

Red Wine and Health: Resveratrol Health Benefits a Myth?

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Resveratrol -- an antioxidant found in red wine, chocolate, and grapes -- didn't correlate with longevity or lower risk of cancer or cardiovascular disease when dietary intake was directly measured in a prospective study.

Older adults in the Chianti wine-making region of Italy with the top dietary intake as indicated by urinary metabolites weren't any less likely to die over nine years of follow-up, Richard D. Semba, MD, MPH, of Johns Hopkins University, and colleagues found.

In fact, the adjusted hazard ratio of 0.80 (95 percent confidence interval 0.54-1.17) numerically favored the lowest intake quartile versus the highest, they reported online in *JAMA Internal Medicine*.

Inflammatory markers, cardiovascular disease, and cancer all showed the same lack of a significant relationship with resveratrol levels.

The findings ran "contrary to all our hypotheses," Semba's group wrote.

The compound has been hailed as a possible key to red wine's heart and other health benefits, leading to substantial supplement sales.

Resveratrol is one of a number of polyphenols found in the skin of grapes, in cocoa powder and dark chocolate, in peanuts, and in certain roots and berries.

However, the Chianti cohort findings really shouldn't have been a surprise, argued Derek Lowe, PhD, a drug development researcher who has been an occasional critic of resveratrol on his blog "In the Pipeline."

Because resveratrol is rapidly metabolized and stays in low concentrations in serum, "there's just no way you're going to get enough of it from diet to have any major effect," he told *MedPage Today*.

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Any heart health or other benefits from red wine would have to be coming from some other source, Lowe noted.

"Personally, I don't see why anyone would take resveratrol supplements," he said. "If it does have an effect it's sure not a very robust or reproducible one."

The American Heart Association (AHA) doesn't recommend antioxidant supplements for cardiovascular risk reduction, although it does not address resveratrol specifically in its guidelines.

"We've really rarely found a cardiovascular benefit from just one food substance or supplement alone," said Nieca Goldberg, MD, a cardiologist at NYU Langone Medical Center in New York City and spokesperson for the AHA.

A balanced diet with exercise and an overall healthy lifestyle is a better strategy, Goldberg told MedPage Today.

However, Nate Berger, MD, an oncologist at University Hospitals Case Medical Center, noted that there was no significant evidence of harm in the study to argue against higher resveratrol doses.

"The study is absolutely not definitive," he argued. "Maybe you need to start having higher levels of resveratrol when you're 50 or 40 to have a benefit."

Most of the positive data with resveratrol has come from in vitro or animal studies (some later found to be falsified), with contradictory results in trials of supraphysiologic supplement doses in people.

Lowe predicted that resveratrol research has about reached the end of the line because the compound has little to teach about mechanisms for further development.

"Pharmacologically it's a very dirty compound," he said. "It hits all kinds of stuff, and none of it very potently."

Semba's group analyzed the prospective Invecchiare in Chianti (InCHIANTI, "Aging in the Chianti Region") Study, which followed a population-based cohort of 783 men and women ages 65 years and older in two Tuscan villages from 1998 to 2009.

Baseline levels of 24-hour urinary resveratrol metabolites ranged widely, with the lowest quartile defined by less than 1,554 nmol/g creatinine compared with more than 15,010 nmol/g creatinine in

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the highest quartile.

Mortality didn't follow a dose-response curve across those categories, with rates of 34% in the bottom quartile, 32% and 34% in the two intermediate quartiles, and 37% in the highest quartile (P=0.67).

The results were similar through various models of confounders and when excluding the 40 participants who consumed more than four drinks of alcohol a day.

Incident cardiovascular disease rates were 22.3% in the lowest resveratrol quartile, 29.6% and 28.4% in the intermediate quartiles, and 28.0% in the highest quartile (P=0.44).

Incident cancer likewise showed no significant difference across groups, from a rate of 4.4% in the lowest, 4.9% and 5.0% in the intermediate, and 4.3% in the highest quartile of resveratrol intake (P=0.98).

Baseline biomarkers also failed to show resveratrol dose effects, including tumor necrosis factor (TNF, P=0.78), the inflammatory cytokines IL-1-beta and IL-6 (P=0.24 and P=0.18), and C-reactive protein (CRP, P=0.52).

The researchers cautioned that while urinary resveratrol levels seemed on par with what's been reported elsewhere, a much larger sample size may be needed to detect associations due to the large variability in exposure, inter-individual variation, and differences in gut microbiota.

Berger also questioned whether the study looked at the right urinary metabolites to link to resveratrol.

Source: Crystal Phend, MedPage Today