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THE IMPACT OF MICRONUTRIENTS IN PERIODONTAL HEALTH AND DISEASE: A NEGLECTED PATHWAY- A REVIEW

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Abstract:
Micronutrients, which have anti-oxidant and anti-inflammatory characteristics, are essential for the health of the oral mucosa and structures. Many, if not all, of the micronutrients described have an independent relationship with the frequency of periodontal disease. Micronutrient treatment, both systemic and local, can enhance tissue repair and improve the prognosis of periodontal disorders. Few studies have been conducted to investigate the efficacy of vitamin supplementation on periodontal treatment, and even fewer have been conducted to investigate the influence of micronutrient deficiencies on the occurrence of periodontitis. More research is needed to broaden the body of information, which might aid in the prevention of oral inflammatory illnesses and the creation of future therapeutic interventions.

Keywords: Micronutrients, Macronutrients, Periodontitis, Periodontal disease, Vitamins, Minerals.

INTRODUCTION

Periodontitis is a chronic inflammatory condition that affects the tooth's supporting structures and, if not treated promptly, can lead to tooth loss, which can lead to decreased masticatory function and, as a result, changes in dietary intake and nutritional status. The knowledge that periodontitis is a risk factor for a variety of serious systemic disorders has increased the necessity of good periodontitis management and treatment.[1] According to the Global Burden of Disease 2010 survey, the global age-standardized prevalence of severe periodontitis was 11.2%, making it the world's sixth-most frequent ailment, while the Global Burden of Disease 2015 report assessed the prevalence of severe periodontitis to be 7.4%. Milder types of periodontitis may account for up to 50% of all cases.[2] In India, the pooled prevalence percentage stated by a systematic study published in 2020 is 51%. These rising numbers highlight the need of illness knowledge and good management as a top public health goal.

In susceptible people, periodontal disease is defined as a dysregulated host inflammatory response to bacterial plaque.[3] A number of risk factors have been identified that alter the host response, shifting the biological balance from health to illness. These influences are genetic, environmental (e.g., stress, bacterial assault), and lifestyle/behavioral (e.g., diet, physical activity, tobacco).

From research that has cited the significance of nutrition in a range of chronic inflammatory conditions, lifestyle being one of the primary risk factors that contribute to the onset of periodontal disease, but in the last decade the association between periodontal diseases and nutrition is grabbing the spotlight of health care professionals.[4,5]

Dietary nutrients are important for life because they offer a critical energy source (macronutrients) as well as vital cofactors necessary for enzyme function, structural moieties, and transport (micronutrients). Malnutrition results from the depletion or lack of availability of certain nutrients at either the macronutrient or micronutrient levels. Micronutrient consumption is a critical modifiable risk factor for oral inflammatory disorders.[6]

Dietary deficiencies have been proven to have an influence on prognosis, with malnutrition being associated with a faster deterioration. Nutrient abnormalities tend to promote the inflammatory processes involved in periodontal disorders. Dietary variables, according to research, contribute to the regulation of microorganisms in the mouth cavity, which has been connected to periodontal diseases. The sections that follow demonstrate these impacts in terms of micronutrients in periodontal health and disease situations.

NUTRIENTS AND ITS TYPES

"Food is essential—it provides vital nutrients for survival and helps the body function and stay healthy,"[7] according to the Academy of Nutrition and Dietetics. Nutrients are elements that the body need for functioning properly. Because the human body does not synthesize or create nutrients, we must receive them from our food.

Fats, carbs, proteins, minerals, vitamins, and water are the six types of nutrients necessary by the body to function and sustain general health. Non-nutrients in meals can be detrimental (such as natural poisons found in plant foods and additions such as certain colors and preservatives) or helpful (such as antioxidants)[8]. Nutrients can be further subdivided into two broad categories:

1. **Macronutrients** must be acquired in significant amounts from the diet and are biologically converted into energy for cells. Macronutrients are classified into three types. Carbohydrates, lipids, and proteins are the three macronutrients.
2. **'Micronutrients,'** which are only required in little amounts in the diet yet are vital for a variety of biological processes critical to good health.[1]

MICRONUTRIENTS

These are nutrients that the body requires in lesser amounts yet are nonetheless necessary for basic activities. Nutrients that are necessary for body activities but are only required in trace levels. All of the important minerals and vitamins are included in micronutrients (Figure 1). Micronutrients, unlike carbohydrates, lipids, and proteins, do not provide energy, but they do aid in the process of energy metabolism as cofactors or components of enzymes (known as coenzymes). Enzymes are proteins that catalyze (or speed) chemical processes in the body; they are involved in many areas of physiological activities, including energy production, nutrition digestion, and macromolecule formation. Aside from the categories described above, nutrients have also been classified as energy producing, organic, and inorganic .[8]

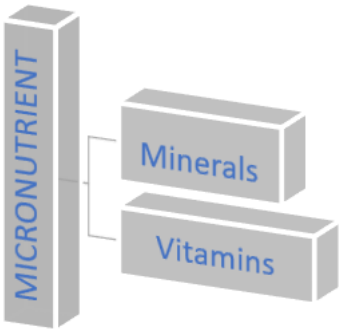


Figure 1: Types of Micro Nutrients.

