

REVIEW

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The use of sugar free chewing gum as a supplement in the prevention of dental caries. Narrative Review

Abstract: Dental caries is one of the most prevalent diseases. The WHO has classified it as one of the major public health problems worldwide. That is why a special emphasis has been paid to developing new preventive methods and the use of gum without sugar has been included as one of them. This strategy has significant benefits on oral health due to: (1) saliva stimulation, which favors teeth clearance and regulates the pH; (2) remineralization promotion as a result of the above and incorporation of minerals to the gum; (3) mechanical control of the bacterial plaque; (4) replacement of sugar by sweeteners which are harmful for bacteria (the most commonly used is xylitol) and (5) incorporation of active agents such as bicarbonate, casein, urea, chlorhexidine and chitosan, among others. Despite these benefits, the effect of the gum is considered to be weak for dental caries prevention when used instead of brushing. Therefore, its implementation must be proposed as a complement to oral hygiene routines and not as a preventive measure by itself. It is necessary to carry out a greater amount of clinical trials to evaluate its effectiveness in a context of high biological variability in the short and long term and including patients of different sex, age, socio-economic status and systemic health.

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INTRODUCTION.

Dental caries is one of the most prevalent infectious diseases and is classified as one of the main worldwide public health problems by the WHO¹. In consequence, prevention has become an important issue for professionals today, especially regarding the development of new methods to prevent plaque formation².

The effective implementation of mechanical methods to reduce bacterial plaque and food debris, such as frequent brushing and flossing, are the main preventive defense method against decay, but there is a high degree of failure to carry out oral hygiene. There are multiple causes for this situation, such as educational and socio-economic level, beliefs and attitudes regarding personal and oral care,

stressful life events, psychomotricity alteration, frequency of dental visits and age³. Therefore, it is necessary to have complementary preventive methods, which are inexpensive and easy to take on part of patients, to fight tooth decay.

In order to do this, current dentistry has added a new alternative to preventive actions: the use of chewing gum⁴. This product is culturally well accepted in various groups of the population and is easily adapted to people's daily routines⁵. It is a habit practiced regularly by a relatively high proportion of individuals in many countries and its use has increased in the last decade, being the most popular confectionery³, selling hundreds of millions of units worldwide annually⁶.

Historically, gum was sweetened with sugar (sucrose)

and its use contributed to developing dental caries. But at the beginning of 1950, sugar-free varieties, sweetened with natural non cariogenic sweeteners were introduced into the market⁶. These products have provided benefits for the oral health as they allow controlling plaque and reducing caries incidence³. Additionally, gum can be used as a vehicle to provide therapeutic components for the oral cavity⁴, which increases the benefits on oral health.

using sugar-free chewing gum for preventing dental caries reported in literature.

Dietary factors

Many epidemiological studies correlate fermentable carbohydrate consumption (FCH) containing sucrose with caries prevalence1 because microorganisms depend on them for their survival and diet provides FCH for the metabolic activity of the oral microbiota⁴. In addition to their use for metabolism, bacteria also need them for the synthesis of insoluble glucans and fructans, which allow adhesion to teeth surface⁷, favoring plaque formation.

FCH which are present in the diet (monosaccharides, disaccharides, oligosaccharides and polysaccharides)¹ have been described as the most popular components of the cariogenic diet. Nevertheless, it is also possible to add cariostatic elements like sugar substitutes, dairy, foods with high fat content, proteins, minerals and vitamins through diet⁸.

EFFECTS OF CHEWING SUGAR-FREE GUM ON THE ORAL CAVITY

Gum is mainly made from a rubber resin and a certain amount of preservatives, flavorings and sweeteners⁹. The labeling of "sugar-free" is allowed for gums which do not depress the pH below 5.7 neither during nor 30 minutes after consumption¹⁰.

Several publications have concluded that these products have an anticariogenic effect, which is mainly attributed to the action of five factors that will be described in detail in the following paragraphs: (1) saliva stimulation through chewing, (2) remineralization promotion, (3) mechanical control of the bacterial plaque, (4) replacement of sugar by sweeteners harmful for bacteria; and

(5) incorporation of therapeutic agents.

