

RAD: 11-116181- -2	FECHA: 2013-09-06 08:40:44
DEP: 2020 DIRECCION DE NUEVAS CREACIONES	EVE: 379 FASE NACIONAL INCLUIDO CAPITULO II
TRA: 11 PCT-PATENTE DE INVENCION CAPITULOS I Y II	FOLIOS: 6
ACT: 519 PRESENTACION	

Abogado(a)/Señor(a)
JUAN PABLO CADENA SARMIENTO

Asunto:	Radicación:	11-116181- -2
	Trámite:	11
	Evento:	379
	Actuación:	519
	Oficio:	16762
	Folios:	6

Patente de Invención	X			Patente de Modelo de Utilidad	
Vía Nacional					
Vía PCT (Fase Nacional)	X	Capítulo I		Capítulo II	X
No. Solicitud Internacional					
Fecha de Presentación Internacional					

Descripción:	Radicación 11-116181-00000	08/Septiembre/2011
Reivindicaciones:	Radicación 11-116181-00000	08/Septiembre/2011
Figuras:	Radicación 11-116181-00000	08/Septiembre/2011
Prioridad:	US2009039184	01/Abril/2009

Se acepta la reivindicación de prioridad porque ésta solicitud fue presentada dentro del plazo establecido (Art. 9 D 486) y su contenido técnico corresponde con el de la prioridad reivindicada.

De acuerdo con lo establecido en el numeral 1.2.2.2 del Título X de la Circular Única para efectos del examen de patentabilidad, se tendrá en cuenta la tasa pagada por el solicitante al momento de comenzar el examen para las reivindicaciones adicionales, por tanto, se estudiarán las reivindicaciones 1 a 28.

Título de la solicitud: “Metabolitos para la salud bucal y usos de los mismos”.

El problema planteado en esta solicitud consiste en la necesidad de desarrollar un método para el diagnóstico de enfermedad periodontal o un estado bucal saludable y

composiciones dentífricas para el tratamiento de dichas patologías.

Para resolver este problema técnico la solicitud en estudio proporciona un método para el diagnóstico de enfermedad periodontal o un estado bucal saludable a partir de la determinación de metabolitos en una muestra de fluido crevicular gingival, composiciones dentífricas que incluyen un agente terapéutico que induce un cambio en los niveles de dichos metabolitos y un dentífrico indicador de metabolitos.

El objeto de la presente solicitud se relaciona con la Clasificación Internacional de Patentes (CIP): A61K 8/19 // 8/34 // 8/44.

4. Excepción a la patentabilidad (Art 20 D 486 literal d)

El objeto de las reivindicaciones 1 a 19 y 23 no son patentables de acuerdo con el artículo citado.

5. De la solicitud de patente

Reivindicaciones (Art 30 D 486, Art 22 PCT)

La reivindicación 20 no es clara toda vez que un kit está conformado por preparaciones combinadas de componentes individuales, donde tales componentes forman una unidad funcional y la presente clausula hace referencia a un elemento tipo tira de recolección de fluidos junto con un diagnóstico de salud oral, lo cual corresponde a la definición de un kit de partes. Se sugiere a la solicitante hacer las aclaraciones respectivas.

Las reivindicaciones 21 y 22 no son claras toda vez que no definen todos los elementos de la composición, ni la proporción de los mismos sino que se limita a establecer el agente terapéutico presente en la misma.

La reivindicación 21 no es clara toda vez que caracteriza una formulación en términos de un resultado a alcanzar. Al respecto se recuerda a la solicitante que la formulación debe caracterizarse en términos de los ingredientes, excipientes y proporciones de los mismos porque de lo contrario la reivindicación incluye todas las alternativas presentes o futuras que permitan alcanzar el resultado mencionado.

Las reivindicaciones 24 a 28 no son claras toda vez que no definen los excipientes de la composición, ni la proporción de los mismos sino que se limita a establecer una categoría funcional de los mismos, por ejemplo composición indicadora de metabolito. Se sugiere a la solicitante caracterizar la formulación en términos de los ingredientes (indicando su nombre IUPAC), excipientes y proporciones de los mismos.

6. Descripción (Art 28 D 486)

La descripción no divulga la composición dentífrica que incluye un agente indicador de metabolito de manera suficientemente completa para que la persona del oficio normalmente versada en la materia pueda ejecutarla, toda vez que no se incluye la descripción química del agente indicador de metabolito, naturaleza química u otras características derivadas de su estructura química que le permitan cumplir dicha

función dentro de la formulación, asimismo, no se mencionan los excipientes y proporciones de los mismos dentro de dicha composición y no se presentan ejemplos de dichas formulaciones que permitan evidenciar el efecto técnico de un indicador discernible por el usuario en exposición a un metabolito asociado con la enfermedad periodontal.

7. Determinación del Estado de la Técnica

El estado de la técnica se determinó con base en la fecha de presentación internacional: abril 1 de 2009, y se encontraron los siguientes documentos que anticipan el objeto de esta solicitud.

Ítem	Documento	Título	Fecha de Publicación
D1	US7402416	"Antibacterial dentifrice exhibiting antiplaque and breath freshening properties"	22/Julio/2008
D2	WO0185116	"Synergistic antiplaque/antigingivitis oral composition"	15/Noviembre/2001
D3	Garcia-Godoy, F., et al. American Journal of Dentistry, Vol. 3, S15-26	"Effect of a triclosan/copolymer/fluoride dentifrice on plaque formation and gingivitis: A 7-month clinical study"	Septiembre/1990

El documento D1¹ divulga una composición dentífrica que comprende una combinación de un compuesto antibacterial no-iónico, específicamente triclosan (2,4,4'-tricloro-2'-hidroxidifenil éter) en una concentración entre 0.1 y 1.5 %p/p, una enzima proteolítica (Col. 2, líneas 1-57), un agente abrasivo del tipo silica coloidal (Col. 3, líneas 1-42) y un vehículo oralmente aceptable (Col. 4, líneas 36-58), donde la composición que incluye el compuesto antibacterial y la composición que incorpora la enzima se encuentran físicamente separados (Col. 7, líneas 40-53).

El documento D2² enseña una composición oral antiplaca y antigingivitis que comprende un difenil éter halogenado no catiónico como triclosan en una proporción entre 0.03 y 2% p/p en combinación con un extracto de magnolia que contiene 0.01 a 0.3% p/p de magnolol y 0.02 a 0.1% p/p de honokiol (Pág. 4, líneas 16-37).

EL documento D3 divulga un estudio clínico que compara el efecto sobre la formación de placa y gingivitis de un dentífrico que contiene triclosan 0.3%, un copolímero de metoxietileno y ácido maléico 2%, fluoruro de sodio 0.243% en una base de silica comparado con un dentífrico de fluoruro de sodio 0.243% en una base de silica (Pág. S16, Col. Der. Párr. 5). Después de 7 meses el grupo que uso dos veces al día el dentífrico de triclosan/copolímero presento una reducción de 58.96% en gingivitis y 97.7% en los depósitos de placa supragingival comparado con el dentífrico placebo (Pág. S15, resumen).

Examen de Patentabilidad (Art 14 D486)

1 http://worldwide.espacenet.com/searchResults?compact=false&ST=singleline&query=US7402416&locale=en_EP&DB=worldwide.espacenet.com

2 http://worldwide.espacenet.com/publicationDetails/claims?CC=WO&NR=0185116A2&KC=A2&FT=D&ND=3&date=20011115&DB=worldwide.espacenet.com&locale=en_EP

Novedad (Art 16 D 486)
Reivindicación 22

La reivindicación 22 consiste en una composición dentífrica que comprende una cantidad efectiva de triclosan como agente terapéutico.

