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# Oral Health Benefits of Cranberry: A Review

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***Abstract:*** *Cranberry has a unique combination of phytochemicals which are used for treatment of various systemic diseases including oral diseases like caries,periodontitis and oral cancer. Many in vitro studies have outlined the potential health benefits of cranberry but in vivo studies are still inconclusive. Cranberry inhibit acid production, attachment and biofilm formation by Streptococcus mutans thereby being an effective anticaries agent. It also inhibits host inflammatory response and adherance of periodontal pathogens on tooth surfaces. Proanthocyanidins in cranberries demonstrate significant cancer prevention. The review aims to well into the potential benefits of cranberry in improving oral health as well as a peep into the still unexplored facets of natural medicaments in oral disease prevention.*

***Keywords:*** *Cranberry, Dental Caries, Periodontitis, Oral health, Antibacterial*

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## I. Introduction

Cranberry (Vaccinium macroporn) is one of the American berries consumed in a broad array of forms including fresh,frozen ,canned as well as dried fruit and fruit juices[1]American cranberry has a complex and rich phytochemical composition,particularly flavan-3-ols,A type procyanidins(PACS),anthocyanins,benzoic acid and ursolic acid[2].Cranberry has often been used for treatment of urinary tract infections.It contains two compounds fructrose and proanthocyaniin that prevent fimbricated Escheresia coli from adhering to uro epithelial cells in urinary tract[3]t.Cranberry has a potential role in eradication of Helicobacter pylori due to the presence of polyphenols.Cranberry induces H.Pylori to develop a coccoid form and thus inhibit its growth bacteriostatically[4].Cranberry juice was found to inhibit heamagglutination induced by influenza virus as well as to neutralize the cytotoxicity of influenza virus in cell cultures[5].Fungastatic effect of cranberry on dermatophytic and other fungi are well documented but it seems to have no effect on oral pathogenic fungi Candida albicans[6]. Flavinoid from Cranberry extracts are seen to inhibit tumor cells of breast ,colon and prostrate[7].Cranberry extracts are believed to have a potential effect in reducing role of cardiovascular diseases by increasing the effect of LDL to oxidise inhibiting platelet aggregation and reduce blood pressure by antithrombotic and anti-inflammatory mechanism[8].In the last two decades research is going on to elucidate the possible role of cranberry extracts in preventing caries, periodontal disease and oral cancer which is highlighted in this review.

**Composition of high molecular constituents of Cranberry**

Cranberry juice is known to inhibit co-aggregation of bacteria like E.coli and H.pylori to host cells. A high molecular weight non-dialysable material (NDM) of cranberry juice was shown to reverse co-aggregation of many oral bacterial species[9].Concentrated juice from the American cranberry Vaccinium macroporn was obtained from the Ocean Spray Cranberries.The juice is exhaustively dialysed (5 days) at 4°C against distilled water in 14000 MW cut off dialysable bags and lyophilized.The NDM was dissolved in distilled water and then lyophilized[10].

**Use of Cranberry non dialysable material(NDM) in periodontal disease**

Periodontitis is an inflammatory disorder leading to destruction of tooth supporting tissues including periodontal ligament and alveolar bone and is caused by specific group of gram negative anaerobic bacteria[11].The continuous challenge to host immune systems is induced by host mediated destructive processes[12].Porphymonas gingivalis is the key pathogen in chronic periodontitis.P.gingivalis is known to express a number of adhesins associated with either outer membrane or fimbria that promote its adhesion to tooth surfaces,gingival epithelial cells,basement membrane components,erythrocytes and oral bacteria[10]. Labercque et.al[10] showed that cranberry NDM could prevent the formation of P.gingivalis biofilm at a concentration of 62.5µg/ml and higher.Cranberry fraction however did not show any capacity to desorb a

preformed biofilm of P.gingivalis. Mechanism of action of cranberry proanthocyanidins (PACs) include 1.inhibition of bacterial and host derived proteolytic enzymes,2.host inflammatory response and 3.osteoclast differentiation and activity[14].

The red complex which included Tanarella forsythia(T.forsythia), Streptococcus sanguis(S.sanguis), Porphymonas gingivalis(P.gingivalis)Capnocytophaga spp and Veilonella parvula(V.parvula) were closely linked to periodontitis particularly pocket depth during probing[15].The strong proteolytic activity of bacteria of red complex causes periodontal destruction by variety of mechanisms including direct tissue degradation and host inflammatory response modulation[16].Bodet (2006)[17] investigated the effect on NDM prepared from cranberry juice concentrate on the proteolytic activities of P.gingivalis,T.forsythia and T.denticola.The effect of NDM on gingipain and dipeptidyl peptidase 1V activities of P.gingivalis ,trypsin like activity of T.forsythia and chymotrypsin activity of T.denticola was evaluated using synthetic chromogenic peptides.The results suggested that NDM has the potential to reduce the proliferation of P.gingivalis,T.forsythia and T.denticola in periodontal pockets or their protienase mediated destructive processes occuring in periodontitis.

High production of cytokines by host cells triggered by periodontopathogens is responsible for destruction of tooth supporting tissues. Bodet et.al(2006)[18] investigated the effect of NDM from cranberry juice on concentrate on pro inflammatory cytokine response of macrophages induced by lipopolysaccarides from Actinobacillus actinomycetocomitans,Fusobacterium nucleatum sub spp,Porphymonas gingivalis ,Treponema denticola,Tanarella forsythia and E.coli.IL-1β,IL-6,IL-8,TNF-α and Regulated on Activation Normal T cell Expressed and Secreted (RANTES) production by macrophages treated with cranberry fraction prior to stimulation by lipopolysaccarides (LPS) was evaluated by ELISA. The results clearly indicate that cranberry fraction was a potent inhibitor of pro-inflammatory cytokine and chemokine response induced by LPS.