SALIVARY FLOW INCREASE

The increase in the flow of stimulated saliva has been associated with an increased anticariogenic potential^{1-3,11,12} since it is related to an increase in the buffer capacity, that is, it increases pH, which reduces the acidogenic effect of the bacterial plaque and improves the remineralization potential of enamel¹¹⁻¹³. This has been demonstrated in clinical trials, where greater remineralization of initial caries lesions has been observed under these circumstances¹¹. Also, it has been proven that the increase in salivary flow rate contributes significantly to oral health; therefore, it allows optimizing clearance or self-cleaning^{1,3,11,12}.

It is important to mention that although some articles confirm an increase in salivary flow when chewing gum, a study in older adults who were indicated to chew sugar-free gum twice a day for 6 months pointed out that it does not increase stimulated saliva flow in these patients¹⁴. The same result was obtained in a prospective study which evaluated the effects of chewing gum in haemodialysed patients for three months¹⁵.

REMINERALIZATION PROMOTION

A few minutes after sugar intake, the dental plaque pH decreases, causing enamel demineralization when the acidity level is under critical pH, which varies among individuals within an approximate range of 5.2 to 5.57. At this point, acids affect the enamel by dissolving apatite crystals and releasing calcium and phosphate ions in the saliva. Although this process takes place naturally, it leads to the destruction of the infrastructure of enamel over time¹⁴.

The first response of the organism to pH lowering is the action of the buffer systems in saliva, which neutralize the pH¹⁶. This system, which includes the action of bicarbonate, phosphate and protein, retrieves the electrolytic balance between the saliva and the tooth, preventing the release of minerals from the enamel⁷.

The remineralization process happens when there is an oversaturation of ions in the oral environment and they incorporate calcium, phosphate, and other minerals in partially decalcified tooth areas as they look for balance in

the enamel surface¹⁵. That way, the minerals added to the gum can improve the tooth remineralization process and have proved to be an effective mechanism for preventing the progression of enamel decay¹³.

MECHANICAL CONTROL OF BACTERIAL PLAQUE

Maintaining effective control of the bacterial plaque is the keystone of all the preventive measures for caries and periodontal disease and this is precisely one of the actions of the gum. Due to its sticky surface, the mechanical forces produced during chewing and the increase in salivary flow (with a consequent increase in clearance) remove a certain amount of plaque from the more exposed teeth surfaces (free faces and occlusal surface)³. This was demonstrated in a study which compared plaque rate before and after chewing sugar-free gum and reported approximately 44% less plaque after consuming chewing gum¹⁷.

Although chewing gum can reduce plaque accumulation in predilection sites of dental caries, it has little or no effect on the predilection sites for gingivitis¹⁷, even though there have been reductions in the gingival index¹⁴.

4) Incorporation of sugar substitutes.

At present, there is a wide variety of sweeteners which replace sugar in chewing gum. These products are non-cariogenic as they make bacterial metabolism more difficult^{2,5} and prevent the production of acids because they are not fermentable^{18,19}. Also their anticariogenic potential is increased because of the provocation of a palatability reflection due to the sweet taste which together with the chewing process increases stimulation of saliva flow^{11, 20}.

Sweeteners that are used with greater frequency in the gum are sorbitol, and xylitol. They are called "alcohols derived from sugar" since their chemical structure is similar to both, sugar and alcohol¹¹.

These products are safe to be used by children⁹ and relatively large quantities of these substances can be consumed without adverse side effects. This makes them excellent candidates for sugar substitutes, although they may act as laxatives when used in excessive quantities⁵. The following describes the scope of both sweeteners.

Xylitol

Xylitol is a 5-carbon alcohol derived from D-xylose (pentose sugars)¹¹ which was approved by the Food and Drug Administration in the 1960s and, since then, has been used as a substitute for refined white sugar⁹.

It is estimated that, in order to prevent dental caries with the use of xylitol, it is not necessary to completely replace sucrose in the diet and it has been shown that relatively small daily doses of xylitol (4 to 10 gr.)⁵ can provide anticaries protection. It has been stipulated that chewing gum sweetened with xylitol from three to five times a day, for a minimum time of five minutes, ideally after food intake, is effective to achieve the desired effect on cariogenic bacteria^{5,21,22}.

It is considered cariostatic since it diminishes the counts of Streptococcus mutans (SM)^{5,11,23-25}, the formation of dental plaque²² and, therefore, dental caries incidence. Therefore, it is particularly effective in those conditions under which it is not possible to make a proper oral hygiene²⁵.

