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[Intervention Protocol]

Herbal medicines to prevent dental caries

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ABSTRACT

Objectives

This is a protocol for a Cochrane Review (intervention). The objectives are as follows:

To assess the effects of herbs/herbal extracts to prevent or minimise tooth decay in children and adults.

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BACKGROUND

Description of the condition

Dental caries is the oldest recognized and most common non-communicable disease worldwide (WHO 2017). The Global Burden of Disease Study of 2019 estimated that nearly 3.5 billion people worldwide have oral diseases, of which dental caries of the permanent teeth is the most prevalent. Dental caries disproportionately affects low- and middle-income countries (LMICs) and is commonly found in people from poor socioeconomic backgrounds (GBD 2020).

The development of dental caries arises from a complex interplay between fermentable carbohydrates, acidogenic bacteria, and tooth enamel, necessitating multifaceted interventions that focus on modifying the substrate (dietary adjustments, fluoride varnish), enhancing enamel integrity (fluoride supplementation, sealants), or disrupting the biofilm and its metabolic activity (mechanical plaque removal, antimicrobial agents) (Yon 2019).

The unequal distribution of healthcare professionals, the cost of oral healthcare infrastructure, and inadequate facilities make access to standardized oral health care difficult for those from low- to middle-income groups. These groups are far less likely to visit a dental healthcare professional for preventive visits (GBD 2020).

The prevalence and severity of oral diseases are correlated consistently with socioeconomic status (income, occupation, and educational attainment). Oral diseases and conditions disproportionately affect the poor and vulnerable members of society throughout life, frequently including those with low incomes, those with disabilities, refugees, and socially excluded groups (Benzian 2021). Higher caries prevalence is associated in children with special needs such as autism (da Silva 2017), cerebral palsy (Cardoso 2014), and children living with disabilities (Uwayezu 2020).

Diagnosis of dental caries is done using a visual examination method which is supplemented by additional diagnostic tools such as bitewing radiography, laser fluorescence, and fibre-optic transillumination methods (Kapor 2021).

Dental caries have a negative impact on the oral health-related quality of life (Haag 2017; Zaror 2022). In addition, it also impacts the health-related cost. The American Dental Association (ADA) reported that national dental expenditures increased by 11% from US dollars (USD) 146 billion in 2020 to USD 162 billion in 2021 (ADA 2021). Similarly, in 2022, consumer spending on dental services in the UK was at approximately British pounds (GBP) 3.1 billion, an increase from the previous year (Yang 2023), while in Australia the dental industry revenue was estimated to be Australian dollars (AUD) 10.6 billion in 2022 (ADIA 2022). In light of these figures, we firmly believe that preventive strategies in oral health care should be prioritized over treatment.

Strategies and methods to prevent the initiation of dental caries have been widely explored in the literature. Numerous systematic reviews have assessed the efficiency of fluorides, dental floss, fissure sealants, dietary recommendations, and antimicrobial therapy in preventing dental caries (Harris 2012; Kashbour 2020; Pereira-Cenci 2013; Worthington 2019). Fluorides have been the most widely reported preventive measure (Benson 2019; Marinho 2016; Marinho 2009; Walsh 2019). Fluoride inhibits demineralization, aids remineralization, and is an effective bacteriostatic agent (Featherstone 1999). While fluoride demonstrably reduces dental caries, its optimal use necessitates balancing its benefits against potential downsides such as dental and skeletal fluorosis. Moreover, the application of fluorides to prevent tooth decay is restricted, and crucial preventive techniques such as community-based approaches, topical fluoride treatments, or access to fluoridated toothpaste are often inaccessible or economically infeasible for a significant portion of the population (Benzian 2021). These preventive strategies vary between patients based on their caries risk assessment. The present clinical practice guidelines have categorized such strategies for low-, moderate-, and high-risk caries groups (AAPD 2022; SDCEP 2018). The American Academy of Pediatric Dentistry suggests that individuals aged six years and above who are at low risk for dental caries should schedule a dental check-up every six to 12 months, and radiographs need to be taken every 12 to 24 months. For individuals at moderate risk, the recommended recall interval is every six months, and radiographs are to be taken every six to 12 months. For individuals at high risk, recall should be every three months, and radiographs should be taken every six months (AAPD 2022; Brown 2008). The Scottish Dental Clinical Effectiveness Programme recommends enhanced preventive measures for children who have increased caries risk (SDCEP 2018).

Description of the intervention

The strategies for the prevention of dental caries have been broadly divided into three categories based on the characteristics of the individuals carrying them out: 1. community-based strategy, 2. professional-based strategy, and 3. individual-based strategy (self-care) (Motallaei 2021). Herbal interventions can be a part of routine self-care due to their economical nature and easy accessibility without prescription and at home.

