Dentalmin PRO™

Remineralizing Toothpaste

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Active Ingredients: NanoXIM•CarePaste (nano-hydroxyapatite), Omyadent® 100 (microhydroxyapatite and calcium carbonate), Cichorium intybus (Chicory) root extract (inulin), Althaea officinalis (Marshmallow) root extract, Ulmus fulva (Slippery elm) bark extract, Sodium bicarbonate, L-arginine, Galactoarabinan‡ (Larix spp. bark), Vaccinium macrocarpon (Cranberry) fruit extract.

Other Ingredients: Vegetable glycerin‡, Sorbitol, Sodium lauroyl sarcosinate, Aqua (deionized water), Natural flavors (mint), Mixed tocopherols, Carbomer
‡Organic

Overview

Dentalmin PRO™ toothpaste provides evidence-based bioactive compounds, nutrients, and botanicals designed to optimize oral health, safely protect and restore dental health and appearance, and preventatively target the etiology of dental caries. Dentalmin PRO™ includes NanoXIM•CarePaste and Omyadent 100 – specially formulated sources of hydroxyapatite and calcium carbonate, the crystals that largely comprise enamel and dentin surfaces. These modern and tested formulations have proven to be both biocompatible and effective, safely remineralizing teeth surfaces and providing protection as well as improvements in teeth appearance, smoothness, and sensitivity.

Dentalmin PRO™ also includes phytochemical-rich botanicals and other active compounds that address the multifactorial nature of dental caries development and progression. This process is largely driven by oral dysbiosis and the presence of cariogenic species, along with the formation of acid-producing bacterial biofilms that erode dental enamel and promote oral disease. Proanthocyanidins from Cranberry fruit extract have been shown to inhibit enzymes needed for bacterial adhesion and the formation of biofilms, as well as biofilm-generated acid production. Galactoarabinan from the Larch tree and inulin from Chicory root act as natural prebiotics, supporting the growth of healthy bacteria while inhibiting the growth and biofilm formation of cariogenic species. Marshmallow root and slippery elm extracts provide protective polysaccharide-rich mucilages, recognized for soothing and protecting mucosal membranes. L-arginine and sodium bicarbonate both improve oral pH through complementary mechanisms, reducing the damage caused by acid-producing bacteria and inhibiting their growth.

Collectively, these compounds favorably modulate the oral environment and microbiome to one that promotes optimal oral health, reducing the risk of dental caries and disease.

Active Ingredients

NanoXIM•CarePaste (nano-hydroxyapatite)

Scientific Evidence:

NanoXIM•CarePaste is comprised of nano-hydroxyapatite (n-HAP), a biocompatible and bioactive form of calcium apatite, recognized as one of the most promising materials in dentistry with the capacity to protect against dental caries, remineralize enamel, and reduce dental hypersensitivity.[1] Hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) is a naturally occurring calcium phosphate compound and the primary component of both the enamel and dentin tooth surfaces. Hydroxyapatite (HAP) crystals in enamel range in size from 20 to 40 nm. The nano-sized particles (< 100nm) found in NanoXIM•CarePaste have a similar morphology and crystal structure to naturally occurring hydroxyapatite, allowing for binding to both enamel and dentin surfaces.[2,3]

n-HAP dentifrices (toothpaste or powders) have been shown to remineralize/repair both dental enamel and dentin surfaces, forming a strong layer of protection against caries and dental erosion.[4] In a scoping review of 28 studies, the use of n-HAP was found to have multiple benefits when used in dentifrices, including improvements in the remineralization of initial enamel lesions and tooth brightness, and a reduction in caries, demineralization, dentinal hypersensitivity, and surface roughness.[5] An *in vitro* study indicated that NanoXIM•CarePaste was among the most effective n-HAP formulations tested for preventing the demineralization associated with orthodontic brackets when used as a daily application.[3]

Dental hypersensitivity is marked by a sharp pain in response to exposed cervical dentin, causally explained by the “hydrodynamic theory,” i.e., that fluid in dentin tubules moves rapidly upon exposure, stimulating pulp nerves. Therapies that reduce dentin permeability also reduce dental hypersensitivity.[6]

