

SYNERGISTIC EFFECTS OF PTEROSTILBENE AND INOSITOL-6-PHOSPHATE ON MELANOMA

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Background: Epidemiologic studies have demonstrated lower rates of cancer in populations with diets rich in fruits and vegetables. We have previously shown that pterostilbene, an antioxidant found in blueberries, inhibits melanoma growth via induction of caspase-dependent apoptosis. We have also described melanoma growth inhibition with inositol-6-phosphate, a phosphorylated carbohydrate found in rice and corn. IP6 growth inhibition was ascribed to decreased VEGF production and increased apoptosis. In this study, we hypothesize that treatment with both agents would potentiate growth inhibition of melanoma as compared to either treatment alone.

Methods: Melanoma cell lines (Sk-Mel 2 and MeWo) were cultured using standard techniques. Cells were treated with increasing doses of pterostilbene (25, 50, 75 μ M), IP6 (250, 500, 750, and 1000 μ M) or combinations thereof. Cell viability was measured at 24, 48, and 72 hours using a MTT assay. VEGF production was measured using ELISA. ANOVA with Bonferroni correction was used for statistical analysis.

Results: Lower doses of pterostilbene and IP6 alone resulted in minimal growth inhibition, whereas increased single agent doses produced 17- 20 percent growth inhibition by 48 hours ($P < 0.001$). The addition of either high dose IP6 or pterostilbene to lower doses of the other agent produced 66 and 43 percent growth inhibition respectively ($P < 0.001$). High dose combinations also resulted in greater growth inhibition than single agent treatment ($P < 0.001$), with similar results observed in both cell lines. VEGF production was decreased with 50 μ M pterostilbene treatment alone and in combination with IP6 ($P < 0.05$).

Conclusions: Currently, no effective chemotherapy exists for melanoma. Herein, we have demonstrated that treatment of melanoma with both pterostilbene and IP6 is more effective than either agent alone in vitro. These results suggest a possible therapeutic or adjuvant role for this combination in the management of melanoma. Further mechanistic studies and in vivo experiments are warranted.