

Clinical Evaluation of the Ability of CaviStat® in a Mint Confection to Inhibit the Development of Dental Caries in Children

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Abstract

- **Objective:** The aim of the present study was to determine if a sugarless mint containing CaviStat® (an arginine bicarbonate calcium carbonate complex) is capable of preventing the development of dental caries in the primary molars and first permanent molars of 10½- to 11-year-old Venezuelan children.
- **Methods:** Two-hundred children were entered into this one-year study who showed the following: (i) age between 10½ and 11 years; (ii) first and second primary molars still present; (iii) sound primary molars or early caries lesions in any of these teeth; and (iv) at least some caries in the primary or permanent teeth as evidence of caries activity. Out of the 200 children initially selected, 195 finished and provided complete data. Children entered into the study were examined and then randomly divided into two groups (A and B), with distribution performed on the basis of the DMFS levels of the first permanent molars. All subjects were examined visually by a single examiner using good artificial light, mirror, and probe. Group A received a sugarless confection containing CaviStat (BasicMints®); Group B received a sugarless mint control that contained all ingredients except for the CaviStat. Packaging and appearance of both types of mints were identical, except for their A and B designations.
- **Results:** Mean differences in DMFS, defs, and DMFS + defs scores between Groups A and B were determined. In the first permanent molars and some early erupting premolars and second molars, the data showed 75.6% fewer caries in Group A than in Group B children after six months, and 50.7% fewer after 12 months. Corresponding defs scores showed reduced development of dental caries in deciduous molars of 76.7% after six months and 131.3% after 12 months. Combined DMFS and defs scores showed 76.2 and 74.8% fewer caries lesions at six and 12 months, respectively. As exfoliation of primary molars occurred during the study period (approximately equal in the two groups), a proportion correction was made to allow for caries score reductions due to lesions lost because of such exfoliation. When this was done, the results at the end of the study still showed larger caries reductions in Group A than in the Group B subjects, and statistical analyses showed these differences were still highly significant ($p < 0.001$). Non-cavitated caries lesions in the first permanent molars were also determined. These showed once again less caries development in Group A than in Group B subjects, and did so at both six and twelve months (57.0 and 52.4%, respectively). Levels of statistical significance at these times were $p = 0.013$ and 0.005 .
- **Conclusion:** It was evident from this clinical trial that mint confections containing CaviStat are able to inhibit both caries onset and caries progression. As a result, one can conclude that CaviStat mint confection technology is a simple and economical means for reducing substantially one of the most prevalent diseases in these children.

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Introduction

In 1890, Miller¹ provided the rudiments of a scientific basis for the initiation and development of dental caries, one of the most prevalent diseases in humans. Apparently, this is still true today. Involved in caries initiation and development are the acidogenic bacteria that are a major component of the mixed bacterial biofilms (dental plaque) that collect and grow best on the hard-to-clean surfaces of the teeth. Commonly, they are able to produce ample quantities of acid from fermentable carbohydrates, mostly

provided from the diet. A second step consists of the accumulation of sufficient acid to dissolve the calcium phosphate mineral, the major component of the hard tissues that comprise human teeth. Despite the tremendous amount of serious research that has been done for more than 100 years on dental caries causation and treatment, this disease has continued to be a major problem for the human population worldwide, especially in children.

Numerous therapeutic agents have been proposed and examined for their ability to prevent and control dental caries. Many

have been directed towards affecting either or both of the acid production and enamel demineralization processes that are basic to caries development. It is well known that saliva² is capable of significantly counteracting both processes. Hence, it has been logical to try to understand how saliva accomplishes these benefits, and to develop insights that lead to a means of providing the same or greater caries protection where this is deficient.

