

# The enhanced anticaries efficacy of a sodium fluoride and dicalcium phosphate dihydrate dentifrice in a dual-chambered tube. A 2-year caries clinical study on children in Brazil

MILTON F. DE A. SILVA, DDS, PHD, EDGLEI V. DE S. MELO, DDS, BERNAL STEWART, BS ENG, WILLIAM DE VIZIO, DMD, JORGE L. SINTES, DMD, PHD, MARGARET E. PETRONE, JD, ANTHONY R. VOLPE, DDS, MS, YUN PO ZHANG, PHD, JAMES J. MCCOOL & HOWARD M. PROSKIN, PHD

**ABSTRACT:** *Purpose:* To clinically evaluate and compare a dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate (Test Dentifrice delivering 0.243% sodium fluoride), to a dentifrice containing 0.243% sodium fluoride in a silica base (Positive Control Dentifrice). *Materials and Methods:* This study was conducted in harmony with the published 1988 American Dental Association guidelines for studies geared toward the comparison of fluoride dentifrices. This 2-yr caries clinical study employed a double-blind, parallel-group design, and involved 6-10 yr-old children from the metropolitan area of Maceio, Alagoas, Brazil. Qualifying subjects were stratified according to age and sex, and were randomly assigned to the two treatment groups, with multiple subjects in the same household all assigned to the dentifrice randomly allocated to the first among them. Caries examinations were conducted in accordance with U.S. Food and Drug Administration guidelines for the clinical evaluation of drugs to prevent dental caries. One calibrated examiner performed all the measurements. After treatment assignment, study participants were instructed to brush their teeth at home with their assigned dentifrice at least twice daily. Brushing instructions were reinforced by indoctrination in proper oral hygiene techniques by dental professionals, supplemented by pamphlets supplied by the sponsor and yearly mailings to participants, emphasizing good oral hygiene and the need to enforce compliance with the study. Post-baseline examinations were performed after 1 yr of product use, and again after 2 yrs of product use. *Results:* Two thousand four hundred thirty-two (2,432) subjects completed this 2-yr study. For these subjects, the mean caries scores (DMFS, decayed, missing and filled tooth surfaces) at baseline were 3.84 for the Test Dentifrice group, and 4.06 for the Positive Control Dentifrice group. For caries increments after 1 yr, the respective means were 2.02 for the Test Dentifrice group and 2.12 for the Positive Control Dentifrice group. Finally, after 2 yrs, the mean caries increments were 4.30 for the Test Dentifrice group, and 4.83 for the Positive Control Dentifrice group. No statistically significant difference was indicated between the treatment groups at baseline or between the 1-yr caries increment scores. However, there was a statistically significant difference in the 2-yr caries increment scores between the treatment groups. Relative to the Positive Control Dentifrice group, the Test Dentifrice group presented a 10.97% reduction in caries increment scores at 2 yrs. In accordance with the procedures and standards provided by the published guidelines of the American Dental Association for the comparison of the anticaries efficacy of fluoride dentifrices, the results of this study support the conclusion that the dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, provided a superior level of anticaries efficacy than did the dentifrice containing 0.243% sodium fluoride in a silica base. (*Am J Dent* 2001;14:19A-23A).

**CLINICAL SIGNIFICANCE:** A dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, provided a superior level of anticaries efficacy than did a dentifrice containing 0.243% sodium fluoride in a silica base.

**CORRESPONDENCE:** Dr. Milton F. de A. Silva, Laboratory of Preventive Dentistry, Federal University of Alagoas, Maceio, Brazil. Fax: 55 82 358-5724. E-mail: mfas@sunnet.com.br

## Introduction

The anticaries efficacy of fluoride containing agents can be improved by creating fluoride "reservoirs" on tooth surfaces.<sup>1-3</sup> Further, the deposits of calcium fluoride would provide the optimum form for such a fluoride "reservoir".<sup>4-5</sup>

A two-component dentifrice system, wherein one chamber contains sodium fluoride in a silica base and the other chamber contains dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, has been developed. It is reasonable to believe that the teeth of subjects using this dentifrice sys-

tem will retain greater amounts of applied fluoride, when compared to the teeth of subjects using sodium fluoride dentifrices, thus resulting in a decreased rate of caries formation.

