

## Formulation of Antibacterial Mouthwash from Local Herbs: A Mini-Review

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### ABSTRACT

Commercially available mouthwash formulations are often medicated and contain chemicals that may elicit adverse effects to the users. A mouthwash may be recommended for its efficacy in preventing dental caries and other oral conditions due to its antimicrobial, anti-inflammatory and analgesic properties. Therefore, it is essential to raise awareness in selecting for an appropriate mouthwash that is safe to be applied to the oral cavity and its natural microflora. The interest towards the incorporation of herbal ingredients in oral products has been increasing exponentially over the years. The main objective of this review is to highlight our consumption of food and herbal products, such as Aleppo oak, clove and turmeric, that contain medicinal properties and have the potential to be developed as key components in mouthwash formulations. Thus, reliance on the use of chemicals may lessen as they could have a negative impact to one's oral health.

### INTRODUCTION

There is an increasing awareness of the disadvantages of alcoholic mouthwash formulations due to their harmful chemicals, such as the cetylpyridinium chloride [CPC] and therefore an extemporaneously prepared herbal mouth-washes will be an option [1]. Thus, there is an increasing tendency towards replacing the commonly used mouthwashes with safer products made from natural ingredients that are less harmful and amenable of giving the same or better effects compared to chemical mouthwash. Several mouthwash companies are now trying to reduce the number of harmful chemicals in their mouthwash formulations by replacing them with more natural

ingredients inspired by homemade-developed recipes. This mini review aims to look into the potential of developing a new kind of mouthwash that is safer, user friendly, and made mainly from herbal ingredients.

Studies on the development and commercialization of a mouthwash made mainly from herbs are gaining popularity. Understanding the role of naturally existing chemicals in herbs and the overall benefits they could impart to oral health and hygiene are the focused of this review. This could also raise awareness of the potential harm that chemical mouthwash formulations may exert on the oral cavity and to its natural and beneficial microbiota. Therefore, investigation in this aspect will

provide a better understanding of the oral microbe, their growth requirements, and their inhibition.

### Oral microbiota

The human body is continuously inhabited by different kinds of microorganisms. The microorganisms in the oral cavity, in particular, take advantage of the watery, mucosal environment, the nutrient leftovers, and the warm temperature in the mouth which are essential for microbes to flourish [2]. The microbes that permanently reside within or onto the oral surfaces are referred to as the oral microbiota. The oral cavity is a non-homogenous environment for microbial colonization as it contains mucosal surfaces in the lips, cheek, palate, and tongue, and hard teeth surfaces. Oral microflora mostly varies from facultative, microaerophilic, capnophilic, and obligately anaerobic species [3]. In addition, the oral cavity is continuously bathed with saliva which has a big influence on the ecology of the mouth. The mean pH of the saliva is maintained between 6.7-7.3, which is favorable for microbial growth and colonization [4].

According to Gao, Xu [5], oral microorganisms were first discovered and described by Antonie van Leeuwenhoek, a Dutch businessman and scientist. In 1680, he reported the presence of “little living animalcules” in his own dental plaque [6]. Oral microbes are considered to be “chemoparasitic” that consume carbohydrates and convert them into acid which damages the teeth [7]. In 1924, J. Clarke isolated an organism which we now know as *Streptococcus mutans* from cariogenic lesions. Unfortunately, he was not able to attribute *S. mutans* as a causative agent of dental plaques [8]. Since 1950, there has been an increasing interest in using experimental animal models to better understand the nature and etiology of oral diseases, including dental caries. In 1960, [9] published two important papers using hamsters as animal models that showed the infectious and transmissible nature of dental caries [10]. Moving further, [11] tackled the “nonspecific plaque hypothesis” that pointed out that dental caries arises from the combined efforts of all organisms in the oral biome. This also postulated that the accumulation of activity of all types of dental plaque is responsible for oral disease, regardless of the virulence of the specific pathogens involved. The improvement of culturing techniques and sampling strategies over the years led to the identification of several oral microbiomes and the characterization of their lifestyle where they mainly exist as biofilms. Biofilms are defined as aggregates of microorganisms in which the associated cells are frequently embedded in a self-produced matrix of extracellular polymeric substances [12] that are adherent to surfaces [13]. Further discoveries of oral microbes resulted from technological advancements that enabled the efficient tracking of microbial DNA and RNA.

