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Der Pharmacia Lettre, 2017, 9 (3):74-79  
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## Anti-carcinoma activity of *Vaccinium oxycoccos*

Mansoureh Masoudi<sup>1</sup>, Milad Saiedi<sup>2\*</sup>

<sup>1</sup>Valiasr Eghlid hospital, Shiraz University of medical sciences, Shiraz, Iran

<sup>2</sup>student of medicine, international Pardis University of Yazd, Yazd, Iran

\*Corresponding author: Milad Saiedi, student of medicine, international Pardis University of Yazd, Yazd, Iran

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### ABSTRACT

**Introduction:** *Vaccinium oxycoccos* or cranberry are evergreen shrubs in the subgenus *Oxycoccos* of the genus *Vaccinium*. The aim of this study was to overview anti-carcinoma activity of *Vaccinium oxycoccos*.

**Methods:** This review article was carried out by searching studies in PubMed, Medline, Web of Science, and IranMedex databases. The initial search strategy identified about 79 references. In this study, 56 studies were accepted for further screening and met all our inclusion criteria [in English, full text, therapeutic effects of *Vaccinium oxycoccos* and dated mainly from the year 2002 to 2016]. The search terms were “*Vaccinium oxycoccos*”, “therapeutic properties”, “pharmacological effects”.

**Result:** the result of this study showed that *Vaccinium oxycoccos* possess anti-carcinoma activity against the following cancers: prostate, bladder, lymphoma, ovarian, cervix, breast, lung, and colon.

**Conclusion:** the results from this review are quite promising for the use of *Vaccinium oxycoccos* as an anti-cancer agent. *Vaccinium oxycoccos* possess the ability to suppress the proliferation of human breast cancer MCF-7 cells and this suppression is at least partly attributed to both the initiation of apoptosis and the G1 phase arrest.

**Keywords:** *Vaccinium oxycoccos*, Phytochemicals, Therapeutic effects, Pharmacognosy, Alternative and complementary medicine.

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### INTRODUCTION

Herbal medicine is shown to contribute effectively in remedy and well-being of many diseases [1-24]. *Vaccinium oxycoccos* is evergreen shrubs in the subgenus *Oxycoccos* of the genus *Vaccinium* [25]. The plant is cultivated in central and northern Europe [26]. They have slender, wiry stems that are not thickly woody and have small evergreen leaves [27].

The flowers are dark pink, with very distinct *reflexed* petals, leaving the style and stamens fully exposed and pointing forward [28]. They are pollinated by bees. The fruit is a berry that is larger than the leaves of the plant; it is initially light green, turning red when ripe [29]. It is edible, with an acidic taste that can overwhelm its sweetness [30].

Raw cranberries are a source of phytochemicals, particularly polyphenols[31] which are under active research for possible effects on the urinary tract infection[32, 33], cardiovascular system [34], immune system [35] and wound healing[36] cancer[37, 38]. *Vaccinium oxycoccos* juice contains a high molecular weight non-dializable material that is under research for its potential to affect formation of plaque by *Streptococcus mutans* pathogens that cause tooth decay[39, 40].

## RESULTS

### *Prostate cancer*

*Vaccinium oxycoccos* -mediated cytotoxicity in DU145 human prostate epithelial tissue cells was investigated. The findings indicate that *Vaccinium oxycoccos* phytochemicals can induce apoptosis in prostate cancer cells in vitro [41].

The effects of proanthocyanidins (PACs) from *Vaccinium oxycoccos* on matrix metalloproteinase (MMP) activity in DU145 human prostate cancer cells was examined. The results suggest that *Vaccinium oxycoccos* PACs lessened MMP activity via inducing and inhibiting specific temporal MMP regulators, and by affecting either the phosphorylation status and/or expression of MAP kinase, PI-3 kinase, and NF- $\kappa$ B and AP-1 pathway proteins [42].

In an animal study, the potential protective effect of *Vaccinium oxycoccos* extract against DOX-induced cardiotoxicity in rats was investigated. CRAN alleviated histopathological changes in rats' hearts treated with DOX. The result suggested that CRAN protects against DOX-induced cardiotoxicity due to CRAN's antioxidant activity [43].

