

# Therapeutic oral rinsing with commercially available products: Position paper and statement from the Canadian Dental Hygienists Association

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## ABSTRACT

**Background:** Mechanical methods of oral hygiene have been shown insufficient in controlling biofilm and preventing the initiation and progression of gingival inflammation and disease. These findings provide the impetus for additional research and the broader use of therapeutic oral rinses by adults. This position paper updates and replaces the 2006 Canadian Dental Hygienists Association position paper on oral rinsing to guide dental hygienists and other dental professionals in making client recommendations. **Methods:** A literature search using MEDLINE-PubMed, the Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) databases was conducted in stages. The search was limited to English language articles published between 2006 and 2016. Articles were selected if they focused on predetermined variables. Each article was reviewed utilizing an analysis table to identify the study parameters. **Results:** The search returned 452 studies, and initial screening of titles and abstracts identified 42 papers for full review. An additional 24 articles identified through hand searching resulted in 66 full-text articles retrieved. Of these, 46 studies were included in the final review. Studies were categorized and reviewed according to a research-stage taxonomy. **Discussion and Conclusions:** The research demonstrates that a commercially available essential oil oral rinse, with a fixed combination of thymol 0.063%, eucalyptol 0.091%, and menthol 0.042%, provides statistically and clinically significant plaque and gingival inflammation reductions beyond that accomplished by mechanical means. While chlorhexidine gluconate rinse remains the gold standard with regard to plaque reduction, its negative side effect profile precludes long-term use. Several other products demonstrated superior efficacy to placebos and require further research. Among non-prescription oral rinses, the essential oil rinse was most effective, safe, and acceptable to study subjects, and should be recommended as a daily complement to tooth brushing and interdental mechanical cleansing for adult clients.

## RÉSUMÉ:

**Contexte :** Il a été démontré que les méthodes mécaniques d'hygiène dentaire ne suffisent pas à contrôler la formation de biofilms ni à prévenir le déclenchement et la progression de l'inflammation et de l'affection des gencives. Ces constatations donnent l'élan nécessaire à des recherches supplémentaires et à l'utilisation plus répandue de rince-bouches thérapeutiques par les adultes. Le présent exposé de position actualise et remplace l'exposé de position de 2006 de l'Association canadienne des hygiénistes dentaires sur le rinçage buccal afin d'orienter les hygiénistes dentaires et autres professionnels dentaires lorsqu'ils formulent des recommandations aux clients. **Méthodes :** Une recherche documentaire a été effectuée en étapes à l'aide des bases de données de MEDLINE-PubMed, du Cochrane Central Register of Controlled Trials et du Cumulative Index to Nursing and Allied Health Literature (CINAHL). La recherche était limitée aux articles de langue anglaise publiés entre 2006 et 2016. Les articles étaient sélectionnés s'ils étaient axés sur des variables prédéterminées et chaque article a été examiné au moyen d'un tableau d'analyse pour cerner les paramètres de l'étude. **Résultats :** La recherche a produit 452 études et la vérification initiale des titres et des résumés a répertorié 42 articles pour examen complet. L'ajout de 24 articles supplémentaires par recherche manuelle a permis d'obtenir le texte intégral d'un total de 66 articles. Parmi ces articles, 46 études ont fait partie de l'examen final. Les études ont été classées et révisées en fonction de la taxonomie par phase de recherche. **Discussion et conclusions :** La recherche démontre qu'un rince-bouche aux huiles essentielles, offert sur le marché, composé d'une association médicamenteuse fixe de thymol à 0,063 %, d'eucalyptol à 0,091 % et de menthol à 0,042 %, permet des réductions statistiques et cliniques considérables de plaque et d'inflammation gingivale qui vont au-delà de celles produites par des moyens mécaniques. Bien que les rince-bouches au gluconate de chlorhexidine demeurent l'étalon de référence lorsqu'il s'agit de la réduction de la plaque, leur profil d'effets secondaires négatifs empêche leur utilisation à long terme. Plusieurs autres produits ont montré une efficacité supérieure à celle des placebo et requièrent davantage de recherches. Parmi les rince-bouches vendus sans ordonnance, le rince-bouche aux huiles essentielles était le plus efficace, sécuritaire et acceptable de la part des sujets de l'étude et devrait être recommandé aux clients adultes comme complément quotidien au brossage de dents et au nettoyage mécanique interdentaire.

**Key words:** dental plaque, oral antiseptic, oral biofilm, oral chemotherapeutic, oral hygiene, oral rinse, mouth rinse, mouthwash

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## CANADIAN DENTAL HYGIENISTS ASSOCIATION POSITION STATEMENT

Based on the current research, dental hygienists are encouraged to recommend oral rinsing with a commercially available therapeutic over-the-counter oral rinse (mouthwash) to their adult clients as a long-term complement to usual mechanical plaque control measures. An accumulation of research, including well-conducted long-term clinical studies ( $\geq 6$  months), has shown that oral rinses with a fixed combination of 3 essential oils—thymol 0.063%, eucalyptol 0.091%, and menthol 0.042%, along with other ingredient(s) (e.g., methyl salicylate 0.0660%)—produce statistically and clinically significant reductions in plaque and gingival inflammation beyond that accomplished by mechanical means alone. Other oral rinses demonstrate some reductions in plaque and gingivitis, but the research on these formulations is less conclusive. While prescription chlorhexidine gluconate oral rinse has been the gold standard with regard to reductions in plaque and gingival inflammation parameters, it is recommended for short-term use only due to a negative side effect profile. Dental hygienists can recommend alcohol-containing therapeutic oral rinse products as these have not been demonstrated to have adverse effects; the exception remains for clients who are unable to tolerate alcohol for personal or health reasons. Dental hygiene interventions should be client-specific and should be based on current evidence, which indicates that therapeutic oral rinses are an important complement to home care routines to achieve optimal oral hygiene and promote oral health for adult clients.

## INTRODUCTION

Dental hygiene clients find it challenging to maintain satisfactory oral hygiene through mechanical methods and, as a result, therapeutic oral rinsing has been advanced as an important addition to home care for reducing oral biofilm. Oral biofilm is the primary etiology for gingivitis, periodontitis, and caries, and also contributes to halitosis and systemic well-being.<sup>1</sup> Traditional mechanical methods for achieving oral cleanliness, such as tooth brushing and interdental cleansing, have been mainstays in controlling oral biofilm, but have in the last several years been recognized as insufficient in preventing oral disease initiation and progression.<sup>2,3</sup> The effectiveness of dental flossing, a pillar of oral hygiene recommendations, has recently been questioned in the media because of a lack of supporting research.<sup>4</sup> The addition of a therapeutic oral rinse to home care routines has been recommended as an important complement to mechanical methods.<sup>5</sup> However, with many oral rinse formulations available on the market and numerous others in development, product selection for both the client and the dental hygienist is challenging.

This position paper, endorsed by the Canadian Dental Hygienists Association (CDHA), provides a comprehensive review of the research on therapeutic oral rinsing, including commercially available over-the-counter (OTC) and prescription oral therapeutic agents. This review was conducted to update CDHA's 2006 position paper and statement<sup>6</sup> on home mouth rinsing as a preventive oral health behaviour particularly as it relates to periodontal disease initiation and progression. While the review included research on oral rinse products in early development and not yet commercially available, those findings will be published separately. The present review updates and replaces the 2006 CDHA position paper and statements, written by the same author. A summary of the updates is found in the Appendix.

Studies testing the effectiveness of therapeutic oral rinse agents have been extensively conducted, but readers will note a wide variety of study designs and protocols, which makes the research difficult to compare

and interpret, subsequently complicating evidence-based decision making in clinical practice. Study designs range from very short-term in vitro and in vivo studies to long-term clinical trials lasting 6 months or more. All of these studies contribute to researchers' and clinicians' understanding of the efficacy of oral rinse formulations designed to control oral biofilm and reduce gingival inflammation. This comprehensive review paper aims to summarize, interpret, and make recommendations based on the research published since the previously published 2006 review.

