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## Probiotics in the dental practice: A review

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During the last decade an increased interest in alternative, preventive, and therapeutic strategies in dentistry has arisen. Probiotics are living microorganisms which, if administered in sufficient amounts, provide a health benefit to the host. Their precise mechanisms of action have not been identified, but they are able to interfere with the imbalance occurring in biofilm-associated infections. In other fields of medicine, mainly in gastroenterology, their usefulness is already proven. Concerning oral threats, probiotic bacteria may reduce the

numbers of pathogens associated with dental caries (mutans streptococci). Clinically, results are encouraging, but further research is needed to demonstrate apparent effects of certain probiotic strains on oral health as well as their desired concentration and vehicle. The use of probiotics in prevention and treatment of caries, periodontal diseases, halitosis, and other oral diseases needs to be further investigated. (*Quintessence Int* 2015;46:255–264; doi: 10.3290/j.qi.a33182)

**Key words:** caries, periodontal disease, probiotics, tooth decay

To date, it is clear that despite the myriad of available mechanical cleaning devices (electrical toothbrushes, interdental brushes, tongue scrapers, etc), not everyone is able to achieve an acceptable level of plaque control.<sup>1</sup> To improve oral health in the population, new approaches that have inflammatory modulating effects and preserve beneficial bacteria rather than reducing the amount of plaque or microorganisms are needed. Moreover, the attitude towards the use of antibiotics has changed. Antibiotic resistance is a significant problem nowadays, rendering many antibiotics useless against important and even possibly deadly diseases. Conventional antimicrobial therapy also has side-effects, such as antibiotic-associated diarrhea (AAD).<sup>2</sup>

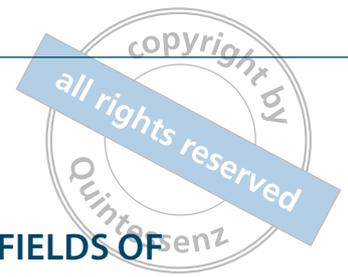
This has led to a growing interest in novel strategies to combat dental biofilm diseases, including probiotics.

There is a long history of recommending the use of microorganisms, particularly lactic acid bacteria, to promote health. The oldest traces date back to classical Roman literature when Plinius Secundus maior wrote that fermented milk products could be beneficial for the stomach. The Nobel prizewinning scientist Eli Metchnikoff is seen as one of the pioneers of modern probiotic research. In "The Prolongation of Life", written in the beginning of the 20th Century, he claimed that Bulgarians lived longer than other populations, due to the consumption of fermented milk.<sup>3</sup> However, it was not until 1965 that the word probiotic itself was introduced by Lilly and Stillwell as "substances produced by microorganisms that stimulate the growth of another".<sup>4</sup> This term, the antonym of antibiotics, is derived from the Greek language and literally means "for life". Since the 1960s, several definitions have been proposed.<sup>5-10</sup> The currently used definition is: "probiotics are living microorganisms which, when administered in adequate

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amounts, confer a health benefit for the host", and has been approved by the World Health Organization (WHO) and the United Nations Food and Agriculture Organization (FAO). In the 1990s, another related term was introduced: prebiotics. These are to date defined as non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth/or activity of one or a limited number of bacteria, that can improve host health. When a product contains both probiotic and prebiotics, the term synbiotic applies.

## BACKGROUND

At this moment at least 700 different bacterial species are known that can colonize the different surfaces of the oral cavity.<sup>11-13</sup> More than 400 of these are found in the periodontal pocket. The remaining can be detected at other oral sites, such as the tongue and mucosa. Every human being is colonized with about 100 to 200 of these 700 species. There is thus a substantial diversity between different people.<sup>11,14</sup> These oral microorganisms grow, interact together, and form a biofilm, called dental plaque.<sup>15</sup> Homeostatic mechanisms help maintain a stable microbial community associated with oral health. However, due to selective pressure of certain environmental factors, the balance of the resident microorganisms at a niche in the mouth may be disrupted and this can predispose to disease. In dental caries, there is an increase in acidogenic and acid-tolerating species such as mutans streptococci and lactobacilli, although other species may be involved like bifidobacteria, non-mutans streptococci, *Actinomyces* species, *Propionibacterium* species, *Veillonella* species, and *Atopobium* species.<sup>16,17</sup> In periodontal disease there is a shift towards obligate anaerobic and proteolytic, mainly Gram negative, bacteria. The tissue damage to both soft and hard periodontal tissues that occurs during periodontitis is the result of the combined effect of the subgingival biofilm and the host response to this bacterial population.<sup>17</sup> The rationale for probiotic use is to interfere with the microbial imbalance in caries and periodontal diseases by adding beneficial species.

