

Resveratrol, found in red wine, worsens MSlike symptoms and neuropathology in mice

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Resveratrol, a naturally occurring polyphenol compound produced by the skin of red grapes and peanuts, and found in red wine, has been touted as a beneficial supplement due to its anti-inflammatory and antioxidant properties. This has been supported by some experimental studies, whereas others suggest a lack of benefit. A new study using two multiple sclerosis (MS) models published in *The American Journal of Pathology* has found that resveratrol actually worsened MS-like neuropathology and inflammation and had no neuroprotective effects.

"Resveratrol may have detrimental effects in some disease conditions and should be discouraged for supplemental use by MS patients pending further research," says lead investigator Ikuo Tsunoda, MD, PhD, Assistant Professor in the Department of Microbiology and Immunology, Center for Molecular & Tumor Virology of the Louisiana State University Health Sciences Center, Shreveport, LA.

Investigators (Fumitaka Sato, PhD, et al) tested resveratrol in autoimmune and viral models of MS. In the autoimmune model, experimental autoimmune encephalomyelitis (EAE) was induced in 6-week-old mice using myelin oligodendrocyte glycoprotein (MOG)35-55 peptide. Mice were fed either a control diet or a diet containing resveratrol for 2 months or only during the early (days -1 to 8) or the late (days 14 to 23) phases of EAE. Around 12 days after MOG sensitization, all groups started to develop clinical signs, such as tail and hind limb paralysis, and the symptoms worsened and peaked by 3 weeks. After 5 weeks, mice fed the control diet showed either complete



recovery or mild paralysis, but all three groups fed resveratrol exhibited severe and lasting EAE without remission.

Spinal cord neuropathology showed higher pathology scores in demyelination, meningitis, perivascular cuffing (inflammation), and overall pathology in mice that had been given resveratrol during the early phase compared with mice fed a control diet, whereas mice treated with resveratrol during the entire treatment period had significantly higher pathology scores in meningitis and overall pathology than controls. Groups did not differ in brain pathology scores.

Although it has been suggested that resveratrol has anti-inflammatory properties, in this study resveratrol did not suppress autoimmune responses as measured by levels of MOG35-55-specific lymphoproliferative responses and pro-inflammatory cytokine production.

To see whether resveratrol had anti-viral properties, as has been reported, 5-week-old mice were infected intracerebrally with the Daniels (DA) strain of Theiler's murine encephalomyelitis virus (TMEV) to induce TMEV-induced demyelinating disease (TMEV-IDD). The mice were fed either a control diet or one containing resveratrol from days 35 to 48 (the chronic phase). Similar to the findings from the EAE model, mice treated with resveratrol developed significantly more severe TMEV-IDD compared with the controls. Another study using the GDVII strain of TMEV to see whether resveratrol could suppress neurodegeneration caused by direct viral infection, not by immunopathology, found that resveratrol had no neuroprotective activity against the virus.

"Resveratrol did not show anti-viral effects in TMEV infection," says Dr. Tsunoda, although he notes that resveratrol has been shown by others to have anti-viral effects on some viruses related to MS, such as herpes simplex virus and Epstein-Barr virus.



To explain their findings, the authors suggest that resveratrol's vasodilating effects via endothelial cells might enhance infiltration of inflammatory cells into the central nervous system, which in turn might play a key role in the pathogenesis of MS.

The degree to which resveratrol exacerbated demyelination and inflammation surprised the research team. "Our findings illustrate that caution should be exercised for potential therapeutic application of <u>resveratrol</u> in human inflammatory demyelination diseases, including MS," says Dr. Tsunoda.

More information: "Resveratrol Exacerbates Both Autoimmune and Viral Models for Multiple Sclerosis," by Fumitaka Sato, Nicholas E. Martinez, Maira Shahid, John W. Rose, Noel G. Carlson, and Ikuo Tsunoda. <u>dx.doi.org/10.1016/j.ajpath.2013.07.006</u>. It appears in The *American Journal of Pathology*, Volume 183, Issue 5 (November 2013)

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