The dentition sites most prone to dental caries development are the posterior teeth. Thus, there is only superficial and nominal protection against caries development. What is needed to control this situation in children is a multiple approach that includes a saliva-based composition that is effective,² and an effective device as a means of its delivery. Such a composition has been formulated to include the amino acid arginine² (CaviStat®, Ortek Therapeutics, Inc., Roslyn, NY, USA). Ammonia formation therefrom by bacteria within dental plaque results in the elevation of plaque pH. It does this not only through provision of substrate, but also by favoring the growth and metabolism of arginolytic bacteria.² CaviStat is also comprised of bicarbonate, the main buffer in saliva for neutralizing plaque acid and a poorly soluble calcium salt, calcium carbonate. The latter component provides a source of calcium to prevent tooth solubilization and, under appropriate conditions, favors pH elevation and tooth remineralization. The bicarbonate and carbonate provide substantial pH buffering and necessary pH control that is important for effective arginine catabolism.³

Arginine is unique among the 20 or so common amino acids that are found in the human body and elsewhere. It can produce large amounts of base to effectively counter any cariogenic acid that is present, while favoring the emergence of arginolytic over non-arginolytic acidogens.² This results in a less cariogenic plaque microflora. Studies⁴ have confirmed that this microflora change actually occurs when subjects brush their teeth with a dentifrice containing CaviStat.

A recent two-year study⁵ demonstrated that arginine bicarbonate/calcium carbonate reduces caries development in children when delivered in a toothpaste formulation. In this study, caries development overall was significantly less in the subjects that used the CaviStat-containing paste than in those who used the fluoride dentifrice control. The CaviStat toothpaste was more effective both clinically and statistically in inhibiting caries initiation and progression. This manifested its effects differently in the already-erupted first molars than in the later-erupting premolars and second molars.

The arginine bicarbonate/calcium carbonate composition also has been used successfully in the treatment of dentinal hypersensitivity. This painful condition occurs when acid, mostly from foods in the diet, facilitates the breaching of tooth cementum and exposure, and opening of underlying dentinal tubules. CaviStat (called SensiStat® when used to treat dentinal hypersensitivity⁶) counters this condition by plugging opened dentinal tubules.^{6,7} Plugging occurs as a result of soluble arginine bicarbonate forming a complex with poorly soluble calcium carbonate, an aggregate with adhesive properties.⁷ This enables it to not only fill open dentinal tubules, but to also adhere to the dentinal tubule walls and form plugs that are more or less secure. Because of the alkalinity, the composition can also react with calcium and

phosphate ions in dentinal fluid⁷ to make the plugs chemically contiguous with the dentinal tubule walls and thereby add to its retentivity.

The aim of the present study was to determine if a sugarless mint containing CaviStat, easy to administer to children, is capable of preventing the development of caries in the primary and first permanent molars of 10½- to 11-year-old Venezuelan children. As there were some permanent premolars and second molars in the beginning stages of eruption, these were also examined at the same time.

Materials and Methods

A double-blinded, randomized and controlled clinical trial of one year's duration was initiated in children from 10 schools in the Municipality of Sucre in Miranda State, Venezuela. Human use approval was obtained from the Research Foundation Institutional Review Board at the State University of New York at Stony Brook, and informed consent was obtained from the parents or guardians of the children prior to examination.

Subjects selected were at an age when the deciduous molars exfoliate, and where it might be possible to biopsy (*i.e.*, section and examine microscopically) a sampling of these teeth after exfoliation. In this way, this method of assessment of caries development during the period of study could be included in this investigation.

Subject Selection

Initially, 2,547 children were processed to obtain the number of children needed to meet the criteria required for inclusion in this investigation. The children were processed into two segments. The first involved 2,135 children, of which 152 were chosen for entry into the study. The second involved 412 children, from which 48 were selected. This produced 200 study entrants. The children in the first cluster had their baseline visit in March, 2005, and the second cluster had theirs in June, 2005. Loss of some subjects from both clusters occurred. To meet the 200-subject target, a third cluster of children was processed in November, 2005 and the subjects needed were selected from this cluster. Out of the 200 children selected, 195 ultimately finished the one-year study with complete data. All subjects were studied for one year. Data for primary first and second molars still exfoliating were collected for various times thereafter.

Subjects entered into the study were examined visually by a single examiner using good artificial light, a mirror, and probe. The following criteria were used for selection: (i) age between 10½ and 11 years; (ii) presence of the first and second primary molars; (iii) sound primary molars or early carious lesions in any of these teeth; and (iv) at least some caries in the primary or permanent teeth as evidence of caries activity.

