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Herbal Dentifrices for Children

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Additional information is available at the end of the chapter

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1. Introduction

The use of plant extracts as antimicrobial agents has been increasing every day. Currently, these applications are mainly found in dentistry with the increased use of plant extracts in toothpastes for both adults and children. This finding results from the fact that the oral cavity is considered a favorable environment for the colonization and growth of a wide range of microorganisms, bacteria being the most common [1, 2]. One of the core arguments for the pharmaceutical industry to use toothpastes made from plant extracts is that they can act as antibiotics, analgesics, sedatives, and anti-inflammatories, in addition to being less likely to cause side effects. In the case of toothpastes for children's use where the presence of fluoride can lead to fluorosis, the presence of extracts with antimicrobial activity is quite interesting, given that these combat microorganisms by preventing the formation of biofilms [3].

The presence of microorganisms in the physiology of the oral cavity is essential for normal development, since most species are commensal microorganisms. In some cases, these microorganisms contribute to preventing the establishment of pathogenic microorganisms [4]. However, some of these microorganisms are considered to be opportunistic pathogens that play an important role in the etiology of periodontitis and dental caries, which are believed to be the most prevalent diseases in the world [5]. These microorganisms have also regularly been involved in the etiology of a number of systemic diseases, such as respiratory infections, infective endocarditis, and cardiovascular diseases [6, 7].

Dental caries is a complex oral disease, caused mainly by dental plaque. Dental plaque has been described as an ordered structure in which the primary colonizers are *Actinomyces* and *Streptococci*. These microorganisms bind tightly to one another, in addition to the solid tooth surface, by means of an extracellular matrix consisting of polymers of both host and microbial origin [8-10]. The formation of dental plaque includes a series of steps that begins with the

initial colonization of the pellicle and ends with the complex formation of a mature biofilm. Additionally, through the growth process of the biofilm, the microbial composition changes from one that is primarily Gram-positive and *Streptococcus*-rich to a structure filled with Gram-negative anaerobes in its more mature state [11]. It is widely accepted that the accumulation of microorganisms plays a key role in the initiation and progression of gingivitis and other oral diseases [12].

Gram-positive bacteria, such as *Lactobacilli* and the *Streptococci* species are associated with the formation of dental caries. As a result, strategies for treating this disease must concentrate on controlling the growth of these bacteria [13-15].

According to data from the World Health Organization (WHO), the prevalence of caries in schoolchildren is 60-90%, while among adults it is universal in most countries [16]. Biofilm formation is a natural process in the oral environment, and its control should be done through chemical and mechanical means. Brushing is a preventive measure considered essential for the prevention of caries and periodontal diseases, and can be effectively increased by using the toothpaste formulations containing antimicrobial agents [17-19].

1.1. Dental fluorosis

Dental fluorosis is the exposure of the tooth germ during its formation process at high concentrations of fluoride, resulting in defects of enamel mineralization with severity directly linked to the amount ingested. Clinically, the formation of opaque spots on the enamel of homologous teeth turning to a yellow or brown color, can be observed in more severe cases. In addition to the high dosage of fluoride, other factors contribute to the onset of fluorosis: low body weight, nutritional status, rate of skeletal growth and bone remodeling periods. In this sense, dental fluorosis is a more common disease in teeth of late mineralization (permanent teeth) in children with a low weight or poor nutritional state, occurring mainly at the ages of the first to second stages of childhood where there is a high incidence of systemic fluoride intake and subsequent harmful effects [20].

The decrease in the prevalence of dental caries has been attributed in large part to the use of fluoride toothpastes when brushing, one of the most accepted measures for the control of dental caries [21, 22]. By contrast, the prevalence of dental fluorosis has increased worldwide. The use of fluoride toothpaste before 6 years of age has been identified as one of the main risk factors for dental fluorosis [23]. However, other factors have also been found to cause fluorosis, especially commercially sold drinks, such as mineral water and soft drinks, among others, a fact that has increased the incidence of fluorosis in both places with fluoridated water consumption as well as in areas with non-fluoridated water consumption. This finding indicates that there is an intake of fluoride from other sources as well, in addition to the public water supply. Several studies have been conducted in many countries to determine the amount of fluoride in mineral waters, especially in soft drinks. The values obtained range from 0.007 mg/L to more than 4.1 mg/L for mineral waters and from 0.02 to 1.28 ppm, an average level of 0.72 ppm, for soft drinks, with no significant difference when the tastes of diet sodas are compared [24].

