

Effects of Fluorine and Xylitol in the Antimicrobial Activity of Child Dentifrices
Efeito do flúor e do xilitol na atividade antimicrobiana de dentifrícios infantis
Efecto del flúor y xilitol en la actividad antimicrobiana de dentífricos infantiles

Received: 10/04/2016
Approved: 18/10/2016
Published: 15/02/2017

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The aim of this study was to evaluate the antimicrobial effect toothpastes for infants containing fluoride and xylitol presented against *Streptococcus mutans*, through an agar diffusion test. Six toothpastes were categorized according to the presence/concentration of fluoride and xylitol: 1-Condor Bambinos; 2-Bitufo Cocoricó; 3-Colgate Smiles; 4-Bitufo Penelope; 5-Tandy and 6-Aquafresh Kids. After the solidification of an agar medium in the dishes, 200 µL of the inoculum (*S. mutans* UA 159) were dispensed on the medium and five holes were made in it for the application of the dentifrices, totalizing 10 wells for each one. The plates were incubated at 37°C for 48h. The inhibition zones were analyzed through the ANOVA one-way and Tukey ($\alpha=0.05$) tests. There was a significant difference between fluoridated dentifrices, as the Aquafresh showed the biggest inhibition halos against *S. mutans*. The concentration of fluoride influenced the antimicrobial activity of child toothpastes; xylitol, however, had no influence.

Descriptors: Fluorine; Xylitol; *Streptococcus mutans*; Dentifrices.

O objetivo deste estudo foi avaliar o efeito do flúor e do xilitol na atividade antimicrobiana de dentifrícios infantis contra *Streptococcus mutans* por difusão em ágar. Seis dentifrícios foram testados de acordo com a presença/concentração de flúor e xilitol: 1-Condor Bambinos; 2-Bitufo Cocoricó; 3-Colgate Smiles; 4-Bitufo Penélope; 5-Tandy e 6-Aquafresh Kids. Após a solidificação do meio ágar em placas, 200µL do inóculo (*S. mutans* UA 159) foram dispensados sobre o meio e cinco poços foram confeccionados em cada placa para preenchimento com os dentifrícios, totalizando dez poços para cada dentifrício. As placas foram incubadas a 37°C por 48h. Os valores de halos de inibição foram analisados por ANOVA one-way e Tukey ($\alpha=0,05\%$). Houve diferença significativa entre os dentifrícios fluoretados, de modo que o dentifrício Aquafresh apresentou o maior halo de inibição contra *S. mutans*. A concentração de flúor influenciou a atividade antimicrobiana dos dentifrícios infantis, entretanto, o xilitol não exerceu influência.

Descritores: Flúor; Xilitol; *Streptococcus mutans*; Dentifrícios.

El objetivo de este estudio fue evaluar el efecto del flúor y xilitol sobre la actividad antimicrobiana en dentífricos para niños contra *Streptococcus mutans* por difusión en ágar. Seis dentífricos fueron probados de acuerdo con la presencia/concentración de flúor y xilitol: 1-Condor Bambinos; 2-Bitufo Cocoricó; 3-Colgate Smiles; 4-Bitufo Penelope; 5-Tandy y 6-Aquafresh Kids. Después de la solidificación del medio de cultivo agar en placas, 200µL de inóculo (*S. mutans*UA 159) fueron dispersados sobre el medio y cinco pocillos fueron confeccionados en cada placa para llenar con pastas de dientes, totalizando diez pocillos para cada dentífrico. Las placas fueron incubadas a 37°C durante 48 h. Los valores de halos de inhibición se analizaron mediante ANOVA one-way y de Tukey ($\alpha=0,05\%$). Existió diferencia significativa entre los dentífricos fluorados, por lo que el dentífrico Aquafresh presentó el mayor halo de inhibición contra *S. mutans*. La concentración de flúor influyó en la actividad antimicrobiana de los dentífricos infantiles, pero, el xilitol no ejerció influencia.

Descriptores: Flúor; Xilitol; *Streptococcus mutans*; Dentífricos.

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INTRODUCTION

A highly effective method to control the development and progression of dental decay is the mechanical control of the biofilm, through hygienisation, associated to the use of dentifrices¹.

