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## STRATEGIES TO CONTROL DENTAL PLAQUE BIOFILMS- A REVIEW

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### ABSTRACT

Periodontal disease is a highly prevalent infection that affects the human dentition and mainly characterised by extensive inflammation and destruction of the alveolar bone. Bacterial plaque is known to be the most common aetiology of periodontal disease. Many theories have been put forward that aims to describe the pathogenesis of periodontal diseases. Eliminating plaque and preventing its formation continues to be the mainstay of periodontal therapy. It should also be learnt that not all bacteria are harmful. There is a balance between the commensals and the pathogenic bacteria that gets shifted more toward the pathogenic bacteria in disease. The various physiologic, therapeutic and novel strategies that are carried out to combat the plaque biofilms are also discussed in this review.

**KEYWORD:** *Biofilm, dental plaque, plaque hypothesis.*



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## INTRODUCTION

Dental plaque is a structured resilient, grayish-yellow structure that tenaciously adheres to the intra oral hard surfaces including removable and fixed restorations.<sup>1</sup> [In 1999, the concept of plaque as a biofilm was suggested. Dental plaque is also the term commonly used for the biofilm formed on teeth surfaces. The term plaque has now been extended to encompass biofilms on all the oral surfaces. Biofilms are defined as matrix embedded microbial populations, that develops on teeth immediately following cleaning of the teeth and directly influences the pattern of initial microbial colonisation.<sup>2</sup> Plaque mainly comprises of bacteria, which are suspended in a matrix consisting of salivary glycoproteins and polysaccharides. This matrix gives it the ability to attach firmly to the tooth surfaces making it difficult to remove by rinsing or with the help of sprays. It is invisible to the naked eye and visualisation is possible only with the help of disclosing solutions. The development of dental plaque is an orderly sequence of events, resulting in a structurally and functionally organised, species-rich microbial community.<sup>3</sup> The dental plaque was considered to have similar structure as a biofilm. It is heterogenous in composition with open fluid filled channels running through the plaque mass. The fluid channels act as a circulatory system which enables the bacteria to absorb the nutrients and proliferate within the matrix. The bacterial substrates are retained within the matrix and favours metabolic interactions among different colonies of bacteria.<sup>4</sup> This complexity of the plaque biofilm and its inherent pathogenicity makes its removal and prevention of its formation an important aspect of treatment of periodontal disease

### **PATHOGENESIS OF PERIODONTAL DISEASES**

Many theories have been put forward that aims to describe the pathogenesis of periodontal diseases and to develop strategies based on the same. One of the very first theories included the Non specific plaque hypothesis proposed in the 1950's.<sup>5</sup>

### **NONSPECIFIC PLAQUE HYPOTHESIS**

This hypothesis proposed that the entire microbial community of plaque that stagnated the tooth surfaces and the gingival crevice contributed to the development of periodontal disorders. Bacterial plaque produced virulent factors and toxic products that initiated inflammation process, challenged the host defence mechanism, and resulted in the destruction of periodontal tissues. Under the nonspecific plaque hypothesis, the quantity of plaque was considered to be the main factor in the progression of periodontal diseases. Thus, increase in the quantity of plaque, as opposed to the quality of specific pathogenic microorganisms, were shown to be primarily responsible for initiating disease and disease progression.<sup>5,6</sup>

### **SPECIFIC PLAQUE HYPOTHESIS**

In non-specific plaque hypothesis, most of the bacterial plaque was viewed to be bad plaque and, henceforth, more plaque meant more disease. Identifying certain microorganisms was shown to be unimportant here. However, not all those with increased plaque deposits

developed severe periodontal disease and those with minimal plaque deposits had severe attachment loss and bone loss. So, then came the specific plaque hypothesis. The pathogenicity of dental plaque depends on the presence of or an increase in specific microorganisms.<sup>7</sup> It was stated that only certain microbial species within the plaque complex were pathogenic, and the pathogenicity depended on the selection of more virulent microorganisms. The pathogenesis of aggressive periodontitis was explained based on this specific plaque hypothesis. The use of systemic antimicrobials in 1980 was suggested to reduce the number of bacterial pathogens in the plaque, consequently leading to reduction in the disease process. The causative organism for the disease was identified and the most effective antibiotic agent was selected using an antibiotic sensitivity tests.<sup>8</sup>

