Milk Helps Build Strong Teeth and Promotes Oral Health

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ABSTRACT

A great deal of research into the benefits of milk consumption has gone largely under the radar for many decades. There is a wealth of studies both in the United States and abroad to suggest that milk consumption is largely anti-cariogenic when combined with a typical routine of oral hygiene. This effect can be mostly attributed to several factors: tooth remineralization, inhibition of bacterial colonization, and biofilm inhibition. These abilities have been studied in detail and are likely due to numerous proteins found in milk. An attractive feature of milk from the community health perspective is its widespread consumption throughout the world. For this reason, studies have been initiated to investigate the possibilities of using milk to deliver fluoride and antibacterial antibodies to high-risk populations worldwide. This review will focus on the various components of milk, which promote oral health, and will also discuss common approaches to improve upon the oral health benefits of milk consumption.

Section 1: A Brief Overview of Milk's Benefits for Oral Health

Got milk? Thanks to a plethora of high-profile milk mustaches, there is now widespread recognition of the benefits of milk for maintaining healthy bones. However, little has been described about the effects of milk on oral health. To obtain a comprehensive overview on the subject, the authors conducted an extensive survey of literature related to milk and oral health. With hundreds of research reports surveyed, the general consensus has indicated that milk provides numerous components associated with improved oral health.

Studies on the benefits of milk in caries control can be traced back more than

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50 years. Since then, a global research effort has been devoted to determining the relationship between milk or dairy product consumption and the prevention of tooth decay. Research suggests that the benefits of milk and related products can be traced to several principal factors: remineralization of the tooth, prevention of bacterial attachment to the tooth, and inhibition of bacterial biofilm formation ability. In addition to the most obvious beneficial factor, calcium, milk has also been shown to contain multiple proteins that serve a variety of functions important for oral health. For example, casein is a family of proteins, which comprise 80 percent of the milk protein. They can actually help to recruit calcium phosphates to demineralized surfaces on the tooth. Casein is also able to prevent the adhesion of caries-causing bacteria to the tooth surface as well. Besides casein, milk contains whey proteins, lactoferrin, lysozyme, and antibodies, which all serve to promote oral health via their interactions with various cariogenic bacteria.

These properties of milk have prompted some suggestions for its use as an artificial saliva for those suffering from xerostomia or hyposalivation.[1] It is well-established that those afflicted with the condition have a greatly increased risk for developing dental caries, in addition to suffering from many other discomforts. While milk offers many of the lubricating features of saliva, it can also provide some of the anti-cariogenic protection found in saliva as well. Animal studies validate the utility of milk for this purpose.[2] However, a well-controlled comparison of milk versus commercially available saliva substitutes is currently lacking.

Section 2: A Detailed Overview of Literature on the Benefits of Milk on Oral Health

Many health benefits of milk consumption have yet to incorporate themselves into the psyche of the general public, despite a wealth of supporting data. This is especially true for the association of milk with maintaining oral health. There are numerous studies beginning as far back as the 1950s that have investigated the role of dietary milk consumption and caries experience in both animals and humans.[3-5] Since that time, research has continued to develop into a more detailed analysis of dairy product consumption. Current research focuses largely on oral health issues related to specific types of dairy product consumption, analysis of bioactive compounds

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contained within milk, and even using milk as a delivery vehicle for anti-cariogenic agents. These studies have provided substantial evidence for the role of milk in promoting oral health.

Given the early association of milk consumption with reduced caries experience, numerous groups have probed the cariogenic potential of milk and other dairy products under the controlled laboratory setting using both *in vitro* and *in vivo* approaches. For example, using an *in vitro* caries model, it was shown by Bibby et al. that incorporating milk solids into laboratory cakes containing sucrose and starch reduced its capacity to promote the dissolution of enamel chips by lactic acid-producing bacteria, whereas, removing the milk component resulted in a higher caries rate.[6] Animal studies have also shown a positive role of milk in the prevention of caries. Desalivated rats fed with a diet of either 2 percent milk or lactose-reduced milk remained largely caries-free, which even suggested a possible application for xerostomia patients.[2]

Furthermore, a recent study in Brazil aimed at comparing the cariogenic potential of cow's milk versus several infant formulas found that cow's milk had the lowest cariogenic potential of the substances fed to Wistar rats infected with a high dose of *Streptococcus sobrinus*.[7] A similar conclusion was also reached by a comparative study at the University of Rochester. Researchers found several commonly used infant formulas to be largely cariogenic in rats, whereas milk proved to be the least cariogenic.[8]