This clinical study was specifically designed to investigate the degree of anticaries efficacy of a dentifrice system in a dual-chambered tube, relative to that provided by a sodium fluoride dentifrice and, in particular, to ascertain whether it can be concluded that the new dentifrice provides a superior level of anticaries efficacy.

Table 1. Coronal caries examination criteria for permanent teeth. (Adapted from the Oral Health Surveys of the National Institute of Dental Research).

Tooth Categories	
S	= Sound (no caries)
P	= Primary (deciduous)
M	= Missing (due to caries)
U	= Unerupted
N	= Not scoreable (fractured, crowned extracted for orthodontics, extracted for periodontics, fluorosis, or composite veneers)

Surface Categories			
<b>Caries</b>		<b>Restoration</b>	
X	= Occlusal	Y	= Occlusal
0	= Lingual	6	= Lingual
1	= Buccal	7	= Buccal
2	= Mesial	8	= Mesial
3	= Distal	9	= Distal
<b>Ortho Bands</b>		<b>Sealants</b>	
40	= Lingual	55	= Occlusal
41	= Buccal	56	= Lingual
42	= Mesial	57	= Buccal
43	= Distal		

## Materials and Methods

This 2-year clinical study was conducted in harmony with the published 1988 American Dental Association guidelines<sup>6</sup> for studies geared toward the comparison of the clinical anticaries efficacy of fluoride dentifrices. The study employed a double-blind, parallel-groups, two-treatment design.

Male and female children (age 6-10 yrs at baseline) participated in the 2-yr clinical study. The children were from the metropolitan area of Maceio, Alagoas, Brazil, where the communal water supplies had less than optimal fluoride concentration.<sup>7</sup> Subjects were enrolled in the study based upon the following criteria:

1. An informed consent form must have been signed by a parent or legal guardian;
2. Subjects were attending an elementary grade school;
3. Subjects were excluded from the study if they had no evidence of clinical caries activity in their dentition or if they had orthodontic appliances;
4. Subjects were excluded from the study if they had participated in any other clinical study during the 3 months prior to the baseline examination, or if they presented with any condition which, in the opinion of the investigator, would impede on their ability to participate.

Baseline examinations were conducted in accordance with U.S. Food and Drug Administration (FDA) guidelines<sup>8</sup> for the clinical evaluation of drugs to prevent dental caries. Qualifying subjects were stratified according to age and sex, and were randomly assigned to the two treatment groups, with multiple subjects in the same household all assigned to the dentifrice randomly allocated to the first among them. The two treatments were:

**Test Dentifrice:** A dentifrice system in a dual-chambered tube, wherein one chamber contains sodium fluoride in a silica base

and the other chamber contains dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride.<sup>a</sup>

**Positive Control Dentifrice:** A dentifrice containing 0.243% sodium fluoride in a silica base.<sup>a</sup>

The Test and Positive Control Dentifrices were packaged in white tubes so as to mask the identity of the products. The dentifrices were provided to the study subjects four times per year, along with two youth-size, soft-bristled toothbrushes. When new tubes of the dentifrice were delivered, subjects returned their previous tubes so that compliance with dentifrice use could be monitored.

After treatment assignment, study participants were instructed to brush their teeth at home with their assigned dentifrice at least twice daily. Brushing instructions were reinforced by the presentation of educational films and lectures at school, and through the periodic distribution of small novelty gifts along with the dentifrice deliveries, in order to enhance the interest and enthusiasm of study participants.

Post-baseline examinations were performed after 1 yr of product use, and again after 2 yrs of product use. One examiner performed all of the measurements for the study. The study was concluded after the completion of the 2-yr examination.

### Clinical examinations and scoring procedure

The clinical caries examinations and scoring procedure were conducted in accordance with U.S. Food and Drug Administration guidelines for the clinical evaluation of drugs to prevent dental caries.<sup>8</sup> Dental caries was scored by an independent, calibrated examiner in accordance with criteria established by the National Institute of Dental Research.<sup>9</sup> Table 1 provides the criteria used to score caries in this clinical study.

