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A Review of the Effectiveness of Antiseptic Mouth Rinses for Oral Health

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Abstract

This narrative review evaluates current evidence related to the effectiveness of various mouth rinses available in retail outlets considered to be anti-plaque and anti-gingivitis agents. There is a plethora of commercial mouth rinses available and it becomes mandatory for a clinician to understand the specifics of oral rinses to be able to choose an appropriate rinse for a patient. This review provides an insight on the available mouth rinses for the reduction of plaque and gingivitis as well as the rationale for their use, mechanisms of action, benefits, adverse effects and precautions.

Keywords: Mouth rinse; Essential oils; Chlorhexidine; Cetylpyridinum chloride; Antiplaque agents; Antigingivitis agents; Anti-infective agents

Introduction

Gingivitis, an inflammatory condition of the gingiva at the necks of the teeth, becomes a serious health concern when it progresses to periodontitis. The most common type of gingivitis is a chronic form induced by bacterial biofilms known as plaque [1]. Chronic gingivitis can progress to periodontitis, where the gingival inflammation results in tissue destruction and bone resorption around the teeth that can ultimately lead to tooth loss. Not all cases of gingivitis progresses to periodontitis; the patient must be susceptible to the development of periodontitis [1]. As per the literature, periodontitis is always preceded by gingivitis, supporting the need for control [2].

As a primary etiological factor, control in plaque is mandatory for primary prevention of gingivitis [1,3]. Plaque is essential, but insufficient to cause periodontitis [3] and should be controlled.

Although mechanical plaque control is the most effective method of plaque removal [4], mechanical removal alone is insufficient to control plaque as some residual plaque is frequently left behind after brushing and flossing [5-8]. A chemotherapeutic agent could be beneficial as an adjunct to self-performed oral hygiene [5,6].

Many types of mouth rinses, claiming anti-plaque effects, are available. Commonly found mouth rinses include bisbiguanides, phenolics and quaternary ammonium antiseptics, as well as oxygenating agents, metal ions and natural products [9,10]. Numerous studies have been done recently to determine the efficacy of these mouth rinses against supragingival plaque and gingivitis. To date, essential oil mouth rinses (such as Listerine®) and Bisbiguanide mouth rinses (such as Chlorhexidine) have been accepted as adjuncts to mechanical cleaning by the American Dental Association (ADA) [11,12]. Following is a narrative of literature focusing on mouth rinse research. The literature was sourced from databases searches of MEDLINE, PubMed, Web of Science and Embase.

Bisbiguanides

Chlorhexidine is a bisbiguanide cation, popular as a mouth rinse due to its anti-plaque and anti-gingivitis effect and considered as the 'gold standard' [13,14]. It has a broad spectrum antibacterial action [15] and removes plaque by its cationic action. The positive charges of chlorhexidine react with the negatively charged microbial cell surface. This action increases the cellular membrane permeability by disrupting the osmotic barrier and interfering with membrane transport [16]. It also has the ability to bind to the outer membrane of plaque bacteria and reduce their adherence to epithelial cells as proven in Porphyromonas gingivalis [17]. By its actions, it inhibits new plaque formation rather than reducing pre-existing plaque deposits [10]. It is the least toxic, since it is poorly absorbed by the gastrointestinal tract [18]. Also, there has been no evidence of risk of cancer or teratogenesis with long term use [19].

The adverse effects of chlorhexidine include staining of teeth, mucous membranes, tongue, supragingival calculus and restorations [20]. Tooth staining seems to be the result of a local precipitation reaction between tooth-bound chlorhexidine and chromogens found within foodstuffs and beverages [21,22]. The stains produced by this mouth rinse are very difficult to remove and requires the use of ultrasonic scalers [10]. Other adverse effects reported are alteration of taste sensation for up to 4 hours after rinsing [20], rare occurrences of parotid swelling, mucosal erosion and risk of the formation of supragingival calculus and slight elevation in blood pressure [23]. Therefore, its use should be limited to not more than two to three weeks.

