Investigations and Insights in Gingival Health

Dr. Sebastian Ciancio

Introduction

One of the major innovations in dental home care therapy was the introduction of fluorides in the 1950s for the management of dental caries. Since that time, fluoride has not only been incorporated into dentifrices, but also into a variety of delivery systems. It was not until the 1990s that the next significant advance in patient home care occurred with the introduction by the Colgate-Palmolive Company of a dentifrice called Colgate® Total® Toothpaste. Total® contains triclosan, a proven antibacterial/anti-inflammatory agent, a copolymer which enables a greater uptake and retention of triclosan to enamel and buccal epithelial cells, and sodium fluoride in a silica base. The addition of the copolymer to the dentifrice formulation provides a long-lasting effect that has been well documented.1 Well-designed clinical studies have demonstrated the efficacy of Total® against plaque and gingivitis, calculus, stain, malodor, and caries. This research has proven that Colgate® Total® is safe, not only for the oral soft tissue and teeth, but it also does not impact the microflora, either through the development of resistant strains or by shifting the oral flora to more opportunistic species. These studies are summarized later in this article.

Mode of Action

Triclosan is a broad-spectrum antibacterial agent, effective against both gram-positive and gram-negative bacteria.2 The chemical structure of triclosan is shown in Figure 1. The primary site of triclosan’s antimicrobial action is the bacterial cytoplasmic membrane. At bacteriostatic concentrations, triclosan prevents essential amino acid uptake; at bactericidal concentrations, it causes cytoplasmic disorganization of the bacterial cytoplasmic membrane, and leakage of cellular contents.

Because of its antibacterial activity, triclosan is a beneficial addition to oral products because it has a broad spectrum of activity on oral bacteria, is compatible with the ingredients in oral products, and has a long history of safe use in consumer products. Triclosan is considered safe for use in dentifrice and mouthrinse products.2

PVM/MA Copolymer is the non-proprietary designation for a polyvinylmethyl ether/maleic acid copolymer. Studies have demonstrated that there was a greater uptake of triclosan to enamel and buccal epithelial cells from the use of a fluoride dentifrice containing triclosan and the PVM/MA copolymer than from a dentifrice containing triclosan alone.2 Further studies demonstrated that the efficacy of triclosan lasted for up to 12 hours when combined with the copolymer.2

Antibacterial Activity

The antibacterial activity of triclosan has been well documented. A 1994 study demonstrated that the level of triclosan retained in plaque 14 hours after brushing significantly exceeds the MIC for plaque bacteria (which ranges from 0.2 to 3 g/ml).2 The overall conclusion from long-lasting...
antibacterial action studies supports the concept that a fluoride dentifrice containing triclosan and the PVM/MA copolymer will substantially impact on the level of viable plaque present in the mouth over a 12-hour post-brushing period.3

**Anti-Inflammatory Effects**

Studies have suggested an anti-inflammatory effect of the triclosan/copolymer formulation, so Colgate® Total® could be classified as a “dual-action antiseptic,” with both antibacterial and anti-inflammatory properties. Research suggests that the antigingivitis and beneficial periodontal effect of the triclosan/copolymer dentifrice results from this dual-action effect. Dental biofilms release a variety of biologically active products as a result of bacterial activity, and the periodontium, in turn, responds through a variety of inflammatory responses (Figure 2). As a consequence, there is a spectrum of periodontal response, from mild gingivitis to severe periodontitis. These, and other host products and responses, may influence a variety of important disease pathways which can have both local and systemic adverse effects.3

Modeer and others4-9 conducted laboratory studies to assess the anti-inflammatory action of triclosan. These studies demonstrated that triclosan inhibited the production of two major cytokines: interleukin-1 beta (IL-1β) and tumor necrosis factor alpha (TNF-α). The major effect of these cytokines is to stimulate the inflammatory response that often results in both soft and hard tissue destruction. In addition, IL-1β and TNF-α can induce prostaglandin E2 (PGE2) production, another potent inflammatory mediator, during the early stages of inflammation. PGE2 is a potent stimulator of collagen breakdown and bone resorption, and exhibits a broad range of inflammatory effects. These studies found that triclosan inhibited both IL-1β- and TNF-α-induced PGE2 production for up to 24 hours, most probably due to the inhibition of PGE2 biosynthesis.

