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# A systematic review of medicinal plants and herbal products' effectiveness in oral health and dental cure with health promotion approach

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## Abstract:

Medicinal plants and herbal drugs are being used increasingly as part of primary health care in most parts of the world. As important adjunctive and alternative treatments for oral health care, herbal products' use may continue to increase and become more widespread. The objective of this study is to present a comprehensive systematic review of the current published literature on the effectiveness of medicinal plants and herbal products employed to improve oral health in adolescents with a health promotion approach. The systematic review was conducted according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines. The keywords "herbal medicine," "herbal extract," "herbal supplements," "plant extract," "natural drug," "pulpitis," "dental caries," "oral viral diseases," and "abscess" were used in combination with the Boolean operators OR and AND. PubMed, Embase, Scopus, and Web of Science were searched. Quality assessment of the included studies was performed using the Cochrane Handbook for Systematic Reviews of Interventions. The search yielded 49 original research studies. A total of 22 studies had low or unclear risk bias. The geographical distribution of included studies was primarily concentrated on western countries. Overall, studies reported herbal product users' age, ranging from young adults aged 18 years to elderly people aged 75 years or older. Most studies reported multiple compounds, including herbal drugs and herbal extracts. Chamomile and Aloe vera were the most frequently reported herbal compounds. The most commonly described herbal products to treat oral diseases were gels, mouth rinses, and pastes. The studies included a range of people with oral diseases, including periodontal and gingival diseases, recurrent aphthous stomatitis, oral lichen planus, and oral candidiasis. Herbal product interventions were found to be effective and safe alternatives for oral health care. One of the most important goals of the World Health Organization (until 2015) is the oral health index, so it is important that dental services be followed up more seriously. Considering the problems in reaching this goal of the World Health Organization in our country, herbal products have the ability to improve clinical oral health outcomes in adolescents. Limited adverse side effects indicate the overall safety of these treatments for a wide range of oral diseases. Therefore, the use of medicinal plants as well as alternative medicine is one of the useful methods in achieving this important goal of public health.

## Keywords:

Dental cure, herbal preparations, medicinal plants, oral health, stomatognathic diseases

## Introduction

Oral diseases are considered one of the most prevalent diseases worldwide and have posed serious health and economic

burdens for many countries. Patient rights are the most important ethical rights which equally belong to every human kind.<sup>[1,2]</sup> It is estimated that about 3.5 billion people around the world are affected by a wide

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range of oral diseases, including dental caries (tooth decay), periodontal (gum) disease, tooth loss, and oral cancers.<sup>[3]</sup> As oral diseases are significantly associated with socioeconomic status (income, education, and occupation) and social determinants of health, the prevalence of oral diseases is seriously rising among poorer, marginalized, and socially disadvantaged groups in society.<sup>[3,4]</sup>

Despite the fact that oral diseases are highly preventable and can be treated in their early stages, they are highly prevalent. Several explanations have been offered to explain this rising pattern, but attention has focused on the cost's oral health treatments. Available treatments for oral diseases are expensive<sup>[4,5]</sup> and not a part of universal health coverage programs<sup>[6,7]</sup> in many developing countries. Payments for oral health care can place a significant burden on households, even preventing them from spending on basic necessities.<sup>[8-10]</sup>

Since the burden of out-of-pocket payments for oral health care is high in many countries, and the health system fails to protect households against the catastrophic consequences of healthcare services, oral diseases are largely neglected.<sup>[3,11]</sup> In addition, treatment of oral diseases may cause some unwanted side effects such as teeth stains, oral mucosal peeling, and allergic contact stomatitis.<sup>[12,13]</sup> Oral health education is an educational process that aims to form or change people's behaviors through knowledge and to maintain or improve their health.<sup>[14,15]</sup> Therefore, fear of adverse side effects and dental fear are considered as negative contributing factors to avoiding necessary oral healthcare services by some patients.<sup>[16,17]</sup> In contrast to the above, it has been reported that alternative approaches based on traditional medicine and herbal products can lead to successful treatment of oral diseases. Since traditional medicine is affordable, safe, easily accessible, and culturally familiar,<sup>[18,19]</sup> medicinal plants and herbal drugs are being used increasingly as part of primary health care in most parts of the world.<sup>[20]</sup> An increasing body of literature has been published in recent years concerning the use of traditional medicine and herbal products for different oral diseases. For example, natural phytochemicals isolated from plants are considered to be good alternatives to synthetic chemicals used in the treatment of dental problems. The Ayurvedic medical materials have been found to be safe and effective through several hundred to several thousand years of use.<sup>[21]</sup> Some articles use procedures that have the potential to be used as an adjunct to conventional chemical means of dental plaque control, such as mouth rinses. Incorporating oil swishing as a component of daily oral hygiene can significantly improve oral and general health, specifically in lower

socioeconomic groups.<sup>[22]</sup> If traditional medicine is to be acknowledged as part of primary health care, the use of safe, quality products and practices should be ensured based on available evidence.<sup>[23]</sup>

Plants have been used for centuries to prevent and control dental diseases. Plant extracts are effective because they interact with certain chemical receptors in the body. Herbal medicines have fewer side effects compared to traditional medicines. The biggest challenge and problem is the lack of information about the effects of herbs on oral tissues, the mechanism of action, and their side effects.<sup>[24]</sup> In some countries like India, due to the use of medicinal plants by different generations, especially in the control and treatment of some oral diseases, it is considered important to preserve this heritage and identify them.<sup>[25]</sup>

Enzo A. Palombo studied traditional medicinal plant extracts and natural products with activity against oral bacteria, and reported plant extracts or phytochemicals that inhibit the growth of oral pathogens, reduce the development of biofilms and dental plaque, influence the adhesion of bacteria to surfaces, and reduce the symptoms of oral diseases. These will be discussed further.<sup>[26]</sup> A randomized, placebo-controlled study in which two commercial tea extracts were used as mouth rinses showed that each was able to significantly reduce the microbial load of the oral cavity.<sup>[27]</sup> A systematic review of randomized clinical trials entitled as a study surveying the efficacy of medicinal plant extracts as dental and periodontal antibiofilm agents, reported that the main active components of herbal plants used as an alternative treatment for dentures., However, more studies are needed to further understand the clinical relevance of their application.<sup>[28]</sup> However, existing evidence on the effectiveness of these interventions is extremely limited. As important adjunctive and alternative treatments for oral health care, herbal products use may continue to increase and become more widespread. The objective of this study is to present a comprehensive systematic review of more recent published literature on the effectiveness of medicinal plants and herbal products employed to improve oral health in adolescents.