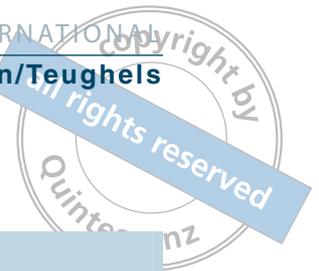
## PROBIOTICS IN OTHER FIELDS OF MEDICINE

Traditional applications of probiotics are in gastroenterology. However, a considerable number of studies are available that describe the use of probiotics in various fields of medicine. There is strong evidence that probiotics, in particular *Saccharomyces boulardii*, have a positive effect on the prevention of AAD.<sup>18</sup> AAD is a condition of diarrhea that is associated with antibiotic usage and has no other identifiable causes. The incidence of this condition is rather high and depends upon the population and the used antibiotic(s). The latter is a strong predictor. A high incidence of AAD (25% to 50%) has been described for ampicillin/amoxicillin, cephalosporin, and clindamycin.<sup>19</sup> AAD is thus a major problem. Seeing the high incidence of this problem associated with antibiotics frequently prescribed in the dental practice, it is also an important concern for the dental practitioner. Additionally, there is strong evidence for the application of probiotics in the treatment of infectious diarrhea in children and adults. The use of, for example, *Lactobacillus casei* strain GG shortens the duration and reduces the stool frequency.<sup>20,21</sup> Finally, strong evidence is available supporting the use of *S. boulardii* in the treatment of a *Helicobacter pylori* infection. This probiotic can decrease the side-effects and enhance the efficacy of the prescribed drug treatment.<sup>20</sup> Promising results are also shown in the treatment of *Clostridium difficile* associated diarrhea, irritable bowel disease, allergic reactions, and acute respiratory infections.<sup>22-25</sup> Potential future applications include the use of probiotics in the fields of rheumatoid arthritis, cancer, ethanol-induced liver diseases, and bacterial vaginosis.<sup>26-29</sup>

## MECHANISMS OF ACTION

The suggested effects of probiotics in the oral cavity can be broadly divided into three groups:

- modulation of the host inflammatory response
- direct effects against pathogenic bacteria
- indirect effects against pathogenic bacteria.



Study	No. of participants	Age range (years)	Strain	Vehicle, time	Authors' conclusion
Hasslöf et al <sup>45</sup>	179	9	<i>L paracasei</i> F19	Cereals, 9 mo	An early probiotic intervention did not affect frequency of dental caries at the age of 9 years.
Näse et al <sup>40</sup>	594	1–7	<i>L rhamnosus</i> GG	Milk, 7 mo	Probiotic intervention reduced the risk of caries significantly, particularly in the 3- to 4-year-olds.
Petersson et al <sup>42</sup>	52	58–84	<i>L rhamnosus</i> LB21	Milk, 15 mo	Daily intake of milk supplemented with fluoride and/or probiotic bacteria may reverse soft and leathery primary root caries lesions in older adults.
Stecksén-Blicks et al <sup>41</sup>	248	1–5	<i>L rhamnosus</i> LB21	Milk, 21 mo	The daily consumption of milk containing fluoride and probiotics reduced the caries activity compared to the control group (preventive fraction: 75%).
Stensson et al <sup>43</sup>	113	9	<i>L reuteri</i> ATCC 55730	Drop, 1 y	Less approximal caries and fewer sites with gingivitis in 9-year-olds when probiotics were administered during the last month of gestation and first year of life.
Taipale et al <sup>44</sup>	106	4	<i>Bifidobacterium animalis</i> subspecies <i>lactis</i> BB-12	Slow releasing pacifier, 2 y	In 4-year-olds, the administration of BB-12 in infancy does not influence the caries occurrence.

