Dentalflora™

Author: Joseph Katzinger, ND

Active Ingredients: Xylitol, Organic Spearmint Leaf extract, Dentalflora™ Blend (BLIS M18™ *Streptococcus salivarius*, *Lactobacillus paracasei*, *Lactobacillus salivarius*, *Lactobacillus reuteri*)

Other Ingredients: Frutafit® HD (inulin), Stearic acid, Hydroxypropyl Cellulose (HPC), Spearmint flavor (natural)

Overview

Dentalflora™ provides an evidence-based blend of probiotics and active compounds designed to improve oral health through diverse and complementary mechanisms. BLIS M18™ *S. salivarius* synthesizes localized and targeted antimicrobial compounds, and three proven species of *Lactobacillus* help to reduce the abundance of pathogens responsible for many oral diseases. These probiotics directly compete with pathogenic bacterial and fungal species, such as *Streptococcus mutans* and *Porphyromonas gingivalis,* by producing organic acids and antimicrobials, upregulating salivary IgA levels, preventing attachment to teeth surfaces, disrupting biofilm and plaque formation, and even downregulating acid tolerance genes among pathogenic bacteria. Xylitol has well-established efficacy for reducing *S. mutans* abundance by interfering with its biofilm formation as well as its energy and acid production, and organic spearmint leaf extract provides many bioactive and antimicrobial compounds that reduce the oxidative stress and inflammation associated with many oral diseases. The components of Dentalflora have individually been shown to reduce dental caries, halitosis, gingivitis, and periodontitis in many randomized and controlled clinical trials, and their complementary mechanisms of action help to support optimal oral health and hygiene.

Xylitol

Scientific Evidence:

Xylitol is a 5-carbon polyol, a natural sugar alcohol found in plums, strawberries, and pumpkins, notable because it is not fermented by oral microorganisms, and appears to have beneficial effects on oral health.[1] Regular consumption of xylitol has been associated with decreased caries incidence and plaque formation, as well as a reduced abundance of *S. mutans*, a major cariogenic species. Xylitol has also been shown to inhibit the formation of biofilms by *S. mutans*, in part by decreasing the viable number of *S. mutans* cells, as well as by inhibiting biofilm polysaccharides and attachment.[2] Xylitol

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[1] Chen, S. Y., Delacruz, J., Kim, Y., et al. (2023). Effect of xylitol on Porphyromonas gingivalis: A systematic review. Clinical and experimental dental research, 9(2), 265–275.

[2] Loimaranta, V., Mazurel, D., Deng, D., et al. (2020). Xylitol and erythritol inhibit real-time biofilm formation of Streptococcus mutans. BMC microbiology, 20(1), 184.

disrupts the energy production processes of *S. mutans*, both starving it and impairing its adhesion to teeth surfaces and its acid production potential.[3] A review of *in vitro* studies suggests that xylitol may also inhibit the growth of *P. gingivalis*, a major contributor to periodontitis, along with the expression of pro-inflammatory cytokines by this pathogenic species.[1]

A systematic review that included 21 randomized and controlled trials (after inclusion/exclusion criteria were applied) concluded that regular exposure to xylitol reduces *S. mutans* abundance without broader effects on the oral microbiota.[4] A second systematic review also found that xylitol appears to reduce gingival inflammation, likely via inhibition of *S. mutans* and biofilm formation.[5] A reduction in dental plaque with xylitol chewing gum (but not xylitol candy) was also recently highlighted in a systematic review of randomized and controlled clinical trials.[6] In a review of controlled trials at least 12 months in length, xylitol was shown to have a small effect on reducing dental caries in children, though a dose-dependent effect was observed, with higher doses demonstrating a medium reduction in caries.[7] Xylitol also reduces the adherence of *S. pneumoniae* and *H. influenzae* to nasopharyngeal cells *in vitro*; a Cochrane systematic review (which included over 1800 participants in randomized controlled trials) found a 25% reduction in acute otitis media following xylitol supplementation (in any form) to healthy children attending daycare.[8]

Organic Spearmint Leaf Extract

Scientific Evidence:

