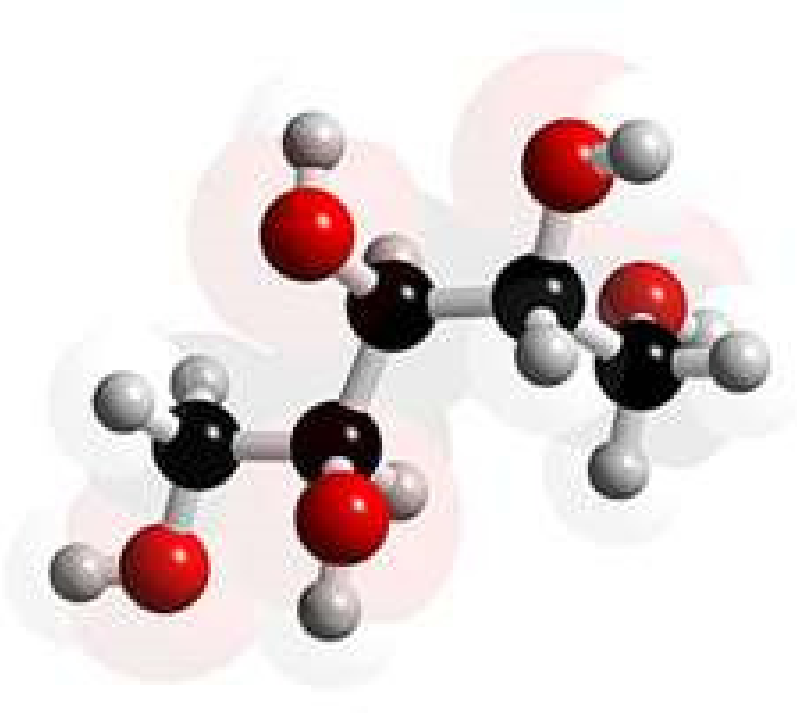
2010

Topical, Annotated Xylitol References



John N. Peldyak

Advanced Developments

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Topical, Annotated Xylitol References

Books

B. L. Horecker, K. Lang, Y. Takagi (eds), *International symposium on metabolism, physiology and clinical uses of pentoses and pentitols* Springer-Verlag, Berlin, 1969.

Proceedings of symposium held in Hakone, Japan August 27-29, 1967. Includes information about xylitol before major dental benefits were demonstrated.

H. L. Sipple, K. W. McNutt (eds) *Sugars in Nutrition* Academic Press, New York 1974.

Xylitol featured in several sections including: Sugars in foods, recent technological developments, digestion and absorption of sugars, metabolism of sugars, diabetes, therapeutic use of sugars, and sugars in the oral cavity.

A. Scheinin, K.K. Mäkinen (eds) *The Turku Sugar Studies, I-XXI* Acta Odontologica Scandinavia, vol. 33, supplement 70, 1975.

The classic series of investigations which revealed the remarkable potential of xylitol.

J. N. Counsell (ed) *Xylitol* Applied Science, London, 1977.

Collects and updates xylitol findings at an International Symposium in London, May 5, 1977. Includes discussions of xylitol as a new ingredient along with biochemical and dental aspects of xylitol.

K. K. Mäkinen, *Biochemical principles of the use of xylitol in medicine and nutrition with special consideration of dental aspects* Birkhäuser Verlag, Basel, 1978.

This monograph details virtually all xylitol-related research published before 1978 on dental caries, oral microbiology, human physiology, and animal and human nutrition.

J. J. Hefferen, H. M. Koehler (eds) *Foods, Nutrition and Dental Health* Pathotox Publishers, Park Forest South, IL 1981.

Contains interesting background "discussions" including insights into the original xylitol programs.

W. J. Loesche, *Dental Caries, a Treatable Infection* University of Michigan, 1987.

"*S. mutans* and *L. casei* can ferment sorbitol and mannitol (sweeteners in sugar-free gum) but are inactive towards xylitol. Xylitol is comparable to sucrose in sweetness and has been shown to be noncariogenic, possibly anticariogenic."

I. D. Mandel (chairman), *Dental Dialogue -- Caries Prevention with Xylitol* (synopsis of symposium held at University of Michigan) Medec Communications, Oradell NJ 1988.

"Clearly, xylitol exhibits more dental benefits than any other sweetener.

We are talking about xylitol not as a sole preventive agent but as an agent used in conjunction with available preventive services."

T. H. Grenby (ed) *Progress in Sweeteners* Elsevier Applied Science, London, 1989.

Includes sections on dental considerations and xylitol in caries limitation.

A. J. Rugg-Gunn (ed) *Sugarless, the Way Forward: Proceedings of an International Symposium Held at the University of Newcastle at Tyne, U.K.* Elsevier Applied Science, London, September 1991.

General information about sugar substitution along with some specific topics such as sweeteners in children's medications, mostly from the British and European regulatory perspective.

N. Kretchmer, C. B. Hollenbeck (eds) *Sugars and Sweeteners* CRC Press, London 1991.

See chapters 8-10.

A. J. Rugg-Gunn, (with) A. F. Hackett, *Nutrition and Dental Health* Oxford University Press, 1993.

"There is no doubt that xylitol is the most expensive sweetener (about ten times more expensive than sucrose)."

J. N. Peldyak, *Sweet Smart – Xylitol* Advanced Developments, MI, 1996.

Focuses on dental aspects of sugars and sweeteners with practical consumer advice on xylitol use.

A. J. Rugg-Gunn, J. H. Nunn, *Nutrition, Diet and Oral Health* Oxford University Press, 1999.

"The reduction of caries prevalence in Finnish children is not likely to be fully explained exclusively in terms of fluorides and improved oral hygiene. In Finland, the widespread use of xylitol as a sweetener may have been a factor in the improvement of dental health."

L. O'Brien Nabors (ed) *Alternative Sweeteners* Marcel Dekker, NY, 2001.

Contains sections on individual sweeteners, including xylitol, and potential mixed sweetener blends with xylitol.

K. Edwards, *Sweeten your Life the Xylitol Way* Armour & Armour (dsgn), Nashville, 2003.

Cookbook utilizes xylitol in recipes.

J. V. Wright, L. Lenard, *Xylitol – Dental and Upper Respiratory Health* Dragon Art, WA, 2003.

Provides overview for dental and upper respiratory benefits of xylitol.

F. Gare, *The Sweet Miracle of Xylitol* Basic Health Publications, North Bergen, NJ, 2003.

Describes xylitol as a healthy sugar alternative; provides suggested uses with recipes.

H. Mitchell, *Sweeteners and Sugar Alternatives in Food Technology* Wiley-Blackwell, 2006.

"Xylitol" section by M. Bond and N. Dunning, pp. 295-317.

E. Phillips, *Kiss Your Dentist Goodbye: a do-it-yourself mouth care system* Greenleaf, Austin TX, 2010.

"The first step my preventive program involves getting rid of damaging mouth bacteria by using xylitol."

L. Jones, *No more allergies, asthma, or sinus infections… The revolutionary approach to eliminating upper respiratory problems without drugs* Freedom Press, 2010.

"Xylitol is like soap for the nose, and a soap that can be used regularly and easily."

General and Review Articles

G. E. Demetrakopoulos, H. Amos, "Xylose and xylitol – metabolism, physiology and nutritional value," *World Review of Nutrition and Dietetics* vol. 32, pp. 96-122, 1978.

"Their (xylose and xylitol) known effects in prevention, maintenance, and therapy of a variety of pathologic conditions could prove them unique among the rest of the dietary carbohydrates. …To this end (xylose or xylitol) with other carbohydrates may be superior to the current refined dietetic sugars."

M. T. Smits, *Xylitol and dental caries*, Academic dissertation, University of Groningen, Amsterdam, The Netherlands, 1987.

Describes xylitol's role in reducing demineralization and enhancing remineralization.

A. Bär, "Caries prevention with xylitol," *World Review of Nutrition and Dietetics* vol. 55, pp. 1-27, 1988.

"Xylitol may be regarded as the best of all nutritive sugar substitutes with respect to caries prevention. It is concluded that partial sugar substitution by xylitol is a powerful tool in preventing caries and should be considered together with fluoridation and oral hygiene measures as an equally important factor in the maintenance of individual oral health."

B. R. Ashpole, "Caries prevention with xylitol," *Journal of the Canadian Dental Association* vol. 55, no. 9, pp. 713-714, September 1989.

Xylitol has a favorable influence on all of the major factors involved in tooth decay.

F. A. Toors, "Chewing gum and dental health," *Revue Belge de Medecine Dentaire* vol. 47, pp. 67-92, 1992.

There are no concerns with any harmful adaptations to long-term xylitol use.

D. Birkhed, "Cariologic aspects of xylitol and its use in chewing gum: a review," *Acta Odontologica Scandinavica*, vol. 52, no. 2, pp. 116–127, 1994.

"Chronic consumption of xylitol-sweetened chewing gum resulted in reduction of dental plaque, suppression of mutans streptococci, and reduced adhesiveness of plaque."

W. H. Bowen, "Food components and caries," *Adv Dent Res* vol. 8, no. 2, pp. 215-220, July 1994.

Replacing sugar in foods with xylitol may lead to a reduction of dental caries.

J. Tanzer, "Xylitol chewing gum and dental caries," *The International Dental Journal*, vol. 45, supplement 1, pp. 65–76, 1995.

"The literature not only supports the conclusion that xylitol is non-cariogenic but it is now strongly suggestive that xylitol is caries-inhibitory, that is, anti-cariogenic."

L. Trahan, "Xylitol: a review of its action on mutans streptococci and dental plaque—its clinical significance," *The International Dental Journal*, vol. 45, supplement 1, pp. 77–92, 1995.

I. D. Mandel, "Caries prevention – current strategies, new directions," *Journal of the American Dental Association*, vol. 127, pp. 1477-1488, October 1996.

"The aggregate caries increment may now be higher in the over-55 age group than in children.

The most promising dietary approach on the current scene is the use of the nonacidogenic sweetener xylitol. The evidence is accumulating that the benefits of xylitol extend beyond 'does not promote tooth decay' to acting as a cariostatic agent."

A. A. Scheie, O. B. Fejerskov, "Xylitol in caries prevention: what is the evidence for clinical efficacy?" *Oral Dis,* vol. 4, no. 4, 1998.

"Essentially all clinical studies concerning the effect of xylitol on caries development consent to its non-cariogenicity and to the beneficial effect of substituting sucrose with xylitol in chewing gums and sweets. However, claims of anti-caries or therapeutic effects, and superiority of xylitol over other polyols are still to be confirmed by well designed and conducted studies from independent research groups."

W. M. Edgar, "Sugar substitutes, chewing gum and dental caries—a review," *British Dental Journal*, vol. 184, no. 1, pp. 29–32, 1998.

"Xylitol's antibacterial properties seem likely to lead to caries reductions superior to the more modest reductions with sorbitol gum."

R. S. Levine, "Briefing paper: xylitol, caries and plaque," *British Dental Journal*, vol. 185, no. 10, p. 520, 1998.

"Xylitol has a clear advantage over sorbitol and all other bulk and intense sweeteners. It is the only one to show both passive and active anti-caries effects."

E. Crates, M. Pilling, R. Rowe (eds), "Xylitol: Something to smile about," *Functional Foods and Nutraceuticals,* vol. 2, no. 11, December 1999.

"Increasing interest in xylitol's dental benefits provided the commercial incentive necessary for large-scale production" (which began in 1975 using birchwood as a source).

C. Hayes, "The effect of non-cariogenic sweeteners on the prevention of dental caries: a review of the evidence," *Journal of Dental Education*, vol. 65, no. 10, pp. 1106–1109, 2001.

"These studies demonstrated a consistent decrease in dental caries, ranging from 30 to 60 percent, among subjects using sugar substitutes. The highest caries reductions were observed in subjects using xylitol.

Furthermore, since the evidence suggests a strong caries protective effect of xylitol, it would be unethical to deprive subjects of its potential benefits."

J. N. Peldyak, K. K. Mäkinen, "Xylitol for caries prevention," *Journal of Dental Hygiene*, vol. 76, no. 4, pp. 276–285, 2002.

"Although underutilized and often overlooked, xylitol use is compatible with and complementary to current oral hygiene recommendations. Xylitol is not a panacea, but is a practical and effective adjunct to "state of the art" caries prevention programs."

G. Livesey, "Health potential of polyols as sugar replacers, with emphasis on low-glycemic properties," *Nutrition Research Reviews,* vol. 16, pp. 163-191, 2003.

Polyols are in general toothfriendly, low-glycemic, low- insulinemic, help reduce overall glycemic load, and contribute to healthy colonic environment and function.

This is the best article to find comparative glycemic discussions.

A. Maguire, A. J. Rugg-Gunn, "Xylitol and caries prevention – is it a magic bullet?" *British Dental Journal*, vol. 194, no. 8, pp. 429–436, 2003.

"Xylitol exhibits dental benefits which are superior to other polyols in all areas where polyols have been shown to have an effect."

J. Peldyak, "Xylitol: sweet and good for teeth," *Christina's Living Healthy Journal* vol. 6, no. 1, 2004.

"Xylitol works very nicely in place of sugar to lightly sweeten tea and herbal teas, instantly creating an effective mouth rinse that is safe to swallow."

S. Gutkowski, "X marks the spot," *Contemporary Oral Hygiene* vol. 5, no. 5, pp. 10-13, 2005.

"Xylitol can and does take the burden of biofilm reduction off the person with the teeth. Everyone can eat a couple pieces of candy a day, even if they cannot motivate themselves to brush and floss."

M. Rothen, "The wonder of xylitol," *Dimensions of Dental Hygiene* pp.18-20, October 2005.

Reduction of MS by xylitol is related to sufficient amount (6 to 10 grams per day), and with increasing frequency of administration (3 or more uses per day).

B. A. Burt, "The Use of Sorbitol- and Xylitol-sweetened Chewing Gum in Caries Control." *Journal of the American Dental Association* vol. 137; pp. 190–196, February 2006.

"The evidence is strong enough to support the regular use of xylitol-sweetened gum as a way to prevent caries, and it can be promoted as a public-health preventive measure."

S. N. Beebe, The expanding utility of xylitol," *Dimensions of Dental Hygiene* pp.34-36, October 2006.

"Xylitol may not only be useful in caries reduction. New benefits are being discovered ranging from children with acute otitis media to elderly people with candidiasis."

S. Mickenautsch, S. C. Leal, V. Yengopal, A. C. Bezerra, V. Cruvinel, "Sugar-free chewing gum and dental caries—a systematic review," *Journal of Applied Oral Science*, vol. 15, no. 2, pp. 83–88, 2007.

"The evidence suggests that sugar-free chewing gum has a caries-reducing effect."

T. E. O'Hehir, "Beyond brushing & flossing," *Hygienetown* pp. 9-12, June 2008.

"The United States has been slow in realizing and promoting the benefits of xylitol as a supplement to brushing and flossing. Adding at least five grams of xylitol, five times daily is a good idea for everyone, not just those at risk of caries."

P. Lif Holgerson, "Xylitol and its effect on oral ecology," Umeå University Odontological Dissertations (Sweden), no. 97, 2007.

"Xylitol-containing products gave elevated concentrations of xylitol in saliva and dental plaque for at least 8 minutes after intake. …A 6g daily dose of xylitol reduced dental plaque and lactic acid production in saliva in schoolchildren after chewing for 4 weeks."

A. Deshpande, A. R. Jadad, "The impact of polyol-containing chewing gums on dental caries: a systematic review of original randomized controlled trials and observational studies," *Journal of the American Dental Association*, vol. 139, no. 12, pp. 1602–1614, 2008.

"We conclude from our quantitative systematic review of the available research that there is consistent evidence to support the use of xylitol- and sorbitol-containing chewing gum as part of normal oral hygiene to prevent dental caries." Xylitol gave the best results, followed by xylitol-sorbitol mixtures.

S. Twetman, "Consistent evidence to support the use of xylitol- and sorbitol-containing chewing gum to prevent dental caries," *The Journal of Evidence-Based Dental*, vol. 10, pp. 10–11, 2009.

"Although research gaps exist, particularly on optimal dosing and relative polyol efficacy, there is consistent evidence to support the use of xylitol- and sorbitol-containing chewing gum as part of normal oral hygiene to prevent dental caries."

It was noted that a sweetener blend of sorbitol and mannitol was *not* effective.

E. Söderling, "Controversies around xylitol," *European Journal of Dentistry,* vol. 3, no. 2, pp. 81-82, April 2009.

"Critical evaluation of the existing literature is a positive goal, but if it leads to a situation where no treatment guidelines can be given, something is wrong. This also applies to xylitol studies. …Xylitol is a useful adjunct to traditional methods for caries control and prevention."

S. Berger, "The many sides of xylitol," *Hygiene Tribune,* vol. 3, no. 5, May 2010.

"Xylitol was once only found in health food stores, however, it has become much more mainstream and is now readily available at retail outlets."

K. K. Mäkinen, "Sugar alcohols, caries incidence, and remineralization of caries lesions: a literature review," *International Journal of Dentistry*, vol. 2010, doi:10.1155/2010/981072, ID 981072, 23 pp, 2010.

"The scientific and clinical information available today indicates that habitual use of xylitol can be associated with significant reduction in the incidence of dental caries and with remineralization of both enamel and dentin caries lesions."

Acid

D. Edwardsson, D. Birkhed, "Acid production from xylitol by oral streptoccoci and lactobacilli," *Acta Odont Scandinavia* vol. 35, pp. 257-263, 1977.

Only minor subspecies of *L. salivarius* and *S. avium* were able to metabolize xylitol, and no tooth-damaging lactic acid was produced.