Probiotic bacteria or their products can modulate the innate immune system (humoral and cellular). Furthermore, probiotic bacteria can produce antimicrobial substances such as lactic acid, hydrogen peroxide, bacteriocins, and bacteriocin-like substances, which can directly inhibit periodontopathogens. Indirect effects against periodontopathogens can originate from competitive exclusion mechanisms by which bacteria compete for essential nutrients or chemicals and can passively occupy a niche previously occupied by a pathogen or actively restrict the adhesion capability of pathogens to surfaces.<sup>30</sup>

## PROBIOTICS AND ORAL HEALTH

The available studies on probiotics and oral health are heterogenous in terms of set-up, used probiotic strains, vehicles, and concentrations (Tables 1 to 3). The vast majority of the strains used belong to the genera *Lactobacillus* and *Bifidobacterium*. Possible vehicles for the application of probiotics are also very diverse, such as lozenges, gum, milk, cheese, yogurt, kefir, ice cream, straw, drops, powder, and mouthwash. In addition, the evaluation of these studies is hampered by their often short follow-up period. The latter results in true parameters of interest (especially in relation to caries) being

rarely described, but rather surrogate endpoints. This heterogeneity makes comparing articles difficult.

### The role of probiotics for controlling caries

The current view on the etiology of dental caries includes three factors: the presence of cariogenic bacteria, a susceptible host, and nutrients.<sup>31,32</sup> Time is important for the production of acids by endogenous, acidogenic bacteria (largely *Streptococcus mutans*, *Streptococcus sobrinus*, and *Lactobacillus* species)<sup>33-37</sup> and the subsequent demineralization of tooth structures, which ultimately leads to cavity formation.<sup>31,32</sup> When one (or more) of these factors is interfered with, the disease process may be stopped. Traditionally, preventive strategies encompass the use of topical fluorides, dietary monitoring, and mechanical and chemical plaque control.<sup>33</sup> More recently, “probiotic methods”, focusing on interfering with the cariogenic bacteria, have been introduced.

A recent systematic review showed that probiotics have demonstrated the capacity to reduce mutans streptococci counts in saliva and/or plaque in the short term.<sup>38</sup> This was confirmed by a recent meta-analysis.<sup>39</sup> For this meta-analysis, an electronic search was conducted in PubMed Medline, ISI Web of Science, and the Cochrane Library at the end of June 2013 in order to



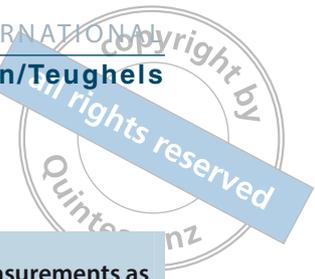
**Table 2** Clinical periodontitis studies included in this review with clinical periodontal parameters as outcome

Study	No. of participants	Age range (years)	Strain	Vehicle, time	Authors' conclusion
Hallström et al <sup>52</sup>	18	–	<i>L reuteri</i> ATC 55730 and <i>L reuteri</i> ATC PTA 5289	Tablets, 3 wk	During experimental gingivitis, daily intake of probiotic lozenges did not significantly affect the PI, GI, and BOP measurements.
Iniesta et al <sup>51</sup>	40	20–24	<i>L reuteri</i> DSM 17938 and <i>L reuteri</i> ATC PTA 5289	Tablets, 8 wk	No clinical impact of the probiotic use in gingivitis patients could be demonstrated concerning PI and GI.
Krasse et al <sup>48</sup>	59	–	<i>L reuteri</i> (2 formulas)	Chewing gums, 2 wk	In patients with moderate to severe gingivitis a significant reduction in PI for both probiotic groups was shown in contrast to no reduction in the placebo group. In one of the probiotic groups a significantly higher reduction of the GI compared with the placebo group was shown.
Riccia et al <sup>56</sup>	26	24–51	<i>L brevis</i>	Lozenges, 4 d	With the use of the probiotic lozenges all clinical parameters (GI, PI, BOP, calculus, and temperature sensitivity) decreased significantly in periodontitis patients.
Shah et al <sup>58</sup>	30	14–35	<i>L brevis</i>	Lozenges, 2 wk	The administration of a probiotic tended to lead to a significant decrease in PI, GI, PPD, and CAL at 2 mo in aggressive periodontitis patients.
Shimauchi et al <sup>57</sup>	66	–	<i>L salivarius</i> WB21	Tablets, 8 wk	GI, PI, and BOP scores were improved after intervention, but no significant differences between placebo and probiotic group could be shown.
Slawik et al <sup>60</sup>	28	20–33	<i>L casei</i> strain <i>Shirota</i>	Milk drink, 4 wk	Daily consumption of a milk drink reduces the effect of plaque-induced gingival inflammation associated with a higher plaque score due to the high carbohydrate content of the probiotic milk drink.
Staab et al <sup>61</sup>	50	–	<i>L casei</i> strain <i>Shirota</i>	Milk drink, 8 wk	Beneficial effect of the probiotic milk drink on gingival inflammation in experimental gingivitis patients.
Szkaradkiewicz et al <sup>54</sup>	38	31–46	<i>L reuteri</i> ATC PTA 5289	Tablets, 2 wk	Improved clinical parameters (GI, PPD, CAL) after probiotic use in chronic periodontitis patients. The measurements in the probiotic group were significantly lower than in the control group.
Teughels et al <sup>55</sup>	30	–	<i>L reuteri</i> DSM 17938 and <i>L reuteri</i> ATC PTA 5289	Tablets, 12 wk	Significantly more pocket depth reduction and attachment gain in the moderate and deep pockets in the probiotic group when compared with the control group.
Twetman et al <sup>49</sup>	38	–	<i>L reuteri</i> ATC 55730 and <i>L reuteri</i> ATC PTA 5289	Chewing gums, 2 wk	BOP improved statistically significantly after probiotic usage.
Vicario et al <sup>53</sup>	20	44–65	<i>L reuteri</i> ATC 55730 and <i>L reuteri</i> ATC PTA 5289	Tablets, 4 wk	Probiotic usage improved PI, BOP, and PPD in non-smoking patients with initial-to-moderate chronic periodontitis. In the control group no statistically significant changes could be shown.
Vivekananda et al <sup>50</sup>	30	35–50	<i>L reuteri</i> DSM 17938 and <i>L reuteri</i> ATC PTA 5289	Lozenges, 3 wk	In chronic periodontitis patients PI, GI, GBI, PPD, and CAL were significantly more reduced in the patients where scaling and root planing were supplemented with a probiotic compared with scaling and root planing alone.