Características esenciales	D1
Composición dentífrica que comprende:	Composición dentífrica que comprende:
Triclosan	un compuesto antibacterial no-iónico, específicamente triclosan (2,4,4'-triclora-2'-hidroxidifenil éter) en una concentración entre 0.1 y 1.5 %p/p (Col. 2, líneas 1-57)
	una enzima proteolítica (Col. 2, líneas 1-57)
	un vehículo oralmente aceptable (Col. 4, líneas 36-58)

Las características esenciales de la composición de la reivindicación 22 habían sido divulgadas previamente en el documento D1, el cual divulga una composición dentífrica que comprende una combinación de un compuesto antibacterial no-iónico, específicamente triclosan (2,4,4'-triclora-2'-hidroxidifenil éter) en una concentración entre 0.1 y 1.5 %p/p, una enzima proteolítica (Col. 2, líneas 1-57), un agente abrasivo del tipo silica coloidal (Col. 3, líneas 1-42) y un vehículo oralmente aceptable (Col. 4, líneas 36-58).

En consecuencia, la reivindicación 22 carece de novedad, según lo divulgado en el documento D1.

Reivindicación 22

La reivindicación 22 consiste en una composición dentífrica que comprende una cantidad efectiva de triclosan como agente terapéutico.

Características esenciales	D2
Composición dentífrica que comprende:	Composición dentífrica que comprende:
Triclosan	un difenil éter halogenado no catiónico como triclosan en una proporción entre 0.03 y 2% p/p
	un extracto de magnolia que contiene 0.01 a 0.3% p/p de magnolol y 0.02 a 0.1% p/p de honokiol (Pág. 4, líneas 16-37)
	un vehículo oralmente aceptable

Las características esenciales de la composición de la reivindicación 22 habían sido divulgadas previamente en el documento D2, el cual divulga una composición oral antiplaca y antigingivitis que comprende un difenil éter halogenado no catiónico como triclosan en una proporción entre 0.03 y 2% p/p en combinación con un extracto de magnolia que contiene 0.01 a 0.3% p/p de magnolol y 0.02 a 0.1% p/p de honokiol (Pág. 4, líneas 16-37).

En consecuencia, la reivindicación 22 carece de novedad, según lo divulgado en el documento D2.

Reivindicación 22

La reivindicación 22 consiste en una composición dentífrica que comprende una cantidad efectiva de triclosan como agente terapéutico.

Características esenciales	D3
Composición dentífrica que comprende:	Composición dentífrica que comprende:
Triclosan	triclosan 0.3%,
	un copolímero de metoxietileno y ácido maléico 2%,
	fluoruro de sodio 0.243%
	base de sílica

Las características esenciales de la composición de la reivindicación 22 habían sido divulgadas previamente en el documento D3, el cual divulga la reducción en gingivitis y en los depósitos de placa supragingival por el uso dos veces al día durante 7 meses de un dentífrico que contiene triclosan 0.3%, un copolímero de metoxietileno y ácido maléico 2%, fluoruro de sodio 0.243% en una base de sílica (Pág. S16, Col. Der. Párr. 5).

En consecuencia, la reivindicación 22 carece de novedad, según lo divulgado en el documento D3.

8. Conclusión

Los requisitos de Patentabilidad de la presente solicitud están afectados así:

Item	Documento	Reivindicaciones afectadas	Requisito que afecta
D1	US7402416	21 – 22	Novedad
D2	WO0185116	21 – 22	Novedad
D3	Garcia-Godoy, F., et al. American Journal of Dentistry, Vol. 3, S15-26	21 – 22	Novedad

En cumplimiento del artículo 45 de la Decisión 486 de la Comisión de la Comunidad Andina, se le indica que debe dar respuesta dentro del término de sesenta (60) días contados a partir de la fecha de notificación de la presente comunicación. En caso de no dar respuesta al presente requerimiento, o si a pesar de la respuesta subsistieran los impedimentos para la concesión, se denegará la patente.

Se invita al solicitante se sirva indicar, si así lo considera, su renuncia al término faltante de sesenta (60) días para dar respuesta a este requerimiento y presentarla por escrito.

Finalmente, se le recuerda al solicitante que si como respuesta a este requerimiento llegara a modificar el capítulo reivindicatorio y éste contenga más de diez (10) reivindicaciones, no pagará la tasa de modificación voluntaria pero sí la correspondiente al pago por reivindicación adicional.

Notifíquese el presente oficio conforme a lo dispuesto en el numeral 5.2, literal e), del capítulo quinto del título primero de la Circular Única No. 10 de 2001.



JOSÉ LUIS SALAZAR LÓPEZ
Director de Nuevas Creaciones (c)

El anterior requerimiento fue notificado por fijación en lista, de fecha 2013-09-10

Elaboró: John Fredy Hernandez Montaño
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Revisó: Jose Luis Salazar Lopez

Effect of a triclosan/copolymer/fluoride dentifrice on plaque formation and gingivitis: A 7-month clinical study

Franklin Garcia-Godoy, DDS, MS, Federico Garcia-Godoy, DDS, William DeVizio, DMD, Anthony R. Volpe, DDS, MS, Robert J. Ferlauto, MS & Jeffrey M. Miller, BS

Garcia-Godoy F, Garcia-Godoy F, DeVizio W, Volpe AR, Ferlauto RJ, Miller JM. Effect of triclosan/copolymer/fluoride dentifrice on plaque formation and gingivitis: A 7-month clinical study. *Am J Dent* 1990; 3: S15-S26.

Abstract: A total of 108 adult male and female subjects completed a 7-month, double-blind clinical study designed to compare the effect of a dentifrice containing 0.3% triclosan and 2% of a copolymer of methoxyethylene and maleic acid on plaque formation and gingivitis, as compared to a placebo dentifrice. The subjects were stratified into two balanced groups according to baseline plaque and baseline gingivitis scores. They then received an oral prophylaxis and were assigned to the use of either a placebo dentifrice or the triclosan/copolymer dentifrice for the next 7 months. After this time, the dentifrice containing triclosan/copolymer provided a 58.96% statistically significant (99% level of confidence) reduction in gingivitis, as compared to the placebo dentifrice. Further, after 7-months' use, the dentifrice containing triclosan/copolymer also provided a 30.17% statistically significant (99% level of confidence) reduction in gingivitis as compared to the placebo dentifrice. The results after 7 months also indicated that the dentifrice containing triclosan/copolymer provided a 97.74% statistically significant (99% level of confidence) reduction in the supragingival plaque deposits on those tooth surfaces with the greatest amount of plaque formation, when compared to the placebo dentifrice. The dentifrice containing triclosan/copolymer also provided 87.56% less sites with the most severe amount of gingival disease, as compared to the placebo dentifrice. This decrease in diseased gingival sites was statistically significant at the 99% level of confidence. It was concluded that the twice daily use of a dentifrice containing 0.3% triclosan and 2% of a copolymer reduces supragingival plaque deposit formation and gingivitis to a highly significant degree, without any extrinsic stains observed.

Key words: Copolymer; dentifrice; fluorides; gingivitis; plaque; toothpaste; triclosan.

Reprint requests: Dr. Franklin Garcia-Godoy, Dept. of Pediatric Dentistry, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, TX 78284-7888, USA.

Introduction

Experimental gingivitis studies have shown the role of plaque in the etiology of gingivitis.^{1,2} The same studies also demonstrated that plaque control and prevention would reverse the gingivitis condition.

It is now well known that the prevention of bacterial plaque by good oral hygiene is necessary to achieve and maintain oral health. An antibacterial agent included as part of an oral hygiene regimen would be expected to reduce plaque formation and enhance gingival health.