A healthy mouth represents a good example of a host supporting millions of microbes without disrupting commensal and mutualistic relationships in the body. The bacterial-oral cavity mutualistic relationship starts after birth when bacterial species begin to inhabit and colonize the mouth. Other factors like diet, environment, hormones and personal hygiene could encourage for more microflora to inhabit the mouth [14]. A common example of an oral bacterium that has a commensal relationship with the human mouth is *Streptococcus salivarius*, a Gram-positive, facultative anaerobic bacterium, that colonizes the oral cavity and the upper respiratory tract of humans just a few hours after birth. Some strains of *S. salivarius* produce bacteriocin which targets cariogenic bacterial species, such as *S. mutans*. Some of these strains were even effective in antagonizing growth of other pathogenic bacteria in the mouth. Several studies associated the presence of *S. salivarius* in the

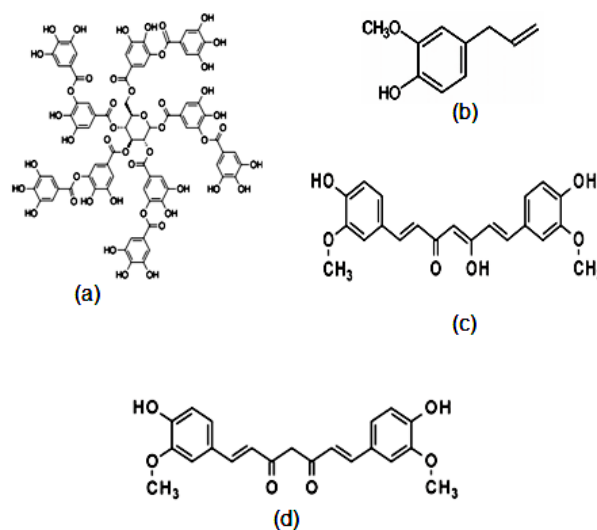
mouth with lesser incidence of streptococcal-induced pharyngitis and reduced susceptibility to rheumatic heart disease [15].

Apart from the beneficial role of oral microbes, a myriad of bacterial species has also been shown to cause serious oral conditions leading to dental caries and gingivitis among others. Some of these microbes were even reported of spreading to other body parts and organs. *S. mutans*, in particular, is a commonly isolated bacterium in the oral cavity which is a significant contributor to tooth decay. *S. mutans* and other tooth decay-causing bacteria adhere sufficiently to dental tissues which may cause destruction of the tooth following the active metabolism of sucrose and release of lactic acid as byproduct. Consequently, the acidic pH would then mineralize the tooth enamel eventually leading to tooth decay [16].

There are bacterial species other than *S. mutans* that have been linked to pathogenic cases not only in the oral cavity, but also affecting the general health of the body. Although there have been attempts to develop vaccines against parasitic oral bacteria, majority of which failed to confer positive results in humans [17]. As of the moment, the most effective solution to ward off harmful microorganisms is by maintaining proper mouth hygiene. This may take the form of regularly brushing the teeth and of using dental floss and a suitable mouthwash.

### Herbs as ingredients for mouthwash formulations

The earliest use of natural mouthwash is credited to Indians and Chinese [18]. The ancient people, who lived more than 1800 years ago, used mouthwash as part of their culture [19]. Since then, herbs and their natural oils (Fig. 1) have been incorporated in several mouthwash recipes [20]. These herbs include clove, oak gall, turmeric, neem, rosemary, ginger, peppermint and tea leaves [21]. In addition to herbs, other ingredients like salt and vinegar are also added to provide better mouth protection and to preserve the quality of the mouthwash. In the succeeding sections, we enumerated several herbs that may have the potential to be used in mouthwash formulations.



**Fig. 1.** Chemical structures of secondary compounds from selected herbs that may be used in mouthwash formulations. (a) tannin; (b) eugenol (c) curcumin in enol form (d) curcumin in keto form. [22].

### Aleppo Oak

*Quercus infectoria* or Aleppo oak is a herbal plant that grows in the Central, South, and Southwest Asia, as well as some parts of the Southern Europe around the Mediterranean Ocean. The oak tree belongs to the Fagaceae family and is commonly referred to as gall oak [23] or manjakani among the local people in Malaysia [24]. Various parts of the plant are used in herbal medicine, including its leaves, seeds, bark and galls. Aleppo oak is valued in traditional medicine due to its high tannin content, approximately 50-70% [25]. The tannin within the oak is a weak acid polyphenol and is considered a potent antioxidant agent [26]. Furthermore, this secondary compound is also valued for its industrial application in the production of leather, feed stocks and beverages [27]. In addition to that, it is also used in medical laboratory techniques as in the case of immunocytochemistry. Apart from its antioxidant property, Aleppo oak has been found to confer antibacterial effects. Its hydrolyzable tannin was found to degrade bacterial cell wall and disturb the integrity of the cytoplasmic membrane and the inner content of the cell [28]. Aleppo oak is also known to confer anticancer and analgesic properties [29]. These characteristics make Aleppo oak one of the most useful ingredients in formulating an antibacterial mouthwash as it can degrade bacteria, especially the gram-positive ones, and can provide relief from toothache and gingivitis [30].