Depending on its severity, dental fluorosis may not only have aesthetic consequences, but it may also cause pain and affect masticatory efficiency [25]. Due to these facts, it is necessary to develop alternative formulations of toothpaste based on plant extracts with proven antimicrobial activity for use in children's dentistry to minimize the risk of dental fluorosis in infants and children from 1 to 6 years of age. Thus, many plant extracts with antimicrobial activity have been incorporated into toothpastes to prevent oral diseases. The plant extracts of the *Chordata macleya* and *Prunella vulgaris* species are examples of plants with an anti-inflammatory activity used in the international toothpaste market [26].

2. Toothpastes and antimicrobial agents

Common antimicrobial compounds added to toothpastes include: triclosan, stannous fluoride, and chlorhexidine. Nevertheless, despite the effectiveness of many formulations of toothpaste with antibacterial properties, the search for natural products with these properties has been increasing. Thus, plant extracts are being investigated as potential sources of new antibacterial compounds [27-29]. Dental plaque is considered an essential factor linked to the onset of caries, thus justifying the measures taken to control it. It is well-known that many metabolites produced by plants, such as tannins, terpenoids, flavonoids, and alkaloids, may represent a new source of antimicrobial substances [30, 31].

Natural toothpastes are considered to be those that do not incorporate the antimicrobial triclosan and fluoride. These toothpastes contain natural ingredients, such as the salts of sodium fluoride and sodium chloride and plant extracts, such as lemon, eucalyptus, rosemary, chamomile, sage, and myrrh [32]. Chamomile extract, for example, exhibits anti-inflammatory properties. By contrast, salvia extract decreases the tissue bleeding, whereas the extract of myrrhis, a natural antiseptic and extract of mentha, presents antiseptic, anti-inflammatory, and antimicrobial activities [33, 34]. Terpenoid compounds derived from medicinal plants and natural products, such as ursolic acid (UA) and oleanolic acid (OA), inhibited the growth of cariogenic microorganisms in a study conducted by Zhou and co-workers [35], suggesting that both compounds have the potential for use as antibacterial agents in the prevention of dental caries. Oral care products that are incorporated together with plant extracts are widely used due to their low toxicity, as compared to oral care products that contain antimicrobials, such as triclosan, cetyl pyridinium chloride, chlorhexidine, and fluoride [36, 37].

Toothpastes for children's use have had their contents changed in the name of progress and development in dentistry. In the past, toothpastes consisted of creams with a high fluorine content, masked by packaging illustrated with children's themes and flavored goodies that attracted children to the product. Nowadays, the cosmetics industry has reduced the fluorine content in these toothpastes to minimize the risk of fluorosis in children of less than 5 years of age, where fluorosis primarily affects the aesthetic appearance of their teeth [38].

3. Medicinal plants with antibacterial activity used in dentistry

The use of medicinal plants for the treatment of dental problems has widely been discussed by many researchers. Many cultures still use medicinal plants for the treatment of oral diseases, including caries for the cleaning and brushing of teeth, especially in rural areas of underdeveloped countries where people still brush their teeth without toothpaste [39]. The scientific field that uses the knowledge of medicinal plants for use in oral health is called Ethno-dentistry, which combines the knowledge of plants used by rural populations, indigenous populations, and communities in general. A brief description of some of the most common plants used in oral health was compiled, as described below.

3.1. *Myristica fragrans*

Myristica fragrans (Myristicaceae) is grown to be used as a spice and for medicinal purposes [40]. Its main constituents include alkylbenzenes (myristicin, elemicin, safrole, etc.); terpenes (α -pinene, β -pinene, myristic acid, trimyristin); and neolignans (myrislignan and macelignan) [41-43]. Its seed (known as nutmeg) is widely used in traditional medicine as an antithrombotic and antifungal drug, for the treatment of nausea and dyspepsia, and as an anti-inflammatory drug [44-46].

