

## Resveratrol: Does it really work? (Part 2)

Since I first decided in 5th grade that I wanted to be a heart surgeon, I have been on a mission to seek out the truth in medicine. Along my journey, I have learned that in many cases there is no one absolute truth but many schools of thought on different medical topics. The question that keeps rearing its head; however, is that one wonders who are these thought leaders... these medical professionals that can have such an influence on health issues on a day to day basis and possibly cause havoc on a patient's life by uttering a simple sentence that may be taken out of context or not? The media feels that many are doctors in name only who don't practice their trade or see patients, but may look good on TV, speak well, or know the right people. Their credentials are never mentioned. Indeed, many doctors themselves don't know where to turn to find the best possible answers to medical questions. When I first started writing, I made a promise to present the newest and most accepted schools of thoughts on topics based on well-performed studies published in the most prestigious peer review journals. If I am just going to give my personal opinion I will say so. That is the promise I make to my patients. It is within this context that I will continue to talk about resveratrol.

In part one, I discussed the basic thoughts on resveratrol and the reason for the current uproar in the media about this "miraculous" new compound that is thought to keep people alive longer, help fight cancer, and have positive effects on cardiovascular disease. I mentioned in part 1 the fact that the supplement industry is not well regulated and therefore, it is very difficult to know if the labeled dosages are accurate.

The anti-aging effects of resveratrol are being studied. Recent studies in laboratory mice have found increased survival and lower incidence of several diseases and conditions associated with aging, but the results are contradictory. Protective effects have been found in mice fed a high-fat or a low-calorie diet, but one study found that mice fed a standard diet beginning at age 12 months did not live longer. One of the studies was reported in a *New York Times* article that described how a researcher was taking resveratrol himself and had founded a pharmaceutical company to develop chemicals that mimic the role of resveratrol but at much lower doses. GlaxoSmithKline acquired his company, Sirtris for \$720 million in 2007 and hopes to develop "drugs that target the sirtuins, a recently discovered family of seven enzymes associated with the aging process." After reviewing the animal studies, the highly respected *Medical Letter* concluded: "Resveratrol appears to produce some of the same effects as calorie-restricted diets that have reduced the incidence of age-related diseases in animals. Whether it has any benefit in humans remains to be established." Another supplement named Protandim, which contains mainly green tea extract and tumeric, has been shown to reduce TBARS (a measure of cellular oxidative stress) by 40% in human subjects. Decreasing cellular oxidative stress could also have profound anti-aging effects, but the long term results on humans for both Resveratrol and Protandim may never be known unless long term prospective human studies are performed.

Many studies suggest that consuming alcohol (especially red wine) may reduce the incidence of coronary heart disease (CHD). Several studies have demonstrated that resveratrol has antioxidant properties. It is claimed that because resveratrol contains highly hydrophilic and lipophilic properties, it may provide more effective protection than other well-known antioxidants such as vitamin C and E. On the other hand, it is less effective than the antioxidants quercetin and epicatechin found in red wine. Reduced platelet aggregation has also been demonstrated in studies on resveratrol, which could contribute to prevention of atherosclerosis. To date, however, most of the research on resveratrol's antioxidant and anti-platelet properties has been done using test-tube or tissue-culture preparations and none have been tested in human trials. In addition, alcohol consumption raises triglyceride levels in the blood stream. Besides the negative effect on the cardiovascular profile, alcohol use and high triglycerides can cause pancreatitis.

Resveratrol is also being studied to see how it affects the initiation, promotion, and progression of cancer. With regard to tumor initiation, it has been shown to act as an antioxidant by inhibiting free radical formation and as an anti-mutagen in rat models. Studies related to progression have found that resveratrol induced human promyelocytic leukemia cell differentiation, inhibited enzymes that promote tumor growth, and exerted antitumor effects in neuroblastomas (the most common solid tumor in childhood). In animal studies, resveratrol was effective against tumors of the skin, breast, gastrointestinal tract, lung, and prostate.

gland, a recent review concluded that during the last decade, resveratrol has been shown to possess a fascinating spectrum of pharmacologic properties. Multiple biochemical and molecular actions seem to contribute to resveratrol effects against precancerous or cancer cells. Resveratrol affects all three discrete stages of carcinogenesis (initiation, promotion, and progression) by modulating signal transduction pathways that control cell division and growth, apoptosis, inflammation, angiogenesis, and metastasis. The anticancer property of resveratrol has been supported by its ability to inhibit proliferation of a wide variety of human tumor cells in vitro; however, its role as a potentiator of breast cancer may limit its clinical use. Numerous preclinical animal studies to evaluate the potential of this drug for cancer chemoprevention and chemotherapy are currently underway.

In summary, epidemiologic studies can find associations between the consumption of foods or dietary supplements and various health outcomes. Animal experiments can demonstrate what can happen in the species tested. However, only clinical trials can determine whether supplementation is useful for humans. Resveratrol has not been tested in human clinical trials, and most clinical trials of other antioxidants have failed to demonstrate the benefits suggested by preliminary studies. Some substances—most notably beta-carotene—have even produced adverse effects. My advice is to ignore the hype surrounding resveratrol until more is known!