Oral and Physiological Benefits of Cranberries

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Running title: Periodontal disease and Cranberries

Abstract

Cranberries are known to prevent urinary tract infection and it is also helpful in maintaining the oral health. Cranberry juice is a widely consumed and recommended beverage for preventing urinary tract infection. Clinical studies in women have shown that cranberries help to stop the recurrence of infection, as the evidence showed the presence of various extracts of cranberries in the patients’ urinary tracts, proving the effectiveness and the mechanism. The primary compound involved in fight against the infection is Proanthocyanidin A that is now the focus of studies to treat common diseases such as *Helicobacter pylori*-associated gastritis, as well as dental caries and periodontal disease, from which it is speculated the mechanism to involve disrupting the bacterial adhesion.

Keywords: Periodontal disease; Cranberries; Biofilm; Dental caries; Dental plaque

Introduction

Cranberries are now known to help in the oral health, especially when the juice is already a popular beverage and an advised dietary remedy for the prophylaxis of urinary tract infection (UTI). Clinical trials showed that cranberries did improve the condition of recurrent urinary tract infection in females. There were traces of cranberry extracts in the urine samples and could be inked to proanthocyanidins, which is now a hot compound for studies on its use in other common diseases, such as Helicobacter pyloric-associated gastritis, dental caries and periodontal disease, given that it is suspected to play a role in inhibiting the adhesion of bacteria on tissues or cells. Proanthocyanidins (PACs)[1-5], the most abundant flavonoid extracted from cranberries, have been reported to show antimicrobial, antioxidant and anti-inflammatory activities and prevent adhesion of microorganisms. Recent in vitro studies have shown that PACs may be a potential therapeutic agent for the prevention and management of periodontitis, an inflammatory disease of bacterial origin affecting the tooth-supporting tissues. Since the phytochemicals in cranberries have been proven to benefit human health, this review would focus on the specific preventive effect of PACs on the breakdown of connective tissues and alveolar bone destruction, as well as their potential for controlling periodontal disease. Possible mechanisms may include inhibiting bacterial and host-derived proteolytic enzymes, inflammatory response in the host, and osteoclast differentiation and activities. With the interesting properties exhibited by PACs in these in vitro studies, the evidence does warrant further investigation by clinical trials to better evaluate the potential of the compound to control periodontal disease[6-11].

**Cranberry Extract**

In the past few years, cranberry extract has increasingly attracted more attention from dental researchers [12-14]. This paper would explore the potential benefits of the extract in oral diseases, such as dental caries and periodontal disease. Cranberries are rich in high-molecular-weight polyphenols and they exist in thousand different forms, all of which are very promising in fixing caries (dental plaques) and periodontal disease, as well as controlling the inflammatory response and enzymes that break down the extracellular matrix. The cranberry extract is now characterized as an anti-caries agent, for its ability to inhibit acid production, bacterial adhesion and biofilm formation, targeting specifically the *Streptococcus* strains, in which the production of glucan-binding protein, the activities of extracellular enzymes, the metabolism of carbohydrates and bacterial hydrophobicity are affected [15-20]. For periodontal disease, the cranberry extract acts to suppress the host’s inflammatory response, inhibit the production and destructive activities of bacterial enzymes in the plaques, and prevent the formation of biofilm for adhesion, proteolytic activities and aggregation of pathogens in the periodontium. These show that cranberries, especially its high-molecular weight ingredient, can be used as bioactive substance for the prevention and treatment of oral diseases [21-26].