Studies have shown that *M. fragrans* has a great potential benefit in the field of dentistry, as its ethanol extract has proven to provide antibacterial activity against cariogenic bacteria [47]. According to Chung [42], the macelignan, an active compound isolated from *M. fragrans*, also presents an antibacterial activity against *Streptococcus mutans* and other oral microorganisms, such as *Streptococcus sobrinus*, *Streptococcus salivarius*, *Streptococcus sanguinis*, *Lactobacillus acidophilus*, and *Lactobacillus casei*, which indicates that it can be used as a natural antibacterial agent in oral hygiene products.

3.2. Propolis

Propolis, a natural antibiotic, is a resinous yellowish-brown to dark-brown substance collected by bees (*Apis mellifera*) from tree buds and is mixed with secreted beeswax. Bees use propolis as a glue to seal the opening of the hives protecting it from outside contaminants, which features over 300 compounds in its composition [48]. Among these constituents, one can find: flavonoids, steroids, sugars, and amino acids. The composition depends on the vegetation of the place from which it was collected and the season [48-50]. Thus, its biological activity is related to the plant ecology of the region visited by bees [51, 52]. Propolis has been outstanding for its anesthetic anti-inflammatory, healing, anti-trypanosome, and anti-cariogenic activities [53-56]. Brazilian propolis is one of the most active resinous substance, whose major components include diterpenes, lignans, *p*-coumaric acid, and flavonoids. A flavonoid is a compound with a wide range of biological activities, mainly antioxidant, anti-inflammatory, and antimicrobial activities [57, 58, 49].

Ikeno *et al.* [59] and Park *et al.* [60], respectively, have shown that propolis has *in vitro* effects on bacterial growth as well as on the activity of the glucosyltransferase enzyme (GTF),

responsible for the formation of *S. sobrinus*, *S. mutans*, and *S. cricetus* biofilms in caries developed in rats. These studies demonstrate that propolis may well become a promising alternative for the prevention of caries and other oral diseases [61-63].

3.3. Chitosan

Chitin and chitosan are copolymers consisting of *N*-acetyl-D-glucosamine and D-glucosamine units in varying proportions. Chitin is the second most abundant polysaccharide in nature and is the main component of the exoskeleton of crustaceans and insects, but can also be found in nematodes, fungal cell walls, and yeasts. Chitosan has interesting medicinal properties, especially the antimicrobial activity *in vitro* against oral biofilm formations. This finding was reported in studies conducted by Verkaik *et al.* [64-66], who found that chitosan-based toothpaste, when compared with chlorhexidine-based toothpaste, traditionally used as an antimicrobial agent in toothpastes, may be equally as effective.

Chitosan showed a significant action in reducing dental plaque and presented antimicrobial activity *in vitro* against several pathogens in the oral cavity associated with the formation of dental plaque and periodontal disease, such as *Actinobacillus*, *S. mutans*, and *P. gingivalis* [67, 68]. Tarsie *et al.* [69] demonstrated that chitosan could influence the adherence of *S. mutans* to tooth surfaces, thus confirming the possibility of using this polysaccharide as a preventive agent in the formation of biofilms. According to the literature [70, 71], chitosan mouthwash was quite effective in reducing plaque that adheres to the teeth and reducing the count of *S. mutans* in saliva.

According to Mohiree Yadav [72], the addition of chitosan to toothpastes reduced plaque levels by 70% and caries caused by bacteria by 85%, respectively. Thus, toothpastes containing plant extracts and chitosan present an antibacterial efficacy comparable to those containing chlorhexidine [65]. The proven antimicrobial, anti-inflammatory, and healing effects of chitosan, coupled with their ability to inhibit the formation of biofilms, may well represent a formidable advantage in the treatment of diseases associated with the oral cavity [73].

3.4. *Punica granatum* Linn.