Spearmint (*Mentha spicata L.*), though often used as a flavoring agent, has demonstrated both antioxidant and anti-inflammatory effects, and is used traditionally for both gastrointestinal and respiratory support. It contains a wide variety of active compounds with antimicrobial effects, most notably rosmarinic acid (RA), as well as carvone, limonene, 1,8-cineole, menthone, menthol, eucalyptol, luteolin, and apigenin derivatives.[9] Spearmint essential oils have been shown to inhibit *S. mutans* growth as well as biofilm formation in an *in vitro* model, suggesting a possible role in preventing dental caries.[10] Although the essential oil of spearmint is often used, the leaf extract contains more bioactive compounds, potentially augmenting its antioxidant and anti-inflammatory effects.[11] RA alone has been

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[3] Nayak, P. A., Nayak, U. A., & Khandelwal, V. (2014). The effect of xylitol on dental caries and oral flora. Clinical, cosmetic and investigational dentistry, 6, 89–94.
[4] Söderling, E., & Pienihäkkinen, K. (2020). Effects of xylitol and erythritol consumption on mutans streptococci and the oral microbiota: a systematic review. Acta odontologica Scandinavica, 78(8), 599–608.
[5] Söderling, E., Pienihäkkinen, K., & Gursoy, U. K. (2022). Effects of sugar-free polyol chewing gums on gingival inflammation: a systematic review. Clinical oral investigations, 26(12), 6881–6891.
[6] Söderling, E., & Pienihäkkinen, K. (2022). Effects of xylitol chewing gum and candies on the accumulation of dental plaque: a systematic review. Clinical oral investigations, 26(1), 119–129.
[7] Marghalani, A. A., Guinto, E., Phan, M., et al. (2017). Effectiveness of Xylitol in Reducing Dental Caries in Children. Pediatric dentistry, 39(2), 103–110.
[8] Azarpazhooh, A., Lawrence, H. P., & Shah, P. S. (2016). Xylitol for preventing acute otitis media in children up to 12 years of age. The Cochrane database of systematic reviews, 2016(8), CD007095.
[9] Cirlini, M., Mena, P., Tassotti, M., et al. (2016). Phenolic and Volatile Composition of a Dry Spearmint (Mentha spicata L.) Extract. Molecules (Basel, Switzerland), 21(8), 1007.
[10] Landeo-Villanueva, G. E., Salazar-Salvatierra, M. E., Ruiz-Quiroz, J. R., et al. (2023). Inhibitory Activity of Essential Oils of Mentha spicata and Eucalyptus globulus on Biofilms of Streptococcus mutans in an In Vitro Model. Antibiotics (Basel, Switzerland), 12(2), 369.
[11] Direito, R., Rocha, J., Lima, A., et al. (2019). Reduction of Inflammation and Colon Injury by a Spearmint Phenolic Extract in Experimental Bowel Disease in Mice. Medicines (Basel, Switzerland), 6(2), 65.

shown to have a variety of antimicrobial as well as antioxidant and anti-inflammatory effects. It has been speculated that RA may help to address the pathogenesis of periodontitis by limiting oxidative damage and inflammatory compounds in gingival fibroblasts, though clinical trials are lacking.[12]

Dentalflora™ Blend

BLIS M18™ *Streptococcus salivarius*

Scientific Evidence:

The probiotic *Streptococcus salivarius* is considered to be a natural pioneer of the oral cavity, present as a predominant member of the oral microbiota throughout the lifespan, usually becoming established within hours of birth.[13] It is a spherical, gram-positive, oxidase-negative, and catalase-negative bacterium recognized for its ability to survive on the dorsum of the tongue.[14] Increased abundance of *S. salivarius* has been observed in healthy subjects, and appears to have a protective effect, demonstrated by *in vitro* inhibition of respiratory pathobionts.[15]

Some strains of *S. salivarius* are capable of producing streptococcal bacteriocin-like inhibitory substances (BLIS), compounds with antimicrobial activity that either inhibit or kill other potentially pathogenic bacteria, one putative mechanism for the health benefits associated with probiotic use. These substances have been defined as “bacterial peptide or protein molecules, released extracellularly, that in low concentrations are able to kill certain other closely related bacteria by a mechanism against which the producer cell exhibits a degree of specific immunity”.[16] A distinct advantage of BLIS as compared to antibiotics is the more targeted and local effect they have on bacterial species, without disruption of the larger microbiome.