Deficits in micro nutrients can be triggered by drugs (antacids, antibiotics, antihypertensives, chelation agents, corticosteroids, diuretics, laxatives, NSAIDs), inadequate absorption or diarrhea, factors related to lifestyle (diet, malnutrition, chronic alcohol or nicotine abuse, and intake of fast food or processed foods), systemic disorders (diabetes mellitus, thyroid and parathyroid disorders), and higher requirements (pregnancy, growth, mental or physical stress, breastfeeding). Nutrient absorption and utilization are affected by physiologically and dietary variables that change over life.[4] Bioavailability, on the contrary, is affected by the chemical form as well as presence of other micronutrients such as vitamin D and calcium.[33,34,35] The various vitamins have been discovered to have beneficial impacts on periodontal health.[39](Figure 2)

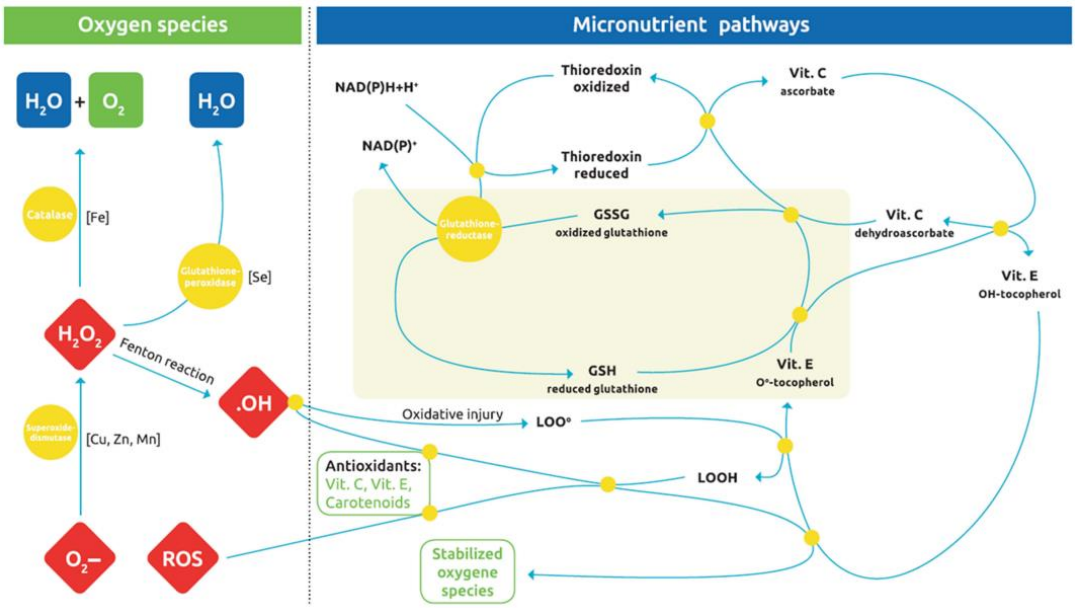


Figure 2: The intricate oxidation-reduction pathways through which several antioxidant micronutrients alleviate oxidative stress via redox-cycling processes. Glutathione is last antioxidant element in the cycle that creates the nonradical GSSG (oxidised glutathione), as well as a key controller of cellular redox status and inflammatory gene transcription factors. *Reproduced from Dommisch H, Kuzmanova D, Jönsson D, et al. Effect of micronutrient malnutrition on periodontal disease and periodontal therapy. Periodontol. © 2018 John Wiley & Sons A/S. Published by John Wiley & Sons Ltd.*[4]

Abbreviations: Cu, copper; Fe, iron; H2O2, hydrogen peroxide; LOO, peroxyl radical; LOOH, lipid hydroperoxide; Mn, manganese; ROS, reactive oxygen species; Se, selenium; Zn, zinc.

MINERALS

Minerals are substantial inorganic compounds that form crystals, and the amount of each mineral contained in human bodies varies substantially, as does mineral intake (Figure 2). Many minerals are required for enzyme activity, while others are utilized to preserve fluid balance, form bone tissue, synthesize hormones, convey nerve impulses, contract and relax muscles, and protect the body from damaging free radicals.

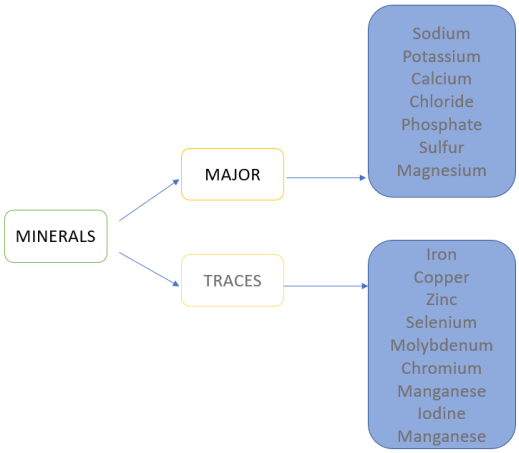


Figure 3: Types of Minerals

Minerals' Function

- Regional calcium administration improves osseointegration, and calcium supplementation improves nonsurgical periodontal treatment results.
- Magnesium supplementation enhances noninvasive periodontal treatment results as well.
- Iron and zinc have antioxidant properties that benefit the periodontium.
- Zinc also lessens the severity of diabetes-related periodontitis. Fluoride is another crucial element that preserves the teeth.

Topical Fluoride applications and supplementation therapy help to prevent tooth cavities.

VITAMINS

Organic compounds are necessary in little quantities in the diet to execute certain cellular processes for the regular upkeep of an individual's optimum growth and health. [11,12]

They have historically been classified as either fat-soluble (hydrophobic) or water-soluble (hydrophilic). Water-soluble vitamins work in the cytoplasm of cells or extracellular fluids like blood, whereas fat-soluble vitamins are primarily important for defending cell membranes from free radical damage. Some vitamins can be synthesized by the body, but others must be acquired from diet.[7,15,16]

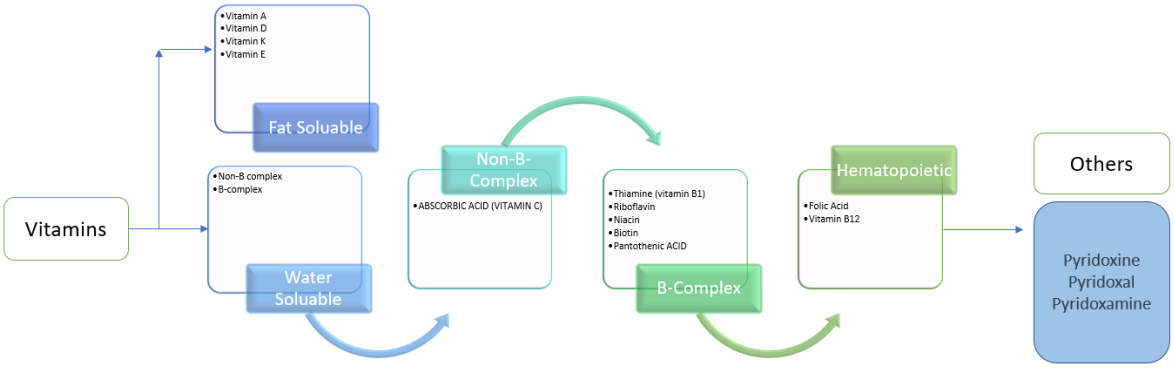


FIGURE 4: Types of Vitamins

LITERATURE REVIEW OF VITAMINS and their Significant Effect on Periodontitis:

