

Review Article

Therapeutic Uses of Cranberry (*Vaccinium Macrocarpon*) Extract - A Review

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ABSTRACT

Cranberry (*Vaccinium macrocarpon*) is a fruit native to North America which is rich in nutrients. It is most commonly taken by humans as cranberry juice cocktails. This super-fruit has antioxidant properties, is anti-cancer and used for treatment in urinary tract infections, intestinal infections as well as oral infections. Its main antioxidant and protective action are due to its high polyphenolic and organic acid content. Its low toxicity and high biocompatibility gives it a great advantage and a promising future as a therapeutic agent. This review discussed the uses of cranberry extract.

Keywords: Cranberry; Urinary Tract Infections; Cancer; Oral infections; Antioxidant

INTRODUCTION

Cranberry, *Vaccinium macrocarpon*, is a native North American fruit. Cranberries consist of 80% water and 10% carbohydrates, ¹while the other 10% are flavonoids, catechins, triterpenoids, organic acids and ascorbic acid. Citric acid, gallic acid, quinic acid, also a lesser content of benzoic acid and glucuronic acid are the organic acids present. Cranberries can be eaten as fresh fruits or more commonly processed into fruit juices, sauces, jams, fruit concentrate and dried cranberries. In recent years, cranberries been extensively investigated for its diverse health benefits to human. Its antioxidant activity can be attributed to its polyphenolic and organic acid components. Cranberries have one of the highest flavanol content among berries of 50-200mg/kg fresh weight.²

The wide array of therapeutic uses of cranberries together with its low toxicity and high biocompatibility gives it great potential for use in treatment and prevention of infections and diseases. It may be easily introduced as dietary supplements, which enables a large scale application. Cranberry extract can be considered as a non-antibiotic alternative for treatment of intestinal and urinary tract infections. It is also more advantages as it prevents development of drug resistant microorganisms, as usage of antibiotics decreases.

Therapeutic actions and uses

A. Intestinal infections: *Helicobacter pylori* is an organism that lives in the stomach of humans. It causes inflammation of the stomach mucosa and is believed to be the cause for peptic ulcer, stomach cancer, idiopathic thrombocytopenic purpura and mucosa-associated lymphoid tissue lymphoma. Cranberry extract was shown to suppress *H. Pylori* growth. Combination of extract with other food products or probiotics is required for more effective eradication of *H. pylori*.³ It has also been shown to inhibit adherence of bacteria to gastric cells.⁴ Cranberry extract is effective against *Bacillus cereus* and *Clostridium perfringens*.

The outer membrane of Gram negative bacteria contains lipopolysaccharides, that if it's disintegrated, it will release the lipopolysaccharides. This increases the permeability of the cell and leakage of cell contents resulting in cell death. Cranberry extract has been seen to release lipopolysaccharide from *Salmonella typhimurium* and *Salmonella infantis*⁵

Gallic acid gives cranberry extract its antimicrobial property. The partial hydrophobicity of gallic acid allows it to act on bacterial membranes by destabilizing them.⁶ Gallic acid increased permeability of *Salmonella* strains and destabilized the bacterial membrane by chelating divalent cations.⁵ Antibacterial action of cranberry extract against *Staphylococcus aureus* is by disruption of cell wall biosynthesis. A combination of cranberry extract and β -lactam antibiotics show great potential in treatment of *S. aureus* infections.⁷

Cranberry extract can also be active in the colon.⁸ Metabolites of proanthocyanidins could bind to colonic bacterial receptors and prevent binding of bacteria to uroepithelium as well as prevent its multiplication.⁹

B. Urinary Tract infections

Urinary tract infections are caused by uropathogens and is most commonly seen in women. Cranberries have been used as traditional medicine for urinary tract infections. Cranberry extract has antibacterial activity against uropathogens such as *Escherichia coli*, *Staphylococcus aureus*, *Enterobacter aerogenes*, and *Klebsiella pneumoniae*.¹⁰ It reduces biofilm formation on uroepithelial cells¹¹. The extract also inhibits bacterial adherence to uroepithelial cells,¹² which is essential if bacteria is to cause infection. Quinic acid inhibits bacterial growth when present in urine.¹³

Consumption of cranberry juice reduces urinary odour.¹⁴ Burning on micturition, among other symptoms are also reduced. A reduction of urinary calcium excretion in patients with renal stones was observed after daily consumption for cranberry juice.¹⁵