N. Sasaki, V. Topitsoglou, G. Frostell, "Effects of xylitol on the acid production activity from sorbitol by Streptococcus mutans and human dental plaque," *Swedish Dental Journal,* vol. 7, no. 4, pp. 153-160, 1983.

Xylitol had an inhibitory effect on acid production from sorbitol by MS or plaque.

C. Vadeboncoeur, L. Trahan, C. Mouton, D. Mayrand, "Effect of xylitol on the growth and glycolysis of acidogenic oral bacteria," *Journal of Dental Research* vol. 62, no. 8, pp. 882-884, 1983.

"Xylitol inhibited the growth of all but one of ten strains of *S. mutans*. …However, the rate of acid production of the *S. mutans* strains was not equally affected by xylitol."

E. Söderling, J. Talonpoika, K. K. Mäkinen, "Effect of xylitol-containing carbohydrate mixtures on acid and ammonia producton in suspensions of salivary sediment," *Scandinavian Journal of Dental Research,* vol. 95, no. 5, pp. 405-410, 1987.

Xylitol inhibits acid production when used alone or in mixtures with slowly fermentable carbohydrates like sorbitol or HSH.

M. Rekola, "Acid production from xylitol products," *Proceedings of the Finnish Dental Society,* vol. 84, pp. 39-44, 1988.

100% xylitol-sweetened products without any added acids yield the best pH plaque response.

B. G. Bibby, J. Fu, "Changes in plaque pH in vitro by sweeteners," *Journal of Dental Research,* vol. 64, no. 9, pp. 1130-1133, 1989.

There was negligible acid production with aspartame, saccharine, or xylitol. Xylitol gave better results with increasing concentration.

O. Aguirre-Zero, D. T. Zero, H. M. Proskin, "Effect of chewing xylitol chewing gum on salivary flow rate and the acidogenic potential of dental plaque," *Caries Research*, vol. 27, no. 1, pp. 55–59, 1993.

After a sucrose rinse, xylitol gum users had oral pH that was significantly less acidic than no gum, sucrose gum or sorbitol gum chewers. Salivary stimulation was not responsible for the pH effects.

S. Twetman, C. Stecksén-Blicks, "Effect of xylitol-containing chewing gums on lactic acid production in dental plaque from caries-active pre-school children," *Oral Health Preventive Dentistry* vol. 1, no. 3, pp. 195-199, 1993.

A 14-day use of xylitol gum (5 grams of xylitol per day) significantly reduced lactic acid concentration. Sorbitol gum had no effect.

V. Topitsoglou, "Acid production from bread containing xylitol or sorbitol or sucrose in suspensions of human dental plaque," *Hellenic Dental Journal* vol. 4, pp. 51-54, 1994.

Unsweetened wheat bread caused as much acid production as a sucrose solution; xylitol bread produced the least acid.

"The results indicated that wheat bread is fermentable by plaque bacteria. Addition of xylitol reduced the acid production from bread by about 30%."

K. K. Park, B. R. Schemehorn, G. K. Stookey, H. H. Butchko, P. G. Sanders, "Acidogenicity of high-intensity sweeteners and polyols," *American Journal of Dentistry* vol. 8, no. 1, pp. 23-26, February 1995.

Aspartame, saccharin, acesulfame-K (high-intensity sweeteners) and xylitol were all non-acidogenic. Both sucrose and fructose were highly acidogenic.

K. K. Park, D. Hernandez, B. R. Schemehorn, B. P. Katz, G. K. Stookey, P. G. Sanders, H. H. Butchko, "Effect of chewing gums on plaque pH after a sucrose challenge," *Journal of Dentistry for Children,* pp. 180-186, May-June 1995.

All sugar-free gums helped reduce acid production after a sucrose sugar rinse. Xylitol gave the best response, followed by paraffin.

H. Kakuta, Y. Iwami, H. Mavanagi, N. Takahashi, "Xylitol inhibition of acid production and growth of mutans Streptococci in the presence of various dietary sugars under strictly anaerobic conditions," *Caries Research,* vol. 37, no. 6, pp. 404-409, 2003.

"Xylitol decreases the growth and acid production of mutans streptococci in the presence of various dietary sugars except fructose."

H. Miyasawa-Hori, S. Aizawa, N. Takahashi, "Difference in the xylitol sensitivity of acid production among Streptococcus mutans strains and the biochemical mechanism," *Oral Microbiol Immunol,* vol. 21, no. 4, pp. 201-205, August 2006.

Xylitol reduces acid production in different strains of *S. mutans* to different degrees by different biochemical mechanisms, such as disruption of glucose cell-wall transport or intracellular glycolysis.

J. D. Ruby, K.-L. Hsu, S. Momeni, D. Denney, R. Osgood, A. P. Dasanayake, "Effect of xylitol on Streptococcus mutans acid production and growth," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

Cell suspensions remained above pH 6 in the presence of xylitol. Glucose added to xylitol reduced the pH levels, but increased concentrations of xylitol did slow MS growth.

Biofilm; Dental Plaque; Bacteria

C. Mouton, A. Scheinin, K. K. Mäkinen, "Effect of a xylitol chewing gum on plaque quantity and quality," *Acta Odontologica Scandinavia* vol. 33, pp. 251-257, 1975.

The xylitol group had a lower plaque index, 40% less plaque, and lower invertase plaque activity than the sucrose group.

J. M. Wood, "An investigation of the effect of xylitol on the production of polysaccharide from sucrose by *Streptococcus mutans,*" Report on special project P506, pp. 1-9, 1977.

Polysaccharide exposed to xylitol was more water-soluble and the structure was more amorphous and granular. This could make dental plaque looser and less adhesive.

G. Frostel, "Behaviour of xylitol in isolated plaque," in *Xylitol,* J. N. Counsel (ed) Applied Science Publishers, Ltd. London, pp. 133-138, 1977.

"There was no adaptation to fermentation of xylitol after three months' frequent consumption of the substance."

E. M. Plüss, "Effect on plaque growth of xylitol- and sucrose-containing chewing gums," *Journal of Clinical Periodontology,* vol. 5, no. 1, pp. 35-40, February 1978.

Subjects using xylitol gum developed less plaque than those who chewed sucrose gum or a flavored gum base.

T. H. Grenby, A. H. Bashaarat, K. H. Gey, "A clinical trial to compare the effects of xylitol and sucrose chewing gums on dental plaque growth," *British Dental Journal*, vol. 152, no. 10, pp. 339–343, 1982.

There was significantly less plaque in the xylitol group than the sucrose or plain gum base groups.

V. Topitsoglou, D. Birkhed, L.-A. Larsson, G. Frostell, "Effect of chewing gums containing xylitol, sorbitol, or a mixture of xylitol and sorbitol on plaque formation, pH changes and acid production in human dental plaque," *Caries Research,* vol. 17, pp. 369-378, 1983.

Xylitol gum chewers had less plaque and acid formation than other groups.

H. Tuompo, J. H. Meurman, K. Lounatmaa, J. Linkola, "Effect of xylitol and other carbon sources on the cell wall of *Streptococcus mutans*," *Scandinavian Journal of Dental Research*, vol. 91, no. 1, pp. 17–25, 1983.

Xylitol caused distinct alterations in bacterial ultrastructure.

S. Wåler, S. Assev, G. Rölla, "Metabolism of xylitol in dental plaque," *Scandinavian Journal of Dental Research*, vol. 93, pp. 218–221, 1983.

Suggests a buildup within plaque cells of xylitol metabolites inhibits glycolysis.

S. Assev, G. Rölla, "Further studies on the growth inhibition of *Streptococcus mutans* OMZ 176 by xylitol," *Acta Pathologica, Microbiologica et Immunologica Scandinavica* vol. 94, pp. 97-102, 1986.

Demonstrates a "futile energy cycle" of MS phosphorylating, dephosphorylating and expelling xylitol, or having phosphorylated xylitol build up to toxic levels within MS cells.

E. Söderling, K. K. Mäkinen, C.-Y. Chen, H. R. Pape Jr., W. Loesche, and P.-L. Mäkinen, "Effect of sorbitol, xylitol, and xylitol/sorbitol chewing gums on dental plaque," *Caries Research*, vol. 23, pp. 378–384, 1989.

Using xylitol chewing gum significantly lowered plaque weight and increased pH; sorbitol gum increased plaque weight and lowered pH.

A. Pihlanto-Leppälä, E. Söderling, et al, "Expulsion mechanism of xylitol 5-phosphate in S. mutans," *Scandinavian Journal of Dental Research* vol. 98, no. 2, pp 112-119, 1990.

In MS, the first step of xylitol metabolism is phosphorylation. The xylitol phosphate cannot be processed for energy by MS, so it builds up to toxic levels within the bacterial cell, or is expelled (as xylitol) back into the plaque.

In humans xylitol is first oxidized (dehydrogenated), and can be used for energy.

A. H. Rogers, K. A. Pilowsky, et al, "Effects of pulsing with xylitol on mixed continuous cultures of oral streptococci," *Australian Dental Journal* pp. 231-235, June 1991.

Uptake of xylitol by MS sets up a "futile metabolic cycle" that leads to depressed growth or even bacterial cell death.

M. Cronin, J. Gordon, R. Reardon, F. Balbo, "Three clinical trials comparing xylitol- and sorbitol-containing chewing gums for their effect on supragingival plaque accumulation," *The Journal of Clinical Dentistry* vol. 5, no. 4, pp. 106-109, 1994.

"Our findings from three separate studies further support that administration of xylitol-containing chewing gum, in a manner consistent with practical use (3-5 times per day), can reduce plaque

accumulation (and) further underscores the importance of considering frequency of exposure to achieve an optimal result.

Both xylitol gums (stick and pellet) were superior to sorbitol gum in retarding plaque regrowth"

D. Almarza-Ortega, M. E. Gomez, et al, "Behavior of S. mutans under prolonged exposure to xylitol," *Invest-Clin* pp. 77-90, June 1994.

"The present study confirmed the SM inability to metabolize xylitol, even after a prolonged adaptative period."

L. Trahan, "Xylitol: a review of its action on mutans streptococci and dental plaque—its clinical significance," *International Dental Journal* vol. 45(Supplement 1), pp. 77–92, Feb. 1995.

Detailed, comprehensive review of xylitol interactions with plaque bacteria.

L. Trahan, G. Bourgeau, R. Breton, "Emergence of multiple xylitol-resistant (fructose PTS-) mutants from human isolates of Mutans streptococci during growth on dietary sugars in the presence of xylitol, *Journal of Dental Research* vol. 75, pp. 1892-1900, Nov. 1996.

A. A. Scheie, O. Fejerskov, B. Danielsen, "The effects of xylitol-containing chewing gums on dental plaque and acidogenic potential," *Journal of Dental Research* vol. 77, no. 7, pp. 1547-1552, July 1998.

Suggests that frequent gum chewing in itself is dentally beneficial – xylitol had no added effect on plaque deposits or acid production.

D. J. Bradshaw, P. D. Marsh, "Effect of sugar alcohols on the composition and metabolism within in vitro dental bacterial communities and biofilms," *Caries Research* vol. 36, no. 2, pp. 81-86, 2002.

Xylitol helped to suppress the growth of *Streptococcus mutans* and *Lactobacillus rhamnosus* in a culture pulsed with glucose without pH control.

M. C. Roberts, C. A. Riedy, S. E. Coldwell, S. Nagahama, K. Judge, M. Lam, T. Kaakko, J. L. Castillo, P. Milgrom, "How xylitol-containing products affect cariogenic bacteria," *Journal of the American Dental Association*, vol. 133, no. 4, pp. 435–441, 2002.

In some subjects the MS levels did not decrease after 4 weeks of xylitol use. However, the MS became more "xylitol-tolerant" which indicates that the cariogenic potential had decreased.

E.-M. Decker, G. Maier, D. Axmann, M. Brecx, C. von Ohle, "Effect of xylitol/chlorhexidine versus xylitol or chlorhexidine as single rinses on initial biofilm formation of cariogenic streptococci," *Quintessence International*, vol. 39, no. 1, pp. 17–22, 2008.

C. Badet, A. Furiga, N. Thébaud, "Effect of xylitol on an in vitro model of oral biofilm," *Oral Health & Preventive Dentistry*, vol. 6, no. 4, pp. 337–341, 2008.

"Xylitol has a clear inhibitory effect on the formation of the experimental biofilms. This study shows that xylitol is not only efficient in inhibiting the acid production of cariogenic bacteria, but also in preventing the formation of a multispecies biofilm; it confirms the relevance of the use of this polyol for the prevention of oral diseases caused by dental plaque."

C. H. Splieth, M. Alkilzy, J. Schmitt, C. Berndt, A. Welk, "Effect of xylitol and sorbitol on plaque acidogenesis," *Quintessence International*, vol. 40, no. 4, pp. 279–285, 2009.

"The regular consumption of xylitol lozenges modifies dental plaque, resulting in a marked reduction in the plaque acidogenicity, which could not be detected using sorbitol lozenges. Therefore, xylitol could have an additional benefit in caries prevention."

P. D. Marsh, "Dental plaque as a biofilm: the significance of pH in health and caries," *Compendium of Continuing Education in Dentistry* vol. 30, no. 2, March 2009.

Xylitol inhibits acid production, which helps to block selection for cariogenic bacteria.

"Xylitol can interfere with sugar transport in MS, and therefore cannot be metabolized to acid nor generate a low pH in plaque."

Y. E. Lee, Y. H. Choi, S. H. Jeong, H. S. Kim, S. H. Lee, K. B. Song, "Morphological changes in *Streptococcus mutans* after chewing gum containing xylitol for twelve months," *Current Microbiology*, vol. 58, pp. 332–337, 2009. (Korea)

"In the xylitol group, the colony counts of *S. mutans* decreased steadily over time. In addition, the adherence of the colonies in the xylitol group became weak, and the size of the colonies decreased compared to the control. The secretion of sticky substances from the surface of *S. mutans* colonies and *gtfB* gene expression also decreased in the xylitol group. These findings indicate that regular chewing of xylitol gum over a long period may lead to decreased *gtfB* expression, which can negatively affect the synthesis of extracellular polysaccharides by *S. mutans,* which could reduce the size and growth of *S. mutans* colonies and change their morphology as a result."

S. E. Dowd, Y. Sun, E. Smith, J. P. Kennedy, C. E. Jones, R. Wolcott, "Effects of biofilm treatments on the multi-species Lubbock chronic wound biofilm model," *Journal of Wound Care* vol. 18, no. 12, pp. 510-512, Dec. 2009.

Xylitol particularly inhibited the growth of *Pseudomonas aeruginosa*, one of the most important species in chronic wound biofilms.

E. M. Söderling, A. M. Hietala-Lenkkeri, "Xylitol and erythritol decrease adherence of polysaccharide-producing oral streptococci," *Current Microbiology*, vol. 60, no. 1, pp. 25–29, 2010.

"Both xylitol and erythritol can decrease polysaccharide-mediated cell adherence contributing to plaque accumulation through a mechanism not dependent on growth inhibition."

A.-E. Hirvonen, Jr., S. Karjalainen, M. Fontana, D. Catt, Sr., L. Seppä, E. Söderling, "Effect of xylitol on the composition of the oral flora," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

Plaque counts and percentage of MS in plaque decreased in the xylitol group. MS appeared to be specifically targeted by xylitol during 4-week test period.

Body Composition/Weight Management

K. Schultis, C. A. Geser, "Observations on the anticatabolic effect of xylitol," in: *International symposium on metabolism, physiology and clinical uses of pentoses and pentitols.* B. L. Horecker, K. Lang, Y. Takagi (eds), Springer-Verlag, Berlin, 1969.

"By giving xylitol to operated patients, we can observe a normalization of the disturbances of glucose utilization, as well as an obviously reduced loss of nitrogen… Compared with sorbitol and fructose, xylitol utilization shows some advantages. The serum insulin values in healthy persons are not influenced by xylitol."

M. Ohnuki, "Clinical study on preventing effect of xylitol on adrenocortical suppression by steroid therapy," *Z Ernährungswiss* vol.11 (supplement 1), pp. 71-80, 1971.

Xylitol stimulates the synthesis of RNA and corticoids, which counteracts the inhibition of adrenal secretion caused by long-term steroid therapy.

E. Salminen, S. Salminen, L. Porkka, P. Koivistoinen, "The effects of xylitol on gastric emptying and secretion of gastric inhibitory polypeptide in the rat," *Journal of Nutrition* vol. 114, pp. 2201-2003, 1984.

Xylitol slows stomach emptying.

R. B. Shafer, A. S. Levine, "Effects of xylitol on gastric emptying and food intake," *American Journal of Clinical Nutrition,* vol. 45, pp. 744-747, 1987.

Xylitol delayed stomach emptying and decreased food intake.

"Our data suggest a role for xylitol as a potentially important agent in dietary control."

B. Leibowitz, "Nutritional alternatives to anabolic hormones, Part 8: Xylitol," *Muscular Development,* vol. 29, pp. 69, 130, Feb. 1992.

"The bottom line is that xylitol is an anticatabolic sugar with potential applications to sports and athletic performance."

M. Colgan, "Sugar highs: Sugar blues," *Muscular Development,* vol. 30, pp. 16, 128, 168, May, 1993.

"This ability of xylitol to keep blood glucose and insulin levels stable is crucial to muscle building. Recovery supplements that do not contain xylitol may well be considered obsolete."

M. DiPasquale, "Research update: unique carb helps burn fat," *Muscle Media,* April, 1998.

"All of these properties make xylitol an excellent addition to a nutritional supplement designed to help you lose body fat while maintaining or even increasing muscle."