Oral rinse studies can be placed on a continuum from early- to late-stage research. New product formulations, often testing active ingredients before commercial products are developed, are typically initially studied using short-term in vitro studies and, if found to be effective, may proceed to longer-term studies, which are more expensive and ethically bound. Thus, where formulations are found to be ineffective in early-stage research, progression to later-stage trials is not warranted.<sup>7</sup> Conducting later-stage research on products without confirmed efficacy in early stages may be inappropriate and unethical. In fact, there has been a call from researchers in the field to standardize studies on therapeutic mouthrinses.<sup>7</sup> This review is framed according to research design stages described in the literature in order to situate oral rinse products on this continuum and clarify for dental hygienists and other readers the practical relevance of oral rinse products.<sup>7</sup>

## Research designs

Although attempts to reach consensus on oral rinse research designs have been made, there is a recognized need to better standardize oral antiseptic research to reduce variability in designs and subsequent outcomes.<sup>7</sup> Research has been conducted to evaluate and describe suitable study designs and other parameters in order to make recommendations for future therapeutic rinse studies.<sup>7</sup> For example, substantivity studies, plaque regrowth studies, experimental gingivitis models, and long-term ( $\geq 6$  months) home use trials were identified as the most often applied

Table 1. Stages of therapeutic oral rinse research

Stage	Classic design	Measured outcomes	Comments
Stage 1	In vitro kill ability; 8-hour in vivo substantivity	Bacterial vitality (vital fluorescence technique), minimal inhibitory concentrations (MIC), colony forming units (CFU)	Measures bactericidal activity and plaque inhibitory effects in cleaned surfaces after single rinse over 8± hours; other oral hygiene suspended; MIC is the lowest concentration of a formulation that will inhibit bacterial growth after a period of incubation; crossover designs suitable
Stage 2	4-day plaque regrowth in vivo	Plaque indices, gravimetry, planimetry	Plaque inhibitory effects in cleaned surfaces while rinsing daily (1-3x); other oral hygiene suspended; crossover designs suitable
Stage 3	21-day experimental gingivitis study in vivo	Plaque and gingivitis indices; bleeding indices	Plaque and gingivitis inhibitory effects in cleaned surfaces while rinsing daily (1-3x); other oral hygiene suspended; shorter than 21 days insufficient time for gingivitis to occur in all study subjects; should use parallel groups to minimize # times undergoing gingivitis
Stage 4	Home use studies; long term; in vivo; requirements for safety records	Plaque and gingivitis indices (i.e., Plaque index [PI], Modified Gingival index [MGI]); bleeding indices (i.e., bleeding index [BI]); side effects; favourability	Typically 6 months; plaque and gingivitis inhibitory effectiveness in real-life conditions while rinsing daily (1-3x) and while using other mechanical methods; parallel groups

study models and were described as the “classical methods” to evaluate therapeutic oral rinses as these approaches have demonstrated reliability, validity, responsiveness, and interpretability.<sup>7</sup> It is a given formulation’s degree of development and demonstrated efficacy that should determine the appropriate research design when planning new studies.<sup>7</sup>

Table 1 has been specifically developed for this review and is based on descriptions of these classical methods to help orient the reader and assist in navigating the text. Stage 1 research is designed to determine whether or not a product works and its level of substantivity in order to establish how often the product would need to be administered to inhibit plaque. Stage 2 studies are designed to determine, in the absence of any other oral hygiene measures, a product’s level of plaque inhibition on initially plaque-free sites over the short term, typically 4 days. Stage 3 studies utilize experimental gingivitis models intended to determine the influence of an oral rinse on plaque development and gingival inflammation over at least 3 weeks, again, in the absence of other oral hygiene measures. Stage 4 research is comprised of home use studies designed to replicate “real-life” conditions most closely over the long term, ideally 6 months or more, thus measuring product effectiveness and safety.

#### Other research parameters

##### Outcome parameters and measures

In addition to the research design, other parameters in oral rinse studies contribute to standardization. Outcome parameters include various measures to determine a product’s efficacy or effectiveness and should not only be aligned with the study design but also be well accepted, reliable, and valid to allow for interpretation and comparison across studies, which may include subsequent systematic reviews and meta-analyses. In vitro and in vivo outcomes measured in early-stage research include bacterial vitality quantified through vital fluorescence technique

and counting colony forming units (CFU). Clinical plaque measures used in intermediate and long-term research can be conducted by calibrated clinicians using well-validated indices or through the use of computer-based measurement tools like gravimetry (weight/mass measure) and planimetry (surface area measure). Gingival indices may be invasive and include measures of bleeding, or alternatively, may be non-invasive. Gingival crevicular fluid (GCF) and, more recently, its composition are also measured in some studies given the positive association found between changes in GCF and inflammation.<sup>8</sup> Outcome measures of side effects include discolouration or staining, taste alterations, and other unfavourable consequences.<sup>7</sup>

##### Study populations

Inclusion and exclusion criteria for study samples would also benefit from standardization as some medical and behavioural factors may influence outcomes. Typically, individuals with systemic diseases, those with a history of severe oral diseases, those who have untreated caries, dentures, are undergoing treatment with antibiotics or other drugs (including those that may significantly impact saliva output), and women who are pregnant or breast feeding should be excluded from oral rinse studies.<sup>7</sup> Some studies will control for tobacco use given its relationship to periodontal disease progression and its ability to mask gingival inflammation.

##### Sample sizes

For studies in stages 1 to 3, sample sizes of a minimum of 20 subjects per group are recommended based on anticipated drop-out rates, a normal distribution, a significance level of  $\alpha = 0.05$  and a power of 80% to determine if there is a real effect.<sup>7</sup> Sample size calculations for long-term home use clinical trials require the application of sample size statistical formulas selected in collaboration with experienced biostatisticians.<sup>9</sup>

## MATERIALS AND METHODS

Along with the author and CDHA staff, a committee was convened to oversee the development of the position paper and assist in defining the scope of the review. Committee members were selected based on content and/or research expertise and communicated with the author via teleconference throughout the review process.

The first step in the investigation was to develop a PICO question, which subsequently guided the literature search and review. The PICO question was as follows:

Do healthy adults who have plaque or biofilm or gingivitis or early periodontitis [Population] who use home mouthrinse or mouthwash or oral rinse according to manufacturer's directions with a commercially available non-prescription or prescription formulation as an adjunct to mechanical cleansing including tooth brushing alone or tooth brushing and flossing or interdental cleansing [Intervention] compared to not using oral rinse [Comparison] have improved plaque or biofilm or inflammation or gingivitis scores [Outcome]?

The literature search was conducted in stages from January 4, 2016, to April 30, 2016, using the following electronic databases: MEDLINE-PubMed, Cochrane Central Register of Controlled Trials, and the Cumulative Index to Nursing and Allied Health Literature (CINAHL).

The initial search focused on primary original research studies and excluded reviews. The search was limited to articles written in English and published between 2006 (when the first CDHA position paper was released) and April 30, 2016. Papers were selected for retrieval if they focused on:

- *Independent variables:* home, commercially available oral rinse product (prescription or non-prescription)
- *Dependent/outcome variables:* impact on bacteria/plaque/biofilm and inflammation/gingivitis

The second phase involved a manual search of references from papers retrieved in the first phase. Systematic reviews, meta-analyses, reports, and grey literature were also hand searched to ensure that no original research meeting the inclusion criteria was missed in the initial review.

To ensure consistency and minimize researcher bias, the author reviewed each paper utilizing an analysis table to identify the study parameters, including the researchers, date of publication, stage of research (according to Table 1), active ingredients, outcome measures, results (effect sizes; *p* values), and any other notes regarding the study.

Many natural-compound-based oral rinses are currently being studied but are not yet found in commercially available formulations. Dental hygienists have expressed interest in natural products, perhaps in response to client

inquiries, and these products will be reviewed in a second article focused on non-commercially available rinses, which are primarily natural compound formulations.

## RESULTS

The initial electronic search of the databases returned 452 research papers, of which 42 papers were selected for full review. An additional 24 articles were identified through the hand search, which resulted in a total of 66 full-text articles retrieved. Of these, 46 studies were found to:

- focus on the research question
- be original research
- include a commercially available rinse
- include an appropriate outcome measure
- be available in English

and were, thus, included in the review. Twenty studies retrieved in full text were excluded, primarily due to a lack of a commercially available rinse formulation in the study, and were referred to Part 2 of the review. In addition, several studies lacked an appropriate outcome measure or a suitable study population. For example, some studies focused on caries as an outcome measure or included children as a population group. The studies included were reviewed within the study stages framework described above and were summarized according to this taxonomy. Only stage 4 studies examining commercially available non-prescription products were reviewed in the 2006 position paper.

### Commercially available products

Oral rinse products have been available commercially for over a century and are supported by a substantial body of research. In fact, systematic reviews and meta-analyses of randomized controlled trials (RCT) have been conducted on several of these products.<sup>10-13</sup> Research conducted to date on commercially available products has focussed primarily on 3 active ingredients: chlorhexidine gluconate (CHG), essential oils (EO), and cetylpyridinium chloride (CPC). While no Cochrane trials have been conducted on commercial oral rinse products, one on CHG is in the protocol stage.<sup>14</sup>

Historically, CHG has been viewed as the gold standard for therapeutic home oral rinse but has been available only by prescription (e.g., PERIDEX™ 0.12%) and has a negative side effect profile primarily due to staining of oral tissues and also to taste alterations and increased calculus accumulation.<sup>6,7</sup> One EO rinse is available commercially (LISTERINE®) as an OTC product in a consistent formulation of naturally derived compounds, and new formulations have emerged with fluoride and without alcohol (LISTERINE TOTAL CARE®, LISTERINE ZERO®). OTC commercially available CPC formulations (e.g., Crest® PRO-HEALTH™) are also widely available and have been included in various studies in the past.<sup>6</sup>

### Stage 1 summary

Stage 1 studies include in vitro and in vivo designs, several of which were conducted with commercially available oral rinse formulations. Many of the products studied demonstrated positive effects in early-stage research and have undergone research in long-term models. However, these studies may be looking at specific bacteria as an outcome measure or at novel concentrations or combinations of established commercial products.