## Materials and Method

In this study, a systematic review of literature was conducted according to the systematic review and meta-analysis (PRISMA) checklist<sup>[30]</sup> (PRISMA checklist). A comprehensive search strategy was developed to locate published and unpublished citations in order to build a database of using herbal products in oral health literature from January 2000 to January 2020. The search incorporated automatic search of bibliographic

databases including PubMed, Embase, Scopus and Web of Science database. These searches utilized both index terms from MeSH headings or Emtree thesaurus and truncation, proximity, and phrases. The search concepts included subject heading terms/keywords for herbal products (e.g., "herbal medicine" or "herbal extract" or "herbal supplements" or "plant extract" or "natural drug") and oral diseases (e.g., "pulpitis" or "dental caries" or "oral viral diseases" or "abscess"). The automated search strategy was finalized using Boolean operators to combine concepts within domains ("OR") and cross-referencing between domains ("AND"). See the complete automated search strategies.<sup>[30]</sup> Hand searching of relevant textbooks and reference list checks were used to complement the automated search and to provide additional search coverage for potentially eligible studies.

### Inclusion criteria and study selection

Preliminary studies including randomized controlled trials, cross-over studies, clinical trials, and *in vitro* studies were included for this review to investigate the effectiveness of herbal products in oral disease. Observational studies (e.g., case controls, cohorts, and cross-sectional studies), editorials, commentaries, letters, and review articles were excluded. All retrieved citations were independently screened and reviewed by two reviewer authors S A and MA. Title and abstract of all citations were primarily evaluated to identify relevant citations. Then, full-texts of citations were finally reviewed to assure the eligibility of potential citations for inclusion in data synthesis.

### Data extraction

Two review authors HS and MM independently extracted data from all included studies. Characteristics of included studies were extracted onto simple forms designed by the research team. These characteristics included bibliographical information (e.g., title, authors, date of publications, and affiliations), patients' information (e.g. age, gender, oral disease subgroup), and methodological information (name of herbal products, intervention group, control group, outcome assessment, and follow-ups).

### Quality assessment of the evidence

The Cochrane Handbook for Systematic Reviews of Interventions<sup>[29]</sup> is used to assess the quality of included randomized trials. The criteria suggested by the Cochrane handbook to assess quality include five items for randomized controlled trials including random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. Effectiveness of interventions was also assessed by the Health Gains Notation framework.<sup>[30]</sup>

## Results

### Quality assessment of included studies

Out of the 7,206 retrieved unique citations, 49 studies met the inclusion criteria and were finally selected for this review<sup>[31-79]</sup> (see PRISMA diagram; Figure 1). Among the 49 included studies, 15 studies<sup>[37,39-41,43,51,59,60,66,67,69,72,73,75,76]</sup> were at low risk for all five methodological quality items (see Appendix 1). The remaining 33 studies were at high or unclear risk of at least one of the bias items; one study<sup>[58]</sup> was at high risk for all bias items. Five studies<sup>[50,56-58,78]</sup> were high or unclear risk for random sequence generation. Seven studies<sup>[35,42,58,71,77-79]</sup> were high or unclear risk for blindness. Twelve studies<sup>[31,32,38,44,46,47,50,53,54,56,58,68,71]</sup> were high or unclear risk for incomplete outcome data.

### The design of herbal products interventions

Of the 49 included studies, 45 studies used parallel design<sup>[31-44,46,47,49-51,53-62,64-79]</sup> and four studies used cross-over design.<sup>[45,48,52,63]</sup> Shortest study duration was 5 days,<sup>[41,57]</sup> and the longest was 180 days.<sup>[51,55]</sup> The average length of trials was 57 days. The average number of participants was 59, ranging from 5<sup>[69]</sup> to 330.<sup>[36]</sup> A total of 2,909 participants were randomized. Publication dates from January 2000 to January 2020 studies were from 17 countries [Table 1].

Geographical distribution of included studies was mainly concentrated on countries from western and southeastern parts of Asia. Thirteen studies described participants located in Iran.<sup>[32,34,35,45,47,50,52,56,57,59,65,67,74]</sup> Ten studies described participants located in India.<sup>[46,48,49,51,58,62,66,71,75,77]</sup> Three studies described participants located in some parts of Thailand.<sup>[36,43,68]</sup> Two studies described users located in China.<sup>[41,42]</sup> One study described herbal products users located in Saudi Arabia.<sup>[69]</sup> One study described herbal products' users located in Lebanon.<sup>[44]</sup> Six studies described herbal users located in American countries including USA,<sup>[39,53]</sup> Brazil,<sup>[37,38,60,61,63,70]</sup> and Cuba.<sup>[33]</sup> Some included studies described a wide range of participants from European countries including Germany,<sup>[54,64]</sup> Switzerland,<sup>[73]</sup> Sweden,<sup>[76]</sup> Spain,<sup>[72]</sup> Czech republic,<sup>[40]</sup> and Cyprus.<sup>[40]</sup> One study described herbal products users located in South Africa.<sup>[79]</sup>

In overall, studies reported herbal products users' age, ranging from young adults aged 18 years to elderly people ages 75 years or older. Thirty-three Studies reported herbal product users' gender; one study only included females<sup>[78]</sup> and one study only included males.<sup>[75]</sup> Of the 31 studies that included both females and males, 17 studies had a majority of female participants.<sup>[32-34,39,41,43,45,54,62,66,68,72-74,76,77,79]</sup>

Most studies reported multiple compounds including herbal drugs and herbal extracts. Chamomile