N. A. King, S. A. Craig, T. Pepper, J. E. Blundell, "Evaluation of the independent and combined effects of xylitol and polydextrose consumed as a snack on hunger and energy intake over 10 d." *British Journal of Nutrition* vol.93, no. 6, pp. 911-915, June 2005.

"The usefulness of xylitol and polydextrose as ingredients in functional foods for appetite control are as a result of their lower energy content and suppression of appetite."

Bones

J. Tenovuo, H. Mielityinen, and K. Paunio, “Effect of dental plaque grown in the presence of xylitol or sucrose on bone resorption in vitro,” *Pharmacology and Therapeutics in Dentistry*, vol. 6, no. 1-2, pp. 35–43, 1981.

M. M. Hämäläinen, K. K. Mäkinen,“Relationship between mineral metabolism and peroral consumption of sugar alcohols,” *Mineral and Electrolyte Metabolism,* vol. 15, pp. 346-352, 1989.

“Absorption-promoting effect of xylitol can perhaps be applied to mineral therapy.”

M. M. Hämäläinen, M. Knuuttila, et al, “Comparison of the effect of xylitol on bone recalcification in calcium-deficient rats,” *Bone* vol. 11, pp. 429-438, 1990.

“These results suggest advantages in the use of xylitol in calcium supplements.”

M. Svanberg, M. Knuuttila M. Dietary xylitol prevents ovariectomy-induced changes of bone inorganic fraction in rats. *Bone Miner* vol. 26, pp. 81-88, 1994.

P. Mattila, “Dietary xylitol in the prevention of experimental osteoporosis -- Beneficial effects on bone resorption, structure and biomechanics,” academic dissertation, University of Oulu, 1999.

P. Mattila, M. Svanberg, M. Knuuttila, “Increased bone volume and bone mineral content in xylitol-fed aged rats” *Gerontology* vol. 47, pp. 300-305, 2001.

Candy

F. Voirol, “The value of xylitol as an ingredient in confectionery,” in *Xylitol*, J. N. Counsel (ed), Applied Science, London 1977.

Xylitol has approximately the same sweetness as sucrose sugar. Depending on the application, xylitol may seem slightly more or less sweet.

“To sweeten a cup of coffee, 13 grams of xylitol will be needed to replace 10 grams of sugar.”

T. Pepper, P. M. Olinger, “Xylitol in sugar-free confections,” *Food Technology*, Oct. 1988.

“Xylitol can bring new value to sugar-free confections. The cariostatic advantage and sensorical properties of xylitol can enable confectioners to create dentally safe products with wider consumer appeal.”

P. M. Olinger, “Sweetening the sugar-free challenge,” *The Manufacturing Confectioner*, May 1990.

Xylitol provides the highest dental benefit, sweetness and cooling effect. Xylitol can be combined with other ingredients to optimize manufacturing requirements, cost considerations, shelf stability, eating qualities and label claims.

P. M. Olinger, “New options for sugar-free chocolate,” *The Manufacturing Confectioner*, pp. 77-84, May 1994.

Combining xylitol with a dimeric polyol such as maltitol or lactitol reduces the cooling effect, which would only be desirable in a mint chocolate.

P. M. Olinger, "Xylitol as a sanding medium," *The Manufacturing Confectioner*, pp. 92-95, Nov. 1995.

"Xylitol provides several advantages as a sanding compound. In addition to enhancing the visual appeal of the product, the increased sweetness provided by xylitol helps to potentiate product flavor."

P. Alanen, P. Isokangas, K. Gutmann, "Xylitol candies in caries prevention: results of a field study in Estonian children," *Community Dentistry and Oral Epidemiology*, vol. 28, no. 3, pp. 218–224, 2000.

Demonstrated that xylitol candy can be as effective as xylitol chewing gum, therefore the caries protection is not just a salivary effect from chewing.

R. C. Deis, "Polyols in confectionery," *The Manufacturing Confectioner*, pp. 53-57, Oct. 2000.

Xylitol has some interesting properties that can result in greater stability for sensitive ingredients and thereby increased self life.

I. Fairs, "Formulating confectionery with xylitol," *The Manufacturing Confectioner*, pp. 39-42, Oct. 2005.

Xylitol is sweet enough to be used without the addition of artificial high-intensity sweeteners. The high cooling effect of xylitol can be used to enhance certain flavors.

E. Honkala, S. Honkala, M. Shyama, S. A. Al-Mutawa, "Field trial on caries prevention with xylitol candies among disabled school students," *Caries Research* vol. 40, no. 6, pp. 508-513, 2006.

Xylitol candy was used 3 times during the school day. "Xylitol seemed to have a strong preventive and a clear remineralizing effect on caries." Relatively small amounts of xylitol cut caries rate in half.

K. A. Ly, C. A. Riedy, P. Milgrom, M. Rothen, M. C. Roberts, L. Zhou, "Xylitol gummy bear snacks: a school-based randomized clinical trial," *BMC Oral Health*, vol. 8, no. 1, article 20, 2008.

In a six-week trial, *S. mutans/sobrinus* levels were reduced with three uses of xylitol gummy bears per day.

Y. Nakai, C. Shinga-Ishihara, K. Moriya, K. Murakami-Yamanaka, "Effect of xylitol-containing tablets on *Mutans streptococci* in children," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

Study included children age 1-6 for 6 months duration. "These results suggest that a xylitol tablet may be an alternative to xylitol chewing gum for dental caries prevention."

Chewing Gum

F. N. Hattab, R. M. Green, K. M. Pang, Y. C. Mok, "Effect of fluoride-containing chewing gum on remineralization of carious lesions and on fluoride uptake in man," *Clinical Preventive Dentistry*, vol. 11, no. 6, pp. 6–11, 1989.

P. Isokangas, J. Tiekso, P. Alanen, K. K. Mäkinen, "Long-term effect of xylitol chewing gum on dental caries," *Community Dentistry and Oral Epidemiology*, vol. 17, no. 4, pp. 200–203, 1989.

"About 85% (*n*= 269) of the subjects who participated in the Ylivieska follow-up studies on the effect of xylitol chewing gum on dental caries during 1982–84 or 1982–85 were re-examined in 1987 for the analysis of possible long-term preventive effects. Further caries reduction was found 2 or 3 yr after the discontinuation of the use of xylitol. …In teeth erupting during the first year of the use of xylitol gum the long-term preventive effect was greater than in other teeth."

J. Arends, M. Smits, J. L. Ruben, J. Christoffersen, "Combined effect of xylitol and fluoride on enamel demineralization in vitro," *Caries Research*, vol. 24, no. 4, pp. 256–257, 1990.

P. Isokangas, J. Tenovuo, E. Söderling, H. Männistö, K. K. Mäkinen, "Dental caries and mutans streptococci in the proximal areas of molars affected by the habitual use of xylitol chewing gum," *Caries Research*, vol. 25, no. 6, pp. 444–448, 1991.

"Those children who had used xylitol chewing gum regularly since 1982 showed significantly lower caries indices in 1988, including the proximal caries scores. The presence of MS in the proximal areas studied was significantly lower in habitual xylitol consumers."

L. M. Steinberg, F. Odusola, I. D. Mandel, "Remineralizing potential, antiplaque and antigingivitis effects of xylitol and sorbitol sweetened chewing gum," *Clinical Preventive Dentistry*, vol. 14, no. 5, pp. 31–34, 1992.

P. Isogangas, K. K. Mäkinen, J. Tiekso, P. Alanen, "Long-term effect of xylitol chewing gum in the prevention of dental caries: a follow-up 5 years after termination of a prevention program," *Caries Research*, vol. 27, no. 6, pp. 495–498, 1993.

J. M. Tanzer, "Xylitol chewing gum and dental caries," *International Dental Journal* vol. 45, pp. 65-76, 1995.

"The literature not only supports the conclusion that xylitol is non-cariogenic, but it is now strongly suggestive that xylitol is caries-inhibitory, that is, anti-cariogenic in human subjects, and it supplies reasonable mechanistic explanations."

E. Söderling, P. Isokangas, J. Tenovuo, J. Tiekso, "Oral biochemical status and depression of streptococcus mutans in children during 24 to 36 month use of xylitol chewing gum," *Caries Research* vol. 23, pp. 261–267, 1998.

"The xylitol-consuming subjects (age 11-12) showed at the end of the study significantly smaller (p less than 0.004) salivary S. mutans counts than the control children. These effects were achieved after using up to 3 xylitol gums/day (daily xylitol dose per child was 7-10 g)."

G. H. Hildebrandt, B. S. Sparks, "Maintaining mutans streptococci suppression with xylitol chewing gum," *Journal of the American Dental Association*, vol. 131, no. 7, pp. 909–916, 2000.

"Xylitol chewing gum appears to have the ability to prolong the effect of chlorhexidine therapy on oral MS." Without xylitol, pathogens quickly returned to baseline levels.

V. Machiulskiene, B. Nyvad, V. Baelum, "Caries preventive effect of sugar-substituted chewing gum," *Community Dentistry and Oral Epidemiology*, vol. 29, no. 4, pp. 278–288, 2001.

"Compliance was better in school C (xylitol gum) than in the other schools."

Trial was conducted in Lithuania. The authors concluded that the caries preventive effect was due more to the chewing process than the ingredients in chewing gum.

C. Hayes, "Xylitol gum decreases the decayed, missing, and filled surfaces (DMFS) score over a 3-year period by an average of 1.9," *Evidence-Based Dental Practice*, vol. 2, no. 1, pp. 14–15, 2002.

Statistical analysis of Machiulskiene (Lithuania trial) revealed that a caries preventive effect was indeed produced by xylitol use.

S. Thaweboon, B. Thaweboon, S. Soo-Ampon, "The effect of xylitol chewing gum on mutans streptococci in saliva and dental plaque," *Southeast Asian J Trop Med Public Health,* vol. 35, no. 4, pp. 1024-1027, 2004.

Both 55% and 100% xylitol-sweetened chewing gum use reduced MS in plaque (trial conducted in Thailand). Only the 100% xylitol gum also reduced MS in saliva.

B. A. Burt, "The use of sorbitol- and xylitol-sweetened chewing gum in caries control," *Journal of the American Dental Association*, vol. 137, no. 2, pp. 190–196, 2006.

"The evidence is strong enough to support the regular use of xylitol-sweetened gum as a way to prevent caries, and it can be promoted as a public-health preventive measure."

P. Milgrom, K. A. Ly, M. C. Roberts, M. Rothen, G. Mueller, D. K. Yamaguchi, "Mutans streptococci dose response to xylitol chewing gum," *Journal of Dental Research*, vol. 85, no. 2, pp. 177–181, 2006.

In adults using chewing gum, xylitol at 6.4 to 10.3 grams per day reduced MS in plaque after 5 weeks, and in both saliva and plaque in 6 months, whereas 3.4 grams did not. It was suggested that two-thirds of the participants had been exposed to some xylitol in their diet, which could mask an effect at low levels.

"A plateau effect is suggested between 6.44 and 10.32 g xylitol/day."

K. A. Ly, P. Milgrom, M. C. Roberts, D. K. Yamaguchi, M. Rothen, G. Mueller, "Linear response of mutans streptococci to increasing frequency of xylitol chewing gum use: a randomized controlled trial," *BMC Oral Health*, vol. 6, article 6, 2006.

Frequency of daily xylitol exposures is important. The reduction of MS in adults increased in a linear fashion with 2, 3 and 4 uses per day. Unlike the previous dose study, there was no plateau effect, suggesting that there was still room for improvement.

W. A. Bretz, O. P. S. Rosa,S.M. Silva, P. M. Corby, O. C. Lima, M. Milanda, W. J. Loesche, "Compliance with xylitol and sorbitol chewing gum regimens in clinical trials," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 25-27, 2006.

"Results clearly suggest that compliance, and possibly acceptance, were superior for xylitol chewing gum."

A. Trummler, W. Strübig, "Beeinflussung verschiedener speichelparameters nach täglicher verwendung von xylit-kaugummi in der schule," *Oralprophylaxe Kinderzahnheilkunde*, vol. 30, pp. 101–105, 2008.

Xylitol gum was more effective in reducing MS than sorbitol-mannitol gum.

K. A. Ly, P. Milgrom, M. Rothen, "The potential of dental-protective chewing gum in oral health interventions," *Journal of the American Dental Association*, vol. 139, no. 5, pp. 553–563, 2008.

K. K. Mäkinen, "Oral care gum products," in *Food Constituents and Oral Health*, M. Wilson, Ed., pp. 433–454, Woodhead, Cambridge, UK, 2009.

Cosmetic

K. Masako, K. Yusuke, I. Hideyuki, M. Atsuko, M. Yoshiki, M. Kayoko, K. Makoto, "A novel method to control the balance of skin microflora," *Journal of Dermatological Science*. vol. 38, no. 3, pp. 207-213, June 2005.

"This study provides evidence supporting a cream containing xylitol as a useful skin-care agent for atopic dry skin colonized by *Staphylococcus aureus*, a bacteria that can worsen atopic dermatitis (AD)."

P. T. Mattila, P. Pelkonen, M. L.E. Knuuttila, "Effects of a long term dietary supplementation on the collagen content and fluorescence of the skin in aged rats" *Gerontology* vol. 51, no. 3, pp. 166-169, 2005.

Dietary xylitol has been shown to increase the amounts of newly synthesized collagen, and to decrease cross-linked collagen. Dietary xylitol supplementation may protect against some degenerative changes during aging.

J. N. Peldyak, L. W. Bybee, E. Johnson, L.R. Misner, "Practical application of xylitol in dentistry," *Finnish Dental Journal,* supplement 1, pp. 54-61, 2006.

"Unsightly white spot lesions, fluorosis and other staining can be cosmetically improved with a xylitol mineralizing solution (~35% xylitol plus calcium glycerophosphate.)"

Dental Caries (Tooth Decay)

A. Scheinin, "Xylitol: An update – Will it be *the* sugar alternative of the future?" *Oral Health* vol. 71, no. 7, pp. 33-35, July 1981.

"The real basis for the sugar-caries ratio—the frequency of sugar intake between meals in solid form—is much more important than overall consumption."

A. Scheinin, "Xylitol: An update – Recent studies, indications," *Oral Health* vol. 71, no. 8, pp. 43-46, August 1981.

"I have never seen as many cases of rampant caries as I saw in French Polynesia… Once an extraction has been performed, the patient takes the extracted tooth and, as a revenge for the pain he has suffered, smashes it with a hammer."

A. Scheinin, E. Söderling, "Carbohydrate sweeteners and dental caries," *Proc Finnish Dental Society* vol. 82, 276-289, 1986.

"Attempts toward reduction of the use of sucrose should be aimed at products found particularly cariogenic." Xylitol appears to reduce caries in a dose-dependent manner.

K. K. Mäkinen, "Sweeteners and prevention of dental caries," *Oral Health* vol. 78, no. 9, pp. 57-66, September 1988.

"Mere sucrose restriction without suggesting alternatives does not take into account human behavior. Complete prevention should always include the use of sucrose substitutes.

Ideal xylitol products include chewing gums, sweet snacks, dentifrices, lozenges, chewable tablets and sweetened medicines."

K. K. Mäkinen, "Latest dental studies on xylitol and mechanism of action of xylitol in caries limitation," in *Progress in Sweeteners*, T. H. Grenby, Ed., pp. 331–362, Elsevier, London, UK, 1989.

"The caries-preventive effect of xylitol is both dose- and concentration-dependent."

P. Isokangas, J, Tenovuo, E. Söderling, H. Männistö, K. K. Mäkinen, "Dental caries and mutans streptococci in the proximal areas of molars affected by the habitual use of xylitol chewing gum" *Caries Research* vol. 25, pp. 444-448, 1991.

K. K. Mäkinen, "Prevention of dental caries by xylitol," *Environmental Management and Health* vol. 2, no. 2, pp. 6-11, 1991.

"The most impressive results have been achieved when a xylitol program has been added to existing prevention efforts."

H. Lynch, P. Milgrom, "Xylitol and dental caries: an overview for clinicians," *Journal of the California Dental Association,* March 2003.

"There is sufficient evidence for clinicians to consider including xylitol-containing products in their clinical armamentarium for the prevention of dental decay in high-risk populations."

K. K. Mäkinen, "Prevention of dental caries by xylitol: issues relating to health claims," in *America's Foods Health Messages and Claims*, J. E. Tillotson (ed), pp. 167–192, CRC Press, Boca Raton, Fla, USA, 1993.

"The consumption of xylitol-containing foods will significantly reduce the incidence of dental caries."

K. A. Ly, P. Milgrom, M. Rothen, "Xylitol, sweeteners, and dental caries," *Pediatric Dentistry,* vol. 28, no. 2, pp. 154-163; discussion 192-198, April 2006.

"Sufficient evidence exists to support the use of xylitol to reduce caries. Clinicians and dental associations should push for clear recommendations of efficacious dose and frequency of xylitol use and for clear labeling of xylitol content in products to help consumers choose appropriately."

T. C. Silva, A. F. Faustino Pereira, M. A. Moreira Machado, M. A. Rabelo Buzalaf, "The use of xylitol as a strategy for prevention of dental caries," *Revista Odonto Ciência,* vol. 24, no. 2, pp. 205-212, 2009.

"Xylitol must not represent a single preventive strategy but should be considered as an auxilliary agent mainly used when the mechanical control of dental biofilm is unsatisfactory and insufficient to avoid the development of dental caries lesions."

Diabetes

G. H. Mellinghoff, "Ueber die verwendbarkeit des xylit als ersatzzucher bie diabetikern," *Klin. Wschr,* vol. 39, pp. 447, 1961.

Up to 60 grams of xylitol per day had no adverse effects on diabetic patients.

F. Manenti, L. Della Casa, "Effetti dello xylitolo sull equilibrio glicidico del diabetico *Boll. Soc. Medico-Chirugia de Modena* pp. 1-8, 1965.

