INTRODUCTION

The chemo-mechanical control of supra- and subgingival bacterial plaque, by associating antimicrobial agents to mechanical therapy, finds its rationale in a series of particular features of the periodontal disease.
4. *Actinobacillus actinomycetemcomitans* and eradication of other potential tissue-invasive germs cannot be achieved without simultaneous antibiotic treatment.\(^1\)

Generally, the mechanical therapy (manual and/or ultrasonic root instrumentation) is the primary treatment method, recommended for most periodontal infections.\(^2\) The clinical re-attachment after scaling and root-planing (SRP) varies with the initial pocket depth. (Table 1)

**Table 1.** Medium clinical attachment level gains after SRP in non – molar sites (in mm, a systematic review of 27 trials, modified after Cobb\(^2\)).

<table>
<thead>
<tr>
<th>Probed depth</th>
<th>PD reduction</th>
<th>Clinical attachment gain</th>
</tr>
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<tbody>
<tr>
<td>1-3</td>
<td>0.03</td>
<td>-0.34</td>
</tr>
<tr>
<td>4-6</td>
<td>1.29</td>
<td>0.55</td>
</tr>
<tr>
<td>&gt;6</td>
<td>2.16</td>
<td>1.19</td>
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One can see that mechanical therapy in sites with initial probing depths of 1-3 mm can lead to the occurrence of an average recession of 0.34 mm, while the greatest average clinical attachment level of 1.19 mm is registered in pockets with a probing depth greater than 6 mm.

A variety of antimicrobial agents used in oral hygiene, such as toothpastes or mouthwashes, containing either essential oils, triclosan or chlorhexidine become useful adjuvant methods, next to teeth brushing and flossing, in patients with gingivitis and periodontitis, because of their ability to decrease plaque accumulation and gingivitis up to 75 %.\(^1\)

**Table 2.** Plaque and gingivitis decrease using different antimicrobial agents (at least 2 trials were considered, trial duration at least 6 month) (after Fine, quoted by Cobb\(^2\)).

<table>
<thead>
<tr>
<th>Agent</th>
<th>Plaque reduction</th>
<th>Gingivitis reduction</th>
<th>Trials</th>
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<tr>
<td>Essential oils</td>
<td>19-35%</td>
<td>15-37%</td>
<td>DePaola et al., 1989, Gordon et al., 1985, Lamster et al., 1983</td>
</tr>
</tbody>
</table>

Plaque and gingivitis reduction using the above mentioned antimicrobial agents is summarized in Table 2, the trials showing a plaque reduction of up to 75% and a gingivitis reduction between 20% and 75%, when triclosan was used.

Gingival inflammation, as understood today, is initiated by a cellular lesion (traumatic, chemical, radiative, bacterial invasion etc.). The immediate response triggers the mastocytes degranulation, with subsequent release of histamine, and the release of chemotactic factors of granulocytes and eosinophiles. The delayed response includes prostaglandins and leukotrienes synthesis and release, plasma systems activation (the complement, the clot-forming system, and the kinin–kalikrein system). On the long term, lymphocytes and macrophages trigger the chronic inflammatory process and the histological reaction in inflamed tissue: chronic inflammatory infiltrate including lymphocytes and plasma cells, macrophages, fibroblasts proliferation, along with increased angiogenesis leading to tissue volume expansion.\(^3\)

The bacterial biofilm releases toxins that penetrate the inner epithelium of the gingival sulcus, triggering inflammatory cell mediators production (cytokines - interleukins IL-1β, IL-8, prostaglandins, TNF α, metalloproteinases), T-lymphocytes, granulocytes and monocytes recruiting factors production, as well as the increase in plasma concentration of the C-reactive protein (CRP), an inflammation marker.\(^4,5\)

The particular way in which triclosan acts against inflammation has made it interesting as therapeutic agent to be used in periodontal therapy. Triclosan seems to simultaneously act as an antibacterial and anti-inflammatory agent. It inhibits the cyclooxygenase (COX – the enzyme that modulates the arachidonic acid conversion into prostaglandins, inflammatory mediators) and the lipoxygenase (LOX – modulates the arachidonic acid conversion into leukotrienes and other chemical mediators of inflammation).\(^4\) A frequent question nowadays is whether triclosan combines in a synergic mode its antibacterial and anti-inflammatory actions, given the fact that the inflammation is responsible for the most clinical features of the periodontal disease.

