

## Role Of Dietary Antioxidants In Periodontitis: A Preventive Approach

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**Abstract:** In periodontitis, one of the major pathologic patterns is an increased production of reactive oxygen species (ROS). Reactive oxygen species are produced by polymorph nuclear cells as an inflammatory response to invading pathogenic bacteria. This imbalance among the production of free radicals and local antioxidants results in periodontal tissue destruction and a state of oxidative stress develops. In recent years, beneficial effects of antioxidants against various chronic disorder induced by oxidative stress have received much attention. This review is intended to summarize the role of dietary antioxidants in prevention of periodontal disease.

**Keywords:** antioxidant, oxidative stress, periodontitis, ROS,

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### I. Introduction

Oxidative stress is a state of altered equilibrium when antioxidant system of body fails to regulate the levels of free radicals produced in the body.<sup>1</sup> At low concentration, free radicals are involved in various cell functions as cell signaling but at high concentrations, they react with cell molecules especially protein, DNA and lipid molecules and mediate tissue damage.<sup>2</sup> Excessive production of free radicals are involved in pathogenesis of various chronic inflammatory disorders including periodontal disease.<sup>3</sup>

Periodontal disease is a chronic inflammatory disorder that leads to tissue damage as a result of complex interactions between pathogenic bacteria and the host immune system.<sup>4,5</sup> Patients with periodontal disease display increased PMN number and activity, resulting in high degree of ROS release, culminating in heightened oxidative stress in gingival tissue, periodontal ligaments, and alveolar bone.<sup>6</sup> Recent reports have also suggested that ROS are produced by osteoclast at the ruffled border interface and may play a role in resorption<sup>7</sup>.

Cells require adequate levels of Antioxidants in order to prevent tissue damage caused by excessive production of reactive oxygen species (ROS). This has been shown that additional intake of high grade antioxidants can reduce periodontal pocket depths as much as 3 times compared to scaling and root planning alone.<sup>8</sup> Due to possible health benefits of antioxidants against periodontitis, increased intake of such nutrients have been recommended. The aim of this article is to provide an overview of the effects of antioxidant nutrients in periodontal health and disease.

### II. Antioxidant Micronutrients:

Natural antioxidants are molecules that prevent cell damage against free radicals and are critical for maintaining optimum health in humans.<sup>9</sup> Major sources of antioxidants in the human diet include cereals, fruits, vegetables, chocolate, oils and beverages such as tea, coffee, wine and fruit juices etc. Dietary antioxidants which possess strong antioxidant activities include vitamin C (ascorbate), vitamin E, beta-carotene and the polyphenols.<sup>10</sup> Now days, among the recommendations for the maintenance of healthy periodontal tissues, focus is given on the value diet and nutritional supplementation also.

#### 2.1 Vitamin C:

The importance of ascorbic acid, better known as vitamin C, for periodontal health has long been known. The most appropriate sources of vitamin C are natural fruits such as kiwi fruit, citrus fruits, pepper etc. Green kiwi fruit is a rich source of vitamin C and it contains 93 mg vitamin C/100 g fruit whereas e.g. oranges contain vitamin C up to 53 mg/100 g fruit.<sup>11</sup>

Vitamin C is a most powerful antioxidant radical scavenger within the aqueous phase.<sup>12</sup> It is a co-factor for lysyl and prolyl hydroxylase, involved in stabilization of the collagen triple helix.<sup>13</sup> it act as acts as regenerator for other antioxidants in body such as vitamin E.<sup>14</sup> Different PDL respond differently to ascorbic acid. Bone-forming PDL cells may differentiate further in the presence of ascorbic acid.<sup>15</sup> In contrast, ascorbic acid may cause fibroblastic PDL cells to increase both collagen and collagenase-1 expression, maintaining a high state of matrix turnover.<sup>16</sup>

Due to high intracellular ascorbic acid concentrations in leukocytes especially PMN and macrophages (approx 10-40 times), these cells are capable to react in response to inflammatory stimuli.<sup>17</sup> It not only enhances chemotaxis of normal PMNLs but also correct abnormal chemotaxis and lysosome degranulation in PMN from patients with Chediak–Higashi syndrome.<sup>18</sup>

Leggott et al.<sup>19</sup> studied the effect of a nutrient rich diet but lacking vitamin C, on periodontal health. The results suggested that ascorbic acid may influence early stages of gingivitis, particularly increased crevicular bleeding. However, in subsequent studies, no significant changes in plaque accumulation, probing pocket depth, or attachment level were noted.<sup>20</sup> Blignaut & Grobler showed that deeper pockets (CPITN code 3 and 4) occurred far less frequently in citrus fruit-producing farm workers than that of workers in grain-producing farms.<sup>21</sup> Based on NHANES III survey, Nishida et al.<sup>22</sup> revealed that the dietary vitamin C have a weak, but statistically significant inverse relationship to periodontal disease in current and former smokers. Using the same NHANES III data set Chapple et al. found a strong and consistent inverse association between serum vitamin C levels and the prevalence of periodontitis.<sup>23</sup>

Vitamin C can be well tolerated at doses well above the RDA recommendations, but high doses of vitamin C may generate toxicity due to the formation of vitamin C radicals. For many years the recommended daily intake of vitamin C was 60 mg. In 2000 Recommended Dietary Allowance (RDA) of vitamin C was increased by the Food and Nutrition Board from 60 to 90 mg daily for men to 75 mg daily for women.<sup>24</sup>

## **2.2 Vitamin E :**

$\alpha$ -tocopherol is the most active biological form of vitamin E. It is a fat soluble antioxidant, found most abundantly in nuts, seeds and vegetable oil as wheat germ oil, sunflower, and safflower oils.<sup>25</sup> Vitamin E transfers phenolic hydrogen to the recipient free radical and gets converted into phenoxyl radical. However, this phenoxyl radical is no longer an antioxidant and it must be recycled or repaired.<sup>26</sup> Water-soluble vitamin C is the popular candidate for this role but thiols and particularly GSH can also function in this role in vitro. Vitamin E can help to control periodontal disease through its ability to prevent inflammation. Taking vitamin E might helps diabetics, control their blood glucose levels thereby it might help reduce the side effects of the disease including the development of periodontal disease.