A series of clinical investigations have evaluated the use of dentifrices containing triclosan (Irgacare MP^a) for their effect on oral health.³⁻¹¹

Recent clinical studies have shown that a dentifrice containing 0.3% triclosan and 2.0% of a copolymer of

methoxyethylene and maleic acid (Gantrez^b) significantly reduces supragingival plaque formation and gingivitis.^{12,13}

The purpose of this double-blind, clinical study was to determine the effect on supragingival plaque formation and gingivitis, following an oral prophylaxis, of a dentifrice containing 0.3% triclosan and 2.0% of a copolymer of methoxyethylene and maleic acid, as compared to a placebo dentifrice over a 7-month period.

Materials and Methods

Adult male and female subjects from Santo Domingo, Dominican Republic, were evaluated by the dental examiner for the presence of supragingival plaque and gingivitis on the buccal and lingual surfaces of all teeth present in the mouth (except third molars and

prosthetic crowns). These initial plaque and gingivitis scores were considered a subject's baseline plaque and gingivitis score.

The clinical scoring procedure used to assess plaque formation was a modification of the Quigley-Hein (Turesky Modification) Plaque Scoring Index.¹⁴ The modified Quigley-Hein Index uses erythrosin disclosing solution and scores plaque formation on a numerical scale according to the following criteria:

- 0 = No plaque present.
- 1 = Separate flecks of plaque at the cervical margin.
- 2 = A thin, continuous band of plaque (up to 1 mm) at the cervical margin.
- 3 = A band of plaque wider than 1 mm but covering less than one-third of the surface.
- 4 = Plaque covering at least one-third but less than two-thirds of the surface.
- 5 = Plaque covering more than two-thirds of the surface.

Each tooth was scored in six areas: 1) mesio-facial, 2) mid-facial, 3) disto-facial, 4) mesio-lingual, 5) mid-lingual, 6) disto-lingual. The maximum score per tooth therefore is 30. All teeth are included except third molars, and those teeth with prosthetic crowns or cervical restorations.

A modified Quigley-Hein Plaque Index for each subject was determined by adding all the individual plaque scores (six per tooth) and dividing this sum by the total number of measurements (number of teeth scored multiplied by six).

The clinical scoring procedure used to assess gingivitis was the Loe-Silness gingival scoring Index as modified by Talbott *et al.*^{15,16} The Loe-Silness Index scores gingivitis on a numerical scale according to the following criteria:

- 0 = Absence of inflammation.
- 1 = Mild inflammation: moderate glazing, redness, edema and hypertrophy. There is no bleeding upon probing.
- 2 = Moderate inflammation: moderate glazing, redness, edema and hypertrophy. There is bleeding upon probing.
- 3 = Severe inflammation: There is marked redness and hypertrophy, a tendency to spontaneous bleeding and ulceration.

Each tooth is scored in six areas: 1) mesio-facial, 2) mid-facial, 3) disto-facial, 4) mesio-lingual, 5) mid-lingual, 6) disto-lingual. The maximum score per tooth therefore is 18. All teeth are included except third molars and those teeth with prosthetic crowns or cervical restorations.

A Loe-Silness Index (Talbott-Mandel-Chilton modification¹⁶) for each subject is determined by adding all the individual scores (six per tooth) and dividing this total by

the number of measurements (number of teeth scored multiplied by 6).

A total of 120 healthy, adult subjects with a modified Quigley-Hein Plaque Index score of 1.5 or greater, and a modified Loe-Silness Gingival Index score of 1.0 or greater at the baseline examination were entered into the clinical study.

All individuals received a complete and thorough oral prophylaxis, including the removal of supragingival and subgingival plaque and calculus deposits. The teeth were then polished and complete plaque removal was verified by use of an erythrosin disclosing solution.

The subjects were stratified into two balanced groups, according to their baseline modified Quigley-Hein Plaque Index and Loe-Silness Gingival Index (Talbott-Mandel-Chilton modification) scores.

Each group was randomly assigned to use either the dentifrice containing 0.3% triclosan and 2% of a copolymer in a 0.243% sodium fluoride/silica base, or a 0.243% sodium fluoride/silica placebo dentifrice. The dentifrices were distributed to the subjects in identical plain white tubes to ensure that neither the subjects nor the dental examiner knew the identity of the dentifrices.

All subjects were instructed to brush their teeth twice daily (morning and evening) for 1 minute each tooth-brushing in their usual and customary manner. They were instructed to use only their assigned dentifrice and soft-bristled toothbrush for the entire 7-month duration of the study. The dentifrices and toothbrushes were supplied to the subjects on a regularly scheduled basis throughout the course of the study.

After 2.5, 5 and 7 months' use of their assigned dentifrice, the subjects were evaluated by the same dental examiner for plaque formation, using the modified Quigley-Hein procedure, and for gingivitis, using the Loe-Silness procedure (Talbott-Mandel-Chilton modification).

The presence or absence of extrinsic staining was visually inspected at every recall visit.

Results

Of the 120 subjects entered into the study, 112 were available for the 2.5 month examination, 108 were available for the 5-month examination, and 108 completed the entire 7-month study.

The subjects that did not complete the study did so for reasons unrelated to the use of any of the dentifrices.

COMPARISON OF MEAN MODIFIED QUIGLEY-HEIN PLAQUE INDEX SCORES.

The characteristics at baseline for the 112 subjects examined for plaque deposits at 2.5 months are presented in Table 1. The two dentifrice groups were well-balanced in relation to number of subjects, age, sex, Quigley-Hein Plaque Index scores and Loe-Silness Gingival Index scores.

Table 1. Baseline characteristics and mean modified Quigley-Hein Plaque Index scores for the subjects completing the first 2.5 months of the study.

Dentifrice group	Number of subjects			Age		Mean Q-H Plaque Index scores*
	Male	Female	Total	Mean	Range	
Placebo	25	31	56	27.30	18-63	2.45 $\pm$ 0.40
Triclosan with copolymer	17	39	56	29.29	18-52	2.50 $\pm$ 0.42

*Mean and standard deviation.

The baseline mean Quigley-Hein Plaque Index score for the placebo dentifrice group was 2.45, while the baseline mean Quigley-Hein Plaque Index score for the triclosan/copolymer dentifrice group was 2.50. An analysis of variance (ANOVA) confirmed that there was no statistically significant difference between the two groups with regard to baseline Quigley-Hein plaque scores.

A comparison of the mean Quigley-Hein Plaque Index scores for the two dentifrice groups after 2.5 months' use of the assigned dentifrice regimen is presented in Table 2. The placebo dentifrice group had a mean Quigley-Hein Plaque Index score of 1.41, while the triclosan/copolymer dentifrice had a mean Quigley-Hein Plaque Index score of 1.22. The triclosan/copolymer dentifrice was associated with a 13.48% reduction in plaque formation, as compared to the placebo dentifrice. This reduction was statistically significant at the 98% level of confidence, as determined by an ANOVA (F value = 5.16).

Table 2. Comparison of the mean modified Quigley-Hein Plaque Index scores for the two dentifrice groups after 2.5 months.

Dentifrice group	Number of subjects	Mean Q-H Plaque Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	56	1.41 $\pm$ 0.45	---	---
Triclosan with copolymer	56	1.22 $\pm$ 0.45	-13.48%	P = 0.02

The baseline characteristics for the 108 subjects who completed 5 months of the study are presented in Table 3. The baseline mean Quigley-Hein Plaque Index score for the placebo dentifrice group was 2.45, and the baseline mean Quigley-Hein Plaque Index score for the

triclosan/copolymer dentifrice group was 2.49. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Quigley-Hein Plaque Index scores.