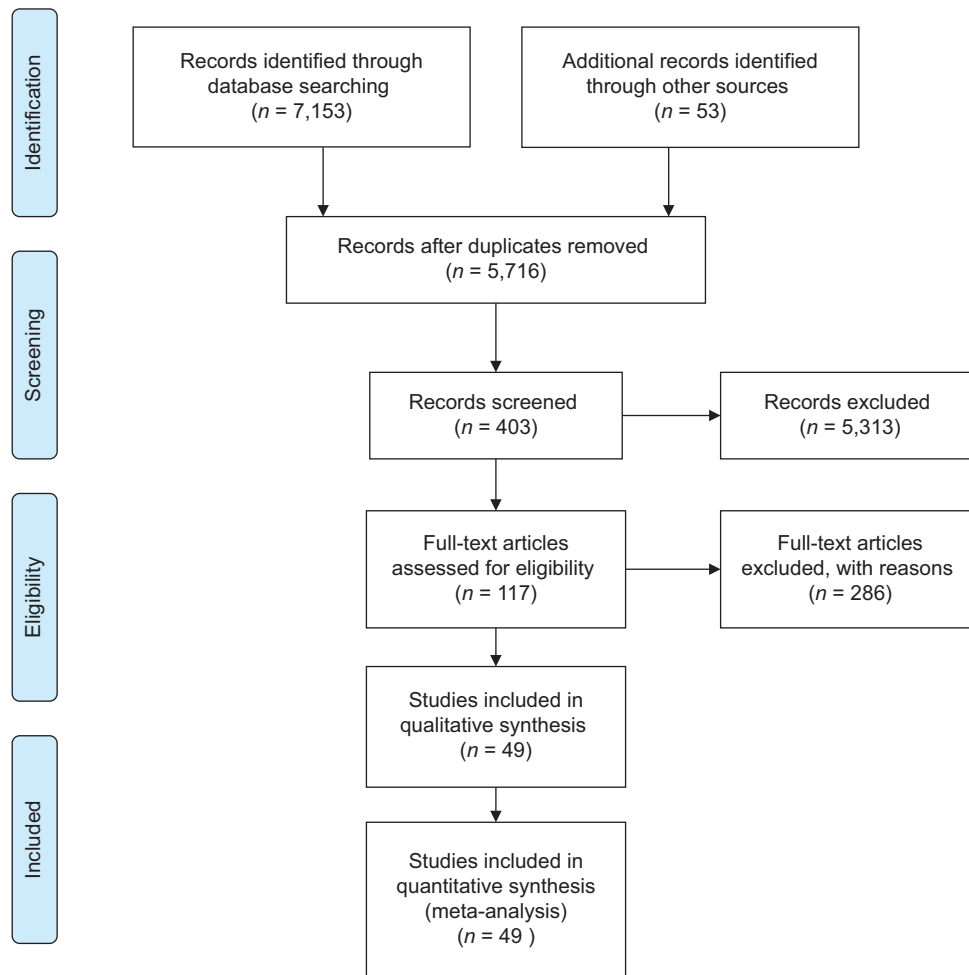


Figure 1: PRISMA diagram describing study selection process

(5 studies)<sup>[45,46,50,64]</sup> and Aloe vera (4 studies)<sup>[36,43,60,72]</sup> were the most frequently reported herbal compound by the included studies. Two studies reported using *Lippia sidoides*,<sup>[37,70]</sup> two studies reported using green tea (*Camellia sinensis*),<sup>[54,67]</sup> and two studies reported using *Calendula officinalis*.<sup>[45,51]</sup> Two studies reported using Myrrh (*Commiphora molm*).<sup>[46,64]</sup> Two studies reported using Sage (*Salvia officinalis*).<sup>[46,73]</sup> One study reported using garlic (*Allium sativum*).<sup>[71]</sup> One study reported using ginger (*Zingiber officinalis*).<sup>[49]</sup> One study reported using Haritaki (*Terminalia chebula*).<sup>[66]</sup> One study reported using Neem (*Azadirachta indica*).<sup>[48]</sup> One study reported using Thyme (*Thymus vulgaris*).<sup>[40]</sup> One study reported using Triphala.<sup>[66]</sup>

The most commonly described herbal product to treat oral diseases was gels,<sup>[38,43,47,56,57,62,63,68-70,77]</sup> mouth rinse,<sup>[37,40,44,48,51,52,64,66,67,74]</sup> and paste.<sup>[31,34,45,46,49,58,60,61,71,78]</sup> (The full list of herbal products is provided in Table 2).

The studies included a range of people with oral diseases including periodontal and gingival diseases (28 studies),<sup>[31,37,41,42,44-46,48-54,58,60-64,66-70,75-77]</sup> recurrent aphthous

stomatitis (6 studies),<sup>[33,34,36,47,57,65]</sup> oral lichen planus (5 studies),<sup>[32,39,43,59,72]</sup> and oral candidiasis (4 studies). Two studies included patients with oral mucositis due to chemotherapy or radiotherapy.<sup>[40,78]</sup> One study included patients with xerostomia in head and neck cancers.<sup>[55]</sup> One study included patients with Herpes labialis.<sup>[73]</sup> One study included patients with fluorosis<sup>[35]</sup> and one study included patients with pulpitis.<sup>[56]</sup>

### The effectiveness of herbal products interventions on oral health

Most studies reported multiple outcomes including gingival, periodontal, and plaque scores; clinical assessment of oral lesions, visual pain score, and quality of life. Of the 28 studies measuring gingival and periodontal outcomes, 17 studies reported gingival index measurements, and 14 studies (82.3%) found statistically significant positive results versus control.<sup>[37,41,46,48,50,51,62,64,66-70,75-77]</sup> Of the 24 studies reporting outcomes related to plaque control, 21 studies (87.5%) reported statistically significant positive results.<sup>[31,37,42,45,46,49-51,53,54,58,62,64,66-70,75-77]</sup> Of the 11 studies reporting clinical assessment of recurrent aphthous ulcers or