The most important property of chlorhexidine which makes it very popular is substantivity. It is adsorbed into the mucosal surfaces and remains for more than 12 hours [24]. This prolonged action makes it suited for plaque formation inhibition [25,26]. Due to the cationic nature of the chlorhexidine molecule, the activity of the agent is rapidly reduced in the presence of anionic agents, particularly those found within certain types of toothpaste. It is best to have an interval between tooth brushing and chlorhexidine rinsing of at least 30 minutes to two hours after brushing to prevent interaction between the negatively charged sodium lauryl sulphate and sodium monofluorophosphate in the toothpaste and chlorhexidine [27]. This interaction makes the chlorhexidine ineffective [27].

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There are two common preparations of chlorhexidine available; 0.2% and 0.12%. A systematic review by Berchier et al. [28] evaluated the effects of 0.12% chlorhexidine mouth rinse compared with 0.2% on plaque and periodontal parameters. Little information related to the effect on gingival inflammation was available. With respect to plaque inhibition, the results showed a small but significant difference in favor of the 0.2% chlorhexidine concentration; the clinical relevance of this difference is probably negligible. It can be concluded that both formulations are equally effective [28,29]. It is important to note that the lower concentration reduces the side effects but maintains the benefits [30].

Until now, chlorhexidine has been proven to be the most effective anti-plaque agent. Gunsolley's systematic review provides strong evidence regarding the anti-plaque and anti-gingivitis agents that are efficacious [31]. His meta-analysis concluded that there is strong evidence supporting the efficacy of chlorhexidine as an anti-plaque and anti-gingivitis agent [31,32]. Six studies supported the strong anti-plaque and anti-gingivitis effect of mouth rinses with 0.12% chlorhexidine mouth rinse and the results were remarkably consistent and statistically significant [31].

Van Leewen and colleagues conducted a systematic review to evaluate the effects of essential oil mouth rinse compared to chlorhexidine mouth rinse in terms of plaque and gingival inflammation parameters. The results revealed that compared to essential oil mouth wash, chlorhexidine mouth rinse provided better results against plaque. However, for long-term control of gingivitis, the essential oil mouth wash is not different from the chlorhexidine [33]. This was reconfirmed in a systematic review in 2012 [34], which included 19 randomized clinical or controlled trials comparing the effects of essential oil mouth wash with chlorhexidine on plaque and calculus accumulation, tooth staining and gingival inflammation. This review concluded that, in short and long term studies, chlorhexidine were significantly better at reducing plaque accumulation than the essential oil mouth wash. However, as far as staining and calculus accumulation were concerned, they were greater among chlorhexidine users compared to essential oil mouth wash users. Both mouth rinses were not different with respect to the long-term control of gingival inflammation [34].

The anti-plaque and anti-gingivitis effect of chlorhexidine is well documented [35]. Chlorhexidine 0.2%, irrespective of the formulation, either gel or mouthwash, is equally effective in reducing plaque and gingival indices [36]. Moreover, a double-blind cross over study by Papaionnou and colleagues (2015) compared the clinical efficacy of alcohol and alcohol free formulations of 0.2% chlorhexidine rinses and found that the alcohol-free rinse had comparable levels of action as the alcoholic rinse of chlorhexidine [37].

Two recent meta-analyses which included all randomized controlled clinical trials comparing chlorhexidine to placebo/control mouth rinses for oral hygiene of at least 4 weeks duration, showed that chlorhexidine together with oral hygiene versus placebo or control mouth rinse provided significant reductions in plaque and gingivitis scores, but a significant increase in staining scores [38,39].

The comprehensive body of evidence supports chlorhexidine gluconate as the gold standard mouth wash and its use as the comparator in research studies due to its superior anti-plaque and substantivity properties [21,24].

Phenolics: essential oils

Phenolic compounds have been used as antiseptics for over a century [4,40]. They exert their antibacterial action by disrupting cell membranes and inhibiting enzyme activity [41,42] and are known to have anti-inflammation effects [43,44].