The effect of highly standardized *Vaccinium oxycoccos* capsules compared with that of placebo capsules on the incidence and severity of radiation cystitis was determined. Result showed men receiving radiation therapy for prostate cancer may benefit from using *Vaccinium oxycoccos* capsules, particularly those on low hydration regimens or with baseline urinary symptoms [44].

The phytochemical extracts from the American *Vaccinium oxycoccos* showed to affect the behavior of human prostate cancer cells in vitro and further support the potential health benefits associated with *Vaccinium oxycoccos* [45].

The effects of *Vaccinium oxycoccos* consumption on PSA values and other markers in men with PCa before radical prostatectomy was evaluated. Regular intake of a powdered *Vaccinium oxycoccos* fruit reduce serum PSA in patients with prostate cancer. The whole fruit contains constituents that may regulate the expression of androgen-responsive genes [46].

### *Bladder cancer*

Anti-proliferative activities of *Vaccinium oxycoccos* derived flavonoids and some of their in vivo metabolites were evaluated. The result suggest that isorhamnetin and quercetin 3-O-glucoside may be the active forms of quercetin in prevention of bladder cancer in vivo and diets rich in cranberries were emphasized for the prevention of bladder carcinoma [47].

***Lymphoma Cancer***

Mechanisms of *Vaccinium oxycoccos* -linked cancer suppression include cellular death induction via apoptosis, necrosis and autophagy; reduction of cellular proliferation; alterations in reactive oxygen species; and modification of cytokine and signal transduction pathways [48].

***Ovarian cancer***

In an in vitro study, Cytotoxicity of Polyphenolic extracts of *Vaccinium oxycoccos* were assessed against tumor cells lines. *Vaccinium oxycoccos* proanthocyanidins exhibit cell-line specific cytotoxicity, induce apoptotic markers and augment cytotoxicity of paraplutin in platinum-resistant SKOV-3 ovarian cancer cells [49].

Differential cell viability reduction of ovarian cancer cells treated with *Vaccinium oxycoccos* flavonoids was observed. This study demonstrates encouraging in vitro cytotoxic and anti-proliferative properties of two newly characterized *Vaccinium oxycoccos* flavonoids, quercetin aglycone and PAC DP-9, against ovarian cancer cells [50].

The ovarian cancer viability and angiogenesis in vitro effect of a proanthocyanidins of *Vaccinium oxycoccos* was evaluated. result suggest that PAC-1 exerts potent anticancer and anti-angiogenic properties and that highly purified PAC from *Vaccinium oxycoccos* can be further developed to treat ovarian cancer in combinational or single-agent therapy [51].

***Cervix cancer***

The effectiveness of *Vaccinium oxycoccos* juice on the incidence of urinary tract infections and urinary symptoms in patients undergoing pelvic radiotherapy for cancer of the bladder or cervix was evaluated. Further research is recommended focusing on the limitations of this study.

***Breast cancer***

The results of a study suggest that *Vaccinium oxycoccos* phytochemical extracts possess the ability to suppress the proliferation of human breast cancer MCF-7 cells and this suppression is at least partly attributed to both the initiation of apoptosis and the G1 phase arrest.

Antioxidant activity and biomarkers of oxidative stress of daily consumption of anthocyanin-rich *Vaccinium oxycoccos* juice was investigated. *Vaccinium oxycoccos* juice consumption did not alter blood or cellular antioxidant status or several biomarkers of lipid status pertinent to heart disease. The results show the importance of distinguishing between the in vitro and in vivo antioxidant activities of dietary anthocyanins in relation to human health.

***Lung cancer***

The ability of a proanthocyanidins rich *Vaccinium oxycoccos* fraction to alter gene expression, induce apoptosis and impact the cell cycle machinery of human NCI-H460 lung cancer cells was investigated. The result showed that PAC is a promising drug to treat lung cancer.

**Colon cancer**

Extracts of six popularly consumed berries were evaluated for their phenolic constituents. The result showed the chemo preventive and chemotherapeutic effects of berries using in vivo models.

**CONCLUSION**

The results from this review are quite promising for the use of *Vaccinium oxycoccos* as an anti-cancer agent. *Vaccinium oxycoccos* possess the ability to suppress the proliferation of human breast cancer MCF-7 cells and this suppression is at least partly attributed to both the initiation of apoptosis and the G1 phase arrest.

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