Punica granatum Linn. (Punicaceae), known in Brazil as “romã”, is a small shrub cultivated worldwide in tropical and subtropical climates, has been used in traditional medicine as an astringent, hemostatic agent, and in the control of diabetes [74]. It is also commonly used to treat throat infections, cough and fever due to its anti-inflammatory and antimicrobial potential [75]. The antibiotic activity of the *P. granatum* extract is associated with its chemical constituents, including tannins and alkaloids found in the leaves, roots, stems and fruits [76, 77]. The alcoholic extract obtained from the fruit of *P. granatum* has shown effective antimicrobial activity against cariogenic bacteria, such as *S. mitis*, *S. mutans*, *S. sanguinis*, *S. sobrinus*, and *L. casei* [78, 79]. Toothpaste obtained from the alcoholic extract of *P. granatum* showed activity against cariogenic *S. mutans*, *S. sanguinis*, and *S. mitis* bacteria, demonstrating its antibacterial effect, suggesting the effective use of this herbal agent in the control of the adherence of different microorganisms within the oral cavity [80].

3.5. *Lentinus edodes* and *Cichorium intybus*

Lentinula edodes is the second most cultivated species of edible mushroom in the world, behind only champignon (*Agaricus bisporus*) [81]. It can be grown on tree trunks or on prepared substrates, and has attracted the interest of researchers, as it presents scientifically proven nutritional and therapeutic qualities [82].

Cichorium intybus (Compositae) has been used by humans as food since the dawn of civilization. It is a native plant of Europe that can be grown virtually everywhere [83, 84]. Studies have shown that various plant foods contain components with antibacterial and anti-dental plaque activity [85], including the alcoholic extracts of edible mushrooms, namely *L. edodes* and *C. intybus*, which can be used in products formulated for daily oral hygiene, such as mouthwashes and toothpastes [86-88].

3.6. *Copaifera officinalis* L.

Copaifera officinalis L. (Fabaceae) is a tree found mainly in Latin America and West Africa, also known as “Copaiba”, copaiba balsam, Jesuit's balsam, copal, and capivi [89-91]. The copaiba oil has been documented to contain antibacterial activity. It corresponds to an excretion product, whose purpose is most likely to protect the plant against animals, fungi, and bacteria [92]. It is a liquid of varying viscosity and color, which can vary from yellow to brown [93, 94]. The extracted oil can vary in relation to its concentration of diterpenes and sesquiterpenes [95]. It is popularly used as an anti-inflammatory and healing agent whose actions are related to the presence of diterpenes within its composition [96]. Pieri *et al.* [97] studied the antimicrobial activity of copaiba oil on plaque-forming bacteria in dogs. The results showed that the oil was active against cariogenic bacteria, presenting an inhibitory effect on the adhesion of plaque-forming bacteria.

3.7. *Rosmarinus officinalis* Linn.

Rosmarinus officinalis Linn. (Labiatae) is a small shrub whose leaves have small glands containing essential oils. Tests performed *in vitro* with the essential oil showed an inhibitory effect on the adherence of *S. mutans* and the inhibitory growth activity of Gram-negative bacteria [98-100]. This plant has great potential in inhibiting bacterial growth and in the synthesis of glucan, suggesting its potential use in the control of cariogenic bacteria, whose activities were observed when its hydro-alcoholic extract showed significant activity on the glucosyltransferase enzyme produced by *S. mutans* [101-103]. It could also be observed that the alcoholic extract proved to be efficient in inhibiting the adherence of *S. mitis*, *S. mutans* and *S. sobrinus*, which suggests that it contains compounds with antibacterial activity against oral bacteria [104].

3.8. *Lippia sidoides* Cham.

Lippia sidoides Cham. (Verbenaceae) is a shrub originating from northeastern Brazil, popularly known as “alecrim pimenta”. It is used in the treatment of allergic rhinitis, sore throat, gum inflammation, and the treating of skin wounds and cuts [105, 106]. *L. sidoides* contains an

essential oil rich in thymol, which contains bactericidal properties [107, 108]. Tests performed *in vivo* have proven the effectiveness of a mouthwash and toothpaste-based essential oil of *L. sidoides*. An inhibition of approximately 12% of the microorganisms could be observed, with a 6% of reduction in the biofilm formation rate, thus demonstrating the efficiency of this essential oil in oral-based hygiene products [109, 110].

3.9. *Calendula officinalis* L.