Research Author & year	Nutrient	Source of diet	Significance in Periodontal health and disease.
Yan K et al., 2020 [36] ***Timmerman et al., 2007*** [37]	Vit A	Cod liver oil, broccoli capsicum, liver, sweet potato, carrots, leafy vegetables	It's not clear. According to investigations, supplementing has no effect on periodontal health.
Mustafa M et al., 2013 [38]	Vit B	B1—Liver, oats, pork, potatoes, eggs B2—Bananas, dairy, green beans B3—Eggs, fish, meat, mushrooms, nuts B5—Avocados, meat, broccoli B7—Raw egg, liver, leafy vegetables, peanuts B9 —Cereals, leafy vegetables B12—Animal products	The supplementation could/may hasten postsurgical healing.
Freeland-Graves et al., 1991 [39]	Vit C	Citrus fruits, vegetables, liver	Gingival bleeding and Inflammation are hallmarks of scurvy. Supplementation may improve outcomes of periodontal therapy
Mustafa M et al., 2013 [38] ***Lee JH et al., 2017*** [40] ***Staudte et al., 2010*** [41]	Vit D	Fish eggs, mushrooms, liver, milk	Deficiency may lead to delayed postsurgical healing. Local application may accelerate post-surgical healing/ osseointegration
Amaliya et al., 2015 [42] ***Jacob RA et al., 1987*** [43] ***Nakamoto T et al., 1984*** [44]	Vit E	Green vegetables, egg yolk	Deficiency may lead to gingival bleeding. No known effects on periodontal therapy if supplementation used as an adjunct.

Note: *Adapted from Najeeb S, Zafar MS, Khurshid Z, Zohaib S, Almas K. The Role of Nutrition in Periodontal Health: An Update. Nutrients. 2016;30;8(9):530.*

BIOCHEMICAL FUNCTIONS OF MICRONUTRIENTS

Understanding the biochemical actions of micronutrients is essential for understanding their role in optimizing health, disease prevention, and therapy.[10]

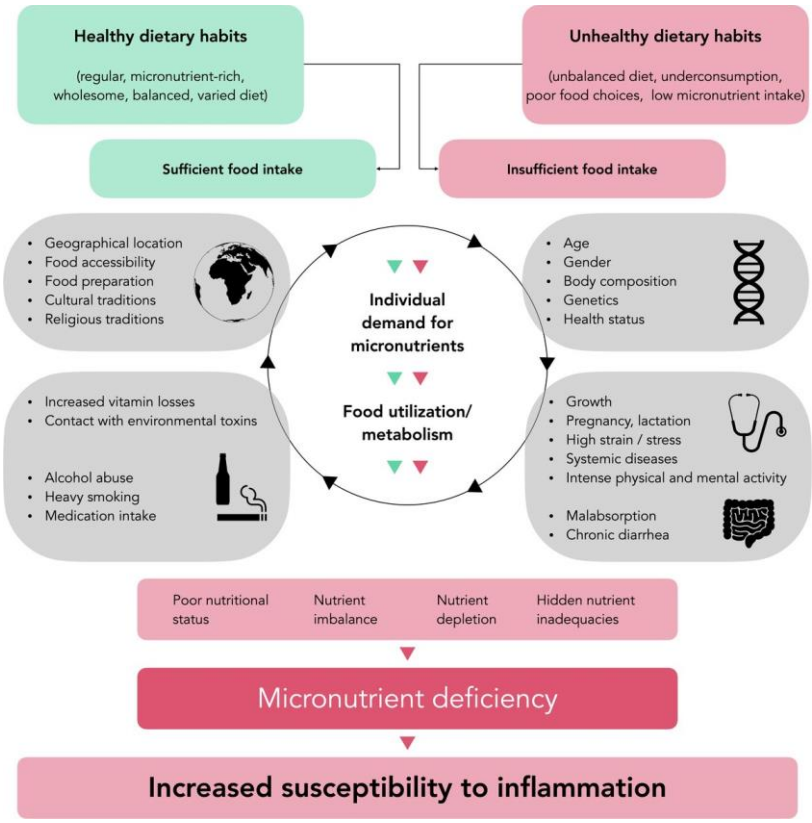
1. ***Cofactors in metabolism***: Trace elements are typically involved in modifying enzyme activity or are an important part of enzyme prosthetic groups, such as zinc, which is needed in the form of selenocysteine inside the enzyme glutathione peroxidase.
2. ***Coenzymes in metabolism***: Many vitamins or vitamin metabolites are needed to play an active role in complicated biochemical events, such as riboflavin and niacin in the electron transport chain or folic acid in methyl group transfer. These processes are crucial to intermediate metabolism because they guarantee that the primary nutrients used to create energy, proteins, and nucleic acids are used.
3. Genetic Control: Zinc "Fingers" are transcription-controlled factors that bind to DNA and govern transcription of steroid hormone receptors and other variables as well.

4. Anti-oxidants: Much of public fascination with micronutrients originates from the discovery that several of them have antioxidant capabilities. Oxidative metabolism invariably results in formation of ROS, which has the potential to induce further oxidative reactions, particularly in portions of cell that are relatively reduced, such as cell membranes or nucleic acids.

The potential for damage is limited by mechanisms such as direct quenching of oxidant activity by tocopherols or Carotenoids or enzyme systems to dispose of oxidation products such as superoxide dismutase and glutathione peroxidase.