C.Oral infections and diseases: Biofilms contains enzymes, bacteria, polysaccharides and host constituents which are considered to initiate and progress oral diseases. *Streptococcus mutans* an obligate biofilm organism gives rise to dental caries. The virulent factors of this bacterium are enzymes, fructosyltransferase (FTF) and glucosyltransferase (GTF). Cranberry juice constituents are an anti-biofilm agent by inhibiting biofilm formation and disrupting already existing biofilms. The anti-biofilm activity is due to its ability to inhibit FTF and GTF. It is also an anti-adhesion agent for several microbial pathogens.¹⁶

An overgrowth of *Candida albicans* will result in a fungal infection called candidiasis. A-type Cranberry proanthocyanidin (AC-PAC) inhibits biofilm formation and decreases adherence of *C. albicans* to oral epithelial cells. Prolonged exposure of AC-PAC resulted in detachment of biofilms. AC-PAC also decreased secretion of cytokines, hence reduced inflammation. AC-PAC could be used in the prevention and treatment of oral candidiasis.¹⁷

Cranberry polyphenols decreases the cell surface hydrophobicity of *Streptococcus mutans* and *Streptococcus sorbinus*.¹⁸ It also decreases the adhesion between cariogenic bacteria and enamel-like structures in the oral environment.¹⁹ Adhesion between bacteria and enamel-like structure is inhibited even with the presence of salivary coating.²⁰ Polyphenols also cause desorption of *S. sorbinus* from artificial dental biofilm.²¹ It also reduces formation of biofilm by *S. mutans*. Hence, caries development and progression is also avoided.²²

Resorption of alveolar bone is a typical hallmark of periodontal disease. Cranberry extract decreases formation of differentiated osteoclast as well as decreases osteoclastic activity. Also, interferes with the physiology of bone matrix. It could be used in the treatment and prevention of bone loss related to inflammatory disorders such as periodontal diseases.²³

D.Cancer: Cranberry proanthocyanidin (PAC) treatment for human oesophageal adenocarcinoma inhibited multiple carcinogenic-associated processes. PAC treatment up regulated BH3 interacting domain death antagonist, TRADD and TP73 which increases apoptosis.²⁴

PAC treatment significantly modulated cancer-related biological processes and key signalling pathways in NCI-H460 lung cancer cells. PAC has highly significant and rapid apoptosis inducing effects and potent effects on multiple cell cycle linked genes resulting in decreased cell proliferation and increased cell death. Specifically, PAC increased P21 expression levels, which has been linked to apoptosis resistance.²⁵

Cranberry extract significantly decreased cell growth and proliferation of oral squamous cell carcinomas. There was a dramatic up-regulation of mRNA expression in apoptosis initiator, caspases-2, and apoptosis effector, caspases-8. The extract also reduced cellular adhesion.²⁶ In prostate cancer, whole cranberry extract induced cytotoxicity, inhibited the expression of cell cycle proteins and slowed the progression of DU145 cells through the cell cycle.²⁷ Proanthocyanidins inhibit expression of matrix

metalloproteinase in DU145 cells and decrease translocation of NFkB p65 protein to nucleus.²⁸ In breast cancer, cranberry extract induced apoptosis and arrested cell cycle in MCF-7.²⁹

E.Antioxidant effects: Doxorubicin is a cancer chemotherapeutic agent. Administration of this drug causes cardiotoxicity in humans, due to formation of free radicals. This increased oxidative stress that leads to cardiac failure is counteracted by cranberry extract which is rich in flavonoids and phenolic acids. Flavonoids and phenolic acids have a high antioxidant effect.³⁰ These compounds inhibit oxidative processes in other tissues as well.³¹ Proanthocyanidins scavenge superoxides and 1,1-Diphenyl-2-picrylhydrazyl.³² It also enhance the ferric-reducing antioxidant power in plasma.³³ This accounts for cranberry extract protective property.

CONCLUSIONS

Cranberry extract has numerous protective functions in the human body. The antioxidant effect in addition to its other effects can serve as potential treatment alternatives in the case of cancers, infections of the gastrointestinal system, urinary tract and oral infections. Further research should study the antimicrobial effects of cranberry extracts and establish the active components of this wonder fruit.

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