



# **Nutrigenomics As a Diagnostic Tool in Periodontology: The New Kid in The Block**

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## **Authors' contributions**

*This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.*

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## **ABSTRACT**

Periodontitis is known to be a progressive inflammatory lesion that may lead to the deterioration of the attachment of the periodontal apparatus & loss of structures involved in the apparatus, mainly the gingiva, pdl, cementum & alveolar bone leading to loss of teeth. Therefore, the interest in learning more about the connections between periodontal disease and nutrition has increased as research on the pathophysiology of periodontal disease and the function of nutrition has progressed. A subfield of nutritional science called nutrigenomics focuses on understanding the molecular interactions of nutrients and genomes. This enables us to recognize early-stage abnormalities in this control and tells us of the impact of nutrition on metabolic pathways & homeostatic regulation. In this review, the role of nutrition in periodontal disease is thoroughly discussed, and dietary recommendations are made for preventing periodontal disease.

*Keywords: Nutrition; epigenetics; periodontal health; nutrigenomics.*

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## 1. INTRODUCTION

The term periodontitis refers to a collection of some chronic, progressive bacterial infection that cause inflammation followed by degeneration of the tissues that support teeth. The words "perio" and "don't" refer to the gingiva and other tissues around teeth, while "itis" refers to inflammation [1]. It is known to be the most contagious chronic diseases in whole world, according to WHO. With a prevalence rate of 50% in the adult age group, periodontal diseases are very common, and their severity increases in 3rd and 4th decades of life with a prevalence rate of 10% [2].

A person is more likely to acquire a disease, such as, whenever there is an inflammatory response in the body, antioxidant vitamins, and trace elements are depleted, as a result of various biological, environmental, and behavioral "risk factors". In the later stage, the reactive oxygen species (ROS) neutralize these deficient molecules, causing periodontal alterations [3]. Nutrient components of the body act as dietary signals. The biological system (bacteria), environmental, genetic, and dietary factors interact critically to promote vulnerability to periodontal disease [4].

Due to advances in our understanding of the mechanisms underlying the degeneration of periodontal tissue, the potential defensive role of nutrients, and the creation of state-of-the-art genomic measurement tools, the field of nutrigenomics, which examines the relationship between nutrition and periodontal disease, has gained more attention [5]. Thus aim of this article is to elaborate the importance of nutrition in maintaining the periodontal health. In 1997, the first nutrigenomics business was established and was renamed genomics by Nancy Fogg-Johnson & Alex Merolli in the year 1999, and Pelegrin coined the word "nutrigenomics" in the year 2001 [6].

**Nutrigenomics:** Nutrigenomics is defined as the science which assesses the individual's response to foods, diet, and dietary compounds with the help of post-genomic and other similar technologies. (Proteomics, Metabolomics, Epigenomics & Transcriptomics) [6].

**Epigenetics:** Through a process known as "epigenetics," which involves histone modification and methylation, changes the

structure of chromatin which produce a somatically heritable state of gene expression [7].

**Proteomics; transcriptomics and metabolomics:** "Proteomics" is defined as study and examination of biological features of proteomes. The entire set of Ribonucleic acid (RNA) can be synthesized from genome is known as transcriptomics. "Metabolomics" is the name given to the scientific study of chemical reactions involving metabolites. There are several different biomarkers for periodontal disorders, including genetic, proteomic, microbiological, and others [8].

### Goals of nutrigenomics [9]:

1. Identifying the transcription factors, which further operates food sensors for targeted genes and subsequent characterisation in main dietary signals.
2. Measuring and validating the gene expression effects in various macronutrient and micronutrient on cells and organs.
3. Clarifying about the relationships between regulatory mechanisms related to nutrition and stress pathways that promote inflammation.
4. To comprehend the mechanism by which metabolic dysregulation causes diet-related disorders.
5. The early development of metabolic dysregulation & susceptibility biomarkers, regulated through diet using nutritional systems biology.

### Impact of nutrition on the epigenetic mechanism: [7]

1. **DNA Methylation:** S-adenosyl methionine (AdoMet) and S-adenosyl homocysteine are two metabolites of one-carbon metabolism (AdoHcy). Therefore, any food that may change tissue amounts of AdoMet/AdoHcy can hamper DNA methylation. Genistein, which is found in foods including soybeans, tea polyphenols, and isothiocyanates from plants, lowers the state of DNA hypermethylation, which prevents cancer.
2. **Modifications to the Histone:** Histone adenosine diphosphate (ADP) ribosylation is influenced by niacin.
3. **Acetylation of histones:** Histone acetylation is facilitated by vitamins B3 and

**Table 1. Transcription factors mediating nutrition gene interaction [9]**

<b>Nutrient</b>	<b>Compound</b>	<b>Transcription Factor</b>
<b>Macronutrient</b>		
Fats	Fatty Acid Cholesterol	PPARs, SREBPs, LXR, HNF 4, ChREBP SREBPs, LXRs, FXR
Carbohydrates	Glucose	USFs, SREBPs, C hREBP
Protein	Amino Acids	C/EBPS
<b>Micronutrients</b>		
<b>Vitamins</b>	Vitamin A Vitamin D Vitamin E	RAR, RXR VDR PXR
<b>Minerals</b>	Calcium Iron Zinc	Calcineurin/NF-Ats IRP1, IRP2 MTF 1
<b>Other food Compounds</b>	Flavonoids Xenobiotics	ER, AP1 CAR, PXR

B5. Histone acetyltransferases (HATs) and histone deacetylases (HDACs) are histone acetylating enzymes (HAT). HDAC is inhibited by resveratrol, a bioactive substance found in grape skins. Curcumin prevents histone acetyltransferase from working.