–, not reported/only mean age reported; BOP, bleeding on probing; CAL, clinical attachment level; GBI, gingival bleeding index; GI, Gingival Index; PI, Plaque Index; PPD: probing pocket depth.

identify articles in which the outcomes were presented as the effect of probiotics on the incidence of caries or on the levels of mutans streptococci and/or *Lactobacillus* species. Human studies, written in English, with at least 15 participants, comparing a probiotic product

with a placebo/no probiotic were included. Where possible a meta-analysis was performed to obtain quantitative data. Nineteen studies could be included for the descriptive analysis and 12 for the meta-analysis. A disadvantage of this review was that there had to be a



**Table 3** Clinical halitosis studies included in this review with organoleptic evaluation or VSC measurements as outcome

Study	No. of participants	Age range (years)	Strain	Vehicle, time	Authors' conclusion
Burton et al <sup>74,75</sup>	23	18–69	<i>S salivarius</i> K12	Lozenge, 1 wk	Significantly lower VSC values for the probiotic group when compared to the placebo group.
Iwamoto et al <sup>76</sup>	20	30–66	<i>L salivarius</i> WB21	Tablet, 4 wk	Oral administration of probiotic lactobacilli primarily improved organoleptic and VSC scores in genuine halitosis patients.
Keller et al <sup>78</sup>	25	19–25	<i>L reuteri</i> DSM 17938 and <i>L reuteri</i> ATCC PTA 5289	Gum, 2 wk	Probiotic chewing gums may have some beneficial effect on oral malodor assessed by OLS in patients with morning bad breath. No significant differences on VSC measurements could be shown.
Sutula et al <sup>79</sup>	21	–	<i>L casei</i> strain <i>Shirota</i>	Milk drink, 4 wk	Morning breath VSC scores were not significantly affected throughout the trial.
Suzuki et al <sup>77</sup>	23	22–67	<i>L salivarius</i> WB21	Tablet, 2 wk	VSC were significantly reduced in the probiotic period compared with the placebo period.

–, not reported/ only mean age reported; OLS, organoleptic scoring; VSC: volatile sulfur compounds.

focus on surrogate endpoints, namely microbiologic measurements, since there were only two studies with caries as outcome that met the inclusion criteria at that time. A second drawback was that the available studies almost never used “state of the art” microbiologic techniques, but mainly utilized chairside tests. This affected the manner in which the meta-analysis was performed; all microbiologic counts had to be arranged in groups in analogy with the interpretation charts of these chairside tests to make a meta-analysis possible. It was shown that when the probiotic and control group are compared after treatment, significantly more patients in the probiotic group had low mutans streptococci (< 10<sup>5</sup> CFU/mL) counts and significantly fewer patients had high (> 10<sup>6</sup> CFU/mL) counts. Regarding the *Lactobacillus* counts, comparing the probiotic and control group at the end of the probiotic use, no significant differences could be observed, either in low (< 10<sup>4</sup> CFU/mL) or in high *Lactobacillus* (> 10<sup>6</sup> CFU/mL) counts.