The anti-inflammatory action of triclosan was demonstrated mainly within gingival cell cultures research. Thus, in human gingival fibroblast cultures, triclosan inhibits COX1 and 2, and LOX5 and 15 (the 4 main enzymes of the arachidonic acid metabolism), at 50 % inhibitory concentrations (50% IC) of 43 and 227 μM, and 43 and 61 μM, respectively.\(^4\) It has also been noticed that, in similar cultures, Triclosan inhibits TNF-α and IL1β production and inhibits the interferon gamma production (IFN-γ – the cytokine for response to antiviral, antiparasite infections and

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1. Actinobacillus actinomycetemcomitans and eradication of other potential tissue-invasive germs cannot be achieved without simultaneous antibiotic treatment.
2. Generally, the mechanical therapy (manual and/or ultrasonic root instrumentation) is the primary treatment method, recommended for most periodontal infections. The clinical re-attachment after scaling and root-planing (SRP) varies with the initial pocket depth.
3. One can see that mechanical therapy in sites with initial probing depths of 1-3 mm can lead to the occurrence of an average recession of 0.34 mm, while the greatest average clinical attachment level of 1.19 mm is registered in pockets with a probing depth greater than 6 mm.
4. A variety of antimicrobial agents used in oral hygiene, such as toothpastes or mouthwashes, containing either essential oils, triclosan or chlorhexidine become useful adjuvant methods, next to teeth brushing and flossing, in patients with gingivitis and periodontitis, because of their ability to decrease plaque accumulation and gingivitis up to 75%.
5. Plaque and gingivitis reduction using different antimicrobial agents (at least 2 trials were considered, trial duration at least 6 month) is summarized in Table 2, the trials showing a plaque reduction of up to 75% and a gingivitis reduction between 20% and 75%, when triclosan was used.
6. Gingival inflammation, as understood today, is initiated by a cellular lesion (traumatic, chemical, radiative, bacterial invasion etc.). The immediate response triggers the mastocytes degranulation, with subsequent release of histamine, and the release of chemotactic factors of granulocytes and eosinophiles. The delayed response includes prostaglandins and leukotrienes synthesis and release, plasma systems activation (the complement, the clot-forming system, and the kinin–kalikrein system). On the long term, lymphocytes and macrophages trigger the chronic inflammatory process and the histological reaction in inflamed tissue: chronic inflammatory infiltrate including lymphocytes and plasma cells, macrophages, fibroblasts proliferation, along with increased angiogenesis leading to tissue volume expansion.
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9. The anti-inflammatory action of triclosan was demonstrated mainly within gingival cell cultures research. Thus, in human gingival fibroblast cultures, triclosan inhibits COX1 and 2, and LOX5 and 15 (the 4 main enzymes of the arachidonic acid metabolism), at 50 % inhibitory concentrations (50% IC) of 43 and 227 μM, and 43 and 61 μM, respectively.
10. It has also been noticed that, in similar cultures, Triclosan inhibits TNF-α and IL1β production and inhibits the interferon gamma production (IFN-γ – the cytokine for response to antiviral, antiparasite infections and
tumors) and the major histocompatibility complex antigen (MHC II). Also, in gingival fibroblasts cultures marked with the carbon 14 isotope, triclosan is bound to the nucleus (probably to the nuclear lipids) and interferes with the intracellular signaling pathways involved in inflammatory mediators production. It also decreases the prostaglandin E2 production by reducing the TNF-α effect on the prostaglandin E–synthetase.

Triclosan’s effect in reducing the gingival inflammation can be summarized as follows:
1. Decrease of Prostaglandin E2 synthesis.
2. Decrease of IL1β, IFN-γ, and MHC II expression.
3. Persistent binding to fibroblast cell – nucleus.

Of a great interest in periodontal therapy remains the anti-inflammatory and antibacterial synergy of triclosan.

THE TRICLOSAN-PVM/MA COPOLYMER COMBINATION AND GINGIVITIS

Triclosan action against gingivitis is a subject of special interest, given the current prevalence of gingivitis which remains high, exceeding 80% in Europe and North America, even if these continents have an excellent state of oral hygiene among population in general. Antibacterial agents with an anti–gingivitis effect that are currently added in toothpaste and mouthwash composition are the chlorhexidine, the stannium fluoride, essential oils, quaternary ammonium compounds (cetylpiridinium chloride), Sanguinaria extract, and Triclosan. From this list, in the United States, at the beginning of 2007, the American Dental Association (who’s Council for Scientific Affairs is conducting a plaque–control agents certification program, in which the subjects must be evaluated in controlled clinical trials vs. placebo with a minimal duration of 6 months) only accepts for gingivitis therapy two agents: prescription mouthwashes containing chlorhexidine gluconate, and non–prescription mouthwashes containing essential oils. Methodologically, the clinical evaluations of the anti–gingivitis effect include periods reaching from 4 days (studying the anti–plaque effect), periods between 2 weeks and 2 months for the anti–plaque AND anti–gingivitis effect, and periods between 3 weeks and 6 months for experimentally-induced gingivitis.

