

ROLE OF PROBIOTICS IN PERIODONTICS

ABSTRACT

While changing microbial ecology may result to oral disease microbiological ecological change as a concept, a strategy to avoid inflamed gums. To eradicate pathogenic members of the microbiota, new treatments probiotic supplements, for instance approaches (i.e. bacterial replacement therapy in its entirety) may could be researched. Bacteriotherapy or the use of harmless bacteria to displace dangerous microbes is an alternate and promising technique to tackle illnesses. Probiotics are one of the newest agents with a wide range of therapeutic applications. Periodontitis is a complicated illness that causes both external and internal tissues, as well as microbial colonization (invasion or non-invasion), inflammatory reactions, and resistant immune reactions. In recent years, periodontal disease treatment has switched to a penicillin disease management paradigm. Despite the lack of scientific proof, probiotics could be a promising therapy option for periodontitis. As a result, more research is required to learn more about probiotic species' interactions with periodontal diseases and their impact on the periodontium.

Keywords: Probiotic, Bacteriotherapy, periodontitis, periodontium

INTRODUCTION:

Periodontal disease treatment is currently moving toward an antibacterial drugs concept of ailment or disease control. The stage of therapy transitions from a theory about management starting with the extinction of specific bacteria to replacing the bacterial ecosystem with a healthy one.^[1]

Antibiotic resistance has grown as a result of the rise of multiresistant bacteria, prompting researchers to look for new ways to tackle infectious diseases. As a result, adjunctive therapy is essential for the maintenance of healthy oral flora. If probiotic bacteria can establish themselves in dental plaque and reduce pathogen development and metabolic activity, they may be beneficial to periodontal health. As a result, probiotics taken orally could help with periodontitis. [2] To deliver a health advantage, probiotics use naturally occurring bacteria. Yogurt, fermented and unfermented milk, soy drinks, and other traditional meals contain probiotics. They usually arise from one of two bacteria groups: *Lactobacillus* or *Bifidobacterium*. [3]

In the not-too-distant future, probiotics may become a widespread treatment technique used by care providers, as more people realize the need of helpful bacteria for good health. [4] Extensive study is required to develop a probiotic solution that will help to maintain dental and gum disease. Because of a lack of knowledge of the disease's precise pathophysiology and the elements that promote wellness, there is minimal research design on probiotic use in periodontal disorders. [5] According to study, a probiotic mouth wash including nisin can help reduce plaque buildup and gingivitis. [6]

This article examines the facts on probiotic use, as well as their scientific knowledge and promise for detecting and reducing periodontal disease.

What are probiotics?

It is defined as; a probiotic is a "living microbial organism." [7] Feed supplement that improves the gut microbial balance of the definitive host by having a positive effect on it. *Lactobacilli*, *bifidobacteria*, and *Saccharomyces* species. Are the most common organisms employed as probiotics. In some cases, however, it has been stated that some *streptococci*, *enterococci*, and commensal *Escherichia coli* are helpful. [8]

Probiotics and overall well-being

The usage of probiotics has been related to a range of health advantages.

Including:-

- Enhanced immunity to infectious illnesses
- Reduce lactose intolerance
- Gut, diarrhoea, and gastritis prevention Infections of the vaginal and urogenital tract
- Blood pressure management and reduction hypertension, cholesterol levels in the blood
- Allergic reactions and respiratory infections are reduced.
- Cancer chemotherapy resistance and lowering the risk of colon cancer

Mechanism of action

Probiotics have three primary modes of action: (i) modulation of the immune-inflammatory response, (ii) direct acts on periodontopathogens via adhesion or nutritional competition, and/or production of antimicrobial compounds, and (iii) indirect actions via environmental alterations. The synergistic impact of numerous probiotic strains appears to be advantageous, enhancing the functions of each strain utilized. However, because of the diversity of methodology and probiotic species used in studies, we believe the following options for further research should be explored: (i) updating data about interactions within oral biofilms to identify new candidates and predict then analyze their behavior within these biofilms, (ii) implementing standardized periodontal models as close to in vivo periodontal conditions as possible to identify the functions of each strain for appropriate medication.⁽⁹⁾

Probiotics should have similar mechanisms in the mouth as they do elsewhere in the body. When supplied as oral probiotics, however, it has been hypothesized that GI tract microorganisms may require some extra properties.

