

Effect of Delphinidin and Resveratrol on Oxidative Stress: Impact on Endothelial Cell Survival and Vascular Function.



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Introduction

Resveratrol has been implicated as a major player in the cardioprotective effects of red wine, however many of the *in vitro* experiments conducted with resveratrol are at concentrations that are not attainable through oral ingestion. Pilot experiments with delphinidin, another polyphenolic compound found in soft berries, suggested that this anthocyanin might have more dramatic benefits than resveratrol at physiologically relevant concentrations. The aim of the study was to test the hypothesis that exposing endothelial cells in culture to delphinidin has significantly greater protective effects than equivalent concentrations of resveratrol in the face of oxidative stress.

Methods

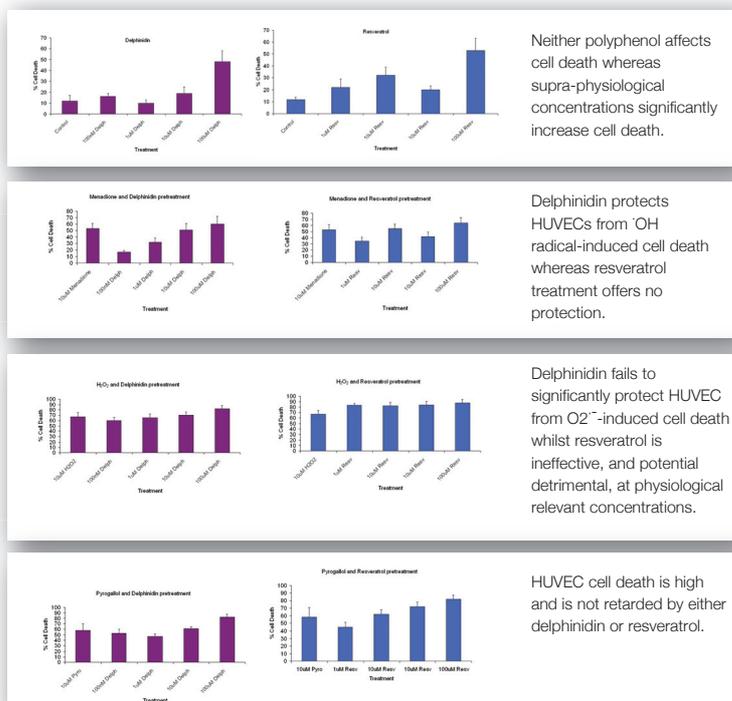
Human umbilical vein endothelial cells (HUVECs) were treated with delphinidin and resveratrol (100nM-100µM) alone or as a pretreatment to incubation with the following oxidizing agents: hydrogen peroxide (H₂O₂; 200µM), pyrogallol (superoxide generator; 100µM) or menadione (hydroxyl radical, ·OH; 10µM). Cell survival was assessed by trypan blue exclusion (cells counted immediately after addition of dye).

Results and Discussion

In the absence of exogenous oxidizing agents, most concentrations of delphinidin or resveratrol had no impact on endothelial cell survival. The exception was the highest concentrations of both which proved deleteriously pro-oxidant.

Delphinidin had a profound impact on menadione-induced endothelial cell death, particularly at low concentrations, reducing cell death from 53% to 17% (100nM) and 32% (1µM). Indeed the effect was dose-dependent and displayed a classic bell shape with reducing efficacy below 100nm (data not shown). The cytotoxic effects of H₂O₂ and pyrogallol were not reversed by either resveratrol or delphinidin.

The results suggest that neither delphinidin nor resveratrol are effective inhibitors of H₂O₂ or superoxide-induced cell death, and that at supra-physiological concentrations the polyphenols might be detrimental. Nanomolar concentrations of delphinidin are, however, protective against ·OH-mediated cell death, a property that is not shared by resveratrol.



Conclusion

Delphinidin is an effective ·OH scavenger that offers protection, at biologically relevant concentrations, against menadione-induced death in endothelial cells. The mechanism by

which this protective effect is mediated has yet to be elucidated, but the low concentrations at which protection is achieved suggests that it is not through direct inactivation of free radicals.

Further experiments are underway to explore whether the effect is due to up-regulation of intracellular antioxidant systems.