At each examination (baseline, 1-yr, 2-yr), scores were recorded for every surface of every permanent tooth, with the exception of third molars. Based on these, a DMFS (decayed, missing and filled tooth surface) score was determined for each participant and a mean DMFS score was calculated for each dentifrice group. From the post-baseline examinations, the mean incremental DMFS score was calculated for each dentifrice group.

### Examiner calibration

The calibration of the caries examiner was conducted by an experienced caries clinician and epidemiologist. The first part of the calibration included a discussion focusing on the diagnostic criteria, examination methods and procedures. In the second part, the examiner was calibrated using a representative sample of subjects. Examiner reliability was quantified through the calculation of Kappa statistics. The Kappa statistic, a widely used measurement of reliability (agreement) for categorical parameters, expresses the degree of improvement over random agreement between repeated measurements of the same individual units. A value of 0 indicates no improvement over random agreement, while a value of 1 indicates that the maximum possible improvement over random agreement has been attained.

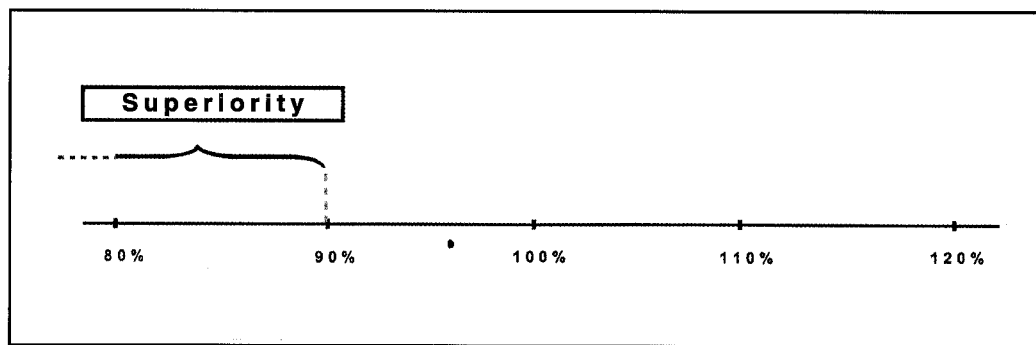


Fig. 1. Illustration of the underlying principle for the comparative attribute "superiority".

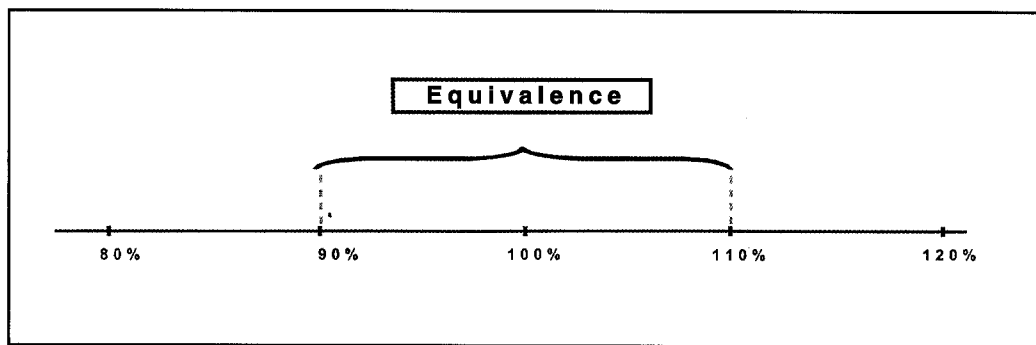


Fig. 2. Illustration of the underlying principle for the comparative attribute "equivalence".

### Statistical methods

An ANOVA was employed to compare the mean incremental DMFS scores obtained for the two study dentifrices at the 1-yr and 2-yr examinations; and as well, to compare the two treatment groups with respect to DMFS scores at baseline. All comparisons of post-baseline means were adjusted for baseline scores. All statistical tests of hypotheses employed a level of significance of  $\alpha = 0.05$ .

