

Review Article

Nutraceutical basis for drug delivery in periodontal disease

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ABSTRACT

Background: Periodontal disease is an infectious, inflammatory disease associated with overgrowth of certain pathogenic bacteria, release of bacterial toxins and inflammatory response of the host. The management of human periodontitis suggests therapies with Nutraceuticals, Surgical therapy and use of Antimicrobial agents. Odonto-nutraceuticals may play a significant role in the care of dental patients, with complex and multifactorial disorders, involving deregulated pathways, like Periodontitis. The present article highlights the role of nutraceuticals in the prevention of periodontal disease.

Key words: periodontitis, nutraceuticals, free radical, antimicrobial therapy.

Introduction

“Odonto” arises from the Greek word odontos for “tooth”, whereas the term nutraceuticals refers to bioactive phytochemicals, which can provide health-promoting effects. A plethora of Plants have been an exemplary source of pharmaceuticals and a preclinical and epidemiological studies have documented the role of nutraceuticals in the prevention of degenerative diseases, by virtue of their cardioprotective, neuroprotective, anti-inflammatory and anticancer properties¹.

Periodontal disease, an inflammatory disease, associated with overgrowth of certain pathogenic bacteria, liberation of bacterial toxins and inflammatory response of the host. The treatment of human periodontitis suggests therapy with Nutraceuticals, surgical therapy and Antimicrobial agents.² Highly organized

bacterial populations forms the periodontal pockets and alveolar bone destruction. Elimination of periodontopathic microorganisms in the subgingival microbiota is essential for periodontal healing.³

Odonto-nutraceuticals may play a significant role in the care of dental patients, in controlling complex and multifactorial disorders, often involving multiple deregulated pathways, like Periodontitis. In these terms, odonto-nutraceuticals represents promising agents in dentistry, because of their ability to regulate different molecular and biochemical targets. Interestingly, recent findings suggest that plant extracts, composed by a number of bioactive components, are more effective than individual compounds, because of additive and/or synergistic effects.^{4,5} Relevant examples of odontonutraceuticals include

Vitamins (A,C,E,B-complex, D), Minerals (Magnesium, Calcium) and Black Seed Grapes rich in polyphenols, particularly catechins, a group of flavonoids, and proanthocyanidins⁵. Association have been found between Periodontal disease Incidence or Prevalence and the intake of these and other nutrients through epidemiological studies. This paper highlights the role of different odontonutraceuticals in Periodontal disease prevention and also highlights different delivery systems in periodontal pockets.

Role of Vitamins (Nutraceuticals) in Periodontal Disease Prevention-

Vitamins play an interesting role for prevention and treatment of some pathological conditions, particularly periodontal disease .

1. Vitamin A

Vitamin A, helps in maintaining periodontal health and prevents disease progression. Moreover, role of vitamin A in immune system could be also important for maintaining some bacteria at adequate levels and for preventing over-inflammation.⁶

2. Vitamin D

Vitamin D, an active form is 1,25-dihydroxycholecalciferol (1,25(OH)₂D₃). Vitamin D helps in bone remodelling. Also vitamin D plays an important role in altering the immune system of a person thereby suppressing inflammation and by inhibiting inflammatory cells. Thus Vitamin D plays a role by improving the health of periodontal tissues.^{7,8,9}

3. Vitamin C

Vitamin C stabilizes the collagen structure by hydroxylation. It maintains the integrity of connective tissues such as the alveolar bone, periodontal ligament and cementum. Furthermore Vitamin C improves the immune system, and accelerates the wound healing. Ascorbic acid is a powerful antioxidant in living organisms, at intracellular level. In the supplemented diet with vitamin C decreased RANKL expression was seen and also osteoclastogenesis stimulation was diminished.^{10,11}

4. Vitamin E

Vitamin E is known for its antioxidant activity.¹² It stops the production of Reactive Oxygen Species by terminating the free radical chain reaction.¹³⁻¹⁴ Vitamin E has been found to protect the periodontal health by increasing the nitric oxide synthetase levels and prevents the oxidative stress.