### **ECOLOGICAL PLAQUE HYPOTHESIS**

The Ecological plaque hypothesis was put forth by Marsh in 1994. This theory stated that a change in the nutrient status of a pocket or chemical and physical changes to the habitat are considered the primary cause for the overgrowth by pathogens. The plaque accumulation will lead to an increased inflammatory response. A major ecological shift is noticed from predominantly gram positive facultative anaerobes to gram negative obligate anaerobic microflora. This hypothesis was believed to lead to new treatment opportunities. For periodontal diseases attempts could be made to change the local environment by reducing the gingival crevicular fluid (GCF) rate, or the site could be made less anaerobic by the use of redox agents.<sup>9</sup> Strategies that are consistently carried out with the aim of preventing disease through the principles of the ecological plaque hypothesis include: (a) inhibition of plaque acid production by incorporating fluoride that increases the acid resistance of enamel (b) avoidance between main meals of foods and drinks containing fermentable sugars, (c) the consumption of foods/drinks that contain non-fermentable sugar substitutes and (d) the stimulation of salivary flow after main meals due to consumption of bulk agents such as sugar alcohols and intense sweeteners. Some of these approaches have been investigated using the mixed culture system.<sup>10</sup>

### **KEYSTONE PATHOGENIC HYPOTHESIS**

The Keystone-Pathogen Hypothesis (KPH) was proposed by Hajishengallis and his colleagues in the year 2012. The KPH indicates that the microbial pathogens are the main cause for inflammatory disease by increasing the quantity of the certainly normal microbiota and by altering its composition.<sup>11</sup> The hypothesis states that the pathogenic microbes can execute the inflammatory disease by remodelling a normal benign microbiota into a dysbiotic one. The microorganisms that support a microbiota associated with disease states are referred to as the "keystone pathogens". The identification of these pathogens would have significant benefits as it facilitates the development of new treatments for polymicrobial diseases by concentrating therapeutic strategies on a limited number of bacterial targets that stabilises the dysbiotic microbial community.<sup>12</sup>

**MICROBIAL HOMEOSTASIS**

Microbial homeostasis is maintained by the equilibrium between the beneficial species and the oral environment. Due to dysbiosis the symbiotic relationship between the host and the microorganism is disrupted leading to the initial development of the disease process. Simultaneously during this phase there is a shift in the oral microbiota from gram positive to gram negative anaerobes. This process continues to occur until the disease begins to manifest clinically.<sup>13</sup>

**PHYSIOLOGIC STRATEGIES FOR THE CONTROL OF ORAL BIOFILMS**

The various physiologic strategies carried out to combat the oral biofilms are,

**CONTROL OF NUTRIENTS**

Anti-inflammatory agents can eliminate tissue destruction caused by bacterial and host-derived proteases. This would aim to minimise the supply of GCF, and thereby restrict the availability of nutrients that are important for the growth of some periodontopathogens.<sup>14</sup>

**CONTROL OF PLAQUE PH**

The strategies to induce salivary flow would help control the plaque pH at favourable values, and increase clearance of fermentable substrates. Disruption of bacterial homeostasis in plaque biofilms is less likely to happen if the frequency of acidic conditions, following sugar intake could be reduced. This is achieved physiologically by incorporating the inhibitors of acid production such as non-fermentable sweetening agents, fluorides and antimicrobial agents and the local generation of base such as arginine, urea and peptides in plaque. This strategy would not only help remove the major environmental pressure selected for cariogenic species, and also aim to prevent the inhibition of species predominating in health, that are generally acid-sensitive.<sup>15</sup>

**CONTROL OF REDOX POTENTIAL**

It is shown that the subgingival environment is anaerobic with low oxygen tension. Raising the redox potential of the periodontal pocket helps to create an environment incompatible with the growth of anaerobic periodontal pathogens, and thereby helps to allow control of these organisms. There are a variety of substances that raise the redox potential of an ecosystem by acting as electron receptors. The redox dyes, such as methylene blue and ferric ions have been used.<sup>16</sup>

**THERAPEUTIC STRATEGIES FOR THE CONTROL OF ORAL BIOFILMS**

Measures that are used to therapeutically alter the ecological environment of the biofilms include the use of mouthrinses, full mouth disinfection, photodynamic therapy and probiotics.

**MOUTHRINSES**

Chlorhexidine mouth rinses are available in formulations of 0.2% and 0.12%. It is said to be a potent inhibitor of dental plaque and has been proved to be so in many literature studies.<sup>17</sup> Chlorhexidine

gluconate (CHX), a positively charged bisguanide, is currently the most effective compound with immense antimicrobial effects on numerous bacterial organisms. Though its usage has been proven to be undebatable in reducing the formation of plaque, it has not been recommended for prolonged periods as it is attributed to certain adverse effects such as altered taste sensation, desquamation of oral mucosa, parotid gland swelling and staining of teeth and mucous membranes.<sup>18</sup>