Calendula officinalis L. (Asteraceae) is an herbaceous plant that is widely cultivated in many parts of the world for ornamental, medicinal, and cosmetic purposes [111]. In the dental field, this plant has been tested as regards its capacity to control the growth of biofilm-forming bacteria. Tests performed *in vivo* have demonstrated the effect of a 10% tincture of *C. officinalis* against chronic gingivitis, presenting significant improvement in the gingival tissues, with no apparent side effects [112, 19]. From these results, a toothpaste and a mouthwash containing 10% tincture of *C. officinalis* was developed. Tests performed *in vivo* using the type of toothpaste have demonstrated the effectiveness of this dental cream on gingival inflammation and the reduction of biofilm formation caused by *S. mutans* [113, 103]. Tests performed *in vivo* using a mouthwash containing 10% tincture of *C. officinalis* verified its efficiency in improving periodontal health, concluding that the performance was similar to mouthwashes prepared with 0.12% chlorhexidine in most evaluated parameters [114]. Another test performed *in vivo* using a toothpaste containing hydroalcoholic extracts of *C. officinalis* and *C. sylvestris* also showed bacteriostatic and fungistatic actions against microorganisms, such as *S. aureus*, *S. mutans*, and *C. albicans*, showing the associated therapeutic properties of these extracts [115].

3.10. *Schinus terebinthifolius* Raddi and *Myracrodruon urundeuva* Fr. All.

Schinus terebinthifolius Raddi and *Myracrodruon urundeuva* Fr. All. (Anacardiaceae), known in Brazil as “aroeira da praia” and “aroeira do sertão”, respectively, are plants that are commonly found in South America. These plants are still used in traditional medicine in the northeastern regions of Brazil [116-119]. A 10% tincture of *S. terebinthifolius* showed efficacy in controlling biofilms formed by *S. mutans*, with a significant reduction in colony-forming units, as well as in the treatment of chronic gingivitis, presenting similar results when compared to 0.12% chlorhexidine-based toothpastes. This tincture also showed anti-inflammatory and antifungal activities against *Candida albicans*, suggesting its potential as an antibacterial agent, especially in the prevention oral cavity disease [120-123]. By contrast, the alcoholic extract of *M. urundeuva* also showed significant antimicrobial and anti-adherent activities against microorganisms that form biofilms [124].

3.11. *Matricaria recutita* Linn.

Matricaria recutita Linn. (Compositae) is a native plant of Europe and western Asia and is known for its variety of active flavonoids as well as for its essential oil, which is rich in terpenoids and is responsible for its anti-inflammatory and antibacterial activities [125, 126]. This plant has been widely used in inflammatory and infectious processes of the oral cavity [127]. Costa *et al.* [128] found that the alcoholic extract of *M. recutita* has antibacterial and anti-

adherent activities against cariogenic bacteria *S. mutans*, *S. sanguinis* and *L. casei* [129]. According to studies performed by Lins *et al.* [130], a simple application of a mouthwash based on the hydroalcoholic extract of *M. recutita* proved effective in controlling biofilm formations caused by microorganisms, such as *S. mutans* and *S. sanguinis*, found in the oral cavity. In addition, this plant has been used in commercial toothpastes formulations for adults and children.

3.12. *Eugenia uniflora* L.

Eugenia uniflora L. (Myrtaceae), popularly known as “pitangueira”, is a fruitful plant that is native to Brazil but can also be found in northern Argentina and Uruguay. [131]. Its leaves have been related to the treatment of various ailments, including fever, stomach ailments, hypertension, and obesity [132]. Antimicrobial activity was observed in this plant’s leaves and cherries against *S. mutans*, *S. sanguinis*, *S. salivarius*, *S. mitis*, and *S. oralis* bacteria. Toothpastes containing the alcoholic extract of the ripe fruit of *E. uniflora* showed a similar efficacy to the Colgate Total 12 toothpaste, used as controlling agents in tests performed *in vivo* by Jovito *et al.* [133]. Castro *et al.* [134] demonstrated that hydroalcoholic extracts of *E. uniflora* showed antibacterial activity against *L. casei*.

3.13. *Myrciaria cauliflora* (Mart.) O. Berg.

Myrciaria cauliflora (Mart.) O. Berg. (Myrtaceae) is a native plant from Brazil and can be found throughout the country [135]. Tests performed *in vitro* using the alcoholic extract of this plant’s leaves against *S. mutans* demonstrated that this extract acts on biofilm formation and could be an alternative for use in toothpastes [136, 137].