Its mechanism of action is to create an unfavorable environment for bacterial growth, especially for SM, as it reduces its ability to adhere to oral tissues by affecting the insoluble glucans that were involved in such process. This property reduces the possibility of forming dental plaque and therefore the local effect of the lactic acid^{2,4}. On the other hand, xylitol penetrates in the bacterial cytoplasm interfering with glycolysis and inhibiting growth of microorganisms².

Other species that are affected are Streptococcus sobrinus (SS), Lactobacillus (LB) and Actinomyces viscosus (AV)²⁶. As a result, a less cariogenic environment is created⁹.

A clinical trial carried out in pairs of mothers and children with high counts of SM, randomly put participants together into two groups: experimental, which received chewing gum with xylitol (21 pairs) and control (13 pairs), to which fluoride varnishes were applied. They were examined 18 months later and the levels of SM in the experimental group decreased significantly in comparison with the control group²⁷.

There have also been positive effects of xylitol in cases

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of gingivitis, decreasing the gingival index significantly in comparison with the ordinary gum^{26,28}.

Sorbitol

Sorbitol is a hexatol derived from glucose¹¹ with has a low cariogenic potential⁵. Like xylitol, it causes a decrease in SM, SS, AV, LB and the insoluble glucans, with an elevation of salivary pH, which give it an anticariogenic potential⁹.

Current evidence establishes that pentatoles and xylitol as well as hexatoles and sorbitol had good results in reducing dental caries. However, the first ones are more effective and so they are more commonly used¹⁰.

Because of that, a study carried out in 2009 compared variations of salivary pH by using both sweeteners and concluded that xylitol significantly reduces acidogenicity in dental plaque. However, this effect was not observed with sorbitol²⁹.

INCORPORATION OF ACTIVE AGENTS

Chewing gum represents a useful vehicle for some active agents^{1,4,12,13,30,31} such as fluorides, bicarbonate, calcium phosphate, sodium trimetaphosphate, casein, urea, chlorhexidine and chitosan, among others. Generally, these products have antimicrobial action, which can reduce caries incidence by controlling plaque formation, affecting the cariogenic species or creating an oral environment which is favorable for remineralization²¹. The mechanisms of action of each of them are described below.

Fluorides.

The application of fluoride in its various forms is one of the most commonly used preventive methods and its topical effect is considered to be the most important; then, its incorporation into the gum is highly beneficial³². Fluorine is present in saliva in very low concentrations, but plays an important role by means of four mechanisms: (1) it participates in the remineralization process, because when combined with the crystals of the enamel, it forms fluorapatita, which is much more resistant to acid attack^{7,21,33}; (2) it prevents demineralization in its liquid phase (salivary medium) by inhibiting the release of F+ ion from the enamel²¹; (3) it inhibits reactions of glycolysis in den-

tal plaque bacteria, especially SM^{7,21,33}; and (4) reduces polysaccharides production of the extracellular matrix of bacterial plaque and produces changes in the surface charge of the tooth, which prevents acquired pellicle formation and, therefore, the adhesion of microorganisms to the tooth^{7,33}.

Bicarbonate

Bicarbonate is part of the buffer systems in saliva, hence its incorporation to chewing gum helps preserve pH above critical pH³⁴.

A study conducted by Anderson (2008) noted that it was possible to obtain a maximum salivary pH of 8.06 by chewing gum with bicarbonate³⁵.

Calcium phosphate

The release of calcium and phosphate ions on the tooth surface causes a saturation of these elements on the enamel surface²², thus inhibiting demineralization and remineralization. Amorphous calcium phosphate (ACP) is an ideal system to prevent tooth decay and achieve incipient lesions remineralization¹⁶.

By incorporating calcium in the form of hydroxyapatite, it has also been possible to obtain significant reductions in dental sensitivity within one or two weeks³⁶.

Sodium Trimetaphosphate (TMP)

Its incorporation causes the same effect as ACP because it increases the concentration of phosphate ions, hindering demineralization and promoting remineralization⁷.

A recent study proved its use provides greater efficiency in the reduction of enamel demineralization by incorporating it to toothpaste³⁷. Another in vitro study corroborated an increase in remineralization by applying fluoride varnish in conjunction with TMP, significantly improving effectiveness³⁸.