BLIS M18™ *S. salivarius*, a strain previously known as Mia, has a unique genome that has been shown to produce four BLIS referred to as salivaricins A2, 9, M, and MPS. These BLIS have demonstrated antibacterial activity against a wide range of species associated with oral pathologies such as gingivitis, halitosis, and dental caries.[13] *In vitro*, BLIS M18™ *S. salivarius* has strongly inhibited the growth of two of the major cariogenic species, *S. mutans* and *S. sobrinus*, as well as species associated with upper respiratory tract infections, including *Actinomyces viscosus*, *Actinomyces naeslundii*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, *Enterococcus faecalis*, *Listeria monocytogenes*, *Haemophilus influenzae*, *Staphylococcus saprophyticus,* and *Staphylococcus cohnii*.[13] In addition, BLIS M18™ *S. salivarius* has been shown to drastically disrupt biofilm formation by the oral pathogen, *Pseudomonas aeruginosa*, inhibit its growth, and sensitize it to antibiotics (along with *Klebsiella pneumonia*).[17] BLIS

[12] Luo, C., Zou, L., Sun, H., et al. (2020). A Review of the Anti-Inflammatory Effects of Rosmarinic Acid on Inflammatory Diseases. Frontiers in pharmacology, 11, 153.
[13] Wescombe, P. A., Hale, J. D., Heng, N. C., et al. (2012). Developing oral probiotics from Streptococcus salivarius. Future microbiology, 7(12), 1355–1371.
[14] Burton, J. P., Chilcott, C. N., Wescombe, P. A., et al. (2010). Extended Safety Data for the Oral Cavity Probiotic Streptococcus salivarius K12. Probiotics and antimicrobial proteins, 2(3), 135–144.
[15] Jörissen, J., van den Broek, M. F. L., De Boeck, I., et al. (2021). Case-Control Microbiome Study of Chronic Otitis Media with Effusion in Children Points at Streptococcus salivarius as a Pathobiont-Inhibiting Species. mSystems, 6(2), e00056-21.
[16] Tagg, J. R., Harold, L. K., Jain, R., et al. (2023). Beneficial modulation of human health in the oral cavity and beyond using bacteriocin-like inhibitory substance-producing streptococcal probiotics. Frontiers in microbiology, 14, 1161155.
[17] Tunçer, S., & Karaçam, S. (2020). Cell-free supernatant of Streptococcus salivarius M18 impairs the pathogenic properties of Pseudomonas aeruginosa and Klebsiella pneumonia. Archives of microbiology, 202(10), 2825–2840.

M18™ *S. salivarius* also synthesizes both dextranase and urease, which inhibit biofilm/plaque formation and raise salivary pH, respectively.[18] *In vitro* reduction of volatile sulfur compound (VSC) production by *P. gingivalis* and *Treponema denticola* also suggests efficacy for improving halitosis, which was observed in a triple-blind placebo-controlled trial among children with orthodontic braces. After 3 months of treatment, VSCs continued to decrease, compared to a return to baseline among those receiving placebo.[19,20]

In additional clinical trials, BLIS M18™ *S. salivarius* has been shown to reduce the likelihood of caries development in children, and to reduce gingivitis and periodontitis in adults. In one randomized trial, children taking 1 lozenge per day of BLIS M18™ *S. salivarius* (taken 30 minutes after a meal with instructions to let it slowly dissolve) were found to have reduced counts of *S. mutans* (correlated directly with caries experience), as well as increased buffering capacity compared to children taking a placebo, after only 7 days.[21] In a randomized and double-blind, placebo-controlled trial that enrolled 100 children with active dental caries, lozenges (BLIS M18™ *S. salivarius* or placebo) were given after brushing in the morning and night, in addition to standard care. After 3 months, children given active treatment had significant reductions in their plaque scores, especially those with the highest baseline levels of plaque.[22] Among children at high risk for dental caries, a slowly dissolving tablet given before bedtime over a 90-day period was shown to improve Cariogram scores compared to an untreated group.[18]

Additionally, 1 tablet of BLIS M18™ *S. salivarius* allowed to dissolve at bedtime was shown to significantly reduce the return of black stains on the teeth of children 6 months after professional removal of these stains, compared to professional removal alone. Gram-positive bacteria embedded in an intermicrobial matrix are thought to be the primary etiological agent responsible for this black discoloration.[23]

