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# The Use of Antibiotics *vs*. Probiotics in Periodontitis Therapy

***Nada Tawfig Hashim****

*Department of Dentistry, University of Khartoum, Sudan*

## Abstract

Periodontal disease is an inflammatory disease, provoked in response to periodontopathogens in the biofilm of the subgingival plaque, affecting tissues supporting the teeth. Members of the red complex, such as *Porphyromonas gingivalis* and *Tannerella forsythia* are considered as the most pathogenic microbial components at present. Likewise, *Aggregatibacter actinomycetemcomitans* is associated with periodontal disease, but it does not belong to the red complex. The gold standard in periodontal treatment is scaling and root planning. Systemic antibiotic therapy is indicated to control deep periodontal pockets with microbial invasion at epithelial level that are difficult to access with disease progressing overtime. Resistance of bacterial species to antibacterial treatment has been considered as a global problem following the excessive use of these drugs. In recent years, the use of probiotics which display a strong inhibitory effect against certain periodontal pathogens has become more prevalent. Thus, this review deliberates the adjunctive use of antibiotics versus probiotics in periodontitis therapy.

**Keywords: Periodontitis; Antibiotics; Probiotics; Biofilm; Root planning**

## Introduction

Periodontal diseases are plaque-induced inflammatory conditions affecting the periodontium, characterized by mononuclear cell infiltration into gingival tissues, leading to connective tissue destruction and alveolar bone resorption and if left untreated, they may lead to destruction of the tooth-supporting apparatus and ultimately tooth loss that potentially damages the dentition [1,2]. The primary etiological factor for periodontal diseases is the dental plaque biofilm which is defined as organized and complex aggregations of bacteria and their products on the tooth surface. Approximately 700 different bacterial species have been identified in the oral microbiota, among which only a small group of 10 to 15 species has been recognized as being significantly associated with the initiation and progression of periodontitis [3]. It is generally approved that microorganisms residing in periodontal pockets are responsible for periodontitis however uncertainty exists concerning the exact mechanisms by which periodontal tissues are destroyed [4]. The principal organisms correlated with the initiation and progressions of periodontitis are *P. gingivalis*, *Treponema denticola*, *T. forsythus*, and *A. actinomycetemcomitans* [1]. However other bacteria such as gram-negative anaerobic rods, some gram-positive bacteria and even enteric rods/pseudomonas could contribute in the etiopathogenesis of periodontitis [5]. Nonsurgical Periodontal Therapy (NSPT) is the foundation of periodontal therapy by which a mechanical root surface debridement is performed. Therefore, the first suggested solution to combat periodontal infection is by NSPT [6]. In spite of the microbial specificity of periodontal infection, however, mechanical debridement of the root surface for treatment of periodontitis remains highly unspecific. This nonspecific treatment approach has proven successful on a long-term basis for many patients, although a small, but significant proportion of sites and patients may not respond satisfactorily [6,7]. A successful treatment of periodontitis thus requires decrease of the bacterial load to enhance the ability of the periodontal tissue to repair itself [8]. Mechanical debridement is a highly challenging therapeutic procedure that doesn't eliminate all periodontopathic bacteria from the sub gingival environment, particularly in inaccessible areas such as furcations, grooves, concavities, and tortuous pockets [9]. Given the infectious nature of periodontal diseases and the minimal efficacy of conventional mechanical therapy for the treatment of certain forms of periodontal diseases, the usage of antibiotics in certain instances necessary to boost clinical outcomes and periodontal conditions [3,10].

## Rationale for the Use of Antibiotics in Periodontal Therapy

The dynamic and complex structure of the periodontal biofilm, which includes several bacterial

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***Correspondence:***
*Nada Tawfig Hashim, Department of Dentistry, University of Khartoum, Sudan, Tel: 00249912347374; E-mail: nadatawfig@yahoo.com*