Vitamin B complex

Vitamin B-complex refers to all of the known essential water-soluble vitamins except for Vitamin C. These include thiamine (vitamin B1), riboflavin (vitamin B2), niacin(vitamin B3), pantothenic acid (vitamin B5), pyridoxine (vitamin B6), biotin (vitamin B7 or B8), folic acid (vitamin B9) and cobalamin (vitamin B12).

Vitamin B complex has been found to prevent gingival inflammation. Few Japanese studies recommend vitamin B complex not to have any role in periodontal disease.^{15,16}

Role of Minerals in Periodontal Disease prevention¹⁷

1. Calcium-

Vitamin D along with calcium plays an important role in maintaining the periodontium. It helps in maintaining the cementum and alveolar bone height.

2. Magnesium-

Though the evidence is lacking, magnesium has shown a positive correlation with periodontal disease suppression.

Other food supplements

1. Probiotics; Probiotics contains beneficial bacterial strains. They help in decreasing the pathogenic bacteria which cause periodontal disease. Lactobacillus reuteri showed significant change in the plaque flora which was pathogenic.
2. Resveratrol; It is isolated from grape, has been used as an antioxidant in anticancer therapy and also to reduce oral mucosal and gingival inflammation.
3. Cranberry; It inhibits biofilm formation and prevents adherence of P. gingivalis, thereby preventing periodontal disease.

Nutraceutical basis for drug delivery in Periodontal disease-

Drug delivery-

Sustained ,prolonged, self controlled release at the site so that pathogens are destroyed. They may not be accessible to mechanical debridement.¹⁸

Ideal requirements of drug delivery system¹⁸

1. The delivery system should deliver the nutraceutical at the base of periodontal pocket in higher concentrations. It should be effective in killing the microorganism.
2. It should be biodegradable.
3. It should be with minimal side effects.
4. It should be retained in the pocket for sufficient duration of time.

Advantages of Nutraceutical based drug delivery system¹⁸

1. Reduction in total drug usage when compared with systemic therapy.
2. Superinfection and drug resistance are rare.
3. Minimal side effects of the nutraceutical.
4. Improved patient compliance.

Disadvantages of Nutraceutical based drug delivery system¹⁸

1. The drug may reach the deeper areas of pocket.
2. It may be time consuming and requires special efforts.

Indications of Drug delivery system¹⁹

1. Patients with chronic periodontitis where initial therapy has been done, but certain are not responsive for the therapy.
2. Patients with localized recurrent deep pockets.
3. Ailing / failing dental implants(peri-implantitis) where surgical procedure cannot be carried out.
4. Grade II furcation involvement where surgical procedure is not planned.

Contraindications of drug delivery systems^{19,20}

1. Patients allergic to any component of delivery system.
2. As a replacement to surgical periodontal therapy.

3. As a replacement for scaling and root planing.

4. Patients susceptible for infective endocarditis.

Nutraceutical based Drug delivery carrier/vehicle in Periodontal disease

These include different types of delivery vehicles-

Fibres²¹

The fibres system act as reservoir for active drug. These fibres which contains the drug is released for a prolonged duration when in place. These fibres are secured with cyanoacrylates

Films²¹

Fims, made of polylactide-co-glycolide, are inserted in the periodontal pockets. Studies have shown that post insertion of films in the pockets, results in reduction of the pocket depth.

Injectable systems²¹

These are comparatively easy systems for delivering the antimicrobial agents in the periodontal pockets. The drug is delivered at the site without pain and reaches deeper parts of pocket thus getting better access to the microflora.