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[1] Bordea, I. R., Candrea, S., Alexescu, G. T., et al. (2020). Nano-hydroxyapatite use in dentistry: a systematic review. Drug metabolism reviews, 52(2), 319–332.
[2] Tschoppe, P., Zandim, D. L., Martus, P., et al. (2011). Enamel and dentine remineralization by nano-hydroxyapatite toothpastes. Journal of dentistry, 39(6), 430–437.
[3] Singh, A., Shetty, B., Mahesh, CM, et al. (2017). Evaluation of Efficiency of Two Nanohydroxyapatite Remineralizing Agents with a Hydroxyapatite and a Conventional Dentifrice: A Comparative In vitro Study. J Indian Orthod Soc, 51, 92-102.
[4] Pepla, E., Besharat, L. K., Palaia, G., et al. (2014). Nano-hydroxyapatite and its applications in preventive, restorative and regenerative dentistry: a review of literature. Annali di stomatologia, 5(3), 108–114.
[5] Anil, A., Ibraheem, W. I., Meshni, A. A., et al. (2022). Nano-Hydroxyapatite (nHAp) in the Remineralization of Early Dental Caries: A Scoping Review. International journal of environmental research and public health, 19(9), 5629.
[6] Amaechi, B. T., Mathews, S. M., Ramalingam, K., et al. (2015). Evaluation of nanohydroxyapatite-containing toothpaste for occluding dentin tubules. American journal of dentistry, 28(1), 33–39.

Multiple *in vitro* and *in situ* models indicate that n-HAP dentifrices occlude dentin tubules, both blocking tubule openings as well as providing a template or scaffolding for remineralization by attracting calcium and phosphate, thereby reducing dental hypersensitivity.[7,8] Fluoride dentifrices, in contrast, have a relatively small effect on hypersensitivity because fluoride ions have a limited ability to occlude dentin tubules, and do not have the same capacity to deposit precipitate layers over the tubules that n-HAP dentifrices do.[6]

When compared directly to two other desensitizing agents in an *in vitro*-based analysis, NanoXIM•CarePaste was the most effective, showing almost complete tubule occlusion (a 97.6% occlusion rate).[9] Similarly, NanoXIM•CarePaste most efficiently occluded dental tubules in an *in vitro* study that compared it to bioactive glass and a tri-calcium phosphate desensitizing agent.[10] In a clinical trial comparing NanoXIM•CarePaste to both propolis or potassium nitrate (Sensodent K), 45 patients with dental hypersensitivity were assessed after 1 and 4 weeks of receiving one of the three treatments. The group receiving NanoXIM•CarePaste had the largest reduction in hypersensitivity after 4 weeks (a reduction of approximately 79%), a significant improvement compared to people receiving potassium nitrate.[11]

n-HAP dentifrices also whiten and smooth rough teeth surfaces by binding to small holes and depressions on the enamel surfaces, acting as a filler and protective layer against various insults.[4] An *in vitro* study concluded that not only did a mouth rinse containing NanoXIM•CarePaste have similar whitening properties to a commercial whitening mouth rinse, but NanoXIM•CarePaste was also superior to mouth rinses containing larger size HAP particles, with a greater effect over time.[12] In a controlled trial, patients received tooth bleaching treatments with hydrogen peroxide, either with or without n-HAP. While bleaching efficacy was similar in both groups, people who also received n-HAP had significantly lower

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[7] Gupta, I., Chauhan, S., Amaranath, B. J. J., et al. (2023). Effect of Commercially Available Nano-Hydroxyapatite Containing Desensitizing Toothpaste and Mouthwash on Dentinal Tubular Occlusion: A SEM Analysis. Journal of pharmacy & bioallied sciences, 15(Suppl 2), S1027–S1029.

[8] Pei, D., Meng, Y., Li, Y., et al. (2019). Influence of nano-hydroxyapatite containing desensitizing toothpastes on the sealing ability of dentinal tubules and bonding performance of self-etch adhesives. Journal of the mechanical behavior of biomedical materials, 91, 38–44.

[9] Kulal, R., Jayanti, I., Sambashivaiah, S., et al. (2016). An In-vitro Comparison of Nano Hydroxyapatite, Novamin and Proargin Desensitizing Toothpastes - A SEM Study. Journal of clinical and diagnostic research : JCDR, 10(10), ZC51–ZC54.

[10] Jalaluddin, M., Hashmi, A., Devi, K. B., et al. (2022). Assessment of the Efficacy of Different Desensitizing Agents on Dentinal Tubules Occlusion- An In vitro Study. Journal of pharmacy & bioallied sciences, 14(Suppl 1), S585–S588.