Further evidence from studies of infant and child beverage consumption has also supported the data found in animal studies. The data are especially striking when milk consumption is compared with children fed sweetened drinks. Invariably, milk consumption was associated with significantly lower proportions of mutans streptococci on the teeth.[9,10] However, it should be noted that there is a general concern among pediatric dentists concerning the lactose content in milk. Since lactose is itself a fermentable sugar, certain conditions can favor caries formation from milk consumption. This is true for nursing or bottle-feeding mothers who feed continually for prolonged periods or bottle feed milk immediately before sleep.[11] Since sleeping with a bottle in the mouth can interfere with the protective action of saliva, any sugars, such as the lactose found in milk, are much more likely to promote caries than during typical consumption patterns.[12] Therefore, it is generally advised that bottle-fed children about to sleep should not be given any beverages containing sugars.

Several recent studies from the United States and Europe have all associated milk or dairy product consumption with lower caries experience when combined with a normal routine of oral hygiene.[13-15] In a study by Petti et al., they also noted a caries preventive effect from milk consumption in a subgroup of their subjects that consumed high levels of sucrose.[13] Much attention has also been given to the effects of cheese consumption. Studies suggest that not only does cheese have a cariostatic effect, but it exerts this effect by efficiently increasing the saliva and plaque concentrations of calcium.[16,17] Additionally, this phenomenon has also been observed when cheese was consumed in a more typical fashion: as part of a mixed meal.[18] Hard cheeses have even been suggested as a remedy to offset the effects of radiation caries in individuals experiencing xerostomia from neck cancer radiation therapy.[19]

While very few studies have probed the effect of milk on issues related to periodontal health, it was recently reported that in a group of Italian adolescent females aged 17 to 19, nutrition, specifically, milk consumption, could account for the differences in observed gingival health at the conclusion of the study. The authors of the study inferred that the increased riboflavin and calcium intake in the milk drinkers was a major contributing factor to the reduced risk of gingivitis.[20] Similarly, it was found from separate studies that a low dietary intake of calcium resulted in more severe periodontal disease, whereas increased calcium and vitamin D intake seemingly yielded protective effects against tooth loss.[21-23] Therefore, it should be quite interesting to further examine dairy product consumption in patients at risk for periodontal disease.

Given the numerous studies indicating milk and other dairy products as beneficial for promoting oral health, it is not surprising that there has been a large amount of effort devoted to determining the mechanisms associated with these benefits. Interestingly, a large volume of data has accumulated to suggest that milk and other dairy products contain numerous bioactive compounds relevant to preventing caries and are not simply calcium delivery vehicles. These compounds are generally derived from the various proteins found in milk. By far, the most extensively studied group of these bioactive milk proteins is the caseins. This group of proteins also accounts for the largest percentage of milk proteins (80 percent).[24]

Caseins actually comprise a family of proteins subdivided into the α/α_{s1} and α/α_{s2}), α, and κ-caseins.[25] These proteins are generally thought to have a positive effect on cariogenesis via two mechanisms: prevention of demineralization and inhibition of bacterial attachment and/or biofilm formation.

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The protective properties of casein against demineralization were demonstrated in an intraoral caries model using sodium caseinate, α_{s1} casein, and a tryptic digest of α_{s1} casein (TD-casein). Supragingival plaque was inoculated onto bovine enamel chips that were treated with either a 3 percent sucrose + 3 percent glucose-salt (wt/vol) solution, or the same solution with the addition of 2 percent sodium caseinate (wt/vol). After 10 days of exposure, the chips incubated with the addition of sodium caseinate showed no evidence of subsurface enamel demineralization as determined by microradiography and microdensitometry.

In the author's next experiment, the enamel chips were exposed to the sucrose-glucose sugar solution six times per day for 10 days and given a treatment of either a 2 percent (wt/vol) solution of sodium caseinate, α_{s1} casein, or TD-casein. Similarly, all three forms of casein were found to be protective against subsurface enamel demineralization and both α_{s1} casein and TD-casein were shown to be incorporated into the enamel plaques. It was suggested that protection from demineralization was mediated by the ability of casein to incorporate into the plaque and thereby increase plaque calcium phosphate concentration as well as to create a buffering capacity derived from the various phosphorylated residues within the protein.[26]

In a follow-up study by the same investigator, the ability of a tryptic digest of casein to remineralize enamel lesions was investigated. This digested form of casein, known as casein phosphopeptide, CPP, was able to stabilize amorphous calcium phosphate and, therefore, stimulate the remineralization of subsurface lesions in the enamel by maintaining a local high concentration gradient of calcium phosphate. After a 10-day period of remineralization in the presence of 1 percent (wt/vol) CPP + calcium phosphate, sectioned enamel lesions were analyzed by microradiography and microdensitometry and found to have an average of 63.9 percent replacement of the lost mineral within the lesions.[27]

Thus, it seems that the anti-caries effect of added casein is largely dependent upon the ability of casein or casein fragments to localize a high concentration gradient of calcium phosphate into the plaque structure where it can prevent, or even reverse the process of demineralization.

