Dental Probiotics in Oral Health: A Short Communication

INTRODUCTION
In recent years, there have been significant changes with respect to the effectiveness of, and attitudes towards, conventional antimicrobial therapy to combat disease. With the threat of widespread antibiotic resistance rendering many antibiotics useless against important diseases, there is an increased necessity not only to minimise antibiotic use and develop novel nonantibiotic based treatments, but also to raise the profile of disease prevention. There is a public appetite for new therapies that are perceived to be natural through, for example, manipulation of the resident microbiota by the ingestion of probiotic bacteria or prebiotics. These changing attitudes are also relevant to the prevention of dental diseases and there is an increased interest in the use of strategies that do not involve conventional antimicrobial agents for oral care. There has been a paradigm shift away from treating dental diseases by targeting specific oral pathogens towards an ecological and microbial community-based approach to understand conditions, such as caries and periodontal diseases. These approaches recognize the importance of maintaining the natural balance of the resident oral microbiota and the need to carefully modulate host immune responses to the microflora at a site.

Probiotics; There is a long tradition, particularly in parts of Europe and Asia, of ingesting microbes or food products that affect the intestinal microbiota in ways that are believed to provide beneficial health effects, i.e. intake of probiotics and prebiotics. Probiotics are defined as viable microorganisms that confer health benefit when administered in sufficient doses.

Prebiotics; The ability of certain oligosaccharides to enhance the growth of resident commensal gut bacteria, particularly bifidobacteria and lactobacilli, is well documented. Thus, the major mechanism of action of prebiotics is assumed to be indirect, i.e. facilitating the proliferation of beneficial components of the resident microflora, with probiotic effects resulting from the actions of these bacteria as described above. Cellobiose has the additional property of down-regulating virulence factors of Listeria monocytogenes.

Mechanism of action; Prevention of adhesion of pathogens to host tissues; Stimulation and modulation of the mucosal immune system, e.g. by reducing production of pro-inflammatory cytokines through actions on NFKB pathways, increasing production of anti-inflammatory cytokines such as IL-10 and host defence peptides such as b-defensin 2, enhancing IgA defences and influencing dendritic cell maturation; Modulation of cell proliferation and apoptosis through cell responses to, for example, microbially produced short chain fatty acids; Improvement of intestinal barrier integrity and upregulation of mucin production; Killing or inhibition of growth of pathogens through production of bacteriocins or other products, such as acid or peroxide, which are antagonistic towards pathogenic bacteria.

The oral microbiota in health and disease; To be able to develop probiotic or prebiotic interventions for applications in oral health care and to understand their mechanisms of action and potential risks, it is essential to have a clear understanding of the oral microbiota and their functions in oral health and disease. This is not always easy, given the complexity of the oral microbiota; more than 700 species have been detected in the human mouth and the resident microbiota of one individual may comprise 30 to 100 species. A wide variety of sites in the mouth are heavily colonised. Supragingival and subgingival plaque form through sequential and specific adhesive interactions that result in a complex climax community. The tongue is heavily colonised and microorganisms on the dorsum of the tongue are reservoirs for supragingival and subgingival plaque and salivary microbial populations. Many oral bacteria, especially streptococci, also survive within buccal epithelial cells.

Functions of the resident microbiota; The main focus of research has been defining the microorganisms and their traits that are responsible for disease, but there is an increased awareness that the resident microbiota does not play merely a passive role, but actively contributes to the maintenance of health. The large, diverse resident microbial communities that
colonise mucosal sites co-exist with a host, with harmful effects only if the host becomes immunocompromised, if the resident microbial populations are suppressed or if micro-organisms reach sites to which they do not normally have access (e.g. through trauma). Studies, mostly of gastrointestinal bacteria, have shown that resident microbial populations contribute to host protection through blocking of colonisation by pathogens, development of cell structure and function, development of the immune system and modulation of inflammatory responses. Evidence is accumulating to support a similar role for oral commensal bacteria in the development of the immune system, the maintenance of healthy oral tissue by influencing expression of mediators such intracellular adhesion molecule 1 (ICAM-1), E-selectin and IL-8, modulating immune responses and enhancing cellular homeostatic mechanisms.

The potential for probiotics in prevention and control of oral diseases: Probiotics in prevention of caries The oral health applications of either probiotics or 'replacement therapy' with Streptococcus mutans strains of attenuated virulence and increased competitiveness were first suggested for prevention of dental caries more than 20 years ago. Despite this, and the fact that some products have reached the market, there remains a paucity of clinical evidence to support the effectiveness of probiotics to prevent or treat caries. Many early studies concentrated on utilising bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances (BLIS) that specifically prevented the growth of cariogenic bacteria. Another approach has been to identify food grade and probiotic bacteria that may have potential in caries prevention.

Probiotics in prevention of periodontal diseases
There are fewer experimental studies exploring probiotic use in periodontal diseases, partly reflecting a poorer understanding of the precise aetiology of the disease and of the conditions that promote health. However, 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. Similarly, 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. 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 and bifidobacteria have been reported to have in vitro inhibitory activity against periodontal pathogens, while others are more active against mutans streptococci. The subgingival application of beneficial oral bacteria (e.g. Streptococcus sanguinis, Streptococcus salivarius and S. mitis) (replacement therapy) has been shown to delay recolonisation by periodontal pathogens, reduce inflammation, and improve bone density and bone levels in a beagle dog model. Lactobacillus gasseri strains isolated from periodontally healthy subjects were more efficient at inhibiting the growth of A. actinomycetemcomitans than strains from periodontally diseased subjects, and also inhibited the growth of P. gingivalis and P. intermedia; this correlated with an inverse relationship between carriage of homofermentative lactobacilli and subgingival colonisation by A. actinomycetemcomitans, P. gingivalis and P. intermedia. Ishikawa et al. 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 H2O2 or bacteriocin production. 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.

Probiotics in prevention of caries: The oral health applications of either probiotics or 'replacement therapy' with Streptococcus mutans strains of attenuated virulence and increased competitiveness were first suggested for prevention of dental caries more than 20 years ago. Despite this, and the fact that some products have reached the market, there remains a paucity of clinical evidence to support the effectiveness of probiotics to prevent or treat caries. Many early studies concentrated on utilising bacteria that expressed bacteriocins or bacteriocin-like inhibitory substances (BLIS) that specifically prevented the growth of cariogenic bacteria. Another approach has been to identify food grade and probiotic bacteria that may have potential in caries prevention.
Are there potential risks? It is worth sounding a note of caution concerning the use of probiotics for the purpose of preventing oral disease. 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. Some probiotic strains have been in use for many years and have excellent safety records. Most probiotic bacteria are weakly proteolytic and, for example, Lactobacillus bulgaricus, was shown to be incapable of degrading some host tissue components. However, there have been some cases of bacteraemia and fungaemia associated with probiotic use, although these have been in subjects who are immunocompromised, or who suffer from chronic disease or short gut syndrome.

In conclusion, 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 optimise 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.

REFERENCES