[11] Narmatha VJ, Thakur, S. (2014). An In-Vivo Comparative Study of the Efficacy of Propolis, Nano-Hydroxyapatite and Potassium Nitrate Containing Desensitizing Agents. Research & Reviews: Journal of Dental Sciences, 2(2), 113-118.

[12] Shang, R., & Kunzelmann, K. H. (2021). Biomimetic tooth-whitening effect of hydroxyapatite-containing mouthrinses after long-term simulated oral rinsing. American journal of dentistry, 34(6), 307–312

tooth sensitivity during treatment.[13] It should be noted that most teeth-whitening agents are abrasive, leading to dental wear and potential erosion of the enamel over time, highlighting the advantage of HAP, which whitens while also remineralizing enamel.[14,15]

Omyadent 100 (micro-hydroxyapatite and calcium carbonate)

Scientific Evidence:

Omyadent 100 comprises particles with calcium carbonate at the core, surrounded by a shell of naturally sourced micro-HAP, with particles between 5–10 microns in size. Comparable to n-HAP, the microcrystals of HAP found in Omyadent 100 resemble naturally occurring HAP crystals in enamel and can bind and strengthen tooth enamel and dentin, filling and smoothing any porous surface irregularities.[16] Similarly, micro-HAP has been shown to improve enamel and dentin remineralization, promote tooth whitening, control biofilms, and reduce dentin sensitivity.[17] In addition to micro-HAP, Omyadent 100 also provides calcium carbonate, helping to maintain a reservoir of calcium, supersaturating saliva and tooth surfaces. Calcium carbonate-based toothpastes increase the calcium level found in plaques, which is inversely related to caries progression, perhaps by neutralizing plaque acids.[18]

In a comparison *in situ* trial, HAP toothpaste was found to be equally effective (non-inferior) to fluoride toothpaste in the remineralization of caries lesions, and in preventing enamel demineralization and carious lesion progression.[19] A randomized and controlled 6-month trial enrolled 147 participants at higher risk for caries development (they were being fitted for orthodontics of at least 6 months duration and had elevated salivary counts of *Streptococcus mutans (≥105 c.f.u./mL*)). In this susceptible group of participants, HAP toothpaste was found to be equally effective as fluoridated toothpaste in the prevention of caries (the primary outcome); and in secondary measures including the plaque and gingival indices.[20] In a systematic review and meta-analysis of randomized controlled trials, HAP-based fluoride-free oral care products were found to have a variety of benefits, including protection against dental caries and acid

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[13] Vano, M., Derchi, G., Barone, A., et al. (2015). Tooth bleaching with hydrogen peroxide and nano-hydroxyapatite: a 9-month follow-up randomized clinical trial. International journal of dental hygiene, 13(4), 301–307.

[14] Schemehorn, B. R., Moore, M. H., & Putt, M. S. (2011). Abrasion, polishing, and stain removal characteristics of various commercial dentifrices in vitro. The Journal of clinical dentistry, 22(1), 11–18.

[15] Coceska, E., Gjorgievska, E., Coleman, N. J., et al. (2016). Enamel alteration following tooth bleaching and remineralization. Journal of microscopy, 262(3), 232–244.

[16] O'Hagan-Wong, K., Enax, J., Meyer, F., et al. (2022). The use of hydroxyapatite toothpaste to prevent dental caries. Odontology, 110(2), 223–230.

[17] Chen, L., Al-Bayatee, S., Khurshid, Z., et al. (2021). Hydroxyapatite in Oral Care Products-A Review. Materials (Basel, Switzerland), 14(17), 4865.

[18] Lynch, R. J., & ten Cate, J. M. (2005). The anti-caries efficacy of calcium carbonate-based fluoride toothpastes. International dental journal, 55(3 Suppl 1), 175–178.

[19] Amaechi, B. T., AbdulAzees, P. A., Alshareif, D. O, et al. (2019). Comparative efficacy of a hydroxyapatite and a fluoride toothpaste for prevention and remineralization of dental caries in children. BDJ open, 5, 18.