These results are in accordance with the articles that describe caries incidence as a primary outcome measure directly after probiotic usage. In 2001, Näse et al<sup>40</sup> examined the effect of milk supplemented with *Lactobacillus rhamnosus* or control milk administered in day-care centers 5 days a week for 7 months in 1- to 6-year-olds. They showed that milk containing *L rhamnosus* GG reduced the risk of caries significantly. This effect

was particularly clear in the group with the 3- to 4-year-olds. Stecksén-Blicks and coworkers<sup>41</sup> examined the effect of *L rhamnosus* and fluoride-containing milk on caries. At the end of usage of this probiotic product, after 21 months, there was a statistically significant difference in caries activity between the probiotic and control group, with a preventive fraction of 75%. Unfortunately, with this study design it cannot be determined if the positive effect is attributable to fluoride, the probiotic, or the combination of both. In 2011, Petersson et al<sup>42</sup> investigated the effect of milk supplemented with *L rhamnosus* LB21 and/or fluoride on caries, in particular root surface caries in older patients. It was shown that daily consumption of milk supplemented with fluoride and/or probiotic bacteria may reverse primary root caries lesions in older adults. The combination of fluoride and a probiotic showed better results than when only one of those two products was administered.

However, the three available articles that describe caries-related parameters several years after probiotic usage show mixed results. StenSSon and coworkers<sup>43</sup> investigated the effect of daily oral supplementation with *Lactobacillus reuteri* ATCC 55730 during the last month of gestation and the first year of life on the primary dentition in 9-year-olds. Fewer sites with gingivitis could be detected and less approximal caries lesions



were noticed in the probiotic group compared with the placebo group. In contrast, Taipale et al<sup>44</sup> and Hasslöf et al<sup>45</sup> did not find differences between the probiotic and control groups. Taipale and coworkers<sup>44</sup> gave babies a slow-releasing pacifier with *Bifidobacterium animalis* subspecies *lactis* BB-12 (BB-12), xylitol, or sorbitol twice a day from the age of 1 to 2 months until the child turned 2 years. At the age of 4 years there appeared to be no differences between the three groups in the occurrence of caries. Instead, this was associated with daily consumption of sweet drinks, visible plaque observed, and mutans streptococci counts. Hasslöf and coworkers randomized full-term babies to a daily diet of control cereals or cereals supplemented with *Lactobacillus paracasei* F19 (LF19) from 4 to 13 months of age. When these subjects were 9 years old, neither decayed, missing, and filled surfaces for primary teeth (dmfs) nor decayed, missing, and filled surfaces for permanent teeth (DMFS) differed significantly between baseline and the end of the study. Significant differences concerning the microbiologic counts could not be found. No evidence of the colonization of the oral cavity with LF19 in the probiotic group could be found.<sup>45</sup>

### The role of probiotics for controlling periodontal disease

It is generally accepted that in a susceptible host, the presence of pathogenic bacteria and the absence of beneficial bacteria play a role in the development of periodontal disease.<sup>46</sup> Since it is difficult to interfere with host susceptibility, actual treatments focus on reducing the pathogenic bacteria. Current treatment strategies include mechanical subgingival debridement (sometimes supplemented with antimicrobial aids) and oral hygiene improvement.<sup>47</sup> However, there has recently been increased interest in the third etiologic factor through restoring the reduced number of beneficial bacteria by the usage of probiotics.