Children entered into the study were randomly divided into two groups (A and B), with distribution being performed on the basis of matching the DMFS (decayed, missing, filled surfaces) levels of their first permanent molars as closely as possible. Children entered into the study from each school were distributed into both groups (Table I). Group A received the sugarless confection containing CaviStat (called BasicMints®). The other (Group B) received a sugarless mint control that contained all

Table I
Number of Male and Female Students Examined in
Groups A and B at the Various Schools

School Examined	Number of Students	Sex		Group	
		M	F	A	B
1. U.E. Cosme Damian	29	20	9	15	14
2. U.E. Ravel	8	4	4	4	4
3. U.E. Socorro González	6	3	3	3	3
4. U.E. Baute	57	35	22	28	29
5. U.E. Ortega Ordoñez	9	6	3	5	4
6. U.E. Negro Primero Nac	11	5	6	4	7
7. U.E. Negro Primero Est	21	14	7	9	12
8. U.E. Magali Burgos	15	10	5	6	9
9. U.E. Simón Bolívar	17	6	11	9	8
10. U.E. Leoncio Martínez	5	5	0	4	1
11. U.E. El Llanito	17	9	8	9	8
Total	195	117	78	96	99

ingredients except for the CaviStat. Packaging and appearance of both types of mints were identical, except for their A and B designations.

Both groups of children continued with their normal hygiene regimens, which included brushing the teeth at baseline and throughout the whole study with a commercially available toothpaste containing 1450 ppm fluoride and dehydrated dicalcium phosphate (Colgate® with Calcium Maxima Protección Anticaries, Colgate-Palmolive C.A., Cali, Colombia). Both groups also received fluoride via the National Salt Fluoridation Program which began in 1995. As a consequence, fluoride was introduced into table salt to compensate for the lower level of fluoride in the drinking water in the Caracas Metropolitan Area, which is at 0.12 ppmF.⁸

Each group then received a monthly allotment of mints, and parents or guardians were instructed in their use. The children were to take four mints daily; two in the morning after brushing the teeth and before eating breakfast, and the other two in the evening after brushing the teeth and before going to bed. Parents or guardians reported no difficulty with compliance.

At each use, one of the mints was introduced into the mouth, held there for about 30 seconds to enable moistening and softening through mixing with the saliva. The mint was moved to one side of the mouth and crushed by the primary molars and the first permanent molars. Modest pressure was used to facilitate packing of the mint confection into the pits and fissures, and the approximating surfaces of the teeth (Figure 1). The second mint was handled similarly, but on the opposite side of the mouth.

Caries Examination

Caries examinations of all subjects at baseline, and at six and 12 months thereafter were performed by a single calibrated examiner (CM) using #5 dental mirrors and #23 explorers. The examiner has served as such in prior clinical trials.⁵ In the present study, suspected lesions were classified as cavitated or non-cavitated. Cavitated caries lesions were identified and scored using the DMFS and defs (decayed, indicated for extraction, filled surfaces) caries method and criteria reported by Radike,⁹ except that slight or no, rather than moderate pressure of exploring was used.⁵ Frank cavitation was detected as a discontinuity of the

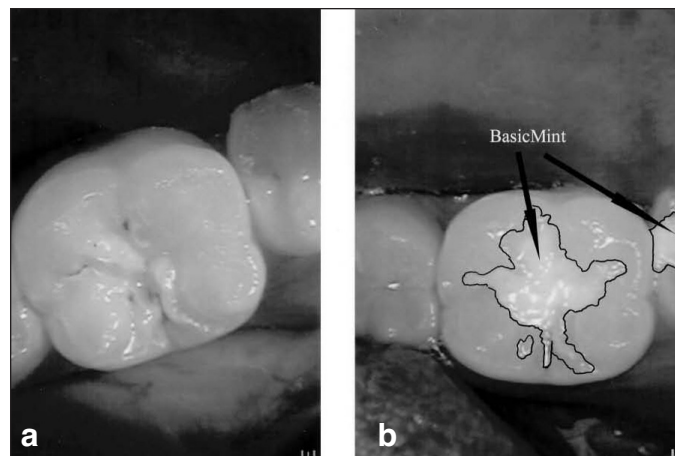


Figure 1. In vivo retention (a) before and (b) after chewing BasicMint on the occlusal surface of a molar tooth.

enamel surface caused by loss of tooth substance as distinct from fracture, erosion, or abrasion. Non-cavitated lesions were scored carious after gentle and careful cleaning to remove plaque, and before and after air drying when the following was observed: (i) opacity (white spots) or loss of normal translucency adjacent to a pit or fissure hardly visible on a wet surface, but distinctly visible after air drying; (ii) opacity or discoloration distinctly visible without air drying; and (iii) localized enamel breakdown in opaque or discontinuous enamel. Generally, there were indications of beginning demineralization or undermining of the enamel. The caries experience was expressed as DMFS, and the total number of initial lesions was calculated only for the first permanent molars by summing the total number of such demineralization lesions detected before and after drying the enamel surface.