[20] Schlagenhauf, U., Kunzelmann, K. H., Hannig, C., et al. (2019). Impact of a non-fluoridated microcrystalline hydroxyapatite dentifrice on enamel caries progression in highly caries-susceptible orthodontic patients: A randomized, controlled 6-month trial. Journal of investigative and clinical dentistry, 10(2), e12399.

erosion, as well as strengthening enamel surfaces through HAP deposits. Mechanisms were distinct from fluoride's mechanism of action and included reversal of carious lesions, remineralization, and increasing the concentrations of calcium and phosphate in saliva.[21]

Cichorium Intybus (Chicory) root extract (inulin)

Scientific Evidence:

Chicory root is a dietary source of inulin, a prebiotic dietary fiber with favorable effects on the oral microbiota. Dental caries are largely driven by dysbiotic oral microbiota and the cariogenic biofilms they create, creating an acidic microenvironment that demineralizes enamel. For example, the canonical cariogenic species *S. mutans* is recognized to be an exceptional biofilm former, and somewhat disproportionately promotes dental caries because of its uniquely efficient biofilm-forming abilities. Yet, other cariogenic species (*Prevotella*, for example) may also be present and driving disease processes.[22] In contrast, multiple *Lactobacillus* species have been shown to inhibit the growth of *S. mutan*s through multiple mechanisms, including interrupting the adherence and integrity of biofilm structures and downregulating virulence genes.[23]

An *ex vivo* model demonstrated that inulin caused a dose-dependent increase in the relative abundances of *Lactobacillus* and *Bifidobacterium* species in plaque specimens from donors with periodontitis. Additionally, inulin decreased the relative abundance of cariogenic bacteria, including *Streptococcus*, *Veillonella*, *Fusobacterium*, *Parvimonas*, and *Prevotella* species, and also reduced biofilm alpha diversity.[24] Furthermore, an *in vitro* analysis indicated that inulin from Chicory root could be utilized by both *Lactobacillus plantarum* and *Lactobacillus casei*, encouraging their growth, while it had no effect on *S. mutans*, suggesting it is not an acceptable nutrient for this cariogenic species.[25] Notably, *L. plantarum* has been found to disrupt biofilms from both *S. mutans* and *Candida albicans*, while surfactants from *L. casei* downregulate genes associated with *S. mutans* adhesion.[26,27]

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[21] Limeback, H., Enax, J., & Meyer, F. (2021). Biomimetic hydroxyapatite and caries prevention: a systematic review and meta-analysis. Canadian journal of dental hygiene : CJDH = Journal canadien de l'hygiene dentaire : JCHD, 55(3), 148–159.

[22] Baker, J. L., Morton, J. T., Dinis, M., et al. (2021). Deep metagenomics examines the oral microbiome during dental caries, revealing novel taxa and co-occurrences with host molecules. Genome research, 31(1), 64–74.

[23] 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.

[24] Colamarino, A. N., Johnson, T. M., Boudreaux, D. M., et al. (2023). Influence of Lactobacillus reuteri, Bifidobacterium animalis subsp. lactis, and prebiotic inulin on dysbiotic dental biofilm composition ex vivo. Journal of periodontology, 94(6), 793–804.

[25] Gupta, A., Mitra, R., Bandyopadhyay, P., et al. (2023). Role of Prebiotic Inulin extracted from chicory root in Oral care, In-vitro study. Indian Journal of Applied Microbiology. 25. 24-33.

[26] Zeng, Y., Fadaak, A., Alomeir, N., et al. (2022). Lactobacillus plantarum Disrupts S. mutans-C. albicans Cross-Kingdom Biofilms. Frontiers in cellular and infection microbiology, 12, 872012.

[27] Savabi, O., Kazemi, M., Kamali, S., et al. (2014). Effects of biosurfactant produced by Lactobacillus casei on gtfB, gtfC, and ftf gene expression level in S. mutans by real-time RT-PCR. Advanced biomedical research, 3, 231.

Althaea Officinalis (Marshmallow) root extract

Scientific Evidence:

Marshmallow root includes multiple bioactive compounds, including polysaccharides (mainly galacturorhamnans, arabinans, glucans, and arabinogalactan), tannins, volatile oil, pectin, flavonoids, phenolic acids, and asparagine.[28] The polysaccharides in Marshmallow root create a natural mucilage, a natural demulcent that acts as a bioadhesive to the oral epithelial mucosa, soothing irritated cells and protecting against inflammation. This bioadhesive polysaccharide layer provides shielding of the mucosal barrier against physical or microbial stress.[28]