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species residing in a glycocalyx matrix, decreases susceptibility to antimicrobials relative to planktonic or free floating bacteria. Hereafter, mechanical debridement is important to removing the biofilm when systemic antibiotics are used to treat periodontitis. The justification for the use of adjunctive systemic antimicrobials is to encourage a reduction in the bacterial load that promotes resolution of inflammation in the periodontal pocket. The recommendation for using antibiotics is restricted to limiting the development of microbial antibiotic resistance in general [11]. Non-surgical scaling and root planning may eliminate sub gingival *Campylobacter rectus* however; it is often ineffectual against *P. gingivalis*, *Prevotella intermedia*, *T. forsythusand* enteric rods and may not considerably decrease the amount of *A. actinomycetemcomitans* or *Peptostreptococcus* [12]. Systemic antibiotics enter the periodontal tissues and periodontal pocket *via* serum and can affect microorganisms outside the reach of cleaning by periodontal instruments. Additionally, systemic antibiotic therapy has the potential to suppress periodontal pathogens residing on the tongue or other oral surfaces, and by this means delaying sub gingival recolonization of pathogens [13]. The use of systemic antibiotics as a part of the periodontal therapy has been recommended as an adjunctive therapy in specific situations such as with patients showing progressive periodontal breakdown even after conventional mechanical treatment, aggressive periodontitis, necrotizing periodontal diseases and periodontal abscess [14]. The main methods to systemic antibiotic therapy for periodontal treatment are focused on mono-therapy, even though combinations of antibiotics are becoming more effective. Metronidazole, the tetracyclines, clindamycin, ciprofloxacin and amoxicillin are the antibiotics most widely used [10]. It has been stated that most patients diagnosed with chronic periodontitis can be managed successfully after mechanical debridement, proper oral hygiene and routine maintenance care. In their study, Hererra et al. [15] concluded that systemic antibiotics used in combination with scaling and root planing could have potential advantages over scaling and root planing alone in terms of minimizing probing depth and clinical attachment level. Another review by Haffajee et al. [16] reported additional clinical outcomes in attachment level gain after prescribing systemic antibiotics as an adjunct to surgical mechanical debridement in deep pockets. However, this conclusion was refuted by Hererra et al. [17]. Who argued that there was inadequate evidence to establish whether or not adjunctive antibiotics were effective when paired with periodontal surgery? Fin comparison, aggressive periodontitis is frequently associated with the presence of elevated levels of *A. actinomycetemcomitans*, and/or *P. gingivalis*, bacteria that have the ability to invade the periodontal tissues. The adjunctive use of antibiotics in this situation is sufficient to eliminate and kill such pathogens [13]. A variety of studies evaluated antibiotics usage to control or decrease the progression of periodontitis. Systemically prescribed antibiotics demonstrated a statistically significant improvement in attachment and reduction in depth of periodontal pockets, irrespective of initial probing methods or therapeutic modalities (antibiotic therapy alone, in combination with scaling and root planing, or in combination with scaling and root planing plus surgical therapy). However, the therapeutic effects identified are clinically relevant in a small range of cases. For instance, attachment gain in patients with aggressive periodontitis is greater than in those with chronic periodontitis [4,16,18].

## Disadvantages of Antibiotics

The application of systemic antibiotics in the treatment of periodontitis is effective only when used in combination with adequate mechanical debridement to remove subgingival biofilm. However, it remains controversial due to the abuse of antibiotics that results from the wider context of the over-prescription which consequently leads to the development of Antimicrobial Resistance (AMR) [13,19]. Nowadays, AMR forms a great threat to humanity and it is evenly balanced to that from terrorism and climate change. The consensus report of the sixth European Workshop in Periodontology in 2008 was that, in this context, antibiotics would be restricted for usage in particular patients' categories and circumstances such as in cases with aggressive and severe forms of periodontitis. In addition, the use of the broad-spectrum antibiotics, such as amoxicillin and metronidazole, has no specific microbiological target and only a small portion of the intake dose enters the target tissue. The leftover dosage is distributed to reach all other organs and systems in the body, with little positive benefits and only side-effects. The "price" that is paid to the community for the extensive use of antibiotics is the increase in antibiotic resistance which is considered as life-threatening. So it is noteworthy to control such a price by ensuring that all antibiotics are appropriately prescribed and develop novel non-antibiotic-based treatments by application of selected beneficial bacteria, as an adjunct to Scaling and Root Planing (SRP), that would also inhibit the periodontopathogens recolonization of periodontal pockets and consequently attain and sustain periodontal health [20,21].