For example, several of these studies focused on CPC rinses. One 24-hour study compared a 0.075% CPC rinse with alcohol (6%) to a version without alcohol and to a negative control to determine differences in plaque reductions.<sup>15</sup> Both formulations significantly reduced plaque ( $p < 0.05$ ) compared to the negative control, but there was no difference between the CPC groups. In another in vitro CPC study, 0.05% CPC with and without alcohol were compared to a negative control in relation to minimal inhibitory concentration (MIC) levels against 25 bacterial species and also to 0.12% CHG with regard to plaque scores. The results showed both CPC rinses to have lower MIC levels than the control and, while the CPC rinses significantly reduced plaque compared to the negative control ( $p < 0.001$ ), the CHG was more effective ( $p < 0.05$ ).<sup>16</sup> In a 5- and 10-day study using 3D confocal laser scanning microscopy and fluorometric analysis, an alcohol-free 0.075% CPC rinse was compared to a placebo control and demonstrated a statistically significant ( $p < 0.001$ ) increase in the number of damaged biofilm cells after 5 days. But, while remaining statistically significant, the effect diminished by the 10-day point.<sup>17</sup> A further study examined viable *Fusobacterium nucleatum* counts following exposure either to an alcohol-free 0.075% CPC rinse or to a control rinse. The CPC rinse showed a significant inactivation of bacterial cells compared to the negative control ( $p < 0.05$ ).<sup>18</sup>

Several other CPC studies examined outcomes when combined with other products. For example, an alcohol-free 0.075% CPC with 0.05% NaF rinse was compared to an alcohol-containing (6%) 0.075% CPC also with 0.05% NaF and to a 0.05% NaF-only negative control with regard to planktonic bacteria. Both of the CPC rinses showed greater than 99.9% reductions in viable bacteria following 30 seconds of treatment.<sup>19</sup> Another study compared CHG, EO, 2 CPC rinses, and a commercially available stabilized chlorine dioxide product on CFU of gingivitis-associated oral bacteria. The EO and the 0.07% CPC rinses showed a complete bacterial kill within one minute, whereas the 0.075% CPC rinse showed the weakest bactericidal effects and the stabilized chlorine dioxide and 0.12% CHG demonstrated 100% kill at 5 minutes.<sup>20</sup>

Additional short-term studies were conducted with other products. For example, in a study comparing 0.2% CHG to a combination 1% povidone-iodine and EO rinse on the impact on *Porphyromonas gingivalis*, all treatment

groups reduced the bacteria, however the EO rinse was the most effective.<sup>21</sup> Another study compared 3 CHG rinses—an experimental 0.05% CHG rinse incorporating EO and alcohol, a 0.05% CHG rinse, and a 0.2% CHG rinse—to a negative control in order to examine the reduction of total viable bacterial counts and growth of microbial populations, including 14 bacterial and fungal species. The results demonstrated a statistically significant reduction ( $p < 0.05$ ) of viable counts of microbial populations of the test and standard CHG solutions over the control, but the standard CHG formulations were superior to the experimental product.<sup>22</sup> An in vitro study examined the maximum inhibitory dilution (MID) capable of inhibiting microbial growth of two 0.12% CHG formulations compared to a polyhexamethylene biguanide-based mouthwash (PHMB), which is a medical antiseptic commercially available in Brazil. No statistically significant difference between the CHG groups ( $p > 0.05$ ) was demonstrated, and the PHMB was statistically significantly less effective.<sup>23</sup> Further, a study comparing 2 versions of a commercially available rinse formulated with soluble bioflavonoids obtained from citrus fruits to a control rinse measured both the MIC against a range of microorganisms and the ability to inhibit microbial growth. The results showed a non-significant ( $p > 0.05$ ) reduction in planktonic and biofilm bacteria by the experimental rinse compared to the control.<sup>24</sup>

### Stage 2 summary

Several plaque regrowth studies have been conducted with commercially available mouthrinses, ranging in duration from 8 hours to 9 days. Some of these trials have extremely small sample sizes,<sup>25-32</sup> and they have inconsistencies in rinsing exposure times and rinse amounts, which may influence outcomes. Many of the stage 2 studies in this review included CHG either as a test group or as a positive control. Of these, 3 studies compared a standard CHG formula to a novel formula and/or to a control group. For example, a recent 4-day plaque regrowth study compared 0.05% CHG to a 0.05% CHG with 0.05% fluoride solution; both demonstrated equal effectiveness in depressing plaque regrowth.<sup>31</sup> A 7-day plaque regrowth study compared 0.12% CHG with alcohol to a 0.1% CHG alcohol-free formulation and to a control and showed the 0.12% CHG with alcohol rinse to be statistically significantly ( $p < 0.05$ ) more effective in plaque inhibition than either the non-alcohol version or the control.<sup>27</sup> An 8-hour plaque regrowth study demonstrated a 0.2% CHG rinse to be more effective ( $p < 0.05$ ) in reducing bacterial growth and adherence compared to a German-manufactured commercially available amine/NaF rinse (ELMEX®) and a negative control.<sup>32</sup>

In several of these plaque regrowth studies, CHG served as a positive control and was compared with another product. In most of these studies, CHG was shown to be statistically significantly more effective than comparison groups. For example, in one 4-day study 0.12% CHG was

compared to 0.05% CPC and a negative control. While both CHG and CPC were statistically significantly superior in reducing CFU compared to the control, CHG demonstrated a statistically significant decrease in values compared to the other groups ( $p < 0.001$ ). With regard to plaque outcomes, CHG suppressed plaque significantly better than both CPC and negative control ( $p < 0.05$ ). While the study was just 4 days in duration, the negative control had significant increases in inflammation from baseline scores ( $p < 0.47$ ), and the CHG was statistically significantly superior to both CPC and the negative control in controlling gingival outcomes ( $p < 0.05$ ).<sup>28</sup>

Two studies compared 0.12% CHG to EO and amine/stannous fluoride (ASF) rinse groups; both found the CHG to be most effective in plaque suppression, although the EO and fluoride rinses were also found to be statistically significantly better than the control.<sup>26,30</sup> In a 2008 study, while there was no statistically significant difference ( $p > 0.05$ ) between the ASF and EO, both significantly inhibited plaque regrowth compared to saline ( $p < 0.001$ ). However, statistically significantly greater plaque reductions were shown with the CHG ( $p < 0.01$ ).<sup>26</sup> In a 2015 study, an ASF rinse was compared to an alcohol-free EO with fluoride rinse and a 0.2% CHG group and, while the ASF was statistically significantly better at inhibiting plaque than the EO plus fluoride group, CHG was again superior to both the ASF and the EO rinses ( $p < 0.001$ ).<sup>30</sup>

CHG has also been compared to commercially available natural compound products. A 3-day study compared an herbal mouthrinse available from India (Herboral®), which is a combination of 10 natural herbs, to 0.2% CHG. The study demonstrated CHG to significantly inhibit plaque compared to the herbal rinse ( $p < 0.001$ ).<sup>33</sup> There were 2 studies conducted with a commercially available product (HiOra®) containing 3 natural compounds: Meswak (persica), Betel leaf, and Belleric Myrobalan or, more correctly termed, *Terminalia bellirica*. In a 2015 5-day plaque regrowth study, both the test formulation and the 0.02% CHG rinse significantly ( $p < 0.001$ ) suppressed plaque and inflammation compared to a negative control and, while the CHG outperformed the test rinse, its results were not statistically significant.<sup>34</sup> An earlier 2013 study compared the same natural compound rinse to 0.2% CHG and EO, and demonstrated the test rinse and the EO to inhibit plaque regrowth significantly over 4 days compared to placebo ( $p < 0.001$ ). The lowest values were found with CHG, which was statistically significantly better than the test rinse and EO ( $p < 0.001$ ).<sup>35</sup> A 5-day plaque regrowth study comparing a commercially available tea tree oil rinse (Tebodont®) to 0.12% CHG, 0.05% CPC, and a placebo demonstrated both CHG and CPC to be significantly more effective ( $p < 0.001$ ) in suppressing plaque than the experimental group and placebo, but there was no statistical difference between them.<sup>36</sup>

Three plaque regrowth studies examined the effects of CPC rinses. Two of these compared different concentrations of CPC to each other and to controls, whereas another study compared CPC to a European commercially available hexitidine rinse (Hextril™). The 2008 3-day study compared 0.1% CPC to 0.05% CPC and to a negative control. Both CPC rinses were significantly superior ( $p < 0.05$ ) to the control, while no difference was evident between CPC groups.<sup>25</sup> A 2011 study compared a 0.075% CPC with 0.05% NaF to an alcohol-free version of the same product and an alcohol-free NaF control rinse. Both CPC rinses performed significantly better ( $p < 0.05$ ) compared to the control rinse in reducing anaerobic bacterial counts.<sup>37</sup> Finally, a 3-day study comparing 0.07% CPC to hexitidine 0.1% and a negative control showed both test rinses to be significantly better ( $p < 0.001$ ) in suppressing plaque than the negative control, but there was no statistical difference between treatment groups or differences detected in inflammation.<sup>29</sup>