Casein

Casein is a protein derived from milk^{22,39}. It can stabilize ACP that is located in the medium²², substantially increasing calcium phosphate level in dental plaque. The combination of casein phosphopeptide and amorphous calcium phosphate (CPP-ACP) softens the activities of the calcium ions and free phosphate, thus helping to maintain

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a state of oversaturation with respect to the enamel of the teeth, which reduces demineralization and promotes remineralization^{22,39}.

A double-blind randomized study conducted with the objective to compare remineralization of enamel produced with sugar free gum with and without CPP-ACP concluded that sugar-free gum containing CPP-ACP promotes higher levels of remineralization than gum without CPP-ACP⁴⁰.

Yengopal (2009) found similar results when comparing both types of chewing gum and also concluded that subjects who chewed gum with 54mg of CPP-ACP were 18% less likely to develop decay compared with the control group without CPP-ACP⁴¹.

The benefits of CPP-ACP have also been highlighted in cases of erosion⁴², white spots and dentin hypersensitivity³⁹.

Urea

Ammonia is produced from urea by urealisis and arginine deiminase system in the oral environment. This represents an important endogenous factor which potentially inhibits the development of dental caries by neutralizing acids and stabilizing oral microbiota, thus favoring the conditions for maintaining health oral⁴³.

Chlorhexidine

Chlorhexidine is a cationic broad-spectrum antimicrobial. Its mechanism of action is given by the reduction in the formation of the acquired pellicle by altering microbial adhesion to tooth surface⁷. Chewing gum with chlorhexidine has obtained a beneficial effect on inhibiting cariogenic plaque, although its effect is considered weak when there are not oral hygiene measures²⁸.

Chitosan

Chitosan is a natural substance with antibacterial effect commonly used in cosmetics industry. Recent research indicates a strong effect on cariogenic bacteria, especially on SM and LB, whose colonies decrease between 70 and 60% respectively by chewing gum with chitosan for 30 minutes, three times a day, during 14 days³¹. Other studies have shown similar results44,45.

DISCUSSION.

Most of chewing gum with sugar substitutes, antimicrobial agents, minerals and other compounds have demonstrated to have a positive effect on reducing plaque⁶, controlling salivary pH, stimulating salivation, and remineralization process^{1,3,10,12,13}. All this provides an important anticaries prevention which has been described by many authors. This relationship has not been established as clearly regarding gingivitis and periodontal disease, even when significant decreases have been found in gingival index14.

Of all the therapeutic agents mentioned, chlorhexidine is described as the one with greater inhibitory effect on bacterial plaque²⁸ and chewing gum with urea, followed by the chewing gum containing fluoride, produce a more effective buffer effect than chewing gum with other therapeutic components after consumption of acidogenic food⁴⁶.

In spite of providing all the benefits described above, it is considered that the effect of gum as a means to provide therapeutic agents, as well as the gum with xylitol, is weak in the prevention of dental caries when used instead of brushing²⁸. Therefore, its implementation must be proposed as a complementary measure to oral hygiene routines and not as a preventive measure by itself.

Even though, and considering that sugar-free chewing gum represents an economic far reaching tool which can increase the impact of other preventive measures⁴⁷, such as promotion, education and application of fluoride, it may become a viable option able to improve oral health, since it has been shown that an increase in frequency of sugar-free chewing gum consumption decreases the amount and severity of carious injuries⁴⁸.

Despite the large amount of information available regarding the effects of sugar-free chewing gum in the prevention of dental caries, it is necessary to perform a greater number of clinical trials in the short and long term. Then, they can directly assess the effectiveness of the products described independently and combined with the objective of determining the most effective method to reduce bacterial plaque and its acidogenic potential. Likewise, these studies should be performed in a context of high biological variability11, including patients of different sex, age, socio-economic status and systemic health; since studies reporting possible beneficial effects in patients with metabolic abnormalities, renal, bone and respiratory tract by incorporating various substances in the sugar-free chewing gum have been published. For the same reason, research must be expanded considering a larger spectrum of parameters on which it is possible to find beneficial effects.

Uso del chicle libre de azúcar como complemento en la prevención de la caries dental. Revisión narrativa.