Cranberry has been shown to reduce the expression of cyclo-oxygenase -2 an enzyme involved in PGE- production. Cranberry was seen to limit the inflammatory responses of both macrophages and gingival fibroblasts elicited by periodontopathogens[19].

Matrix metalloprotienases(MMPs) produced by resident and inflammatory cells in response by periodontopathogens play a major role in periodontal tissue destruction[20].La et.al (2009)[21] investigated the effects of A-type cranberry proanthocyanidins (AC-PACs) on the production of various MMPs by human monocyte derived macrophages stimulated with Aggregatibacter actinomycetocomitans and the catalytic activity of recombinant MMP-1 and MMP-9.The results showed that AC-PACs inhibit the production of MMPs in a concentration dependent manner and also inhibited catalytic activity of MMP-1 and MMP-9

**Cranberry NDM and Dental Caries**

Dental plaque is a structurally and functionally organized biofilm. Plaque forms in an ordered way and has a diverse microbial components that in health remains stable over time. In dental caries,there is a shift towards community dominance by acidogenic and acid tolerating species such as S.mutans and lactobacilli. Oral biofilms provide an ideal platform for caries devolepment . Stratergies to control caries should include inhibition of biofilm devolepment like prevention of attachment of cariogenic bacteria,manipulation of cell signaling systems,enhancement of host defences and delivery of effective anti microbials[22]Dental plaque samples when observed microscopically showed intimate contact between vast majority of bacteria in biofilm. In several areas of oral cavity the acquired pellicle serves as substrate for adhesion of so called early colonizing bacteria predominantly streptococci and actinomycetes.The late colonizers include P.gingivalis ,P.intermedia, T.forsythia, A.actinomycetocomitans ,F.nucleatum etc[23].Streptococcus mutans ,the main pathogenic bacteria associated with dental caries produces a number of extracellular sucrose metabolizing enzymes such as glucosyltransferases (GTFB,GTFC and GTFD)and fructosyltransferase (FTF).The cooperative action of these enzymes is essential for sucrose dependent cellular adhesion and biofilm formation[24]. Cariogenic bacteria which are highly acidogenic and aciduric get embedded into the dental biofilm.Acids like lactic acid produced by these bacteria reduce pH below 5.5 initiating a favorable environment for enamel dissolution [25].

Cranberry NDM inhibits mutans streptococcal adhesion and biofilm formation as well as a co-aggregation of oral streptococci.Salivary counts of oral streptococci are reduced in volunteers using mouthwash supplemented with NDM from cranberry juice[26].Cranberry causes disruption of acidogenic/aciduric properties of planktonic and biofilm cells of S.mutans.It has inhibitory effects on GTF activity and adherance by S.mutans and causes reduction in the formation of S.mutans biofilms and EPS contents[27].Yamanaka et.al[28] examined the effects of cranberry polyphenols fraction on hydrophobicity,biofilm formatation and bacterial growth of mutans streptococci strains.The results suggest that daily uses of mouthwashes ,tooth paste or chewing gum containing cranberry polyphenol fraction might prevent the development of dental plaque.

The use of mouthwash supplemented with NDM on oral hygiene was investigated by Weiss et.al[29].Following 6 weeks of daily usage of cranberry by an experimental groups compared with those using

placebo ,significant reduction of total bacterial count was observed. Data suggests the ability to reduce mutans streptococci counts in vivo due to anti adhesion activity of cranberry constituent.

The dental biofilm once formed causes bacteria on its surface to release organic acids especially lactic acid which cause the demineralization of enamel with cavity formation. The glucan binding protiens (GBP) present in streptococcal membrane helps in adhesion of streptococci to the biofilm[30].Durate et.al(2006)[31] examined the influenze of flavanols,proanthocyanidins and anthocyanins from cranberry on virulence factor of S.mutans biofilm devolepment and acidogenicity.Biofilm devolepment and acidogenicity were significantly affected by topical applications of flavanols and proanthocyanidins.Steinberg et.al[32] examined the effects of NDM on several constituents of dental biofilm,glucosyl transferase (GTF) and fructosyl transferase as well as adhesion of S.sobrinus.They concluded that NDM may affect biofilm formation by inhibition of extracellular polysaccaride synthesis that promote the sucrose dependent adhesion of oral bacteria as S.sobrinus.Koo et.al (2006)[33] used cranberry juice (pH 5.5) to evaluate its ability to influence the adherance of S.mutans to either saliva (sHA) or glucan coated hydroxyapatite(gSHA) and to inhibit the glucan production by purified glucosyltransferases absorbed by SHA. The results showed that cranberry juice inhibit glucan mediated biofilm devolepment and acid producton and holds promise as a natural product to treat biofilm related oral diseases.

## II. Conclusion

Cranberry juice may fight oral diseases but its high dextrose and fructose content in addition to its hyperacidity limits its potential. However the NDM fraction of cranberry is highly effective in control of dental caries as well as periodontitis.NDM fraction of cranberry incorporated in mouthwashes or toothpastes have shown lot of promise in the control of oral diseases. Even though cranberry and its extracts hold lot of promise, much work needs to be done to unearth the true potential of this natural fruit.

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