### Stage 3 summary

Six stage 3 suspended oral hygiene experimental gingivitis studies were included in this review. Of these, 4 were only 2 weeks in length and, therefore, would not necessarily be long enough to induce gingivitis in all participants.<sup>7</sup> Four of these studies compared EO to CPC and/or a negative control in relation to plaque and gingival parameters.<sup>38-41</sup> These showed expected outcomes, with EO and CPC both statistically significantly outperforming the control rinse and also demonstrating that the EO rinse was superior to CPC regardless of the latter's concentration. Specifically, the 2009 2-week study demonstrated the EO rinse to be significantly better ( $p < 0.001$ ) than the 0.05% CPC and control rinses in plaque and gingival parameters.<sup>38</sup> Similarly, the 2011 study, also only 2 weeks in length, demonstrated the EO rinse to be significantly better ( $p < 0.011$ ) in both plaque and gingival outcomes than a 0.07% CPC rinse.<sup>39</sup> Another 2-week study compared an alcohol-free EO rinse to placebo and showed the EO to significantly outperform the control ( $p < 0.001$ ) in plaque and gingival measures.<sup>40</sup> Finally, a 2-week trial conducted in 2013 compared an EO rinse to a 0.075% CPC and a negative control. That study also demonstrated significant ( $p < 0.001$ ) reductions in plaque and gingival measures by the EO rinse compared to the control. The EO rinse significantly ( $p < 0.001$ ) reduced bleeding compared to the CPC rinse.<sup>41</sup>

Both of the 3-week studies were conducted with CHG. One small ( $n = 20$ ) study compared 0.12% CHG on plaque-free surfaces versus plaque-covered surfaces.<sup>42</sup> Results were significantly better ( $p < 0.05$ ) with the plaque-free surfaces, demonstrating the importance of surfaces initially being cleaned to inhibit plaque and gingivitis over time.<sup>42</sup> The final experimental gingivitis study included in the review compared a 0.2% CHG rinse to a triclosan 0.3% plus 0.025% NaF with alcohol rinse and to a 0.2% CHG

rinse also with 0.3% triclosan, 0.3% NaF, and 0.09% zinc chloride. The findings showed 0.2% CHG to be significantly most effective ( $p = 0.046$ ) in reducing plaque and gingivitis, but also had significantly ( $p = 0.03$ ) more stain than the other groups, highlighting the trade-off between efficacy and side effects associated with CHG.<sup>43</sup>

#### Stage 4 summary

**Short-term (6-week) home use trials:** Short-term home use studies were not described by Lorenz and colleagues in their research on appropriate study designs for therapeutic oral rinses,<sup>7</sup> but 6 studies falling within this category were identified and reviewed, and ranged from as short as 7 days to 6 weeks. Those that were shorter than 3 weeks, again, need to be viewed cautiously with regard to gingival parameters. Two of these studies compared CPC to an EO formulation. A 4-week study comparing an EO rinse to 0.075% CPC and a negative control demonstrated both the EO and CPC rinses to be statistically significantly superior to the control, but the EO rinse was superior to the CPC formulation in plaque and gingival outcome measures ( $p < 0.001$ ).<sup>44</sup> Another recent 6-week study compared 0.075% CPC to EO rinse and again showed the EO rinse to be superior to the control ( $p < 0.001$ ) and the CPC rinse ( $p < 0.05$ ) in plaque and gingivitis measures.<sup>45</sup>

Several studies compared CPC rinses to a positive or negative control. For example, two 7-day studies compared 0.05% CPC rinse to a control rinse; both showed the CPC rinse to significantly reduce plaque scores compared to the control ( $p < 0.05$ ;  $p < 0.05$ ).<sup>46,47</sup> A longer 6-week trial also conducted on 0.05% CPC and a control had similar outcomes ( $p < 0.05$ ).<sup>48</sup> A small ( $n = 30$ ) 28-day study comparing alcohol-free 0.2% CHG to an alcohol-containing 0.2% CHG and a placebo demonstrated both CHG rinses to be significantly better ( $p < 0.05$ ) in reducing plaque and gingival scores than the control.<sup>49</sup>

**Long-term ( $\geq 6$  months) home use trials:** Nine long-term clinical home use trials investigating commercially available products were included in the review. All of these trials included EO, CPC, and placebos in various combinations typically in addition to usual mechanical oral home care routines. Two studies compared EO rinse to a control group only and showed expected results. The 2013 study demonstrated that the EO rinse group significantly ( $p < 0.001$ ) reduced all outcome measures at all time points including both plaque and gingival parameters. In addition the effect increased over the duration of the study and no negative outcomes occurred.<sup>50</sup> The 2009 study also showed significantly greater reductions by the EO rinse compared to control ( $p < 0.05$ ) in plaque and gingivitis scores.<sup>51</sup>

Additional long-term clinical trials conducted with EO rinses included other test groups. For example, a large trial comparing EO rinse, a 0.07% CPC rinse, and negative control showed a statistically significant reduction in plaque and inflammation by both test groups compared to the control, but the EO rinse group was significantly

superior to the CPC at all time points after baseline ( $p < 0.05$ ). There were no adverse outcomes other than staining reported by the CPC group.<sup>52</sup> Another large trial compared an alcohol-free EO rinse to a 0.05% alcohol-free CPC rinse and a control and again showed both to significantly reduce plaque compared to the negative control ( $p < 0.001$ ). However, the EO rinse also significantly decreased plaque and gingivitis compared to CPC ( $p < 0.001$ ).<sup>53</sup> An earlier, very large trial compared EO rinse with zinc chloride and NaF to a 0.05% CPC also with NaF and to a control. Although the CPC produced a statistically significant reduction in plaque and inflammation scores compared to the control, the EO rinse was significantly better ( $p < 0.05$ ) than the CPC rinse in all parameters and at all time points post baseline, and, again, the improvements increased over time.<sup>54</sup> Another long-term clinical trial compared an EO rinse to a 0.05% CPC and a placebo control and showed similar results, with the EO rinse demonstrating significantly lower plaque and inflammation scores than the control ( $p < 0.001$ ) and CPC ( $p < 0.001$ ). The CPC did show significantly lower outcome scores ( $p < 0.001$ ) than the control group and no adverse events occurred with either group.<sup>55</sup>

Two other long-term CPC studies were conducted. One compared an alcohol-free 0.075% CPC with 0.05% NaF to a control 0.05% NaF rinse. The CPC rinse group had significant reductions in gingival and plaque scores ( $p < 0.05$ ) as compared to the control group.<sup>56</sup> In another study comparing a 0.07% CPC rinse to placebo, both the test ( $p < 0.001$ ) and the control ( $p = 0.003$ ) groups had significant reductions in outcomes, but the CPC group significantly reduced plaque compared to the placebo ( $p < 0.001$ ). While bleeding was also lower in the CPC group, the findings were not significant ( $p = 0.052$ ).<sup>57</sup> However, staining of teeth was also measured using the Gründemann Modification of the Stain Index (GMSI); there was significantly more staining with the test rinse as compared to the negative control at 3 ( $p = 0.007$ ) and 6 months ( $p < 0.001$ ).<sup>57</sup>

Only one of these long-term clinical home use studies did not confirm previous findings, demonstrating no statistically significant difference between the EO rinse and the 0.07% CPC rinse in plaque or gingivitis measures ( $p = 0.05$ ).<sup>58</sup> However, the study did not include a negative control group as is recommended in the American Dental Association (ADA) guidelines, and when the study was later critically reviewed, it was found to be flawed because of its lack of a control group and its analysis of the results as a traditional comparative study rather than more appropriately as an equivalence study.<sup>59,60</sup>

Long-term clinical trials are expected to evaluate and report safety outcomes. Other than what has been indicated above, none of the studies reported adverse events as an outcome of the test rinses included. One study examined salivary output and pH associated with EO rinse with

Table 2. Oral rinse systematic reviews (2007 to present)

Study authors, date	Active ingredient(s) (# of studies included)	Overall conclusions
Araujo et al. (2015) <sup>10</sup>	EO (29)	Meta-analysis demonstrates clinically significant, site-specific benefit of adjunctive EO treatment within a 6-month period
Van Strydonck et al. (2012) <sup>12</sup>	CHG (30)	CHG with oral hygiene versus placebo or control mouthrinse provides significant reductions in plaque and gingivitis scores, but a significant increase in staining score
Van Leeuwen et al. (2011) <sup>11</sup>	EO, CHG (19)	EO appears to be a reliable alternative to chlorhexidine mouthwash with respect to parameters of gingival inflammation
Haps et al. (2008) <sup>13</sup>	CPC (3)	Provides small but significant adjunctive benefit to mechanical cleansing
Stoeken et al. (2007) <sup>79</sup>	EO (11)	EO provides additional benefit with regard to plaque and gingivitis reductions

alcohol and found no alterations to either outcome.<sup>51</sup>

### Systematic reviews

Since the 2006 CDHA position paper was published, several systematic reviews and meta-analyses have been carried out on commercially available oral rinse products. These reviews (Table 2) compare CHG, EO, and CPC rinses to each other and/or to placebo and reaffirm the continued focus on these 3 active ingredients found in commercially available products. A recently published systematic review on natural-compound-containing mouthrinses, primarily focused on non-commercial formulations,<sup>61</sup> will be discussed in a separate article. Overall, the results of these systematic reviews and meta-analyses demonstrate that, while CHG consistently reduces plaque beyond that achieved with EO rinse, the latter appears to reduce gingival inflammatory outcomes similarly to CHG without the negative side effect profile.<sup>10,11</sup> CPC rinses have shown less compelling results with regard to plaque and gingival outcomes.<sup>13</sup>

