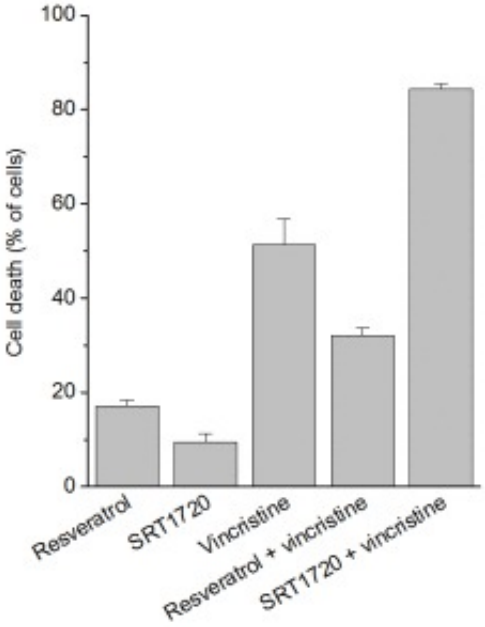
Effect of resveratrol on chemotherapy of a fatal childhood cancer

The natural polyphenolic compound resveratrol, found in red wine, dark chocolate, and peanuts, may confer health benefits in humans. It is a powerful antioxidant that has been suggested to alleviate age-related pathologies, such as type II diabetes, neurodegenerative disorders, cardiovascular diseases, and cancer. In fact, the so-called "French paradox", which defines the phenomenon that French people enjoy a low incidence of coronary heart disease despite a diet rich in cholesterol and saturated fat, has been attributed to the consumption of resveratrol present in red wine. As a consequence, the use of resveratrol as a dietary supplement has become quite popular. Prevailing evidence indicates that resveratrol exerts its favorable effects by activating an enzyme known as sirtuin-1.



Resveratrol impairs and SRT1720 enhances vincristine-induced cancer cell death. Ewing‘s sarcoma cells were treated with 5 µM resveratrol, 2.25 µM SRT1720, 3 nM vincristine or combinations of 5 µM resveratrol plus 3 nM vincristine or 2.25 µM SRT1720 plus 3 nM vincristine for 48 h.

However, current research studies indicate that sirtuin-1 has an ambiguous role in cancer: it may work either as a tumor suppressor or as a tumor promoter. Complimentary findings have recently been reported by a study that aimed at uncovering the effect of sirtuin-1 activation in Ewing's sarcoma cells. Ewing's sarcoma is one of the most aggressive cancers in childhood and

adolescence. In particular, Ewing's sarcoma patients with detectable metastases at diagnosis have a dismal prognosis. More effective treatment regimens for these patients are clearly needed.

Ewing's sarcoma patients are *treated* with surgery and multiagent chemotherapy, which includes the anticancer drugs etoposide and vincristine (marketed under the names Etopophos and Oncovin, respectively). In the new study, a novel treatment regimen consisting of either of these drugs in combination with resveratrol was investigated for its effectiveness against Ewing's sarcoma cells in a cell line model. For comparison, a synthetic sirtuin-1-activating compound, termed SRT1720, was also tested. Both resveratrol and SRT1720 were found to be effective against Ewing's sarcoma cells when applied as single agents. Strikingly, however, when applied in conjunction with etoposide or vincristine, they displayed reverse effects: SRT1720 enhanced chemotherapy-induced anticancer effects while resveratrol inhibited them.

These findings suggest that the synthetic compound SRT1720 may be useful to boost the efficacy of anticancer therapy in Ewing's sarcoma. But they also suggest that the dietary intake of the natural compound resveratrol may be detrimental during chemotherapy of Ewing's sarcoma and should, thus, best be avoided during treatment.

Publication

Reverse chemomodulatory effects of the SIRT1 activators resveratrol and SRT1720 in Ewing's sarcoma cells: resveratrol suppresses and SRT1720 enhances etoposide- and vincristine-induced anticancer activity.
Sonnemann J, Kahl M, Siranjeevi PM, Blumrich A, Blümel L, Becker S, Wittig S, Winkler R, Krämer OH, Beck JF
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