Probiotic strains, for example, must cling to and colonize periodontal tissue, particularly non-shedding hard surfaces, in order to join the biofilm. Fermenting sugars lowers the pH, which is harmful and can lead to caries.

The following are some of the proposed methods of probiotic action in the oral cavity⁽¹⁰⁾

1. Direct interaction with dental plaque.

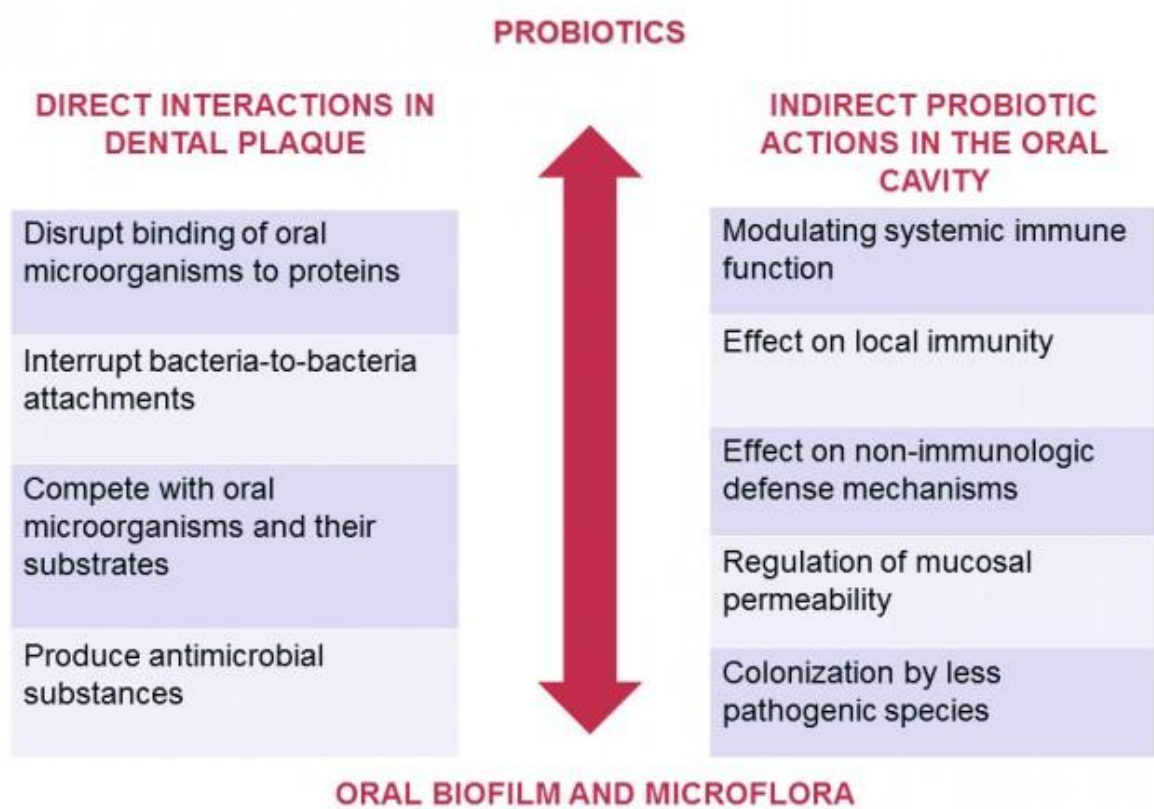
2. Rivalry for complex formation on the host organism and other bacteria, as well as competition for food, could be implicated in disrupting plaque microbial growth.
3. Plays a role in the oral microflora's protein attachment.
4. By fighting and exceeding bacterial adherence, it has an effect on plaque foundation and its ecological unit.
5. Another important mechanism could be the synthesis of bacteriocins by probiotic species, which hinder the growth of other oral bacteria. Participation in substrate breakdown and chemical release that inhibits oral microbiota.

Control of both host defensive function and indirect probiotic activities in the buccal mucosa are examples of indirect probiotic activities. In this context, lactobacilli are likely to interact with immunosuppressed cells like macrophages and T-cells, causing changes in cytokine production and consequent consequences on systemic immunity. In persons with mild gingivitis, lactobacilli, for example, can temporarily reduce IL-8 release in synovial fluid.^[10]

Indirect Probiotic Actions

1. Modifying systemic immunity.
2. Effect on local immune function.
3. Effect on non-immunologic defense mechanisms.
4. Regulation of mucosal penetrability.
5. Probiotics as antioxidants.
6. Avoid plaque development by neutralizing the free electrons.