Studies on vitamin E showed Mixed Results. Sobaniec found that there are significantly low levels of vitamin E and other antioxidants in saliva of epilepsy patients with periodontal disease.<sup>27</sup> Cohen RE et al compared the use of a 5% vitamin E gel, a chlorhexidine rinse and a placebo on plaque and periodontal disease<sup>28</sup>. After two weeks, participants using the placebo and the vitamin E gel showed no improvement in the amount of plaque or gum inflammation but chlorhexidine significantly reduced plaque. In another study no significant difference in the levels of serum vitamin E in patients with and without periodontal disease was found.<sup>29</sup> Although it has been suggested that vitamin E might be beneficial in the prevention of periodontal disease, but its overall effect on periodontal health is not fully understood. Data do not provide sufficient support for the treatment of inflammatory periodontal disease with vitamin E and more researches are needed in this area.

## **2.3 Carotenoids:**

Carotenoid antioxidants (alpha carotene, beta-carotene, cryptoxanthin, lutein, lycopene, zeaxanthin) are a group of natural colored pigments, usually yellow, red or orange, that are widespread in plants.<sup>30</sup> They act as free radical traps. They have protective effects on vitamin C and E and have synergistic effects by scavenging reactive nitrogen species.<sup>31</sup>  $\beta$ -carotene is the main source of provitamin A in the diet. Due to the fact that carotenoid levels have influence on other antioxidant molecules therefore they are regarded as cardinal in antioxidant defense system. Svilaas et al revealed that carotenoids are predictors of all in all antioxidant status.<sup>32</sup>

Carotenoids are powerful antioxidants. They may also be involved in regulating cell-to-cell communication or gene expression. Carotenoid rich diet is correlated with a diminished risk various degenerative disorders including cancer, cardiovascular or ophthalmological diseases.<sup>33</sup>

Linden et al. evaluated the correlation between periodontal health and serum levels multiple antioxidants.<sup>34</sup> He noticed that levels of  $\alpha$  and  $\beta$  carotene,  $\beta$  cryptoxanthin, and zeaxanthin were significantly lower in moderate and severe periodontitis patients however no such association was found in the levels of lutein, lycopene,  $\alpha$  tocopherol or retinol with periodontitis. Walston et al found that patients with low levels of  $\alpha$ - and  $\beta$ -carotene and total carotenoids were more likely to have high interleukin-6.<sup>35</sup>

$\beta$ -Cryptoxanthin has an anabolic effect on bone metabolism. It has been shown to stimulates bone formation and inhibit bone resorption.<sup>36</sup> Also it inhibits gene expression of osteoclastic enzymes which are involved in bone resorption. It is suggested that increased intake of fruit and vegetables containing  $\beta$ -cryptoxanthin could reduce the risk of osteoporosis.<sup>37</sup> Therefore  $\beta$ -Cryptoxanthin could be relevant to periodontal destruction, given its potential osteogenic activity on bone rather than through its activity as an antioxidant.

## 2.4 Flavonoids :

Flavonoids are polyphenolic compounds found in fruits, vegetables and certain beverages. Dietary intake of flavonoids is quite high compared to other dietary antioxidants. They have antioxidant, anti-inflammatory, anti-allergic, antiplatelet and antitumor activities.<sup>38</sup> It also has an inhibitory action on bacterial collagenase. Synergistic relationship between flavonoids and vitamin C has also been established.<sup>39</sup> High-flavonoid foods help to protect blood vessels from rupture or leakage, protect cells from oxygen damage, and prevent excessive inflammation throughout body.<sup>40</sup> Green tea has flavonoid components called catechin that may reach 1 gram per cup. Other rich sources of flavonoids are Cocoa, berry, onion, apple etc.

Tomofuji et al showed that rats feasted on a cocoa enriched diet could develop experimental periodontitis, however the serum ROS levels and the GSH ratio was shown to be maintained in gingival tissues.<sup>41</sup> Sonia N. revealed that there is significant reduction of the gingival bleeding index in the green tea consumers group as well as in the group of patients that followed the flavonoid treatment.<sup>42</sup> Kushiyama et al. demonstrated that the intake of green tea was inversely related with mean pocket depth, bleeding on probing and clinical attachment level.<sup>43</sup> Balbin showed that green tea can completely inhibit the activity of collagenase in GCF in aggressive periodontitis patients.<sup>44</sup> It was demonstrated that flavonoids may restore the alveolar bone therefore provide a bone mass by inhibiting LPS-induced bone resorption.<sup>45,46</sup> Therefore increased intake of flavonoids may proved to be beneficial prevention of periodontal disease.

## III. Conclusion:

Specific foods and combinations of various micronutrients can improve the response to therapies. Also nutritional counseling and supplementation reduces inflammation and hence can complement treatment concepts. Due to the potential health benefits, antioxidant nutrients have opened a new window for prevention and treatment of periodontal diseases and diet should be supplemented with natural antioxidants. However to correctly evaluate the relationship of dietary antioxidants and periodontal health, further controlled clinical studies are needed.

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