A comparison of the mean Quigley-Hein Plaque Index scores for the two dentifrice groups after 5 months' use of the assigned dentifrice regimen is presented in Table 4. The placebo dentifrice group had a mean Quigley-Hein Plaque Index score of 1.85, while the triclosan/copolymer dentifrice had a mean Quigley-Hein Plaque Index score of 0.99. The triclosan/copolymer dentifrice provided a 46.49% reduction in plaque formation, as compared to the placebo dentifrice. This reduction was statistically significant at the 99% level of confidence, as determined by an ANOVA (F value = 161.86).

Table 4. Comparison of the mean modified Quigley-Hein Plaque Index scores for the two dentifrice groups after 5 months.

Dentifrice group	Number of subjects	Mean Q-H Plaque Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	1.85 $\pm$ 0.29	---	---
Triclosan with copolymer	54	0.99 $\pm$ 0.41	- 46.49%	P = 0.001

The baseline characteristics for the 108 subjects who completed the entire 7 months of the study are presented in Table 5. The baseline mean Quigley-Hein Plaque Index score for the placebo dentifrice group was 2.45, and the baseline mean Quigley-Hein Plaque Index score for the triclosan/copolymer dentifrice group was 2.49. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Quigley-Hein Plaque Index scores.

Table 3. Baseline characteristics and mean modified Quigley-Hein Plaque Index scores for the subjects completing the first 5 months of the study.

Dentifrice group	Number of subjects			Age		Mean Q-H Plaque Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	2.45 $\pm$ 0.39
Triclosan with copolymer	17	37	54	29.26	18-52	2.49 $\pm$ 0.42

Table 5. Baseline characteristics and mean modified Quigley-Hein Plaque Index scores for the subjects completing the entire 7 months of the study.

Dentifrice group	Number of subjects			Age		Mean Q-H Plaque Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	2.45 $\pm$ 0.39
Triclosan with copolymer	17	37	54	29.26	18-52	2.49 $\pm$ 0.42

A comparison of the mean Quigley-Hein Plaque Index scores for the two dentifrice groups after 7 months' use of the assigned dentifrice regimen is presented in Table 6. The placebo dentifrice group had a mean Quigley-Hein Plaque Index score of 1.73, while the triclosan/copolymer dentifrice had a mean Quigley-Hein Plaque Index score of 0.71. The triclosan/copolymer dentifrice provided a 58.96% reduction in plaque formation, as compared to the placebo dentifrice. This reduction was statistically significant at the 99% level of confidence, as determined by an ANOVA (F value = 294.03).

Table 6. Comparison of the mean modified Quigley-Hein Plaque Index scores for the two dentifrice groups completing the entire 7 months of the study.

Dentifrice group	Number of subjects	Mean Q-H Plaque Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	1.73 $\pm$ 0.36	---	---
Triclosan with copolymer	54	0.71 $\pm$ 0.25	-58.96%	P = 0.000

Figures 1 and 2 illustrate the comparison of mean Quigley-Hein Plaque Index scores at 2.5, 5 and 7 months.

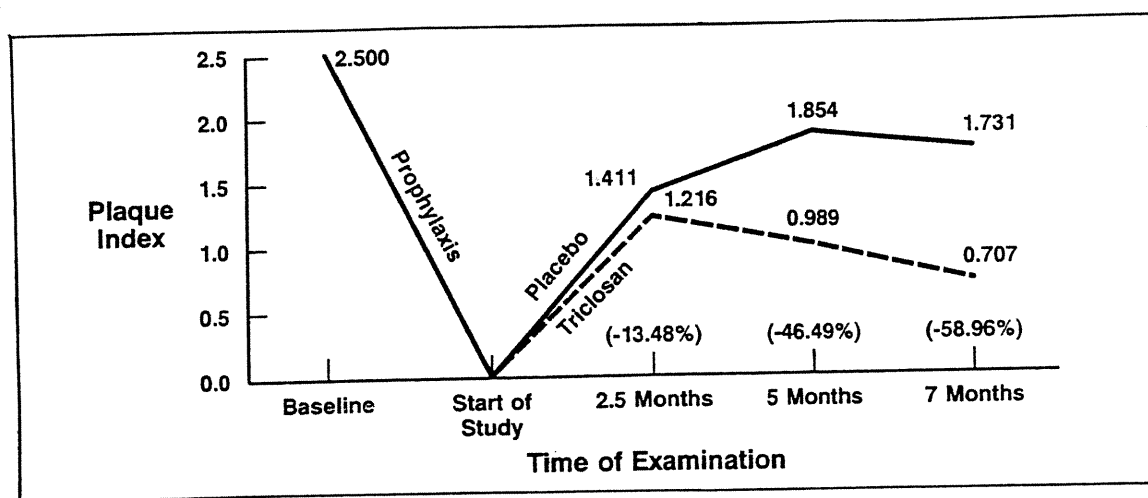


Fig. 1. Quigley-Hein Plaque Index. Placebo vs. triclosan/copolymer dentifrice.

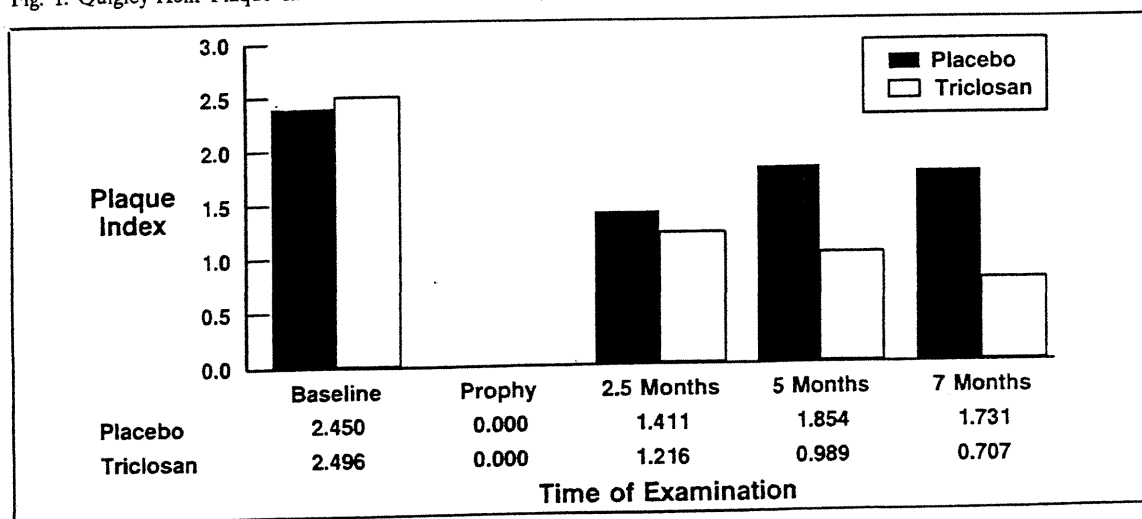


Fig. 2. Quigley-Hein Plaque Index. Placebo vs. triclosan/copolymer dentifrice.

Table 7. Baseline characteristics and mean Plaque Severity Index scores for the subjects completing the first 2.5 months of the study.

Dentifrice group	Number of subjects			Age		Mean Plaque Severity Index scores
	Male	Female	Total	Mean	Range	
Placebo	25	31	56	27.30	18-63	0.474 ± 0.156
Triclosan with copolymer	17	39	56	29.29	18-52	0.488 ± 0.160

COMPARISON OF MEAN PLAQUE SEVERITY INDEX SCORES.

