Cranberry – A Boon in Periodontal Therapy

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Abstract

Cranberry juice has been used in medical fields for the past decade because of its several health benefits. Due to its properties, cranberries and its molecular components have gained attention by the researchers. The chief bioactive component of cranberry is proanthocyanidins. Its improved health benefits are already being found in treating UTI and many systemic diseases. But only a few studies have shown its effect on oral health.

Keywords: *Cranberry juice, Periodontal Disease, Functional Food, Vaccinium macrocarpon, Proanthocyanidins.*

Introduction

The native North American fruit cranberryhas currently gained some interest in the medical field for its several health benefits. Widely grown in the peat bogs of the cooler northeastern part of North America, it is one of the three original fruits of the country, which grows as a vine or low trailing shrub, bears a red fruit and is acidic in taste.Cranberry itself is a unique, good source of several classes of bioactive flavonoids includingflavonols, anthocyanins, and proanthocyanidins which confer it the significant therapeutic potential. The cranberry fruit is commonly consumed via several foodproducts, including the fruit itself and also in powder form incorporated in capsules and tablets.[1]

Therapeutic applications of cranberries started during the17th century which includes the treatment of blood disorders, stomach ache, liver problems, vomiting, appetite loss, scurvy, and cancer. Recently, cranberry extract has gained enormous attention in various areas of health research, including infectious and non-infectious diseases.Cranberry (Vaccinium macrocarpon) is a berry bush found in North America as one of the original fruit of the country. It has a mild acidic taste. It is consumed via different ways like fresh and dried form, juices and sauces and also in capsules and tablets in granulated form. It is an exclusive source of bioactive flavonoids which includes anthocyanins,proanthocyanidins and flavanols. These components in cranberry are solely responsible for its distinct therapeutic properties.[2]

Structure of proanthocyanidins

The procedure of making it includes extensive dialization of cranberry juice along with some other modifications. This process results in a product which is devoid of sugar and acids, containing 0.35% anthocyanin and 65.1% proanthocyanidins[2].Prof. Jacques Masquelier is the first one to develop the distillation procedure for extracting the proanthocyanidins from pine bark and grape seeds. Proanthocyanidins are mainly of two types: type A and B. Type A can be found in apricot, cranberry and type B can be found in other berries. Proanthocyanidins are mainly composed of multiple epicatechin units along with a minimum of one A-type

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linkage (O7 C2).[2] Other tannin-rich food contains B type linkage. The typical structure of cranberries is thought to be essential for the anti-adhesion property which can be used against the colonization of periodontopathogens in supragingival and subgingival regions.[3]

Nonetheless activation of the host immune system by bacteria and their products initiates a cascade of host-mediated noxious process which leads to the accumulation of inflammatory mediators. This reaction is succeeded by the inflammatory reaction normally caused by MMPs which will ultimately lead to tissue destruction. Degradation of tissue protein and invasion of periodontium occurs because of the bacteria secreted soluble and insoluble proteases.[4]

Periodontitis is a disease caused by chiefly the colonization of particular gram-negative bacteria. This ultimately leads to the impairment of soft and hard tissues of the periodontium and finally results in tooth loss. The pathogenesis of periodontitis is consisting of two major factors. First is microbial, which includes colonization of periodontal-pathogenic bacteria subgingivally, which destroys the soft tissue and junctional epithelium. The second is the host response of periodontopathogens which leads to increased production of inflammatory mediators and MMPs which are chiefly responsible for the initiation and progression of periodontitis. It was reported that cranberry has significant inhibitory effects on these two stages.[5]

Effects on periodontopathogens (adhesion and biofilm formation)

For the periodontal progression, the microbial colonization is an essential step. the ability of periopathogens to form biofilm and to generate adhesins which ultimately helps them to attach to the tooth surface, basement membrane or host cells. Thecranberry NDM fraction helps in inhibition of biofilm formation of but it does not affect the bacterial growth. This cranberry NDM fraction reduces the attachment of P. gingivalisto various proteins like Type I collagen and fibrinogen[3].

This fraction also inhibits the bacterial co-aggregation. They target those bacteria which are gram-negative anaerobes frequently responsible for periodontal diseases. These findings guides us to the decision that cranberry NDM fraction functions by preventing the bacterial adhesion rather than only by hindering the bacterial growth.

Proteolytic enzymes

Socransky et al. (1998) described that the members of the red complex which include P. gingivalis, T. forsythia, and T. denticola are the chief causative factors of periodontitis.[12] These periodontopathogens are closely related to periodontitis particularly in the destruction of junctional epithelium, increasing in pocket probing depth and bleeding on probing. The cranberry NDM fraction reacts with the period onto pathogens proteinases. It inhibits the action of gingipain (both Arg- and Lys-gingipain) depending on the dose. It also downregulates P. gingivalis activity, the trypsin-like activity of T. forsythia, and the chymotrypsin-like activity of T. denticola.[4] It also preventsP. gingivalis to denaturize proteins like collagen and transferrin. All these functional values of NDM fraction proposes that it can inhibit the production of red-complex bacteria in periodontal pockets.[6]

The destructive period onto pathogens produce proteinases. NDM fraction may reduce these tissue destruction mediators. Additional proof was given by Yamanaka et al. (2006) about the inhibitory efficacy of cranberry polyphenols action. Among the three fractions of cranberry polyphenols (anthocyanin, proanthocyanidin, and flavonol), the proanthocynidin fraction is highly effective and anthocyanin fraction is the least effective[5]. It has been suggested that these inhibitors can suppress bacterial pathogenicity and henceforth it can beassessed as a novel therapeutic agent for treating periodontitis.