### Criteria for assessment of results

The assessment of the results of this comparative study were performed in accordance with the criteria established in the aforementioned American Dental Association guidelines<sup>6</sup>, as further described and enumerated by Proskin *et al.*<sup>10</sup> These guidelines provide three terms (often called "comparative attributes") which can be applied to describe the comparative efficacy of fluoride dentifrices: these are (1) superior, (2) equivalent, and (3) "at least as good as". As explained by Proskin *et al.*,<sup>10</sup> these terms are based on the relative values of the mean incremental caries scores associated with the dentifrices over the period of use, and are most commonly discussed by expressing the mean incremental caries score for the "test" dentifrice as a percentage of the mean incremental caries score for the "control" dentifrice.

When the "test" dentifrice results in a substantial reduction in incremental caries relative to the "control" dentifrice, the term "superiority" is applied to express this relationship. Current American Dental Association guidelines indicate that a 10% reduction in caries increment is sufficient to warrant this term. An illustration of this principle is provided in Fig. 1. According to the criteria described in Proskin *et al.*,<sup>10</sup> a study will support such a conclusion if: 1) the "test" dentifrice exhibits a statistically significant reduction in incremental

caries compared to the "control" dentifrice (one-sided test,  $\alpha = 0.05$ ); and 2) the observed mean incremental caries score associated with the "test" dentifrice is at least 10% lower than that associated with the "control" dentifrice.

When the "test" and "control" dentifrices provide levels of anticaries efficacy which are very close to each other, the term "equivalent" is applied. Current American Dental Association guidelines indicate that this term is applicable if the mean caries increment associated with the "test" dentifrice does not differ from that associated with the "control" dentifrice by more than 10%, *i.e.*, if the mean caries increment associated with the "test" dentifrice is between 90% and 110% of that associated with the "control" dentifrice. This principle, which is investigated through the use of Fieller confidence intervals,<sup>11</sup> is illustrated in Fig. 2.

When the "test" dentifrice provides a level of anticaries efficacy which is not substantially worse than that provided by a "control" dentifrice, we say that the "test" dentifrice is "at least as good as" the "control" dentifrice. Current American Dental Association guidelines indicate that this term is applicable if the mean caries increment associated with the "test" dentifrice is below 110% of that associated with the "control" dentifrice. Figure 3 provides an illustration of this principle. Note that as the figure illustrates, the range of percentages associated with "at least as good as" consists of the combined ranges for the aforementioned properties "superiority" and "equivalence".

### Results

Two thousand four hundred thirty two (2,432) subjects completed the entire 2-yr study. A summary of the age (at baseline) and sex of the study population is presented in Table 2. The treatment groups were well balanced with respect to these characteristics.

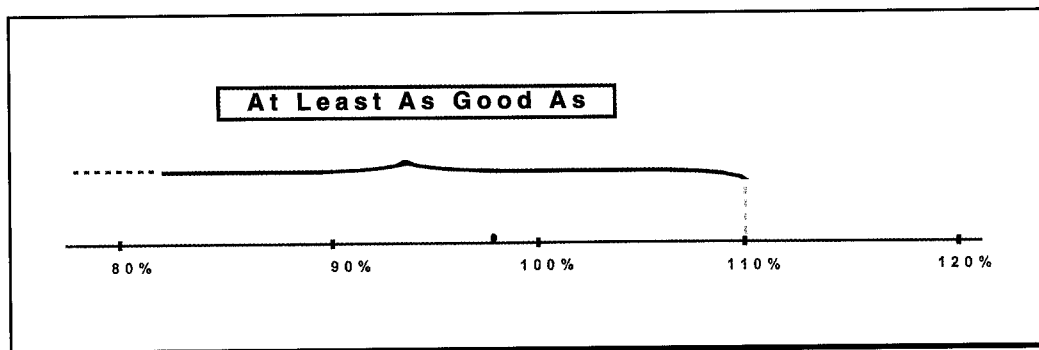


Fig. 3. Illustration of the underlying principle for the comparative attribute "at least as good as".

Table 2. Summary of age at baseline and sex characteristics for subjects who completed the 2-yr clinical study.

Dentifrice group	Number of Subjects			Age at baseline	
	Male	Female	Total	Mean	Range
Test <sup>1</sup>	577	607	1184	8.26	6-10
Positive Control <sup>2</sup>	584	664	1248	8.28	6-10

<sup>1</sup> A dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride.