**Table 1: Summary of the included studies considering the effectiveness of herbal products for oral health in adolescents**

Study ID	Country	Compound	Forms of preparation
Krahwinkel and Willershausen <sup>[54]</sup>	Germany	Green tea	Chew candies
Kimbrough <i>et al.</i> <sup>[53]</sup>	United States	Pycnogenol (a standardized extract of <i>Pinus pinaster</i> bark)	Chewing gums
Pereira <i>et al.</i> <sup>[64]</sup>	Germany	Mixture of <i>salvia officinalis</i> , <i>mentha piperita</i> , menthol, <i>matricaria chamomilla</i> , <i>commiphora myrrha</i> , <i>carum carvi</i> , <i>Eugenia caryophyllus</i> , and <i>Echinacea purpurea</i>	Mouth rinse
Pannuti <i>et al.</i> <sup>[61]</sup>	Brazil	Parodontax (chamomile, echinacea, sage, rhatany, myrrh, and peppermint oil)	Paste
de Oliveira <i>et al.</i> <sup>[60]</sup>	Brazil	Aloe vera	Paste
Sharath <i>et al.</i> <sup>[75]</sup>	India	Sesame	Oil
Pereira <i>et al.</i> <sup>[63]</sup>	Brazil	Copaifera	Gel
Jayashankar <i>et al.</i> <sup>[49]</sup>	India	Mixture of <i>Acacia chundra</i> Willd, <i>Adhatoda vasica</i> Nees., <i>Mimusops elengi</i> L., <i>Piper nigrum</i> L., <i>Pongamia pinnata</i> L. Poir., <i>Quercus infectoria</i> Olivier., <i>Syzygium aromaticum</i> L., <i>Terminalia chebula</i> Retz., <i>Zingiber officinale</i> Roscoe.	Paste
Chen <i>et al.</i> <sup>[41]</sup>	China	<i>Rabdosia Rubescens</i>	Oral tablets
George <i>et al.</i> <sup>[46]</sup>	India	Herbal toothpaste containing calcium carbonate, chamomile, sage, myrrh eucalyptus, and sodium monofluorophosphate	Paste
Rodrigues <i>et al.</i> <sup>[70]</sup>	Brazil	<i>Lippia Sidoides</i>	Gel
Rassameemasmaung <i>et al.</i> <sup>[68]</sup>	Thailand	<i>Garcinia mangostana</i> L. Pericarp extract	Gel
Botelho <i>et al.</i> <sup>[37]</sup>	Brazil	<i>Lippia sidoides</i>	Mouth rinse
Adámková <i>et al.</i> <sup>[31]</sup>	Czech Republic	Herbal toothpaste containing <i>P. vulgaris</i> extract (0.5%), <i>M. cordata</i> extract (0.005%), a silica abrasive system, humectants and surfactants, but no fluoride	Paste
Jalaluddin <i>et al.</i> <sup>[48]</sup>	India	The 2% neem mouthwash	Mouth rinse
Khairnar <i>et al.</i> <sup>[51]</sup>	India	<i>Calendula officinalis</i> (C. officinalis)	Mouth rinse
Pradeep <i>et al.</i> <sup>[66]</sup>	India	Triphala, a traditional Ayurvedic medicine made from fruits of three medicinal trees: <i>Amalaki</i> ( <i>Embllica officinalis</i> ); <i>Bibhitaki</i> ( <i>Terminalia belerica</i> ); and <i>Haritaki</i> ( <i>T. chebula</i> ).	Mouth rinse
Sofrata <i>et al.</i> <sup>[76]</sup>	Sweden	Active <i>Salvadora persica</i> miswak	Chewing sticks
Somu <i>et al.</i> <sup>[77]</sup>	India	Pomegranate extract	Gel
Mohire <i>et al.</i> <sup>[58]</sup>	India	Chitosan-based polyherbal compound containing <i>Pterocarpus marsupium</i> aqueous extract (PM), <i>Stevia rebaudiana</i> aqueous extract (SR), <i>Glycyrrhiza glabra</i> aqueous extract (GG)	Paste
Cheng <i>et al.</i> <sup>[42]</sup>	China	<i>Ginkgo biloba</i> extract (EGB)	Chewing tablets
Pappu <i>et al.</i> <sup>[62]</sup>	India	Flax seed extract ( <i>Linum usitatissimum</i> )	gel
Diab <i>et al.</i> <sup>[44]</sup>	Lebanon	<i>Solanum melongena</i> ( <i>Solanaceae</i> ) peduncles extracts	Mouth rinse
Khoramian-Tusi <i>et al.</i> <sup>[52]</sup>	Iran	<i>Teucrium Polium</i>	Mouth rinse
Esfahani-Zadeh <i>et al.</i> <sup>[45]</sup>	Iran	SILCA herbal toothpaste containing <i>Achillea millefolium</i> , <i>Matricaria chamomilla</i> Syn. <i>Matricaria recutita</i> , and <i>Calendula Officinalis</i> extracts	Paste
Rabienejad <i>et al.</i> <sup>[67]</sup>	Iran	Green tea ( <i>Camelia sinensis</i> )	Mouth rinse
Karimi <i>et al.</i> <sup>[50]</sup>	Iran	SUAB2 (mixture of sumac, <i>Matricaria chamomilla</i> , and <i>Quercus Infectoria Oliv</i> )	Dental floss
Rayyan <i>et al.</i> <sup>[69]</sup>	Saudi Arabia	Grape seed extract	Gel
Babae <i>et al.</i> <sup>[34]</sup>	Iran	<i>Myrtus communis</i> (Myrtle)	Paste
de Armas <i>et al.</i> <sup>[33]</sup>	Cuba	<i>Rhizophora mangle</i> aqueous bark extract (RMABE)	Solution
Pourahmad <i>et al.</i> <sup>[65]</sup>	Iran	Camel thorn distillate	Solution
Moghadamnia <i>et al.</i> <sup>[57]</sup>	Iran	Bioadhesive patches	Gel
Bhalang <i>et al.</i> <sup>[36]</sup>	Thailand	Containing licorice extract	Skin patch
Ghalayani <i>et al.</i> <sup>[47]</sup>	Iran	<i>Acemannan</i> , a polysaccharide extracted from <i>Aloe vera</i>	Skin patch
Mousavi <i>et al.</i> <sup>[59]</sup>	Iran	<i>Punica granatum</i> (PG) extract	Gel
Salazar-Sánchez <i>et al.</i> <sup>[72]</sup>	Spain	<i>Ignatia amara</i>	Solution
Salazar-Sánchez <i>et al.</i> <sup>[72]</sup>	Spain	<i>Aloe vera</i>	Suspension
Agha-Hosseini <i>et al.</i> <sup>[32]</sup>	Iran	<i>Purslane</i>	Capsules
Choonhakarn <i>et al.</i> <sup>[43]</sup>	Thailand	<i>Aloe vera</i>	Gels

Contd...