Fluorine is the main component of dentifrices; it acts as a chemical auxiliary in the prevention of dental decay and in the processes of demineralization and remineralization of the enamel, reducing its solubility². Thus, the dentifrices are considered to be the main reason for the decline of tooth decay². Therefore, for the fluorine to have a meaningful antimicrobial effect, its use in high concentrations is required, as long as they are higher than the concentration of the solubility of apatite³.

However, the decline of tooth decay was accompanied by an increase in the prevalence of dental fluorosis⁴. Dental fluorosis is a defect in enamel composition during the development of the teeth; the extent to which it aesthetically compromises the teeth depends on the dose to which the child is subjected². To minimize the risk of fluorosis, dentifrices with a low concentration of fluorine (500-750 ppm) or without any fluorine at all started being commercialized⁵. The anti-decay effect of dentifrices with low fluorine concentration has not been proven in literature⁶, and there are controversies regarding the antimicrobial effect of dentifrices devoid of fluorine⁷.

Some dentifrices included xylitol in their composition, which as a non-cariogenic sugar with pentol in its base, and cannot be metabolized by oral bacteria⁸. Therefore, xylitol can be an effective tool in the control of the micro-organisms which are responsible for the process of demineralization and remineralization of dental enamel, inhibiting the growth and metabolism of the *Streptococcus mutans* and of biofilm⁸.

It has been shown that fluorinated dentifrices and xylitol presented a higher enamel remineralization rate when compared to dentifrices without xylitol, and when associated to fluoride, they can have a stronger action in the prevention of dental

decay^{8,9}. Information regarding the antimicrobial activity of fluorinated and non-fluorinated xylitol containing dentifrices still is scarce in the literature. Thus, the objective of this work is to perform an *in vitro* evaluation of fluorine and xylitol in the children dentifrice antimicrobial activity against *S. mutans*.

METHOD

The antibacterial activity of six children dentifrices in the market was identified, according to the presence or lack of fluorine and xylitol; the concentration of fluoride ions varied. The composition and concentration of fluoride, as well as the presence of xylitol, according to the information given by the producers, are described in Table 1. Six groups were formed:

- Group 1: Condor Bambinos (no fluorine and no xylitol) - NEGATIVE CONTROL;
- Group 2: Bitufo Cocoricó (no fluorine, with xylitol);
- Group 3: Colgate Smiles Barney (500 ppm of fluorine, no xylitol);
- Group 4: Bitufo Penélope (750 ppm of fluorine, with xylitol) - POSITIVE CONTROL.
- Group 5: Tandy (1100 ppm of fluorine and no xylitol);
- Group 6: Aquafresh kids (1500 ppm of fluor, no xylitol).

Antimicrobial activity - Test of Diffusion in Agar

The antimicrobial activity of the dentifrices was evaluated against a strain of *S. mutans* (UA 159) ceded by the University of Campinas (UNICAMP). The colonies of *S. mutans* were cultivated from a stock culture frozen in a broth of brain and heart infusion (BHI, DIFCO Laboratories, Detroit, MI, USA). 100 µL of the stock culture was added to 8ml of BHI broth and maintained there for 24 h, at a temperature of 37°C, in microaerophilic conditions, and with the deployment of the candle flame method. After confirming the viability and absence of contamination, the culture was adjusted to a concentration of 10⁸ cells/MI of the McFarland scale in a spectrophotometer (Fluostar Optima, BMG-Labtech, Cary, NC, USA), so that the inoculum which was used for the test of diffusion in agar could be obtained.

Table 1. Composition of dentifrices investigated in the study.