MICRONUTRIENTS INADEQUACY AND INVOLVEMENT OF ENVIRONMENTAL FACTORS:

A lack of vitamins and minerals in the diet can lead to deficiency illness or deficiencies, which is a health issue that is not limited to low- and middle-income nations. This "hidden hunger" can be induced by either chronic underconsumption or poor food selection. Selective micronutrient deficits can coexist with both undernutrition and obesity. Such shortages may emerge in persons with appropriate nutritional intake during periods of elevated individual micronutrient requirements, but also in situations of increased micronutrient loss, such as alcohol misuse and severe smoking. (Figure 4) Malnutrition and poor oral hygiene are two major risk factors for necrotizing gingivitis. According to one comprehensive review, micronutrient deficiencies, such as vitamin C, vitamin D, or vitamin B12, may be linked to the initiation and progression of periodontal disorders.



Adapted from: *The Role of Micronutrients in Periodontal Disease Prevention and Therapy EFP, Dommisch H, Kuzmanova D, Jönsson D, Grant M, Chapple I. Effect of micronutrient malnutrition on periodontal disease and periodontal therapy. Periodontology 2000. 2018 Oct;78(1):129-53.* [58]

INFLUENCE OF MINERALS ON PERIODONTAL HEALTH

Mineral nutrients are components that organisms require to exist and operate correctly (other than oxygen, carbon, nitrogen, and hydrogen). Mineral shortage has ramifications for periodontal health, ***according to Najeeb et al. in 2016.***[32]

According to Zahrani et al., there is an inverse relationship between dairy product consumption and the prevalence of periodontitis. A research on elderly Danish patients found that consuming more dairy products reduces the severity of periodontitis later in life.[45]

Miley et al. and Gracia et al. found that, whereas periodontal clinical measures improved independent of supplementation during the maintenance programme, calcium supplements had a slight, favorable influence on periodontal treatment results.[46,47]

Meisel et al. found a strong relationship between periodontal health and blood magnesium levels. They emphasized that dietary magnesium supplementation may enhance periodontal health and prevent or postpone tooth loss in those in their forties and fifties.[48]

Yamori et al. conducted a cross-sectional research to examine the relationship of periodontitis and tooth loss with conventional risk factors for hypertension in middle-aged (46-58 years) non-smoking and non-alcohol drinking Tanzanian women who were not on medication. They concluded that a low potassium consumption in the diet, along with a low Fibre intake, may elevate blood pressure and periodontal inflammation.[49]

Park et al. completed a research on young individuals aged 19 to 39 years old using data from *the Fourth Korean Health and Nutrition Examination Survey*. They discovered a link between periodontitis and reduced iron consumption in women. However, no research has attempted to identify an association between iron supplementation and periodontal treatment results.[50]
In two separate case control investigations, ***Thomas et al.*** compared blood zinc levels in patients with diabetes and periodontitis to those in patients with periodontitis but no diabetes. Periodontitis patients, both with and without diabetes, had considerably lower zinc levels than healthy people.[25] Indeed, a comprehensive study by ***Pushparani*** found that zinc can help prevent diabetes-related periodontitis by having an anti-oxidant impact. As a result, zinc supplementation may be able to enhance the therapeutic effects of periodontal treatment.[51]

EFFECTS OF VITAMINS ON PERIODONTAL HEALTH

Zong et al. investigated the possible link between blood vitamin B12 and periodontitis alterations in a prospective population. They discovered that an increase in blood vitamin B12 was linked to a decrease in the clinical markers of Parkinson's disease (probing pocket depth, clinical attachment loss, and tooth loss).[33]
PMNs (polymorphonuclear leukocytes) and macrophages had 10-40 times greater intracellular ascorbic acid concentrations than plasma.[52] It has been proposed that increased ascorbic acid levels in leukocytes contribute to their ability to respond to inflammatory stimuli.[53]
Vitamin C insufficiency has been linked to an increased risk of periodontal disease. It is generally documented that a lack of vitamin C in the diet causes scurvy, an inflammatory condition of the gingiva that causes bleeding gums and was first discovered by ***James Lindhe***. ***Kaur K et al.*** state that Vitamin C's anti-inflammatory, antioxidant, and regenerative properties are well recognized, suggesting that it may have a role in moderating inflammatory responses in periodontal disorders.[5]

Dietrich et al conducted the first study to report an association between serum vitamin D levels and periodontitis and gingivitis, utilizing data from the US National Health and Nutrition Examination Survey, and discovered a lower prevalence of periodontitis in individuals with elevated concentrations of serum Vitamin D.[54]

ROLE OF ANTIOXIDANTS IN PERIODONTAL HEALTH AND DISEASE

Oral hygiene is commonly neglected in patients who have undergone radiotherapy and they often develop dry mouth, mucositis due to radiation therapy, etc., as side effects. [55] An emergency is a significant, unforeseen, and frequently dangerous circumstance that demands a quick response. [56]

Because of disease and trauma, the mouth cavity, like any other tissue, experiences inflammation and damage. Inflammatory processes entail immune cells producing reactive oxygen species (ROS) when provoked by pathogens. ROS and highly reactive free radicals (molecules with unpaired electrons) can cause cellular and tissue damage by changing the chemical structure of molecules. They specifically harm lipids by starting a chain reaction called lipid peroxidation. Aerobic respiration normally results in the formation of ROS. Antioxidant defense enzymes, on the other hand, lower ROS to minimize cellular damage. However, if there is an excess of ROS generation owing to inflammation or tissue injury, the antioxidant system is insufficient to reduce oxidative damage. When the equilibrium between ROS generation and antioxidant enzymes (e.g., glutathione) is upset, oxidative stress ensues. [36]

The periodontium can also become oxidatively damaged as a consequence of disease and/or trauma-induced inflammation, as reported by ***Najeeb S et al.*** By intercepting ROS, antioxidants can assist in lessening disease intensity.[32]

LITERATURE REVIEW:

SL NO.	Authors and year of research	Research focus	Methods	Results	Conclusion
1	Hans A et al., 2023 [2,12]	To assess if a deficiency of certain essential vitamins is a risk factor for developing periodontitis	The subjects consisted of 100 subjects, 50 with generalized chronic periodontitis and 50 periodontally healthy volunteers. The following clinical parameters were measured: Gingival Index, pocket depth (mm); Clinical Attachment Loss (mm). Serum samples were collected and analyzed for levels of cis-β- carotene, β-cryptoxanthin, vitamin B 12, folate, vitamin D, and vitamin E. Individual data collected was summarized and analyzed using statistical software	All the clinical parameters for periodontal status in the periodontitis group compared to healthy volunteers were highly significant ($p < 0.0001$). The mean levels of all the micronutrients, vitamin A precursors cisβ-carotene and β-cryptoxanthin, folate, vitamin B 12, D & E were lower in the periodontitis group than the healthy volunteers, although the difference was statistically significant only in case of β-cryptoxanthin, Vitamin B12 and Vitamin D ($p < 0.05$).	The findings of our study suggest that serum micronutrient levels especially Vitamin A, Vitamin B 12, and Vitamin D may be modifiable risk factors for periodontal disease. Providing an optimized combination of various vitamins in each meal in combination with sufficient measures of standard oral hygiene care may provide an important role in the prevention ofperiodontitis
2	Shankarai Malaipan et al., 2022 [15]	To assess the salivary micronutrient levels in healthy and chronic periodontitis	N/A	The salivary micronutrient zinc, copper, iron levels are significantly reduced in chronic periodontitis than in healthy individuals	Within the limitations of the present study, it can be concluded that there is a significant reduction in salivary micronutrient levels of iron, copper and zinc in chronic periodontitis when compared to healthy individuals

3	Blessy Pushparathna., 2022 [57]	To assess the correlation between salivary micronutrient levels in chronic periodontitis patients before and after non-surgical periodontal therapy	A total of 50 chronic periodontitis patients who reported to the Department of Periodontics, Saveetha Dental College and Hospitals, Chennai were enrolled. Levels of Zinc [Zn], Copper [Cu], Iron [Fe], and Selenium [Se] were measured from unstimulated saliva samples before and after scaling and root planing. Paired t-test was done and the results were considered to be statistically significant when the p-value was <0.05	At baseline (before SRP), the levels of Zn, Cu, Fe and Se were 3.05± 0.53, 8.45± 0.73, 7.30± 2.21 and 2.2± 1.23 respectively. At 3 weeks follow-up (after SRP), the levels of Zn, Cu, Fe and Se were 4.95± 0.48, 5.95± 0.48, 5.74± 0.34 and4.8± 1.01 respectively. The difference between levels of Zn, Cu, Fe and Se before and after nonsurgical periodontal therapy was statistically significant with $p < 0.05$.	The salivary levels of Zn and Se were increased and levels of Cu and Fe were decreased in chronic periodontitis after non- surgical periodontal therapy. This indicates that the levels of micronutrients can be used as effective biomarkers for chronic periodontitis
4	Patricia Daniela Costa et al., 2021 [14]	To evaluate the relationship between micronutrient intake, sociodemographic behavioral characteristics, and periodontal health in adults assisted by a public health care system	Data collections related to nutritional variables and the periodontal status of the population were carried out in a cross-sectional design, through home visits. In each visit, general and nutritional interviews were carried out, also applying the food frequency questionnaire, followed by anthropometric and periodontal assessments	The prevalence of at least one periodontal pocket ≥ 4mm was 67.4%. Three clusters were identified according to periodontal status. Cluster 1 "poor periodontal status" was characterized by older individuals (n = 202; 85% females) with poor periodontal status, lower education level, mainly smokers with non-transmissible chronic diseases (NTCD), with lower energy, omega-3, fiber, Zn, K, Cu, and vitamin C intake Cluster 3 "healthy periodontal status" included younger individuals (n = 54) with the healthiest periodontal status, a higher education level, without NTCD, and with	Diet can significantly affect periodontal status, and nutritional deficiencies are very important factors in countries with upper middle- income economies. Brazil has a public health system that greatly modifies the context of oral assistance in relation to other countries. This study highlights the influence of nutritional and sociodemographic behavioral factors on periodontal status, which may guide population- based measures for low-income populations

				higher energy, omega-3, fiber, Zn, calcium, retinol, and riboflavin intake. Cluster 2 was labeled as "intermediate periodontalstatus	
5	Mohamed El-Mofty et al., 2021 [15]	To compare the efficacy of intra-mucosal injection (mesotherapy) with topical gel as non-surgical methods for managing gingival hyperpigmentation	20 healthy non-smokers with mildto severe hyperpigmented gingiva were randomly assigned for Mesotherapy (G1); intra-mucosal injection of ascorbic acid or Gel (G2), topical ascorbic acid gel. Pigmentation index (DOPI), patient satisfaction, as well as histological analysis for Fontana-Masson-stained specimens were performed at baseline and after 6 months. Comparison between groups and changes by time were analyzed using Mann Whitney and Friedman's tests	The median DOPI significantly decreased after 1 month in G1 (P value < 0.001, r = 0.9) compared with non-significant change in G2. No pain experienced during or after treatment in both groups. G1 patients showed significantly higher satisfaction with treatment than G2. Mean area fraction of melanin forming cells was significantly reduced in both groups after 6 months, but the effect size was higher in G1 (r = 0.886) than in G2 (r = 0.797	Vitamin C mesotherapy showed better and early effect than topical gel, and both techniques were not painful and esthetically satisfying in managing gingival hyperpigmentation
6	Islam S. Bakr., et al., 2020 [16]	To evaluate the effectiveness of topical oral vitamin D gel in prevention of radiation induced oral mucositis	A three-armed randomized controlled clinical trial on forty-five head and neck cancer patients was conducted. First group: conventional treatment. Second group: Topical oral vitamin D gel. Third group: topical oral vitamin D gel plus the conventional treatment. All the patients were examined clinically three and six weeks after the start of radiotherapy for pain and WHO mucositis score	After 6 weeks of radiotherapy, (33.5%) the patients in control group developed high- grade severity of oral mucositis while the patients in the two-test groups "vitamin D group& combined therapy group" remained with low-grade severity or with complete remission. Mean Pain scores showed a significant decrease in the combined therapy group and to a close degree in vitamin D group rather than thecontrol group	Topical oral vitamin D gel has a beneficial effect in lowering oral mucositis development and in reducing pain sensation during the radiation period especially when combined with conventional therapeutic agents
7	H. Gencay Keceli	To evaluate clinical and biochemical	60 CGP patients (30 per group) were	Significant time-dependent	Both modalities exhibited clinical