There is vast literature concerning the anti–gingivitis effect of triclosan and copolymers, but the clinical efficacy is, for various reasons, difficult to quantify: the use of different copolymers as additives, the different products (toothpaste or mouthwash), and different formulations available on different markets. However, the 1997 classification of oral antiseptic agents issued by the Second European Workshop on Periodontology, and completed by Brecx, includes under “anti–gingivitis” agents triclosan and aspirin only, and only triclosan is considered to have both an anti–plaque and anti–gingivitis action.

The main problem of topic antimicrobial therapy is the necessity to achieve a high concentration in order to be effective, as well as the need of a prolonged contact time with the tissue. The triclosan – PVM/MA copolymer combination increases the ability to maintain triclosan within levels above the minimal inhibitory concentration (MIC) even 12 hours after the dental brushing.

The ideal clinical trial for the study of the antimicrobial effect of an agent contained in a toothpaste against gingivitis should embrace the following pattern: double-blind, controlled, randomized, preceded by a rigorous prophylaxis, with initially homogenous study- and control populations, with the subjects brushing the teeth twice a day for 6 months, using at least two different toothpastes.

A systematic review showed that most clinical trials evaluating the effect of triclosan-containing toothpaste against gingivitis are in its favor, resulting in absolute reductions of 15% of the sites with plaque, as well as 12% reductions of the gingival bleeding sites. In 2006, a meta–analysis of similar clinical trials showed identical results. These results focused in two directions: 1. There is a certain benefit in associating triclosan with the copolymer, given that triclosan alone or combined with other substances does not have the same efficacy against plaque or gingivitis as the one of the mentioned combination; 2. Is the degree of inflammation reduced enough to avoid evolution towards periodontitis? In this respect, more studies are necessary to achieve relevance, but it is certain that the inhibition of inflammation needs to occur to prevent the evolution of gingivitis towards periodontitis.

Another group of trials allows some other interesting conclusions:
- The triclosan-PVM/MA copolymer combination has a more pronounced effect in sites with more plaque and inflammation.
- Gingivitis reduction can reach 55 – 57 % in very inflamed areas.
- Gingivitis reduction continues even after 6 months.

Another interesting finding is that the toothpastes containing the triclosan - copolymer combination are effective in all sectors of dental arches, even in the less accessible ones (lingual and interproximal surfaces),
this effect being due not only to plaque reduction.\textsuperscript{21} The efficiency against gingivitis is also confirmed in pregnant and breast-feeding women.\textsuperscript{22}

The characteristic indicating the antiinflammatory role of triclosan is that after using a toothpaste containing the triclosan-copolymer combination for some time, the correlation between plaque quantity and gingival bleeding decreases, while with control toothpastes, this relation is not modified (low bleeding index and not reduced plaque and tartar index).\textsuperscript{23,24}

Some less favorable trials for the triclosan-copolymer combination have reported improved efficacy for toothpastes associating triclosan with zinc citrate, (regarding the plaque- and gingivitis control), while other trials only reported only a modest effect of triclosan against plaque accumulation and gingivitis development, and that only for patients presenting with at least 45 bleeding sites upon probing.\textsuperscript{25-28}

In conclusion, the use of toothpaste containing the triclosan-PVM/MA copolymer combination offers a pronounced antibacterial effect and reduces the gingival bleeding, especially in areas initially presenting more plaque and inflammation, as well as in inaccessible areas. The quantity and viability of bacterial plaque are diminished even 12 hours after teeth brushing with this formulation. The synergic anti-inflammatory effect of the triclosan-PVM/MA copolymer combination can explain the bleeding reduction in areas with unmodified plaque quantity.

**ACKNOWLEDGEMENT**

The content of this publication is part of the Report of the Consensus Meeting “Applications of Triclosan in Dental Medicine. The Triclosan-Copolymer Technology”, Athenee Palace Hilton Hotel, Bucharest, February 15, 2008. Published with the permission of Colgate-Palmolive Romania.

**REFERENCES**