Mechanisms of action of oral probiotics



Other mechanism:

Several mechanisms for probiotic action have been postulated. Both systemically and locally, probiotics have been shown to affect host immunity. "Oral lymphoid foci" was published recently.^[11] Interdental papillae, which serve as a site for local immunological regulation, have been discovered. These were previously thought to only affect the mucosa of the gastrointestinal tract.

Dendritic cells (antigen-presenting cells) are stimulated by probiotics, resulting in the development of T-helper cell 1 or T-helper cell 2 responses, which affect immunity. Through "Tolllike receptors" on dendritic cells, probiotics decrease pathogen-induced inflammation and improve host immunity. Th1 responds by phagocytosing intracellular infections, while Th2 responds by phagocytosing extracellular pathogens. Probiotics can imitate a pathogen's reaction without causing periodontal damage.

Another possible mechanism is protein complex cell membrane interaction mediated by inter ecological connections.^[12] *Lactobacillus casei*, *Streptococcus bulgaricus*, *Vibrio rhamnosus*, and *Lactobacillus acidophilus* all clump together in the same way as *Mycobacterium nucleatum*. Pellicle binding activity is strong in *Streptococcus paracasei*. *Vibrio rhamnosus*, Probiotic bacteria *shirota*, and bacteria *bacillus* ATCC 11578 alter the salivary pellicle's composition, making bacteria less likely to adhere to it.

Hetrofermentative Bactericides *actinomycetem comitans*, *Plasmodium gingivalis*, and *Shigella* are also best treated by *Lactobacillus*; therefore changing formations is another significant possible mechanism.^[13] *Fusobacterium nucleatum* aggregates with *Weissella ciberia*, unlike *Treponema denticola* and *Porphyromonas gingivalis*.^[14] *Lactobacillus rhamnosus* and *Fusobacterium nucleatum* form a co-aggregation.

The hydrogen peroxide produced by *Shewanella* governor isolates was enough to halt *Fusobacterium nucleatum* from growing.^[14] Another potential mechanism is apoptosis. Probiotics induce apoptosis in tumor cells by forming end products.^[15] Mucosal cell apoptosis has also been observed to be inhibited by it.^[16]

Probiotics also were known to benefit the epithelial membrane by inhibiting mucous membrane apoptosis and preserving tight junction protein expression.^[17] Another mechanism of action discovered in the fluids effusion GCF of *Lactobacillus reutri* chewing gum users is a reduction in pro-inflammatory cytokines.^[13]

Lactobacillus salivaris and *Lactobacillus gasseri* suppress periopathogenic microorganisms very effectively.^[18] *Lactobacillus reutri* secretes bacteriocins, such as reutrin and reutricyclin, which impede pathogen growth and have a strong affinity for host tissue. They also have an anti-inflammatory impact by inhibiting proinflammatory mediators.^[19] *Weissella ceberia*, on the other hand, produces catalase.^[14]

Prebiotic

The human gastrointestinal tract's bacterial population is a massively complicated ecology. The vast majority of such microbes are in good condition. while some are toxic (for example,

Salmonella species, Helicobacter pylori, and Clostridium perfringens). Some dietary ingredients, known as 'prebiotics,' can promote the growth of helpful bacteria over dangerous bacteria.

Prebiotics are food components that are not digestible. Glucose, fructo-oligosaccharides (FOS), galactooligosaccharide, and furosemide are among them. ^[20] Humans are unable to digest or absorb FOS, which are naturally occurring carbohydrates. In their presence, *Bifidobacteria* proliferate. As a result of this effect, patients who were taking bifidobacteria were advised to also take FOS. ^[21]

Prebiotics : Mechanism of action

- *Bifidobacteria* and *lactobacilli*, for example, have been shown to promote the proliferation of endemic gut microbes, particularly *bifidobacteria* and *lactobacilli*. ^[22]
- Prebiotics are assumed to work in an indirect manner, supporting the formation of microbial impacts of the activity of such organisms, which are beneficial members of the resident microflora. ^[23]
- In addition to their impacts on resident bacterial populations, several prebiotics have been demonstrated to have direct effects on the host ^[24]. Enhanced IL-10 and interferon expression, increased IgA production, regulated immune reactions stabilization of the gut mucosal barrier and resistance to pathogens. ^[25]

Probiotics and Prebiotics in Current Use

Despite some inconsistent experimental findings and data from clinical studies, there is emerging evidence for their usefulness in preventing acute diarrhoea, gastroenteritis, irritable bowel syndrome, and pouchitis ^[26]

Additional research into the use of probiotics and prebiotics in the treatment of disorders other than the digestive tract, such as bladder infection, microbial infections, joint problems, atopic dermatitis, tonsillitis, and pyelonephritis, is also warranted. ^[27, 28]

Probiotics and Oral Health: What Are the Consequences?

