric oxide synthase (iNOS) and cyclooxygenase-2 (COX-2) *via* its inhibitory effects on nuclear factor κ B (NF- κ B) or the activator protein-1 (AP-1). More recent data provide interesting insights into the effect of this compound on the lifespan of yeast and flies, implicating the potential of resveratrol as an anti-aging agent in treating age-related human diseases. It is worthy to note that the phenolic compound possesses a low bioavailability and rapid clearance from the plasma. As the positive effects of resveratrol on inflammatory response regulation may comprise relevant clinical implications, the purpose of this article is to review its strong anti-inflammatory activity and the plausible mechanisms of these effects. Also, this review is intended to provide the reader an up-date of the

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Biological effects of resveratrol

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Abstract

Resveratrol (3, 4', 5 trihydroxystilbene) is a naturally occurring phytoalexin produced by some spermatophytes, such as grapevines, in response to injury. Given that it is present in grape berry skins but not in flesh, white wine contains very small amounts of resveratrol, compared to red wine. The concentrations in the form of trans- and cis- isomers of aglycone and glucosides are subjected to numerous variables. In red wine, the concentrations of the trans-isomer, which is the major form, generally ranges between 0.1 and 15 mg/L. As a phenolic compound, resveratrol contributes to the antioxidant potential of red wine and thereby **may play a role in the prevention of human cardiovascular**

diseases. Resveratrol has been shown to modulate the metabolism of lipids, and to inhibit the oxidation of low-density lipoproteins and the aggregation of platelets. **Moreover, as phytoestrogen, resveratrol may provide cardiovascular protection. Resveratrol compound also possesses anti-inflammatory and anticancer properties.**