The most recent of these systematic reviews was published in 2015 and examined 29 RCTs of 6 months in duration conducted with commercially available EO rinse, including both published and unpublished trials. While this research was sponsored by the EO manufacturer, it included a meta-analysis with results from over 5000 participants thereby providing a comprehensive summary of the outcomes of EO rinse as compared to mechanical cleansing alone in both whole mouth means and “site specific” data.<sup>10</sup> In addition, the review provided summary odds ratios for plaque-free and inflammation-free sites and a responder analysis to help guide clinical decision making.<sup>10</sup> All statistical measures showed a statistically and clinically significant adjunctive benefit of EO rinsing over 6 months.<sup>10</sup>

In 2012, Van Strydonck and colleagues published a systematic review of 30 studies on CHG.<sup>12</sup> The authors concluded that CHG oral rinses, together with oral hygiene, provide significant reductions in both plaque and gingivitis scores ( $p < 0.00001$ ) compared to placebo-control mouthrinse in clients with gingivitis, but statistically significant side effects were found.<sup>12</sup> Staining was the most

common observation, but increased calculus formation and taste alterations were also frequently reported.<sup>12</sup> In a 2011 systematic review, Van Leeuwen and co-researchers compared EO and CHG, concluding that, in long-term use, EO rinse appeared to be a reliable alternative to CHG with respect to parameters of gingival inflammation without the negative side effects.<sup>11</sup> Although the CPC systematic review included products with different concentrations and studies with considerable heterogeneity, from the meta-analysis the authors concluded there was a small but statistically significant additional benefit in reducing plaque accumulation ( $p < 0.00001$ ) and gingival inflammation ( $p < 0.00003$ ).<sup>13</sup>

### DISCUSSION

Four stages of research on commercially available oral rinses have been conducted, ranging from short-term in vitro and in vivo studies to long-term ( $\geq 6$  months) home use clinical trials. The studies primarily focused on the more established formulations, including CHG, EO, and CPC rinses, although shorter trials tended to compare novel concentrations and combinations of these and other products.

Commercially available oral rinses are supported by a large body of research, some of which has been funded by product manufacturers. While clinicians should always approach research with healthy skepticism, industry-conducted or sponsored research can be of high quality and, like all scholarly research, is scrutinized by peer review committees prior to publication to ensure scientific rigour. Clinical trials involving human subjects must undergo ethical review and, in most countries, drug trials must be registered so they can be followed through to the publication phase.<sup>62-64</sup> Given this concerted effort to reduce reporting bias, it would be imprudent to discount research solely because it was supported or conducted by industry.

In Canada, most oral rinses are categorized as a “consumer health product” and fall within one of over 80 categories of non-prescription products approved for use.<sup>65</sup> These products can be identified by their product number on the label, which also indicates whether the product is approved by the Food and Drug Regulations or by the

Natural Health Products Regulations.<sup>65</sup> In addition, these products must have a valid product licence issued by Health Canada, which requires the brand to demonstrate product safety and efficacy.<sup>65</sup> Products requiring a prescription are regulated under the Food and Drug Regulations.<sup>65</sup>

The Canadian Dental Association provides reviews of submissions from consumer oral health product manufacturers, verifying that the research methods and product claims are scientifically supported by the evidence.<sup>66</sup> The ADA has specific and rigorous criteria for granting the ADA seal of acceptance to chemotherapeutic oral rinses. These criteria include proof of objective clinical/laboratory studies demonstrating safety and effectiveness, FDA-approved ingredients, manufacturer assured purity and uniformity and, finally, packaging and advertising claims supported by science.<sup>67</sup> As part of these rigorous criteria, clinical trials must also be at least 6 months in duration and must demonstrate statistically significant reductions in both plaque and gingivitis. To date, only CHG and EO rinses have received the ADA seal, but because the ADA has moved away from approving prescription products, CHG has lost its ADA seal.<sup>68</sup>

Most of the short-term studies included in this review were *in vitro* or *in vivo* studies examining effects after single exposure to rinses over 8 or more hours without other oral hygiene interventions. These studies primarily compared CPC rinses to negative controls or placebos or to CHG, serving as a positive control, and examined bacterial vitality, MIC to oral microbiota, and/or CFU counts. Overall, this research did not present any unexpected results in that the CPC formulations in various concentrations were consistently significantly more effective than negative controls but less effective than CHG. Interestingly, no differences in outcomes were demonstrated when an alcohol-free formulation was compared to an alcohol-containing counterpart in early-stage research models.

Stage 2 studies examined plaque regrowth over several days of suspended oral hygiene (with the exception of the rinse) and are too short to draw conclusions about gingival inflammatory outcomes, although many of the studies did. The stage 2 studies demonstrated the greatest inconsistencies in study design and also had very small sample sizes, potentially affecting statistical power. These studies were largely conducted with CHG and CPC rinse formulations, but a few less-established products were evaluated. Again, CHG in various concentrations (i.e., 0.05%, 0.1%, 0.12%, and 0.2%) was found to be superior in inhibiting plaque regrowth compared to other products including CPC, A/NaF, EO with fluoride, and a commercially available herbal rinse. One study demonstrated alcohol-containing CHG rinse to be superior to an alcohol-free version.<sup>27</sup> In addition, an herbal based product (HiOra<sup>®</sup>) and the antiseptic hexitidine produced, in separate studies, statistically significant results, suggesting that more and possibly higher level research is warranted to investigate

potential therapeutic activity. However, a systematic review conducted on hexitidine concluded that it was consistently less effective than and not a good alternative to CHG.<sup>69</sup>

Research shows that maturing biofilm bacteria is profoundly more resistant to antimicrobials than those in planktonic states. Therefore, it is essential for potentially effective antimicrobial agents to demonstrate activity within biofilm models.<sup>24</sup> Few stage 3 experimental gingivitis studies were conducted, which, when conducted well, would have the potential to demonstrate plaque and gingival effects. Instead, most of the stage 3 studies were only 2 weeks in length, and may not have provided sufficient time for gingivitis to occur. Within this model, both EO and CPC formulations significantly reduced plaque and gingivitis compared to controls, but the EO rinse consistently outperformed the CPC. Given the demonstrated effects, additional stage 3 studies with these products are likely unwarranted at least with current formulations.

If they are of sufficient duration, short-term ( $\leq 1$  month) home use studies have the potential to show both plaque and gingival outcomes and are more authentic to real-life conditions than stage 3 studies in that other oral hygiene measures are not suspended. Few of these studies were identified for review. In those that were, however, expected outcomes prevailed with EO, CPC, and CHG rinses all outperforming negative controls and EO rinse significantly reducing plaque and inflammation compared to CPC rinse.

Long-term ( $\geq 6$  months) home use clinical trials provide the most compelling results for clinicians because they have typically gone through all earlier stages of research and likely have the demonstrated efficacy warranting a long-term trial. These studies must report safety, efficacy, and compliance. Of the long-term clinical trials reviewed, most compared EO rinse to CPC and/or a negative control. With only one exception, the EO rinse was superior in reducing plaque and gingivitis when compared to the CPC. Studies examining the addition of zinc chloride and fluoride did not alter these outcomes. Two of the long-term trials demonstrated CPC to have increased staining associated with its use, which has been confirmed in a systematic review on CPC rinse.<sup>12</sup>

It is generally accepted that plaque biofilm is the primary etiology for gingival inflammation and periodontal disease progression.<sup>3,70</sup> However, some researchers have concluded that EO rinses possess a synergistic anti-inflammatory effect<sup>71</sup> and, notwithstanding well-demonstrated plaque reductions, provide enhanced anti-inflammatory benefits.<sup>51,72,73</sup> While CHG remains the gold standard in terms of plaque outcomes, EO rinse performs well in reducing plaque and demonstrates comparable outcomes to CHG with regard to gingival inflammation reductions.

EO rinses are a group of plant extracts and, currently, only one EO rinse is commercially available, having a

greater than 100-year history of use. This rinse includes a fixed combination of 3 essential oils: thymol 0.063%, eucalyptol 0.091%, and menthol 0.042%, as well as additional ingredients such as methyl salicylate 0.0660%.<sup>74</sup> Other EO rinses have not been studied to the same degree and consist of various formulations. As a result, similar conclusions cannot be made. Over a decade of research reviewed here shows a benefit of using EO rinse in addition to mechanical methods, thereby substantiating its use with clients.

To enhance rinse activity, research reviewed recommended that mechanical therapy be performed prior to rinsing to disrupt biofilm and decrease the microbial load, allowing for a more effective penetration by the chemotherapeutic agent into the plaque biofilm.<sup>71</sup> It should be recognized that no mechanical method or therapeutic oral rinse has demonstrated the ability to completely eliminate oral biofilm. Therefore, a daily combination of both interventions should be recommended. This review validates the importance of a multitherapeutic approach involving traditional mechanical methods, such as tooth brushing and interdental cleansing, and therapeutic oral rinsing. Therapeutic oral rinse should be considered complementary to mechanical oral hygiene.