4. Vitamins B9, B12, choline, methionine, and betaine have an impact on the methylation of histones.
5. **Biotinylation of histones:** The chromatin structure, gene silence, and DNA repair are all significantly impacted by biotin deficiency, a vitamin B7 nutrient.

**Nutrient–gene interactions:** Water, carbs, lipids, proteins, and micronutrients are examples of micronutrients. The transcription of genes is impacted by nutrition (Table 1). To achieve optimal health, it is important to take into account all environmental factors, including smoking, physical activity, and food in addition to genetics and dietary components [8].

## 2. IMPACT OF NUTRIGENOMICS ON THE PERIODONTAL HEALTH

### 1. Role of Carbohydrate

*Porphyromonas gingivalis* and *Aggregatibacter actinomycetemcomitans*, periodontal pathogens, are both susceptible to the artificial sweetener xylitol's antibacterial properties. The periodontal health of the general population is effectively improved by lowering sugar intake, performing SRP, and using gums with xylitol [9].

### 2. Role of vitamins

- Several studies have found that taking vitamin A supplements improve periodontal health.

- While vitamin B supplements may hasten the healing process following surgery, vitamin supplements may enhance the results of periodontal therapy.
- Vitamin D topical administration speeds up osseointegration and healing after surgery.
- Vitamins E and C in food have been demonstrated to reduce oxidative stress in the periodontium, and studies on patients receiving nonsurgical periodontal care have found that vitamin C supplements improve total antioxidant capacity (TAOC).

### 3. Vitamin A

Vitamin A deficiency can cause leukoplakia lesions and mucosal keratinization.

### 4. Vitamin B Complex

Recurrent ulcers and reversible dysplastic alterations to the oral mucosa are brought on by vitamin B12 deficiency. Lack of vitamin B3 causes mucosal atrophy, while a lack of folate causes candidiasis [10].

### 5. Vitamin D & Calcium

Periodontitis is connected with polymorphisms of vitamin D receptor (VDR) gene. Reduced serum levels can result in decreased calcium absorption and increased osteoclastic activity of the bone. In a study by Miley et al. [11] on effects of vitamin D and calcium supplementation, 51 people with chronic periodontitis were divided into 23 groups who got vitamin D treatment (400 IU/day) & calcium supplementation (1,000 mg/day), and 28 groups who did not. For the mandibular posterior teeth, periodontal disease markers including probing depth, attachment loss, gingival index,

bleeding following probing, and furcation involvement were noted. Exclusion criteria include any kind of periodontal surgery in the last year, SRP in the last 6 months, medical history of any medications, or any diseases/conditions that affect bone, mineral metabolism, and periodontal health.

When vitamin D and calcium supplements were added to periodontal maintenance therapy, a tendency toward better periodontal health was seen in the individuals [12].

## 6. Vitamin E

Given how broadly distributed the vitamin is in the diet, vitamin E deficiency in humans is unusual. Therefore, it is impossible to draw a connection between periodontal disease and a lack of vitamin E in the diet [13].

## 7. Vitamin C

Using the NHANES III survey of 12,419 individuals (20-90 years of age), Nishida et al. [14] conducted a study involving dental measures and an evaluation of dietary vitamin C. Those who had clinical attachment levels of less than 1.5 mm were categorized as having periodontal disease. Periodontal disease and vitamin C were found to have a statistically significant dose-response association, with a low intake leading to a higher risk of periodontal disease. Low dietary vitamin C consumption was also linked to an increased risk of disease occurrence in both past and current smokers.

Staff of grain farms and employees of citrus fruit farms were compared in terms of periodontal health by Blignaut and Grobler. 25-grain farm workers served as the controls. The CPITN index was used to track the state of the periodontium. Results showed that subjects who consumed citrus fruit had a lower frequency of deeper pockets. The link between a vitamin C deficit and nug is also widely recognised [15].

The effects of mega dosages of ascorbic acid on neutrophil chemotaxis and gingivitis were studied by Vogel et al. [16] in 24 dentistry students (18 males and 6 females). The study eliminated students who had clinical attachment loss, moderate to severe gingivitis, were using vitamin supplements, had a systemic condition, or was taking any medications that affected the periodontium. The findings showed that as compared to the control subjects, people with periodontitis consumed less vitamin C daily.