In addition to its capacity to alter caries progression, several other studies have demonstrated the ability of various caseins to modulate the ability of bacteria to initiate caries as well. In a study of *S. mutans* attachment to saliva-coated hydroxyapatite beads, it was shown that incubation with milk or κ-casein effectively prevented *S. mutans* from attaching

to the beads.[28] A later study by the same group found that hydroxyapatite beads carried in the mouth had altered salivary pellicle formation on the beads as a result of either milk or κ-casein rinses.

Again, bacteria were found to be inhibited in their ability to attach to these beads in the presence of milk or κ-casein. It was suggested in this study that the attachment defects could be mediated by alterations in pellicle formation as a result of exposure to these proteins.[29] Pellicles formed in the presence of milk and κ-casein were also able to inhibit the glucosyltransferase activity of *S. mutans*, which could yield an additional mechanism to prevent adherence and/or biofilm formation as well.[29,30] In a similar study, *S. sobrinus* attachment to the tooth surface was also found to be potently inhibited by casein derivatives.[31,32] Additionally, *in vivo* studies using a rat model of caries, challenged with a cariogenic diet, plus multiple milk proteins, demonstrated a 73 percent to 80 percent reduction in the numbers of *S. sobrinus* in rats that consumed milk proteins containing casein. This resulted in the inhibition of both advanced dentinal fissure and smooth surface caries lesions.[33] Peptide derivatives of casein have even been shown to prevent oral actinomycete attachment to erythrocytes by inhibiting their hemagglutinin activity.[34] Therefore, it seems that casein not only aids in preventing demineralization, but it may also play an active role in inhibiting the pathogenic potential of a diverse array of oral bacteria.

Despite the wide spectrum of activity associated with casein or casein derivatives, a study by Grenby et al. suggested that one of the main caries protective effects of milk may actually not even reside in the casein fraction of milk. Using typical enamel demineralization tests, the authors examined the ability of milk fractions removed of the lactose, fat, and casein-associated components, and found that the remaining material was still largely protective against demineralization. Further analysis revealed that the activity was associated with two particular fractions enriched for the presence of proteose-peptone, which are minor components of the whey proteins in milk.[35] Further analysis of the remaining fractions confirmed the findings of a previous study in which it was suggested that milk also has a mineral component that can aid in the prevention of buccal and sulcal caries in rats.[35,36]

In those areas that are both remote and economically disadvantaged, milk fluoridation may be the only realistic option to lower caries incidence on a community-wide scale.

Other minor protein components of milk may also yield, as yet, unidentified oral health benefits. Milk contains the iron-chelating protein lactoferrin, which has been previously shown to have activity against *S. mutans*.[37] Interestingly, a portion of the bovine lactoferrin protein was recently shown to be responsible for inhibiting the attachment of *S. mutans* to salivary agglutinin and thus may aid in the prevention of tooth colonization.[38,39] This inhibitory activity was shown to be due to a competition for binding to salivary agglutinin, and was independent of the iron-chelating activity of lactoferrin.[38,39] Milk also has a small amount of lysozyme, which is the same antibacterial agent found in tears and saliva.[24] While there are currently no studies that have suggested a protective role for these proteins during milk consumption, it would be interesting to determine whether these proteins have the ability to induce changes in bacterial plaque populations.

Beginning in the 1950s, it was suggested that milk could also be used as a vehicle for delivering anti-cariogenic substances.[40] Specifically, it was suggested that fluoride salts be added to milk in order to augment the benefits of proper oral hygiene. At that time, fluoride was not a typical additive to public drinking water and, presumably, the ubiquity of milk consumption would have proven useful to increase the amount of fluoride in the diet of the average citizen.