### Clove

Cloves are the aromatic flower buds of the *Syzygium aromaticum* tree which belongs to the Myrtaceae family. It is used as a spice for food seasoning due to its strong flavor and aromatic smell [31]. Clove does not only give flavor to food, but is also used to antagonize growth of foodborne bacteria, such as *Staphylococcus aureus*, *Bacillus subtilis*, *Salmonella typhimurium* and *Listeria monocytogenes* [32]. The compound responsible for clove aroma is eugenol which constitutes about 72-90% of its essential oil [33]. Eugenol is a weak acidic phenylpropanoid which is slightly soluble in water and highly soluble in organic solvents. Similar to tannins found in Aleppo oak, eugenol is also a potent antibacterial agent that could damage the cell wall by denaturing proteins and phospholipids, eventually leading to cell lysis [34].

In addition to its antibacterial activity, clove and its essential oil have been reported to possess analgesic and anti-inflammatory properties. Thus, clove has been a popular ingredient of choice in many oral hygiene products, such as toothpaste and mouthwash formulations [35]. In dentistry, eugenol from clove is combined with zinc oxide and is used as a temporary filler of cavities [36]. Some studies also pointed out the potential application of clove and its essential oil in treating cancer.

### Turmeric

Turmeric or *Curcuma longa* is a flowering plant that belongs to the Zingiberaceae family, the same family as ginger [37]. It mainly grows in South and Southeast Asia, particularly in India. Turmeric is known for its distinctive yellow color and aroma which makes it one of the main spices in Asian cuisines [38]. Ancient people also used turmeric as a colorizing agent and as part of traditional medicine [39]. Different cultures around the world have various applications for turmeric. For instance, in India, turmeric is used in curries; in Japan, it is served as tea; in Thailand, it is used in cosmetics; in China, it is used as a coloring dye; in Korea, it is served in drinks; in Malaysia, it is used as an antiseptic and in many cooking recipes; in Pakistan, it is used as an anti-inflammatory agent; and in the United States, it is used as a preservative and colorizer for many food products, such as the mustard sauce, cheese, butter and potato chips [40]. The main

chemical component in turmeric is the polyphenolic compound curcumin. Curcumin or diferuloylmethane is a water-insoluble pigment extracted from turmeric roots [41]. Curcumin exhibits an enolic form in organic solvents and a keto form in water which give rise to many of its chemical properties [42].

In medicine, curcumin is valued for its inhibition of Gram-positive and Gram-negative bacteria [43]. It showed good antibacterial activity against periodontopathic agents, such as *Porphyromonas gingivalis* and *Prevotella intermedia* [44]. In addition to that, curcumin also harbors an anti-plaque activity and is found to be effective in reducing tooth pain and swelling [41]. These properties further support the potential use of turmeric as an ingredient in mouthwash formulations. Apart from these biological activities, turmeric has also been found to possess an antioxidant, antiapoptotic, anti-inflammatory, anticancer, and wound healing properties [45].

### Current trends in mouthwash formulations and future prospects

According to the World Health Organization [WHO], more than 80% of the world's population depend on traditional medicine for their primary healthcare needs [46]. Mouthwash formulations are frequently prescribed by dentists for the prevention and treatment of pathologic conditions in the mouth [19]. However, the market offers a wide variety of mouth rinses that are freely used by patients without medical supervision. For all kinds of practices, patients need not only to be aware of the benefits they can get from commercial products, but also their relevant adverse effects and harm [47]. One of the most common side effects of a mouthwash is staining the dental enamel. This is attributed to chemicals added to enhance the mechanical property and antibacterial effects of a mouthwash. An example of this is the nano zinc oxide which is an alternative to chlorhexidine [48] and has been extensively employed in dentistry [49].