Community-based strategies encompass practices such as adding fluoride to water, salt, milk, or combinations of these. Dental professionals employ techniques such as oral prophylaxis, fluoride therapy, fissure sealants, and antimicrobial agents. On an individual level, self-care methods involve using fluoride toothpaste, fluoride supplements, fluoride mouthwashes, fluoride gels, as well as chlorhexidine gels and mouthwashes. Additionally, there are slow-release fluoride devices, dietary adjustments, and non-cariogenic sweeteners such as xylitol (Motallaei 2021).

Despite their longstanding use in traditional medicine for millennia, herbal formulations are gaining broader acceptance within the framework of evidence-based medicine (EBM). The once-distinct realms of traditional knowledge and EBM are gradually converging, with herbal formulations emerging as a promising area of exploration and integration for holistic health care (Woo 2012).

Herbal medicines encompass herbs, herbal materials, herbal preparations, and finished herbal products that contain plants, plant materials, or their combinations as active ingredients (Shinde 2009). Herbal medicines are dispensed in traditional forms, such as powder or oil, or commercial forms, such as tablets, pastes, or gels (Sumantran 2011). Beyond their individual chemical components, herbal interventions engage in dynamic interactions within ecosystems, influencing both the plants themselves and the human populations utilizing them. If utilized appropriately, herbs offer economical and accessible adjuncts to routine oral health

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care. Incorporating herbs or herbal extracts may aid in preventing dental diseases with minimal cost.

Besides preventing dental caries, some medicinal plants have proven more effective than drugs at restoring and regulating the body's overall well-being. A synergy of the active ingredients enables the preventive and regulatory activities of the body's defence mechanisms to fight external infections (Cruz 2017).

The interventions for prevention of dental caries in high, moderate, and low caries risk groups vary in the frequency and concentration of the non-herbal interventions such as topical fluoride (SDCEP 2018), and this could be applicable to the herbal interventions also.

How the intervention might work

Herbal interventions are known for their antibacterial properties, and various herbs documented in the literature have been shown to be effective against several oral micro-organisms that contribute to dental caries.

Limited studies have reviewed the role of sugar substitutes such as xylitol and sorbitol in preventing dental caries (Hayes 2001; Mickenautsch 2007). These findings suggest that replacing sucrose with sorbitol and xylitol can significantly decrease the incidence of dental caries.

Sorbitol, a six-carbon sugar alcohol that exists naturally in several vegetables, fruits, tobacco, and seaweed, is commonly found in pears, apples, peaches, and grapes. Unlike other sugar alcohols, sorbitol is not fermented by oral bacteria, making it non-cariogenic. This non-cariogenic property makes it a popular additive in gums, candies, and toothpaste (Msomi 2021).

Erythritol, a non-fermentable sugar alcohol, resists metabolism by oral bacteria, including *Streptococcus mutans*, a major contributor to dental caries. This prevents acid production in the mouth, a crucial factor in demineralizing tooth enamel and subsequent development of caries (Mäkinen 2010). *In vitro* experiments have shown a direct inhibitory effect of erythritol on the growth of *S mutans* (Loimaranta 2020; Runnel 2013).

Miswak traditionally refers to a twig from the Salvadora persica tree, also known as the toothbrush tree. Miswak (*Salvadora persica*) possesses both antibacterial and anti-inflammatory properties, making its use in mouthwashes and toothpastes beneficial for oral hygiene (Al-Dabbagh 2016). The multifactorial mechanism behind Miswak's effectiveness in preventing dental caries involves several key actions including the presence of antimicrobials such as tannins, flavonoids, and alkaloids, which effectively inhibit the growth of cariogenic bacteria within the oral cavity (Almas 2005). Second, Miswak increases salivary production, a natural defence mechanism against dental caries. Saliva aids in neutralizing the acid produced by cariogenic bacteria and thus promotes remineralization of tooth enamel (Haque 2015).

Grape seed extract (GSE), an easily accessible supplement, holds promising potential as both a dental restorative and a caries preventive agent due to its high content of proanthocyanidins (PACs). These PACs act as potent antioxidants (Delimont 2020), exhibiting significant protective effects on dentine. Studies have shown that PACs reduce degradation rates and improve the mechanical properties of the organic matrix (Bedran-Russo 2011). Furthermore, research by Zhao and colleagues demonstrated that GSE effectively inhibits the growth of *S mutans* biofilm in an in vitro model, suggesting its potential in preventing enamel caries (Zhao 2014).

Triphala translates to 'three fruits,' directly reflecting its composition and capturing its long-standing tradition in Ayurvedic medicine. Triphala, a blend of fruits from *Terminalia bellirica*, *Terminalia chebula*, and *Emblica officinalis*, has been extensively researched for its antimicrobial properties. Triphala demonstrates potent antibacterial activity against *S mutans* biofilm in laboratory-based in vitro studies (Shanbhag 2015).