Dentifrices	Composition	Concentration of fluoride and presence of xylitol
Condor Bambinos (Condor AS, São Bento do Sul, SC, Brasil) Lot:50B11	PEG8, sorbitol, sodium saccharine, sodium benzoate, carboxymethyl cellulose, silica, aroma and water.	No fluorine, no xylitol
Bitufo Cocoricó (IPH&C, Itupeva, SP, Brasil) Lot:074338	Xylitol, sorbitol, glicerine, cellulose gum, xanthan gum PEG-8, methylparaben, propylparaben, hydrated silica, sodium lauryl sulfate, sodium saccharine, titanium dioxide, triclosan, EDTA, aroma, alcohol, water.	No fluor, with xylitol
Colgate Smiles (Colgate Palmolive, São José Iturbe, México) Lot: MX1136	Sodium fluoride, sorbitol, water, hydrated silica, PEG-12, cellulose gum, sodium lauryl sulfate, glycerin, sodium saccharin, eugenol, dipentene, aroma	500 ppm sodium fluoride, no xylitol
Bitufo Penelope (IPH&C, Itupeva, SP, Brasil) Lot:074338	Sodium monofluorophosphate, xylitol, sorbitol, calcium carbonate, cellulose gum, sodium lauryl sulfate, methylparaben, propylparaben, PEG8, sodium saccharin, hydrated silica, aroma and water	750ppm sodium monofluorophosphate, with xylitol
Tandy (Colgate Palmolive, São Bernardo do Campo, SP, Brasil) Lot:2306BR123K	Sodium fluoride, sorbitol, water, hydrated silica, PEG-12, cellulose gum, sodium lauryl sulfate, sodium saccharine, aroma	1,100ppm sodium fluoride, no xylitol
Aquafresh Kids (Glaxo Smithkline, Moon Township, PA, England) Lot.(L)2E07	Sodium monofluorophosphate, sorbitol, calcium carbonate, glycerin, cellulose gum, sodium lauryl sulfate, PEG8, titanium dioxide, sodium bicarbonate, sodium saccharin, calcium caragena, sodium benzoate, water	1,500 ppm sodium monofluorophosphate, no xylitol

A base containing 15 mL BHI agar was prepared and dispensed in each sterile petri dish. After the solidification of the culture medium, 200 µL of the inoculum (*S. mutans*) were dispensed and spread over the medium with the help of a sterile handle. Five holes with a 5mm diameter were made in each dish for posterior inclusion of the dentifrices. For each dentifrice, 10 holes were filled (n=10). All dentifrices were inserted in the holes using a plastic dispenser.

The dishes were maintained for one hour under room temperature so the diffusion of the products could happen, and after that, were incubated at 37°C for 48h in microaerophilic conditions. The candle flame method was also used. After incubation, the inhibition zones formed were measured using a digital caliper.

Data analysis

Data were tested regarding their normality and homogeneity of variance with the Kolmogorov-Smirnov and Shapiro-Wilk tests, so that posterior comparisons of the halos formed by dentifrices was possible, through the ANOVA one-way and Tukey tests, with a significance level of 5%.

RESULTS

Table 2 shows the average and standard-deviation of the dentifrices inhibition halos. All dentifrices presented antimicrobial effects against *S. mutans* ($p < 0.001$). There was a significant difference between fluorinated dentifrices. The dentifrice Aquafresh presented the strongest antimicrobial activity (22.48 ± 1.59), followed by Tandy (20.03 ± 1.09), Colgate Smiles (19.77 ± 1.71) and Bitufo Penelope (18.36 ± 0.98). In turn, there was no statistical difference between

the dentifrices Tandy and Colgate Smiles (Table 2).

The comparison among the non-fluorinated dentifrices has shown that there was a significant statistical difference between Condor Bambinos (17.31 ± 0.72) and Bitufo Cocoricó (19.89 ± 1.36 - $p < 0.001$) (Table 2). The comparison among dentifrices with and without xylitol has shown that the

dentifrice Bitufo Cocoricó (with xylitol) has presented a stronger antimicrobial activity when compared to Condor Bambinos (without xylitol).

There was no statistical difference ($p > 0.05$) between the dentifrices Condor Bambinos and Bitufo Penelope; that was also true among the dentifrices Bitufo Cocoricó, Tandy and Colgate Smiles ($p > 0.05$) (Table 2).

Table 2. Mean value and standard deviation of the inhibition halos of researched dentifrices.