Mouthwash companies are becoming aware of the adverse effects of these chemicals and are directed towards the production of mouthwashes made mainly from herbal ingredients. The leading brand Listerine offers essential oil-based mouthwash formulations that are compellingly effective against plaques and gingivitis. Several studies have been done to evaluate the performance of natural mouthwashes. One of the plants that has found its ways in toothpaste and mouthwash formulations is *Salvadora persica* or miswak that is cultivated in India and Africa [50]. The application of miswak in dentistry dates back to 5000 B.C where it was reported to have been extensively used by Babylonians, Arabians and Muslims [51]. Miswak was proven to be efficient in reducing plaque score and cariogenic bacterial count as it has anti-pyretic, anti-inflammatory and analgesic properties [52]. Thus, it was recommended for use in mouthwash formulations which good antimicrobial effectiveness of herbal-based mouthrinses against oral microorganisms [53].

In addition, the leaves of the fruit-bearing tree *Psidium guajava* are being used in the Thai folk medicine for the management of dental caries [54]. Guava leaves have been found to possess antibacterial and anticariogenic activities against *S. mutans* [55]. Owing to its multiple medicinal properties and favorable public acceptance, clinical trials have approved the use of guava mouth rinse as an empirical adjunct to professional oral prophylaxis [56]. Similar to guava leaves, *Camellia sinensis* or green tea was reported to be effective against *S. mutans* [57]. Green tea extract mouthwash is safe and non-toxic, particularly for children. Recent studies showed that green tea mouthwash is

even more effective than chlorhexidine in the treatment of gingivitis [58].

Aside from the antimicrobial effects that mouthwash formulations may confer, recent studies have tested their effects on orthodontic wires, dental alloys and filling materials. Literatures have indicated that individuals with misaligned teeth are more prone to periodontal problems due to the difficulty in accessing areas which can be a hindrance in maintaining proper oral hygiene [59]. Such patients are more susceptible to dental caries and might benefit from the regular use of a mouthwash formula in addition to regular brushing. Patients with misaligned teeth often receive orthodontic nickel-titanium wires for tooth correction. The long term use of chlorhexidine gluconate mouthwashes, however, can lead to the corrosion of orthodontic wires [60]. Several analytical studies are being conducted to determine the safest mouth rinse brands and types for those who have received orthodontic treatment. Furthermore, the alloys used for fixed prosthodontics are mostly composed of nickel-chromium. Some mouthwashes could play a role in releasing nickel ions from dental alloys and are therefore contraindicated for patients with a medical history of nickel allergy [61].

The most recent global issue is the coronavirus pandemic. On January 8, 2020, a novel coronavirus was officially announced as the causative pathogen of Covid-19 by the Chinese Center for Disease Control and Prevention [62]. Coronaviruses make use of a large, single-stranded positive sense RNA as genome [63]. The common transmission routes for the novel coronavirus include direct [coughing, sneezing and droplet inhalation] and contact [contact with oral, nasal, and eye mucous membranes] transmissions [64]. Since one of the routes used for transmission is the oral pathway and droplets, personal protective measures are required at dental clinics.

One of the proposed procedures is to rinse the patient's mouth with a specific mouthwash to reduce the possibility of transferring the virus to the attending dentist or to the dental equipment if in case the patient is Covid-19 positive. Mouthwash formulations that contain chlorhexidine gluconate were found to be ineffective against coronavirus in general [65]. Since the novel coronavirus is vulnerable to oxidation, a pre-procedural mouth rinse containing oxidative agents such as 1% hydrogen peroxide or 0.2% povidone is recommended, in order to reduce the salivary load of oral microbes, including potential novel coronavirus carriage [66]. A pre-procedural mouth rinse would be most useful in cases when a rubber dam cannot be used [67].

## CONCLUSION

The oral cavity is home to a wide variety of microorganisms. The moist environment and the abundance of nutrients make the mouth a haven for microbial growth and colonization. Thus, oral hygiene is necessary to delimit the number of colonizing microbes and protect the mouth and body from their pathogenic activities. The use of a mouthwash as part of the oral care routine is highly recommended to ensure good hygiene in areas of the mouth that toothbrush is not able to penetrate. Several herbs have been incorporated in mouthwash recipes for hundreds of years. These herbs are widely known for their antibacterial activities and may therefore be used against oral diseases that are mainly caused by bacteria. They are also valued for their ability to reduce inflammation and for relieving tooth and gum pain. The interest towards the incorporation of herbal ingredients in oral products has been increasing exponentially over the years. Herbs definitely have a great potential in the mouthwash industry and can be used as a substitute to chemicals that may be harmful for

the oral cavity. From the general perspectives, it can be concluded that awareness to use mouthwash made of herbal components may depend on the demand for a natural product itself in the market. However, conventional mouth wash is still popular among consumers.

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