Oral rinses are typically well tolerated by most individuals. Discolouration is the most frequent side effect reported and one discolouration index provided a standardized estimate of the amount in study subjects.<sup>7</sup> For the most part, EO rinses do not have side effects like CHG and CPC have demonstrated with regard to stain and, therefore, can be used over the long term.<sup>52,75</sup> The presence of plaque increases CHG side effects and reinforces the necessity of biofilm disruption prior to the start of CHG mouth rinsing.<sup>42</sup> No studies in the review reported poor tolerance of EO rinses with or without alcohol over the long term, including changes to pH and salivary output.<sup>51</sup> This finding confirms research conducted previously, which demonstrated no increase in the perception of oral dryness (xerostomia) or a decrease in salivary output with EO rinse,<sup>76</sup> contrary to commonly perpetuated beliefs.

While controversy has existed surrounding mouthwash use (particularly those containing alcohol) and oropharyngeal cancer, epidemiological research has shown no statistically significant association between the regular use of mouthwash and oral cancer. Neither has a trend in risk of oral cancer with increased daily use of mouthwash been demonstrated. Importantly, there was also no association between alcohol-containing oral rinse and oral cancer.<sup>77</sup>

A recent, large European case-control study aimed to assess the association between mouthwash use and other factors, and upper-aerodigestive tract (UADT) cancer risk. Although the study used hospital patients as the controls, these patients had been admitted for conditions unrelated to oral cancer risk. The study corroborated a

dose-effect relationship between tobacco smoking and alcohol consumption (markedly so when combined) and UADT risk, and demonstrated that both socio-economic status and consumption of fruits and vegetables had an inverse relationship to risk of UADT. Interestingly, after adjusting for tobacco smoking and alcohol, the study concluded that poor oral health and poor dental care were independently associated with increased risk of UADT. While the study did not demonstrate an association between prescribed levels (twice daily use) of oral rinsing and oral cancer, the researchers found an association between frequent mouthwash use ( $\geq 3$  times/day) and oral cavity and pharyngeal cancers. This finding was based on only 1.8% of cases and 0.8% of controls reporting such frequent use. Further, the study did not account for alcohol-containing versus non-alcohol-containing mouthwash.<sup>78</sup> The researchers concluded that the impact of the alcohol content present in most formulations remains to be fully clarified, and they further hypothesized that any risk associated with mouthwash use and oral cancer is likely confined to smokers given that alcohol consumption among “never smokers” has not been shown to be a risk for head and neck cancers.<sup>78</sup>

Ethanol is incorporated in some oral rinses to act as a solubilizer, stabilizer, and preservative, and, although not considered an active ingredient, seems to enhance anti-plaque efficacy.<sup>77</sup> Recently, more alcohol-free formulations have been made commercially available, but there is less research demonstrating equivalency of these products. It is important to recognize that commercial EO rinses have been safely in use for over a century and have not demonstrated adverse effects in long-term clinical trials. While this paper does not attempt to review the literature surrounding an association between mouthwash use, alcohol, and cancer-related health risks, it will be important to review this literature going forward in order to make more definitive statements surrounding safety. Dental hygienists should consider all risks when evaluating therapeutic oral rinsing benefits for their clients, particularly clients who currently engage in high-risk behaviours such as tobacco smoking and high levels of alcohol consumption.

## CONCLUSION

Based on this review, dental hygienists can confidently recommend a commercially available EO mouthrinse for their adult clients, with alcohol where not prohibited by client characteristics (i.e., alcoholism, religious beliefs, ability to expectorate), for long-term, twice daily use to reduce plaque and gingival inflammation, regardless of current home care routines. Clients presenting with high-risk behaviours, such as tobacco smokers, should be viewed holistically and cautioned about demonstrated and potential oropharyngeal cancer risks. Several additional commercial products including CPC have consistently shown efficacy superior to placebos, but not comparatively to EO and CHG and not in long-term clinical trials with

stringent study protocols. These conclusions are aligned with several recently conducted systematic reviews and ADA accepted guidelines and related seals of acceptance. Therapeutic oral rinses should be used together with mechanical cleansing (tooth brushing and interdental cleansing) in order for clients to achieve the highest level of

plaque and gingival inflammatory control. Incorporating an effective therapeutic oral rinse as a complement to home care routines will help dental hygiene clients reduce oral biofilm and achieve more desirable oral health outcomes.

## APPENDIX: UPDATES TO THERAPEUTIC ORAL RINSING RECOMMENDATIONS

2016 updated recommendation	2006 recommendation	Rationale
1. <i>Revised:</i> Over-the-counter (OTC) commercially available therapeutic oral rinses should be viewed as part of an overall plaque control strategy along with mechanical plaque removal methods.	1. Over-the-counter (OTC) commercially available chemotherapeutic oral rinses should be viewed as adjunctive to mechanical plaque removal methods.	Research supports the use of therapeutic oral rinses to complement mechanical methods as it shows a benefit beyond what can be accomplished by mechanical means alone.
2. <i>Revised:</i> While recommendations should remain specific, therapeutic oral rinses are indicated as a complementary oral hygiene component for all adult clients (with exception to those with a contraindication to use).	2. OTC rinses are particularly indicated for clients with uncontrolled plaque, bleeding, inflammation and/or gingivitis; all oral hygiene recommendations should be client specific.	Virtually all study subjects have experienced a reduction in plaque and inflammation with the addition of a therapeutic oral rinse beyond that achieved by mechanical methods alone; even clients with minimal plaque and inflammation can expect improvements.
3. <i>No change:</i> For OTC rinses, a fixed combination of 3 essential oils: thymol 0.063%, eucalyptol 0.091%, and menthol 0.042%, and additional ingredients, such as methyl salicylate 0.0660%, has been demonstrated in rigorous long-term studies to be most effective and safe, with acceptable side effects.	3. For OTC rinses, a fixed combination of 3 essential oils: thymol 0.063%, eucalyptol 0.091%, and menthol 0.042%, and additional ingredients, such as methyl salicylate 0.0660% (Listerine), has been demonstrated in stringent long-term studies to be most effective, safe, with acceptable side effects.	More research conducted since 2006 has accumulated in long-term clinical trials and systematic reviews to substantiate this recommendation.
4. <i>Revised:</i> Several commercial products have shown efficacy superior to placebos (e.g., CPC [in specific % formulations], hexitidine, and one herbal formulation [HiOra®]) and require further stage-appropriate research.	4. Several additional OTC rinse products, including AmF/SnF2, some products containing cetylpyridinium chloride, and triclosan, have shown efficacy superior to placebos but not within stringent study protocols. They therefore warrant further investigation.	Research has demonstrated efficacy of some additional products, but these require further, higher stage research to substantiate findings.
5. <i>Revised:</i> Dental hygienists can recommend alcohol-containing products as these have not been demonstrated to have adverse effects; the exception remains for clients who are unable to tolerate alcohol for personal reasons; clients demonstrating high-risk behaviours such as tobacco smoking should be cautioned regarding (over)use of oral rinses.	5. Dental hygienists can recommend alcohol-containing products as these have not been demonstrated to have adverse effects; the exception remains for clients who are unable to tolerate alcohol for various medically related reasons.	Additional research substantiates this recommendation; no reductions in salivary output or perception of dryness (xerostomia) have been demonstrated; while no adverse outcomes have been reported with prescribed levels of oral rinses, epidemiological data continue to be monitored regarding oropharyngeal cancer risks associated with smoking, alcohol use, poor oral health, poor oral hygiene, and the use of oral rinses.
6. <i>No change:</i> Dental hygienists will need to continue to monitor this field of inquiry as research and development in the area will likely continue; dental hygienists need to recognize the limitations of short-term, early-stage research study methods when determining the efficacy and safety of rinse formulations.	6. Dental hygienists will need to monitor this field of inquiry closely as vigorous research and development in the area will likely continue. Dental hygienists need to recognize the limitations of short-term and less stringent long-term study protocols when determining the efficacy and safety of rinse formulations.	The stages of research framework adopted for use in this paper further substantiates this recommendation. A second review focussed on non-commercially available oral rinse products will be published, which will be of interest to dental hygienists.

## DUALITY OF INTEREST

Joanna Asadoorian was paid as a consultant by the Canadian Dental Hygienists Association (CDHA) for the design, research, and writing of this position paper, and also works on contract with CDHA. She has done short-term contractual work with Johnson & Johnson in the past.