3.14. *Syzygium aromaticum*

Syzygium aromaticum (Myrtaceae), an aromatic flower bud of a tree that is native to the Maluku Islands in Indonesia, is commonly used as a spice. Cloves are commercially harvested primarily in Indonesia, India, Madagascar, Zanzibar, Pakistan, and Sri Lanka. The essential oil of *S. aromaticum* is used for flavoring and as a natural food preservative, as it presents antifungal and antibacterial activities [138, 139]. Its essential oil is rich in the compound eugenol, which is the most abundant substance in the tree’s bark and is widely used in dentistry as an anesthetic in dental hygiene and to relieve toothaches [140]. This tree’s branches contain a predominance of α and β -pinene, α -phellandrene, *p*-cymene, limonene, linalool, α -sequiterpenes copaene, β -caryophyllene, caryophyllene oxide, alilbenzenos ϵ -cinnamaldehyde, and aceto of ϵ -cinnamyl monoterpenes [141]. Tests performed *in vitro* demonstrated that the essential oil of *S. aromaticum*, when pure and incorporated into a toothpaste, presented antibacterial activity against *S. mutans* [142].

3.15. *Cinnamomum zeylanicum*

Cinnamomum zeylanicum (Lauraceae), native to Sri Lanka in South Asia, is a small or medium sized tree, commonly reaching 20 to 40 ft. in height. *C. zeylanicum* was widely used in ancient

times as a spice. It is currently used as a flavoring in cooking food as well as in medicine as an antimicrobial agent. The essential oil extracted from its leaves contain a greater quantity of an aldehyde called cinnamaldehyde. Oliveira *et al.* [142] evaluated the essential oil of this plant against *S. mutans* and *L. casei*. These authors observed that the essential oil of *C. zeylanicum* showed inhibition zones of close to or above those of standard chlorhexidine, which was the same result observed for toothpastes formulated with the oil. Other studies have demonstrated the action of this essential oil on yeasts, such as *C. albicans* and *C. tropicalis*, which produce oral candidiasis in denture users [143].

3.16. *Cymbopogon citratus*

Cymbopogon citratus (Poaceae) is a herbaceous plant that is, native to the tropical regions of Asia, especially India. Also known as *Cymbopogon (nardus)* or by synonyms, such as *Andropogon citratus ceriferus*, *Andropogon citratus*, *Andropogon citriodorum*, *Andropogon nardus ceriferus*, *Andropogon roxburghii*, and *Andropogon schoenanthus*. The essential oil extracted from this plant's leaves contains the main components of citral, geraniol, methyleugenol, myrcene, and citronellal [144]. Oliveira *et al.* [142] evaluated this plant's essential oil against *S. mutans* and *L. casei* and noted that it presented inhibition zones of close to those of standard chlorhexidine against the microorganism *S. mutans*. However, when analyzing the formulation of toothpastes containing the essential oil, it was found that this oil proved ineffective in the concentration tested to inhibit the growth of microorganisms. Perazzo *et al.* [145] also evaluated the essential oil of *C. citratus* on bacterial biofilm formation, especially in strains of *S. mutans* (ATCC 25175), *S. salivarius* (ATCC7073), and *S. oralis* (ATCC1055) and observed that this essential oil was more effective against *S. mutans*.

3.17. *Malva sylvestris*

Malva sylvestris (Malvaceae) is a biennial or perennial erect herbaceous species that is native to Europe and is widely known for its anti-inflammatory and antimicrobial properties [146]. Its phytochemical composition includes tannins, glycolipids, and flavonoids, which were tested as regards their capacity to control the growth of bacteria and biofilm formation [147, 18]. *M. sylvestris* has proven to be so effective that it already exists on the commercial market, called Malvatricin®, which is widely used as an antimicrobial agent against cariogenic bacteria. This effect is most likely due to the action of quinosol, a substance present in its composition [148].

3.18. *Nasturtium officinale*

Nasturtium officinale (Cruciferaeae) is a native plant of Europe and Asia that has many uses in medicine and pharmacology [149]. It is rich in vitamins and active substances, and is most commonly used in the treatment of urinary tract infections in children [150]. Tests performed *in vitro* with a mouthwash containing 10% hydroalcoholic extract of *N. officinale* was effective in controlling the growth of the microorganisms present in the oral cavity and dental plaque [151].