According to a report by the Centers for Disease Control, by the year 2000, 65.8 percent of the American population served by public water systems received optimally fluoridated water. Therefore, the need for widespread fluoridation of milk has waned in the United States. In contrast, in many parts of the world, especially in rural areas and economically deprived regions, milk fluoridation is still pursued as a viable alternative to large-scale water fluoridation. This option has been actively investigated by the World Health Organization to lower the caries incidence in poorer populations with a high-caries burden. In a study aimed at assessing the efficacy of milk fluoridation in Bulgarian school children, it was found that children participating in the program for five years had a DMFT index that was 79 percent lower than those who did not.[41]

A 21-month trial of fluoridated milk in Beijing, China, also reported a highly significant reduction in the DMFT scores of kindergarten-age participants.[42] In those areas that are both remote and economically disadvantaged, milk fluoridation may be the only realistic option to lower caries incidence on a community-wide scale. In Codegua, Chile, a large program was initiated through the National Complementary Feeding Program to include fluoridated powdered milk in the diets of preschool children of various age groups. At the termination of the program four years later, the DMFT indices of the 3- to

6-year-old age group had dropped by 72 percent and the proportion of caries-free children in the community had risen from 22 percent to 48.4 percent.[43]

Interestingly, the authors surveyed the same community several years after the conclusion of their previous study and found that caries prevalence had increased to a level equivalent to the control community which had not received any fluoride supplements.[44] Clearly, there was a marked deterioration in the oral health of this community in the absence of continued supplemented milk consumption.

The potential benefits of fluoridated milk have also been investigated in the laboratory setting as well. Using a rat model of caries, two separate studies have determined that fluoridated milk is a very effective means for caries prevention.[45,46] Interestingly, a study by Banoczy et al. found that fluoridated milk was even more effective than fluoridated water in reducing caries experience.[46] In addition, the utility of fluoridated milk has been well-supported by *in vitro* experiments of enamel demineralization and has even been demonstrated to alter proportions of plaque streptococci as well.[47-49] Therefore, for both practicality and efficacy, it seems that using milk as a means to deliver fluoride into the diet is quite effective and, in some instances, may be the best available option.

Another alternative use of milk has been to deliver antibodies that offer protection from cariogenic bacterial species. Rat studies in the 1970s first investigated the possibility of immunizing pregnant animals against *S. mutans* in order to enrich the milk with anti-*S. mutans* antibodies for the benefit of the offspring (passive immunization). The results indicated that the ingested IgG and IgA antibodies were indeed protective against caries.[50,51] Given the promising results of these early studies, recent research has focused on immunizing cows in order to deliver this same protective benefit to milk consumers. This strategy provides promise since it would not require genetic manipulation of cows and would only change the specificity of the antibodies that are already found in milk.

One approach has been to simply immunize cows with specific bacterial species and allow antibody formation against a whole slew of antigens present on the bacterial surface. This approach has been tested using *S. mutans* as well as *S. sobrinus*. In both instances, it was found to elicit protection from bacterial colonization and stimulated phagocytosis by human leukocytes.[52,53] Other studies have chosen to immunize in a more defined manner, which has the potential advantage of enriching for those antibodies that would theoretically affect specific virulence properties of a cariogenic species. This strategy has been tested by simply injecting cows using specific proteins derived from *S. mutans*. Two of the most heavily studied proteins used for this purpose are the cell surface protein antigen (PAc) and the glucan synthesizing enzyme glucosyltransferase I. Antibodies from immune milk directed against these proteins have been shown to inhibit the colonization ability of *S. mutans* as well as reduce its biofilm-forming capability in *in vitro* studies, animal models, and even in limited human trials.[54-56]

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From a production perspective, one of the major concerns for large-scale passive immunization is whether the antibodies in immune milk have a shelf life that permits reasonable protection for the intended lifetime of the product. This was tested by adding anti-streptococcal antibodies to ultra-high temperature-treated toddler's milk and testing antibody efficacy after storage for two months at various temperatures. It was reported that after two months of storage, the titers of these antibodies did not decrease at any of the tested storage temperatures and all provided protection from bacterial colonization.[57]

Interestingly, using passive immunization with immune milk has also been investigated for other oral diseases, such as oral submucous fibrosis, with promising results.[58] Furthermore, it should also be feasible to use this same strategy to inactivate known periodontal pathogens as well. Undoubtedly, this approach will be investigated in the future if immune milk becomes a common item on grocery store shelves.

With the current abundance of beverage choices available to the consumer, it is not surprising that such a familiar item as milk can be taken for granted. This has not been the case for the scientific community however; as a great deal of attention has been devoted to milk studies for the past 50 years and still continues to this day. In fact, it is actually quite extraordinary to consider the scope and diversity of milk research conducted over the years. Perhaps in the near future, parents will recognize one more reason to promote milk consumption to the next generation: oral health. CDA

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