Finally, recent work indicates that triclosan can inhibit matrix metalloproteinase production in fibroblasts and osteoblasts that were stimulated with inflammatory cytokines.5 Inhibition of matrix metalloproteinases (MMPs) is significant since MMPs are important in the formation of collagen, which is the basis of bone formation. By reducing the possibility of breakdown of these compounds by MMPs, there may be a reduction of resorption of alveolar bone associated with inflammation.

**Safety**

Five long-term safety studies in 1,000 patients have been published,10-14 with the objective of evaluating a dentifrice containing triclosan/copolymer for its effect on oral microflora and the development of bacterial resistance. All of the studies were consistent in finding no emergence of pathogens and no suppression of health-associated bacteria.

In the most recent study involving more than 400 subjects,15 half used a triclosan/copolymer dentifrice, while the other half used a placebo dentifrice for a period of five years. The researchers evaluated both periodontal and microbiologic endpoints. Clinical efficacy was maintained for the five-year period. Measurements of dental plaque bacteria (P. gingivalis, P. intermedia, and A. actinomycetemcomitans) showed a high degree of volatility with subjects acquiring, and then subsequently losing the organisms over the course of the study. These results were consistent in failing to demonstrate resistance to triclosan in any of the organisms studied over the five-year period.

**Clinical Benefits**

**Plaque and Gingivitis**

Fifteen studies in over 2,500 patients examined the effect of triclosan/copolymer on plaque and gingivitis.16-20 Among these studies were 12 independent, long-term, double-blind clinical studies that followed a similar design and demonstrated the clinical efficacy and safety of triclosan/copolymer.21,22-25 The study design was in compliance with various regulatory agencies and professional associations, including the US FDA and the ADA. These studies provided clear evidence that triclosan/copolymer is highly effective against plaque and gingivitis.

The long-term clinical studies, versus fluoride dentifrices without triclosan/copolymer (placebo), demonstrated statistically significant differences (p < 0.01) in favor of the dentifrice containing triclosan/copolymer for the treatment of plaque and gingivitis. The reduction in plaque for the triclosan/copolymer dentifrice, as compared to the placebo dentifrice, was as high as 58.9% for plaque reduction, and as high as 41.9% for gingivitis reduction. Additionally, no significant adverse effects were noted, including the absence of development of bacterial resistance. The lack of adverse effects was not surprising because triclosan has a nearly four-decade history of safe use in soaps and deodorants.30

**Post-Periodontal Therapy**

In this category there were seven studies, of which six were randomized controlled trials.31-36 The sample size ranged from 14 in one study,31 to 480 in another.32 The studies examined the effect of a triclosan/copolymer dentifrice on healing in smokers, healing after non-surgical treatment in recurrent periodontitis, and the incidence of attachment loss in conjunction with other factors in patients with periodontitis. Overall, these studies33-36 demonstrated:

- the efficacy of a triclosan/copolymer dentifrice in reducing the progression of periodontal disease, frequency of deep periodontal pockets, and number of sites that exhibit additional probing attachment and bone loss;31
- the efficacy of a triclosan/copolymer dentifrice in the reduction in attachment loss of 50% when compared with a control dentifrice (p < 0.05), suggesting a potential to minimize the onset of the earliest signs of destructive periodontal disease.33


- the efficacy of a triclosan/copolymer dentifrice in providing a significant periodontal health benefit in those subjects susceptible to periodontal disease;\textsuperscript{33,34} and
- clinically significant gains in attachment levels and reduction in pocket depth and bleeding in patients with recurrent disease among subjects using a triclosan/copolymer dentifrice.\textsuperscript{34}