Research by Ferrazzano and colleagues suggests that the polyphenolic compounds found in pomegranate could be beneficial in both preventing and treating dental caries (Ferrazzano 2017). Similarly, a study conducted by Gulube and colleagues demonstrated that extracts from *Punica granatum* effectively killed cariogenic *S mutans* bacteria at higher concentrations. Interestingly, at lower concentrations, the extract still limited biofilm formation and acid production, suggesting its potential as a preventive agent against dental caries (Gulube 2016).

Fennel seeds, Shataputi (Ayurveda), scientifically known as *Foeniculum vulgare*, are a rich source of various minerals and vitamins, including calcium, phosphorus, iron, sodium, potassium, thiamine, riboflavin, niacin, and vitamin C (Rather 2016). One randomized controlled trial (RCT) conducted by Sultan and colleagues demonstrated that chewing fennel seeds significantly increases plaque pH, calcium, and phosphate concentration (Sultan 2016). This, in turn, can help neutralize acids produced by bacteria and promote tooth remineralization, both of which are crucial for preventing dental caries.

Cardamom, Ela (Sanskrit), and Elaichi (Ayurveda) has been shown to exhibit antibacterial and antifungal properties, demonstrating effectiveness against oral pathogens such as *S mutans* and *Candida albicans* (Karimi 2020). While its mildly pungent yet pleasant flavour stimulates saliva production, the fibrous exterior of cardamom pods provides mechanical cleansing of the teeth, contributing to overall oral hygiene.

Syzygium aromaticum, commonly known as clove, Lavanga (Sanskrit), belongs to the Myrtaceae family. Uju and colleagues investigated the *n*-hexane extract of clove seeds, demonstrating its specific growth-inhibitory activity against *S mutans* (Uju 2011). This finding suggests the potential application of clove extract as an ingredient in toothpaste formulations. Further research by Oluwasina and colleagues evaluated the antibacterial efficacy of a toothpaste containing *Syzygium aromaticum* (Oluwasina 2019). The results revealed the formulation's strong antibacterial activity against cariogenic pathogens, attributed to the presence of bioactive components within the clove.

Oil pulling, Gandoosha (Sanskrit), a traditional oral hygiene practice, involves swishing a small amount of edible oil, such as coconut, sesame, or sunflower oil, around the mouth for a specific period, typically around 15 to 20 minutes. The practice aims to improve oral health and hygiene by drawing out toxins, bacteria, and other impurities from the mouth. Sesame oil is traditionally used in Ayurveda for gandoosha (Peng 2022).

Commonly known as holy basil, Tulsi (Ocimum sanctum), Thulasi (Siddha), and Tulsi (Ayurveda), is a widely recognized

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medicinal herb in Ayurveda. Agarwal and colleagues evaluated the antimicrobial activity of Tulsi and concluded that its effectiveness was attributed to the presence of eugenol, ursolic acid, and carvacrol (Agarwal 2010). The authors recommended utilizing Tulsi in an ethanolic extraction form as a caries-preventive agent due to its ease of availability, cost-effectiveness, minimal to no adverse effects, and widespread cultural acceptance.

Stevia rebaudiana is a perennial shrub belonging to the Asteraceae family (Brambilla 2014). Stevia extracts have been proposed to possess a caries-preventing effect due to their potential antibacterial properties and ability to decrease the consumption of fermentable carbohydrates.

Curcumin, the active compound in turmeric, Haridra (Ayurveda), is widely recognized for its antibacterial properties. Song and colleagues demonstrated that curcumin ingestion significantly reduced the adherence of *S mutans* to tooth surfaces (Song 2012). This suggests that curcumin consumption may potentially prevent the adhesion of this cariogenic bacterium, thereby inhibiting the development of dental caries and plaque.

Studies have shown that theobromine present in cacao, the unprocessed version of cocoa, can harden tooth enamel and therefore decrease the likelihood of dental caries (Nimbulkar 2020). In addition, Babu and colleagues compared cacao bean husk extract mouthwash and chlorhexidine mouthwash in the reduction of *S mutans* count (Venkatesh Babu 2011).

Aprillia and colleagues found that applying rice husk nano silica significantly increased the amount of hydroxyapatite in dentine (Aprillia 2022). Additionally, a 2% concentration of rice husk nano silica exhibits antimicrobial properties, effectively killing *S mutans* bacteria.

Liquorice (*Glycyrrhiza* spp), a common herb in traditional Chinese medicine and Ayurveda, also known as 'gancao' (sweet grass), is believed to possess antimicrobial, antiviral, anti-inflammatory, and antitumor properties (Wang 2015). Several short-term RCTs have demonstrated its anticariogenic effects by showing its ability to reduce *S mutans* counts.