With regard to the studies examining the effect of probiotics on periodontal diseases, there is pronounced heterogeneity, which makes comparing the available research difficult. To start with, there is a very diverse patient population: healthy patients, experi-

mental gingivitis models, and patients with gingivitis, chronic periodontitis, and aggressive periodontitis. There is also a large variety in the studied parameters, such as microbiologic parameters in saliva and plaque, different plaque and gingivitis indices, bleeding on probing, and probing pocket depth. In addition there is often only a short period of probiotic use, with a maximum of 3 months, so it seems logical that real periodontal parameters such as probing pocket depth are not described or not significantly different when compared to baseline data. However, it is notable that there are many studies that use the same mixture of two *L reuteri* strains.<sup>48-55</sup>

In the majority of these studies on real periodontitis patients a significant decrease in terms of gingivitis and plaque index could be noted in the probiotic group when the measurements after probiotic usage were compared with those at baseline.<sup>48,50,53,55</sup> However, in (experimental) gingivitis patients this significant difference was not observed.<sup>51,52</sup> Three studies on periodontitis patients with a longer follow-up are available showing significant differences in pocket depth reduction in initial moderate (4 to 5 mm) and deep ( $\geq 6$  mm) pockets. Other studies using *Lactobacillus* species (*L brevis*, *L salivarius* WB21) show significant decreases in gingivitis and plaque index when the results at the end of the probiotic usage are compared to baseline data.<sup>56-58</sup> Additionally, a significant decrease in five periodontopathogens is described in subgingival plaque.<sup>59</sup> The use of a probiotic drink with *L casei Shirota* in healthy patients and in an experimental gingivitis model failed to demonstrate significant clinical changes.<sup>60,61</sup> However, in healthy patients the increase in gingival crevicular fluid volume in the probiotic group was significantly lower compared with the control group.<sup>60</sup> Additionally, in the experimental gingivitis group the elastase activity and matrix metalloproteinase-3 amount were significantly lower after the intake of the probiotic milk drink. This could suggest a beneficial effect of this probiotic milk product on gingival inflammation.<sup>61</sup>

A study examining the effect of a mouthwash with a mixture of *Streptococcus oralis* KJ3sm, *Streptococcus*



*uberis* KJ2sm, and *Streptococcus rattus* JH145 on microbiologic parameters, showed that this mouthwash was able to substantially affect the levels of periodontal pathogens in subgingival plaque.<sup>62</sup>

### The role of probiotics for controlling halitosis

Halitosis and breath malodor are general terms used to define an offensive odor emanating from someone's breath.<sup>63,64</sup> In more than 90% of the patients, the origin of this foul smell can be localized in the oral cavity.<sup>65,66</sup> In these cases the term oral malodor applies. It is the result of the microbial degradation by anaerobic bacteria of proteins present in saliva, food debris, gingival crevicular fluid, interdental plaque, shed epithelial cells, postnasal drip, and blood. Thereby a range of volatiles are produced, of which the volatile sulfur compounds (VSCs) are the most studied.<sup>67-69</sup> The clinical detection of bad breath can be done by smelling (organoleptic evaluation) and/or by using certain machines to analyze volatile compounds (mainly volatile sulfur compounds) in the breath.<sup>70</sup> The treatment of halitosis focuses on reducing the bacterial load and the micro-nutrients in the oral cavity by use of a variety of mechanical and chemical aids. To date, there are very few studies available examining the effect of probiotics on bad breath. The rationale for using probiotics is to avoid the re-establishment of volatile sulfur producing bacteria.

The probiotic effect of *Streptococcus salivarius* K12, *Weissella cibaria*, and *Streptococcus thermophilus* on halitosis parameters was shown in vitro.<sup>71-73</sup> Kang and coworkers<sup>71</sup> showed that *W. cibaria* inhibits hydrogen peroxide production by *Fusobacterium nucleatum* by inhibiting the replication of this microorganism. Masdea et al<sup>72</sup> demonstrated that *S. salivarius* K12 has antimicrobial activity against bacteria involved in halitosis. Lee and Baek<sup>73</sup> showed that *S. thermophilus* may reduce the VSC measurement by inhibition of *Porphyromonas gingivalis* growth and neutralizing VSCs.<sup>73</sup> Clinically, Burton and coworkers<sup>74,75</sup> demonstrated the effect of *S. salivarius* K12 in 2006. Twenty-three subjects with halitosis were assigned after thorough mechanical and

chemical oral cleansing to a test group receiving a K12 lozenge ( $10^9$  *S. salivarius*/lozenge; 13 subjects) or the control group (10 subjects) receiving a placebo tablet for 2 weeks. After 1 week the VSC readings of the probiotic group were significantly lower than in the placebo group. A positive effect after 12 and 29 days of usage of three tablets a day containing *L. salivarius* WB21 was shown on organoleptic scores and VSC measurements.<sup>76</sup> This was an open-label pilot study on 20 halitosis patients. Moreover, it was shown in a cross-over trial that 14-day use of these tablets significantly reduced VSCs compared with the use of a placebo.<sup>77</sup>