In a small trial among adults with moderate to severe gingivitis or moderate periodontitis, in addition to receiving scaling and root planing, participants that dissolved 1 tablet BLIS M18™ *S. salivarius* twice per day for 30 days had significant improvements in all parameters measured, including plaque index, gingival index, modified sulcus bleeding index, and probing pocket depth when compared to scaling and root planing alone.[24] Similarly, in a randomized and double-blind placebo-controlled trial, young adults with gingivitis had improvement in gingival inflammation after 4 weeks of active treatment which persisted after a 4-week washout period. Reduced plaque scores were also observed during the active treatment period.[25]

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[18] Di Pierro, F., Zanvit, A., Nobili, P., et al. (2015). Cariogram outcome after 90 days of oral treatment with Streptococcus salivarius M18 in children at high risk for dental caries: results of a randomized, controlled study. Clinical, cosmetic and investigational dentistry, 7, 107–113.
[19] Yoo, H. J., Jwa, S. K., Kim, D. H., et al. (2020). Inhibitory effect of Streptococcus salivarius K12 and M18 on halitosis in vitro. Clinical and experimental dental research, 6(2), 207–214.
[20] Benic, G. Z., Farella, M., Morgan, X. C., et al. (2019). Oral probiotics reduce halitosis in patients wearing orthodontic braces: a randomized, triple-blind, placebo-controlled trial. Journal of breath research, 13(3), 036010.
[21] Salim, H. P., Mallikarjun, S. B., Raju, S., et al. (2023). Randomized Clinical Trial of Oral Probiotic Streptococcus salivarius M18 on Salivary Streptococcus mutans in Preprimary Children. International journal of clinical pediatric dentistry, 16(2), 259–263.
[22] Burton, J. P., Drummond, B. K., Chilcott, C. N., et al. (2013). Influence of the probiotic Streptococcus salivarius strain M18 on indices of dental health in children: a randomized double-blind, placebo-controlled trial. Journal of medical microbiology, 62(Pt 6), 875–884.
[23] Bardellini, E., Amadori, F., Gobbi, E., et al. (2020). Does Streptococcus Salivarius Strain M18 Assumption Make Black Stains Disappear in Children?. Oral health & preventive dentistry, 18(1), 161–164.
[24] Litty S, Nagarathna D, Merline V. (2015). Probiotics in periodontal therapy. Int J Pharm Bio Sci, 6(1):242–250.
[25] Babina, K., Salikhova, D., Doroshina, V., et al. (2023). Antigingivitis and Antiplaque Effects of Oral Probiotic Containing the

Lactobacillus paracasei

Scientific Evidence:

Multiple species of *Lactobacillus* are present as major constituents of oral microbiota, and are thought to inhibit the growth of pathogenic bacterial species such as *S. mutans* through a variety of mechanisms. For example, several *Lactobacillus sp*. were shown to inhibit the growth of *S. mutans in vitro* by generating organic acids and hydrogen peroxide, reducing cellular adherence and biofilm structures, modulating immune function, and downregulating virulence genes of *S. mutans*, including those related to acid tolerance and quorum-sensing.[26] Experimental models suggest *Lactobacillus paracasei* may also target *S. mutans* biofilms by decreasing exopolysaccharide (EPS) production.[27]

Lactobacillus paracasei has demonstrated antibacterial and anticandidal activities against multiple oral pathogens, including *S. mutans*, *Streptococcus sanguis*, *Staphylococcus aureus*, *Actinomyces viscosus*, P. *gingivalis*, *Candida albicans*, *Candida tropicalis*, and *Candida glabrata.*[28] In clinical trials, *L. paracasei* has been shown to reduce both *S. mutans* abundance as well as dental caries, and to modulate local immunity. In a randomized controlled clinical trial, 122 children with good oral health (median age of approximately 13 years) received either a strain of *L. paracasei* mixed in milk powder or a placebo milk powder for 6 months. Those receiving active treatment had both lower levels of *S. mutans* and incidence of caries; among those at high risk for caries, the risk was decreased 4.5-fold in the active group.[29] An additional 12-month controlled trial with this strain found a reduction in caries formation on pit and fissure surfaces (but not smooth surfaces), associated with an increase in salivary human neutrophil peptides 1–3 (HNP1-3), small antimicrobial peptides found in higher amounts in caries-free children.[30] A subsequent controlled trial also found an upregulation of salivary IgA levels with supplementation; IgA is known to prevent microorganisms from binding to mucosal membranes as well as teeth.[31] Similar benefits were observed in a younger population of preschool children in a 3-month controlled clinical trial, with a reduction in *S. mutans* and caries compared to placebo.[32]

Lactobacillus salivarius

Scientific Evidence:

Lactobacillus salivarius has also demonstrated an ability to inhibit the growth of *S. mutans* and other pathogenic species, reduce halitosis and dental caries, improve periodontal health, and help

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Streptococcus salivarius M18 Strain: A Randomized Clinical Trial. Nutrients, 15(18), 3882.

