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REPORT

Resveratrol

Powerful Protection Against Prostate Cancer

By Terri Mitchell

Good news for men concerned about prostate cancer: resveratrol is a supplement that blocks it at every stage, from beginning to end. A polyphenol found in grapes and other plants, resveratrol was first identified as a multistage protector in 1997,¹ and now is considered a leading agent against prostate cancer by researchers at Houston's MD Anderson Cancer Center and other institutions.^{2,3} Resveratrol works through more than a dozen different anticancer mechanisms and selectively targets cancer cells. This single supplement modulates hormones, has several mechanisms that stop cancer cells from multiplying, and even has the ability to destroy cancer cells.



Resveratrol originally gained notice when researchers suggested that it is the agent in wine that protects against heart disease. Because of its antioxidant and anti-inflammatory actions, resveratrol also was investigated as a possible anticancer supplement. Since research began in earnest in the 1990s, resveratrol has been the subject of hundreds of scientific papers, making it one of the most intensely studied supplements on the market today.

In one review of resveratrol, University of Wisconsin researchers set out six criteria for a good anticancer agent: it should a) have no toxic effects in healthy cells; b) work against different types of cancers; c) be administered orally; d) have known mechanisms of action; e) be inexpensive; and f) be acceptable to humans.⁴ Resveratrol met all six criteria.

Cancer-Preventive Effects

Age, chemicals, radiation, and other factors can overwhelm the body's capacity to counteract abnormal cells, which may then progress silently to cancer. This invisible aspect of cancer is important. As a working group for the American Association for Cancer Research has stated: "We need an intensive educational effort to convince people that absence of clinical symptoms may not guarantee that one is "healthy."⁵

The best approach to cancer is prevention. By augmenting the body's natural scavenging and repair mechanisms, cancer cells can be prevented from forming and destroyed immediately if they do. If one has been treated for cancer already, preventing recurrence is paramount. Resveratrol is a "chemopreventive" supplement that prevents DNA damage and destroys cancer cells from the earliest to the latest stages in both human and animal experimental models.

One remarkable aspect of resveratrol is that it can be very toxic to cancer cells but does not harm healthy cells; in fact, a person taking resveratrol for protection against prostate cancer may receive cardiovascular benefits as a side effect.

Another important aspect of resveratrol is that it may be combined with other phytochemicals to potentially enhance its effects. Resveratrol naturally occurs with other polyphenols such as quercetin in plants such as grapes. Quercetin may enhance resveratrol's bioavailability and cancer-killing effects.^{6,7} Another plant extract, indole-3-carbinol, or I3C, may work synergistically with resveratrol to kill more cancer cells because I3C stops cell growth at one point in the cell cycle while resveratrol stops it at another point.^{8,9} Physicians employ this same concept when prescribing combinations of chemotherapeutic drugs for their patients—each drug halts cancer cell growth at a different stage of the growth cycle.

Researchers who have studied the effects of grape extract containing resveratrol and quercetin in advanced human prostate cancer cells that were transplanted into rodents have proposed these agents as a possible therapy for prostate cancer in humans, though such therapies have not yet been tried.¹⁰ After studying the effects of grape seed extract on advanced prostate cancer cells, researchers at the University of Colorado concluded that combining the extract with a natural cancer-killing cytokine (tumor necrosis factor) "might prove to be a more effective and less toxic alternative in clinical therapy of prostate cancer."³ In another study that examined different types of prostate cancer cells, resveratrol was the most potent of all polyphenols tested against advanced prostate cancer cells.¹¹



Austrian researchers report that resveratrol works through a tamoxifen-like mechanism to block bone cells' ability to respond to messages from cancer in other parts of the body, potentially preventing cancer from spreading to the bone.¹² While resveratrol alone is a powerful polyphenol, combining it with other plant-derived compounds may further enhance its strength. Researchers increasingly are requesting grants to study such combinations of phytochemicals.¹³

Taking Aim at Hormones

Indole-3-carbinol has shown impressive results in fighting hormones that enhance cancer growth.¹⁴⁻¹⁷ I3C is converted into various products, including diindolylmethane, or DIM. Various I3C metabolites have been shown to have different beneficial effects. Resveratrol also is recognized for its ability to modulate estrogen, testosterone, and other androgens.^{18,19} After examining its effects on hormone-responsive genes in prostate cancer cells, researchers concluded that "resveratrol may be a useful chemopreventive/chemotherapeutic agent for prostate cancer."²⁰ Among other things, resveratrol reverses increased prostate-specific antigen (PSA) in cancer cells. In one study, four days of treatment with resveratrol reduced PSA levels in prostate cancer cells by 80%.²¹ Blocking growth-promoting hormones alone would justify the use of resveratrol and I3C against prostate cancer, but they do even more.