<sup>2</sup> A dentifrice containing 0.243% sodium fluoride in a silica base.

Table 4. Summary of 1-yr incremental caries (DMFS) for subjects who completed the 2-yr clinical study.

Dentifrice group	N	Incremental DMFS*	Percent reduction <sup>3</sup> (Test vs. Positive Control)	Sig. <sup>4</sup>
Test <sup>1</sup>	1184	2.02 ± 2.26	-4.72%	NS
Positive Control <sup>2</sup>	1248	2.12 ± 2.62		

\* Mean ± standard deviation.

<sup>1</sup> A dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride.

<sup>2</sup> A dentifrice containing 0.243% sodium fluoride in a silica base.

<sup>3</sup> There was 4.72% less caries in the group using the Test Dentifrice as compared to the group using the Positive Control Dentifrice.

<sup>4</sup> Significance of comparison of baseline-adjusted means, NS = not significant ( $P > 0.05$ ).

Throughout the study, there were no adverse effects on the oral hard or soft tissues, which were observed by the dental examiner, or reported by the subjects when questioned concerning adverse effects.

The Kappa statistic for intra-examiner reproducibility of caries scores was greater than 0.9, indicating a high level of examiner reliability.

#### Baseline data

Table 3 presents a summary of the DMFS scores observed at the baseline examination for those subjects who went on to complete the entire 2-yr study. At baseline, the Test Dentifrice group presented a mean DMFS score of 3.84, while the Positive Control Dentifrice group presented a mean DMFS score of 4.06. No statistically significant difference was indicated between the treatment groups with respect to this parameter.

Table 3. Summary of baseline caries prevalence (DMFS) for subjects who completed the 2-yr clinical study.

Dentifrice group	N	Baseline DMFS*	Significance <sup>3</sup>
Test <sup>1</sup>	1184	3.84 ± 4.38	NS
Positive Control <sup>2</sup>	1248	4.06 ± 4.66	

\* Mean ± standard deviation.

<sup>1</sup> A dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride.

<sup>2</sup> A dentifrice containing 0.243% sodium fluoride in a silica base.

<sup>3</sup> Significance of comparison of means, NS = not significant ( $P > 0.05$ ).

Table 5. Summary of 2-yr incremental caries (DMFS) for subjects who completed the 2-yr clinical study.

Dentifrice group	N	Incremental DMFS*	Percent reduction <sup>3</sup> (Test vs. Positive Control)	Sig. <sup>4</sup>
Test <sup>1</sup>	1184	4.30 ± 3.22	-10.97%	$P < 0.05$
Positive Control <sup>2</sup>	1248	4.83 ± 4.07		

\* Mean ± standard deviation.

<sup>1</sup> A dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride.

<sup>2</sup> A dentifrice containing 0.243% sodium fluoride in a silica base.

<sup>3</sup> There was 10.97% less caries in the group using the Test Dentifrice as compared to the group using the Positive Control Dentifrice.

<sup>4</sup> Significance of comparison of baseline-adjusted means.

#### 1-year data

Table 4 presents a summary of the incremental DMFS scores observed at the 1-yr examination for those subjects who went on to complete the entire 2-yr study. The mean DMFS increment was 2.02 for the Test Dentifrice group, and 2.12 for the Positive Control Dentifrice group. There was no statistically significant difference indicated between the two treatment groups with respect to this parameter.

#### 2-year data

Table 5 presents a summary of the incremental DMFS scores observed at the 2-yr examination. The mean DMFS increment was 4.30 for the Test Dentifrice group, and 4.83 for the Positive Control Dentifrice group. Thus, the Test Dentifrice group presented a statistically significant 10.97% reduction in the mean incremental DMFS scores in comparison to the Positive Control Dentifrice group ( $P < 0.05$ ).

## Discussion

The aim of the present clinical study was to compare the anticaries efficacy of a dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, to a dentifrice containing 0.243% sodium fluoride in a silica base.