	et al., 2020 [17]	effects of adjunctive systemic folic acid (FA) intake with scaling and root planing (SRP) in periodontitistreatment	randomly assigned into study groups and treated with either SRP + placebo (SRP + P) or SRP + folic acid (SRP + F). In addition to clinical parameters (plaque index [PI], gingival index [GI], probing pocket depth [PPD], clinical attachment level [CAL] and gingival recession [GR]), gingival crevicular fluid (GCF) samples were obtained at baseline and post-treatment (PT) periods, three and six months for C-reactive protein (CRP) and homocysteine (Hcy) evaluation	reduction was detected at all clinical parameters for both groups ($p < .001$). Compared to SRP + P, CAL was lower in SRP + Fat PT-1 ($p = .004$) and PT-3 ($p = .035$), whereas GR was lower at only PT-1 ($p = .015$). GCF volume and CRP did not show inter-group differences, whereas Hcy was higher in SRP + F at PT-3 ($p = .044$) and PT-6 ($p = .041$). GCF volume and Hcy showed reduction after treatment in both groups ($p < .001$)	improvement and change in biochemical parameters. Adjunctive systemic FA intake may be recommended adjunctive to periodontitis treatment to reveal better outcomes. However, its impact mechanisms should be further enlightened
8	B. Nandlal et al., 2020 [18]	To examine the effects of brushing with a test toothpaste containing natural ingredients, that is, clove (Syzgium Aromaticum), aloe vera (Aloe Barbadensis), amla (Emblica Officinalis), neem (Azadirachta Indica), tulsi (Ocimum Basillicum) and honey (from Apis Mellifera) along with zinc salts and fluoride in comparison with a dentifrice formulated with fluoride alone on dental plaque and gingivitis over a 6-month period.	Subjects were evaluated for plaque and GI scores and were randomly assigned to perform twice daily oral hygiene with either the test or the control toothpaste for the next 6 months. Assessments were conducted after 3-month and 6-month use of an assigned product after subjects refrained from oral hygiene for 12 h prior to each evaluation. Comparisons of the treatment groups with respect to baseline-adjusted GI, PI and bleeding index scores at the follow-up examinations were performed using analyses of covariance (ANCOVA).	At 3-month and 6-month examination, the test toothpaste exhibited progressive reductions in plaque, gingival and bleeding scores as compared to control toothpaste as showed by ANCOVA ($p < 0.001$). In comparison with the control, the test demonstrated reductions in 23.5%, 25.6%, and 73.3% for dental plaque, gingival index and bleeding index outcomes, respectively, at the finalvisit	Routine oral hygiene with the test toothpaste formulated with herbal ingredients and zinc demonstrated a clinical adjunctive improvement in oral hygiene and parameters of gingival health as compared to brushing with a fluoride toothpaste
9	Ji-Youn Hong et al., 2019 [19]	To evaluate gingival inflammation from fixed-dose combinations of vitamin C, vitamin E,	One hundred patients were randomly assigned to receive CELC (test) or placebo	Ninety-three patients completed the study. The GI in the test group significantly	Within the study, CELC showed a significant reduction in gingival inflammation

		lysozyme and carbazochrome (CELC) in the treatment of chronic periodontitis following scaling and root planing	(control) for the first 4 weeks at a 1:1 ratio, and both groups received CELC for the remaining 4 weeks. Primary outcome was the mean change in the gingival index (GI) after 4 weeks. Secondary outcomes included mean change in GI after 8 weeks and plaque index, probing depth, clinical attachment level at 4 weeks and 8 weeks	decreased after 4 weeks ($p < 0.001$) and 8 weeks ($p < 0.001$). The mean change from baseline in GI significantly decreased in the test group compared to the control group after 4 weeks ($p = 0.015$). In the GEE model adjusting for age, gender and visits, the test group showed 2.5 times GI improvement compared to the control group ($p = 0.022$	compared with a placebo. Other parameters, however, weresimilar between groups
10.	Mohamed M. Meghil et al., 2019 [20]	To investigate the influence of 12 weeks of 25(OH) vitamin D supplementation (VDS) on mediatorsof systemic inflammation periodontitis patients	A total of 23 patients with moderate to severe periodontitis were randomly assigned to the vitamin D group or placebo group and received intensive single visit scaling and root planning to elicit a systemic inflammatory response	Vitamin D supplementation increased serum 25(OH)D levels approximately 2-fold over baseline levels; moreover, VDS group had reduced peripheral blood CD3 and CD3+CD8+ cytotoxic T lymphocyte (CTLs) counts and reduced pro-inflamma- tory salivary cytokines. In contrast, VDS group had higher levels of the autophagy- related proteins and other proteins crucial for anti-microbial autophagy in whole blood PBMCs	VDS has multiple benefits for reducing systemic inflammation and promoting induction of autophagy- related proteins related to anti-microbial functions.
11	Elif Inonu et al., 2019 [21]	To determine whether association between mineral elements and periodontal status occur.	190 systemically healthy non-smoker participants (mean age 32.2 ± 6.02; 50 periodontally healthy, 50 gingivitis, 50 chronic periodontitis, and 40 aggressive periodontitis individuals) were included in this cross-sectional study. Salivary levels of some macro and	Statistically significant differences were found in sodium (Na), magnesium (Mg), potassium (K), calcium (Ca), vanadium (V), chromium Cr), manganese (Mn), iron (Fe), rubidium (Rb), strontium (Sr), and selenium (Se) concentrations among the groups. Significant increases in the	The results of this study demonstrated that assessment of mineral element concentrations in saliva might be useful in assessing periodontal health and disease