**FULL MOUTH DISINFECTION THERAPY**

In the year 1995, full mouth disinfection therapy (FMDT) was suggested by Quirynen and was introduced by the Belgian Lowen research group. The FMDT was also known as one stage therapy. This therapy was focused on eliminating the periodontal pathogens from both the gingival pockets as well as the rest of the intraoral habitats which included the mucous membrane, tongue and saliva in a single appointment. In this technique, bacterial re-colonisation through cross-contamination is delayed until the healing of the periodontal pockets occur. The therapy produced positive results which lead to gain in attachment, reduction of pocket depth and an ecological shift in the oral microflora. However, the technique had controversy over its efficacy, patient comfort, rationale and cost effectiveness.<sup>19</sup>

**PROBIOTICS**

Probiotics are being developed in destroying the attachment of periodontopathogenic bacteria via competition for binding sites at the biofilm, and competition for nutrients within the biofilm. Probiotic strains are also being produced that can secrete antimicrobial compounds, potentially inhibiting pathogenic oral bacterium.<sup>20</sup> After profound studies are made in combating periodontal disease, Probiotics have become of interest in the research field. They have been known to effectively delay the pathogenesis of periodontal diseases and to abate periodontal infections. Probiotics are categorised in two genus *Lactobacillus* and *Bifidobacterium*. The other microorganisms classified into this group includes *Saccharomyces cerevisiae*, *Aspergillus niger*, *Aspergillus oryzae*, *Sochromyces boulardii*.<sup>21</sup>

**ANTIMICROBIAL COATINGS**

Pioneer studies were made in literature by Zobell and Henrici whose description about bacteria was that they could attach to the surface and thrive on the surface. The existence of a surface is believed to be the most important prerequisite for biofilm formation. The physicochemical factors govern the initial attachment and adhesion of bacteria to surface. Preventing the formation of a conditioning layer that tolerates the exposed surface chemistry and providing an attachment site for bacteria are the key challenges faced in this area. All materials are subjected to bacterial contaminations since exposed to air, humidity or diverse environmental conditions. To overcome these problems, several strategies have been used to create coatings that are antimicrobial.<sup>22</sup>

**KEYES TECHNIQUE**

In 1978, Paul. H. Keyes, introduced the use of a phase-contrast microscopy in the diagnosis and treatment of

periodontal diseases. This was known as the "Keyes technique" in the treatment of periodontal lesions. The more appropriate term is "microbiologically modulated periodontal therapy". The fundamental goal of this technique was to help keep the bacterial products at non-pathogenic levels and minimise the destruction levels to further allow healing process to occur.<sup>23</sup> The Keyes technique targeted at specific disease-associated bacterial species in the sub-gingival plaque microbiota had also been suggested for treatment of juvenile periodontitis. This rationale was applied initially to the treatment of adult periodontitis lesions.<sup>24</sup> It lost its importance as bacterial monitoring using a phase contrast microscope is a technique sensitive, inaccurate and outmoded technology, which does not accurately differentiate between bacteria associated with a healthy periodontal environment and that associated with aggressive periodontal disease. Studies had shown that adjunctive use of baking soda and hydrogen peroxide have not demonstrated any particular added benefit over conventional techniques.

#### **PHOTODYNAMIC THERAPY**

Photodynamic therapy (PDT) is a non-invasive treatment modality for the various infections caused by bacteria, fungi and viruses. It is useful as an adjunct in eliminating periopathogenic bacteria. PDT may be applied topically into the periodontal sulcus avoiding overdoses and adverse effects associated with the systemic antimicrobial administration. It also reduces the occurrence of bacterial resistance. The therapy utilises low power lasers to kill microorganisms that are treated with a photo-sensitiser drug.<sup>25</sup> The process of killing microorganisms with light by a sensitising agent was done about 100 years back in the year 1908. The therapy was based upon the production of OH radicals, formed by the excitation of a photoactivatable agent. The most commonly tested are the tricyclic dyes-methylene blue and erythrosine, phenothiazine dyes-toluidine blue O, tetrapyrroles- porphyrins, and furo-coumarins.<sup>26</sup>

#### **NOVEL STRATEGIES FOR THE CONTROL OF ORAL BIOFILMS**

##### **ANTI-ADHESION COATING**

Anti-adhesion coatings focuses on preventing the formation of biofilm at early stages, which should be desirable in clinical settings. Due to the complex interaction between the coating surfaces with bacteria, and host proteins, the mechanism of anti-adhesion coatings is also difficult to pinpoint. As a result, more effort is needed to exploit this strategy for prevention of biofilm related infections.<sup>27</sup> The increase in drug-resistant bacteria makes the search for novel strategies in fighting bacterial infections. An attractive approach involves utilising agents that cause interference with the ability of the bacteria to adhere to tissues of the host. However, the future of anti-adhesion coating therapy will depend on having a good knowledge of the properties of bacterial adhesins and on the development of appropriate agents that block adhesion.<sup>28</sup>

##### **ENZYMES**

Combining the polysaccharide-hydrolysing enzymes and oxidoreductases caused removal of bacterial biofilms.