Regulating Genes

The latest trend in oncology and nutritional research is examining how a target phytochemical affects genes, using a new tool known as a "DNA microarray." A microarray reveals a compound's effects on thousands of genes at the same time. Microarrays for resveratrol and I3C show that both compounds exert a striking effect on cancer-related genes. Among other things, these phytochemicals activate tumor suppressor genes, other genes that destroy cancer cells, and genes that detoxify chemicals. They also suppress genes that enable cancer cells to "communicate" with one another.^{22,23} This ability to get inside cancer cells and activate or deactivate genes is a powerful weapon against cancer growth. The ability to exert these effects without toxicity—as resveratrol and I3C do—makes them extremely desirable as chemopreventive agents.



Cutting-Edge Therapeutic Action

In early 2003, a new cancer-fighting compound called "deguelin" made waves in the medical world.²⁴ Deguelin, like resveratrol, is synthesized by certain plants as a natural defense against pests, and has been used as a natural pesticide by indigenous people for centuries. Its anticancer actions against different types of cancer (lung, colon, breast, and skin cancer have been tested to date) have spurred considerable ongoing research.²⁵⁻²⁷ In addition to being effective against different forms of cancer, deguelin works by interfering with a basic cancer mechanism. All cell growth, including cancer cell growth, involves an enzyme known as ornithine decarboxylase. Deguelin, like resveratrol and I3C, blocks this enzyme.²⁸⁻³⁴ Of 90 potential anticancer compounds tested in a study by the National Cancer Institute, I3C was one of eight that scored positively on all six tests of anticancer activity, including the suppression of ornithine decarboxylase.³⁵

Neutralizing Carcinogens

On a per-capita basis, the Japanese smoke much more than their US counterparts, yet their risk of contracting lung cancer is about 10 times less than that of Americans.^{36,37} Some researchers believe that widespread consumption of green tea in Japan may explain this anomaly. Polyphenols in green tea have been shown to prevent DNA damage, block carcinogens, and increase antioxidant enzymes.³⁸

Resveratrol and its related polyphenols also protect DNA, block cancer-causing chemicals and radiation, and fight free radicals and inflammation. They have been shown to be more powerful against some types of radicals than vitamins C and E.³⁹⁻⁴¹ Resveratrol activates the same anticancer gene activated by non-steroidal anti-inflammatory drugs (NSAIDs).⁴² In a recent study, resveratrol, along with quercetin and curcumin, emerged as the most powerful anticancer agents from 22 compounds that were subjected to a battery of tests, including their ability to suppress ornithine decarboxylase, scavenge free radicals, and counteract carcinogens.

Prostate Cancer and Diet

An abundance of evidence suggests that diet may help determine whether a man will contract prostate cancer and whether he will survive it. Plant foods are cancer protective,⁴³⁻⁴⁷ while animal foods tend to be cancer promoters.⁴⁸⁻⁵¹ Can the negative effects of animal foods be offset by plant foods? Studies of Seventh-Day Adventists suggest that it is unlikely.⁵² Adventists are vegetarians but consume large amounts of dairy products, and their rate of prostate cancer is high. A study published in the journal *Cancer* shows that consuming three or more glasses of milk a day more than doubles the risk of prostate cancer.⁵³ Other studies show that hormones implanted in American cattle are stronger than the human body's natural hormones.^{54,55} Diet and supplements may not be enough to overcome this kind of chemical exposure. Although a connection between human prostate cancer and cattle implant drugs has yet to be established, the evidence for such a link is strongly suggestive. Interestingly, vitamin D3, which has been proposed as a treatment for prostate cancer, antagonizes the effects of cattle implants.^{56,57}



In European countries such as France and Switzerland where cattle hormone implants are banned, the incidence of prostate cancer is 50% less than in the US; in Italy and Greece, it is about 75% below the US rate.⁵⁸ Italian and Greek men commonly drink red wine, a good source of resveratrol. (Although moderate consumption of red wine may be effective in reducing the risk of prostate cancer, this has not been demonstrated conclusively.)

Resveratrol, on the other hand, has multiple, anti-prostate cancer effects. Resveratrol halts the growth of hormone-positive and -negative cancers; works through multiple mechanisms to stop cancer cells from multiplying; is effective from the earliest to the latest stages of cancer; protects DNA from damage; and may inhibit cancer metastasis. Combined with quercetin and the powerful anti-hormonal agent I3C, resveratrol may be the best cancer-preventive approach available today.



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