In addition to calculating a mean Quigley-Hein Plaque Index for each subject, a mean Plaque Severity Index was also calculated for each subject at 2.5, 5 and 7 months.^{12,13} This index allows for a comparison of the tooth surfaces from each dentifrice group that received the most severe Quigley-Hein Plaque Index scores, that is, a Quigley-Hein Plaque Index score of 3, 4, or 5. The mean Plaque Severity Index was calculated for each subject by dividing the total number of tooth surfaces scored either 3, 4 or 5 by the total number of tooth surfaces scored in the entire mouth for plaque formation.

The characteristics at baseline and the mean Plaque Severity Index for the subjects examined for plaque deposits after 2.5 months are presented in Table 7. The baseline mean Plaque Severity Index score for the placebo dentifrice was 0.474, while the baseline mean Plaque Severity Index score for the triclosan/copolymer dentifrice group was 0.488.

An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Plaque Severity Index scores.

A comparison of the mean Plaque Severity Index for the two dentifrice groups after 2.5 months' use of their assigned dentifrices is presented in Table 8. The placebo dentifrice group had a mean Plaque Severity Index score of 0.156, while the triclosan/copolymer dentifrice group had a mean Plaque Severity Index score of 0.095.

Table 8. Comparison of the mean Plaque Severity Index scores for the two dentifrice groups after 2.5 months.

Dentifrice group	Number of subjects	Mean Plaque Severity Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	56	0.156 ± 0.130	---	---
Triclosan with copolymer	56	0.095 ± 0.105	-39.10%	P = 0.007

Table 9. Baseline characteristics and mean Plaque Severity Index scores for the subjects completing the first 5 months of the study.

Dentifrice group	Number of subjects			Age		Mean Plaque Severity Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	0.476 ± 0.150
Triclosan with copolymer	17	37	54	29.26	18-52	0.487 ± 0.163

The triclosan/copolymer dentifrice provided a 39.10% reduction of plaque on the tooth surfaces with higher plaque formation, as compared to the placebo dentifrice. An ANOVA confirmed that this reduction was statistically significant at the 99% level of confidence (F value = 7.63).

The baseline characteristics and mean Plaque Severity Index for the 108 subjects who completed 5 months of the study are presented in Table 9. The baseline mean Plaque Severity Index score for the placebo was 0.476, while the baseline mean Plaque Severity Index score for the triclosan/copolymer dentifrice group was 0.487. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Plaque Severity Index scores.

The results of comparing the mean Plaque Severity Index scores for the two dentifrice groups after 5 months' use of the assigned dentifrices is presented in Table 10. The placebo dentifrice group had a mean Plaque Severity Index score of 0.252, while the triclosan/copolymer dentifrice group had a mean Plaque Severity Index score of 0.034.

Table 10. Comparison of the mean Plaque Severity Index scores for the two dentifrice groups after 5 months.

Dentifrice group	Number of subjects	Mean Plaque Severity Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	0.252 ± 0.131	---	---
Triclosan with copolymer	54	0.034 ± 0.089	-86.51%	P = 0.001

The triclosan/copolymer dentifrice provided an 86.51% reduction of plaque in the areas of higher plaque formation as compared to the placebo dentifrice. This reduction was statistically significant at the 99% level of

Table 11. Baseline characteristics and mean Plaque Severity Index scores for the subjects completing the entire 7 months of the study.

Dentifrice group	Number of subjects			Mean	Age Range	Mean Plaque Severity Index scores
	Male	Female	Total			
Placebo	23	31	54	27.20	18-63	0.476 ± 0.150
Triclosan with copolymer	17	37	54	29.26	18-52	0.487 ± 0.163

confidence, according to an ANOVA (F value = 102.35).

The baseline characteristics and mean Plaque Severity Index for the 108 subjects who completed the entire 7 months of the study are presented in Table 11. The baseline mean Plaque Severity Index score for the placebo was 0.476, while the baseline mean Plaque Severity Index score for the triclosan/copolymer dentifrice group was 0.487. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Plaque Severity Index scores.

The results of comparing the mean Plaque Severity Index scores for the two dentifrice groups after 7 months' use of the assigned dentifrices is presented in

Table 12. The placebo dentifrice group had a mean Plaque Severity Index score of 0.221, while the triclosan/copolymer dentifrice group had a mean Plaque Severity Index score of 0.005.

Table 12. Comparison of the mean Plaque Severity Index scores for the two dentifrice groups completing the entire 7 months of the study.

Dentifrice group	Number of subjects	Mean Plaque Severity Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	0.221 ± 0.140	---	---
Triclosan with copolymer	54	0.005 ± 0.030	-97.74%	P = 0.000

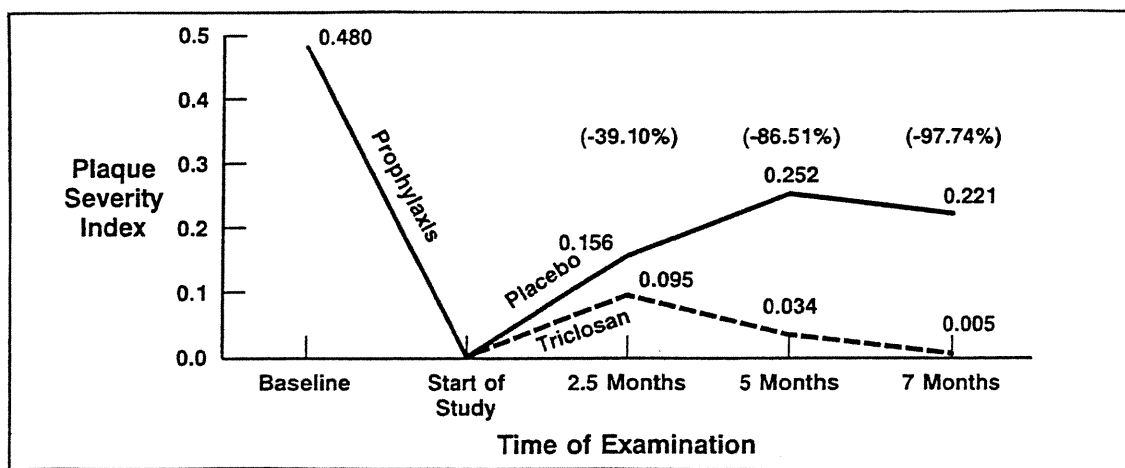


Fig. 3. Quigley-Hein Plaque Severity Index. Placebo vs. triclosan/ copolymer dentifrice.

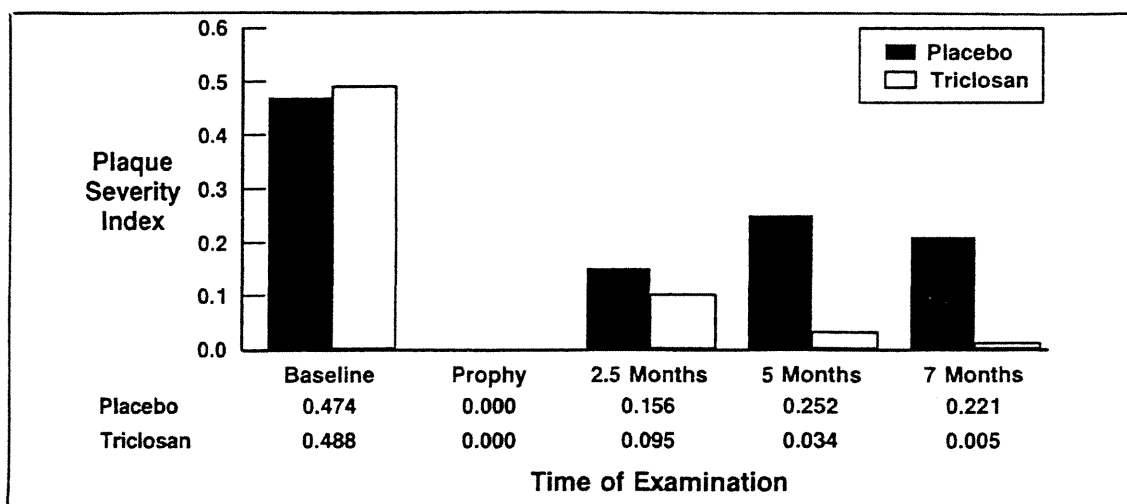


Fig. 4. Quigley-Hein Plaque Severity Index. Placebo vs. triclosan/ copolymer dentifrice.