Resumen: La caries dental constituye una de las enfermedades de mayor prevalencia, siendo catalogada por la OMS como uno de los principales problemas de salud pública a nivel mundial. Por ésta razón se ha enfatizado en el desarrollo de nuevos métodos preventivos a los que se ha incorporado el uso del chicle sin azúcar. Con esta estrategia es posible obtener importantes beneficios para la salud oral producto de: (1) estimulación de la salivación, lo que favorece el aclaramiento y regula el pH; (2) promoción de la remineralización como consecuencia de lo anterior y de la incorporación de minerales a la goma de mascar; (3) control mecánico de la placa bacteriana; (4) sustitución del azúcar por edulcorantes nocivos para las bacterias, de los cuales el más utilizado es el xilitol; e (5) incorporación de agentes activos tales como bicarbonato, caseína, urea, clorhexidina y quitosano, entre otros. Pese a proporcionar ésta serie de beneficios se considera que el efecto del chicle es débil en la prevención de caries cuando éste propósito se busca en ausencia de cepillado dental y por lo tanto debe proponerse su implementación como complemento a las rutinas de higiene oral y no como una medida preventiva por sí sola, siendo necesario realizar una mayor cantidad de ensayos clínicos, a corto y largo plazo, que evalúen la efectividad en un contexto de alta variabilidad biológica, incluyendo pacientes de distinto sexo, edad, situación socioeconómica y salud sistémica.

Palabras clave: Goma de mascar; Caries; Carbohidratos; Prevención primaria.

REFERENCES.

- Salud dental: relación entre la caries dental y el consumo de alimentos. Nutr Hosp. 2013; 28(4): 64-71.
- Velásquez C, Narvárez C. Effect of xylitol chewing gum on dental plaque, saliva flow and saliva buffer capacity in Chilean youngsters. Int J Odontostomat. 2013; 7(1): 133-137.
- 3. Tangade P, Mathur A, Chaudhary S, Gupta R. The effect of sugar-free and sugar chewing gums on plaque deposition. Dent 8. Res J. 2012; 9(3): 309-13.
- Panesso E, Calle M, Meneses E. Salud bucal y xilitol: usos y posibilidades en caries y enfermedad periodontal en poblaciones "PEPE". Univ Salud 2012; 14(2): 205-215.

González A, González B, González E. no invasivo. Rev ADM 2013; 70(2): 54-6.

- N, Van Loveren C, Van der Weijden G. Effects of sugar-free chewing gum sweetened with xylitol or maltitol on the development of gingivitis and plaque: a rando-[Epub ahead of print].
- Núñez D, García L. Bioquímica de la caries dental. Rev Haban Cienc Méd. 2010; 9(2): 156-166.
- Galhotra V, Sofat A, Dua H, Rohila S. Anticariogenic And Cariostatic Potential Of Components Of Diet: A Review. 13. Dodds M, Chidichimo D, Haas M. Indian J Dent Sci. 2014; 6(4): 079.
- Kumar S, Sogi S, Indushekar K. Comparative evaluation of the effects of xylitol and sugar-free chewing gums on sa-Cuadrado D, Peña R, Gómez J. El livary and dental plaque pH in children. J concepto de caries: hacia un tratamiento Indian Soc Pedod Prev Dent. 2013; 31(4): sugar-free chewing gum on the oral health

- Keukenmeester R, Slot D, Rosema 10. Imfeld T. Chewing gum--facts and fiction: a review of gum-chewing and oral health. Crit Rev Oral Biol Med. 1999; 10(3): 405-19.
- 11. Mickenautsch S, Coelho S, Yengomized clinical trial. Int J Dent Hyg. 2014; pal V, Bezerra A, Cruvinel V. Sugar-free chewing gum and dental caries: a systematic review. J Appl Oral Sci. 2007; 15(2):
 - 12. Dodds M. The oral health benefits of chewing gum. J Ir Dent Assoc. 2012; 58(5): 253-61.
 - Delivery of Active Agents from Chewing Gum for Improved Remineralization. Adv Dent Res. 2012; 24(2): 58-62.
 - 14. Al-Haboubi M, Zoitopoulos L, Beighton D, Gallagher. The potential benefits of

and quality of life of older people living in the community: a randomized controlled trial. Community Dent Oral Epidemiol. 2012; 40(5): 415-24.