Polyphenols in Marshmallow root extract may also shift the relative abundances of the oral microbiota and have been shown to inhibit the growth of several oral pathogens, including *Prevotella* spp., *Porphyromonas gingivalis,* and *Streptococcus pyogenes*. An *in vitro* analysis also suggests that Marshmallow root extract has antibacterial effects on *S. mutans*, though to a lesser degree than established antibiotics such as chlorhexidine (CHX) and penicillin.[29]

Ulmus Fulva (Slippery Elm) bark extract

Scientific Evidence:

Slippery elm also has demulcent properties, with polysaccharides that form a natural mucilage, and is often used to protect and support mucosal barrier function. Its polysaccharides are long linear chains of alternating D-galacturonic acid and L-rhamnose residues, as well as α-linkages of both galactose and 3-O-methyl galactose.[30] While largely used as a traditional medicine, slippery elm extract has also been shown to inhibit biofilm formation by *S. pyogenes*, the primary bacterial cause of pharyngitis.[31] As a component of herbal formulas, it is typically included for its suspected anti-inflammatory and mucus membrane soothing properties, likely via similar mechanisms attributed to the mucilage found in *Althaea Officinalis*.[32]

Sodium bicarbonate

Scientific Evidence:

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[28] Deters, A., Zippel, J., Hellenbrand, N., et al. (2010). Aqueous extracts and polysaccharides from Marshmallow roots (Althea officinalis L.): cellular internalisation and stimulation of cell physiology of human epithelial cells in vitro. Journal of ethnopharmacology, 127(1), 62–69.

[29] Haghgoo, R., Mehran, M., Afshari, E., et al. (2017). Antibacterial Effects of Different Concentrations of Althaea officinalis Root Extract versus 0.2% Chlorhexidine and Penicillin on Streptococcus mutans and Lactobacillus (In vitro). Journal of International Society of Preventive & Community Dentistry, 7(4), 180–185.

[30] Peterson, C. T., Sharma, V., Uchitel, S., et al. (2018). Prebiotic Potential of Herbal Medicines Used in Digestive Health and Disease. Journal of alternative and complementary medicine (New York, N.Y.), 24(7), 656–665.

[31] Wijesundara, N. M., & Rupasinghe, H. P. V. (2019). Bactericidal and Anti-Biofilm Activity of Ethanol Extracts Derived from Selected Medicinal Plants against Streptococcus pyogenes. Molecules (Basel, Switzerland), 24(6), 1165.

[32] Ried, K., Travica, N., Dorairaj, R., et al. (2020). Herbal formula improves upper and lower gastrointestinal symptoms and gut health in Australian adults with digestive disorders. Nutrition research (New York, N.Y.), 76, 37–51.

Sodium bicarbonate (baking soda) is often used as a component of dentifrices to aid in plaque removal, both by mechanical disruption of plaque by particles of sodium bicarbonate and by the inhibition of biofilm adhesion.[33] In addition to disrupting biofilm adhesion, sodium bicarbonate also neutralizes biofilm acids that cause demineralization, inhibits *S. mutans* growth, and dose-dependently increases salivary pH.[34,35] Bicarbonate is the principal buffer in the saliva, and a neutral pH or above reduces the cariogenicity of harmful species. Sodium bicarbonate also appears to have bactericidal effects against cariogenic species, along with tooth-whitening effects.[36,37,38]

In a pooled analysis of six studies and nearly 1,500 participants, sodium bicarbonate (67% w/w) was found to significantly improve gingival health and plaque control in people with mild-to-moderate gingivitis at all tooth sites when used twice per day (brushing).[39] A six-month randomized and controlled trial conducted among nearly 250 adults with moderate gingivitis suggests that brushing twice per day with a toothpaste containing sodium bicarbonate reduced gingival bleeding and plaque compared to controls (toothpaste without sodium bicarbonate).[40]

L-arginine

Scientific Evidence:

The amino acid L-arginine is hydrolyzed by the bacterial arginine deiminase system (ADS) pathway, producing ammonia as well as citrulline, ornithine, CO2, and ATP. The net effect of the metabolism of L-arginine by ADS is an increase in salivary pH and an inhibition of biofilm formation by *S. mutans*, reducing cariogenic activity.[41,42] Multiple studies indicate that reduced ADS activity and subsequent decreases in ammonia production are associated with an increased risk of developing

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[33] Putt, M. S., Milleman, K. R., Ghassemi, A., et al. (2008). Enhancement of plaque removal efficacy by tooth brushing with baking soda dentifrices: results of five clinical studies. The Journal of clinical dentistry, 19(4), 111–119.

