In 1994, the World Health Organization

deemed probiotics to be the next-most important immune defense systemwhen commonly prescribed antibiotics are rendered useless by antibiotic resistance.

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in acidogenic and acid-tolerating species such as mutans streptococci and lactobacilli, although other bacteria with similar properties can also be found and bifidobacteria, non-mutans streptococci, Actinomyces spp., Propionibacterium spp., Veillonella spp. and Atopobium spp. have also been implicated as significant in the etiology of this disease. [**23**]

In periodontal diseases, there is an increase in plaque mass and a shift towards obligatory anaerobic and proteolytic bacteria, many of which are Gram negative and currently unculturable. The host damage that occurs during periodontal disease arises through the combined activities of subgingival biofilms and the host responses to these diverse bacterial populations. [**16**]

Candida albicans and other Candida species are present in low levels in oral microbial communities and can cause oral candidiasis and denture- associated stomatitis. [**24**] Halitosis is most often the result of production of malodorous metabolic endproducts (especially volatile sulphur compounds) by oral bacteria, in particular Gram negative anaerobes. [**25**]

Probiotics of interest

The most common probiotic strains belong to the genera *Lactobacillus* and *Bifidobacterium*. *Lactobacillus* species from which probiotic strains have been isolated include *L. acidophilus, L. johnsonii, L. casei, L. rhamnosus, L. gasseri, and L. reuteri.* Similarly, the *bifidobacterium strains include B. bifidum, B. longum, and B. infantis. Lactobacilli* can produce different antimicrobial components including organic acids, hydrogen peroxide, low-molecular weight antimicrobial substances, bacteriocins and adhesion inhibitors and thus have gained prominence as probiotics. *Streptococcus Oralis* and *Streptococcus Uberis* have been shown to inhibit the growth of pathogens both in the laboratory and animal models. [**26**]

Probiotics in prevention of periodontal diseases

Periodontal disease is classified into 2 types: gingivitis and periodontitis. Gingivitis is characterized by inflammation limited to the gingiva, whereas periodontitis is a progressive, destructive disease that affects all supporting tissues of the teeth, including the alveolar bone. [**27**] The main pathogenic agents associated with periodontitis are *P . gingivalis, Treponema denticola, T annerella forsythus* and *Aggregatibacter actinomycetemcomitans*. [**27**] These bacteria have a variety of virulent characteristics allowing them to colonize the subgingival sites, escape the host"s defense system and cause tissue damage. [**27**] The persistence of the host"s immune response also constitutes a determining factor in progression of the disease. [**27**]

There are fewer experimental studies exploring probiotic use in periodontal diseases, partly reflecting a poorer understanding of the precise etiology of the disease and of the conditions that promote health.

Grudianov et al [**28**] studied the effect of probiotic tablets on gingivitis and different grades of periodontitis and observed that probiotic treatment resulted in better microbiota normalization than control group. In one recent study, the prevalence of lactobacilli, particularly *L. gasseri* and *L. fermentum*, in the oral cavity was greater among healthy participants than among patients with chronic periodontitis. [**29**] Various studies have reported the capacity of lactobacilli to inhibit the growth of periodontopathogens, including *P .*

gingivalis, *Prevotella intermedia* and *actinomycetemcomitans*. [**29**] Together, these observations suggest that lactobacilli residing in the oral cavity could play a role in the oral ecological balance.

In a study by Krasse et al, [**30**] patients with moderate to severe gingivitis who were given either one of two L. reuteri formulations had reduced plaque and gingivitis scores compared to a placebo group. Although the exact mechanisms of action of *L. reuteri* remain to be elucidated, previous studies have suggested at least 3 plausible possibilities: first, *L. reuteri* is known for its secretion of 2 bacteriocins, reuterin and reutericyclin, that inhibit the growth of a wide variety of pathogens; [**31**] second, *L. reuteri* has a strong capacity to adhere to host tissues, thereby competing with pathogenic bacteria; [**32**] and third, the recognized anti-inflammatory effects of *L. reuteri* on the intestinal mucosa, leading to inhibition of secretion of proinflammatory cytokines, could be the foundation for a direct or indirect beneficial effect of this bacterium on people with periodontal disease. Vivekanda et al [**33**] also confirmed the plaque inhibitory, anti- inflammatory and antimicrobial effects of *L. reuteri* Prodentis.

Riccia and colleagues [**34**] recently studied the anti-inflammatory effects of *Lactobacillus brevis* in a group of patients with chronic periodontitis. A significant reduction in salivary levels of prostaglandin E2 (PGE2) and matrix metalloproteinases (MMPs) was observed. The authors suggested that the beneficial anti- inflammatory effects of *L. brevis* could be attributed to its capacity to prevent the production of nitric oxide and, consequently, the release of PGE2 and the activation of MMPs induced by the nitric oxide. [**34**] However, *L. brevis* may also be antagonistic, leading to a reduction in the quantity of plaque and therefore an improvement in the gingival index.