Table 13. Baseline characteristics and mean Loe-Silness Gingival Index scores for the subjects completing the first 2.5 months of the study.

Dentifrice group	Number of subjects			Age		Mean L-S Gingival Index scores
	Male	Female	Total	Mean	Range	
Placebo	25	31	56	27.30	18-63	1.51 ± 0.19
Triclosan with copolymer	17	39	56	29.29	18-52	1.48 ± 0.11

The triclosan/copolymer dentifrice provided a 97.74% reduction of plaque in the areas of higher plaque formation as compared to the placebo dentifrice. This reduction was statistically significant at the 99% level of confidence, according to an ANOVA (F value = 117.16).

Figures 3 and 4 illustrate the comparison of mean Plaque Severity Index scores at 2.5, 5 and 7 months.

COMPARISON OF MEAN LOE-SILNESS GINGIVITIS INDEX SCORES (TALBOTT-MANDEL-CHILTON MODIFICATION)

The characteristics at baseline for the 112 subjects examined for gingivitis at 2.5 months are presented in Table 13.

The baseline mean Loe-Silness Index score for the placebo dentifrice group was 1.51, while the baseline mean Loe-Silness Index score for the triclosan/copolymer dentifrice group was 1.48. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Loe-Silness Index scores.

A comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups after 2.5 months' use of the assigned dentifrices is presented in Table 14. The placebo dentifrice group had a mean Loe-Silness Index score of 0.84, while the triclosan/copolymer dentifrice group had a mean Loe-Silness

Table 14. Comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups after 2.5 months.

Dentifrice group	Number of subjects	Mean L-S Gingival Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	56	0.84 ± 0.45	---	---
Triclosan with copolymer	56	0.78 ± 0.45	-7.14%	N.S.

Gingival Index score of 0.78. Thus, the triclosan/copolymer dentifrice was associated with a 7.14% reduction in gingivitis, as compared to the placebo dentifrice. An ANOVA indicated that this reduction was not statistically significant.

The baseline characteristics for the 108 subjects who completed 5 months of the study are presented in Table 15. The baseline mean Loe-Silness Index score for the placebo dentifrice group was 1.51, as compared to 1.49 for the triclosan/copolymer dentifrice group. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Loe-Silness Index scores.

A comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups completing 5 months of the study is presented in Table 16. The placebo dentifrice group had a mean Loe-Silness Index score of 1.21, while the triclosan/copolymer dentifrice group had a mean Loe-Silness Gingival Index score of 0.95. Thus, the triclosan/copolymer dentifrice was associated with a 21.49% reduction in gingivitis, as compared to the placebo dentifrice. An ANOVA indicated that this reduction was statistically significant at the 99% level of confidence (F value = 73.53).

Table 16. Comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups after 5 months.

Dentifrice group	Number of subjects	Mean L-S Gingival Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	1.21 ± 0.13	---	---
Triclosan with copolymer	54	0.95 ± 0.18	-21.49%	P = 0.001

The baseline characteristics for the 108 subjects who completed the entire 7 months of the study are presented in Table 17. The baseline mean Loe-Silness Index score

Table 15. Baseline characteristics and mean Loe-Silness Gingival Index scores for the subjects completing the first 5 months of the study.

Dentifrice group	Number of subjects			Age		Mean L-S Gingival Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	1.51 ± 0.19
Triclosan with copolymer	17	37	54	29.26	18-52	1.49 ± 0.11

Table 17. Baseline characteristics and mean Loe-Silness Gingival Index scores for the subjects completing the entire 7 months of the study.

Dentifrice group	Number of subjects			Age		Mean L-S Gingival Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	1.51 $\pm$ 0.19
Triclosan with copolymer	17	37	54	29.26	18-52	1.49 $\pm$ 0.11

for the placebo dentifrice group was 1.51, as compared to 1.49 for the triclosan/copolymer dentifrice group. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Loe-Silness Index scores.

A comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups who completed the entire 7 months of the study is presented in Table 18. The placebo dentifrice group had a mean Loe-Silness Index score of 1.16, while the triclosan/copolymer dentifrice group had a mean Loe-Silness Gingival Index score of 0.81. Thus, the triclosan/copolymer dentifrice was associated with a 30.17% reduction in gingivitis, as compared to the placebo denti-

frice. An ANOVA indicated that this reduction was statistically significant at the 99% level of confidence (F value = 144.20).

Table 18. Comparison of the mean Loe-Silness Gingival Index scores for the two dentifrice groups completing the entire 7 months of the study.

Dentifrice group	Number of subjects	Mean L-S Gingival Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	1.16 $\pm$ 0.13	---	---
Triclosan with copolymer	54	0.81 $\pm$ 0.17	-30.17%	P = 0.000

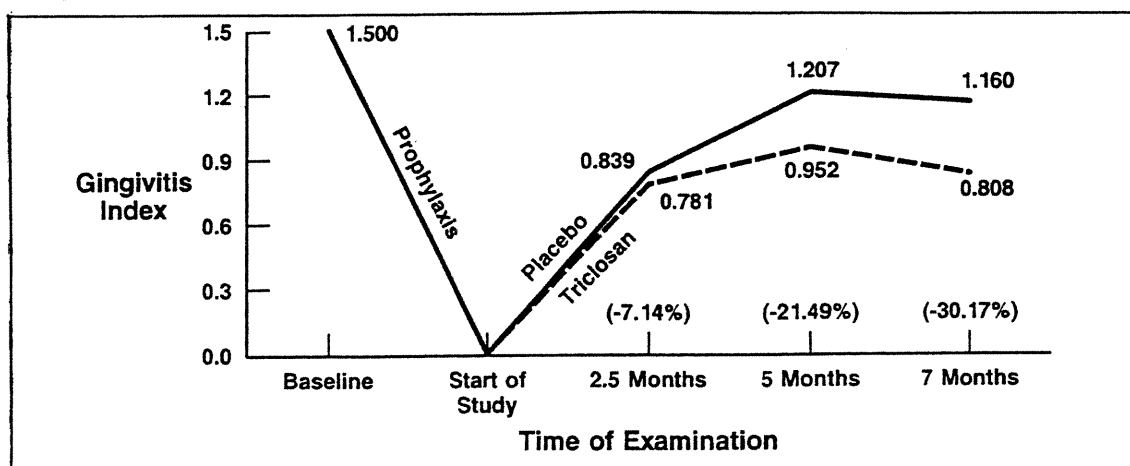


Fig. 5. Loe-Silness Gingival Index. Placebo vs. triclosan/copolymer dentifrice.