One of the most popular phenolic mouth rinses is Listerine® with moderate plaque inhibitory and anti-gingivitis effects [45]. They consist of four phenol-related essential oils eucalyptol, menthol, thymol and methyl salicylate in a 20-26% alcohol medium. The moderate plaque inhibitory effects are less than that of chlorhexidine and could be attributed to its poor oral retention as it does not exhibit the property of substantivity [45]. Being a phenol, it acts by penetrating the lipid cell wall of the bacteria and inhibit the bacterial enzymes, destroying the bacteria [46]. Its anti-inflammatory effects are probably due to its antioxidant activity [47].

There are concerns regarding the high alcohol concentration but the amount has not been found to be harmful to human tissues [48,49]. Listerine does not affect taste perception or increase calculus formation [50] and has no staining effects [51]. It does not have any interaction with toothpaste and can, therefore, be used immediately after brushing [4].

According to Gunsolley's systematic review [31], the highest proportion of randomized clinical trials (21 studies) supported the efficacy of mouth rinses with essential oils [31]. All of the studies, except for one, showed consistent results. It can be concluded that there is a high level of evidence supporting the anti-plaque and anti-gingivitis efficacy of essential oils when used long term with mechanical oral hygiene measures.

Gunsolley's findings are supported by Van Leeuwen and colleagues comparing the anti-plaque and anti-gingivitis efficacy of essential oils and other mouth rinses using a systematic review and meta-analysis [33]. More support is provided by a systematic review by Stoeken including 11 randomized clinical trials on the long-term effect of essential oil mouth washes on dental plaque and gingivitis. The results were consistent and concluded that when used as an adjunct to unsupervised oral hygiene, essential oil mouth washes provide an additional benefit about plaque and gingivitis reduction as compared to a placebo or control [52].

A meta-analysis of epidemiologic studies by Gandini and colleagues [53] and Boyle and others [54] regarding the use of mouth rinse and common oral conditions indicated a clear benefit in reducing the risk of dental plaque, gingivitis and caries with no major adverse effects. Specifically, they found no statistically significant association between the use of mouthwash containing alcohol and oral cancer risk.

A recent meta-analysis by Marcelo and others [55] considered the adjunctive use of essential oil mouth washes relative to mechanical oral hygiene alone. The study included 29 randomized, long term clinical trials and demonstrated clinically significant, site-specific benefits of adjunctive essential oil mouth rinse treatment in people within a 6-month period between dental visits [55].

Due to possible ethanol-induced mucosal irritation and dryness, these mouth rinses have not been recommended to patients suffering from xerostomia, dental erosion due to a low oral pH, or oral mucosal diseases. They are also prohibited for children due to the risk of accidental ingestion of high doses of ethanol [51]. A meta-analysis of 18 epidemiological studies on mouthwash use and oral malignancy specifically, mouthwashes containing >25% alcohol revealed no statistically significant association between mouthwash use and risk of oral cancer including no significant trend in risk with increasing daily

use as well as no association between use of mouthwash containing alcohol and oral cancer risk [53].

Non-alcohol based formulations of Listerine are now available in the market. Systematic review studies on essential oil mouth washes with or without alcohol showed no significant difference in efficacy. Alcohol contributed no added therapeutic value [56].

Quaternary ammonium compounds

Cetylpyridinium is a quaternary ammonium compound with a cationic action similar to chlorhexidine. It has a broad spectrum antimicrobial action and has been found to be effective in preventing supragingival plaque formation and gingivitis [57]. However, these effects are less compared to chlorhexidine probably due to the rapid desorption from the oral mucosa [58]. The side effects of cetylpyridinum are similar to chlorhexidine, however, usually very mild [59]. It has a substantive action of up to 6 hours following rinsing [60]. Similar to chlorhexidine, the activity of cetylpyridinum chloride is adversely affected by toothpaste if used immediately after the antiseptic (Sheen et al., 2001). There are several formulations of cetylpyridinum chloride in the market varying from 0.045 to 0.07%. Both alcohol containing and alcohol free products are available [61].

The clinical benefits of cetylpyridinum chloride as a mouth rinse, when compared to inactive controls, are very limited [59]. According to a systematic review by Haps and colleagues, concerning cetylpyridinum mouth rinses, when used as adjuncts to either supervised or unsupervised oral hygiene, contributed a small but significant additional benefit in reducing plaque accumulation and gingival inflammation [62].