[26] Wasfi, R., Abd El-Rahman, O. A., Zafer, et al. (2018). Probiotic Lactobacillus sp. inhibit growth, biofilm formation and gene expression of caries-inducing Streptococcus mutans. Journal of cellular and molecular medicine, 22(3), 1972–1983.

[27] Guo, M., Wu, J., Hung, W., et al. (2023). Lactobacillus paracasei ET-22 Suppresses Dental Caries by Regulating Microbiota of Dental Plaques and Inhibiting Biofilm Formation. Nutrients, 15(15), 3316.

[28] Sookkhee, S., Chulasiri, M., & Prachyabrued, W. (2001). Lactic acid bacteria from healthy oral cavity of Thai volunteers: inhibition of oral pathogens. Journal of applied microbiology, 90(2), 172–179.

[29] Teanpaisan, R., Piwat, S., Tianviwat, S., et al. (2015). Effect of Long-Term Consumption of Lactobacillus paracasei SD1 on Reducing Mutans Streptococci and Caries Risk: A Randomized Placebo-Controlled Trial. Dentistry journal, 3(2), 43–54.

[30] Wattanarat, O., Makeudom, A., Sastraruji, T, et al. (2015). Enhancement of salivary human neutrophil peptide 1-3 levels by probiotic supplementation. BMC oral health, 15, 19.

[31] Pahumunto, N., Sophatha, B., Piwat, S., & Teanpaisan, R. (2019). Increasing salivary IgA and reducing Streptococcus mutans by probiotic Lactobacillus paracasei SD1: A double-blind, randomized, controlled study. Journal of dental sciences, 14(2), 178–184.

[32] Pahumunto, N., Piwat, S., Chankanka, O., et al. (2018). Reducing mutans streptococci and caries development by Lactobacillus paracasei SD1 in preschool children: a randomized placebo-controlled trial. Acta odontologica Scandinavica, 76(5), 331–337.

maintain optimal oral hygiene. *In vitro* data, for instance, indicates that *L. salivarius* inhibits the growth of potential pathogens linked to peri-implantitis, including P. *gingivalis*, *P. intermedia*, *S. salivarius*, and *S. aureus*.[33] Using plaques extracted from children with early childhood caries, *L. salivarius* was also shown to inhibit the biofilm formation of a "double-species biofilm" formed by *C. albicans* and *S. mutans*. It also reduced the mass and number of *S. mutans* and *C. albicans* in existing biofilms, and appeared to weaken the pathogenic potential of *C. albicans*.[34]

In a randomized but open-label clinical trial, two different strains of *L. salivarius* were shown to decrease levels of *S. mutans* after only 2 weeks of administration, supporting *in vitro* and *in vivo* findings in which *L. salivarius* prevented adhesion of *S. mutans* to hydroxyapatite, the major inorganic component of dental enamel.[35,36] A subsequent randomized and open-label clinical trial with 140 healthy children aged 3-6 years found that *L. salivarius*, provided as chewing tablets, significantly reduced the incidence and prevalence of dental caries for 12 months after only a 2-week long intervention compared to standard treatment alone.[37]

A strain of *L. salivarius* was also shown to improve signs of periodontitis in a double-blind and randomized controlled trial, including plaque index and probing pocket depth, especially in those at higher risk of disease (e.g. smokers).[38] Improvements in both halitosis and bleeding upon probing were also observed in an open-label trial, while a reduction in bleeding upon probing and an inhibition of both VSCs and VSC-producing bacteria was observed in a controlled trial.[39,40] In a double-blind and placebo-controlled randomized cross-over trial, a strain of *L. salivarius* was shown to reduce VSCs, average probing pocket depth, as well as some pathogenic strains (e.g. *Fusobacterium nucleatum*) during the probiotic supplementation period of the cross-over trial.[41] A randomized and controlled trial conducted among an older population (mean age approximately 70 years) found that supplementation with a strain *L. salivarius* also increased salivary IgG production, and was associated with a decrease in the coating of the tongue, a potential indicator of oral hygiene and a healthy oral microbiome.[42]