The examiner performing the clinical examinations did not know which group was which, or which of products A and B contained CaviStat. Dental radiographs were not taken.

Kappa Analysis

Re-examination of 10% of the subjects was done by the single examiner, and the data were used to determine her consistency by Cohen Kappa analysis.¹⁰ Subjects were randomly selected at different times in the study for this re-examination. The Kappa value obtained before the final examination (January, 2006) for the first group of subjects was 0.99, and for the second group (May, 2006) it was 0.99 as well.

Statistical Analysis

At baseline and each test period, DMFS and defs descriptive statistical data were obtained and analysis for significant differences between Group A and B subjects was performed, where appropriate, using analysis of variance, analysis of covariance, and Student's t-test.

Results

A total of 195 subjects completed the study. Distribution of the subjects into two groups is shown in Table I. Group A contained 96 and Group B contained 99 children. Collectively, they were comprised of 117 males and 78 females.

Permanent Posterior Teeth DMFS Score Comparisons

The mean DMFS (\pm SD) scores for the permanent teeth (mostly first permanent molars and some early-erupting premolars and second molars) in the Group A and Group B children are shown in Tables IIa and III. At baseline, scores (\pm SD) for the Group A subjects were 1.18 ± 1.35 , and 1.16 ± 1.64 for Group B. These numbers were essentially the same, because the matching of the two groups of subjects at baseline was performed to try to distribute subjects evenly. After 12 months, scores (\pm SD) were 1.55 ± 1.68 for Group A and 1.91 ± 1.81 for Group B. Accordingly, the permanent teeth of these two groups were subjected to analysis of variance; the difference between their respective means was significant at $p < 0.001$. The Δ DMFS values after six and 12 months were 0.11 and 0.37 for Group A, and 0.45 and 0.75 for Group B, respectively (Table IIa). Reduction in caries in the permanent teeth in Group A, relative to Group B, was 75.6% after six months and 50.7% at the end of 12 months (Table IIb).

Table IIa

Effect of Mints With and Without CaviStat on the Mean DMFS (\pm SD) and defs* (\pm SD) Scores at Six and 12 Months for the Permanent and Primary Teeth of the Children Studied

Group A Subjects					
Scores	0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months
DMFS	1.18 ± 1.35	1.29 ± 1.53	1.55 ± 1.68	0.11	0.37
defs	0.67 ± 1.66	0.81 ± 1.46	0.57 ± 1.43	0.14	-0.10
DMFS + defs	1.85 ± 2.39	2.10 ± 2.37	2.12 ± 2.55	0.25	0.27
Group B Subjects					
Scores	0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months
DMFS	1.16 ± 1.64	1.61 ± 1.97	1.91 ± 1.81	0.45	0.75
defs	0.51 ± 1.21	1.11 ± 1.85	0.83 ± 1.57	0.60	0.32*
DMFS + defs	1.67 ± 2.32	2.72 ± 2.80	2.74 ± 2.35	1.05	1.07*

*The effect of exfoliation of primary teeth has not been dealt with in this table. Its impact has been examined in Table Vb. Exfoliation is approximately equal in the two groups (see Table VI).

Table IIb

Score Differences Between Group A and Group B Subjects

Group B—Group A Subjects						
Score difference	Δ DMFS (B-A)		Δ defs (B-A)		Δ DMFS + defs (B-A)	
	After 6 Months	After 12 Months	After 6 Months	After 12 Months	After 6 Months	After 12 Months
Score difference	0.34	0.38	0.46	0.42	0.80	0.80
% difference $\frac{B-A}{B} \times 100\%$	75.6%	50.7%	76.7%	131.3%	76.2%	74.8%

Breakdown of the results for the permanent DMFS scores are shown in Table III. Interestingly, no caries lesions were seen in the first premolars and very few caries lesions were seen in either the second premolars or second permanent molars in Group A. Some, however, were seen in these teeth in Group B (Table III). Although these numbers for the premolars and second molars are small, the difference of Group B from Group A