A meta-analysis by Herera (2009) on randomized clinical trials and controlled clinical trials using cetylpyridinum mouth rinse longer than 4 weeks, highlighted that its use should be considered with caution owing to the heterogeneity of the pooled studies and limitations of the meta-analyses performed [63]. Support for the caution is provided by Gunsolley's meta-analysis (2006) on mouth rinses used for a period of 6 months, revealed inconsistent results for products containing cetylpyridinum chloride. The author could not draw a conclusion regarding the efficacy of cetylpyridinum chloride-containing mouth rinses since the formulations of the cetylpyridinum chloride-containing mouth rinses varied, with concentrations ranging from 0.045 to 0.07%. There were two studies that evaluated a 7% concentration. One study involved formulations that were alcohol-based [64] and other non-alcohol-based [65]. The six-month results were promising for the non-alcohol-based 7% concentration agent, however more long-term studies are needed to provide the same level of evidence that exists for the other agents [31].

Natural products

Though herbal agents have limited side effects, research should be done to determine their effectivity. Controversial evidence exists regarding the effectiveness of these mouth rinses. A meta-analysis by Manipal and colleagues pooled 11 randomized clinical trials comparing the effects of herbal mouth rinses with chlorhexidine mouth rinse with only two studies favouring the use of herbal products [66]. The successful rinses are neem (Azadirachta indica), Aloe vera (Aloe perfoliata L. var. vera) and tea tree oil (Melaleuca alternifolia) [66].

Aloe vera gel does not contain any alcohol or artificial additives. It consists of three very active ingredients namely Echinecea, golden seal and grape fruit seed extract. They exhibit anti-inflammatory and anti-fungal therapeutic effects [67]. One study by Kaim and colleagues, found Aloe vera gel to be significantly better than chlorhexidine and essential oils [68]. A second study by Haffajee and others, produced controversial results with chlorhexidine superior to Aloe vera and Aloe vera superior to essential oils [67]. Two other studies also gave similar results [68]. Studies done by Gupta and others indicated that Aloe vera mouth rinse is equally effective in reducing gingivitis and plaque as chlorhexidine [69]. Further clinical trials are needed to establish the efficacy of this mouth rinse.

Tea tree oil, a well-known natural disinfectant also called Melaleuca oil, is taken from the leaves of Melaleuca alternifolia, a plant native to Australia. A randomized clinical trial done by Rahman and colleagues supports the use of tea tree oil as an anti-plaque agent in comparison with cetylpyridinum [70]. However, the study has its own weaknesses in terms of duration of study and sample size. Further clinical trials with longer duration are warranted to establish its effectiveness.

Neem leaves, due to their excellent anti-inflammatory properties have been used in the treatment of periodontal diseases. Neem stick extract has been studied extensively and shown to have excellent bacterial aggregation properties [71] suggesting that it could reduce streptococci colonization on the surface of the tooth. A. indica extract has significantly reduced the plaque index and bacterial count as compared to positive controls (chlorhexidine 0.2%) [72,73].

Dill (Anethum graveolens), a herb, is known for its carminative properties that soothes the digestive system. Dill seed oil has been extracted from the dried seeds through a steam distillation method. Considering its antimicrobial and antioxidant properties, a double blind randomized clinical trial has been conducted in 2016 to compare the effectiveness of 0.2% chlorhexidine gluconate and dill seed mouth rinse on plaque levels and gingivitis [74]. Results revealed no significant difference in gingival and plaque scores among two mouth rinses [74]. Further trials are warranted.

Another herb, Ocimum sanctum, known as the "Queen of herbs" has been tested for its anti-plaque and anti-gingivitis properties compared to chlorhexidine and normal saline in a triple blind randomized control trial. The results indicated that Ocimum sanctum mouth rinse may prove to be an effective mouthwash owing to its ability in decreasing periodontal indices by reducing plaque accumulation, gingival inflammation and bleeding [69]. However, clinical trials of longer duration with a larger sample size should be carried out to study the effectiveness of Ocimum sanctum as a mouthwash for commercialization.