## 8. Role of Minerals

- Calcium supplementation has been demonstrated to improve the results of nonsurgical periodontal therapy and local calcium application increases osseointegration.
- Supplemental magnesium enhances the effectiveness of nonsurgical periodontal treatment.
- The periodontium is protected against free radical damage by iron and zinc. Additionally, zinc lessens the severity of periodontitis brought on by diabetes. Fluoride is a crucial element that safeguards the teeth. Dental caries can be avoided by fluoride supplements and topical applications [17].

## 9. Proteins

The accompanying symptoms of protein shortage include osteoporosis of alveolar bone, delayed wound healing, and degeneration of connective tissue of gingiva and periodontal ligament [18].

## 10. Lipids

An advantageous moderating impact of PUFAs on animal gingival inflammation has been proposed by biomarker analysis. Kesavalu et al. [19] proposed that dietary supplementation along with omega fatty acids modifies the inflammatory responses that result in periodontal disease in infected rats. In the investigation, female Sprague-Dawley rats were employed. n-3 fatty acid-rich fish oil or n-6 fatty acid-rich corn oil diets were given to rats for 22 weeks while they were also infected with *Porphyromonas gingivalis*. Elevated blood levels of docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) were evidence of diet-induced alterations in rats fed a -3 FA diet. strains of *Porphyromonas gingivalis* combined with equal parts of 2 percent.

El-Sharkawy et al assessed, effect of nutritional supplements on 80 healthy individuals (40 per group) with advanced chronic periodontitis in their study. The goal of the study was to conduct a parallel-design and double-masked clinical experiment to evaluate a novel periodontal treatment technique. Attachment levels, probing depths, bleeding on probing, and plaque and gingival indices were all measured. The control group received SRP treatment along with a placebo, while test groups received SRP

treatment followed by daily dietary supplementation of omega-3 PUFAs and 81 mg of aspirin. The test group outperformed the control group in terms of pocket depth reduction and attachment growth after 3 & 6 months. To prevent and treat periodontitis, it is crucial to ingest adequate fish oils daily [20].

### 11. Zinc

Dang et al. [21] used nutrigenomic methods to explore the effectiveness of zinc supplements, changed by genotype SLC30A8, to enhance beta cell activity in diabetic rat cell line model. Control interfering RNA knockdown beta cells were employed to investigate potential effects of increased extracellular zinc on insulin secretion in the model, 24 hours prior to being grown with extracellular glucose. Based on the findings, they put out a theory that zinc supplements might modify the expression of the ZnT8 transporter gene, which in turn might have an impact on how periodontal disease develops.

**Benefits from nutrigenomics:** With the ultimate goal of establishing ways to improve health management and to avoid diseases, nutrigenomics research will broaden our awareness and knowledge of phenotype, genotype, and food interactions in a holistic fashion. The discovery of biomarkers that depict the transition from the healthy state to the pre-disease and disease stages is crucial in this regard. Based on expression profiles and patterns derived from genomes, transcriptomics, proteomics, and metabolomics research, nutritional genomics is thought to produce new biomarkers. These biomarkers will serve as indicators of health, predisease, and disease states or homeostasis [22]

**Future:** Even though there are now only a few workable concepts, nutrigenomics is undoubtedly predicted to be the next big thing. The food industry is aware of the importance of nutrigenomics research as a foundation for the idea of "personalized diets," for locating molecular biomarkers or novel bioactive food ingredients, and for confirming the efficacy of these bioactive ingredients as functional food components or nutraceuticals. Detecting indicators in the earliest stages of diet-related disorders is important because this is when nutritional intervention can treat the patient. Through the use of nutrients or their mixtures, markers can modify gene expression to enhance both productivity and overall performance. Although there are high expectations for the

developing field of nutrigenomics, there are two main areas of worry [23]. First of all, it is questionable whether or not the objective of matching foods to certain genotypes in order to improve the health of those individuals can be accomplished. Second, there are many obstacles that must be cleared before individualized nutrigenomics foods may be sold on the global food market, including some that are of a technological and ethical nature.

### 3. CONCLUSION

As the development of individualized nutrition intervention is expected to cause significant, and consistent changes in eating and lifestyle behaviors, enabling new preventative and therapeutic approaches, nutritional genomics is currently demonstrating outstanding success. The dental surgeon should consider using fish oils, fruits & vegetables, fibre, which lowers level of refined sugar in the diet as part of protocol of periodontal treatment, according to the 2011 European Workshop on Periodontology.

For the preventing and further treatment of periodontitis, a sufficient daily consumption of calcium and vitamin D is also advised. Nutrigenomics is anticipated to soon enable the development and validation of novel markers of cancer risk. In order to establish stability throughout the life cycle, which will lead to optimal human health and illness prevention, it is therefore vital to understand the interactions between the dietary components and human genome function.

### CONSENT AND ETHICAL APPROVAL

It is not applicable.

### COMPETING INTERESTS

Authors have declared that no competing interests exist.

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