Table III

Effect of Mints With and Without CaviStat on the Mean DMFS (\pm SD) Scores in the Permanent Teeth of the Children Studied at Baseline, Six and 12 Months

Mean First Premolar DMFS Scores					
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months
Group A	96	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00
Group B	99	0.00 ± 0.00	0.01 ± 0.10	0.03 ± 0.17	0.01
Mean Second Premolar DMFS Scores					
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months
Group A	96	0.00 ± 0.00	0.00 ± 0.00	0.01 ± 0.10	0.00
Group B	99	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00
Mean Second Permanent Molar DMFS Scores					
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months
Group A	96	0.00 ± 0.00	0.01 ± 0.10	0.01 ± 0.10	0.01
Group B	99	0.00 ± 0.00	0.04 ± 0.40	0.08 ± 0.47	0.04
Mean Total Premolar and Second Permanent Molar Scores					
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months
Group A	96	0.00	0.01	0.02	0.02
Group B	99	0.00	0.05	0.11	0.05
Mean First Permanent Molar DMFS Scores					
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months
Group A	96	1.18 ± 1.35	1.28 ± 1.51	1.53 ± 1.66	0.10
Group B	99	1.16 ± 1.64	1.56 ± 1.85	1.80 ± 1.72	0.40

is nonetheless evident and consistent with the first molar data in this table. In contrast, first permanent molar caries was much higher. This is attributable to the longer time the first molars had been in the mouth.

Deciduous Molar defs Score Comparisons

The defs scores for the deciduous molar teeth that had not exfoliated during the one-year study period are shown in Table IIa, and more specifically in Table IV. Since distribution of subjects into Groups A and B at baseline was done on the basis of initially matching permanent first molar DMFS scores, baseline levels for the deciduous molars did not match. Baseline levels were not statistically significantly different; hence, analysis of covariance was used to assess statistical significance (see below). As occurred for the permanent first molars, caries increments in the deciduous teeth were greater in Group B than in Group A. The defs increments for Group A at six and 12 months were 0.14 and -0.10 for Group A, and 0.60 and 0.32 for Group B, respectively (Tables IIa and IV). Reduction in the increase in the deciduous teeth defs score (Group A compared to Group B) was 76.7% after six months and 131.3% after 12 months (Table IIb). Statistical testing for significance by analysis of covariance showed (as before) that Group B increments were significantly larger than those in Group A ($p < 0.001$).

As a result of primary teeth exfoliation, the number of teeth present in the mouth in both Groups A and B at 12 months fell below baseline (Table Va). From this table, the mean number of

Table IV

Effect of Mints With and Without CaviStat on the Mean defs (\pm SD) Scores in the Deciduous Teeth of the Children Studied at Baseline, Six, and 12 Months*

Mean First Premolar DMFS Scores						
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months	
Group A	96	0.60 \pm 1.44	0.56 \pm 1.21	0.30 \pm 0.85	-0.04	-0.30
Group B	99	0.43 \pm 1.10	0.66 \pm 1.32	0.58 \pm 1.16	0.23	0.15

Mean Second Primary Molar defs Scores						
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months	
Group A	96	0.07 \pm 0.33	0.25 \pm 0.65	0.27 \pm 0.64	0.18	0.20
Group B	99	0.07 \pm 0.36	0.45 \pm 0.87	0.26 \pm 0.60	0.38	0.19

Mean First Plus Second Primary Molar defs Scores						
N°	0 Months	6 Months	12 Months	Δ After 6 Months	Δ After 12 Months	
Group A	96	0.67 \pm 1.52	0.81 \pm 1.36	0.57 \pm 1.17	0.14	-0.10
Group B	99	0.51 \pm 1.14	1.11 \pm 1.71	0.83 \pm 1.43	0.60	0.32

*Not taken into account are the primary teeth exfoliated at 6 and 12 months (see Table Va). This apparently results in a decrease, rather than a rise in the defs scores seen at 12 months and a probable lesser increase at six months than would be the case.