[34] Zero D. T. (2017). Evidence for biofilm acid neutralization by baking soda. Journal of the American Dental Association (1939), 148(11S), S10–S14.

[35] Silhacek, K. J., & Taake, K. R. (2005). Sodium bicarbonate and hydrogen peroxide: the effect on the growth of Streptococcus mutans. Journal of dental hygiene : JDH, 79(4), 7.

[36] Legier-Vargas, K., Mundorff-Shrestha, S. A., Featherstone, J. D., et al. (1995). Effects of sodium bicarbonate dentifrices on the levels of cariogenic bacteria in human saliva. Caries research, 29(2), 143–147.

[37] Madeswaran, S., & Jayachandran, S. (2018). Sodium bicarbonate: A review and its uses in dentistry. Indian journal of dental research : official publication of Indian Society for Dental Research, 29(5), 672–677.

[38] Kleber, C. J., Moore, M. H., & Nelson, B. J. (1998). Laboratory assessment of tooth whitening by sodium bicarbonate dentifrices. The Journal of clinical dentistry, 9(3), 72–75.

[39] Parkinson, C. R., Butler, A., & Ling, M. R. (2023). Antigingivitis efficacy of a sodium bicarbonate toothpaste: Pooled analysis. International journal of dental hygiene, 21(1), 106–115.

[40] Akwagyiram, I., Amini, P., Bosma, M. L., et al. (2018). Efficacy and Tolerability of Sodium Bicarbonate Toothpaste in Subjects with Gingivitis: A 6-Month Randomized Controlled Study. Oral health & preventive dentistry, 16(5), 401–407.

[41] Huang, X., Zhang, K., Deng, M., et al. (2017). Effect of arginine on the growth and biofilm formation of oral bacteria. Archives of oral biology, 82, 256–262.

[42] Nascimento M. M. (2018). Potential Uses of Arginine in Dentistry. Advances in dental research, 29(1), 98–103.

caries.[43] In a systematic review and meta-analysis of seven studies, both salivary and plaque ADS activity were found to be predictive of caries risk.[44] Furthermore, increasing the capacity of oral microbiota to neutralize biofilm pH through upregulation of ADS activity may prevent caries development and progression.[45]

Some bacterial species possess ADS activity, such as *S. gordonii* and *S. sanguinis* (*S. mutans* does not), and adding L-arginine has been shown to increase the abundance of ADS-producing strains, having a prebiotic-like effect.[46,47] For example, a small clinical trial found that people without caries at baseline were more likely to have higher ADS activity, but the use of an arginine-containing toothpaste (compared to a fluoride-based toothpaste) increased the ADS activity of people with dental caries at baseline, shifting their oral microbiota to more closely resemble caries-free participants.[48] Adding arginine to toothpaste was also shown to reduce lactic acid production from *in situ* plaques as part of a small but randomized and controlled, double-blind crossover study.[49]

Galactoarabinan (*Larix* spp. bark)

Scientific Evidence:

Galactoarabinan (aka arabinogalactan) is a long and branched, non-starch polysaccharide extracted from the Larch tree (*Larix* spp.), comprised of linkages between galactose and arabinose monosaccharides. Galactoarabinan is characterized as a prebiotic, digested primarily by gut microbiota, with some evidence for immunomodulation achieved at least in part by increasing production of short-chain fatty acids such as butyrate, acetate, and propionate.[50,51] While the majority of metabolism likely takes place in the proximal and distal colon, galactoarabinan is known to be an energy source for beneficial bacterial species, including *Bifidobacterium longum*.[52] Furthermore, arabinose (a

