

Proanthocyanidins from the American Cranberry (*Vaccinium macrocarpon*) Induce Cell Cycle Alterations in DU145 Human Prostate Cancer Cells in Vitro by Affecting the Expression of Cell Cycle-Associated Proteins

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ABSTRACT:

Background: Prostate cancer is one of the most common cancers in the world. There are genetic and environmental factors that can potentially impact the development and progression of many types of cancer, including prostate cancer. As a consequence of environmental factors, such as diet having a potential effect on the development of prostate cancer, considerable interest in the possible health benefits associated with the inclusion and consumption of certain foods in the diet exists.

Context and purpose of this study: This study describes the effects of a proanthocyanidin-enriched fraction (PACs) isolated from the American cranberry (*Vaccinium macrocarpon*) on the behaviour of androgen-refractory (insensitive) DU145 human prostate cancer cells *in vitro*.

Results: Following treatment of DU145 human prostate cancer cells with 25 µg/mL of PACs for six hours, PACs significantly decreased the cellular viability of DU145 cells. PACs treatment (25 µg/mL for 6 hours) of DU145 cells increased the proportion of cells in the G2-M phase of the cell cycle and decreased the proportion of cells in the G1 phase of the cell cycle. These alterations were associated with changes in cell cycle regulatory proteins and other cell cycle associated proteins. PACs increased the expression of cyclin E, cyclin D1, CDK2 and CDK4, and decreased the expression of cyclin A and cyclin B1. The protein expression level of p27 increased, and the protein expression levels of p16^{INK4a}, p21, and pRBp107 decreased in response to PACs treatment. The protein expression level of pRBp130 was unchanged in

response to PACs treatment.

Conclusions: These findings demonstrate that proanthocyanidins from the American cranberry can affect the behaviour of human prostate cancer cells *in vitro* and further support the potential health benefits associated with cranberries.

Keywords: Prostate cancer, proanthocyanidin-enriched fraction (PACs), American cranberry (*Vaccinium macrocarpon*)