Table Va

Fall in the Mean Numbers of Primary Molars in Mouths Because of Teeth Exfoliation*

	Mean Number of Teeth			Mean Tooth Loss/Gain		
	At 0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months	
Primary defs	11.74 \pm 1.25	10.07 \pm 2.62	8.25 \pm 3.65	-1.67	-3.49	Group A
Permanent DMFS	11.71 \pm 1.14	13.35 \pm 2.56	15.34 \pm 3.82	+1.64	+3.63	

	Mean Number of Teeth			Mean Tooth Loss/Gain		
	At 0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months	
Primary defs	11.90 \pm 0.96	10.26 \pm 2.35	9.05 \pm 3.25	-1.64	-2.85	Group B
Permanent DMFS	11.51 \pm 11.05	13.22 \pm 1.05	14.71 \pm 3.82	+1.71	+3.20	

Adjustment Factors for Exfoliating Primary Teeth Obtained from Data in Table IV

$$6 \text{ month} - \frac{11.74}{10.07} = 1.17 \quad 12 \text{ months} - \frac{11.74}{8.25} = 1.42 \quad \text{Group A}$$

$$6 \text{ month} - \frac{11.90}{10.26} = 1.16 \quad 12 \text{ months} - \frac{11.90}{9.05} = 1.31 \quad \text{Group B}$$

These adjustment factors applied to Table IIa defs and DMFS + defs data produces the data allowing for exfoliation in Table Vb.

*Shown for comparison and interest is the corresponding increase in the mean number of permanent molar and premolar replacements that occur at the same time, as a result of premolar and second molar eruptions.

teeth exfoliated per subject at 12 months was calculated. It was -3.49 in Group A and -2.85 in Group B. Also noted was that permanent teeth showed a corresponding rise in their numbers because of premolar and second permanent molar eruptions occurring at the same time (Table Va).

When defs scores are re-calculated to allow for the lost defs surfaces resulting from exfoliation (see determination of a proportion factor in Table Va), substantially fewer caries were

still evident in A than in B (Table Vb). The increment in defs scores at six months in Group A becomes 0.28, and at 12 months it becomes 0.14. The corresponding increments in the Group B subjects becomes 0.78 and 0.58, respectively. This results in 64.1% fewer caries lesions with A relative to B at six months, and 75.9% fewer at 12 months (Table Vb).

Table Vb

Effect of Mints With and Without CaviStat on the Mean defs (\pm SD) Scores*

Scores	Group A Subjects				
	At 0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months
defs	0.67 \pm 1.66	0.95 \pm 1.46	0.81 \pm 1.43	0.28	0.14
DMFS + defs	1.85 \pm 2.39	2.24 \pm 2.37	2.36 \pm 2.55	0.39	0.51

Scores	Group B Subjects				
	At 0 Months	At 6 Months	At 12 Months	Δ After 6 Months	Δ After 12 Months
defs	0.51 \pm 1.21	1.29 \pm 1.85	1.09 \pm 1.57	0.78	0.58
DMFS + defs	1.67 \pm 2.32	2.90 \pm 2.80	3.00 \pm 2.35	1.23	1.33

	Score Differences Between Group A and Group B Subjects			
	Δ defs (B-A)		Δ DMFS + defs (B-A)	
	After 6 Months	After 12 Months	After 6 Months	After 12 Months
Score difference	0.50	0.44	0.84	0.82
% difference	64.1%	75.9%	68.3%	61.7%

$$\frac{B-A}{B} \times 100\%$$

*After adjustment has been made for the effect that exfoliated primary teeth would have had on the defs results had they been included in the core.

Exfoliation is clearly a confounding factor, but its effect was mitigated to a certain degree by the adjustment calculation done here.

Exfoliation of Primary Teeth and Their Scoring

The decreases in the defs scores in Groups A and B at six and 12 months shown in Tables IIa and IV are attributable mostly to the exfoliation of primary teeth (and thus loss of surfaces) which occurred in both groups. A number of exfoliated teeth that could be obtained and their mean times of exfoliation were determined (Table VI). This indicated, as one might have expected, that the numbers and overall times of exfoliation were comparable. Con-

Table VI

Mean Times of Exfoliation of Group A and Group B Primary Molars

	Between Baseline and Exfoliation		Between End of Taking Mints and Time of Exfoliation		Totals	
	Number of Teeth	Mean* Months	Number of Teeth	Mean** Months	Number of Teeth	Mean Months
Group A	42	8.76 \pm 2.31	65	6.95 \pm 4.24	107	14.95
Group B	26	9.08 \pm 2.92	65	6.06 \pm 3.82	91	15.49
Total	68		130		198	

* Period between baseline and time of exfoliation; respective mints were taken by both groups, respectively .