Dentifrices	Mean value \pm Standard Deviation
Condor Bambinos	17.31 ± 0.72^B *
Bitufo Cocoricó	19.89 ± 1.36^C
Colgate Smiles	19.77 ± 1.71^C
Bitufo Penélope	18.36 ± 0.98^B
Tandy	20.03 ± 1.09^C
Aquafresh	22.48 ± 1.59^A

*Equal letters mean that there is no statistical difference between the dentifrices (ANOVA-One way test and Tukey test, $p > 0.05$).

DISCUSSION

Teeth brushing, when coupled with the use of dentifrices, is still the most effective method for the removal of biofilm and the prevention of tooth decay, since dentifrices have in their composition fluorine and other antimicrobials such as xylitol, which significantly aid in the reduction of the incidence of cavities^{10,11}. There are several dentifrices in the market that are suitable for babies and children; however, the diversity of the components in them makes it difficult to identify their antimicrobial action.

Fluoride ions are antimicrobial, but the main anti-decay effect is related to the prevention against the demineralization of enamel, and to the action towards remineralization¹⁻³. The dentifrices Colgate Smiles (500 ppm), Tandy (1100 ppm) and Aquafresh (1500 ppm) presented an antimicrobial action significantly higher than that of the other evaluated dentifrices, these results showing that, the higher the concentration of fluorine, the higher the antimicrobial activity.

Even though the increase in fluorine concentration seems to be connected to an increase in the effect, the utilization of fluorinated dentifrices with a concentration above 1500 ppm is not recommended for children under 6 years of age, as there is a concern regarding the ingestion of fluorine through the swallowing of the dentifrice,

which may lead to the developing of fluorosis¹⁰. An alternative to diminish such a risk is to diminish the amount of dentifrice placed on the brush¹⁰.

One of the most relevant properties of xylitol is its determined anti-cavity action, especially since it can not be fermented by bacteria of the genus *Streptococcus*. The proliferation of bacteria is limited and promotes the diminution of insoluble polysaccharides, forming a biofilm less adherent and more easily removed through teeth brushing¹³⁻¹⁵. In addition, xylitol can promote the remineralization of the enamel through an increase in salivary flux, prevent the drop on the pH of the surface of the teeth, as well as increase the blocking capabilities and bacteriostatic activity of the saliva^{13,16}.

In a study by Björklund, Ouwehand and Forssten¹⁷, the effect of xylitol in the inhibition of the growth of *Streptococcus mutans* in both human and artificial saliva was evident, even with the addition of glucose. Brambilla, Ionescu, Cazzaniga, Ottobelli and Samaranayake¹⁸ observed that the xylitol and the L-carbohydrates led to a decrease in the adhesion and formation of biofilm of the species *Candida albicans* and *Streptococcus mutans*. Another study verified that when xylitol is combined with saccharose, the amount of *Streptococcus mutans* in the artificial saliva diminishes, and

there is a reduction in the amount of bacteria that colonize the hydroxyapatite¹⁹.

Regarding the presence of xylitol in dentifrices, Magalhães et al⁵ reported that the fluorinated dentifrices with xylitol in their composition (in a concentration from 3 to 10%) presented anti-decay action superior to that of fluorinated dentifrices without xylitol. Similarly, it was noted in this study that the antimicrobial activity of the dentifrice without fluorine and with xylitol (Bitufo Cocoricó) was higher than that of the dentifrice without fluorine and without xylitol (Condor Bambinos).

It was also shown that the dentifrice without fluorine but with xylitol (Bitufo Cocoricó) presented an inhibition halo that was not statistically different from that of dentifrices with no xylitol, whether with a high fluorine concentration (1100ppm - Tandy) or a low one (500ppm - Colgate Smiles). Therefore, it can be suggested that the antimicrobial activity of the dentifrice without fluorine is to be attributed to the presence of xylitol⁵.