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[33] Mulla, M., Hegde, S., Koshy, A., et al. (2021). Effect of Probiotic Lactobacillus salivarius on Peri-Implantitis Pathogenic Bacteria: An In Vitro Study. Cureus, 13(12), e20808.
[34] Krzyściak, W., Kościelniak, D., Papież, M., et al. (2017). Effect of a Lactobacillus Salivarius Probiotic on a Double-Species Streptococcus Mutans and Candida Albicans Caries Biofilm. Nutrients, 9(11), 1242.
[35] Nishihara, T., Suzuki, N., Yoneda, M., et al. (2014). Effects of Lactobacillus salivarius-containing tablets on caries risk factors: a randomized open-label clinical trial. BMC oral health, 14, 110.
[36] Sañudo, A. I., Luque, R., Díaz-Ropero, M. P., et al. (2017). In vitro and in vivo anti-microbial activity evaluation of inactivated cells of Lactobacillus salivarius CECT 5713 against Streptococcus mutans. Archives of oral biology, 84, 58–63.
[37] Staszczyk, M., Jamka-Kasprzyk, M., Kościelniak, D., C, et al. (2022). Effect of a Short-Term Intervention with Lactobacillus salivarius Probiotic on Early Childhood Caries-An Open Label Randomized Controlled Trial. International journal of environmental research and public health, 19(19), 12447.
[38] Shimauchi, H., Mayanagi, G., Nakaya, S., et al. (2008). Improvement of periodontal condition by probiotics with Lactobacillus salivarius WB21: a randomized, double-blind, placebo-controlled study. Journal of clinical periodontology, 35(10), 897–905.
[39] Iwamoto, T., Suzuki, N., Tanabe, K., et al. (2010). Effects of probiotic Lactobacillus salivarius WB21 on halitosis and oral health: an open-label pilot trial. Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics, 110(2), 201–208.
[40] Suzuki, N., Tanabe, K., Takeshita, T., et al. (2012). Effects of oil drops containing Lactobacillus salivarius WB21 on periodontal health and oral microbiota producing volatile sulfur compounds. Journal of breath research, 6(1), 017106.
[41] Suzuki, N., Yoneda, M., Tanabe, K., et al. (2014). Lactobacillus salivarius WB21--containing tablets for the treatment of oral malodor: a double-blind, randomized, placebo-controlled crossover trial. Oral surgery, oral medicine, oral pathology and oral radiology, 117(4), 462–470.
[42] Kijima, S., Suzuki, N., Hanioka, T., et al. (2022). Application of Lactobacillus salivarius WB21 to the Oral Care of Healthy Older Adults: A Randomized, Double-Blind, Placebo-Controlled Crossover Comparative Study. Life (Basel, Switzerland), 12(9), 1422.

Lactobacillus reuteri

Scientific Evidence:

Lactobacillus reuteri is a common colonizer of the gastrointestinal tract, widely recognized for its many health benefits, including modulation of immune function, promotion of gut mucosal integrity, and competition with pathogenic species.[43] It secretes multiple antimicrobial substances, including reuterin (3-hydroxypropanal, or 3-HPA), lactic acid, ethanol, and reutericyclin, with numerous clinical studies supporting its safety and efficacy for supporting gastrointestinal health. *L. reuteri* may be the only *Lactobacillus* species to convert glycerol to reuterin, shown to inhibit the growth of gram-positive and gram-negative bacteria, in addition to yeasts, fungi, and even protozoa, primarily by inducing oxidative stress and modifying thiol groups among pathogenic species.[44,45] For example, *in vitro* data demonstrates a nearly complete inhibition of *C. albicans* and *C. parapsilosis*, with antifungal effects against 5 of the 6 most common species of *Candida*.[46]

