Resveratrol and its Structural Analogues as Potential Inhibitors of p53 Protein Aggregation

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INTRODUCTION: p53 protein has an essential role in preventing cancer development by inducing cell cycle arrest and/or apoptosis in response to cellular stress. Mutations in the p53 gene are described in over 50% of all human cancers. Besides the mutations, cellular aggregation of p53 can also inactivate the protein, leading to malignancy. Resveratrol and its structural analogues, pterostilbene and piceatannol, are bioactive food compounds that regulates many cellular targets involved in cancer signaling pathways, including those mediated by the p53 protein. **OBJECTIVES:** Investigate the potential of resveratrol, pterostilbene and piceatannol in preventing p53 aggregation *in vitro* and in tumor cells. **MATERIALS AND METHODS:** Cell viability and apoptosis were measured by MTT reduction and annexin-PI assay, respectively, in human breast cancer cells MCF-7 (wild-type p53) and MDA-MB-231 (mutant p53). p53 aggregation experiments were performed by using fluorescence spectroscopy and fluorescence microscopy techniques. **DISCUSSION AND RESULTS:** Pterostilbene (0-100µM), but not piceatannol, promoted a cytotoxic effect on MCF-7 and MDA-MB-231 breast cancer cells in a dose-and time-dependent manner. Pterostilbene (100µM) increased phosphatidylserine exposure on MCF-7 cells surface, which is suggestive of apoptosis. These effects were partially prevented when cells were pretreated with pifithrin-α, a specific p53 inhibitor. We also found that pterostilbene and resveratrol has the ability to inhibit the p53 core domain undergo *in vitro* aggregation. Additionally, resveratrol (50 and 100µM) reduces the formation of nuclear p53 aggregates in MDA-MB231 cancer cells. **CONCLUSIONS:** Our results indicate that pterostilbene can be suggested as a promising chemopreventive agent and its cytotoxicity possibly requires p53 normal function. We also have evidence that this compound, as well as resveratrol, could prevent p53 protein aggregation and may pave the way for development of new anticancer strategies.

Key Words: cancer, p53 aggregation and resveratrol.
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