The possible elimination of biofilm comes from observing biofilm self-destruction. Citing huge masses of biofilm to be the reason for oxygen depletion, inducing exopolysaccharide lyase helps to digest the biofilm matrix and liberating the cells. Surface finishing treatments including polishing, sandblasting, and grinding slackened the build-up of bacterial biofilms, but electropolishing seemed to work the best.<sup>29</sup>

#### **CHELATING AGENTS**

Calcium, magnesium, iron and some other metal cations have been implicated in maintaining matrix integrity. Chelating agents are known to destabilise biofilm architecture as well as interfering with bacterial membrane stability. For example, tetrasodium-EDTA combats biofilms in an in-vitro biofilm model and disodium-EDTA in combination with gentamicin showed a rapid decline in biofilm formation by *Staphylococcus* species and *P. aeruginosa* species.<sup>30</sup>

#### **GUIDED POCKET RECOLONISATION**

Therapeutic treatments are focused on removing periodontopathogens from the subgingival area and amongst various strategies, scaling and root planing is considered to be the gold standard modality. The concept of periodontal replacement therapy consists of applying beneficial oral bacteria subgingivally to prevent recolonisation of periodontal pockets by pathogens after scaling and root planing. With the advent of antibiotic resistance and lack of non-antibiotic regimen options, this Guided Pocket Recolonisation (GPR) approach may provide a worthy alternative to the armamentarium of treating periodontitis.<sup>31</sup>

#### **BACTERIOPHAGE**

Bacteriophages are natural viruses that infect bacteria. The bacteriophage genomes contain genes that are able to break down elements of the biofilm matrix. It is taken into assumption that the biofilms confer resistance to bacteriophages, due to the impermeability offered by the biofilm matrix. However, though they are larger than chemical agents, bacteriophages are still smaller than their bacterial hosts, and many bacteriophages can still infect bacteria within biofilms.<sup>32</sup>

#### **PERIODONTAL VACCINES**

The process of vaccination is capable of inducing immune resistance to viral or bacterial infectious agents. It was in the 20<sup>th</sup> century that the periodontal vaccines came into existence and some examples are Vancott's vaccine and Inava endocarp vaccine.<sup>33</sup> The role of periodontal vaccines and the need for its development are emphasised on three factors such as elimination of bacteria, example; *P. gingivalis*, which has the capability to evade host immune responses and invade tissues, to reduce the rate of periodontal diseases and to save individuals from the probable financial burden.<sup>34</sup> The bacteria implicated to be the cause for periodontal disease includes *Porphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans*. Research in the field of periodontal vaccines has been forward moving in the identification of antigenic molecules of *P. gingivalis* and *A. actinomycetemcomitans*. These vaccines have the potential to prevent the course of periodontitis and

also greatly enhance the quality of living of people, whom are not able to obtain periodontal treatment easily. Though periodontal vaccines serve definite adjunctive treatment for animal models and have offered many therapeutic advantages, it has not been completely successful for humans and still remains to be elusive.<sup>35</sup>

### NATURAL SOURCES

Herbal extracts have been used as a traditional source of treatment in medicine since ancient times, involving eastern and western medical customs. Many plant-derived antimicrobial components are used in folklore therapeutics for treating periodontal disorders and for the maintenance of oral hygiene.<sup>36</sup> Extracts from aromatic plants are now being investigated as natural agents against bacterial biofilms. They are invariably regarded as safe and so are compatible with current regulations regarding food production.<sup>37</sup> Acacia catechu, a herbal tooth powder was reported to show significant reduction in plaque and gingivitis. Extracts of Aloe barbadensis miller (Aloe Vera) has been useful in treating periodontal diseases by virtue of their antioxidant properties. The anti-inflammatory property of Ocimum sanctum (tulsi) and Curcuma Longa (turmeric)

makes it ideal for treating periodontitis. Various other herbs used in the management of periodontal diseases are Drynaria, Allium sativum, Allium ceta, Magnifera indica, Sisygium aromaticum etc.<sup>38</sup>

### CONCLUSION

Prevention of plaque biofilms and controlling the growth of periodontogenic bacteria continues to be the most challenging aspects of periodontal intervention and numerous strategies have been proposed for the same. Although a plethora of therapeutic and novel strategies have been put forth to abate periodontal infections, most of them are yet to bring about a permanent solution to combat the disease progress. However, amongst the several novel strategies, herbal products have been proved to be the most promising in alleviating the symptoms of periodontal problems with minimal side effects and need to be explored more in the future.

### CONFLICT OF INTEREST

Conflict of interest declared none.

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