Shimauchi et al [**35**] reported that the regular (three times daily for eight weeks) intake of tablets containing Lactobacillus salivarius resulted in benefits in terms of pocket probing depth and plaque index in individuals at high risk of periodontal disease (smokers) compared to a placebo control group. [**35**] Other studies have aimed to identify organisms that have the potential for probiotic action that may protect against periodontal diseases. Some oral strains of lactobacilli and streptococci [**36**] and bifidobacteria [**37**] have been reported to have in vitro inhibitory activity against periodontal pathogens, while others are more active

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against mutans streptococci. [**36**] Koll-Klais et al [**38**] observed that *Lactobacillus gasseri* strains isolated from periodontally healthy subjects were more efficient at inhibiting the growth of *A. actinomycetemcomitans* than strains from periodontally diseased subjects. *L. gasseri* also inhibited the growth of *P. gingivalis* and *P. intermedia*; this correlated with an inverse relationship between carriage of homofermentative lactobacilli and subgingival colonization by *A. actinomycetemcomitans, P . gingivalis* and *P. intermedia.* Ishikawa et al. [**39**] observed in vitro inhibition of *P . gingivalis*, P . intermedia and *Prevotella nigrescens* by *L. salivarius*. Daily ingestion of *L. salivarius*-containing tablets resulted in reduced salivary counts of these black pigmented anaerobes. The mechanisms of inhibition of periodontal pathogens have not been fully clarified. The inhibitory activity displayed by homofermentative lactobacilli against periodontal pathogens was principally related to their production of acid, not to H_2O_2 or bacteriocin production. [**38**] Hojo et al [**37**] suggested that bifidobacteria inhibit some black pigmented anaerobes by competing for an essential growth factor, vitamin K, although there was no significant relationship between higher bifidobacterial counts and lower black-pigmented anaerobe counts. Recently, a bacteriocin purified from *Lactobacillus casei* killed *P. gingivalis* but its use was proposed as a novel chemotherapeutic agent rather than as strain development for probiotic applications. [**40**] During the fermentation process in milk, *Lactobacillus helveticus* produces short peptides that act on osteoblasts and increase their activity in bone formation. [**41**] These bioactive peptides could thereby contribute to reducing the bone resorption associated with periodontitis.

Recently Shimazaki and colleagues [**42**] used epidemiological data to assess the relationship between periodontal health and the consumption of dairy products such as cheese, milk and yoghurt. The authors found that individuals, particularly nonsmokers, who regularly consumed yoghurt or beverages containing lactic acid exhibited lower probing depths and less loss of clinical attachment than individuals who consumed few of these dairy products. A similar effect was not observed with milk or cheese. By controlling the growth of the pathogens responsible for periodontitis, the lactic acid bacteria present in yoghurt would be in part responsible for the beneficial effects observed.

Sunstar (Etoy, Switzerland) recently began marketing the first probiotic specifically formulated to fight periodontal disease. Gum Perio Balance contains a patented combination of 2 strains of *L. reuteri* specially selected for their synergetic properties in fighting cariogenic bacteria and periodontopathogens. Each dose of lozenge contains at least 2×10^8 living cells of *L. reuteri* Prodentis. Users are advised to use a lozenge every day, either after a meal or in the evening after brushing their teeth, to allow the probiotics to spread throughout the oral cavity and attach to the various dental surfaces.

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Guided periodontal pocket recolonization (Bacterial replacement therapy) in Periodontics

“Replacement therapy” is also known as “probiotic therapy”. The concept of bacterial replacement therapy in periodontics was first introduced by Teughels et al in 2007. They reported that the subgingival application of a bacterial mixture including *Streptococcus sanguis, S. salivarius,* and *Streptococcus mitis* after scaling and root planing significantly suppressed the re- colonization of *Porphyromonas gulae* (canine *P . gingivalis)* and *P. intermedia* in a beagle dog model. [**43**] Nackaerts et al [**44**] observed that the subgingival application of beneficial oral bacteria (i.e. *Streptococcus sanguinis, Streptococcus salivarius and S. mitis*) delays recolonization by periodontal pathogens, reduce inflammation, and improve bone density and bone levels in a beagle dog model. This guided pocket recolonization approach may provide a valuable addition or alternative to the armamentarium of treatment options for periodontitis.

Probiotics in prevention of halitosis

Halitosis has many causes (including consumption of particular foods, metabolic disorders, respiratory tract infections), but in most cases it is associated with an imbalance of the commensal microflora of the oral cavity. [**45**] More specifically, halitosis results from the action of anaerobic bacteria that degrade salivary and food proteins to generate amino acids, which are in turn transformed into volatile sulphur compounds, including hydrogen sulphide and methyl mercaptan and dimethyl sulphide. [**45**]

There have also been clinical and laboratory studies of probiotics in their potential for preventing halitosis. Peroxide production by strains of *Weissella cibaria* (commonly present in fermented foods) isolated from the mouths of healthy children, inhibited production of volatile sulphur