Table 1: Contd...

Study ID	Country	Compound	Forms of preparation
Chainani-Wu <i>et al.</i> <sup>[39]</sup>	United States	Curcuminoids	Capsules
Tiemann <i>et al.</i> <sup>[78]</sup>	Germany	Ratanhia	Mouth rinse and paste
Charalambous <i>et al.</i> <sup>[40]</sup>	Cyprus	Thyme honey	Mouth rinse
Lim <i>et al.</i> <sup>[55]</sup>	Malaysia	Mixture of Chinese herbal treatments	Herbal extract
Sabitha <i>et al.</i> <sup>[71]</sup>	India	Garlic	Paste
Sefidgar <i>et al.</i> <sup>[74]</sup>	Iran	Artemisia Sieberi	Mouth rinse
Wright <i>et al.</i> <sup>[79]</sup>	South Africa	Lemon juice and lemon grass (Cymbopogon citratus)	Solution
de Souza Vasconcelos <i>et al.</i> <sup>[38]</sup>	Brazil	Punica Granatum	Gel
Saller <i>et al.</i> <sup>[73]</sup>	Switzerland	Rhubarb extract, sage extract, and Zovirax cream	Cream
Madani <i>et al.</i> <sup>[56]</sup>	Iran	Piperine	Gel
Basir <i>et al.</i> <sup>[35]</sup>	Iran	Shahed-herbal compound	Cream

Study ID	Method of intervention	Number of participants	Oral disease category	Outcome assessed	Intervention length (days)	Effectiveness of interventions
Krahwinkel and Willershausen <sup>[54]</sup>	Clinical randomized double-blind study	47	Gingivitis	API, SBI	28	Beneficial
Kimbrough <i>et al.</i> <sup>[53]</sup>	Clinical randomized double-blind study	40	Gingivitis	PLI, BI	14	Beneficial
Pereira <i>et al.</i> <sup>[64]</sup>	A randomized, double-blind clinical study	84	Gingivitis	PI, SBI, GI, PD	90	Beneficial
Pannuti <i>et al.</i> <sup>[61]</sup>	A double-blind study	30	Gingivitis	GI, PI	21	Likely to be ineffective or harmful
de Oliveira <i>et al.</i> <sup>[60]</sup>	A randomized, parallel, and double-blind clinical trial	30	Gingivitis	GBI, PI	30	Likely to be ineffective or harmful
Sharath <i>et al.</i> <sup>[75]</sup>	A randomized, controlled, triple-blind study.	20	Gingivitis	PI, MGI	10	Beneficial
Pereira <i>et al.</i> <sup>[63]</sup>	A randomized controlled clinical trial	23	Gingivitis	PLI, BI, GI	21	Likely to be ineffective or harmful
Jayashankar <i>et al.</i> <sup>[49]</sup>	A randomized double-blind placebo-controlled study	60	Gingivitis	SAnB, SAB, PI, BOP, PD	84	Beneficial
Chen <i>et al.</i> <sup>[41]</sup>	A randomized controlled trial	136	Gingivitis	GI	5	Beneficial
George <i>et al.</i> <sup>[46]</sup>	A double-blinded controlled clinical trial with parallel groups	30	Gingivitis	PI, GI	30	Beneficial
Rodrigues <i>et al.</i> <sup>[70]</sup>	A double-blind clinical study	26	Gingivitis	PLI, BI, GI	30	Beneficial
Rassameemasuang <i>et al.</i> <sup>[68]</sup>	A randomized controlled trial	31	Periodontitis	PPD, CAL, BOP, GI, PI	90	Beneficial
Botelho <i>et al.</i> <sup>[37]</sup>	A double-blinded randomized controlled trial	31	Gingivitis	PI, GI, BI	7	Beneficial
Adámková <i>et al.</i> <sup>[31]</sup>	A double-blind, placebo-controlled clinical trial	40	Gingivitis	PI, CPITN, PBI	84	Beneficial
Jalaluddin <i>et al.</i> <sup>[48]</sup>	A double-blind cross-over study	40	Gingivitis	GI	7	Beneficial
Khairmar <i>et al.</i> <sup>[51]</sup>	A double-blinded randomized controlled trial	240	Gingivitis	PI, GI, SBI, OHI-S	180	Beneficial
Pradeep <i>et al.</i> <sup>[66]</sup>	A randomized controlled clinical trial	90	Gingivitis	PI, GI, OHI-S	60	Beneficial
Sofrata <i>et al.</i> <sup>[76]</sup>	A double-blinded randomized controlled trial	68	Gingivitis	PI, GI	21	Beneficial
Somu <i>et al.</i> <sup>[77]</sup>	A randomized clinical study	40	Gingivitis	PI, GI, PBI	21	Beneficial
Mohire <i>et al.</i> <sup>[58]</sup>	A randomized clinical study	12	Plaque control	PI	28	Beneficial
Cheng <i>et al.</i> <sup>[42]</sup>	A randomized clinical study	60	Periodontitis	PI, BI, PD, AL	120	Beneficial
Pappu <i>et al.</i> <sup>[62]</sup>	A randomized clinical trial	60	Gingivitis	PI, GI, PD, AL	90	Beneficial
Diab <i>et al.</i> <sup>[44]</sup>	A double-blind clinical study	20	Periodontitis	BI, PD	90	Beneficial

Contd...