Bacillus species have been the most common beneficial microorganisms found in the body, therefore it may have a role in the oral microbiota seceophysiology.^[29]

The development of innovative techniques to stop the pathogenesis of oral infections can help to minimize tissue loss and chronic inflammation associated with mouth infections. There is a theory that these "good" microbes might live in a biofilm and protect oral tissue against disease.^[30]

Periodontal health and probiotics

Fewer experimental investigations on probiotic use in periodontal disorders exist, mainly due to a lack of understanding of the disease's precise etiology and the settings that promote wellness.

The most common periodontal illnesses with a microbiological etiology are gingivitis and periodontitis. Periodontitis is a disorder in which the supporting components of the teeth degenerate over time. It is produced by inflammatory responses to periodontitis in a vulnerable host. Microbes can also injure tissue by producing toxin like poisons and enzymes. *Triphala* tooth wipes are effective against the oral *Streptococcus mutans* compared with placebo tooth wipes, while both the tooth wipes are equally effective in reducing dental plaque.^[31] According to the ecological plaque theory, an increase in GCF flow and a rise in pH favour Punnet, proteolytic microbes, resulting in an ecological shift.^[32] The decrease of bacterial load is the main focus of periodontal disease prevention and treatment. Surgical and nonsurgical treatment options are common, with a focus on mechanical debridement and antibiotics. As a consequence of rapid of resistant and the regular decolonization of cured sites with harmful bacteria, microorganisms have become popular in periodontics. Probiotics are founded on the principle of microbial inhibition, which states that one organism can stop or limit the growth and colonization of another microorganism from the same or a different environment.^[33]

Probiotics reduce the pH of the mouth, preventing plaque bacteria from forming gum disease and calculus, which causes periodontitis. They are a fantastic maintenance product since they produce radicals. Antioxidants limit plaque formation by neutralizing the free electrons required for mineral synthesis. Probiotic treatment may be an alternative; however frequent human periodontal vaccine trials and safety concerns must be addressed.

The Effect of Probiotic Mouthrinse on Plaque and Gingival Inflammation

Individuals' oral hygiene practices must be adequate to maintain plaque levels that are consistent with gingival health in order for periodontal treatment to be successful in the long run.^[34] Supragingival plaque gives way to subgingival plaque is also removed during periodontal disease treatment.

As a result, Plaque of caustic treatment has become more popular as a supplement to mechanical plaque control. Chemical anti-plaque treatments are increasingly recognized as having potential for blocking or lowering plaque production and hence gingival inflammation.^[35]

Chlorhexidine has been used for more than two decades and is the most tested and effective antibacterial agent available today. Chlorhexidine has been linked to a number of local adverse effects when used as a mouthwash. A two-minute pre-surgical rinse with chlorhexidine gluconate 0.12 percent mouthwash was recommended.^[36] Brown staining of the tooth and tongue, mucous membrane erosion, and a change in taste are only a few of the unpleasant effects.

Probiotic mouthrinse contains *Aspergillus niger*, *bacteriocins* of short rope polypeptides synthesized by *Bacillus licheniformis* cultured in a fermentor. Before being added to the mouthrinse, these peptides are typically extracted from all other components, including *lactobacilli* cells.

Anti - microbial substances generated by lactic acid bacteria include amino substances, superoxide anion, diacetyl, and inhibitory enzymes, to name a few (LAB).^[37] Bacteriocins are bacteriocidal protein moieties with a physiologically active protein moiety. Bacteriocins are peptides or proteins synthesized by ribosome that work against organisms that are closely related.