3.19. *Aloe vera*

Aloe vera (L.) Burm and *Aloe barbadensis* Miller (Asphodelaceae), popularly known as "aloe", are native from Africa and are widely used in traditional medicine. The gel of this plant contains healing, antibacterial, and antifungal activities due to the presence of anthraquinones, such as aloenin, barbaloin, and isobarbaloin in its chemical composition [152-155]. Studies have demonstrated the antimicrobial activity of toothpastes containing *A. vera* on oral microorganisms, such as *S. mutans*, *S. sanguis*, *A. viscosus*, and *C. albicans* [27].

3.20. *Magnolia officinalis*

Magnolia officinalis (Magnoliaceae) is a native plant of the mountains and valleys of China at altitudes of 300-1500 meters. The highly aromatic bark is stripped from the stems, branches, and roots, and is used in traditional Chinese medicine, where it is known as "hou po" [156]. The traditional use indications are to eliminate the dampness and phlegm, and relieve the distension. Huang *et al.* [157] have shown that the magnolol isolated from this plant was able to inhibit the growth of cariogenic bacteria.

Plants	Pharmaceutical form	Use
<i>Salvia officinalis</i>	mouthwash	plaque and bleeding on probing
<i>Plantago psyllium L</i>	mouthwash	periodontitis
<i>Punica granatum Linn. and Centella asiatica</i>	mouthwash	periodontitis
<i>Aloe ferox Mill</i>	mouthwash	gingivitis
<i>Calendula officinalis L</i>	mouthwash	Gengivite and periodontitis
<i>Lippia sidoides Cham</i>	mouthwash	plaque and bleeding on probing
<i>Punica granatum Linn.</i>	toothpaste	gingivitis
<i>M. recutita L./Enchinacea angustifolia/ Krameria triandria Ruiz Pavon</i>	toothpaste	gingivitis
<i>Calendula officinalis L</i>	toothpaste	gingivitis
<i>Punica granatum Linn.</i>	Gel	candidiasis, plaque and gingivitis

Table 1. Medicinal plants use in the treatment of oral diseases clinical studies.

3.21. *Salvia officinallis*

Salvia officinallis (Labiatae) is plant that is native to the Mediterranean region, though it has been naturalized in many places throughout the world. It is a perennial, evergreen subshrub that has a long history of medicinal and culinary uses. Its essential oil contains cineole, borneol, and thujone. Sage leaf contains tannic acid, oleic acid, ursonic acid, ursolic acid, carnosol, carnosic acid, fumaric acid, chlorogenic acid, caffeic acid, niacin, nicotinamide, flavones, flavonoid glycosides, and estrogenic substances [158]. Tests performed *in vivo* by Celeste *et*

al. [159] have shown that a mouthwash containing a 10% alcoholic extract of *S. officinalis* reduced the visible plaque index (VPI) of the volunteers in 15.3% and the gingival index (GI) in 9.3% when compared to the chlorhexidine control.

3.22. *Azadirachta indica*

Azadirachta indica (Meliaceae) is native plant of India and the Indian subcontinent including Nepal, Pakistan, Bangladesh, and Sri Lanka. The tree can reach a height of 15 to 20 m (49 to 66 ft.). It has been used in India for decades in the treatment of several diseases in medicine and dentistry. Chatterjee *et al.* [160] evaluated a 0.19% *A. indica* mouthwash in tests performed *in vivo* and observed that the *A. indica* mouthwash is as effective in reducing periodontal indices as is chlorhexidine, which was used as the control, showing a significant reduction in gingival bleeding, and plaque indices.

4. Conclusion

The decrease in the amount of fluoride associated with the presence of plant extracts with proven antimicrobial activity is a positive factor for the reduction of fluorosis. For babies, we recommend the use of toothpastes containing only plant extracts, with no fluoride, since there is no risk of caries at this age. In such cases, these toothpastes can be used to adapt the babies to a proper hygiene of their oral cavity as well as maintain their beneficial microbiota.

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