Table 1: Contd...

Study ID	Method of intervention	Number of participants	Oral disease category	Outcome assessed	Intervention length (days)	Effectiveness of interventions
Khoramian-Tusi <i>et al.</i> <sup>[52]</sup>	A cross-over double-blind randomized clinical trial	22	Plaque control	MS	14	Beneficial
Esfahani-Zadeh <i>et al.</i> <sup>[45]</sup>	A cross-over clinical trial study	60	Plaque control	PI	14	Beneficial
Rabienjad <i>et al.</i> <sup>[67]</sup>	A comparative study	50	Gingivitis	PI, GI, BI	60	Beneficial
Karimi <i>et al.</i> <sup>[39]</sup>	A randomized, split mouth, double-blind clinical trial	10	Gingivitis	PI, GI, PD, BOP	90	Beneficial
Rayyan <i>et al.</i> <sup>[69]</sup>	A randomized clinical study	5	Gingivitis	PD, GI, PI, BOP	28	Beneficial
Babae <i>et al.</i> <sup>[34]</sup>	A randomized controlled trial	45	RAS	SU, VAS, EL, OHIP, PS	6	Beneficial
de Armas <i>et al.</i> <sup>[33]</sup>	A pilot study	32	RAS	ACHT, QL, ADR	14	Beneficial
Pourahmad <i>et al.</i> <sup>[65]</sup>	A randomized controlled trial	93	RAS	ACHT, LD, VAS	14	Beneficial
Moghadamnia <i>et al.</i> <sup>[57]</sup>	A randomized controlled trial	30	RAS	VAS, ACHT, LD	5	Beneficial
Bhalang <i>et al.</i> <sup>[36]</sup>	A randomized controlled trial	330	RAS	VAS, LD	7	Beneficial
Ghalayani <i>et al.</i> <sup>[47]</sup>	A randomized, double-blind, and placebo-controlled study.	40	RAS	VAS, ACHT	7	Beneficial
Mousavi <i>et al.</i> <sup>[59]</sup>	A single-blind randomized control clinical trial	30	OLP	SU, VAS	120	Beneficial
Salazar-Sánchez <i>et al.</i> <sup>[72]</sup>	A randomized double-blind study	55	OLP	SU, VAS, OHIP, HAD	84	"Likely to be beneficial"
Agha-Hosseini <i>et al.</i> <sup>[32]</sup>	A randomized double-blind placebo-controlled trial	37	OLP	SU, VAS	90	Beneficial
Choonhakarn <i>et al.</i> <sup>[43]</sup>	A randomized controlled trial	54	OLP	SU, VAS	54	Beneficial
Chainani-Wu <i>et al.</i> <sup>[39]</sup>	A randomized, placebo-controlled, double-blind clinical trial	33	OLP	VAS, NRS, CSS	49	Likely to be beneficial"
Tiemann <i>et al.</i> <sup>[78]</sup>	A clinical trial	49	OM	PI, GI, DM, ACS	28	Beneficial
Charalambous <i>et al.</i> <sup>[40]</sup>	A randomized controlled trial	86	OM	OMAS, QL	180	Beneficial
Lim <i>et al.</i> <sup>[55]</sup>	An observational study	42	Xerostomia	USFR, SSFR, QL	180	Beneficial
Sabitha <i>et al.</i> <sup>[71]</sup>	A randomized trial	74	OC	CLR	14	Likely to be beneficial"
Sefidgar <i>et al.</i> <sup>[74]</sup>	A preliminary study	30	OC	CS	14	Beneficial
Wright <i>et al.</i> <sup>[79]</sup>	A randomized controlled trial	83	OC	OCG	11	Beneficial
de Souza Vasconcelos <i>et al.</i> <sup>[38]</sup>	A randomized controlled trial	60	OC	CLR	15	Beneficial
Saller <i>et al.</i> <sup>[73]</sup>	A double-blind, comparative, randomized trial	145	Herpes labialis	ACHT, LD, SU, PS	14	Beneficial
Madani <i>et al.</i> <sup>[56]</sup>	A randomized controlled trial	60	Pulpitis	VAS	3	Beneficial
Basir <i>et al.</i> <sup>[35]</sup>	A randomized clinical trial	72	Dental fluorosis	DBI, TD, ACHT	-	Likely to be ineffective or harmful

oral lichen planus lesions, 10 studies reported visual pain score measurements, and 8 studies (72.7%) reported statistically significant positive results versus control.<sup>[32,34,36,43,47,57,59,65]</sup>

### Adverse events

Of the 49 studies included in the review, 24 studies<sup>[31,35,41,42,44-50,52-59,64,67,74-76]</sup> did not report any data about the adverse side-effects of interventions. A total of 19 studies<sup>[32-34,36,40,43,51,60,62,63,65,66,68-72,77,78]</sup> reported no adverse side effects for interventions. Six studies<sup>[37-39,61,73,79]</sup> reported

some sorts of mild and transient side effects for herbal products. Dry mouth was reported by three studies<sup>[39,61,79]</sup> as adverse side effects of interventions. Burning sensation was reported by two studies.<sup>[37,61]</sup> Nausea and gastric disorders were reported by two studies.<sup>[38,79]</sup> Metallic taste was also reported by one study.<sup>[39]</sup>

### Discussion

A variety of approaches have been used to treat stomatognathic diseases, including corticosteroids,

