compounds that contribute to oral malodour by *F. nucleatum* in vitro and in exhalations following mouth-rinsing by adult volunteers with a suspension of *W. cibaria*. [**46**] The success of *W. cibaria* in reducing malodour may have also been because it coaggregated efficiently with *F. nucleatum* [**46**] and therefore competed with other late/secondary colonizers for adhesion sites. Thus, *W. cibaria* may have probiotic activities with potential for prevention of periodontal disease. Volatile sulphur compounds, such as H_2S and mercaptoethanol, are produced by a range of periodontal anaerobes. [**47**] The inhibition of these micro-organisms by peroxide from *W. cibaria* may help reduce subgingival plaque pathogenicity while its competition for coaggregation sites may reduce the reservoir of micro- organisms available for transmission into plaque.

One recent study [**48**] showed that certain bacterial species, including *Atopobium parvulum*, *Eubacterium sulci* and *Solobacterium moorei,* predominate on the dorsal surface of the tongue among people with halitosis. Conversely, another species,

Streptococcus salivarius, was detected most frequently among people without halitosis and is therefore considered a commensal probiotic of the oral cavity. *S. salivarius* is known to produce bacteriocins, which could contribute to reducing the number of bacteria that produce volatile sulphur compounds. [**49**]

S. salivarius K12 produces salivaricin, a lantibiotic with inhibitory activity towards most Streptococcus pyogenes. [**50**] This strain has been commercially promoted as a probiotic that is reported to be protective against throat infections and oral malodour. [**50**] The importance of strain selection for probiotic use is illustrated by the fact that some *S. salivarius* strains differ from K12 in some important activities; one strain increased production of malodorous products by facilitating *P. gingivalis* metabolism of salivary mucins [**51**] and another up-regulated IL-8 secretion by oral epithelial cells [**52**] in contrast to the down-regulation observed in response to K12.

Residence time of probiotics in oral cavity

Residence time of probiotics in oral cavity after treat- ment withdrawal was studied by Çaglar et al. [**53**] A reduced *S. mutans* level was shown after a two-week use of a *L. reuteri*- enriched yoghurt; effects were observed during use and for a few days after discontinuation. A loss of *L. reuteri* colonization was observed by Wolf et al. [**54**] two months after having discontinued probiotic use. *L. rhamnosus* GG administration and oral cavity colonization was studied by Yli-Knuuttila et al [**55**]; the authors concluded that permanent colonization in oral cavity was unlikely (although possible in some cases) and suggested the probiotic to be used on a regular basis. Binding strength of 17 Lactobacillus strains and 7 bifidobacteria strains to saliva and

oral mucous membrane was variable in different strains, according to a study by Haukioja et al. [**56**] Such a strength variation caused an increased residence time of probiotic in oral cavity. Latency time of probiotic *S. salivarius* K12, 4 tablets/day for 3 days, was assessed in several oral cavity areas in a 35-day follow-up, by Horz et al. [**57**] Probiotic could be found on oral mucous membrane, tongue and in stimulated saliva for more than 3 weeks, with a gradually reduced *S. salivarius* K12 level being detected beginning 8 days after treatment withdrawal.

Potential risks of probiotic therapy

Different strains of a species may not all possess characteristics that enable them to be probiotics and rigorous strain selection for the disease concerned is complex but essential. [**58**] Some probiotic strains have been in use for many years and have excellent safety records. [**59**] Most probiotic bacteria are weakly proteolytic and, for example, *Lactobacillus bulgaricus*, was shown to be incapable of degrading some host tissue components. [**60**] However, there have been some cases of bacteraemia and fungaemia associated with probiotic use, although these have been in subjects who are immunocompromised, [**61**] or who suffer from chronic disease [**59**] or short gut syndrome. [**62**] Other predisposing factors include prior prolonged

hospitalization and prior surgical intervention. [**61**] An individual who had been taking *L. rhamnosus* in a probiotic preparation developed Lactobacillus endocarditis following dental treatment. [**63**] In Finland, however, there has not been an increase in bacteremia associated with probiotic lactobacilli following the increase in the use of these products since 1990. [**64**] The species that most commonly exhibit probiotic benefits are lactobacilli and other lactic acid bacteria, and the production of acid is often thought to be an important component of their protection against pathogenic colonization. However, *Lactobacillus spp.* and acid production by acidogenic plaque populations play a significant part in the development of caries, and a probiotic strain of *L. salivarius* has been shown to be cariogenic in a rat model. [**65**] A number of probiotic lactobacilli and bifidobacteria produce acid from fermentation of dietary sugars in vitro. [**66**] There are conflicting data on the salivary lactobacilli levels following probiotic usage. Some studies have reported no effects, [**67**] others have found trends for an increase, [**68**] while others have detected statistically significant rises in counts of salivary lactobacilli. [**69**] There is a converse risk in that the control or prevention of caries may indirectly affect periodontal pathogens. It has been known for many years that streptococci, through production of hydrogen peroxide, inhibit the growth of putative periodontal pathogens, leading to early proposals that interactions between groups of micro-organisms within plaque can influence the development of disease or actively contribute to the maintenance of health, [**70**] and lactobacilli and bifidobacteria also inhibit the growth of a range of periodontal pathogens. [**70**] It is clear that careful selection of the strain to be ingested for a particular disease is essential and the mode and timing of administration can be crucial, as well as the age and health of the individual taking the probiotic. There is a sufficient knowledge base for

major and minor risk factors to have been proposed for administration of probiotics to prevent intestinal conditions, [**59**] but this knowledge base for oral applications is clearly more distant. One of the biggest problems to overcome may be that the probiotic activities and micro-organisms that protect against oral disease could increase the risk of development of dental caries. Therefore, a prebiotic-type approach to enhance endogenous beneficial commensals may be more attractive. It will also be a challenge to ensure that modes of delivery are developed that provide sufficient retention and exposure times in the mouth that will allow probiotics to colonies plaque or prebiotics to enter into plaque or mucosal biofilms and influence microbial metabolism within them.

Conclusion

Probiotics are emerging as a fascinating field in oral medicine. This concept prompts a new horizon on the relationship between diet and oral health. The use of probiotics for use in oral care applications is gaining momentum. There is increasing evidence that the use of existing probiotic strains can deliver oral health benefits. Further work will be needed to fully optimize and quantify the extent of this benefit. In parallel, the potential of prebiotics to maintain and enhance the benefits provided by the resident oral microbiota will be investigated. However, whether considering probiotics or prebiotics, it will be essential to develop an understanding of the broad ecological changes induced in the mouth by their ingestion and the long-term consequences of their use on oral health and disease. Further studies to understand the

ability of probiotic bacteria to survive, grow, and have a therapeutic effect when used for treatment or when added to foods, to fix the doses and schedules of administration of probiotics. Hence, systematic studies and randomized controlled trials are needed to find out the best probiotic strains and means of their administration in different oral health conditions. Finally, possibilities to genetically modify or engineer

potential probiotic strains may offer all new visions. Better scientific understanding and extended research of these tiny forms of life and their effect on humans in the treatment of periodontal diseases might further broaden the field of potential applications.

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