Effect on periodontal bacteria and host mechanisms

Experiments performed by Labreque in 2006 and Yamanaka in 2008 revealed that the NDM fraction revealed that cranberry NDM fraction hinders the aggregation of Porphyromonas gingivalisand Fusobacterium nucleatum in the gingival crevicular fluid.[7]

Cranberries are reported to stop the protein denaturation occurred by the red-complex bacteria. It restrains the gingipain activity of P. gingivalis, the trypsin-like activity of Tanerella forsythia and the chymotrypsin-like activity of T. denticola, thus it leads to the conclusion that this fruit is having the capability to restrain the aggregation and multiplication of bacteria by restricting their growth resources like amino acids, peptides. It also inhibits the bacterial proteinases mediated tissue destruction.[8]

Inflammatory cytokines like (IL-1β, TNF-α) are produced by host macrophages. This process will lead to a cascade of inflammatory reactions like lipopolysaccharide production of A. actinomycetemcomitans, F. nucleatum, P. gingivalis, T. denticola and T. forsythia. A clinical experiment done by Bodet et al in 2006 found that the cranberry fraction helps in inhibiting these cytokines.[15] The NDM fraction acts by inhibiting the cell-signaling proteins and leads to the reduction in regular activator protein (AP-1). This AP-1 protein is an important transcription factor for pro-inflammatory mediators coding genes.[9]

Inflammatory cells chiefly macrophages and fibroblasts produce various enzymes like MMPs and elastase which is the primary cause of tissue destruction. In vitro ELIZA studies revealed that depending on the dose this cranberry NDM fraction has an inhibitory effect on the MMPs[6]. The lipopolysaccharide-induced interleukins and PGE-2 responses as well as Cyclooxygenase-2 expression are suppressed by the cranberry fraction[7].

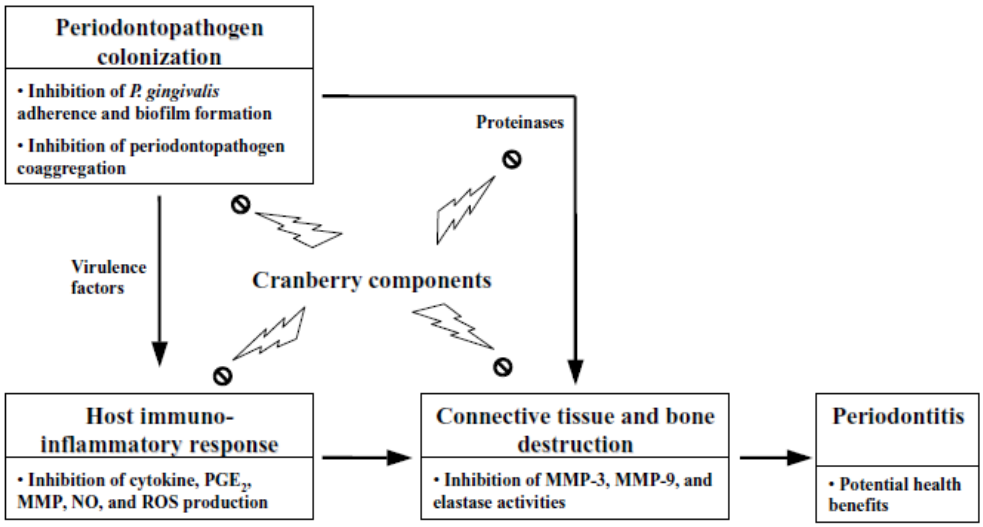

Figure 1. Pathophysiology of periodontal pathogens

Dosage: Various doses and formulations of cranberry are available in the market. This includes unsweetened or sweetened cranberry juice, cranberry extract tablets, pure cranberry extracts in a bottle etc. A recent randomized control trial performed showed that the one tablet of concentrated cranberry extract (300 to 400 mg) twice daily, or 8 oz. of pure unsweetened cranberry juice three times daily for 12 months is safe and effective as an daily systemic treatment doses for antimicrobial therapy.[10, 11]

Contra indications and adverse effects: Cranberry as a dietary supplement has shown a record of safety and it has not shown any particular drug interactions. Still, specific long term safety data is missing. A study found that patients who are under proton pump drug therapy, cranberry enhances the vitamin B12 in them which can ultimately lead to faster metabolization of weakly acidic drugs thereby reducing their effectiveness.[10] A study showed that it can be responsible for the significant rise of urinary oxalate levels and systematic daily use of cranberry may lead to a high risk of kidney stone formation in patients with a history of oxalate calculi.[8, 12-14]

Conclusion

Cranberry extract certainly helps in fighting oral diseases. However, due to high dextrose and fructose content and strong acidic flavour the cranberry juices which are available in the market are inappropriate for daily oral hygiene use. However, cranberry fractions included in the dietary supplements have shown some promising results as suggested by current research.

Remarkably, the cranberry fraction stops the pathologic mechanism of dental caries and periodontal infection. It can be included in various products like toothpastes and mouthrinses as well as gels and strips to arrest the progression or treat the oral diseases. Weiss et al in 2004 showed that NDM supplemented mouth wash reduces the salivary S. mutans levels in healthy adults. The study can lead to the conclusion that the anti-adhesion and anti-plaque therapy by the edible dietary components can be a sustainable way for treating oral diseases like dental caries and periodontal diseases.

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