Microspheres²¹

The active drug in the biodegradable material in the microspheres is released slowly. Rate of degradation determines the rate of drug release. It is made of synthetic polymer or natural polymers. Synthetic polymers are glycolides, poly alkyl cyanoacrylates and poly anhydrides. Natural polymers are proteins(albumin & gelatin) and carbohydrates (agarose and chitosan). Depending on the rate of degradation they are classified into- surface eroding and bulk eroding. The bulk eroding polymers allow the permeation of water into the matrix and whole microsphere is degraded. On the other hand, surface eroding don't allow the water to permeate through the sphere thus allowing slow degradation.

Gels²²

These systems are based on carbopol 974, hydroxyethyl cellulose and polycarbophil. The gel is carried in the pocket with a blunt syringe.

It doesn't dissolve water. Drug delivery occurs at a faster rate.

Strips and compacts²²

The strips are made from mixing polymers, monomers and different agents. They are flexible enough for placing in the periodontal pockets where degradation of the strips occurs similarly to the films.

Vesicular system^{23,24}

These liposome systems are covered by a membranous lipid bilayer, and mainly composed of natural and synthetic phospholipid. They are nontoxic and biodegradable. The drug is protected from immediate dilution or degradation.

Nanoparticle system²⁵

These include nanoparticles, polymeric micelles, nanocapsules, nano-gels, metal nanoparticles and quantum dots. The main advantages of these systems are high dispersibility, controlled release rate and increased stability. They easily reach the deeper parts of pockets. Dung²⁵ prepared oligonucleotide loaded chitosan nanoparticles and investigated release of the same. They found the product to be stable in the oral cavity for 12 hours. Furthermore, many herbal products like Aloe vera, curcuma, cocoa husk, pomegranate, cranberry are potentially effective against periodontitis.

Other applications of Nutraceuticals based drug delivery in Periodontal disease

Dentin Hypersensitivity²⁵

Desensitizing dentifrices containing 15% Hydroxyapatite nanoparticles, fluoride and Nutraceuticals like *Curcuma longa* reduced of dentin hypersensitivity clinically.

Dentifrobots²⁵

Dentifrobots kill the microorganisms in the dental plaque and prevent halitosis. Halitosis is indicative of Periodontal Disease.

Nanorobotic Local Anesthetics²⁵

Nanorobotic local anesthetics when applied to the gingival or the oral mucosa and signaled, the anesthetic travels via the epithelial and connective tissues of the gingiva to reach the pulp, thus providing selective anesthesia, which is under the control of the clinician.

Thus these agents help in alleviation of pain of the patient.

Bone regeneration^{25,26}

The most popular ones are Nano -HAP composite bone graft which are available in crystalline and titanium reinforced forms. These Nano -HAP composite bone graft scaffolds are biocompatible with superior mechanical properties.

Nanoceramic composite materials:

- Nanocrystals of CaSO₄ Particle size ranging from 200-900 nm; improve resistance to degradation, last longer (12-14 weeks) than conventional CaSO₄.
- CaPO₄ + ZnO (antibacterial)
- Carbon nanotubes provides flexible and inert scaffold on which the cell proliferate and deposit new bone.

Future Challenges and Conclusion

Though the science of nutraceuticals appears to be not feasible in the present scenario, the future holds strong promise for the delivery of nutraceuticals for the prevention of periodontal disease. The challenge will be to fabricate the devices which will easily deliver the nutraceuticals in the periodontal pockets and will help in prevention of periodontal disease. The delivery of nutraceuticals with newer technology will definitely benefit the patients and the practicing dentists. More studies are necessary to test the efficacy of these devices in prevention and control of periodontal disease in patients.

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Date of Submission: 19 June 2020

Date of Publishing: 30 September 2020

Author Declaration: Source of support: Nil , Conflict of interest: Nil

Ethics Committee Approval obtained for this study? NA

Was informed consent obtained from the subjects involved in the study? NA

For any images presented appropriate consent has been obtained from the subjects: NA

Plagiarism Checked: Yes

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DOI: 10.36848/PMR/2020/13100.51330