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[43] Nascimento, M. M., Gordan, V. V., Garvan, C. W., et al. (2009). Correlations of oral bacterial arginine and urea catabolism with caries experience. Oral microbiology and immunology, 24(2), 89–95.
[44] Bijle, M. N. A., Yiu, C. K. Y., & Ekambaram, M. (2018). Can oral ADS activity or arginine levels be a caries risk indicator? A systematic review and meta-analysis. Clinical oral investigations, 22(2), 583–596.
[45] Nascimento, M. M., Alvarez, A. J., Huang, X., et al. (2019). Metabolic Profile of Supragingival Plaque Exposed to Arginine and Fluoride. Journal of dental research, 98(11), 1245–1252.
[46] Eick, S., & Lussi, A. (2021). Arginine: A Weapon against Cariogenic Biofilm?. Monographs in oral science, 29, 80–90.
[47] Koopman, J. E., Hoogenkamp, M. A., Buijs, M. J., et al. (2017). Changes in the oral ecosystem induced by the use of 8% arginine toothpaste. Archives of oral biology, 73, 79–87.
[48] Nascimento, M. M., Browngardt, C., Xiaohui, X., et al. (2014). The effect of arginine on oral biofilm communities. Molecular oral microbiology, 29(1), 45–54.
[49] Xue, Y., Lu, Q., Tian, Y., et al. (2017). Effect of toothpaste containing arginine on dental plaque-A randomized controlled in situ study. Journal of dentistry, 67, 88–93.
[50] Sun, Y., Hu, J., Zhang, S., et al. (2021). Prebiotic characteristics of arabinogalactans during in vitro fermentation through multi-omics analysis. Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association, 156, 112522.
[51] Dion, C., Chappuis, E., & Ripoll, C. (2016). Does larch arabinogalactan enhance immune function? A review of mechanistic and clinical trials. Nutrition & metabolism, 13, 28.
[52] Fujita, K., Sakamoto, A., Kaneko, S., et al. (2019). Degradative enzymes for type II arabinogalactan side chains in Bifidobacterium longum subsp. longum. Applied microbiology and biotechnology, 103(3), 1299–1310.

monosaccharide component in galactoarabinan) has been shown to significantly inhibit the biofilm formation of several oral pathogens *in vitro*, including *Porphyromonas gingivalis*, *Fusobacterium nucleatum*, and *Streptococcus oralis*.[53]

Vaccinium Macrocarpon (Cranberry) fruit extract

Scientific Evidence:

Cranberry fruit extracts provide a rich source of many bioactive polyphenols that have demonstrated potential to prevent caries and periodontal disease, including flavonols, proanthocyanidins (PACs), and, to a lesser extent, anthocyanins.[54] Cranberry flavonols and PACs have been shown to inhibit key virulence enzymes produced by *S. mutans* needed for the synthesis of biofilms, glycolysis, bacterial adhesion, and a proton pump that protects acid-sensitive glycolytic bacterial enzymes (glycosyltransferases B and C, and F-ATPase).[55,56] For example, an *in vivo* experimental study indicated that topical application of cranberry PACs reduced biofilm mass in the context of a high-sucrose diet, as well as the incidence and severity of caries on smooth and sulcal surfaces. This same study also published *in vitro* inhibition of *S. mutans* biofilm formation by cranberry PACs, along with reduced acidogenicity within the biofilms.[57] Cranberries contain high amounts of a specific type of PAC, an A-linked PAC, with much more biological activity than PACs found in other fruits, such as blueberries.[58,59]

A systematic review of 22 studies evaluating the *in vitro* use of PACs from cranberry and grape seep extract concluded that these compounds may help reduce the growth, virulence, and colonization of *S. mutans* by inhibiting the synthesis of insoluble glucans (needed for biofilm formation), inhibiting proton-translocating F-ATPase activity, and disrupting acidogenesis.[60] *In vitro* data also suggests

[53] An, S. J., Namkung, J. U., Ha, K. et al. (2022). Inhibitory effect of d-arabinose on oral bacteria biofilm formation on titanium discs. Anaerobe, 75, 102533.
[54] Philip, N., & Walsh, L. J. (2019). Cranberry Polyphenols: Natural Weapons against Dental Caries. Dentistry journal, 7(1), 20.
[55] Duarte, S., Gregoire, S., Singh, A. Pet al. (2006). Inhibitory effects of cranberry polyphenols on formation and acidogenicity of Streptococcus mutans biofilms. FEMS microbiology letters, 257(1), 50–56.
[56] Gregoire, S., Singh, A. P., Vorsa, N., et al. (2007). Influence of cranberry phenolics on glucan synthesis by glucosyltransferases and Streptococcus mutans acidogenicity. Journal of applied microbiology, 103(5), 1960–1968.
[57] Koo, H., Duarte, S., Murata, R. M., et al. (2010). Influence of cranberry proanthocyanidins on formation of biofilms by Streptococcus mutans on saliva-coated apatitic surface and on dental caries development in vivo. Caries research, 44(2), 116–126.
[58] Howell, A. B., Reed, J. D., Krueger, C. G., et al. (2005). A-type cranberry proanthocyanidins and uropathogenic bacterial anti-adhesion activity. Phytochemistry, 66(18), 2281–2291.
[59] Feng, G., Klein, M. I., Gregoire, S., et al. (2013). The specific degree-of-polymerization of A-type proanthocyanidin oligomers impacts Streptococcus mutans glucan-mediated adhesion and transcriptome responses within biofilms. Biofouling, 29(6), 629–640.
[60] Castellanos, J. S., Betancourt, D. E., Díaz-Báez, D., & Baldión, P. A. (2024). Effect of flavonoids from grape seed and cranberry extracts on the microbiological activity of Streptococcus mutans: a systematic review of in vitro studies. BMC oral health, 24(1), 662.