## REFERENCES

- Borgnakke WS. Does treatment of periodontal disease influence systemic disease? *Dent Clin North Am.* 2015;59(4):885–917.
- Teles RP, Teles FRF. Antimicrobial agents used in the control of periodontal biofilms: Effective adjuncts to mechanical plaque control? *Braz Oral Res.* 2009;23(Special Issue 1):39–48.
- Wilder RS, Bray KS. Improving periodontal outcomes: Merging clinical and behavioral science. *Periodontol 2000.* 2016;71:65–81.
- Donn J. Medical benefits of dental floss unproven [Internet]. Associated Press; 2016. Available from: [bigstory.ap.org/article/.../medical-benefits-dental-floss-unproven](http://bigstory.ap.org/article/.../medical-benefits-dental-floss-unproven).
- Rode SM, Gimenez X, Montoya VC, Gómez M, Blanc SL, Medina M, et al. Daily biofilm control and oral health: Consensus on the epidemiological challenge – Latin American Advisory Panel. *Braz Oral Res.* 2012;26(Special Issue 1):133–42.
- Asadoorian J. CDHA position paper on commercially available over-the-counter oral rinsing products. *Can J Dent Hyg.* 2006;40(4):1–13.
- Lorenz K, Bruhn G, Netuschil L, Heumann C, Hoffman T. How to select study designs and parameters to investigate the effect of mouthrinses? Part I: Rationale and background. *J Physio Pharm.* 2009;60(Supplement 8):77–83.
- Bolerazska B, Marekova M, Markovska N. Trends in laboratory diagnostic methods in periodontology. *Acta Medica (Hradec Kralove).* 2016;59(1):3–9.
- Rohrig B, du Prel JB, Wachtlin D, Kwicien R, Blettne, M. Sample size calculation in clinical trials: Part 13 of a series on evaluation of scientific publications. *Dtsch Arztebl Int.* 2010;107(31–32):552–56.
- Araujo MWB, Charles CA, Weinstein RB, McGuire JA, Parikh-Das AM, Du Q, et al. Meta-analysis of the effect of an essential oil-containing mouthrinse on gingivitis and plaque. *J Am Dent Assoc.* 2015;146(8):610–33.
- Van Leeuwen MP, Slot DE, Van der Weijden GA. Essential oils compared to chlorhexidine with respect to plaque and parameters of gingival inflammation: a systematic review. *J Periodontol.* 2011;82(2):174–94.
- Van Strydonck DA, Slot DE, Van der Velden U, Van der Weijden F. Effect of a chlorhexidine mouthrinse on plaque, gingival inflammation and staining in gingivitis patients: a systematic review. *J Clin Periodontol.* 2012;39(11):1042–54.
- Haps S, Slot DE, Berchier CE, Van der Weijden GA. The effect of cetylpyridinium chloride-containing mouth rinses as adjuncts to toothbrushing on plaque and parameters of gingival inflammation: a systematic review. *Int J Dent Hyg.* 2008;6:290–303.
- The Cochrane Collaboration [website]. 2016. Available from: <http://canada.cochrane.org/>.
- Barnes V, Arvanitidou E, Szewczyk G, Richter R, DeVizio W, Cronin M, Michelle S. Evaluation of the antiplaque efficacy of two cetylpyridinium chloride-containing mouthwashes. *J Clin Dent.* 2011;22(6):200–203.
- Sreenivasan PK, Haraszthy VI, Zambon JJ. Antimicrobial efficacy of 0.05% cetylpyridinium chloride mouthrinses. *Lett Appl Microbiol.* 2013;56(1):14–20.
- Rao D, Arvanitidou E, Du-Thumm L, Rickard AH. Efficacy of an alcohol-free CPC-containing mouthwash against oral multispecies biofilms. *J Clin Dent.* 2011;22(6):187–94.
- Latimer J, Munday JL, Buzza KM, Sreenivasan PK, McBain AJ. Antibacterial efficacy of a cetylpyridinium chloride-based mouthrinse against *Fusobacterium nucleatum* and in vitro plaques. *Am J Dent.* 2015;September(28 Spec No A):9A–13A.
- Schaeffer LM, Szewczyk G, Nesta J, Vandeven M, Du-Thumm L, Williams MI, Arvanitidou E. In vitro antibacterial efficacy of cetylpyridinium chloride-containing mouthwashes. *J Clin Dent.* 2011;22(6):183–86.
- Drake D, Villhauer AL. An in vitro comparative study determining bactericidal activity of stabilized chlorine dioxide and other oral rinses. *J Clin Dent.* 2011;22(1):1–5.
- Bercy P, Lasserre J. Susceptibility to various oral antiseptics of *Porphyromonas gingivalis* W83 within a biofilm. *Adv Ther.* 2007;24(6):1181–91.
- Hofer D, Meier A, Sener B, Guggenheim B, Attin T, Schmidlin PR. Biofilm reduction and staining potential of a 0.05% chlorhexidine rinse containing essential oils. *Int J Dent Hyg.* 2011;9(1):60–67.
- Nascimento AP, Tanomaru JM, Matoba-Júnior F, Watanabe E, Tanomaru-Filho M, Ito IY. Maximum inhibitory dilution of mouthwashes containing chlorhexidine and polyhexamethylene biguanide against salivary *Staphylococcus aureus*. *J Applied Oral Sci.* 2008;Sep-Oct 16(5):336–39.
- Hooper SJ, Lewis MA, Wilson MJ, Williams DW. Antimicrobial activity of Citrox bioflavonoid preparations against oral microorganisms. *Br Dent J.* 2011;210(1):1–5.
- Rawlinson A, Pollington S, Walsh TF, Lamb DJ, Marlow I, Haywood J, Wright P. Efficacy of two alcohol-free cetylpyridinium chloride mouthwashes – a randomized double-blind crossover study. *J Clin Periodontol.* 2008;35(3):230–35.
- Pizzo G, La Cara M, Licata ME, Pizzo I, D'Angelo M. The effects of an essential oil and an amine fluoride/stannous fluoride mouthrinse on supragingival plaque regrowth. *J Periodontol.* 2008;79(7):1177–83.
- Ennibi O, Lakhdar L, Bouziane A, Bensouda Y, Abouqal R. Chlorhexidine alcohol base mouthrinse versus Chlorhexidine formaldehyde base mouthrinse efficacy on plaque control: Double blind, randomized clinical trials. *Medicina Oral Patologia Oral y Cirugia Bucal.* 2013:e135–e9.