** Respective mints were only taken between baseline and 12 months by both groups, respectively.

sequently, the proportioning used in the previous section would appear to be reasonable, and enabled statistical comparisons and analyses to be made.

By scoring the exfoliated teeth outside of the mouth, which can be done with greater confidence and accuracy than analysis *in vivo*, it was found once again that more caries lesions occurred in Group B teeth than in the teeth in Group A (Table VII).

Table VII
Effect of Mints With and Without CaviStat on the Mean defs (\pm SD) Scores of Primary Teeth that Exfoliated before End of 12 Months

Score	Mean defs Score Group A	Mean defs Score Group B	p-values for Comparisons Between Group A and Group B defs Scores (Horizontal Comparison)
defs at Baseline	0.13 \pm 0.41	0.08 \pm 0.37	0.23
defs after exfoliation	0.23 \pm 0.53	0.42 \pm 0.70	0.03
p-values for Group A and for Group B before and after exfoliation (Vertical Comparison)	0.08	0.0002	

Mints were available to Group A and Group B respectively between baseline and time of exfoliation.

Deciduous Molar Plus Permanent Posterior Teeth Score Comparisons

When defs and DMFS data were considered together (Table IIa), the increments in caries defs + DMFS scores (\pm SD) at six months was 0.25 for Group A and 1.05 for Group B (Table IIa). At 12 months, it was 0.27 for Group A and 1.07 for Group B (Table IIa). The smaller increase in caries development (*i.e.*, Group A relative to Group B) after six months was 76.2%, and 74.8% after 12 months (Table IIb). When the exfoliation adjustment for the deciduous teeth portion was factored in (Table Vb), caries development after six months was 68.3% less, and after 12 months it was 61.7% less.

New Non-cavitated Initial Lesions in the Permanent Dentition

The criteria for classifying caries lesions as cavitated or non-cavitated are given in the Materials and Methods section. Cavitated lesions in the first permanent molars were detected by gentle probing, whereas the non-cavitated were detected by visualizing white lesions after careful cleaning to remove plaque before and after air drying.

The results for the total number of new non-cavitated lesions, which were mostly seen in the first permanent molars, are shown in Figure 2. A larger number of non-cavitated lesions was detected after drying, and more were observed in the Group B children. In Group A, new non-cavitated lesions increased from zero at baseline to a mean (\pm SD) per subject of 0.21 \pm 0.07 at six, and 0.30 \pm 0.07 at 12 months thereafter. In contrast, they increased in Group B from zero at baseline to 0.49 \pm 0.09 at six, and 0.63 \pm 0.10 at 12 months. Six- and 12-month differences between Groups A and B were both highly significant by Student's t-test analysis. About two thirds of the new lesions were observed in the buccal surfaces of the lower molars. New early non-cavitated lesions were few in the occlusal surfaces, possibly because they are hard to detect visually.

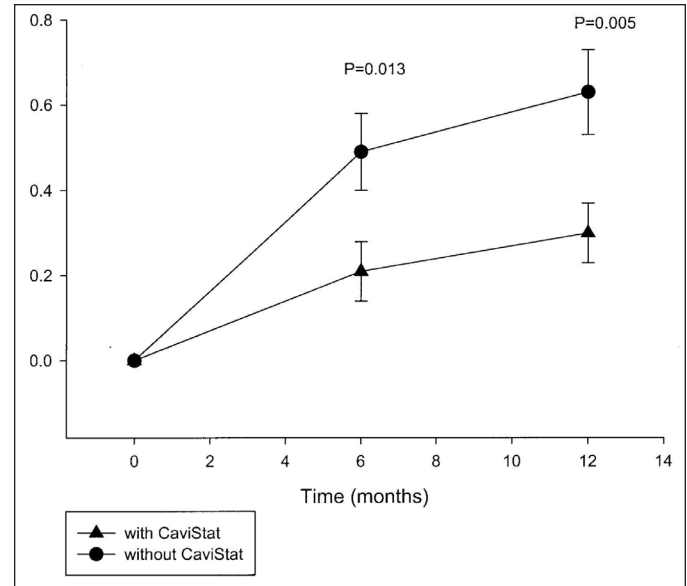


Figure 2. Effect of mints with and without CaviStat on initial (*i.e.*, non-cavitated) occlusal carious lesions in first permanent molars (% reduction at 6 months = 57.0%; at 12 months reduction is 52.4%).