An extract of a herb, Sanguinaria canadensis, has been used to produce a mouth rinse at 0.03% with anti-plaque and anti-gingivitis properties [59]. Its chemical action is due to the iminium ions and may be partly due to the zinc present in the formulation. It exhibits properties of substantivity for several hours and low toxicity due to poor absorption from the gastro-intestinal tract [75]. However, limited evidence is available regarding its effectiveness. Studies comparing Sanguinarine rinse with chlorhexidine and essential oils have shown Sanguinarine to be less effective than the other two mouth rinses in terms of supragingival plaque removal and ineffective as an anti-gingivitis agent [76].

Although several herbal products have been tested, conclusive results are still lacking [77]. According to the meta-analysis by Manipal and colleagues, less documented evidence is available for herbal studies; their use should only be advised with more scientific evidence [66].

Metal ions

Metal ions have demonstrated significant anti-plaque activity. Of these copper, tin and zinc have been studied extensively. Copper and tin show local effects of staining. Stannous fluoride, though, has been found to be an effective anti-plaque and anti-gingivitis agent. However, due to its staining effects it cannot be used on a long term basis. The evidence regarding its efficacy is also limited. Aluminium triformate, an aluminium salt, has been used to control "bleeding gums" for decades in Europe. Other compounds of aluminium salts [aluminium-containing mouth rinses] have shown a reducing effect on bacterial growth and plaque formation [78,79], however further studies with larger sample sizes are needed to confirm the findings. Also, data are not available for its effects on gingival inflammation and plaque formation. Azaripour and colleagues conducted a short-term pilot clinical trial which provided evidence that the modified sulcus bleeding index was significantly reduced in the aluminium triformate group compared to the placebo group [80]. Long-term controlled clinical trials are required to provide evidence of the effectiveness of aluminium triformate.

Miscellaneous

Oxygenating agents such as hydrogen peroxide, sodium peroxiborate and peroxycarbonate have been shown to have excellent broad spectrum antibacterial action [81]. Their action is due to the liberation of nascent oxygen to loosen debris, remove stains and destroy anaerobic organisms. Though used for several years for disinfection purposes of oral tissues, limited evidence is available regarding their use as anti-plaque and anti-gingivitis agents.

Triclosan, a phenol, non-ionic antiseptic agent has plaque inhibitory effects, but to a much lesser extent than chlorhexidine. It has also been proven to be an anti-gingivitis agent due to its anti-inflammatory effects of inhibiting cyclo-oxygenase and lipoxygenase which in turn reduce prostaglandins and leukotrienes mediators of inflammation [82] and lipid penetrating ability.

Triclosan-containing formulations are not as effective as chlorhexidine, probably due to Triclosan's limited ability to bind intra-orally [75]. It is being used in combination with other agents to improve its retention. Triclosan, in combination with gantrez copolymer have been found to be more effective [83]. However, further studies with larger sample sizes are needed to confirm the effectiveness of Triclosan and Gantrez-based mouth rinses.

Short-term trials of Triclosan/copolymer mouth rinses (Colgate® Total Plax) provided evidence of significant effectiveness in plaque outcomes when measured against controls but it is still significantly less effective than chorhexidine [84]. A mouth rinse containing 0.3% Triclosan/2.0% copolymer (Colgate® Total Plax (USA)) has beneficial effects on plaque formation and gingivitis reduction [85,86]. Most of the trials on Triclosan have been performed on dentifrices and long term clinical trials are warranted with regard to the rinses.

Conclusion

Although manufacturers might claim advantages in levels of effectiveness of plaque-inhibiting mouth washes, a dental practitioner, for the safety of their patients, should base their decisions on available scientific level of evidence.

Chlorhexidine still remains the first choice when plaque control is the focus of therapy and the most reliable alternative is essential oil mouth rinses. No difference between chlorhexidine and essential oil mouth rinses with respect to gingivitis was observed (34,87). Systematic reviews have shown beneficial effects of mouth rinses as anti-plaque and anti-gingivitis agents when used as adjunct to mechanical cleaning aids. The strongest level of evidence supports chlorhexidine and essential oils as well as a moderate effect of cetylpyridinium chloride. Long term clinical trials are essential for other mouth rinses.

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