**Caries**

Four large, double-blind studies on nearly 10,000 subjects have demonstrated that a dentifrice containing triclosan/copolymer provides a significant anticaries benefit.\textsuperscript{33,34} These studies, conducted in accordance with ADA guidelines, showed that the reduction of caries ranged from 11-15\% when compared to a positive fluoride control. The reduction in caries associated with the dentifrice containing triclosan/copolymer is due not only to the inclusion of sodium fluoride in the formula, but also to the effect of this product on remineralization and plaque biofilm reduction. Results of an in situ study indicated that the triclosan/copolymer dentifrice was effective in preventing demineralization and enhancing remineralization, as compared to a non-fluoride placebo dentifrice and to a positive control NaF/silica dentifrice.\textsuperscript{31}

**Cosmetic Benefits**

**Calculus**

A triclosan/copolymer dentifrice offers an alternative mechanism to traditional chemical agents (pyrophosphates, zinc compounds) used in dentifrices to reduce calculus formation. Rather than prevent mineralization of plaque by traditional elements, a triclosan/copolymer dentifrice reduces plaque, the substrate for mineralization, directly. Therefore, for patients who cannot use traditional anti-tartar dentifrices due to tooth sensitivity or soft tissue irritation, the triclosan/copolymer dentifrice may be of special value since it has a demonstrated reduction in calculus scores, similar to those obtained with traditional “tartar control” dentifrices.

Seven studies demonstrating effective calculus reduction have been published,\textsuperscript{19,36,42-46} and among them were four that evaluated the triclosan/copolymer dentifrice to determine its effect on supragingival calculus formation in over 400 patients.\textsuperscript{36,42-46} All four studies showed statistically significant differences (p < 0.01) in supragingival calculus in favor of the triclosan/copolymer dentifrice as compared to the placebo dentifrice. Reductions in supragingival calculus formation ranged from 23\% to 57\%, with an average reduction of 37\%, with no adverse events.

**Malodor**

Six studies related to triclosan/copolymer have been published on malodor reduction efficacy.\textsuperscript{32,52-57} These studies involved a total of approximately 250 patients with no adverse events reported. Triclosan was considered to be effective in controlling malodor. Not surprisingly, the studies showed that this dentifrice reduced, in vitro, the bacteria that cause malodor.\textsuperscript{32,52,56}

**Stain**

Seven studies regarding efficacy against stain have been published,\textsuperscript{51,43,47-51} with no adverse events. Overall, the studies demonstrated consistent results with subjects using the whitening formulation of the triclosan dentifrice exhibiting statistically significant reductions in extrinsic tooth stains compared to controls.

**References**


Investigator’s Insights
Augusto Elias Boneta, DMD, MSD

Dental plaque-induced gingivitis is a reversible inflammation of the gingival tissues. The scientific literature supports that the accumulation of dental plaque in susceptible hosts is associated with gingivitis and periodontitis. A long-term goal in dental practice, therefore, is the achievement of sufficient plaque control.

Antimicrobial agents have been employed as adjunctive treatment in the reduction of periodontal pathogens to prevent the progression of periodontal diseases. In the search for antiplaque and/or antigingivitis efficacy agents, research has turned its interest toward those with antibacterial properties, such as triclosan, that could be added to fluoride-containing toothpastes.

Toothpastes containing a combination of 0.3% triclosan/2.0% copolymer/0.243% sodium fluoride in a silica base have been shown through numerous clinical studies to significantly reduce plaque and gingivitis. One example is a study by Mateu, et al. This double-blind clinical study demonstrated that a dentifrice containing 0.3% triclosan/2.0% PVM/MA copolymer/0.243% sodium fluoride in a 17% dual silica base (Colgate® Total® Toothpaste – test dentifrice) is efficacious for the control of established supragingival plaque and gingivitis. Relative to the control dentifrice (Crest® Cavity Protection Toothpaste), the test dentifrice presented statistically significantly lower whole-mouth plaque index and gingival index scores (23.4% and 21.3%, respectively) after six months of product use.