However, a randomized placebo-controlled cross-over trial on self-reported malodorous morning bad breath with probiotic chewing gum (*L. reuteri* DSM 17938 and *L. reuteri* ATCC PTA 5289) could only show significant differences in organoleptic scores, but not on VSC measurements after 14 days of usage.<sup>78</sup> When a 4-week consumption of probiotic-containing milk drink Yakult was examined in healthy dentate people, VSC measurements in the morning were not significantly affected throughout the trial.<sup>79</sup>

### The role of probiotics for controlling other oral threats

Hatakka and coworkers<sup>80</sup> investigated in 2007 if probiotic treatment could reduce the prevalence of oral *Candida* in the elderly; 276 elderly people were enrolled in a randomized, double-blind, placebo-controlled study to receive daily control cheese or a cheese containing a mixture of probiotics (*L. rhamnosus* GG, *L. rhamnosus* LC705, *Propionibacterium freudenreichii* subspecies *shermanii* JS) for 16 weeks. It was shown that probiotic intervention reduced the risk of high yeast counts ( $\geq 10^4$  CFU/mL) significantly.

The effect of probiotic lozenges on radiation- and chemotherapy-induced mucositis was studied in 2012 by Sharma et al.<sup>81</sup> Mucositis is a painful condition that may lead to dose reduction, treatment delays, or even treatment discontinuation. During this randomized, double-blind, placebo-controlled study, 200 chemoradiotherapy patients consumed 6x/day lozenges containing either *L. brevis* CD2 or a placebo. The intake of



probiotic lozenges reduced the incidence of grade III and IV anticancer therapy-induced oral mucositis and was associated with a lower overall rate of mucositis and a higher rate of anticancer treatment completion.

A case report even describes the beneficial effect of *L brevis* CD2 use in an adult hemophilic patient suffering from painful aphthous oral ulcerations.<sup>82</sup> After 3 days of 6×/day usage of these lozenges two large painful ulcerated lesions completely healed. The patient continued to take these probiotic lozenges for 1 month and he had no recurrences of oral ulcers for the following 6 months.

## FUTURE DIRECTIONS

Probiotics for oral health are an emerging and promising new field of research. Further research is needed to show the effects of probiotics in the prevention and treatment of caries, periodontal diseases, and halitosis. When designing future probiotic trials it is important that randomization and blinding are properly described and a sufficiently large study group is taken into account. Moreover, it is important to further explore the strain- and dose-specific effects and the proper vehicle for the probiotics of interest. A sufficiently long follow-up is important so that real dental parameters (such as caries, plaque formation, and probing pocket depth) can be considered instead of intermediate endpoints.

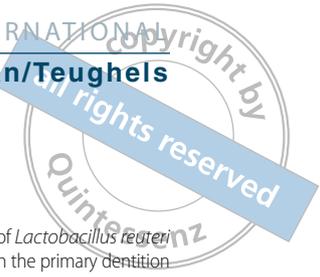
## CONCLUSION

The results are encouraging, but further research is needed to demonstrate apparent effects of certain probiotic strains on oral health and their desired concentration and vehicle. However, probiotics are becoming more and more commercially available. This leads to increasing questions from patients at the dental office about these products. It is therefore important that a dentist can give sound advice about probiotics. Always remember that the effects are strain and dose dependent. Probiotic selection should be based on products clinically tested for the given disorder. The use of probiotic products in healthy patients is safe.<sup>83,84</sup>

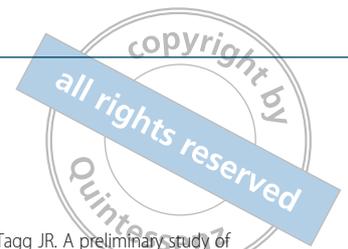
However, it is not advisable to recommend these products in specific risk patients, such as immunocompromised patients or cardiac valvular disease patients. Before the commencement of probiotic use for oral health, prophylaxis should be performed, since it is proven that it is difficult to disrupt an acquired biofilm.<sup>85</sup> It is also important to make clear that probiotics are a supplemental tool and certainly not a substitute for classic mechanical oral hygiene at home. When the probiotic product usage is stopped, then it can be expected that the probiotic effect will also stop.

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