cranberry extract disrupts the architecture of dual-species biofilms, specifically *S. mutans* and *C. albicans*.[61]

Other Ingredients

Sorbitol

Sorbitol is a commonly used polyol in toothpaste formulation.[62] It is primarily used as a humectant to prevent moisture loss and to improve the consistency of toothpaste.[63] In addition, sorbitol acts as a primary or secondary sweetener in toothpaste.[72] Sorbitol has approximately 60 percent of the sweetness of sucrose and is used as a standard sweetener in numerous pharmaceutical products as well as in sugar-free chewing gums.[64] S. mutans cannot use sorbitol for glucan or fructan synthesis, and thus sorbitol has a limited effect on acid production compared to sucrose, glucose, and fructose. Additionally, in the absence of other sugars, sorbitol interrupts the biofilms of both S. mutans and Candida albicans.[65]

Glycerin

Glycerin is used in toothpaste formulations as a humectant to prevent drying out and subsequent hardening of the paste.[72,66] Glycerin is also used as a sweetener in toothpaste to improve flavor.[72,75]

Sodium lauroyl sarcosinate

Sodium lauroyl sarcosinate is a surfactant and is used in toothpaste formulations as a foaming agent to enhance the cleaning effect. Surfactants act by lowering surface tension to solubilize substances, thereby allowing penetration and loosening of surface deposits and plaque dissolution, which makes it easier to clean teeth. Surfactants also aid in dispersing the flavor in toothpaste. Sodium lauroyl sarcosinate has emerged as a safe alternative to other surfactants that may irritate the oral mucosa.[75,67]

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Cellulose gum (carboxymethylcellulose)

Cellulose gum, also known as carboxymethyl cellulose, is derived from plant cell walls and used in toothpaste formulations as a binder. Binding agents are hydrophilic colloids that prevent the separation of the dry and liquid toothpaste components. They also provide viscoelasticity and form to the paste. By binding water, cellulose gum also helps prevent the paste from drying out. Cellulose gum has FDA GRAS status, with well-recognized safety.[75,76,68]

Mixed tocopherols

Mixed tocopherols (vitamin E) are fat-soluble antioxidants that neutralize reactive oxygen species, specifically by quenching reactive singlet oxygen, hydroxyl radicals, and reactive nitrogen species.[69] These vitamin E isomers help protect against peroxidation, particularly when combined with other antioxidants such as ascorbic acid. Ascorbic acid returns tocopherols to a reduced state, effectively renewing their antioxidant potential.[70] For this reason, tocopherols are widely used as antioxidants in many pharmaceuticals, cosmetics, natural supplements, etc., acting to preserve the integrity and prevent the deterioration of other substances.[71] Additionally, the use of tocopherol-containing toothpaste has been shown to enrich the tocopherol levels of gingival tissues.[72]

Carbomer

Carbomer is frequently used in toothpaste as a binding or thickening agent. A polymer of cross-linked polyacrylic acid, its versatility as a gelling agent and well-established safety record has led to its use in a variety of cosmetics, pharmaceuticals, and food products.[73]

Natural flavors, Aqua (deionized water)

Natural mint flavor is sourced from mint leaves and/or anise extracts.

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Overall Safety Summary

The ingredients in Dentalmin PRO™ have an excellent safety record when used as recommended, though should be avoided in individuals with a known sensitivity to any of the ingredients. Both nano- and micro-hydroxyapatite have been used in multiple trials with no safety concerns reported and may be considered as an alternative in those at high risk of fluorosis, as no dose-related toxicities have been observed.[20,74,75,76] No known contraindications exist for the ingredients in Dentalmin PRO™ aside from known hypersensitivity reactions, such as allergy to *Vaccinium* species.[37,77,78,79,80,81,82]

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