**Table 2: Herbal products used in selected studies (n=49)**

Herbal products	Studies
Chewing gum (n=1)	Kimbrough <i>et al.</i> (2009) <sup>[53]</sup>
Dental floss (n=1)	Karimi <i>et al.</i> (2013) <sup>[50]</sup>
Gels (n=11)	Pereira <i>et al.</i> (2010), <sup>[63]</sup> Rayyan <i>et al.</i> (2018), <sup>[69]</sup> Rodrigues <i>et al.</i> (2009), <sup>[70]</sup> Rassameemasmaung <i>et al.</i> (2008), <sup>[68]</sup> Somu <i>et al.</i> (2012), <sup>[77]</sup> Pappu <i>et al.</i> (2019), <sup>[62]</sup> Moghadamnia <i>et al.</i> (2009), <sup>[57]</sup> Ghalayani <i>et al.</i> (2013), <sup>[47]</sup> Choonhakarn <i>et al.</i> (2008), <sup>[43]</sup> de Souza Vasconcelos (2003), <sup>[38]</sup> Madani <i>et al.</i> (2002) <sup>[56]</sup>
Herbal extracts (n=4)	Agha-Hosseini <i>et al.</i> (2010), <sup>[32]</sup> Bhalang <i>et al.</i> (2013), <sup>[36]</sup> Cheng <i>et al.</i> (2014), <sup>[42]</sup> Lim <i>et al.</i> (2019) <sup>[55]</sup>
Liquids and suspensions (n=4)	de Armas <i>et al.</i> (2005), <sup>[33]</sup> Pourahmad <i>et al.</i> (2010), <sup>[65]</sup> Mousavi <i>et al.</i> (2009), <sup>[59]</sup> Wright <i>et al.</i> (2009) <sup>[79]</sup>
Mouth rinse (n=9)	Pistorius <i>et al.</i> (2003), <sup>[64]</sup> Botelho <i>et al.</i> (2007), <sup>[37]</sup> Jalaluddin <i>et al.</i> (2017), <sup>[48]</sup> Khairnar <i>et al.</i> (2013), <sup>[51]</sup> Pradeep <i>et al.</i> (2016), <sup>[66]</sup> Diab <i>et al.</i> (2011), <sup>[44]</sup> Khoramian-Tusi <i>et al.</i> (2015), <sup>[52]</sup> Rabienejad <i>et al.</i> (2018), <sup>[67]</sup> Charalambous <i>et al.</i> (2018), <sup>[40]</sup> Sefidgar <i>et al.</i> (2010) <sup>[74]</sup>
Oils for oral health (n=1)	Sharath <i>et al.</i> (2009) <sup>[75]</sup>
Oral ointments and creams (n=3)	Saller <i>et al.</i> (2001), <sup>[73]</sup> Basir <i>et al.</i> (2013), <sup>[35]</sup> Sabitha <i>et al.</i> (2005) <sup>[71]</sup>
Oral tablets, candies, and capsules (n=3)	Krahwinkel and Willershausen (2000), <sup>[54]</sup> Cheng <i>et al.</i> (2014), <sup>[42]</sup> Chainani-Wu <i>et al.</i> (2007), <sup>[39]</sup> Chen <i>et al.</i> (2009) <sup>[41]</sup>
Toothbrush stick (n=1)	Sofrata <i>et al.</i> (2011) <sup>[76]</sup>
Paste (n=10)	George <i>et al.</i> (2009), <sup>[46]</sup> Adámková <i>et al.</i> (2004), <sup>[31]</sup> Jayashankar <i>et al.</i> (2011), <sup>[49]</sup> Mohire and Yadav (2010), <sup>[58]</sup> Esfahani-Zadeh <i>et al.</i> (2018), <sup>[45]</sup> Babae <i>et al.</i> (2010), <sup>[34]</sup> Tiemann <i>et al.</i> (2007), <sup>[78]</sup> Pannuti <i>et al.</i> (2003), <sup>[61]</sup> de Oliveira <i>et al.</i> (2008) <sup>[60]</sup>

antimicrobial ingredients, retinoids, topical antifungal drugs, calcineurin inhibitors, and surgery. The main disadvantages of these treatments are their adverse effects. Several studies have investigated the application of natural and herbal formulations for treating different oral diseases, particularly gingivitis, mucositis, and stomatitis.<sup>[37-39,61,73,79]</sup> In this scenario, phototherapy has been adopted as a therapeutic alternative to reduce symptoms and improve patients' quality of life; it also offers the advantages of low cost, availability, and absence of adverse effects.

This systematic review assessed applications of herbal drugs for treating oral and dental disorders and included 49 studies, involving 2,909 adolescents that used medicinal plants and herbal products in oral health care.<sup>[57]</sup> Medicinal plants and herbal products have been shown to improve a wide range of clinical outcomes in patients with oral conditions. To our knowledge, this is the first systematic review of the effectiveness of therapeutic approaches based on medicinal plants and herbal products on stomatognathic diseases in adolescents. The overall methodological quality of the included studies was moderate to high.

In most included studies,<sup>[80-83]</sup> the effectiveness and safety of medicinal plants and herbal products were illustrated in comparison with standard or conventional treatments to improve gingivitis, periodontitis, plaque scores, pain, and quality of life in most included studies.<sup>[80-83]</sup> Systemic administration and local drug delivery are both important ways of drug administration. However, systemic administration could cause many other problems, like drug resistance, dysbacteriosis, and systemic side effects. The antibacterial effect is also limited as very little can arrive at the oral lesion area

after systemic circulation. The findings of this systematic review show using topical preparations instead of oral or systemic drugs. Herbal mixtures were prepared in a wide range of forms such as gels, pastes, mouth rinses, capsules, oils, and ointments. The most commonly used herbal formulations were gels, mouth rinses, and pastes, respectively. Despite the absence of pharmacological studies to verify their safety, our findings highlighted encouraging effects and high safety profiles.

Findings demonstrated the clinical effectiveness of herbal products in improving gingivitis and dental plaque formation in patients with oral conditions. These findings are in line with the recent evidence indicating the antimicrobial activity of herbal products and their potential to modulate dental plaque formation and caries development.<sup>[80-83]</sup> The anti-gingivitis and anti-plaque effects of herbal products were previously examined by several randomized controlled trials.<sup>[84-87]</sup> In addition, several *in vitro*,<sup>[88-91]</sup> *in vivo*,<sup>[92-95]</sup> and clinical trials<sup>[96-100]</sup> have demonstrated the effectiveness and safety of herbal products in oral health.