In several randomized and controlled clinical trials, daily administration of *L. reuteri* was shown to reduce counts of periodontal pathogens, such as *P. gingivalis*, and to improve the efficacy of scaling and root planing among participants with chronic periodontitis, as demonstrated by greater pocket depth reduction and attachment gain in moderate and deep pockets, as well as improved probing depth and bleeding on probing.[47,48,49] A systematic review of 9 trials suggests clinical benefit for *L. reuteri* as an adjunct to scaling and planing for the treatment of periodontal disease.[50] Supplementation with *L. reuteri* has also been associated with benefits for gingivitis; in a 2-week randomized and placebo-controlled trial, the gingival and plaque indices improved among participants with moderate to severe gingivitis.[51] *L. reuteri* has also been shown to inhibit *S. mutans* growth in human trials; in a single-blind placebo-controlled trial, supplementation to mothers in the last month of pregnancy, as well as to their children during the first year of life, was associated with a reduction in caries prevalence and gingivitis by

[43] Mu, Q., Tavella, V. J., & Luo, X. M. (2018). Role of Lactobacillus reuteri in Human Health and Diseases. Frontiers in microbiology, 9, 757.
[44] Talarico, T. L., & Dobrogosz, W. J. (1989). Chemical characterization of an antimicrobial substance produced by Lactobacillus reuteri. Antimicrobial agents and chemotherapy, 33(5), 674–679.
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[46] Jørgensen, M. R., Kragelund, C., Jensen, P. Ø., et al. (2017). Probiotic Lactobacillus reuteri has antifungal effects on oral Candida species in vitro. Journal of oral microbiology, 9(1), 1274582.
[47] Iniesta, M., Herrera, D., Montero, E., et al. (2012). Probiotic effects of orally administered Lactobacillus reuteri-containing tablets on the subgingival and salivary microbiota in patients with gingivitis. A randomized clinical trial. Journal of clinical periodontology, 39(8), 736–744.
[48] Teughels, W., Durukan, A., Ozcelik, O., et al. (2013). Clinical and microbiological effects of Lactobacillus reuteri probiotics in the treatment of chronic periodontitis: a randomized placebo-controlled study. Journal of clinical periodontology, 40(11), 1025–1035.
[49] İnce, G., Gürsoy, H., İpçi, Ş. D., et al. (2015). Clinical and Biochemical Evaluation of Lozenges Containing Lactobacillus reuteri as an Adjunct to Non-Surgical Periodontal Therapy in Chronic Periodontitis. Journal of periodontology, 86(6), 746–754.
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[51] Krasse, P., Carlsson, B., Dahl, C., et al. (2006). Decreased gum bleeding and reduced gingivitis by the probiotic Lactobacillus reuteri. Swedish dental journal, 30(2), 55–60.

9 years of age.[52,53,54] A subsequent controlled trial found no improvement in dental caries with *L. reuteri* use, though the study was inadequately powered due to the COVID-19 pandemic.[55]

Overall Safety Summary

The probiotics in Dentalflora™ have an excellent safety record in multiple clinical trials in both adults and children, though Dentalflora™ should be avoided in individuals with a known sensitivity to any of the ingredients. Probiotics in general should be used with caution by those at high risk for adverse effects, such as those who are immune compromised.[56] Hypersensitivity reactions to spearmint, though rare, have been reported even through contact as an ingredient in toothpaste.[57] Xylitol in large amounts is known to induce osmotic diarrhea, but is unlikely to cause any adverse effects in the dose and form of administration in Dentalflora™ when given to both children and adults; a large systematic review of use as xylitol gum reported no adverse effects.[3,58]

Other Ingredients

Frutafit® HD is a natural source of inulin (from chicory roots), a prebiotic fiber (oligosaccharide) utilized by multiple probiotic species, including multiple strains of *Lactobacillus*, and is considered a safe food ingredient with the potential for a wide range of health benefits.[59,60] Stearic acid and spearmint, used as a lubricating agent and flavor respectively, have Generally Recognized as Safe (GRAS) status, and hydroxypropyl cellulose (HPC) is commonly used as a stabilizing agent, recognized by the FDA as safe for human consumption and as a binding agent for dietary supplements.[61,62,63]

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[52] Bolla, V. L., Reddy, M. S., Srinivas, N., et al. (2022). Investigation and comparison of the effects of two probiotic bacteria, and in reducing mutans streptococci levels in the saliva of children. Annals of African medicine, 21(4), 395–402.

[53] Alamoudi, N. M., Almabadi, E. S., El Ashiry, E. A., et al. (2018). Effect of Probiotic Lactobacillus reuteri on Salivary Cariogenic Bacterial Counts among Groups of Preschool Children in Jeddah, Saudi Arabia: A Randomized Clinical Trial. The Journal of clinical pediatric dentistry, 42(5), 331–338.

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