The actual concentration of xylitol in these dentifrices is not informed by the manufacturer, making it difficult to state that the xylitol in combination with the fluoride presented a significant antimicrobial activity. According to a study by Filho et al¹⁵, xylitol (with a concentration from 2.5% to 10%), associated with fluorine was effective against tooth decay, preventing the formation of *S. mutans* biofilm, and suggesting a synergistic effect between both components. Likewise, Mickenautsch and Yengopal⁹ conducted a systematic review, and suggested that the use of xylitol associated to fluoride can be effective in the prevention of tooth decay. In turn, Lee et al²⁰ have shown in a randomized clinical essay that the use of xylitol containing chewing gums did not add any benefit to already existing preventive measures, such as the use of fluorides, when compared to the placebo. Studies which show the effect of dentifrices that contain xylitol associated to fluoride, and compare the effects to dentifrices that only contain fluoride, are still considered to be of little scientific significance, which justifies the

development of randomized clinical studies of a higher quality^{21,22}.

It is likely that other antimicrobial agents present in the composition of the dentifrices are also responsible for the formation of the inhibitory halo. The dentifrice Condor Bambinos, which does not contain neither fluorine nor xylitol, presented an inhibitory halo that was not statistically different to that of the dentifrice Bitufo Penelope, which contains 750ppm of fluorine, and also contains xylitol. It can be suggested that the component sodium lauryl sulfate, present in the Condor Bambinos dentifrice, presented an antimicrobial effect, due to it being a stable anionic detergent, capable of provoking lysis in the membrane of gram-negative microorganisms and deactivate bacterial enzymes associated to the transport of sugars and the extracellular synthesis of polysaccharides^{7,23}.

Xylitol has been gradually added to dentifrices, chewing gums, mouth washers and mints to act as an antimicrobial agent²⁴. This *in vitro* study has, as its limitations, the characteristics of the agar infusion test, whose results depend on the diffusion ability of the antimicrobial agents. In addition, when the dentifrice comes in contact with the saliva, it is diluted, and its antimicrobial effect might be diminished⁷. Since here the effects of undiluted dentifrices were analyzed, it becomes necessary to analyze the antimicrobial activity of them when diluted.

Though these study only presents preliminary results, it has been shown that the concentration of fluoride ions in children dentifrices can influence their antimicrobial activity. More studies should be conducted in order to prove the antimicrobial action of children dentifrices which contain fluoride, xylitol, or both, especially considering how important dentifrices are for the antimicrobial activities of children and babies, as they act in the prevention of enamel demineralization and minimize the risk of dental fluorosis.

CONCLUSION

Within the limits of this *in vitro* study, it was concluded that all tested dentifrices

presented antimicrobial activities against *Streptococcus mutans*.

The dentifrice with a higher fluorine concentration (1500ppm, no xylitol) presented the highest antimicrobial activity, and the presence of xylitol in the dentifrices resulted in an antimicrobial activity similar to that of fluorinated dentifrices.

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CONTRIBUTIONS

Gilmara Medeiros Lucena took part in the conception, design and writing of this study. **Renata Sobreira França** and **Valeska Alves de Oliveira** acted in the writing and critical review. **Hugo Lemes Carlo** and **Fabiola Galbiatti de Carvalho** took part in the design, data analysis and interpretation.

How to cite this article (Vancouver)

Lucena GM, França RS, Oliveira VA, Carlo HL, Carvalho FG. Effects of Fluorine and Xylitol in the Antimicrobial Activity of Child Dentifrices. *REFACS* [Internet]. 2017 [cited in: *insert day, month, and year of access*]; 5(Supl. 1):101-107. Available in: *access link*. DOI: <http://dx.doi.org/10.18554/refacs.v5i0.1978>

How to cite this article (ABNT)

LUCENA, G.M. et al. Effects of Fluorine and Xylitol in the Antimicrobial Activity of Child Dentifrices. *REFACS*, Uberaba, MG, v. 5, p. 101-107, 2017. Supl. 1. Available in: *access link*. Access in: *insert day, month and year of access*. DOI: <http://dx.doi.org/10.18554/refacs.v5i0.1978>

How to cite this article (APA)

Lucena, G. M, França, R. S, Oliveira, V. A, Carlo, H. L & Carvalho, F. G. (2017). Effects of Fluorine and Xylitol in the Antimicrobial Activity of Child Dentifrices. *REFACS*, 5(Supl. 1), 101-107. Recovered in: *insert day, month and year of access*. *Insert access link*. DOI: <http://dx.doi.org/10.18554/refacs.v5i0.1978>