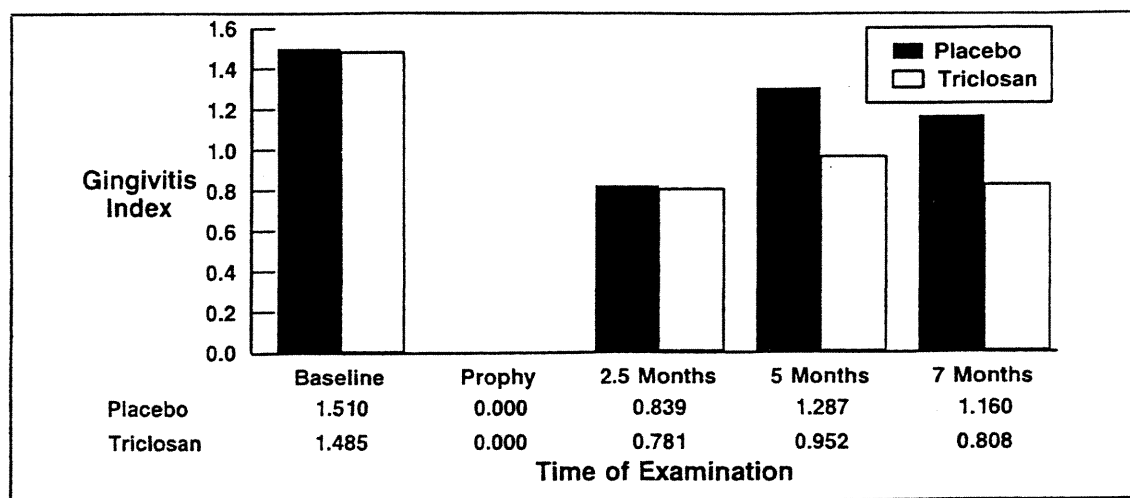


Fig. 6. Loe-Silness Gingival Index. Placebo vs. triclosan/copolymer dentifrice.

Table 19. Baseline characteristics and mean Gingivitis Severity Index scores for the subjects completing the first 2.5 months of the study.

Dentifrice group	Number of subjects			Age		Mean G-S Index scores
	Male	Female	Total	Mean	Range	
Placebo	25	31	56	27.30	18-63	0.488 ± 0.140
Triclosan with copolymer	17	39	56	29.29	18-52	0.479 ± 0.106

Figures 5 and 6 illustrate the comparison of the mean Loe-Silness Gingival Index scores at 2.5, 5 and 7 months.

COMPARISON OF MEAN GINGIVITIS SEVERITY INDEX SCORES (GINGIVAL BLEEDING).

In addition to calculating a mean Loe-Silness Gingival Index score for each subject, a mean Gingivitis Severity Index was also calculated for each subject at 2.5, 5 and 7 months.

This index allows for a comparison of the gingival sites from each dentifrice group that received the highest possible Loe-Silness Gingival Index scores, that is Loe-Silness Gingival Index scores of 2 or 3. The mean Gingival Severity Index was calculated for each subject by dividing the total number of gingival sites scored 2 or 3 by the total number of teeth scored in the entire mouth for gingivitis multiplied by six (total number of sites scored).

The characteristics at baseline and the mean Gingivitis Severity Index for the subjects examined for gingivitis after 2.5 months are presented in Table 19. The baseline mean Gingival Severity Index score for the placebo dentifrice group was 0.488, while the baseline mean Gingival Severity Index score for the triclosan/copolymer dentifrice group was 0.479. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Gingival Severity Index scores.

A comparison of the mean Gingival Severity Index scores for the two dentifrice groups after 2.5 months' use of their dentifrices is presented in Table 20. The placebo dentifrice group had a mean Gingival Severity Index score of 0.184, while the triclosan/copolymer dentifrice group had a mean Gingival Severity Index score of 0.174. Thus, the triclosan/copolymer dentifrice was associated with 5.43% less sites with severe disease, as compared to the placebo dentifrice. An ANOVA indicated that this

Table 20. Comparison of the Gingivitis Severity Index scores for the two dentifrice groups after 2.5 months.

Dentifrice group	Number of subjects	Mean G-S Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	56	0.184 ± 0.174	---	---
Triclosan with copolymer	56	0.174 ± 0.166	-5.43%	N.S.

decrease in severely diseased sites was not statistically significant.

The baseline characteristics and the mean Gingival Severity Index for the 108 subjects who completed 5 months of the study are presented in Table 21. The baseline mean Gingival Severity Index score for the placebo dentifrice group was 0.485, while the baseline mean Gingival Severity Index score for the triclosan/copolymer dentifrice group was 0.479. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline Gingival Severity Index scores.

The results of comparing the mean Gingival Severity Index scores for the two dentifrice groups after 5 months' use of the assigned dentifrices is presented in Table 22. The placebo dentifrice group had a mean Gingival Severity Index score of 0.243, while the triclosan/copolymer dentifrice group had a mean Gingival Severity Index score of 0.060.

Table 22. Comparison of the Gingivitis Severity Index scores for the two dentifrice groups after 5 months.

Dentifrice group	Number of subjects	Mean G-S Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	0.243 ± 0.069	---	---
Triclosan with copolymer	54	0.060 ± 0.042	-75.31%	P = 0.005

Table 21. Baseline characteristics and mean Gingivitis Severity Index scores for the subjects completing the first 5 months of the study.

Dentifrice group	Number of subjects			Age		Mean G-S Index scores
	Male	Female	Total	Mean	Range	
Placebo	23	31	54	27.20	18-63	0.485 ± 0.140
Triclosan with copolymer	17	37	54	29.26	18-52	0.479 ± 0.108

Table 23. Baseline characteristics and mean Gingivitis Severity Index scores for the subjects completing the entire 7 months of the study.

Dentifrice group	Number of subjects			Mean	Age Range	Mean G-S Index scores
	Male	Female	Total			
Placebo	23	31	54	27.20	18-63	0.485 $\pm$ 0.140
Triclosan with copolymer	17	37	54	29.26	18-52	0.479 $\pm$ 0.108

The triclosan/copolymer dentifrice provided 75.31% less sites with severe disease, as compared to the placebo dentifrice. This decrease in severely diseased sites was statistically significant at the 99% level of confidence, according to an ANOVA (F value = 278.96).

The baseline characteristics and the mean Gingival Severity Index for the 108 subjects who completed the entire 7 months of the study are presented in Table 23. The baseline mean Gingival Severity Index score for the placebo dentifrice group was 0.485, while the baseline mean Gingival Severity Index score for the triclosan/copolymer dentifrice group was 0.479. An ANOVA confirmed that there was no statistically significant difference between the two groups with regard to baseline

Gingival Severity Index scores.

The results of comparing the mean Gingival Severity Index scores for the two dentifrice groups after 7 months' use of the assigned dentifrices is presented in Table 24. The placebo dentifrice group had a mean Gin-

Table 24. Comparison of the Gingivitis Severity Index scores for the two dentifrice groups completing the entire 7 months of the study.

Dentifrice group	Number of subjects	Mean G-S Index scores	Percent reduction vs. placebo	Statistical significance
Placebo	54	0.225 $\pm$ 0.090	---	---
Triclosan with copolymer	54	0.028 $\pm$ 0.040	- 87.56%	P = 0.000

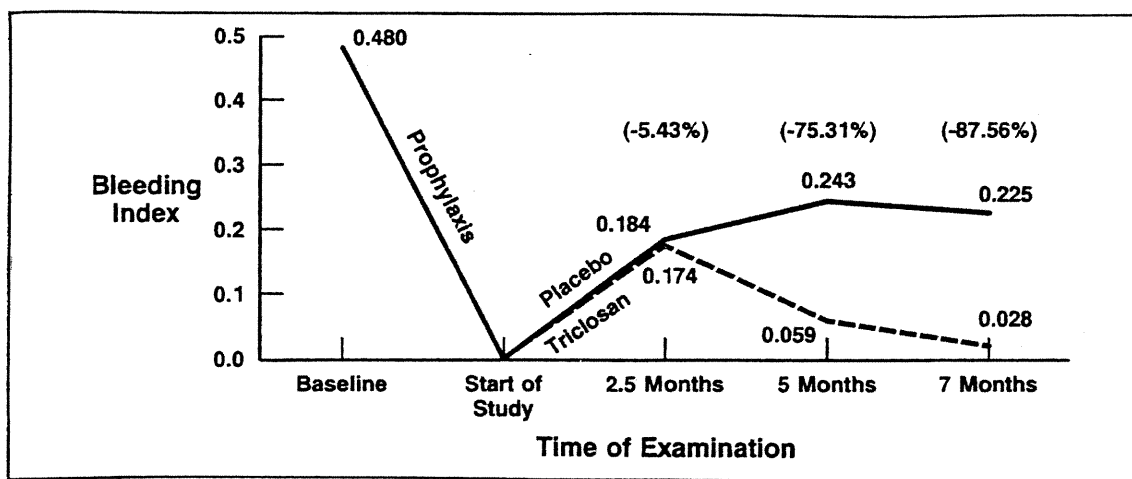


Fig. 7. Loe-Silness Bleeding Index. Placebo vs. triclosan/copolymer dentifrice.