## What are Probiotics?

Probiotics are defined as bacteria with physiological benefits for humans, influencing both the development and stability of microbiota, thus preventing the colonization of pathogens, enhancing the mucosal barrier *via* tropic effects on the epithelium, and stimulating both the innate and the adaptive immune systems [22]. Once probiotics are given in appropriate quantities, they replicate beneficial bacteria that can help kill pathogenic bacteria and combat infection. Oral probiotics can aid oral health by preventing the development of harmful microbiota or by modulating mucosal immunity in the oral cavity [23].

## History of Probiotics

The word probiotic derives literally from Latin (pro) and Greek (bios) meaning for life. Kollath was first used it in 1953 to generically describe various organic and inorganic supplements that were believed to have the potential to improve the health of malnourished patients. In 1965 Lilly and Stillwell used the term probiotics to describe 'substances' secreted by one organism that stimulates the growth of another [24,25]. In 2001, the World Health Organization defined probiotics as "Live microorganisms that confer a health benefit on the host when administered in appropriate amount" [26].

### Criteria for probiotics

The following criteria should be fulfilled by the bacteria to be classified as oral probiotics [27]:

- Scientifically demonstrated beneficial physiologic effects.
- Human origin, safety for human use, and stability in acid and Bile.
- Should adhere to and colonize on dental tissue, and should be a part of the biofilm.
- Should not ferment sugars, which subsequently lowers the pH and is detrimental to dental health.

The most frequently used and studied genera satisfying the above

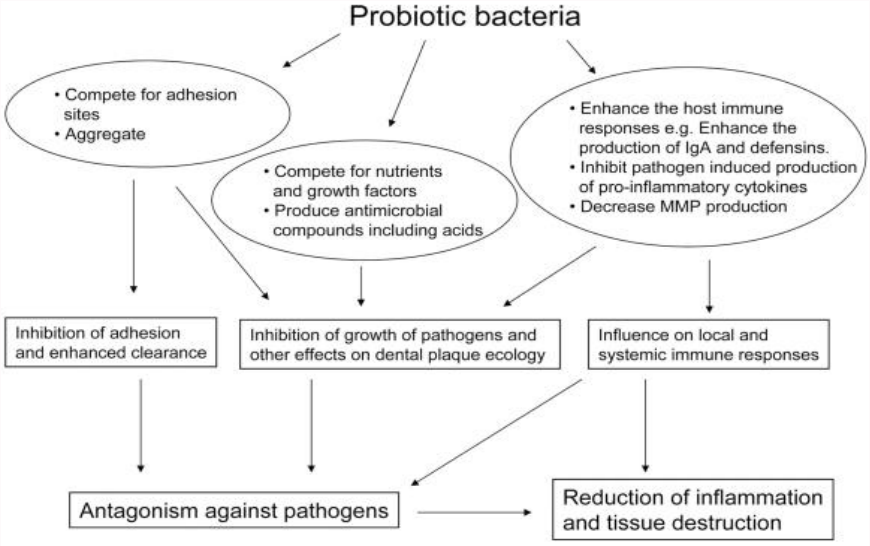


**Figure 1:** Potential mechanisms by which probiotic bacteria could affect oral health.

criteria are *Lactobacillus* and *Bifidobacterium* [23].

*Lactobacilli* make up around 1% of the cultivable oral micro flora in humans. The most commonly occurring species in saliva are *Lactobacillus acidophilus*, *L. scasei*, *L. fermentum*, *L. plantarum*, *L. rhamnosus* and *L. salivarius*. The species found in dairy products are *L. acidophilus*, *L. casei*, *L. fermentum* and *L. rhamnosus*. It has also been reported that individuals who ate *L. rhamnosus* containing yogurt regularly, host this microorganism in the saliva for up to 3 weeks following cessation of yoghurt intake [28,29].

### Potential mechanisms of probiotics effects in the oral cavity

The pathways for probiotics activity in the oral cavity can be grouped into three major categories: Normalization of the oral microbiota, regulation of the immune response, and metabolic impact [30].