- 15. Jagodzińska M, Zimmer-Nowicka J, Nowicki M. Three months of regular gum chewing neither alleviates xerostomia nor reduces overhydration in chronic hemodialysis patients. J Ren Nutr. 2011; 21 (5): 410-7.
- 16. Simeone S. Usos y efectos del fosfato de calcio amorfo (FCA) en la odontología restauradora y preventiva. Acta Odontol Venez. 2010; 48 (3): 1-12.
- 17. Hanham A, Addy M. The effect of 39-46. chewing sugar-free gum on plaque regrowth at smooth and occlusal surfaces. J Clin Periodontol. 2001; 28(3): 255-7.
- 18. Loveren C, Broukal Z, Oganessian E. Functional foods/ingredients and dental caries. Eur J Nutr 2, 2012; 51:15-25.
- Tuncer D, Önen A, Yazici, A. Effect of chewing gums with xylitol, sorbitol and xylitol-sorbitol on the remineralization and hardness of initial enamel lesions in situ. J Dent Res. 2014; 11 (5): 537-543.
- 20. Hanno A, Alamoudi N, Almushayt A, Masoud M, Sabbagh H, Farsi N. Effect of xylitol on dental caries and salivary Streptococcus mutans levels among a group of mother-child pairs. J Clin Pediatr Dent. 2011; 36(1): 25-30.
- 21. Cobos C, Valenzuela Emilia, Araiza M. Influencia de un enjuague a base de fluoruro y xilitol en la remineralización in vitro del esmalte en dientes temporales. Rev Odont Mex. 2013; 17(4): 204-209.
- 22. Portilla J, Pinzón M, Huerta E, Obregón A. Conceptos actuales e investigaciones futuras en el tratamiento de la caries dental y control de la placa bacteriana. Rev Odont Mex. 2010; 14(4): 218-225.
- 23. Seki M, Karakama F, Kawato T, Tanaka H, Saeki Y, Yamashita Y. Effect of xylitol gum on the level of oral mutans streptococci of preschoolers: block-rando-

mised trial. Int Dent J. 2011; 61(5): 274-

- 24. Söderling E, Elsalhy M, Honkala E, Fontana M, Flannagan S, Eckert G, Kokaras A, Paster B, Tolvanen M, Honkala S. Effects of short-term xylitol gum chewing on the oral microbiome. Clin Oral Investig. 2014; [Epub ahead of print].
- 25. Hashiba T, Takeuchi K, Shimazaki Y, Takeshita T, Yamashita Y. Chewing Xylitol Gum Improves Self-Rated and Objective Indicators of Oral Health Status under Conditions Interrupting Regular Oral Hygiene. Tohoku J Exp Med. 2015; 235 (1):
- 26. Thabuis C, Cheng C, Wang X, Pochat M, Han A, Miller L, Wils D, Guerin-Deremaux L. Effects of maltitol and xylitol chewing-gums on parameters involved in dental caries development. Eur J Paediatr Dent. 2013; 14(4): 303-8.
- 27. Alamoudi N, Hanno A, Masoud M, Sabbagh H, Almushayt A, Masoud I. Effects of xylitol on salivary mutans streptococcus, plaque level, and caries activity in a group of Saudi mother-child pairs. An 18-month clinical trial. Saudi Med J. 2012; 33(2): 186-92.
- 28. Keukenmeester R, Slot D, Putt M, Weijden G. The effect of medicated, sugarfree chewing gum on plaque and clinical parameters of gingival inflammation: a systematic review. Int J Dent Hyg. 2014; 12 (1): 2-16.
- 29. Splieth C, Alkilzy M, Schmitt J, Berndt C, Welk A. Effect of xylitol and sorbitol on plaque acidogenesis. Quintessence Int. 2009; 40(4): 279.
- 30. Ly K, Milgrom P, Rothen M. The Potential of Dental-Protective Chewing Gum in Oral Health Interventions. J Am Dent Assoc. 2008; 139: 553-563.
- 31. Wilczynska-Borawska M, Rodakowska E, Lewkowski A, Baginska J, Wilczko M. Chitosan in the chewing gum, an innovative caries prevention method? Initial in ralisation by chewing sugar-free gums in a