After 2 yrs of product use, the dentifrice system in a dual-chambered tube provided a statistically significant 10.97% reduction in caries increment compared to the dentifrice containing 0.243% sodium fluoride in a silica base. With respect to the clinical interpretation of these results, as established by the American Dental Association Guidelines,<sup>6</sup> and as further enumerated by Proskin *et al*,<sup>10</sup> the results of this clinical study, support the conclusion that a dentifrice system in a dual-chambered tube, wherein one chamber contained sodium fluoride in a silica base and the other chamber contained dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, provided a clinically superior level of anticaries efficacy than does a dentifrice containing 0.243% sodium fluoride in a silica base.

## Summary and Conclusion

The results of this 2-yr clinical study support the conclusion that a dentifrice system in a dual-chambered tube, wherein one chamber contains sodium fluoride in a silica base and the other chamber contains dicalcium phosphate dihydrate, delivering 0.243% sodium fluoride, provides a clinically superior level of anticaries efficacy than does a dentifrice containing 0.243% sodium fluoride in a silica base in a single-chambered tube, consistent with the standards established by the published guidelines of the American Dental Association.

a. Colgate-Palmolive Co., New York, NY, USA.

Dr. Silva is Associate Professor, Department of Dentistry and Dr. Melo is Research Associate, Laboratory of Preventive Dentistry, Federal University of Alagoas, Maceio, Brazil. Mr. Stewart is Caries Clinical Research Coordinator, Dr. DeVizio is Worldwide Director of Technology, Dr. Sintes is Director of External Relations/Convention, Ms. Petrone is Associate Director, Dr. Volpe is Vice President of Clinical Research, Dr. Zhang is Senior Technical Assistant, and Mr. McCool is Senior Computer Technologist, all at the Clinical Dental Research Department, Colgate-Palmolive Technology Center, Piscataway, New Jersey, USA. Dr. Proskin is President, Howard M. Proskin & Associates, Inc., Rochester, New York, USA.

## References

1. Blake-Haskins JC, Mellberg JR, Snyder C. Effect of calcium in model plaque on the anticaries activity of fluoride *in vitro*. *J Dent Res* 1992;71:1482-1486.
2. Pearce EIF. The artificial mineralization of dental plaque. In: Ferguson DB. *The environment of the teeth, frontiers of oral physiology*. London: S Karger, 1981; 108-124; Vol 3.
3. Pearce EIF. Effect of plaque mineralization on experimental dental caries. *Caries Res* 1982;16:460-471.
4. Mellberg JR. Enamel fluoride and its anticaries effects. *J Prev Dent* 1977;4:8-20.
5. Rolla G, Saxegaard E. Critical evaluation of the composition and use of topical fluorides, with emphasis on the role of calcium fluoride in caries inhibition. *J Dent Res* 1990;69:780-785.
6. American Dental Association, Council on Dental Therapeutics. Report on workshop aimed at defining guidelines for caries clinical trials: Superiority and equivalence claims for anticaries dentifrices. *J Am Dent Assoc* 1988;117:683-685.
7. Ministerio de Saúde, Secretaria Nacional de Programas Especiais de Saúde, Divisão Nacional de Saúde Bucal, Fundação Serviços de Saúde Pública. Levantamento Epidemiológico em Saúde Bucal: Brazil, zona urbana, 1986. Brasília: Centro de Documentação do Ministerio de Saúde, 1988.
8. United States Department of Health, Education, and Welfare, Public Health Service, Food and Drug Administration. Guidelines for the clinical evaluation of drugs to prevent dental caries. 1978;79: Publication No. 3075.
9. National Institutes of Health, National Institute of Dental Research. Oral health surveys of the National Institute of Dental Research, diagnostic criteria and procedures. 1991; Publication No. 91-2870.
10. Proskin HM, Kingman A, Naleway C, *et al*. Comparative attributes for the description of the relative efficacy of therapeutic agents: General concepts and definitions, and application to the American Dental Association guidelines for the comparison of the clinical anticaries efficacy of fluoride dentifrices. *J Clin Dent* 1995;6:176-184.
11. Wallenstein S, Fleiss JL, Chilton NW. Confidence intervals for percentage reduction in caries increments. *J Dent Res* 1982;61:828-830.