## Probiotics and Periodontal Disease

The most common oral diseases including periodontal diseases are caused by a shift in the balance of the resident microbiota [31-33]. In periodontal diseases, there is an increase in plaque mass and a change to increasingly obligatory anaerobic and proteolysis bacteria. The harm done to the host is attributable to the synergistic effect of subgingival biofilm, and the host response to different bacterial populations [34-36]. In respect to commensal oral microbes, several aspects support the idea that it may be possible to find bacteria that could be useful in prevention or treatment of periodontal disease. The ecological plaque hypothesis proposes that selective pressure in environmental conditions can change the balance between oral health and disease. Because bacteria may also affect their environment, and both synergistic and antagonistic interactions are proposed for bacteria in dental plaque, the environmental pressure identified in the ecological plaque hypothesis may be partially imposed by bacteria [29].

Probiotics conventionally used in the field of medicine are also used to regulate and treat periodontal disease by the application of bacterial replacement therapy. Nowadays, probiotics are commonly used in the oral health perspective as a result of antibiotic resistance and frequent recolonization of treated sites with pathogenic bacteria [37]. Oral probiotics bacteria bind and colonize periodontal tissue including hard non-shedding surfaces and become part of the biofilm. They should not ferment sugars, which instead lower the pH and induce dental caries [38]. Probiotics have demonstrated inhibition of plaque formation by lowering the salivary pH, therefore, disabling bacteria associated with plaque formation to form plaque. Probiotics are also known to produce antioxidants which, in effect, prevent plaque formation by neutralizing the free electrons required for plaque mineralization. Moreover, probiotics are capable of breaking down putrescent odor by fixing on volatile sulfur compounds and changing them to gases needed for metabolism. A few studies have shown that probiotics *Lactobacillus* strains have been effective in reducing gingival inflammation and a number of black-pigmented rods including *P. gingivalis* in the saliva and subgingival plaque. Additionally, Lactobacilli have been found to minimize the levels of periodontal pathogens on the tongue which considered as a significant reservoir for their dissemination and thereby, indirectly minimize the colonization of subgingival plaque by periodontal pathogens [39,40]. Homofermentative *lactobacilli* inhibitory action against periodontal pathogens was mainly associated with their acid production, and not with $H_2O_2$ or bacteriocin production [41]. The method of replacing the pathogenic bacteria in the gingival sulcus with beneficial bacteria is called guided periodontal pocket recolonization. Subgingival utilization of beneficial bacteria, *S. sanguis*, *S. salivarius*, and S. mitmitis, has been effective in delaying the re-colonization by periodontal pathogens, decreasing inflammation and increasing bone density and bone levels in beagle dogs [26,42].

### Products containing probiotics for periodontal disease management

A few products containing probiotics are available in the form of lozenges, toothpaste, chewing gums, or mouthwashes. GUM PerioBalance is the first probiotics sold by Sunstar (Etoy, Switzerland), primarily formulated to combat periodontal disease. GUM PerioBalance comprises an original combination of 2 strains of *L. reuteri* specially chosen for their synergistic properties in battle against cryogenic bacteria and periodontopathogens. PeriBiotic this toothpaste is an all natural, fluoride free oral hygiene supplement

containing Dental-Lac, a functional *L. paracasei* probiotics not found in any other toothpaste. Bifidumbacterin, Acilact, Vitanarthis preparation of probiotics containing a complex of five live lyophilized lactic acid bacteria is believed to enhance both clinical and microbiologic parameters in patients with gingivitis and mild periodontitis [43-46].

## Conclusion

The current understanding of periodontal diseases describes them as infections caused by particular microbiota which live in sub-gingival biofilms on the non-shedding surfaces of the oral cavity. The major etiological causes of periodontal disease tend to be the lack of beneficial bacteria, the existence of pathogenic bacteria, and a susceptible host. Current therapeutic strategies suggest the alteration of ecological niches, from pathogenic bacteria to a biofilm of commensal bacteria. The use of probiotics has re-emerged as a mean to restore and boost the beneficial microbes in the oral cavity. The timing of growing interest in this field coincides with the need to augment or replace antibiotics whose side effects are undesirable and whose efficacy is diminishing due to drug resistance. Evidence that probiotics strains can substitute antibiotic therapy by reducing adverse effects and enhancing mucosal immunity is mounting. Therefore, in order to avoid the deleterious side-effects of antibiotics, the administration of beneficial bacteria in the form of probiotics can be a valuable alternative in the treatment of periodontitis.

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