			trace elements were measured by using inductively coupled plasma mass spectrometry (ICP-MS). Kruskal-Wallis's test was used for statistical analysis.	essential minerals Na, Mg, K, Ca, Fe, and Se occurred in both periodontitis groups when compared to the gingivitis and periodontally healthy groups. Lower Se, Sr, Fe, Mn, and V concentrations were found in the aggressive periodontitis group than in the chronic periodontitis group.	
12	Xiao Li et al., 2018 [22]	To explore the effects of vitamin C supplementation in wound healing, following the placement of dental implants with or without bone grafts and patients with chronic periodontitis	Patients were divided into four groups, group A received dental implants supported GBR technique, group B received dental implants with Bio-Oss Collagen, group C received dental implants in patients with chronic periodontitis, and group D received dental implants without any bone grafting or periodontal disease. Follow-up appointments were performed at day 3, 7, 14 postsurgery, during which soft tissue healing and pain response scores were evaluated using the Landry index and VAS respectively	The experimental subgroups had significantly higher healing indices than the controls ($P < .05$) at day 7 postsurgery for group B and day 14 postsurgery for groups A, B, and C. Group D displayed no difference between the experimental and control groups at any time point. In reference to vitamin C for pain relief, there were no statistically significant differences between the study groups	Using vitamin C supplementation improves postoperative healing following dental implant surgery in patients with chronic periodontitis and patients treated with GBR or Bio-Oss Collagen grafts. However, vitamin C supplementation does not decrease the postoperative pain associated with dental implant surgery.
13	Johan P et al., 2019 [23]	To investigate the influence of an anti-inflammatory diet on different parameters in patients with gingivitis	30 patients were randomly allocated to an experimental and a control group. The experimental group had to change to a diet low in processed carbohydrates and animal proteins, and rich in omega-3 fatty acids, vitamin C, vitamin D, antioxidants, plant nitrates and fibres	No differences regarding the plaque values, the experi- mental group showed a significant reduction in gingival bleeding, a significant increase in Vitamin D values and a significant weight loss. There were no inter-group differences regarding the	The evaluated diet could significantly reduce gingivitis in a clinically rel- evant range, while serological inflammatory parameters and the subgingival microbiome seem to be unaffected in this study duration.

			for 4 weeks. The control group did not change their diet. Both groups suspended inter-dental cleaning. Periodontal parameters were assessed. Serological and subgingival plaque samples were taken atbaseline and end	inflammatory serological parameters, the serological omega fatty acids, nor the sub- gingival composition	
14	Pia- Merete et al., 2019 [24]	This randomized controlled cross- over-design-study investigated short-term effects on oral malodor of a zinc-lactate-containing mouthwash	Sixteen subjects (18–65 years) with an organoleptic score (OLS) ≥ 2 were included. Following rinses were used: A: a zinc-lactate-containing mouthwash (10ml/30s); B: a zinc-lactate-containing mouthwash (15ml/60s); C: a rinse without zinc-lactate (3 droplets/10ml tap water/30s) and D: tap water (10ml/30s). Each formulation was evaluated by two blinded examiners comparing OLS and three volatile-Sulphur-compounds (VSC; H2S (hydrogen sulphone), CH3SH (methyl mercaptan) and (CH3)2S (dimethyl sulphide)) before, one and three hours after rinsing. Subject's perception was investigated with a visual-analogue-scale. Linear mixed models were used to compare all parameters simultaneously with respect to the four treatment groups with a significance level	OLS was significantly reduced by A and B compared to C and D after three hours. The sum of the 3 VSCs as well as H2S alone were significantly reduced by rinses A and B after one and three hours compared to rinses C andD . Significant differences were found between the four rinses for "Taste" (p=0.003), for "Change of mouth feeling" (p=0.001), for "Feeling of freshness" (p=0.002) and for "Effectiveness" (p=0.002) in favor of A & B	A zinc-lactate-containing mouthwash reduced OLS and VSC over a period of three hours with favorable patient reported outcomes

			$\alpha<0.05$		
15	Biju Thomas et al., 2018 [25]	To evaluate the comparison of glutathione, catalase, and selenium levels in the serum of diabetes mellitus type 2 patients and healthy individuals with and without periodontal disease	The study was designed as a case - control study comprising of 150 subjects, inclusive of both sexes and were divided into three groups of 50 patients each. Group I: 50 subjects with type 2 diabetes mellitus and chronic periodontitis. Group II: 50 subjects who are systemically healthy with the chronic periodontitis. Group III: 50 subjects who are systemically healthy and not suffering from Periodontitis	The serum levels of glutathione in diabetic patients with periodontitis were significantly lower with a mean of 61.36 + 8.054 when compared to healthy individuals with and without periodontitis ($P \leq 0.005$). The serum levels of catalase were significantly lower in diabetic patients with periodontitis with a mean of 19.30 + 7.355 when compared to healthy individuals with and without periodontitis ($P \leq 0.005$). The serum levels of selenium were significantly lower in diabetic patients with periodontitis with a mean of 81.41 + 55.419 when compared to healthy individuals withand without periodontitis ($P \leq 0.005$)	The findings from the study suggest that the levels of glutathione, catalase, and selenium are significantly lower in diabetic patients with periodontitis and also in healthy individuals withperiodontitis, but are highestin healthy controls, showing that the serum levels are inversely proportional to inflammation and tissue destruction
16	Gopalakrishnan Sundaram et al., 2017 [26]	To find out the effect of nonsurgical periodontal therapy on serum zinc (Zn), magnesium (Mg), and copper (Cu) concentration and glycemic status in type 2 diabetes with chronic periodontitis (CP).	120 patients were included in this study, which was further divided into three groups. Group 1 consisted of 40 patients with CP, Group 2 of 40 patients of CP with controlled diabetes, and Group 3 of 40 patients of CP with uncontrolled diabetes. Periodontal parameters such as PI,GI, BOP, PD, and CALs were evaluated. Blood samples were collected to assess the levels of fasting blood sugar, glycosylated hemoglobin, Zn,	The results showed statistically significant reduction in all the clinical parameters within the groups except for the CAL in group 1 patients ($P = 0.05$). The glycemic status showed a statistically significant reduction after treatment ($P < 0.001$). The intragroup comparison was taken between the values of micronutrients, showed substantial increase in the levels of both Zn and Mg and	Patients with diabetes and periodontitis had altered metabolism of Zn, Mg, and Cu contributing to the progression and complication of diabetes mellitus and periodontitis. Nonsurgical periodontal treatment improved the variation and concentration of plasma micronutrients and also the periodontal status and glycemic level