According to our results, chamomile was the most frequently used herbal product in the treatment of oral conditions, especially gingivitis and plaque control. Chamomile has been frequently reported as an anti-gingivitis and anti-plaque agent in a number of previous studies.<sup>[101-103]</sup> Chamomile's antimicrobial, antiviral, and anti-inflammatory properties are attributed to a number of pharmacologically active compounds such as bisabolol and related sesquiterpenes, flavonoids, apigenin, luteolin, and quercetin.<sup>[24]</sup> Existing evidence suggests the effectiveness of chamomile in the treatment of different systemic and oral lesions such as aphthous ulcers.<sup>[104,105]</sup> However, evidence on the effectiveness of



this natural compound in the treatment of oral lichen planus is extremely limited.<sup>[106,107]</sup>

According to our findings, Aloe vera was the second most frequently used herbal compound for the treatment of patients with oral conditions. Aloe vera has been used as a therapeutic agent since Roman times.<sup>[100]</sup> The antimicrobial activity of *A. Vera* is attributed to some pharmacologically active compounds, including anthraquinones, aloin A and B, aloe-emodin, aloetic acid, anthracene, aloe mannan, aloeride, antranol, chrysophanic acid, resistanol, and saponin.<sup>[108]</sup> Aloin and aloe-emodin are responsible for the antimicrobial and antiviral activities of *Aloe vera*. In the present study, *Aloe vera* indicated similar effectiveness against gingivitis and dental plaque in comparison with a conventional paste containing fluoride. This finding is confirmed by a number of previous clinical trials that indicated the anti-inflammatory and anti-plaque properties of *Aloe vera* in the treatment of gingival inflammation.<sup>[109-111]</sup> In addition, our results indicated the clinical effectiveness of Aloe vera in improving the quality of life and clinical symptoms of patients with oral lichen planus. According to existing evidence, Aloe vera indicated promising results with no adverse side effects in comparison with placebo<sup>[112]</sup> and triamcinolone acetone<sup>[113]</sup> in patients with oral lichen planus. It can be concluded from the existing evidence that Aloe vera is an effective herbal compound that can be used as an alternative or adjuvant treatment against a number of oral diseases such as gingivitis, oral lichen planus, ulcers, gum abscesses, gingival problems associated with AIDS, candidiasis, desquamative gingivitis, and xerostomia<sup>[24]</sup> These findings are comparable with previous results that varied greatly across different studies.

### Limitations

- Although there are limitations in this review, some of them are considering the small sample size and the short duration of the reported studies, it is not clear whether these results can be considered for all studies
- As gray literature (unpublished, possibly only presented) was not considered, some results may have been missed. The risk of bias in many studies was unclear due to vague description of the studies, making the results more uncertain.
- The actual effect of the treatment measures performed cannot be determined due to the diverse methods used in the studies and the lack of uniform outcome measures.
- Attempts to summarize the results of the studies were difficult because different outcome measures were used; most of the studies did not measure the effectiveness and only mentioned whether the results were significant or not.

### Conclusion

Oral and dental hygiene is one of the most important issues that today, in addition to individuals and families, has attracted the attention of the government and the policy-making of the health sector. Taking into account the policies of the World Health Organization regarding oral and dental health and on the other hand, the low cost and affordability of the therapeutic and preventive measures of traditional medicine and medicinal plants in oral and dental health, it is recommended to familiarize and use them.

This systematic review presents the use of medicinal plants and herbal products for a wide range of oral diseases including gingivitis, plaque, aphthous ulcers, and oral lichen planus. Our findings demonstrate that herbal products have the ability to improve clinical oral health outcomes in adolescents. Limited adverse side effects indicate the overall safety of these treatments for a wide range of oral diseases.

The benefit of the current study is introducing the most common herbal medicines for curing stomatognathic diseases as alternative therapies. Also the writers suggest designing a meta-analysis systematic review entitled a definite oral and dental disorder, and evaluation of herbal medicines effectiveness for treatment. Performing of these studies' series will conduct to introduce herbal protocols for treatment oral and dental diseases as a complementary medicine.

However, numerous studies with reference to the beneficial properties of herbal medicine in dentistry claim that herbal products can be employed as alternatives for conventional drugs, without performing how mechanisms of active ingredients *in vivo* and *in vitro*, and the majority of them. Therefore, these researches are conducted at *in vitro* and pre-clinical settings. Therefore, there is an urgent need to increase research efforts and funding aimed at clinical trials on efficacy, safety, cost-effectiveness, and characterization of these natural compounds.

### Abbreviations

ACHT, Average complete healing time; ACS, Assessment of quality symptoms; ADR, Adverse drug reactions; AL, Attachment loss; API, Approximal plaque index; BI, Bleeding index; BOP, Bleeding on probing; CAL, Clinical attachment level; CLR, Clinical and laboratory response; CPITN, Community periodontal index of treatment needs; CS, Colony size; CSS, Change in symptoms scale; DBI, Dental beauty index; DM, Degree of mucositis; EL, Erythema and exudation level; GBI, Gingival bleeding index; GI, Gingival index; HAD, Hospital anxiety-depression; LD, Lesion diameter; MGI, Modified gingival

index; MS, Streptococcus Mutans; NRS, Numerical rating scale; OC, Oral candidiasis; OCG, Oral candidiasis grading; OHIP, Oral health impact profile; OHI-S, Oral hygiene index simplified; OLP, Oral lichen planus; OM, Oral mucositis; OMAS, Oral mucositis assessment scale; PBI, Papillary bleeding index; PD, Probing depth; PI, Plaque index/score; PPD, Probing pocket depth; PS, Patient satisfaction; PS, Persistence of symptoms; QL, Quality of life; RAS, Recurrent aphthous stomatitis; SAB, Aerobic bacterial counts; SAnB, Anaerobic bacterial counts; SBI, Sulcus bleeding index; SSFR, Stimulated salivary flow rate; SU, Size of ulcers; TD, Tooth discoloration; USFR, Un-stimulated salivary flow rate; VAS, Visual pain scale/score.

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### Conflicts of interest

There are no conflicts of interest.

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