Haraszthy, et al. assessed the antimicrobial efficacy of commercial dentifrices containing fluoride, stannous fluoride, and triclosan/copolymer/fluoride on microorganisms frequently present in the oral cavity. The authors demonstrated that the use of a dentifrice containing triclosan/copolymer/fluoride (Colgate® Total® Toothpaste) resulted in a significantly greater inhibition of bacterial growth compared to both a stannous fluoride (Crest® Pro-Health®) and a sodium fluoride dentifrice (p < 0.00005).

Periodontal care depends on the commitment of both the patient and the dentist. Adequate maintenance care and effective plaque control are the cornerstones of a successful dental practice. Our study supports
the conclusion that a 0.3% triclosan/2.0% copolymer/0.243% sodium fluoride dentifrice provides superior supragingival plaque and gingivitis reduction compared to Crest® Pro-Health® toothpaste.

References

A 6-Month Study of the Effects of 0.3% Triclosan/Copolymer Dentifrice on Dental Implants

(J Clin Periodontol 2010; doi: 10.1111/j.1600-051X.2010.01617.x.)

Summary
According to the American Academy of Periodontology, “dental implants offer an ideal option for those who have lost a tooth or more due to periodontal disease, injury, or some other reason, and who are in good general and oral health” (Perio.org). Implant patients should engage in conscientious at-home oral care and see their dental professional regularly for supportive maintenance visits to minimize the possibility of infection and inflammation, and optimize the health of the tissues surrounding the implant site.

The objective of this double-blind, two-treatment, parallel-group study was to examine the effect of a 0.3% triclosan/2.0% copolymer dentifrice on oral biofilms and gingival inflammation on dental implants and peri-implant tissues.

One-hundred and twenty adults with a dental implant and contralateral tooth were randomly assigned to either a triclosan/copolymer dentifrice group (test) or a fluoride dentifrice group (control), with instructions to brush twice daily for six months. At baseline, three, and six months, dental plaque and gingival inflammation were assessed, and collected supragingival dental plaque was analyzed microbiologically.

At both the three- and six-month assessments, subjects in the triclosan/copolymer dentifrice group demonstrated significantly lower levels of dental plaque, gingivitis, and bleeding on probing at both the implant and contralateral tooth sites compared with the fluoride dentifrice group (p < 0.05). Additionally, there were significantly (p < 0.05) fewer gram-negative anaerobes in the triclosan/copolymer dentifrice group compared with the fluoride dentifrice group.

The authors concluded that twice-daily use of a triclosan/copolymer dentifrice may enhance dental implant maintenance by reducing dental plaque and gingival inflammation.

Investigator’s Insights
Joseph J. Zambon DDS, PhD

Our research was the result of a nearly three-year collaboration by an international group of clinical and laboratory scientists. The study was based on two previously established facts: first, the well-established clinical efficacy of a 0.3% triclosan/copolymer dentifrice – Colgate® Total® Toothpaste – in reducing dental plaque (oral biofilms) and gingival inflammation; and second, the need for therapies to specifically address the growing problem of peri-implant mucositis and peri-implantitis. Analogous to the association between plaque-induced gingivitis and chronic periodontitis, peri-implant mucositis is both a disease in its own right, as well as a likely precursor to the more serious disease, peri-implantitis, that leads to the loss of dental implants.