The later erupting premolars and second molars also showed a clear difference in number of new lesions, albeit the numbers were very small. Nevertheless, the Group A children showed no non-cavitated new lesions in any of the premolars or permanent second molars during the 12 months of treatment. In contrast, in the Group B controls lesions were evident in the second permanent molars at six and 12 months, the first premolars at 12 months, but no lesions were evident as yet in the second premolars (Table IV).

Discussion

Many investigations have been carried out using different therapeutic agents to inhibit caries development and progression in humans. There is a convincing and extensive body of evidence showing that fluoride is a highly effective anticaries agent.¹¹⁻¹⁴ Fluoride is either released into, or present in the fluid phase that bathes the hard tissues, or it may be incorporated into enamel, dentine, or cementum as part of poorly soluble fluorapatite.¹⁵ However, in the last decade, other anticaries agents have been tested, such as casein derivatives¹⁶ that complex with calcium phosphate, cacao mass extract,¹⁷ derivatives from natural products,¹⁸⁻²² and, more recently, a composition containing arginine (CaviStat), which has been incorporated into a toothpaste and proven to be anticariogenic in children.⁵ The results in that study showed it was more effective in inhibiting caries initiation and progression than a fluoride toothpaste control. It manifested its effect differently in the already-erupted first molars than in the later-erupting premolars and second molars.⁵

In the present study, CaviStat was incorporated into a sugarless mint confection, a vehicle that appears to be well-suited for reducing caries development and progression in posterior occlusal surfaces of the primary and permanent teeth. It was clear from the study that the Group A subjects, who received the mint confections containing CaviStat, developed fewer caries lesions than did the subjects in Group B, who received mint confections

that did not contain CaviStat. This was true for comparisons made by standard DMFS examination in the permanent teeth, and its defs counterpart in the deciduous teeth.

The caries-inhibiting effects of CaviStat were also observed for non-cavitated developing lesions. These were mainly seen in the permanent first molars. Since the primary and permanent teeth started essentially with no or few lesions, reversal is not likely to be a significant factor in the caries scoring and only demineralization is of issue. This makes the caries scoring and ability to show effects of an active agent much easier. Of interest, the inhibitory effect of CaviStat on caries lesion development in this study was seen in both primary and permanent teeth (Tables II, III, and IV).

The number of lesions in the premolars and second molars were small since any caries in these teeth would be in an early stage of their development. As a consequence, the period of time these teeth would have been in the mouth was short. Nonetheless, differences between Group A and Group B were evident. Inhibition of very early caries development in the premolars and second permanent molars was a result of the CaviStat provided to the Group A children.

Interestingly, early non-cavitated lesions were few in the occlusal surfaces, possibly because they are hard to detect visually since occlusal caries takes place within, rather than at the mouth of pits and fissures. This situation may arise because of higher fluoride and lower tooth solubility that may be associated more with the orifices²³ than with interior tooth locations.

These results give affirmation to the studies that led to CaviStat development.² Central is that it is a complex designed to counter caries formation by simultaneously inhibiting the two fundamental processes known for more than a hundred years to be responsible for caries development, *viz*, acid generation by bacterial fermentation of appropriate carbohydrate substrates, and solubilization of tooth mineral by the acid so generated.^{1,2,24} Additional affirmation comes from recent results⁴ showing that the use of a CaviStat-containing dentifrice (DenClude®, Ortek Therapeutics, Roslyn, NY, USA) favors an increase in the arginolytic bacterial component of the oral microflora, which in turn will favor an increase in alkalinity when arginine is available. As pointed out earlier, CaviStat can favor remineralization of initial caries lesions by providing calcium from calcium carbonate,^{25,26} which is activated when the plaque pH begins to decrease. Countering such a decrease are the bicarbonate and carbonate anions in CaviStat which provide a more favorable pH for base formation³ from arginine.

Conclusion

Mint confections containing CaviStat are able to inhibit both caries onset and caries progression. As a result, it is reasonable to conclude that one of the most prevalent diseases in humans, namely dental caries, can be substantially reduced by use of CaviStat delivered in a mint confection.

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