Ingestion of 50 grams of xylitol caused only a marginal increase of blood sugar.

S. Yamagata, Y. Gato, "Clinical effects of xylitol on carbohydrate and lipid metabolism in diabetes," *Lancet,* pp. 918-921, Nov, 1965.

"Xylitol produces benefits to the metabolic disorders in diabetes."

H. Förster, S. Böcker, A. Walther, "Verwendung von xylit als zuckeraustauschstoff bei diabetischen kindern," *Fortshr. Med.* vol. 95, pp. 99-102, 1977.

30 grams of xylitol per day was well tolerated by children with Type 1 diabetes.

J. M. Olefsky, P. Crapo, "Fructose, xylitol, and sorbitol," *Diabetes Care* vol. 3, no. 2, 1980.

"(Fructose, xylitol, sorbitol) have been used extensively as sucrose or glucose substitutes in diabetic diets in several Western European countries and provide some theoretical advantages in dietary management."

The review paper goes on to be somewhat dismissive of the practicality of sugar substitution with bulk sweeteners. It raises alarms about the safety of xylitol in some animals (which have been addressed subsequently), stating "If the association between xylitol and tumor induction is confirmed, it is likely that xylitol will be banned."

N. de Kalbermatten, E. Ravussin, E. Maeder, C. Geser, E. Jéquier, J. P. Felber, "Comparison of glucose, fructose, sorbitol, and xylitol utilization in humans during insulin supression," *Metabolism* vol. 29, no. 1, pp. 62-67, January 1980.

"These results indicate that fructose, sorbitol, and xylitol are oxidized at a higher rate than glucose during suppression of endogenous insulin secretion, without any significant rise in glycemia."

J. D. Brunzell, "Use of fructose, xylitol, or sorbitol as a sweetener in diabetes mellitus," *Diabetes Care* pp.223-228, July-Aug. 1978.

"No significant side effects have been demonstrated with ingestion of modest amounts of oral xylitol in normal individuals or treated diabetic patients."

W. Hassinger, G. Sauer, U. Cordes, U. Krause, J. Beyer, K. H. Bässler, "The effects of equal caloric amounts of xylitol, sucrose and starch on insulin requirements and blood glucose levels in insulin dependent diabetics," *Diabetologia* vol. 2, pp. 37-40, 1981.

Insulin requirement after sucrose was significantly higher than after xylitol (30 grams with mixed meals). There were no side effects with 30 grams of xylitol incorporated into breakfast.

"Sucrose, in contrast, induced a greater post-prandial rise in blood glucose levels despite counter-regulation by the glucose-controlled insulin infusion system."

R. A. Bonner, D. C. Laine, "Effects of xylitol, fructose and sucrose on types I and II diabetics," *Diabetes,* vol. 31, supplement 2, 1982.

70 grams of xylitol per day caused no adverse reactions.

A. Bär, "Rationale for the use of sugar substitutes in the diabetic diet," *Bioresco Ltd,* Brussels, Oct. 1990.

"Xylitol offers considerable advantages as a sweetener in the diabetic diet."

A. Bär, "Sugar alcohols in the diabetic diet," in N. Kretchmer, C. B. Hollenbeck (eds) *Sugars and Sweeteners,* pp. 131-149, 1991.

Xylitol can help in the dietary management of diabetes.

C. Otto, A. C. Sonnichsen, et al, "The influence of fiber, xylitol and fructose in enteral formulas on glucose and lipid metabolism in normal subjects," *Clin-Investig.* vol. 71, no. 4, pp. 290-293, April 1993.

"We conclude that a patient with type II diabetes may benefit from replacing glucose and glucose equivalents with… xylitol."

S. S. Natah, K. R. Hussien, J. A. Tuominen, V. A. Koivisto, "Metabolic response to xylitol and lactitol in healthy men," *American Journal of Clinical Nutrition* vol. 65, no. 4, pp. 947-950, 1997.

"The small glucose and insulin responses also suggest that lactitol and xylitol are suitable components of the diet for diabetic patients."

A. Sentko, "The low-glycemic concept," *The Manufacturing Confectioner*, pp. 73-82, June 2004.

Xylitol is partly absorbed and metabolized and is in the "very low" glycemic category.

"A low-glycemic diet may lead to lower insulin levels, to a reduced insulin demand, to improved blood glucose control and reduced blood lipid levels."

Dry Mouth (Xerostomia)

H. Olsson, C. J. Spak, T. Axell, "The effect of a chewing gum on salivary secretion, oral mucosal friction and the feeling of dry mouth in xerostomic patients," *Acta Odontologica Scandinavia* vol. 49, pp. 273-279, 1991.

Xylitol increases salivary secretion rate and decreases feeling of dry mouth.

K. Masalin, “Caries-risk reducing effects of xylitol-containing chewing gum and tablets in confectionery workers in Finland,” *Community Dental Health*,” vol. 9, no. 1, pp. 3-10, March 1992.

Xylitol increased salivary flow and buffer capacity.

Economics and Public Health

A. Nordblad, L. Suominen-Taipale, H. Murtomaa, E. Vartiainen, and K. Koskela, “Smart Habit Xylitol campaign, a new approach in oral health promotion,” *Community Dental Health*, vol. 12, no. 4, pp. 230–234, 1995.

“There seems to be potential for positive health promotion by means of this type of xylitol campaign.”

S. Honkala, E. Honkala, J. Tynjälä, and L. Kannas, “Use of xylitol chewing gum among Finnish schoolchildren,” *Acta Odontologica Scandinavica*, vol. 57, no. 6, pp. 306–309, 1999.

P. Alanen, M.-L. Holsti, K. Pienihäkkinen, “Sealants and xylitol chewing gum are equal in caries prevention,” *Acta Odontologica Scandinavica*, vol. 58, no. 6, pp. 279–284, 2000.

“After 5 years, no statistically significant differences between the sealant and xylitol groups were found.”

K. K. Mäkinen, “The rocky road of xylitol to its clinical application,” *Journal of Dental Research*, vol. 79, no. 6, pp. 1352–1355, 2000.

“Following the publication of the first results, the dental circles divided into two schools: some colleagues readily accepted the “xylitol concept” while others were more reserved.”

R. Widome, “What can oral public health learn from Finland?” *American Journal of Public Health* vol. 94, no. 11, p. 1842, November 2004.

“Distributing gum or candy to children is inherently low-tech. The xylitol research is significant because a low-cost, quickly implementable caries prevention strategy that can circumvent barriers could lessen oral health disparities in the United States.”

J. R. de Magalhães Bastos, L. S. C. Da Cunha, R. H. Alves da Silva, F. Elias, H. J. Gurgel Rodrigues, “Utilization of xylitol as a preventive substance in dentistry,” *Brazilian Journal of Oral Sciences,* vol. 4, no. 15, pp. 891-893, 2005.

“In conclusion, xylitol can be presented in many forms such as chewing gums, tablets, mouthrinses, and associated to fluoride in toothpastes. Its anticariogenic power is due to the impairment of growth of cariogenic bacteria and consequent reduction in the acidity of plaque. Besides, it helps in the remineralization of initial carious lesions, is specific to S. mutans, well accepted by children and may be used with beneficial effects in all ages.”

P. Milgrom, M. Rothen, L. Milgrom, “Developing public health interventions with xylitol for the US and US-associated territories and states,” *Finnish Dental Journal*, vol. 13, supplement 1, pp. 28–37, 2006.

“Steps to develop effective alternative vehicles for the delivery of xylitol particularly useful for young children and institutional settings in America are explored.”

P. Alanen, "Economical aspects of caries protection with xylitol," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 50-53, 2006.

The results from economical point of view seem to be promising if xylitol is used before and around the eruption of teeth, and maybe even better if the aim of the programme is to prevent the colonization of SM in the mouth of early childhood."

P. Milgrom, D. T. Zero, and J. M. Tanzer, "An examination of the advances in science technology of prevention of tooth decay in young children since the Surgeon General's report on oral health," *Academic Pediatrics*, vol. 9, no. 6, pp. 404–409, 2009.

Anonymous, "Xylitol cleared for anti-caries health claims," *British Dental Journal*, vol. 206, no. 3, p. 123, 2009.

Field Trials

A. Scheinin, K. K. Mäkinen, K. Ylitalo, "Turku sugar studies. I. An intermediate report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man," *Acta Odontologica Scandinavica*, vol. 32, no. 6, pp. 383–412, 1974.

A. Scheinin, K. K. Mäkinen, E. Tammisalo, M. Rekola, "Turku sugar studies XVIII. Incidence of dental caries in relation to 1-year consumption of xylitol chewing gum," *Acta Odontologica Scandinavica*, vol. 33, supplement 70, pp. 307–316, 1975.

A. Scheinin, K. K. Mäkinen, K. Ylitalo, "Turku sugar studies V. Final report on the effect of sucrose, fructose and xylitol diets on the caries incidence in man," *Acta Odontologica Scandinavica*, vol. 34, no. 4, pp. 179–216, 1976.

A. N. Galiullin, "Evaluation of the caries-preventive action of xylitol," *Kazan Medical Journal*, vol. 67, pp. 16–18, 1981 (Russian).

Xylitol only replaced about half the usual candy. The xylitol group had a 73% reduction in caries, and the decay they did have was much less severe.

A. Scheinin, J. Bánóczy, J. Szöke, et al., "Collaborative WHO xylitol field studies in Hungary. I. Three-year caries activity in institutionalized children," *Acta Odontologica Scandinavica*, vol. 43, no. 6, pp. 327–347, 1985.

A. Scheinin, K. Pienihäkkinen, J. Tiekso, et al., "Collaborative WHO xylitol field studies in Hungary. VII. Two-year caries indicence in 976 institutionalized children," *Acta Odontologica Scandinavica*, vol. 43, no. 6, pp. 381–387, 1985.

D. Barnes, J. Barnaud, S. Khambonaanda, J. S. Infirri, "Field trials of preventive regimen in Thailand and French Polynesia," *International Dental Journal,* vol. 35, pp. 66-72, 1985.

Preventive effect was seen with a fluoride chewing gum sweetened with xylitol and sorbitol. All children received same basic fluoride prevention.

M. Rekola, “Changes in buccal white spots during 2-year consumption of dietary sucrose or xylitol,” *Acta Odontologica Scandinavica*, vol. 44, no. 5, pp. 285–290, 1986.

M. Rekola, “Approximal caries development during 2-year total substitution of dietary sucrose with xylitol,” *Caries Research*, vol. 21, no. 1, pp. 87–94, 1987.

D. Kandelman, A. Bär, A. Hefti, “Collaborative WHO xylitol field study in French Polynesia. I. Baseline prevalence and 32-month caries increment,” *Caries Research*, vol. 22, no. 1, pp. 55–62, 1988.

P. Isokangas, P. Alanen, J. Tiekso, K. K. Mäkinen, “Xylitol chewing gum in caries prevention: a field study in children,” *The Journal of the American Dental Association*, vol. 117, no. 2, pp. 315–320, 1988.

D. Kandelman, G. Gagnon, “A 24-month clinical study of the incidence and progression of dental caries in relation to consumption of chewing gum containing xylitol in school preventive programs,” *Journal of Dental Research*, vol. 69, no. 11, pp. 1771–1775, 1990.

K. K. Mäkinen, C. A. Bennett, P. P. Hujoel, P. J Isokangas, K. P. Isotupa, H. R. Pape, Jr, P.-L. Mäkinen, “Xylitol chewing gums and caries rates: a 40-month cohort study,” *Journal of Dental Research*, vol. 74, no. 12, pp. 1904–1913, 1995.

This large trial was conducted in Belize, Central America, between 1989-1993 to compare caries rates in groups using chewing gum sweetened with sugar, sorbitol, xylitol, or sorbitol/xylitol mixture. There was also a no-gum group. The caries rates were: sugar>no gum>sorbitol>sorbitol/xylitol mix>xylitol.

K. K. Mäkinen, P. P. Hujoel, C. A. Bennett, K. P. Isotupa, P.-L. Mäkinen, P. Allen, “Polyol chewing gums and caries rates in primary dentition: a 24-month cohort study,” *Caries Research*, vol. 30, no. 6, pp. 408–417, 1996.

This trial was conducted in the Stann Creek district of Belize, Central America, with a population high sugar consumption and high caries rates. There were 7 groups using chewing gums sweetened wiyh sorbitol, xylitol or combinations the best results were obtained wiyh 100% xylitol pellet gum.510 6 yr old children

K. K. Mäkinen, D. Pemberton, P.-L. Mäkinen, et al., “Polyol-combinant saliva stimulants and oral health in veterans affairs patients—an exploratory study,” *Special Care in Dentistry*, vol. 16, no. 3, pp. 104–115, 1996.

Xylitol improved periodontal health and reduced root surface caries in an elderly population.

J. I. Virtanen, R. S. Bloigu, M. A. Larmas, “Timing of first restorations before, during, and after a preventive xylitol trial,” *Acta Odontologica Scandinavica*, vol. 54, no. 4, pp. 211–216, 1996.

K. K. Mäkinen, P.-L. Mäkinen, H. R. Pape Jr., J. Peldyak, P. Hujoel, K. P. Isotupa, E. Söderling, P. Isokangas, P. Allen, C. Bennett, “Conclusion and review of the ‘Michigan Xylitol Programme’ (1986–1995) for the prevention of dental caries,” *International Dental Journal*, vol. 46, pp. 22–34, 1996.

In a series of studies, xylitol demonstrated more dental benefits than typical sugar or sorbitol sweetened products.

K. K. Mäkinen, P. P. Hujoel, C. A. Bennett, et al., "A descriptive report of the effects of a 16-month xylitol chewing-gum programme subsequent to a 40-month sucrose gum programme," *Caries Research*, vol. 32, no. 2, pp. 107–112, 1998.

W. Wenhui, P. Alanen, P. Isokagas, K. Isotupa, P. L. Mäkinen , E. Söderling, W. Weijian, C. Xiaochi, W. Yi, Z. Boxue, K. K. Mäkinen, "Effect of two-year xylitol consumption on mutans streptococci and lactobacilli in saliva and plaque," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 38-43, 2006.

"Long-term use of xylitol chewing gum had an inhibitory effect on mutans streptococci in saliva and dental plaque, and on saliva lactobacilli."

H. Hausen, L. Seppä, R. Poutanen, A. Niinimaa[a], S. Lahti, S. Kärkkäinen, I. Pietilä, "Noninvasive control of dental caries in children with active initial lesions: a randomized clinical trial," *Caries Research*, vol. 41, no. 5, pp. 384–391, 2007.

Nearly 500 children (age 11-12) in Finland participated. "Using a regimen that includes multiple measures (including xylitol) for preventing dental decay, caries increment can be significantly reduced among caries-active children living in an area where the overall level of caries experience is low."

K. K. Mäkinen, "An end to crossover designs for studies on the effect of sugar substitutes on caries?" *Caries Research*, vol. 43, pp. 331–333, 2009.

Some interventions such as xylitol and fluoride may have long-lasting effects which can confound results of cross-over study designs.

Fluoride

A. Cobanera, E. Mopasso, P. White, R. Cuevas, R. Espanosa, "Xylitol-sodium fluoride: effect on plaque," *Journal of Dental Research,* vol. 66, abstract 56, 1985.

Xylitol and fluoride have an additive preventive effect.

J. H. Meurman, J. Suhonen, "Combination chemotherapy of dental plaque infections," *Proceedings of the Finnish Dental Society,* vol. 87, no. 4, pp 549-54, 1991.

Lower concentrations of fluoride and chlorhexidine can be used when combined with xylitol.

A. H. Rogers, A.G. Bert, "Effects of xylitol and fluoride on the response to glucose pulses of S mutans growing in continuous culture," *Oral Microbiology and Immunology* pp.124-126, April 1992.

"Xylitol can augment the metabolic effects on S. mutans of low levels of fluoride."

H. Maehara, Y. Iwami, H. Mayanagi, N. Takahashi, "Synergistic inhibition by combination of fluoride and xylitol on glycolysis by mutans streptococci and its biochemical mechanism," *Caries Research*, vol. 39, no. 6, pp. 521–528, 2005.

"Xylitol inhibited the upper part of the glycolytic pathway, while fluoride inhibited the lower part. This study indicates that fluoride and xylitol together have synergistic inhibitory effects on the acid

production of mutans streptococci and suggests that xylitol has the potential to enhance inhibitory effects of low concentrations of fluoride."

V. G. Petin, J. K. Kim, R. O. Kritsky, L. N. Komarova, "Mathematical description, optimization and prediction of synergistic interaction of fluoride and xylitol," *Chemosphere*, vol. 72, no. 5, pp. 844–849, 2008.

This Russian model predicts optimal use of xylitol with fluoride combinations.

B. T. Amaechi, S. M. Higham, W. M. Edgar, "The influence of xylitol and fluoride on dental erosion in vitro," *Archives of Oral Biology*, vol. 43, no. 2, pp. 157–161, 1998.

"It was concluded that xylitol and fluoride have an additive effect in the reduction of dental erosion by pure orange juice in vitro."

S. Chunmuang, S. Jitpukdeebodintra, C. Chuenarrom, P. Benjakul, "Effect of xylitol and fluoride on enamel erosion in vitro," *Journal of Oral Science*, vol. 49, no. 4, pp. 293–297, 2007.

"This study demonstrated that addition of xylitol, fluoride or a xylitol/fluoride combination to an acidic drink or post-treatment with fluoride or a xylitol/fluoride combination could reduce, but not prevent, enamel erosion."

Fungus (Yeast)

K. K. Mäkinen, A. Ojanotko, H. Vidgren, "Effect of xylitol on the growth of three oral strains of *Candida albicans. Journal of Dental Research,* vol. 54, p. 1239, 1975.