- vitro study. Healthmed. 2012; 6(12): 3957-3960.
- 32. Tubert-Jeannin S, Auclair C, Amsallem E, Tramini P, Gerbaud L, Ruffieux C, Schulte A, Koch M, Rège-Walther M, Ismail A. Fluoride supplements (tablets, drops, lozenges or chewing gums) for preventing dental caries in children. Cochrane Database Syst Rev. 2011:CD007592.
- 33. Miñara V. El flúor y la prevención de la caries en la infancia. Actualización. Acta Pediatr Esp. 2010; 68(3): 129-134.
- 34. Rojas T, Romero M, Navas R, Álvarez C, Morón A. Flujo salival, pH y capacidad amortiguadora en niños y adolescentes cardiópatas: factor de riesgo para caries dental y enfermedad periodontal. Estudio preliminar. Cienc Odontol. 2008; 5(1): 17-26.
- 35. Anderson L, Orchardson R. The effect of chewing bicarbonate-containing gum on salivary flow rate and pH in humans. Arch Oral Biol. 2003; 48(3): 201-4.
- 36. Porciani P, Chazine M, Grandini S. A clinical study of the efficacy of a new chewing gum containing calcium hydroxyapatite in reducing dentin hypersensitivity. J Clin Dent. 2014; 25(2): 32-6.
- 37. de Castro L, Delbem A, Danelon M, Passarinho A, Percinoto C. In vitro effect of sodium trimetaphosphate additives to conventional toothpastes on enamel demineralization. Clin Oral Investig. 2015; [Epub ahead of print]
- 38. Manarelli M, Delbem A, Lima T, Castilho F, Pessan J. In vitro remineralizing effect of fluoride varnishes containing sodium trimetaphosphate. Caries Res. 2014; 48(4): 299-305.
- 39. Reema S, Lahiri P, Roy S. Review of casein phosphopeptides-amorphous calcium phosphate. Chin J Dent Res. 2014; 17(1): 7-14.
- 40. Cochrane N, Shen P, Byrne S, Walker G, Adams G, Yuan Y, Reynolds C, Hoffmann B, Dashper S, Reynolds E. Remine-

randomised, controlled in situ trial including dietary intake and gauze to promote plaque formation. Caries Res. 2012; 46(2): 147-55.

- 41. Yengopal V, Mickenautsch S. Caries preventive effect of casein phosphopeptide-amorphous calcium phosphate (CPP-ACP): a meta-analysis. Acta Odontol Scand. 2009; 67 (6): 321-332.
- 42. Prestes L, Souza B, Comar L, Salomão P, Rios D, Magalhães A. In situ effect of chewing gum containing CPP-ACP on the mineral precipitation of eroded bovine enamel-a surface hardness analysis. J Dent. 2013; 41(8): 747-51.
- 43. Reyes É, Martín J, Yévenes I, Nei-

- ra M, Palma P, Gordan V, Moncada G. 46. Gopinath V, Tandon S, Shirwaikar Actividad y efectos de ureasa y arginina deiminasa en saliva y biopelícula oral humana. Rev Fac Odontol Univ Antioq 2012; 23(2): 343-352.
- 44. Hayashi Y, Ohara N, Ganno T, Ishizaki H, Yanagiguchi K. Chitosan-containing gum chewing accelerates antibacterial effect with an increase in salivary secretion. J Dent. 2007; 35(11): 871-4.
- 45. Hayashi Y, Ohara N, Ganno T, Yamaguchi K, Ishizaki T, Nakamura T, Sato M. Chewing chitosan-containing gum effectively inhibits the growth of cariogenic bacteria. Arch Oral Biol. 2007; 52(3): 290-4.
- A. The effect of chewing gums on acidogenicity of plaque after a sucrose challenge. J Clin Pediatr Dent. 1997; 22(1): 77-81.
- 47. Dodds M, Reeves J. Sugar-free gum and dental caries: a high-impact approach. Dental Nursing. 2014; 10 (7): 175-177.
- 48. Wang, X, Zhong B, Chen Z, Stewart M, Zhang C, Zhang K, Ni J, Dodds M, Hanley A, Miller L. History of frequent gum chewing is associated with higher unstimulated salivary flow rate and lower caries severity in healthy chinese adults. Caries Res. 2012; 46 (6): 513-518.