28. Garcia V, Rioboo M, Serrano J, O'Connor A, Herrera D, Sanz M. Plaque inhibitory effect of a 0.05% cetyl-pyridinium chloride mouth-rinse in a 4-day non-brushing model. *Int J Dent Hyg.* 2011;9:266–73.
29. Versteeg PA, Rosema NA, Hoenderdos NL, Slot DE, Van der Weijden GA. The plaque inhibitory effect of a CPC mouthrinse in a 3-day plaque accumulation model – a cross-over study. *Int J Dent Hyg.* 2010;8(4):269–75.
30. Marchetti E, Casalena F, Capestro A, Tecco S, Mattei A, Marzo G. Efficacy of two mouthwashes on 3-day supragingival plaque regrowth: a randomized crossover clinical trial. *Int J Dent Hyg.* 2015:1–8.
31. De Siena F, Del Fabbro M, Corbella S, Taschieri S, Weinstein R. Evaluation of chlorhexidine 0.05% with the adjunct of fluoride 0.05% in the inhibition of plaque formation: a double blind, crossover, plaque regrowth study. *Int J Dent Hyg.* 2013;11(3):186–90.
32. Hannig C, Gaeding A, Basche S, Richter G, Helbig R, Hannig M. Effect of conventional mouthrinses on initial bioadhesion to enamel and dentin in situ. *Caries Res.* 2013;47(2):150–61.
33. Malhotra R, Grover V, Kapoor A, Saxena D. Comparison of the effectiveness of a commercially available herbal mouthrinse with chlorhexidine gluconate at the clinical and patient level. *J Indian Soc Periodontol.* 2011;15(4):349–52.
34. Prasad KA, John S, Deepika V, Dwijendra KS, Reddy BR, Chincholi S. Anti-plaque efficacy of herbal and 0.2% Chlorhexidine gluconate mouthwash: a comparative study. *J Int Oral Health.* 2015;7(8):98–102.
35. Singh A, Daing A, Dixit J. The effect of herbal, essential oil and chlorhexidine mouthrinse on de novo plaque formation. *Int J Dent Hyg.* 2013;11(1):48–52.
36. Rahman B, Alkawas S, Al Zubaidi EA, Adel OI, Hawas N. Comparative antiplaque and antigingivitis effectiveness of tea tree oil mouthwash and a cetylpyridinium chloride mouthwash: A randomized controlled crossover study. *Contemp Clin Dent.* 2014;5(4):466–70.
37. He S, Wei Y, Fan X, Hu D, Sreenivasan PK. A clinical study to assess the 12-hour antimicrobial effects of cetylpyridinium chloride mouthwashes on supragingival plaque bacteria. *J Clin Dent.* 2011;22(6):195–99.
38. Amini P, Araujo MWB, Wu M-M, Charles CA, Sharma NC. Comparative antiplaque and antigingivitis efficacy of three antiseptic mouthrinses: a two week randomized clinical trial. *Braz Oral Res.* 2009;23(3):319–25.
39. Charles CA, McGuire JA, Sharma NC, Qaqish J. Comparative efficacy of two daily use mouthrinses: randomized clinical trial using an experimental gingivitis model. *Braz Oral Res.* 2011;25(4):338–44.
40. Charles CA, Amini P, Gallob J, Shang H, McGuire JA, Costa R. Antiplaque and antigingivitis efficacy of an alcohol-free essential-oil containing mouthrinse: A 2-week clinical trial. *Am J Dent.* 2012;25(4):195–8.
41. Parikh-Das AM, Sharma NC, Du Q, Charles CA. Superiority of essential oils versus 0.075% cpc-containing mouthrinse: A two-week randomized clinical trial. *J Clin Dent.* 2013;24(3):94–9.
42. Zanatta FB, Antoniazzi RP, Rosing CK. The effect of 0.12% chlorhexidine gluconate rinsing on previously plaque-free and plaque-covered surfaces: a randomized, controlled clinical trial. *J Periodontol.* 2007;78(11):2127–34.
43. Kumar S, Patel S, Tadakamadla J, Tibdewal H, Duraiswamy P, Kulkarni S. Effectiveness of a mouthrinse containing active ingredients in addition to chlorhexidine and triclosan compared with chlorhexidine and triclosan rinses on plaque, gingivitis, supragingival calculus and extrinsic staining. *Int J Dent Hyg.* 2013;11(1):35–40.
44. Charles CA, Cortelli JR, Aquino D, Revankar R, Wu MM. Gingival health benefits of essential oil, 0.075% cetylpyridinium chloride and control mouthrinses: A 4-week randomized clinical study. *Am J Dent.* 2015;28(4):197–202.
45. Elias-Boneta AR, Toro MJ, Noboa J, Romeu FL, Mateo LR, Ahmed R, et al. Efficacy of CPC and essential oils mouthwashes compared to a negative control mouthwash in controlling established dental plaque and gingivitis: A 6-week, randomized clinical trial. *Am J Dent.* 2015;28(Spec No A):21A–6A.
46. Hernandez-Cott PL, Elias Boneta A, Stewart B, DeVizio W, Proskin HM. Clinical investigation of the efficacy of a commercial mouthrinse containing 0.05% cetylpyridinium chloride in reducing dental plaque. *J Clin Dent.* 2009;20(2):39–44.
47. Lotufo R, Calil CM, Feng HS, Sekiguchi RT, Stewart B, DeVizio W, Proskin HM. Clinical investigation of the efficacy of a commercial mouthrinse containing 0.05% cetylpyridinium chloride in preventing dental plaque. *J Clin Dent.* 2009;20(2):50–54.
48. Silva MF, dos Santos NB, Stewart B, DeVizio W, Proskin HM. A clinical investigation of the efficacy of a commercial mouthrinse containing 0.05% cetylpyridinium chloride to control established dental plaque and gingivitis. *J Clin Dent.* 2009;20(2):55–61.
49. Todkar R, Sheikh S, Byakod G, Muglikar S. Efficacy of chlorhexidine mouthrinses with and without alcohol – a clinical study. *Oral Health Prev Dent.* 2012;10(3):291–96.
50. Charles CA, McGuire JA, Qaqish J, Amini P. Increasing antiplaque/antigingivitis efficacy of an essential oil mouthrinse over time: an in vivo study. *Gen Dent.* 2013;61(1):23–28.
51. Cortelli SC, Cortelli JR, Holzhausen M, Franco GC, Rebelo RZ, Sonagere AS, Queiroz CS, Costa FO. Essential oils in one-stage full-mouth disinfection: double-blind, randomized clinical trial of long-term clinical, microbial and salivary effects. *J Clin Periodontol.* 2009;36(4):333–42.
52. Cortelli SC, Cortelli JR, Shang H, Costa R, Charles CA. Gingival health benefits of essential-oil and cetylpyridinium chloride mouthrinses: a 6-month randomized clinical study. *Am J Dent.* 2014;27(3):119–27.
53. Cortelli SC, Cortelli JR, Shang H, McGuire JA, Charles CA. Long-term management of plaque and gingivitis using an alcohol-free essential oil containing mouthrinse: a 6-month randomized clinical trial. *Am J Dent.* 2013;26(3):149–55.
54. Cortelli SC, Cortelli JR, Wu MM, Simmons K, Charles CA. Comparative antiplaque and antigingivitis efficacy of a multipurpose essential oil-containing mouthrinse and a cetylpyridinium chloride-containing mouthrinse: A 6-month randomized clinical trial. *Quintessence Int.* 2012;43(7):e82–e95.
55. Sharma NC, Araujo MWB, Wu M-M, Qaqish J, Charles CH. Superiority of an essential oil mouthrinse when compared with a 0.05% cetylpyridinium chloride containing mouthrinse: a six-month study. *Int Dent J.* 2010;60(3):175–80.

56. Ayad F, Prado R, Mateo LR, Stewart B, Szewczyk G, Arvanitidou E, Panagakos FS. A comparative investigation to evaluate the clinical efficacy of an alcohol-free CPC-containing mouthwash as compared to a control mouthwash in controlling dental plaque and gingivitis: a six-month clinical study on adults in San Jose, Costa Rica. *J Clin Dent*. 2011;22(6):204–12.
57. Costa X, Laguna E, Herrera D, Serrano J, Alonso B, Sanz M. Efficacy of a new mouth rinse formulation based on 0.07% cetylpyridinium chloride in the control of plaque and gingivitis: a 6-month randomized clinical trial. *J Clin Periodontol*. 2013;40(11):1007–15.
58. Albert-Kiszely A, Pjetursson BE, Salvi GE, Witt J, Hamilton A, Persson GR, Lang NP. Comparison of the effects of cetylpyridinium chloride with an essential oil mouth rinse on dental plaque and gingivitis – a six-month randomized controlled clinical trial. *J Clin Periodontol*. 2007;34(8):658–67.
59. Gunsolley JC. Uncontrolled randomized clinical trial demonstrates similar long-term (6 months) antigingivitis and antiplaque efficacy for 2 mouth rinses: One that uses cetylpyridinium chloride (CPC) as an active agent and the other that uses essential oils (EO) as an active agent. *J Evid Based Dent Pract*. 2008;8(2):85–86.
60. Walker E, Nowacki AS. Understanding equivalence and noninferiority testing. *J Gen Intern Med*. 2011;26(2):192–96.
61. Chen Y, Wong RW, McGrath C, Hagg U, Seneviratne CJ. Natural compounds containing mouthrinses in the management of dental plaque and gingivitis: a systematic review. *Clin Oral Investig*. 2014;18(1):1–16.
62. Drugs and Health Products. Health Canada's Clinical Trials Database [website]. Canada: Health Canada; 2016 [updated 2016-06-07]. Available from: <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/databasdonclin/index-eng.php>.
63. BioMed Central. ISRCTN registry [website]. 2016. Available from: <http://www.isrctn.com/>.
64. National Institutes of Health. ClinicalTrials.gov [website]. Available from: <https://clinicaltrials.gov/>.
65. Consumer Health Products Canada [website]. Ottawa: Consumer Health Products Canada; 2012. Available from: <http://www.chpcanada.ca/en/consumer-health-products-you/consumer-health-products>.
66. The Canadian Dental Association [website]. Available from: <https://www.cda-adc.ca/en/index.asp>.
67. American Dental Association. Science and research [website]. 2016. Available from: [www.ada.org/science-research](http://www.ada.org/science-research).
68. American Dental Association. ADA seal of acceptance [website]. 2016. Available from: <http://www.ada.org/en/science-research/ada-seal-of-acceptance/how-to-earn-the-ada-seal/guidelines-for-product-acceptance>.
69. Afenich FS, Slot DE, Hossainian N, Van der Weijden GA. The effect of hexetidine mouthwash on the prevention of plaque and gingival inflammation: a systematic review. *Int J Dent Hyg*. 2011;9(3):182–90.
70. Loe H. Oral hygiene in the prevention of caries and periodontal disease. *Int Dent J*. 2000;50(3):129–39.
71. Sharma N, Charles CH, Lynch MC, Qaqish J, McGuire JA, Galustians JG, Kumar LD. Adjunctive benefit of an essential oil-containing mouthrinse in reducing plaque and gingivitis in patients who brush and floss regularly. *JADA*. 2004;135(4):496–504.
72. Sharma S, Saimbi CS, Koirala B, Shukla R. Effect of various mouthwashes on the levels of interleukin-2 and interferon-gamma in chronic gingivitis. *J Clin Pediatr Dent*. 2008;32(2):111–14.
73. Haas AN, Reis A, Lemos CA, Pannuti CM, Escobar E, Almeida ER, et al. Daily biofilm control and oral hygiene: An epidemiological challenge consensus. *Braz J Periodontol*. 2012;22(3):7–13.
74. LISTERINE® Tips and Practices [website]. Johnson & Johnson Inc.; 2014 [updated May 2016]. Available from: <http://www.listerine.ca/tips-and-practices>.
75. Lisante TA, McGuire JA, Williams KP. The staining potential of various currently marketed mouthrinses. *J Clin Dent*. 2013;24(1):5–11.
76. Kerr AR, Corby PM, Kalliontzi K, McGuire JA, Charles CA. Comparison of two mouthrinses in relation to salivary flow and perceived dryness. *Oral Surg Oral Med Oral Pathol Oral Radiol*. 2015;119(1):59–64.
77. Gandini S, Negri E, Boffett P, La Vecchia C, Boyle P. Mouthwash and oral cancer risk – Quantitative meta-analysis of epidemiologic studies. *Ann Agric Environ Med*. 2012;19(2):173–80.
78. Ahrens W, Pohlabeln H, Foraita R, Nelis M, Lagiou P, Lagiou A, et al. Oral health, dental care and mouthwash associated with upper aerodigestive tract cancer risk in Europe: The ARCADE study. *Oral Oncology*. 2014;50:616–25.
79. Stoeken JE, Paraskevas S, van der Weijden GA. The long-term effect of a mouthrinse containing essential oils on dental plaque and gingivitis: a systematic review. *J Periodontol*. 2007;78(7):1218–28.