There was a slight inhibition of growth on glucose of three oral strains of *Candida albicans* in the presence of xylitol.

K. Izumori, K. Yamanaka, "Selective inhibition of *Klebsiella aerogenes* growth on pentoses by pentitols," *Journal of Bacteriology* vol. 134, no. 3, pp. 713–717, 1978.

Xylitol inhibited the growth of *Klebsiella aerogenes* cultured on xylose.

R. Maleszka, H. Schneider, "Fermentation of D-xylose, xylitol, and D-xylulose by yeasts," *Canadian Journal of Microbiology* vol. 28, no. 3, pp. 360-363, 1982.

"The ability to convert D-xylose to ethanol under these conditions is probably common among yeasts. Growth under the same conditions on xylitol, led to only traces of ethanol."

F. Ameglio, C. Di-Giorgio, "'Giant Cell' production by *C. albicans* cultured in xylitol," *Microbiologia* vol. 13, no. 4, pp. 343-6, 1990.

Buildup of intracellular xylitol catabolites caused cell swelling and weakening in *C. albicans*.

S. L. Vargas, C. C. Patrick, G. D. Ayers, W. T. Hughes, "Modulating effect of dietary supplementation on Candida albicans colonization and invasion in a neutropenic mouse model," *Infection and Immunology* vol. 61, no. 2, pp. 619-626, February 1993.

"Xylitol and glucose have different effects on the GI microflora." Xylitol caused a shift to a simpler, more gram-positive flora. Glucose led to higher rates of candida growth and invasion.

"It (xylitol) may therefore constitute a suitable carbohydrate for use in immunocompromised patients during periods of high risk for mucositis or candidemia."

Y. H. Samaranayake, T. W. MacFarlane, "The *in vitro* lysosyme susceptibility of *Candida albicans* cultured in carbohydrate supplemented media," *Oral Microbiology and Immunology,* pp. 177-81, June 1993.

Yeasts cultured in sucrose developed more resistance than those cultured in xylitol.

J. Chandra, D. M. Kuhn, P. K. Mukherjee, L. L. Hoyer, T. McCormick, M. A. Ghannoum, "Biofilm formation by the fungal pathogen *Candida albicans*: development, archetechture, and drug resistance," *Journal of Bacteriology* vol. 183, no. 18, pp. 5385-5394, 2001.

"These strains (of *Candida albicans)* were found to be positive for glucose, galactose, maltose, saccharose, and raffinose, but they were negative for 2-keto-D-gluconate, arabinose, xylose, adonitol, xylitol, inositol, sorbitol, *N*-acetyl-D-glucosamine, cellobiose, and lactose assimilation tests."

H. Abu-Elteen, H. Khaled, "The influence of dietary carbohydrates on in vitro adherence of four Candida species to human buccal epithelial cells (BEC)," *Microbial Ecology in Health and Disease* vol. 17, no. 3, pp. 156-162, 2005.

"C. albicans grown in galactose elicited maximal increase in adhesion followed by glucose and sucrose. Maltose and fructose also promoted adherence of Candida.

Xylitol significantly reduced adherence of Candida to BECs.

The dietary carbohydrates, therefore, might represent a risk factor for oral candidosis. The limitation of their consumption by substituting xylitol could be of value in the control of oral Candida colonization and infection."

T. Ichikawa, Y. Yano, Y. Fujita, T. Kashiwabara, K. Nagao, "The enhancement effect of three sugar alcohols on the fungicidal effect of benzethonium chloride toward *Candida albicans*" *Journal of Dentistry*, vol. 36, no. 11, pp. 965–968, 2008.

Sugar alcohols, especially erythritol, enhanced the fungicidal effect of BTC toward *in vitro* candidal biofilms.

Intravenous (Infusion Therapy, Parenteral Nutrition)

K. H. Brässler, K. Schultis, "Metabolism of fructose, sorbitol, and xylitol and their use in parenteral alimentation," in: *Total Parenteral Nutrition* H. Ghadimi (ed) John Wiley & Sons, NY, 1975.

Mixtures of carbohydrates (including xylitol) have some advantages in IV (intravenous) nutrition over pure glucose.

M. Georgieff, L. Moldawer, B. Bistrian, G. Blackburn, "Xylitol, an energy source for intravenous nutrition after trauma," *Journal of Parenteral and Enteral Nutrition* vol. 9, no. 2, pp. 199-209, 1985.

"Xylitol may have special pharmacologic properties during trauma or septicemia.

Partial replacement of glucose calories with xylitol may result in an overall better utilization of nutrients."

M. Georgieff, E. Pscheidl, et al,"The mechanism of the reduction of protein catabolism following trauma and during sepsis using xylitol" *Anaesthetist* pp. 85-91, Feb. 1991.

"Maximal glucose utilization is reduced during such states (trauma and sepsis), while the utilization of xylitol is more than doubled."

M. Georgieff, E. Pscheidl, et al, "Artificial Feeding," *Langenbecks-Arch-Chir-Suppl-Kongressbd* pp. 303-307, 1991.

"After trauma (first 4 days) xylitol is superior to glucose with regard to oxidative metabolism and stimulation of visceral protein synthesis." Comparable favorable long-term results were obtained with a 1:1 glucose:xylitol mixture.

G. Gross, T. Schricker, et al, "Carbohydrate and lipid metabolism following heart bypass operations. The effect of the intravenous hypocaloric administration of glucose versus xylitol:glucose (1:1) *Dtsch-Med-Wochenschr* pp. 1669-1674, Oct. 1992.

"Blood glucose and insulin levels were significantly lower in the xylitol:glucose group."

O. Hamberg, T. P. Almdal, "Effects of xylitol on urea synthesis in normal humans: relation to glucagons," *Journal of Parenteral and Enteral Nutrition* vol. 20, no. 2, pp. 139-144, 1996.

Xylitol blocked functional hepatic nitrogen clearace (FHNC) related to elevated glucagons levels.

"The mechanism whereby xylitol reduces nitrogen loss (muscle wasting) in stress metabolic conditions with hyperglucagonemia involves an effect on liver metabolism."

Long-Term Protection

P. Isokangas, J. Tiekso, P. Alanen, K. K. Mäkinen, "Long-term effect of xylitol chewing gum on dental caries," *Community Dentisty Oral Epidemiology,* vol.17, pp. 200-203, 1989.

"Further caries reduction was found 2 or 3 years after discontinuation of xylitol."

P. P. Hujoel, K. K. Mäkinen, C. A. Bennett, et al., "The optimum time to initiate habitual xylitol gum-chewing for obtaining long-term caries prevention," *Journal of Dental Research*, vol. 78, no. 3, pp. 797–803, 1999.

"Xylitol reduced the likelihood of subjects' developing caries in the five-year time period after they chewed the last experimental gum. When teeth erupted during the second year of habitual xylitol gum-chewing, the long-term caries risk reduction was 93%."

P. Isokangas, E. Söderling, K. Pienihäkkinen, P. Alanen, "Occurrence of dental decay in children children after maternal consumption of xylitol chewing gum, a follow-up from 0 to 5 years of age," *Journal of Dental Research*, vol. 79, no. 11, pp. 1885-1889, Nov. 2000.

"The presence of MS colonization in children at the age of 2 years was significantly related to each child's age at the first caries attack in the primary dentition. In children at the age of 5 years, the dentinal caries (dmf) in the xylitol group was reduced by about 70% as compared with that in the fluoride or chlorhexidine group. We conclude that maternal use of xylitol chewing gum can prevent dental caries in their children by prohibiting the transmission of MS from mother to child."

E. Söderling, P. Isokangas, K. Pienihäkkinen, J. Tenovuo, P. Alanen, "Influence of maternal xylitol consumption on mother-child transmission of mutans streptococci: 6-year follow-up," *Caries Research,* vol. 35, no. 3, pp. 173-177, May-June 2001.

"The earlier demonstrated, xylitol-associated reduction in the probability of mother-child transmission of MS was still found in the children's MS counts at the age of 3 and 6 years."

S. Haresaku, T. Hanioka, A. Tsutsui, M. Yamamoto, T. Chou, Y. Gunjishima, "Long-term effect of xylitol gum use on mutans streptococci in adults," *Caries Research* vol. 41, no. 3, pp. 198-203, 2007.

"The present study demonstrated that chewing xylitol gum for 6 months continued to inhibit the growth of mutans streptococci in adults."

The group that used maltitol sugar-free gum had increased levels of MS in plaque.

P. Fraga, M. P. Mayer, C. R. Rodrigues, "Use of chewing gum containing 15% of xylitol and reduction in mutans streptococci salivary levels," *Brazilian Oral Research* vol. 24, no. 2, pp. 142-146, June 2010.

"So, the use of xylitol induced a reduction in MS salivary levels after a short period of usage which persisted beyond its interruption."

P. Lingström, M. G. Cagetti, G. Sacco, L. Strohmenger, S. Sale, G. Campus, "Long-term effect of polyols in high risk caries schoolchildren," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

"Polyol-based chewing gums have a long-term effect on caries prevalence in children with a xylitol-containing gum being most effective."

Medical Uses – Other

T. Asakura, K. Adachi, H. Yoshikawa, "Reduction of oxidized glutathione by xylitol," *J Biochem* vol. 67, pp. 731-733, 1970.

Xylitol helps keep the antioxidant glutathione in its active (reduced) form.

S. G. Vainshtein, M. I. Pivikova, D. Maksudova, "Xylitol action on the gastric secretion and the external secretory function of the pancreas in patients with duodenal ulcer," *Vopr. Pitan.* (Russian) no. 1, pp. 14-17, 1973.

Xylitol has a stimulating effect on digestive enzymes.

J. van Eys, Y. M. Wang, S. Chan, S. Voravarn, S. Tanphaichitr, S. M. King, "Xylitol as a therapeutic agent in glucose-6-phosphate dehydrogenase deficiency," in: *Sugars in Nutrition* (Sipple HL, McNutt KW, eds), pp. 613-631, Academic Press, New York 1974.

Xylitol can help compensate for enzyme deficiency (glucose-6-phosphate dehydrogenase deficiency) by generating NADPH. This reduces red blood cell destruction in certain hemolytic anemias.

H. G. Zimmer, E. Gerlach, "Stimulation of myocardial adinine nucleotide biosynthesis by pentoses and pentitols," *Plügers Arch* vol. 376, pp. 223-227, 1978.

Ribose sugar and xylitol generate energy molecules in heart muscle.

T. Tanaka, H. Arimura, "Validity of xylitol for management of cardiac arrhythmia during aneathesia," *J Uoeh,* vol. 1, no. 3, pp. 365-369, 1979.

"Xylitol was administered in an attempt to normalize the functions of the sinus node and the A-V junction, and brought about a satisfactory result. It is, therefore, suggested that xylitol should be kept in mind for the treatment of cardiac arrhythmias during anesthesia."

N. Yoshimura, H. Yamada, M. Haraguchi, "Anti-arrhythmic effect of xylitol during anesthesia," *Japan Journal of Anesthesiology* vol. 28, pp. 841-848, 1979.

G. Assouline, A. Danon, "Hyperosmotic xylitol, prostoglandins and gastric mucosal barrier," *Prostaglandin Medicine* vol.7, pp. 63-70, 1981.

Xylitol used as an adjunct in gastric ulcer therapy.

W. A. Ukab, J. Sato, Y. M. Wang, J. van Eys, "Xylitol mediated amelioration of actylphenylhydrazine-induced hemolysis in rabbits," *Metabolism* vol. 30, pp. 1053-1059, 1981.

Xylitol helps protect red blood cell membranes.

D. Strauss, "The two-step presentation of red blood cells. A contribution to improve their viability and therapeutic efficiency," *Acta Biol Med Germ* vol. 40, pp. 721-725, 1981.

Added xylitol improves blood storage methods.

V. T. Palchun, V. I. Aslamazova, O. A. Buyanovskaya, T. S. Polyakova, "Employment of xylite for intralabyrinthine hydropsy detection," *Vestn. Otorinolaringol* (Russian) vol. 4, pp. 35-38, July-August 1982.

Single oral administration of xylitol increased the auditory threshold values of patients with Meniere's disease.

M. Bruyland, G. Ebinger, "Beneficial effect of treatment with xylitol in a patient with myoadenylate deaminase deficiency," *Clinical Neuropharmacology,* vol. 17, no. 5, pp. 492-493, October 1994.

Myoadenylate deaminase deficiency is an inherited disease (relatively common but most are not symptomatic) caused by lack of an enzyme used to recycle the energy molecule ATP. MAD is characterized by exercise intolerance, muscle weakness, cramps and soreness. One treatment is to provide the 5-carbon sugar D-ribose. In this trial, 20 grams of xylitol per day resolved the symptoms at a lower cost than ribose (xylitol is a metabolic precursor of ribose).

P. Naaber, E. Lehto, S. Salminen, M. Mikelsaar, "Inhibition of adhesion of Clostridium difficile to caco-2 cells," *FEMS Immunology and Medical Microbiology* vol. 14, no. 4, pp. 205-209, 1996.

Xylitol helped to inhibit adherence of *Clostridium difficile,* which is potentially useful for the prevention and treatment of pseudomembraneous colitis (antibiotic-associated diarrhea).

Metabolism

C. J. Carr and J. C. Krantz, "Metabolism of the sugar alcohols and their derivatives," *Advances in Carbohydrate Chemistry*, vol. 1, pp. 175–192, 1945.

R. L. Lohmar, "The polyols," in *The Carbohydrates, Chemistry, Biochemistry, Physiology*, W. Pigman, (ed), pp. 241–298, Academic Press, New York, NY, USA, 1962.

O. Touster, D. R. D. Shaw, "Biochemistry of the acyclic polyols," *Physiological Reviews*, vol. 42, pp. 181–225, 1962.

K. H. Dehmel, H. Förster, H. Mehnert, "Absorption of xylitol," in: *International symposium on metabolism, physiology and clinical uses of pentoses and pentitols.*
B. L. Horecker, K. Lang, Y. Takagi (eds), Springer-Verlag, Berlin, 1969.
In the small intestine, xylitol is absorbed more slowly than other sugars.

K. H. Bässler, "Biochemistry of Xylitol," in: *Xylitol.* J. N. Counsell (ed) Applied Science, London, 1977.
"Since the conversion to glucose proceeds smoothly with no abrupt effects n the blood glucose level and insulin secretion, xylitol instead of sucrose in the diabetic makes metabolic control easier. In starvation, diabetes and stress situations, xylitol has a normalizing effect on fat metabolism."

A. Bär, G. Ritzel (eds) "Xylitol and oxalate: studies in animals and man," *International Journal for Vitamin and Nutrition Research* supplement no. 28, Huber, Toronto 1985.
Collects, reviews and discusses possible concerns with metabolic effects of high-dose xylitol, based on Australian reports of toxicity from parenteral administration. Nine studies were reported as delivered or designed at a meeting held January 24-25 in Basel, Switzerland.
In general, it was concluded that xylitol is safe for peroral human consumption, and more definitive guidelines should be developed for parenteral administration.

A. Bär, "Effect of high oral doses of xylitol versus sucrose on urinary risk factors of urolithiasis in man," *International Journal for Vitamin and Nutrition Research* supplement no. 28, pp. 91-118, Huber, Toronto 1985.
"In conclusion, an assessment of the effects of high-dose xylitol administration on urinary risk factors for urolithiasis indicates that the observed changes were marginal and devoid of clinical significance."

Mother and Baby

J. Suhonen, B. Sener, "Release of preventive agents from pacifiers in vitro," *Schweiz Monatsschr Zahnmed*, vol. 104, no. 8, pp. 946-951, 1994.
Describes time-release xylitol via pacifier.

E. Söderling, P. Isokangas, Pienihäkinen, J. Tenovuo, "Influence of maternal xylitol consumption on acquisition of mutans streptococci by infants," *Journal Dental Research* vol. 79, pp. 882-887, 2000.

Mothers used xylitol gum from 3 to 24 months after delivery. Control groups received either fluoride or chlorhexidine varnishes on a regular schedule. MS colonization in the children was five-fold higher in the fluoride group, and three-fold higher in the Chlorhexidine group compared to the xylitol group.

Mothers who use xylitol gum are less likely to transmit harmful MS bacteria to their children.

P. Isokangas, E. Söderling, K. Pienihäkkinen, P. Alanen, "Occurrence of dental decay in children after maternal consumption of xylitol chewing gum, a follow-up from 0 to 5 years of age," *Journal of Dental Research*, vol. 79, no. 11, pp. 1885–1889, 2000.

At the age of 5 years, the caries rate was 70% lower in the xylitol than the fluoride or chlorhexidine groups.

S. Aaltonen, J. T. Suhonen, J. Tenovuo, I. Inkilä-Saari, "Efficacy of a slow-release device containing fluoride, xylitol and sorbitol in preventing infant caries" *Acta Odontologica Scandinavica*, vol. 58, no. 6, pp. 285–292, 2000.

Use of a novel "fall asleep pacifier" delivering time-release fluoride, xylitol and sorbitol significantly reduced MS colonization and caries in children.

I. Thorild, B. Lindau, S. Twetman, "Effect of maternal use of chewing gums containing xylitol, chlorhexidine or fluoride on mutans streptococci colonization in the mothers' infant children," *Oral Health Preventive Dentistry*, vol. 1, no. 1, pp. 53–57, 2003.

"Maternal consumption of xylitol- and chlorhexidine/xylitol-containing chewing gums significantly reduced the mother-child transmission of salivary mutans streptococci."