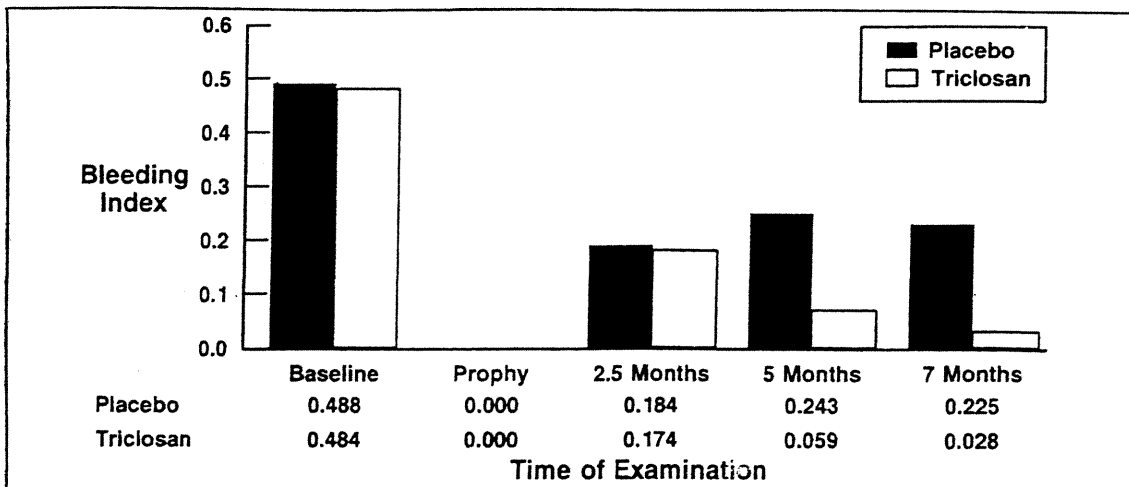


Fig. 8. Loe-Silness Bleeding Index. Placebo vs. triclosan/copolymer dentifrice.

gival Severity Index score of 0.225, while the triclosan/copolymer dentifrice group had a mean Gingival Severity Index score of 0.028.

The triclosan/copolymer dentifrice provided 87.56% less sites with severe disease, as compared to the placebo dentifrice. This decrease in severely diseased sites was statistically significant at the 99% level of confidence, according to an ANOVA (F value = 235.85).

Figures 7 and 8 illustrate the comparison of the mean Gingival Severity Index scores at 2.5, 5 and 7 months.

EXTRINSIC STAINING

No extrinsic staining was observed, no unpleasant taste was reported and there were no adverse side effects involving the oral hard and soft tissues associated with the use of either of the dentifrices.

Discussion

This double-blind clinical study evaluated a dentifrice containing 0.3% triclosan and 2% of a copolymer of methoxyethylene and maleic acid for its effect on plaque and gingivitis formation, after an oral prophylaxis, as compared to a placebo dentifrice. The effect of the triclosan/copolymer dentifrice on plaque and gingivitis was determined after 2.5, 5, and 7-months' use.

After 2.5 months' use of the dentifrices, the triclosan/copolymer group had a statistically significant lessening of plaque formation. An even more significant reduction in plaque formation was recorded on those surfaces of the teeth where the greatest amount of plaque had formed. This is in harmony with previous studies which have used this index (Plaque Severity Index) to examine surfaces with higher plaque formation.^{12,13}

Although not statistically significant, the use of triclosan/copolymer dentifrice provided a reduction in gingivitis at 2.5 months, as compared to the placebo. Also, the use of the triclosan/copolymer dentifrice resulted in a decrease in the number of severely diseased sites, as determined by the Severity Index.

As can be seen at the 2.5-month examination, the subjects in the placebo dentifrice group had substantially lower plaque and gingivitis index scores when compared to their baseline values.

Probably, the cause for this is the "Hawthorne effect". As indicated by Robertson *et al*,¹⁷ the "Hawthorne effect" refers to positive changes in the behavior of subjects as a result of the special attention and status received from participation in an investigation".

As was reported by Robertson *et al*,¹⁷ an average of 20% improvement in all clinical indices was observed on 16 patients who were to begin a study in 3 months time even though they were not given instructions, information or therapy. This 20% improvement was attributed to the "Hawthorne effect".

In this study, the "special attention and status" would be reflected by the subjects' receipt of an oral prophylaxis and the clinical examination procedure itself.

It is interesting to note that at the subsequent 5- and 7-month examinations, subjects' scores in the placebo group reflect a return towards the baseline mean, thus indicating the decreasing influence of the "Hawthorne effect".

After 5-months' use of the dentifrices, a greater effect in all parameters measured was noted. The triclosan/copolymer group had statistically significant reductions of plaque in all areas of the mouth, including those areas of highest plaque formation.

Similarly, after 5-months' use of the triclosan/copolymer dentifrice, a statistically significant reduction in gingivitis was noted. The difference in the number of severely diseased sites for the triclosan/copolymer dentifrice group also decreased to a statistically significant level, as compared to the placebo dentifrice.

After 7-months' use of the dentifrices, a larger difference in all parameters measured was noted. This effect was even greater than that seen at 5 months.

The parameters for the placebo dentifrice remained relatively constant when one compares the 5-month and 7-month examination data. That is, a "plateau" was established and there was not an increased effect with time (*i.e.* plaque and gingivitis indices remained relatively constant).

The triclosan/copolymer dentifrice provided the greatest effect on the more severe manifestations of plaque and gingivitis and continued to demonstrate an increased beneficial effect with time (*i.e.* plaque and gingivitis indices continued to decrease).

In the present study, the absence of staining of the teeth and the positive response to the flavor of the triclosan/copolymer dentifrice are of clinical significance as other antibacterial agents, such as chlorhexidine, stain the teeth after prolonged use and have an unpleasant taste.

Conclusions

The 2.5, 5 and 7-month results from this study indicated that the triclosan/copolymer dentifrice provided statistically significant plaque reductions of 13.48%, 46.49% and 58.96%, respectively, as compared to the placebo dentifrice.

Further, the 5- and 7-month results indicated that the triclosan/copolymer dentifrice also provided statistically significant reductions in gingivitis of 21.49% and 30.17%, respectively, as compared to the placebo dentifrice.

The use of a triclosan/copolymer dentifrice over a 7-month period of time will provide a statistically significant and clinically beneficial effect on plaque and gingivitis formation, as compared to a placebo dentifrice.

No extrinsic staining was observed, no unpleasant taste was reported and there were no adverse side effects

involving the oral hard and soft tissues associated with the use of either of the dentifrices.

- a. Ciba-Geigy, Greensboro, NC, USA.
- b. GAF Corp., New York, NY, USA.

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