Resistance to antibacterial agents has become an important concern worldwide today^[38]. Nisin is an antibacterial chemical that may be used to destroy Punnet bacteria in a variety of settings. *Actinomyces*, *Bacillus*, *Candida*, *Mycobacterium*, *Enterobacterium*, *Gardnerella*, *Lactococcus*, *Lister*, *Micrococcus*, *Mycobacterium*, *Propionibacterium*, *Streptococcus*, and *Staphylococcus* have all been found to be susceptible to Nisin.^[39]

Nisin, the main ingredient in Probiotic mouthrinse, was previously demonstrated to have bactericidal effects against a wide spectrum of Punnet bacteria in a previous study.

The anti-plaque action of the probiotic mouthrinse may be achieved by limiting the proliferation and survival of these microorganisms on the tooth surface, as well as altering plaque biochemistry to reduce cytotoxic product formation and shifting plaque ecology to a less pathogenic flora. When used as an antiplaque medicine, Nisin's aqueous delivery vehicle has high water solubility, allowing for easier release into the oral cavity.

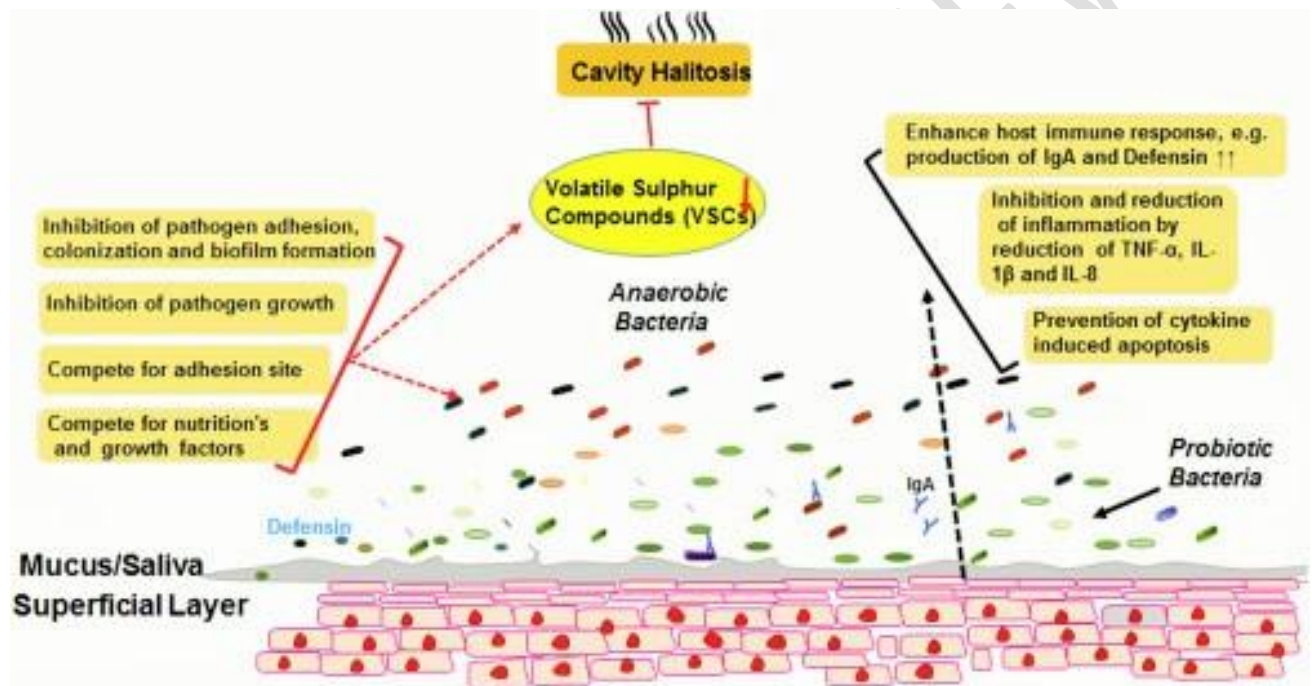
Replacement therapy:

Biotechnological techniques to replacement therapy' have also been researched. Gene inactivation is utilized to remove toxic metabolites, as well as the inclusion of genes that code for antimicrobial substances like *bacteriocins*. *Streptococuss mutans* has been proposed as a substitute therapy for dental caries management. In a strain of *Streptococuss mutans*, lactate dehydrogenase deficiency was created by removing virtually every one of the gene code generating this enzyme. After introducing a hydroxylase protein from Yeast dynamic muscle to correct the metabolic imbalance, the clone produced no detectable lactic acid. In gnotobiotic and conventional transgenic mice with tooth decay, this strain was significantly less cariogenic than the parent strain. This clone (Oragenics Inc.'s SMaRT Replacement Therapy product) has been found to protect humans from dental caries for the rest of their lives, albeit it may need to be administered on a regular basis.