It is important to note that in this trial in Sweeden, all the groups of mothers used chewing gum from child age 6 months to 18 months. The amount of xylitol was rather low, but still showed a positive benefit for the pure xylitol group. Children of high-risk mothers who used 100% xylitol gum had MS colonization rates similar to the low-risk group.

I. Thorild, B. Lindau, S. Twetman, "Caries in 4-year-old children after maternal chewing of gums containing combinations of xylitol, sorbitol, chlorhexidine and fluoride," *European Archives of Paediatric Dentistry*, vol. 7, no. 4, pp. 241–245, 2006.

"Less caries was observed in children of mothers who chewed gums with xylitol as the single sweetener during the time of eruption of the first primary teeth compared with those who used gums containing fluoride, sorbitol and lower amounts of xylitol."

E. Söderling, "Xylitol reduces mother-child transmission of mutans streptococci," *Finnish Dental Journal,* supplement 1, pp. 8-11, 2006.

Follow-ups at age 6 and 10 continued to show lower MS counts in the xylitol group compared with the fluoride and chlorhexidine groups, along with significantly less need for restorative dental treatment.

Y. Nakai, "Influence of maternal xylitol consumption on mother-child transmission of cariogenic bacteria during and after pregnancy – a promising strategy against initiation of caries," *Finnish Dental Journal,* supplement 1, pp. 12-17, 2006.

"Xylitol was effective as an additional caries preventive procedure in pregnant women."

S. E. Coldwell, T. K. Oswald, D. R. Reed, "A marker of growth differs between adolescents with high vs. low sugar preference," *Behavior Physiology* vol. 96, no. 23, pp. 574-580, March, 2009.

Preference for the sweet taste appears to be innate and related to growth.

M. Fontana, D. Catt, G. J. Eckert, S. Ofner, M. Toro, R. L. Gregory, A. F. Zandona, H. Eggertsson, R. Jackson, J. Chin, D. Zero, C. H. Sissons, "Xylitol: effects on the acquisition of cariogenic species in infants," *Pediatric Dentistry*, vol. 31, no. 3, pp. 257–266, 2009.

This study found an association between mother food-tasting and MS colonization. The xylitol effects were not considered significant. Xylitol use was limited to 6 and 9 months.

P. Milgrom, K. A. Ly, O. K. Tut, L. Mancl, M. C. Roberts, K. Briand, M. J. Gancio, "Xylitol pediatric topical oral syrup to prevent dental caries – a double-blind randomized clinical trial of efficacy," *Archives of Pediatrics and Adolescent Medicine*, vol. 163, no. 7, pp. 601–607, 2009.

Xylitol syrup squirted on teeth (8 grams at least twice per day) was effective in reducing early childhood caries by up to 70%.

Anonymous, "Xylitol-containing oral syrup may prevent caries in children," *The Journal of the American Dental Association*, vol. 140, p. 972, 2009.

Xylitol syrup is likely to be effective in populations with high caries rates.

Y. Nakai, C. Shinga-Ishihara, M. Kaji, K. Murakami-Yamanaka, M. Takimura, "Xylitol gum and maternal transmission of mutans streptococci," *Journal of Dental Research* vol. 89, no. 1, pp. 56-60, 2010.

Maternal gum chewing began in the sixth month of pregnancy and ended 13 months later. The children of mothers in the xylitol group had significantly less colonization or at least delayed colonization by MS than the control group.

"In summary, xylitol gum chewing… starting at pregnancy, significantly reduced mother-child transmission of MS in this Japanese population."

M.-L. Laitala, "Dental Health in Primary Teeth After Prevention of Mother-Child Transmission of Mutans Streptococci – A Historical Cohort Study on Restorative Visits and Maternal Prevention Costs," Academic Dissertation presented at the University of Turku Institute of Dentistry, September 24, 2010.

"The ten-year follow-up suggested that the results of the Ylivieska (Finland) mother-child study had not been temporary and that the prevention of MS transmission (with xylitol) in assumed high-risk families can be economically reasonable."

Nose and Ear; Upper Respiratory

T. Kontiokari, M. Uhari, M. Koskela, "Effect of xylitol on growth of nasopharyngeal bacteria in vitro," *Antimicrob Agents Chemother* vol 39, no. 8, pp. 1820-, August 1995.

Xylitol markedly inhibited the growth of alpha-hemolytic streptococci.

M. Uhari, T. Kontiokari, M. Niemelä, "A novel use of xylitol sugar in preventing acute otitis media," *Pediatrics* vol. 102 (4 Pt 1), pp. 879–84, October 1998.

"With the increasing appearance of antimicrobial resistance, alternatives are needed to prevent bacterial diseases. We found xylitol to be a promising new product, effective in syrup and chewing gums, for preventing acute otitis media (AOM) in children."

M. Uhari, T. Kontiokari, M. Koskela, M. Niemelä, "Xylitol chewing gum in prevention of acute otitis media: double blind randomised trial. *British Medical Journal* vol. 313, no. 7066, pp. 1180-1184, 1996.

Xylitol chewing gum reduced the occurrence of otitis media by 40%.

T. Kontiokari, M. Uhari, M. Koskela, "Antiadhesive effects of xylitol on otopathogenic bacteria," *Journal of Antimicrobial Chemotherapy* vol. 41, no. 5, pp. 563-565, May, 1998

Xylitol reduces the adherence of *Streptococcus pneunomiae* and *Hemophilus influenzae* to epithelial cells.

J. Zabner, M. P. Seler, J. L. Launspach, P. H. Karp, W. R. Kearney, D. C. Look, J. J. Smith, M. J. Welsh, "The osmolyte xylitol reduces the salt concentration of airway surface fluid and may enhance bacterial killing." *Proceedings of the National Academy of Sciences USA*. Vol. 97, no. 21, pp. 11614-11619, October 10, 2000.

"Xylitol may be of value in enhancing the innate antimicrobial defense at the airway surface."

A. H. Jones, "Intranasal Xylitol, Recurrent Otitis Media, and Asthma: Report of Three Cases." *Clinical Practice of Alternative Medicine,* vol. 2, no. 2, pp. 112–117, 2001.

L. Vernacchio, R. M. Vezina, A. A. Mitchell, "Tolerability of oral xylitol solution in young children: implications for otitis media prophylaxis," *International Journal of Pediatric Otorhinolargology* vol. 71, no. 1, pp. 89-94, 2007.

Xylitol solutions of 5 to 7.5 grams were well tolerated by toddlers aged 6 to 36 months.

J. L. Danhauer, C. E. Johnson, S. N. Rotan, T. A. Snelson, J. S. Stockwell, "National survey about pediatricians' opinions about and practices for acute otitis media and xylitol use," *Journal American Academy of Audiology*. vol. 21, no. 5, pp. 329-346, May 2010.

Only about half of the pediatricians surveyed knew about medical uses of xylitol. "Future research should focus on prevention and the use of xylitol as a possible prophylaxis regimen for Acute Otitis Media in patients."

Orthodontics

T. M. Graber, T. P. Muller, V. D. Bhatia, "The effect of xylitol gum and rinses on plaque acidogenesis in patients with fixed orthodontic appliances," *Swedish Dental Journal*, vol. 15, pp. 41-55, 1982.

Xylitol helps prevent damage to teeth and gums during fixed orthodontic treatment.

K. P. Isotupa, S. Gunn, C. Y. Chen, D. Lopatin, K. K. Mäkinen, "Effect of polyol gums on dental plaque in orthodontic patients," *American Journal of Orthodontics and Dentalfacial Orthopedics* vol. 107, pp. 497-504, 1995.

100% xylitol-sweetened gum yielded the best results in reducing plaque and MS in young patients wearing fixed orthodontic appliances (braces).

C. Stecksén-Blicks, P. L. Holgerson, M. Olsson, B. Bylund, I. Sjostrom, K. Skold-Larsson, S. Kalfas, S. Twetman, "Effect of xylitol on mutans streptococci and lactic acid formation in saliva and plaque from adolescents and young adults with fixed orthodontic appliances," *European Journal Oral Science,* vol. 112, no. 3, pp. 244-248, 2004.

Xylitol in tablets was used at a low dose of 1.7 or 3.4 g/day for 18 weeks. There were no changes in MS counts in plaque or saliva.

"The lactic acid formation rates decreased slightly (approximately 10%) in the two xylitol groups compared with baseline."

A. Sengun, Z. Sari, S. I. Ramoglu, S. Malkoç, I. Duran, "Evaluation of the dental plaque recovery effect of a xylitol lozenge on patients with fixed orthodontic appliances," *The Angle Orthodontist* vol. 74, no. 2, pp. 240-244, 2004.

"The use of a xylitol lozenge after a sucrose challenge can be an advisable practice for fixed orthodontic patients to prevent future dental caries."

Periodontal (Gum) Disease

V. Luostarinen, K. Paunio, J. Varrela, M. Rekola, S. Luoma, A. Scheinin, K. K. Mäkinen, "Turku sugar studies, XV. Vascular reactions in the hamster cheek pouch to human gingival exudate," *Acta Odontologica Scandinavica*, vol. 33, supplement 70, pp. 287-291, 1975.

There was less inflammation with xylitol users.

U. Harjola, H. Liesmaa, "Effects of polyol and sucrose candies on plaque, gingivitis and lactobacillus index scores," *Acta Odontologica Scandinavica*, vol. 36, no. 4, pp. 237-242, 1978.

There was less gingival bleeding with xylitol.

J. Tenovuo, H. Mielityinen, K. Paunio, "Effect of dental plaque grown in the presence of xylitol or sucrose on bone resorption in vitro," *Pharmacology and Therapeutics in Dentistry*, vol. 6, no. 1-2, pp. 35-43, 1981.

"The inflammatory potential of dental plaque may be reduced during xylitol consumption as compared to sucrose consumption."

H. Mielityinen, J. Tenovuo, E. Söderling, K. Paunio, "Effect of xylitol and sucrose plaque on release of lysosomal enzymes from bones and macrophages in vitro," *Acta Odontologica Scandinavica*, vol. 41, no. 3, pp. 173-180, 1983.

Xylitol plaque was less irritating for macrophages and bones than sucrose plaque.

K. Paunio, H. Hurttia, J. Tenovuo, K. K. Mäkinen, J. Tiekso, "Effects on oral health of mouthrinses containing xylitol, sodium cyclamate and sucrose sweeteners in the absence of oral hygiene. I. Clinical findings and analysis of gingival exudates," *Proceedings of the Finnish Dental Society*, vol. 80, no. 1, pp. 3-12, 1984.

Sucrose rinse was the most irritating for bone.

H. Hurttia, V-M Multanen, K. K. Mäkinen, J. Tenovuo, K. Paunio, " Effects on oral health of mouthrinses containing xylitol, sodium cyclamate and sucrose sweeteners in the absence of oral hygiene, III. Composition and bone resorbing potential of dental plaque," *Proceedings of the Finnish Dental Society*, vol. 80, no. 1, pp. 20-27, 1984.

"The total carbohydrate content was significantly lower in plaque obtained from the xylitol and cyclamate groups than in plaque obtained from the sucrose group. Rinsing with xylitol solution resulted in a higher plaque calcium level than with the two other sweeteners."

V. Luostarinen, K. K. Mäkinen, P.-L. Mäkinen, "Effects on oral health of mouthrinses containing xylitol, sodium cyclamate and sucrose sweeteners in the absence of oral hygiene. V. Response of hamster cheek pouch microcirculation to dental plaque," *Proceedings of the Finnish Dental Society*, vol. 80, no. 1, pp. 35–39, 1984.

Xylitol plaque was less inflammatory than sucrose plaque.

K. K. Mäkinen, D. Pemberton, J. Cole, P.-L. Mäkinen, C.-Y. Chen, P. Lambert, "Saliva stimulants and the oral health of geriatric patients," *Adv Dental Research* vol. 9, no. 2, pp. 125-126, July 1995.

Along with reductions in occurrence of root surface caries, xylitol use also improved gingival health.

S. J. Han, S. Y. Jeong, Y. J. Nam, K. H. Yang, H. S. Lim, J. Chung, "Xylitol inhibits inflammatory cytokine expression induced by lipopolysaccharide from Porphyromonas gingivalis," *Clinical and Diagnostic Laboratory Immunology*, vol. 12, no. 11, pp. 1285–1291, 2005.

"Taken together, these findings suggest that xylitol may have good clinical effect not only for caries but also for periodontitis by its inhibitory effect on the LPS-induced inflammatory cytokine expression." This Korean study also showed that xylitol inhibits the growth of *P. gingivalis,* an important periodontal pathogen.

M. Shyama, E. Honkala, S. Honkala, S. A. Al-Mutawa, "Effect of xylitol candies on plaque and gingival indices in physically disabled school pupils**,"** *Clin Dent* vol. 17, no. 1, pp. 17-21, 2006.

Plaque and Gingival Index scores were significantly improved with the three uses of xylitol candy during school days.

W. A. Bretz, O. P. S. Rosa, S.M. Silva, P. M. Corby, O. C. Lima, M. Milanda, P. Hujoel, W. J. Loesche, "On the acquisition of periodontopathic bacteria by children from mothers," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 18-24, 2006.

"These overall findings of beneficial effects of xylitol-based protocols on periodontal parameters corroborate our findings.

We have demonstrated that a combined treatment consisting of xylitol gum/chlorhexidine- and fluoride- varnish was moderately superior on periodontal parameters of mothers. Similar results were found for (their) infants."

T. Iwamoto, N. Suzuki, K. Tanabe, T. Takeshita, T. Hirofuji, "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* vol. 110, no. 2, pp. 201-208, August 2010.

Use of probiotic/xylitol tablets for 2 and 4 weeks showed improvement in halitosis and gingival bleeding upon probing.

M. Al-Haboubi, L. Zoitopoulos, D. Beighton, J. Gallagher, "Gum-chewing for the prevention of oral diseases in older people," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

Participants, at least 60 years old, who chewed xylitol gum twice a day for 6 months demonstrated significant improvements in Plaque and Gingival Index scores over the control group.

Regulatory and Endorsements

H. Limeback, F. M. Eggert, "Xylitol in chewing gum: A discussion on developing CDA guidelines for the recognition of food products with dental therapeutic claims," *Journal of the Canadian Dental Association* vol. 55, no. 9, pp. 717-719, September 1989.

"These 'cariostatic" effects make xylitol the best sugar substitute for chewing gum, children's medications, and, perhaps, a variety of other sweetened products."

K. K. Mäkinen, "Public use and recommendations of xylitol in the prevention of dental caries," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 66-75, 2006.

"Public policy recommendations regarding dental benefits of such (xylitol) products should be allowed and manufacturers permitted to make scientifically-supported promotional health claims in package labeling and media advertising."

M. Pöyry, "The Finnish endorsement practice for xylitol products," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 62-65, 2006.

Typical approved statement: "The Finnish Dental Association recommends the use of xylitol."

Originating Council, Council on Clinical Affairs, American Academy of Pediatric Dentistry, "Policy on the use of xylitol in caries prevention," *Reference Manual,* vol. 31, no. 6, pp. 9-10, 2006.

"The American Academy of Pediatric Dentistry (AAPD) recognizes the benefits of caries preventive strategies involving sugar substitutes, particularly xylitol, on the oral health of infants, children, adolescents, and persons with special health care needs."

K. W. Shyu and M. Y. Hsu, "The cariogenicity of xylitol, mannitol, sorbitol, and sucrose," *Proceedings of the National Science Council, Republic of China*, vol. 4, pp. 21-26, 1980.

Remineralization

I. Tarján, L.-Å. Linden, "Investigation of enamel permeability with marked saccharose and xylit," *Fogorvos Szle*, vol. 74, pp. 235-238, 1981 (Hungarian).

More than twice as many xylitol as sucrose molecules diffuse through dental enamel.

R. Havenaar, J. H. J. Huis in't Veld, J. D. de Stoppelaar, O. Backer Dirks, "Anti-cariogenic and remineralizing properties of xylitol in combination with sucrose in rats inoculated with *Streptococcus mutans*," *Caries Research*, vol. 18, no. 3, pp. 269-277, 1984.

K. K. Mäkinen, E. Söderling, "Solubility of calcium salts, enamel, and hydroxyapatite in aqueous solutions of simple carbohydrates," *Calcified Tissue International* vol. 36, pp. 64-71, 1984.

"Whereas the more soluble Ca(II) compounds (like $CaSO_4$) exerted measurable complexation with xylitol, no such complexation was found with hydroxyapatite and enamel powder. … Through the retarding effect on calcium phosphate precipitation, alditols may favorably govern remineralization of carious lesions."

M. T. Smits and J. Arends, "Influence of extraoral xylitol and sucrose dippings on enamel demineralization in vivo," *Caries Research*, vol. 22, no. 3, pp. 160-165, 1988.

Mineral loss in enamel was about three times higher with sucrose than xylitol.

R. H. Manning, W. M. Edgar, E. A. Agalamanyi, "Effects of chewing gums sweetened with sorbitol or a sorbitol/xylitol mixture on the remineralisation of human enamel lesions in situ," *Caries Research*, vol. 26, no. 2, pp. 104-109, 1992.

Chewing sorbitol or sorbitol/xylitol gum for 20 minutes after meals and snacks stimulated remineralization by salivary means.

A. Scheinin, E. Söderling, U. Scheinin, R. L. Glass, M.-L. Kallio, "Xylitol-induced changes of enamel microhardness paralleled by microradiographic observations," *Acta Odontologica Scandinavica*, vol. 51, no. 4, pp. 241-246, 1993.

Exposure to xylitol (20 grams per day in candy) resulted in pronounced rehardening.

K. Wennerholm, J. Arends, D. Birkhed, J. Ruben, C. G. Emilson, A. G. Dijkman, "Effect of xylitol and sorbitol in chewing-gums on mutans streptococci, plaque pH and mineral loss of enamel," *Caries Research*, vol. 28, no. 1, pp. 48-54, 1994.