			Mg, and Cu. All parameters were evaluated at baseline and 3 months after nonsurgical periodontal therapy.	decrease inthe level of Cu after nonsurgical periodontal treatment	
17	Aditi Chopra et al., 2015 [27]	To evaluate and compare the beneficial effects of green tea intakeon the total antioxidant capacity of gingival crevicular fluid (GCF) and plasma, and to examine itsrole as an adjunct to nonsurgical periodontal therapy for the management of chronic periodontitis	120 subjects with mild to moderate chronic periodontitis were divided equally into two groups. Afterscaling and root planing in all subjects, green tea supplements were given to the case group and a placebo to the control group. The clinical parameters gingival index, plaque index, clinical probing depth, clinical attachment loss, percentage of sites with bleeding on probing, along with total antioxidant capacity of GCF and plasma were recorded atbaseline, one and three months	There was a significant improvement in all clinical parameters along with an 8-fold greater antioxidant capacity in GCF in the case group than in thecontrol group	Green tea intake as a component of nonsurgical periodontal therapy is promising for superior and rapid resolution of the disease process. Green tea increases the total antioxidant capacity of GCF and plasma along with potent anti-inflammatory, astringent and anti-plaque effects
18	Sathish Manthena et al., 2015 [28]	To evaluate the effectiveness of CoQ 10 supplementation as an adjunct to scaling and rootplaning in reducing gingival inflammation and periodontal pocket depth.	30 subjects with plaque induced gingival inflammation and having atleast three nonadjacent interproximal sites with a probing pocket depth ≥ 5mm were included in the study. The subjects were randomly divided into two groups. The test group (n=15) in which patients were given oral CoQ10 supplements after NSPT and the control group (n=15) in which patients were given an oral placebo after NSPT. The PI, GI and PD were recorded at baseline, 1 month and 3	Both the groups showed marked reduction of periodontal parametersat 1 and 3 months when compared to baseline. Though there was no significant difference in PI and PPD between the two groups at any given time period, test group showed significant difference in gingival inflammation at one month and three months when compared to control group	In the present study use of Coenzyme Q10 oral supplements as an adjunct to scaling and root planing showed significant reduction in gingival inflammation when compared to scaling and rootplaning alone

			months. Statistical analysis done by using Student's paired t-test for intragroup comparison and unpaired t- test for inter-group comparison		
19	Sunita Daiya et al., 2014 [29]	To investigate changes in periodontal parameters and superoxide dismutase activity triggered by root surface debridement with and without micronutrient supplementation in postmenopausal women	Forty-three postmenopausal chronic periodontitis patients were divided into two groups: group 1 (n=22) were provided periodontal treatment in the form of scaling and root planing (SRP) and group 2 (n=21) patients received SRP along with systemic administration of micronutrient antioxidants. Patients in both groups were subjected to root surface debridement. Group 2 patients also received adjunctive micronutrient antioxidant supplementation. Serum and salivary superoxide dismutase (SOD) activity along with periodontal parameters were recorded at baseline and 3 months after therapy.	Salivary and serum SOD values significantly improved with periodontal treatment.	Adjunctive micronutrient supplements reduce periodontal inflammation and improve the status of systemic enzymatic antioxidants in postmenopausal women

RECOMMENDATIONS FOR FUTURE RESEARCH

More research is needed to determine the efficacy of vitamin supplementation on periodontal treatment and the influence of micronutrient deficits on periodontitis incidence.

More study is needed on the function of micronutrients in innate and adaptive immune responses, since the relationship between nutritional status and immunological response to bacterial assault may be a key component in periodontal disease development.

Further research should be conducted to identify specific gene polymorphisms that appear to affect each individual's biological response to a specific nutritional intervention, as well as genetic testing to identify at-risk groups that may benefit from specific nutritional therapies as part of a precision approach to periodontal medicine.

Summary:
To Jot it down, the analysis of the literature revealed that periodontal disease is connected with reduced serum/plasma levels of different micronutrients, primarily vitamin D, vitamin C, and other antioxidants. However, there is a scarcity of longitudinal intervention studies in this critical field to investigate the influence of dietary therapies on periodontal results.

Scientific Hypothesis/Theory behind the Research
Nutrition has been shown to be a significant lifestyle contributor to risk for a variety of inflammatory diseases and conditions, such as cardiovascular disease, type 2 diabetes, rheumatoid arthritis, and inflammatory bowel disease, all of which have been linked to periodontitis. As a result, diet could serve an essential part in the development and treatment of periodontitis.

Inference Obtained:
In deficient patients, the existing information would support the advice of a sufficient daily consumption of foods containing natural sources of antioxidants, as well as vitamin D and calcium supplementation. As a result, the medical history should contain extensive information about the daily food consumption of the major micronutrients, as well as lifestyle factors. Inadequate antioxidant intake can be compensated for by increasing consumption of vegetables, berries, and fruits (e.g., kiwi fruit). Inadequate vitamin D and calcium supply can be corrected by dietary/lifestyle changes or supplementation.

CONCLUSION:

In a nutshell, there is developing proof supporting the role of micronutrients in general and periodontal health. Formerly we as practicing dentists have preferred not to delve beyond the limits of the standard prescription course of antibiotics when treating patients with periodontal diseases or any other ailments. This article is an attempt to draw the attention of the clinicians to take a holistic approach in treating patients and I hope that it will be an eye opener for many readers.

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