**Composition of Cranberries**

Cranberries contain quite a variety of substances, such as Proanthocyanidins A (PACs), tannic acid, organic acids, catechins, iron, zinc and other trace elements. Studies have pointed out that the major antibacterial component is Proanthocyanidins A, which can prevent dental caries, periodontal disease or urinary tract infection [27,28]. Over the last decade, in vitro clinical studies have found that some raspberry extracts are involved in microbial infection and spreading, especially the proanthocyanidins, which have an inhibitory effect on the adhesion of *E. coli* to urothelial cells. According to research, high-molecular-weight extracts in cranberries also showed similar effect to prevent the adhesion of P-fimbriated *E. coli*, as well as *Helicobacter pylori* to the mucosa of gastric wall in humans; thus, preventing the development of gastric ulcers. These in vitro observations are consistent with evidence of cranberry extracts inhibiting urinary tract infection and *Helicobacter pylori* infection. There are also some evidence supporting its inhibitory effect on some skin pathogens, but unfortunately, it has no effect on the oral pathogen, *Candida albicans* [29-36].

**Pathophysiological Mechanism of Preventing Periodontal Disease**

Proanthocyanidins are extracted from cranberries the fruit and are the most abundant flavonoid among the ingredients. They are anti-bacterial, anti-adhesion, antioxidant and anti-inflammatory. Recent experiments have all pointed to its therapeutic potential as an agent in the prevention and treatment of periodontitis, which is an inflammatory disease of bacterial origin affecting the tooth-supporting periodontium [11-14], beside its potential to prevent urinary tract infection and oral health, as well. Studies have shown that PACs in cranberries will help the connective tissues such as the gums and alveolar bones to resist breakdown and destruction by bacteria. It is speculated that it can: 1) inhibit bacterial and host-derived proteolytic enzyme activities; 2) inhibit the inflammatory response in host; and 3) prevent the differentiation and activities of osteoclasts. These were proven in animal experiments, but it will require more clinical trials (randomized and controlled) to better assess its potential in the prevention and treatment of periodontal disease [37-41].

Studies have found that the flavonoids in cranberry extract can inhibit the Glucosyltransferase enzymes (GTF) required for the formation of dental plaque, and an average of 250 mg of flavonoids can effectively inhibit 50% of GTF activities, while the teeth are naturally built to resist the bacteria by as much as 40%. Furthermore, experimental data showed that the active substances of cranberries, specifically the flavonoids (including Quercetin and Myricetin) can resist some degree of acidification and control the bacterial strain, *S.mutans*, that causes tooth decay. By reducing the chance of forming dental plaque, it will help to prevent tooth decay. In addition, cranberries stop Haemophilus bacteria from adhering to the mucosal epithelial cells; hence, reducing the chance of urinary tract infection. Recently, it was confirmed that PACs can prevent periodontal disease and dental caries by inhibiting the proteolytic enzymes from bacteria and the host, or inhibiting the host's inflammatory response, as well as inhibiting the differentiation and activities of osteoclasts. For periodontal disease and the necrosis of the tissues that are induced by gram-negative bacteria, the cranberry extract is highly effective in inhibiting MMPs and elastase secreted by inflamed oral cells. Plus, it plays to stop the acid-producing enzyme B and C (GTF-B, GTF-C), as well as F-Type ATPase in bacterial mitochondria. Overall, the evidence showed the cranberry extract with function to prevent periodontal disease and tooth decay, in addition to the inhibition of plaque formation and bacterial adhesion [42-46].

**Conclusion**

Cranberries are rich in healthy ingredients with nutritional value. Over the last decade, there was an increase in the public’s attention to the use of cranberries (Vaccinium macrocarpon) in North America, specifically the phytochemicals, namely anthocyanins, flavonols, flavan-3-ols, phenolic acid derivatives, proanthocyanidines, etc. These chemicals are the highlight of the cranberries’ inhibitory effect on bacteria, helping to fight against urinary tract infection and childhood diseases [47,48]. PACs are flavonoid-rich substances extracted from the cranberries, which are known to be anti-bacterial, anti-adhesion, antioxidant and anti-inflammatory. In recent years, more experiments have extracted PACs from cranberries as the potential agent to treat periodontitis. Thus, it is expected for the cranberries to show unlimited potential in oral health care in the future.

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