This 25-day study suggested a concentration response with xylitol.

"The pH drop in plaque, measured in vivo after a 1-min mouthrinse with a 10% sorbitol solution, was least pronounced after the 70% xylitol gum and most pronounced after the 70% sorbitol gum period."

K. K. Mäkinen, P.-L. Mäkinen, H. R. Pape Jr., P. Allen, C. A. Bennett, P. J. Isokangas, K. P. Isotupa, "Stabilization of rampant caries: polyol gums and arrest of dentine caries in two long-term cohort studies in young subjects," *International Dental Journal*, vol. 45, pp. 93-107, 1995.

These observations are from the chewing gums field trials carried out in Belize.

"The usage of 100 per cent xylitol pellet-shaped gum was more frequently associated with arrest of dentine caries than other treatments. … High-xylitol chewing gum usage can retard or arrest even rampant caries."

K. K. Mäkinen, D. J. Chiego Jr., P. Allen, et al., "Physical, chemical, and histologic changes in dentin caries lesions of primary teeth induced by regular use of polyol chewing gums," *Acta Odontologica Scandinavica*, vol. 56, pp. 148-156, 1998.

Primary teeth with dentin caries that remineralized during xylitol use were examined by electron microscope and for microhardness. "The rehardened surface layer (normally <0.1 mm in thickness) was significantly harder than sound dentin and nearly as hard as sound enamel."

Y. Miake, M. Takahashi, Y. Saeki, T. Yanagisawa, "Effect of xylitol on remineralization of demineralized enamel," *The Shikwa Gakuho*, vol. 99, pp. 393-399, 1999 (Japanese).

"When remineralizing solution containing xylitol is used, xylitol may act as Ca2+ ion carrier and may maintain constant Ca2+ ion content by introducing Ca2+ ions from the surface layer to the middle and deep demineralized layers, thereby enhancing total remineralization. The present study demonstrates that remineralization occurs over the entire demineralized layers via the utilization of xylitol."

Y. Miake, T. Yanagisawa, "Effects of xylitol on remineralization of artificial demineralized enamel," *Japanese Journal of Oral Biology*, vol. 42, pp. 580-589, 2000.

"Remineralization near the surface layer advanced because of crystal formation resulting from fluoride action. Xylitol additives working as calcium-ion carriers possibly promoted remineralization in the intermediate and deep layers."

M. Takahashi, Y. Saeki, Y. Miake, T. Yanagisawa, "Effects of sugar alcohols and calcium compounds on remineralization," *Shikwa Gakuho*, vol. 100, pp. 755-762, 2000 (Japanese).

"It was found that among sugar alcohols and calcium compounds tested, the combination of xylitol and calcium hydrogenphosphate strongly enhanced the remineralization of demineralized layers."

Y. Saeki, M. Takahashi, S. Kamikawa, T. Tokumoto, Y. Miake, S. Yamada, K. Okuda, T. Yanagisawa, "Remineralization effect of xylitol chewing gum containing *Gloipeltis furcata* extract and calcium hydrogenphosphate on initial caries-like enamel lesions," *Japanese Journal of Oral Biology*, vol. 42, pp. 590-600, 2000 (Japanese).

Xylitol chewing gum is even more effective with the addition of calcium and seaweed extract.

M. Takahashi, Y. Saeki, K. Fujimoto, H. Matsuzaki, Y. Miake, and T. Yanagisawa, "Remineralization effects of xylitol dragee gum containing *Gloipeltis furcata* extract and calcium hydrogenphosphate on initial caries-like enamel lesions in vivo," *The Shikwa Gakuho*, vol. 101, pp. 1033-1042, 2001 (Japanese).

"Xylitol gum containing G. furcata extract and calcium hydrogenphosphate amplified the remineralization throughout all demineralized layers. Furthermore, the effect of this gum stronger than that of maltitol gum."

Y. Miake, M. Takahashi, Y. Saeki, T. Yanagisawa, "Remineralization effects of xylitol on demineralized enamel," *Journal of Electron Microscopy* vol. 52, pp. 471-476, 2003.

"Xylitol can induce remineralization of deeper layers of demineralized enamel by facilitating Ca^{2+} movement and accessibility."

T. Yanagisawa, Y. Miake, Y. Saeki, M. Takahashi, "Remineralization in enamel caries and restoration of carious lesions by enhanced remineralization induced by saliva and xylitol," *Dentistry in Japan*, vol. 39, pp. 208-215, 2003.

Xylitol gum enhanced the remineralization of initial caries-like enamel lesions

T. Yanagisawa, Y. Miake, "Prevention of caries and restoration of initial enamel caries by remineralization enhanced with xylitol +2 gum," *Finnish Dental Journal*, vol. 13, supplement 1, pp. 44-49, 2006.

"Remineralization becomes all the more remarkable in the presence of xylitol. Xylitol strongly stimulated saliva-induced remineralization in deep layers."

R. Suda, T. Suzuki, R. Takiguchi, K. Egawa, T. Sano, and K. Hasegawa, "The effect of adding calcium lactate to xylitol chewing gum on remineralization of enamel lesions," *Caries Research*, vol. 40, no. 1, pp. 43-46, 2006.

Adding calcium to xylitol gum increased the remineralizing effect.

S. Thaweboon, S. Nakornchai, Y. Miyake, T. Yanagisawa, B. Thaweboon, S. Soo-ampon, D. Lexomboon, "Remineralizaron of enamel subsurface lesions by xylitol chewing gum containing funoran and calcium hydrogenphosphate," *Southeast Asian Journal of Tropical Medicine and Public Health*, vol. 40, no. 2, pp. 345-353, 2009.

"Chewing xylitol gum containing funoran and calcium hydrogenphosphate has a significant effect on the remineralization of initial caries-like lesions of the teeth."

Safety

K. H. Bässler, W. Toussaint, G. Stein, "Xylit-verwertung bei fruehgeborenen, saeuglingen, kindern und erwachsenen kinetic der elimination aus dem blut," *Klin Wochenschr* vol. 14, pp. 212-215, 1966.

Even premature babies are fully capable of metabolizing xylitol.

U. C. Dubach, E. Feiner, "Orale vertaglichkeit von xylit bei stoffwechselgesunden probanden," *Schweiz med Wschr* vol.99, pp. 190-194, 1969.

Adaptation up to 200 grams per day in divided doses is possible.

T. Asano, et al, "Xylitol absorption in healthy men," *Diabetes* vol. 21, pp. 350-351, 1972.

Absorption decreases with increasing dosage. Blood chemistries were all normal.

M. Brin, O. N. Miller, "The safety of oral xylitol," in: "*Sugars in Nutrition*" (H. L. Sipple, K. W. McNutt, eds), pp. 591-605, Academic Press, New York 1974.

"Xylitol, with adaptation, is well-tolerated and safe to levels of at least 90 grams per day, with no subjective or objective adverse findings."

H. Förster, "Tolerance in the human. Adults and children," in *Xylitol,* J. N. Counsel (ed) Applied Science Publishers, Ltd. London, pp. 42-46, 1977.

"In our own experiments, 100 grams (per day, after adaptation) was well-tolerated without much difficulty."

A. Scheinin, "Xylitol in relation to oral and general health," *International Dental Journal,* vol. 29, pp. 237-243, 1979.

"Recent metabolic studies have further indicated the safety of perorally administered xylitol at the present dosage levels. Comprehensive blood and urinary analysis on human subjects have revealed no untoward side effects."

K. K. Mäkinen, R. Ylikahri, P.-L. Mäkinen, E. Söderling, M. Hämäläinen, "Turku Sugar Studies XXIII. Comparison of metabolic tolerance to high oral doses of xylitol and sucrose after long-term regular consumption of xylitol," *International Journal of Vitamin and Nutrition Research* (Supplement 22) pp. 29-51, 1981.

"The subjects' body weights and blood values remained normal throughout the whole, more than 5-year period involving the regular consumption of substantial amounts of xylitol."

H. K. Åkerblom, T. Koivukangas, et al, "The tolerance of increasing amounts of dietary xylitol in children," *International Journal of Vitamin and Nutrition Research* vol. 22 (supplement), pp. 53-66, 1982.

Even in small children there are usually no side effects with the amount of xylitol needed for dental protection.

R. Senti, "Health aspects of sugar alcohols and lactose," *US Department of Health and Human Services* Life Sciences Research Office, Federation of American Societies for Experimental Biology. Report prepared for Food Safety and Applied Nutrition, Food and Drug Administration (Contract no. FDA 223-83-3020) 1986.

The safety profile of xylitol was reviewed and found similar to the milk sugar lactose. Any adverse effects in animals were species-specific and not significant for humans.

S. J. Culbert, Y. M. Wang, H. A. Fritsche Jr, D. Carr, E. Lantin, J vanEys, "Oral xylitol in American adults" *Nutrition Research* vol. 6, pp. 913-922, 1986.

The only adverse reports were transient gastrointestinal discomfort with xylitol over-consumption.

K. K. Mäkinen, "Dietary prevention of dental caries by xylitol – clinical effectiveness and safety," *Journal of Applied Nutrition* vol. 43, no. 1, 1991.

"The accumulated scientific evidence demonstrates that xylitol meets the safety and efficacy prerequisites for use in caries prevention programs."

Special Properties

L. Hyvoenen, R. Kurkela, P. Koivistoinen, P. Merimaa, "Effects of temperature and concentration on the relative sweetness of fructose, glucose and xylitol," *Lebensm Wiss Technol* vol. 10, pp. 316-320, 1977.

Sweetness of xylitol is similar to sucrose. Fructose is sweeter; glucose less sweet.

J. F. Back, D. Oakenfull, M. B. Smith, "Increased thermal stability of proteins in the presence of sugars and polyols," *Biochemistry*, vol. 18, no. 23, pp. 5191-5196, 1979.

Polyols stabilize proteins against heat denaturation.

K. K. Mäkinen, E. Söderling, "Effect of xylitol on some food-spoilage microorganisms" *Journal of Food Science* vol. 46, no. 3, pp. 950-951, 1981.

Xylitol inhibits several important food-spoilage organisms.

M. Brin, Discussion in *Foods, Nutrition and Dental Health Vol 1* Pathotox, Park Forest South, Il, 1981.

"There may be some inadvertent health and nutritional benefits from the presence of xylitol in the diet."

A. M. Rofe, R. Krishnan, R. Bais, J. B. Edwards, R. Conyers, "A mechanism for the thiamine-sparing action of dietary xylitol in the rat" *Australian Journal of Exp Biol Med Science* vol. 60, pp. 101-111, 1982.

Dietary xylitol helped prevent B-vitamin deficiencies.

K. K. Mäkinen, E. Söderling, "Solubility of calcium salts, enamel, and hydroxyapatite in aqueous solutions of simple carbohydrates," *Calcified Tissue International*, vol. 36, no. 1, pp. 64-74, 1984.

"Alditols (such as xylitol) do not function as demineralizing agents of the teeth, however. Through the retarding effect on calcium phosphate precipitation, alditols may favorably govern remineralization of carious lesions."

E. Söderling, K. K. Mäkinen, "Aggregation of human salivary Ca-proteinates in the presence of simple carbohydrates in vitro," *Scandinavian Journal of Dental Research*, vol. 94, no. 2, pp. 125–131, 1986.

Xylitol inhibits aggregation of calcium-proteinates.

K. K. Mäkinen, E. Söderling, D. R. Peacor, P.-L. Mäkinen, L. M. Park, "Carbohydrate-controlled precipitation of apatite with coprecipitation of organic molecules in human saliva: stabilizing role of polyols," *Calcified Tissue International*, vol. 44, pp. 258–268, 1989.

"Aldo- and ketosugars and disaccharides (maltose, sucrose, lactose) generally enhanced precipitation, whereas all polyols (xylitol, D-sorbitol, mannitol, and maltitol) retarded the formation of turbidity in saliva. Xylitol inhibited formation of precipitates also in the presence of D-xylose, dextrans, and starch."

E. Sjökvist, C. Nyström, "Physiochemical aspects of drug release. XI. Tableting properties of solid dispersions, using xylitol as a carrier," *International Journal of Pharmaceutics* vol. 67, pp. 139-153, 1991.

"The results indicate that xylitol can be used as a carrier in tablets of solid dispersions, when a fast drug release is desired."

M. Carlevaro, E. R. Caffarena, J. R. Grigera, "Hydration properties of xylitol: computer simulation," *International Journal of Biological Macromolecules*, vol. 23, no. 2, pp. 149–155, 1998.

"There is a relatively strong hydration of xylitol. This polyol adopts a single linear conformation and, from the point of view of the hydration dynamics, it should be classified as positively hydrated."

M. Soleimani, L. Tabil, S. Panigrahi, "Bio-production of a polyalcohol (xylitol) from lignocellulosic resources: a review," *The Canadian Society for Bioengineering* presentation at CSBE/SCGAB Annual Conference, no. 06-106, Edmonton, Alberta, July 16-19, 2006.

"Xylitol is being used as a highly valued ingredient with some interesting and useful properties in food and pharmaceutical products. It can be produced from xylose-rich (hemicellulose fraction of lignocellulose) resources by chemical or biotechnological method."

Special Situations

U. Pakkala, H. Liesmaa, and K. K. Mäkinen, "Use of xylitol in the control of oral hygiene in mentally retarded children: a clinical and biochemical study," *Proceedings of the Finnish Dental Society*, vol. 71, no. 5, pp. 271–277, 1981.

Over a period of 60 days, 20 grams of xylitol per day (as tablets with meals) improved plaque index, gingival bleeding scores, and overall oral hygiene.

L. Turtola, "A trial of adding xylitol chewing gum to a part of university students' meals," *Finnish Student Health Service Publications* vol. 30, pp. 1-55, Health Service Office, Helsinki, 1990.

College students surveyed gave almost unanimous, unconditional support for a program of including xylitol gum routinely with school-based meals.

K. Masalin, "Caries-reducing effects of xylitol-containing chewing gum and tablets in confectionery workers in Finland," *Community Dental Health* vol. 9, pp. 3-10, 1992.

"An ordinary commercial xylitol-containing chewing-gum can be used to decrease caries risk factors in confectionery workers."

K. K. Mäkinen, "A dietary procedure for preventing dental caries in young adults," *Journal of American College Health* vol. 41, pp. 172-180, January 1993.

"Xylitol should always be used immediately after exposure to sugar or other carbohydrates."

S. Twetman, L. G. Petersson, "Influence of xylitol in dentifrice on salivary microflora of preschool children at caries risk," *Swedish Dental Journal* vol. 19, no. 3, pp. 103-108, 1995.

After 3 months twice daily use of fluoride toothpaste in a preschool setting, more children in the xylitol group had reduced MS scores (toothpaste had 9.7% added xylitol).

E. Honkala, A. Rimpelä, S. Karvonen, M. Rimpelä, "Chewing of xylitol gum – a well adopted practice among Finnish adolescents," *Caries Research* vol. 30, no. 1, pp. 34-39, 1996.

From 1977 use of xylitol gum in Finland has increased dramatically: among teenage girls, from 1% to 81%, with 61% reporting regular daily use.

"The increase in use of xylitol gum is an example of the positive effect of health education given by a comprehensive, preventively oriented system of dental health care in association with commercial interests."

K. K. Mäkinen, D. Pemberton, P.-L. Mäkinen, C.-Y. Chen, J. Cole, P. Hujoel, D. Lopatin, P. Lambert, "Polyol-combinant saliva stimulants and oral health in veterans affairs patients—an exploratory study," *Special Care in Dentistry*, vol. 16, no. 3, pp. 104–115, 1996.

Xylitol was more effective than sorbitol in reducing the incidence of root surface caries. Xylitol use also stimulated saliva, improved gingival health, and even help reduced cravings for cigarettes in several smokers.

L. Erickson, "Oral health promotion and prevention for older adults," *Dental Clinics of North America,* vol. 41, no. 4, pp. 727-747, October 1997.

"Chewing gum containing xylitol as the sweetener has resulted in reduced risk of root surface caries. It may effectively reduce plaque, the virulence of plaque, the acidity of plaque after a sucrose challenge, and gingivitis."

M. Lam, C. A. Riedy, P. Milgrom, S. E. Coldwell, R. Craig, "Children's acceptance of xylitol-based foods," *Community Dentistry Oral Epidemiology* vol. 28, no. 2, pp. 97-101, 2000.

"These results suggest that snack foods developed with xylitol are generally well accepted by children." Most children aged 3 to 6 years found at least 5 of 6 snack foods sweetened with xylitol acceptable or very good.

J. T. Autio, F. J. Courts, "Acceptance of the chewing gum regimen by preschool children and teachers in a Head Start program: a pilot study," *Pediatric Dentistry* vol. 23, no. 1, pp. 71-74, 2001.

"Children's acceptance and compliance for chewing was excellent. Children chewed the gum at designated times and none of the children swallowed the gum. Teachers' acceptance of the chewing program was low."

J. T. Autio, "Effect of xylitol chewing gum on salivary streptococcus mutans in preschool children," *Journal of Dentistry for Children,* vol. 69, no. 1, pp. 81-86, 2002.

"This study supports the suggestion that chewing xylitol gum may reduce salivary S. mutans levels. Xylitol chewing gum may provide a feasible caries prevention method for preschool children."

K. K. Mäkinen, K. P. Isotupa, T. Kivilompolo, P.-L. Mäkinen, S. Murtomaa, J. Petäjä, J. Toivanen, E. Söderling, "The effect of polyol-combinant saliva stimulants on *S. mutans* levels in plaque and saliva of patients with mental retardation," *Special Care in Dentistry*, vol. 22, no. 5, pp. 187–193, 2002.