To answer the question, “Does Colgate® Total® Toothpaste inhibit dental plaque and peri-implant mucositis?”, we designed and performed a 6-month, randomly controlled clinical trial involving 120 adults who had both dental implants and natural teeth. Among the many possible choices for designs of a clinical trial, the randomly controlled clinical trial is generally acknowledged to provide the strongest evidence for evaluating different therapies. Furthermore, by comparing the effect of the twice-daily use of a triclosan/copolymer toothpaste on natural teeth and dental implants in the same patient, rather than comparing separate dental implant patient groups and natural teeth patient groups, each patient served as his/her own control, and between-patient differences could be minimized. Finally, the study was designed with numerous microbiological assessments performed independent of the clinical assessments. In this way, we could study both the clinical effects of a triclosan/copolymer toothpaste on dental plaque and gingival inflammation, as well as its effect on the underlying microbial cause of peri-implant mucositis.

The study clearly shows that patients brushing twice a day with a triclosan/copolymer toothpaste accumulate significantly less dental plaque on their dental implants, and demonstrate significantly less...
gingival inflammation in the tissues surrounding their dental implants compared to patients brushing twice a day with a fluoride control dentifrice. Consistent with the significantly reduced peri-implant tissue inflammation — that is, the lower levels of gingival redness and bleeding — the microbiological assessments demonstrate that patients using a triclosan/copolymer toothpaste have significantly less peri-implant infection with anaerobic bacteria, and a greater than 90% reduction in the number of specific pathogenic oral bacteria.

Thus, the microbiological data explain the significant reduction in gingivitis seen in patients using a triclosan/copolymer toothpaste. The reduction in gingival inflammation is due to decreased levels of dental plaque, specifically, decreased numbers of bacterial anaerobes and pathogens. Triclosan may also have a separate anti-inflammatory effect around dental implants, but more research is necessary to confirm this.

As with all carefully designed clinical trials, the results of this study are applicable primarily to the target group, in this case, peri-implant mucositis patients. This trial did not examine peri-implantitis patients. While peri-implant mucositis may be a precursor to peri-implantitis, analogous to the relationship between plaque-induced gingivitis and chronic periodontitis, the effect of the triclosan/copolymer dentifrice in the treatment of peri-implantitis is unknown. However, as oral hygiene regimens that reduce the prevalence and severity of plaque-associated gingivitis are thought to reduce the prevalence and severity of chronic periodontitis, a similar relationship may exist between peri-implant mucositis and peri-implantitis. In other words, it may well be that oral hygiene regimens that reduce peri-implant mucositis may reduce peri-implantitis and the loss of dental implants. This, however, needs to be confirmed in future studies.

Based on this study, oral health care professionals can recommend the twice-daily use of Colgate® Total® Toothpaste to enhance the oral hygiene of their dental implant patients.

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Colgate® Total® Toothpaste was introduced globally in 1992, and is sold today in more than 170 countries. Dental associations in over 30 countries, including the US, Canada, and the UK, have conferred seals of acceptance on Colgate® Total® Toothpaste based on their high standards for safety and efficacy.

Today, there are hundreds of oral care products available for sale directly to your patients. Because a professional product recommendation is vital for optimal oral healthcare, equally vital is the need for the profession to be well informed of the differences between the various products to which your patients are exposed on store shelves and in the media. And education is the cornerstone for a well-informed profession.

To better understand the unique action of the triclosan/copolymer components of Colgate® Total® Toothpaste and the significant clinical benefits it offers your patients, a highly informative, 4-minute animated video has been produced and is available at www.colgateprofessional.com/colgateTotaltechnology. In it, you will see how the triclosan/copolymer technology not only exerts its antibacterial action on viable plaque residing along the gum line, but prevents the regrowth of plaque bacteria, giving your patients antibacterial protection for 12 hours.

Recent clinical investigations have been conducted at universities and clinical research facilities in the US and elsewhere comparing Colgate® Total® Toothpaste to Crest® Pro-Health® Toothpaste for their antibacterial action, as well as their efficacy in the reduction of plaque and gingivitis. The results of these studies have been published in The Journal of Clinical Dentistry and are available online at _____URL_____.

Additional professional and patient education resources are available at www.colgateprofessional.com.