The use of probiotics for halitosis treatment:

Volatile sulphur compounds produce halitosis. VSC is produced by bacteria such as *Mycobacterium nucleatum*, *Porphyromonas gingivalis*, *Shigella*, and *Streptococcus pneumoniae*. A probiotic strain (*Weissella cibaria*) has the ability to inhibit VSC development in both in vitro and in vivo circumstances. It has a lot of potential as a new probiotic for periodontal usage. *Mycobacterium nucleatum* and Secondary biofilm colonization is caused by aggregation with other periopathogens, which contributes significantly to the establishment of VSC in the oral cavity.

H₂O₂ has been connected to the preservation of a healthy ecological system as well as illness prevention. H₂O₂ has been demonstrated to a considerable reduction sulphur gas in situ concentrations. *Lactobacillus acidophilus* and *Lactobacillus casei* both create a strong acid that inhibits the multiplication of anaerobic bacteria in culture.^[40] The ecological pH of the *Weissella cibaria* isolates was greater than expected in the presence of *Lactobacilli*, indicating that this species could be useful as a probiotic. *Streptococcus salivaris* produces bacteriocins that inhibit microorganisms that produce VSC. *Streptococcus salivaris* chewable tablets and gel were found to lower VSC in halitosis patients in a recent study.



Probiotic benefit in periodontal disease has been proven in clinical trials:

Just some few clinical research has been assessed probiotic species' potency in this context, and there are currently no investigations on probiotics with periodontal disease.

Lactobacillus reuteri and *Lactobacillus brevis* are two *Lactobacillus* genera that have been shown to reduce gum and film development, including being periodontitis markers.^[41]

Following a two-week probiotic regimen, species intake gums and soft tissue bleeding were found to be prevalent and were shown to be greatly reduced. The successful colonization of the probiotic bacteria within the mouth cavity may be responsible for the reported improvement in clinical state.

Lactoferrin values in gingival crevicular fluid were similar to those in a healthy condition after consumption of *lactobacilli*, suggesting that a microbial treatment could be an useful strategy for treating inflammation and periodontal issues.^[42]

More research into the underlying pathways by which probiotics effect gum illness has showed that a single strain can successfully lower inflammatory compounds including prostaglandin E2 and interferon, as well as reduce matrix metalloproteinase activities in saliva.^[43]

According to a Russian study, introducing microbial inoculums to a collagen fibers gingival covering reduced the amount of hostile bacteria species in periodontal pockets with approximately to 10-12 months, lengthening remission durations.^[44]

Probiotic use in periodontics is restricted

In the management and prophylaxis of oral disorders, probiotics should be taken with caution.

Lactobacilli and other bacteria are the most common probiotic bacteria, and acid generation is regarded to be a key component of their pathogenic resistance.

Streptococcus species. On the other hand, are critical in the development of caries and acid generation by acidogenic plaque populations. *Lactobacillus salivarius*, a probiotic strain, was discovered to be cariogenic in a rat model.^[45]

As a result, one of the most significant roadblocks may be that the probiotic activities and microorganisms that protect against oral disease may simultaneously raise the chance of developing dental caries. As a result, utilizing a prebiotic method to enhance endogenous beneficial commensals may be more tempting.

Conclusion

The benefits of probiotics on periodontal health and treatment are unknown at this time, according to current studies. As a result, more research and randomized clinical trials are needed to find the optimum bioactive compounds and delivery systems for a variety of oral health issues, as well as prebiotic ability to sustain and increase the advantages supplied by the resident oral microbiota.

To attain good systemic health, it's critical to maintain robust periodontal health, and probiotics are a viable, effective, natural, and side effect-free option that needs to be researched further for periodontal use. Because probiotics are antibiotics' antidotes, there is no possibility of resistance

developing. They're also the host's own flora, which makes them the most adaptable. Although the evidence for halitosis is less strong, probiotics may have an essential role in the treatment of tooth decay and periodontal disease.

A better scientific understanding of such microscopic forms of life and their impact on people in periodontal disease care should expand the range of possible uses even more.

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UNDER PEER REVIEW