"The results suggest that xylitol-containing saliva stimulants may be more effective than sorbitol-containing products in controlling some caries-associated parameters in people who are mentally disabled."

H. Kovari, K. Pienihäkkinen, P. Alanen, "The use of xylitol chewing gum in kindergartens," *Acta Odontologica Scandinavia* vol. 61, pp. 367-370, 2003.

"Oral health status in the xylitol group was a little bit better than in the control group. The use of xylitol can therefore be recommended, especially if the personnel do not have the possibility to supervise the brushing."

P. Richter, J. Chaffin, "Army's 'Look for Xylitol First' program," *The Dental Assistant* vol. 73, pp. 38-40, March-April 2004.

"The U.S. Army Dental Command's Health Promotion Program is constantly seeking additional prevention measures to enhance the oral health of America's Army. The Dental Command has created the "Look for Xylitol First" initiative aimed at training all members of the dental care team on the positive benefits of xylitol and to teach patients how to be smart consumers and evaluate products for their xylitol content."

K. K. Mäkinen, K. P. Isotupa, P.-L. Mäkinen, E. Söderling, K. B. Song, S. H. Nam, S. H. Jeong, "Six-month polyol chewing-gum programme in kindergarten-age children: a feasibility study focusing on mutans streptococci and dental plaque," *International Dental Journal,* vol. 55, no. 2, pp. 81-88, April 2005.

"Habitual use of relatively small daily quantities of polyol-containing chewing gum by young children may be regarded as an important additional caries-preventive procedure in a combined day-care centre and home setting. Especially xylitol-containing chewing gum may significantly reduce the growth of mutans streptococci and dental plaque which may be associated with dental caries."

D. H. Kitchens, "Xylitol in the prevention of oral diseases," *Special Care in Dentistry*, vol. 25, no. 3, pp. 140-144, 2005.

"The purpose of this paper is to review information for the inclusion of xylitol in primary preventive regimens as an adjunct for the prevention of oral diseases for special needs patients."

J. L. Castillo, P. Milgrom, S. E. Coldwell, R. Castillo, R. Lazo, "Children's acceptance of milk with xylitol or sorbitol for dental caries prevention." *BMC Oral Health,* vol. 22, no. 5, 2006.

"Milk sweetened with xylitol is well accepted by Peruvian children ages 4-7 years." Xylitol in milk was preferred over plain milk or milk with sorbitol.

J. D. Featherstone, "Delivery challenges for fluoride, Chlorhexidine and xylitol," *BMC Oral Health,* vol. 15, no. 6, supplement 1, p. S8, June 2006.

"Xylitol delivered by gum or lozenge appears to be effective clinically in reducing cariogenic bacteria and caries levels, but novel systems that deliver therapeutic amounts when needed would be a major advance, especially for young children."

E. Honkala, S. Honkala, M. Shyama, S. A. Al-Mutawa, "Field trials on caries prevention with xylitol candies among disabled school students," *Caries Research*, vol. 40, no. 6, pp. 508–513, 2006.

Tooth decay rates were cut in half by relatively small amounts of xylitol in hard candy.

S. Gutkowski, "Dental hygiene for dependent adults," *Dental Tribune International* October 2009.

"It is prudent for clinicians to advise all patients approaching declining age to start using xylitol products as a preventive. Use of these products may be the answer everyone has been waiting for."

M. Seki, F. Karakama, T. Kawato, H. Tanaka, Y. Saeki, Y. Yamashita, "Effect of xylitol gum on the oral health of preschoolers," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

Xylitol gum was used 4 times a day for 3 months by chidren 3 to 4 years old. "Xylitol gum consumption is effective in avoiding increased plaque mutans streptococci in young children."

Sweeteners (Other)

C. Aminoff, "New carbohydrate sweeteners," In: *Sugars in Nutrition* (Sipple HL, McNutt KW, eds), Chapter 10, Academic Press, New York 1974.

"Xylitol has first been used for parenteral nutrition and subsequently as a sweetener in diets for diabetics."

H. Förster, in: *Xylitol* J. N. Counsell (ed) 1977.

"(Gastrointestinal) tolerance to maltitol is very low. My volunteers said that maltitol did the most terrible things to them and they would not take part in any more tests."

J. Ainamo, S. Asikainen, A. Ainamo, A. Lahtinen, M. Sjöblom, "Plaque growth while chewing sorbitol and xylitol simultaneously with sucrose flavored gum," *Journal of Clinical Periodontology* vol. 6, no. 6, pp. 397-406, 1979.

A mixture of sucrose and xylitol in chewing gum was not effective in reducing plaque.

K. K. Mäkinen, E. Söderling, "A quantitive study of mannitol, sorbitol and xylose in wild berries and commercial fruits," *Journal of Food Science* vol. 45, pp. 367-371, 1980.

Xylitol is found in a wide variety of fruits and vegetables, but in small quantities.

K. K. Mäkinen, "New biochemical aspects of sweeteners," *The International Dental Journal*, vol. 35, no. 1, pp. 23–35, 1985.

A. Vissink, E. J. S'Gravenmade, T. B. F. M. Gelhard, A. K. Panders, and M. H. Franken, "Rehardening properties of mucin- or CMC-containing saliva substitutes on softened human enamel," *Caries Research*, vol. 19, pp. 212–218, 1985.

The best rehardening properties were for saliva substitutes with xylitol.

K. K. Mäkinen, P. Isokangas, "Relationship between carbohydrate sweeteners and oral diseases," *Progress in Food and Nutrition Science* vol. 12, pp. 73-109, 1988.

"More research is needed to assess the ability of mixtures of xylitol with sorbitol, maltitol, other sugar alcohols and intense sweeteners to prevent oral plaque diseases.

Xylitol (is) an exceptionally effective caries-reducing instrument provided that xylitol is not mixed in foods containing large amounts of sucrose."

W. Strübig, "Caries etiologic aspects of sugar and sugar substitutes," *Zahnärztlicher Gesundheitsdienst*, vol. 19, no. 2, pp. 10–13, 1989.

T. H. Grenby, A. Phillips, M. Mistry, "Studies of the dental properties of lactitol compared with five other bulk sweeteners," *Caries Research* 23, pp. 315-319, 1989.

Acid and polysaccharide production were reduced with xylitol.

"The amounts of polysaccharide synthesized by the microorganisms in the incubations decreased in the order: glucose>sucrose>sorbitol>mannitol>lactitol>xylitol."

S. D. Hogg, A. J. Rugg-Gunn, "Can the oral flora adapt to sorbitol?" *Journal of Dentistry* vol. 19, pp. 263-271, 1991.

"Frequent use of sorbitol may present a small cariogenic risk in people with low salivary flow."

E. Newbrun, "Dental effects of sugars and sweeteners," in N. Kretchmer, C. B. Hollenbeck (eds) *Sugars and Sweeteners,* pp. 175-202, 1991.

"The central role of sucrose in promoting dental caries is beyond reasonable dispute. Other fermentable sugars such as glucose, fructose, corn syrups, and high fructose corn syrups, are also cariogenic.

Most sugar alcohols (sorbitol, mannitol, lactitol, maltitol and hydrogenated starch hydrolysate (HSH) are fermented at much slower rates by oral flora than sucrose; however, with long-term use the oral microflora will adapt and they are then more acidogenic. Xylitol is an exception in that it is not fermented at all by normal oral flora and produces no caries."

R. J. Verdi, L. Hood, "Advantages of alternative sweetener blends," *Food Technology* pp. 94-101, June, 1993.

An expensive ingredient like xylitol is often blended with less costly bulking agents along with intense sweeteners. Xylitol is sometimes used in small amounts to potentiate flavor in sugar-free applications.

J. M. Navia, "Carbohydrates and dental health," *American Journal of Clinical Nutrition* vol. 59, no. 3 (supplement) Proceedings of a symposium "Carbohydrates in human nutrition" held in Ystad, Sweden May 19-22, 1992, pp. 719S-727S, March 1994.

"The final conclusion has always been that consumption of sugars is a risk factor for caries.

The previously mentioned characteristics of sorbitol and xylitol make sorbitol a very low caries-promoting sugar alcohol, and xylitol either a non- or even anticarious ingredient in foods."

K. K. Mäkinen, "Sugar alcohols," in *Functional Foods, Designer Foods, Pharmafoods, Nutraceuticals*, I. Goldberg, (ed.), pp. 219–241, Chapman & Hall, New York, NY, USA, 1994.

Catalogs common sugar alcohols -- their occurrence, uses and selected properties.

D. Kandelman, "Sugar, alternative sweeteners and meal frequency in relation to caries prevention: new perspectives," *British Journal of Nutrition,* vol. 77, supplement 1, pp. S121-S128, April 1997.

Caries risk is related to the frequency of carbohydrate consumption. "The use of chewing gum and other xylitol-containing products have resulted in defined reduction in caries and represent interesting alternatives for high-caries-risk populations."

K. K. Mäkinen, "Can the pentitol-hexitol theory explain the clinical observations made with xylitol?" *Medical Hypotheses*, vol. 54, no. 4, pp. 603–613, 2000.

Not all sugar alcohols share the same characteristics. The uncommon 5-carbon structure of xylitol may help explain some unique health benefits.

M. A. Gales, T. M. Nguyen, "Sorbitol compared with xylitol in the prevention of dental caries," *Ann Pharmacother* vol. 34, pp. 98-100, 2000.

K. K. Mäkinen, K. P. Isotupa, T. Kivilompolo, P.-L. Mäkinen, J. Toivanen, and E. Söderling, "Comparison of erythritol and xylitol saliva stimulants in the control of dental plaque and mutans streptococci," *Caries Research*, vol. 35, no. 2, pp. 129–135, 2001.

R. Touger-Decker, C. van Loveren, "Sugars and dental caries," *American Journal of Clinical Nutrition,* vol. 78, no. 4 (supplement), pp. 881S-892S, October 2003.

"Xylitol—a 5-carbon sugar that oral microflora cannot metabolize—has additional anticariogenic effects attributable to antimicrobial action, stimulation of saliva resulting in increased buffer activity and an increase in pH, and enhanced remineralization."

K. K. Mäkinen, "Sweeteners and dental health," in *Functional Foods, Degenerative Disease, and Ageing*, C. Remacle and B. Reusens, (Eds), pp. 200–219, Woodhead, Cambridge, UK, 2004.

K. K. Mäkinen, M. Saag, K. P. Isotupa, et al., "Similarity of the effects of erythritol and xylitol on some risk factors of dental caries," *Caries Research*, vol. 39, pp. 207–215, 2005.

"Erythritol and xylitol may exert similar effects on some risk factors of dental caries, although the biochemical mechanism of the effects may differ."

D. T. Zero, "Are sugar substitutes also anticariogenic?" *Journal of the American Dental Association* vol. 139, supplement 2, pp. 9S-10S, 2008.

"Unlike sorbitol, which can be metabolized slowly by some oral bacteria, xylitol has a bacteriostatic effect on mutans streptococci. It also has been reported to reduce mutans streptococci levels in plaque and saliva, block mother-to-child transmission of mutans streptococci and alter the acidogenic potential of plaque to subsequent sugar challenges. Xylitol-containing chewing gum and mints can be recommended as an adjunct to other preventive intervention strategies if cost considerations do not outweigh effectiveness."

Toothpaste and Oral Care Products

J. D. B. Featherstone, T. W. Cutress, B. E. Rodgers, and P. J. Dennison, "Remineralization of artificial caries-like lesions in vivo by a self-administered mouthrinse or paste," *Caries Research*, vol. 16, pp. 235–242, 1982.

The authors did not pay attention to the possible role of xylitol (2.5% as a flavoring agent) as a contributor to enhanced remineralization of one of the rinses.

K. K. Mäkinen, E. Söderling, H. Hurttia, O.-P. Lehtonen, E. Luukkala,"Biochemical, microbiologic and clinical comparisons between two dentifices that contain different mixtures of sugar alcohols," *Journal of the American Dental Association,* vol. 111, pp. 745-751, 1985.

"The reduction of dental plaque and caries is achieved regardless of how the xylitol is administered. The only prerequisite is to get the xylitol into contact with the teeth."

M. Svanberg and D. Birkhed, "Effect of dentifrices containing either xylitol and glycerol or sorbitol on mutans streptococci in saliva," *Caries Research*, vol. 25, no. 6, pp. 449–453, 1991.

"Significant reduction of MS was found in subjects using the xylitol/glycerol dentifrice."

L. G. Petersson, D. Birkhed, A. Gleerup, M. Johansson, G. Jönsson, "Caries-preventive effect of dentifrices containing various types and concentrations of fluorides and sugar alcohols," *Caries Research*, vol. 25, no. 1, pp. 74–79, 1991.

"Children with no detectable approximal caries at baseline, who used the MFP toothpaste with the xylitol-sorbitol mixture, showed a lower ($p < 0.05$) caries increment as compared with children who used the MFP toothpaste with sorbitol alone."

J. L. Sintes, C. Escalante, B. Stewart, J. J. McCool, L. García, A. R. Volpe, C. Triol, "Enhanced anticaries efficacy of a 0.243% sodium fluoride/xylitol/silica dentifrice: 3-year clinical results," *American Journal of Dentistry*, vol. 8, no. 5, pp. 231–235, 1995.

Fluoride toothpaste with added 10% xylitol provided a significantly greater anticaries benefit than similar fluoride toothpaste without xylitol.

A. Surdacka, J. Stopa, "The effect of xylitol toothpaste on the oral cavity environment," *The Journal of Preventive Medicine* vol. 13, no. 1-2, pp. 98-107, 2005.

"Xylitol added to toothpastes has a positive influence on the quality of the oral environment and, as a result, it would be purposeful to introduce it into prophylactic programmes."

P. Lif Holgerson, C. Stecksén-Blicks, I. Sjöström, M. Öberg, "Xylitol concentration in saliva and dental plaque after use of various xylitol-containing products," *Caries Research* vol. 40, pp. 393-397, 2006.

"All xylitol-containing products resulted in significantly increased levels immediately after intake and remained elevated for 8–16 min in the different groups. The highest mean value in saliva was obtained immediately after use of chewing gums and the lowest was demonstrated after using toothpaste. No significant differences were demonstrated between chewing gums, sucking tablets, candyand rinses."

S. E. Calamari, A. I. Azcurra, E. R. Luna Maldonado, L. J. Battellino, S. T. Cattoni, R. G. Colantonio, "Effects of xylitol, sorbitol and fluoride mouthrinses on glucose clearance in adolescents," *Acta Odontológica Latinoamericana* vol. 10, no. 1, pp. 25-36, 1997.

Xylitol treatment (14 days) provoked an increase in oral glucose clearance, which was proportional to its concentration in the mouthrinse formula, up to 40% with 1% xylitol concentration.

P. Lingström, F. Lundgren, D. Birkhed, I. Takazoe, G. Frostell, "Effects of frequent mouthrinses with palatinose and xylitol on dental plaque," *European Journal of Oral Science* vol. 105, no. 2, pp. 162-169, April 1997.

The most pronounced pH drop for the sugar substitutes was found when rinsing with palatinose, and the least with xylitol. MS counts and plaque index scores decreased after xylitol.

L. Jannesson, S. Renvert, D. Birkhed, "Effect of xylitol in an enzyme-containing dentifrice without sodium lauryl sulfate on mutans streptococci in vivo," *Acta Odontologica Scandinavia* vol. 55, no. 4, pp. 212-216, August 1997.

"Thus, this study demonstrated 1) that addition of 10% xylitol to an enzyme-containing dentifrice without sodium lauryl sulfate has an inhibitory effect on MS counts in saliva and dental plaque, and 2) that the inhibitory effect seems to be dose-dependent."

E. Cutler, W. Bruce, J. Phillips, "Effect of high-xylitol-content dentifrice on periodontal markers," (Unpublished results of 6-months trial), October 2000.

Toothpaste containing 36% xylitol (Squigle Enamel Saver®) was superior to regular, (non-xylitol) fluoride toothpaste with respect to bleeding index, gingival index and plaque index in a group of 78 periodontal patients.

L. Jannesson, S. Renvert, P. Kjellsdotter, A. Gaffer, N. Nabi, "Effect of a triclosan-containing toothpaste supplemented with 10% xylitol on mutans streptococci in saliva and dental plaque. A 6-month clinical study," *Caries Research* vol. 36, no.1, pp. 36-39, 2002.

"The addition of 10% xylitol to a triclosan-containing dentifrice reduces the number of MS in saliva and dental plaque."

J. L. Sintes, A. Elías-Boneta, B. Stewart, A. R. Volpe, J. Lovett, "Anticaries efficacy of a sodium monofluorophosphate dentifrice containing xylitol in a dicalcium phosphate dihydrate base. A 30-month caries clinical study in Costa Rica," *American Journal of Dentistry*, vol. 15, no. 4, pp. 215–219, 2002.

H. Sano, S. Nakashima, Y. Songpaisan, P. Phantumvanit, "Effect of a xylitol and fluoride containing toothpaste on the remineralization of human enamel in vitro," *Journal of Oral Science*, vol. 49, no. 1, pp. 67–73, 2007.

Adding xylitol to fluoride toothpaste enhanced the remineralizing effect.

A. F. F. Pereira, T. C. Silva, T. L. Silva, M. L. Caldana, J. R. M. Bastos, M. A. R. Buzalaf, "Varnish, a new vehicle to increase xylitol release in saliva," International Association for Dental Research, 88th General Session, Barcelona, Spain, July 2010.

"Xylitol varnish can be regarded as a promising vehicle for increasing xylitol release along time."

WWW.

National Institutes of Health, "Consensus development conference statement. Diagnosis and management of dental caries through life," March 2002, http://nidcr.gov/news/consensus.asp.