Magnoliae Officinalis Cortex, also known as 'Houpo' in Chinese, has been extensively used in Southeast Asia for treating abdominal distension and relieving anxiety (Luo 2019). In vitro testing of magnolia bark extract (MBE) against multispecies oral biofilms demonstrated a significant reduction in their biomass, thickness, and viability (Komarov 2017). Furthermore, short-term use of MBE chewing gum has shown beneficial effects on oral health.

Goenka 2013 reported that tea leaves from the *Camellia sinensis* plant can be processed into three different types of tea: green tea, black tea, and oolong tea. These medicinal plants contain compounds with diverse effects beneficial to oral health, including antibacterial properties, inhibition of bacterial and salivary amylase activity, and suppression of acid production, ultimately contributing to the prevention of dental caries.

A 2021 review by Abuzenada and colleagues highlighted the effectiveness of several medicinal herbs in preventing tooth decay (Abuzenada 2021). These herbs include *Medicago sativa* (alfalfa), *Aloe barbadensis Miller* (aloe vera), and *Trifolium pratense* (red clover).

Propolis, a natural resinous substance produced by bees, contains flavonoids that are known to have antibacterial, antifungal, and anti-inflammatory effects. Most commercially available propolis extracts were found to be effective against oral bacteria associated with dental caries, periodontal disorders, and Candida infections (Stähli 2021). In one RCT, Bapat and colleagues found propolis to be as efficient as chlorhexidine in the reduction of plaque and pathogens causing dental caries when used as a mouth rinse (Bapat 2021).

Xanthorrhizol, a bioactive compound isolated from the *Curcuma xanthorrhiza* rhizome (Java turmeric), has been shown to possess significant antibacterial effects against caries-associated bacteria. This species, native to Southeast Asia, possesses distinct properties and applications, often used in local traditional medicine systems such as Jamu in Indonesia. In vitro experiments demonstrated its efficacy against a range of bacterial species while exhibiting a selective inhibitory action on the growth of *S mutans* (Cho 2020; Philip 2020).

Native to South America, Bauhinia forficata link (BFL), also known as Brazilian orchid tree has a history of being used in Brazilian folk medicine for treating diabetes. Notably, BFL tincture exhibits significant antimicrobial activity against *S mutans*, a key bacterium associated with dental caries, demonstrating its potential as an effective agent against tooth decay (Ferreira-Filho 2020).

Some of the traditional medicinal systems such as Ayurveda use combinations of various herbs. In such poly-herb combinational interventions, one or two ingredients will be active and the remaining ingredients have a supporting role (Kumar 2017). Therefore, it is beyond the scope of this review to describe the action of all such interventions. However, if available in the included studies, we will include textual inputs about such poly-herb combination to enable the reader to interpret the results contextually to the respective traditional medicinal philosophy.

Why it is important to do this review

The James Lind Alliance identified the top 10 priorities for oral and dental health, with the highest priority being the search for the most effective way to prevent tooth decay and reduce oral health inequalities at the community or population level (JLA 2018). This highlights the critical need for effective and accessible solutions to address this widespread issue. Growing interest in natural products and traditional medicine extends to their potential for preventing and treating various diseases, including dental caries. Many herbal remedies, used for centuries in traditional medicine to promote oral health, possess demonstrably beneficial properties, such as antibacterial and anti-inflammatory effects, that could contribute to the prevention of tooth decay. Therefore, exploring the potential of herbal remedies for preventing dental caries represents a crucial area of research. In light of this, we propose including a comprehensive systematic review that compiles and critically analyzes various herbal agents with the potential to aid the general population in preventing and minimizing dental caries.

While several systematic reviews have assessed the effectiveness of herbal products for reducing dental plaque (Lima 2021; Mathur 2018; Shui 2021), preventing gingivitis, oral mucositis, and denture stomatitis (Shui 2021), research on their role in dental caries prevention remains limited. Existing scientific reviews and clinical trials primarily compare the efficacy of individual herbal products

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or two at most for routine oral health care. Notably, one 2015 Cochrane review investigated the use of xylitol-containing products for preventing dental caries in children and adults, highlighting the potential of specific ingredients (Riley 2015).

While a systematic review and meta-analysis conducted by Kengadaran and colleagues compared the effectiveness of herbal and conventional toothpaste, no comprehensive systematic review to date has investigated the efficacy of herbal interventions for dental caries prevention (Kengadaran 2022). This present systematic review aims to address this gap by providing evidence-based knowledge about the role of herbal products in preventing dental caries, ultimately contributing to a better understanding of their potential benefits, risks, limitations, and informing oral healthcare decisions.

The COVID-19 pandemic severely disrupted the delivery of essential oral healthcare services worldwide, leading to postponed treatments, increased antibiotic prescriptions, and exacerbated disparities in oral health. However, instead of solely posing a challenge, the pandemic presented an opportunity to further integrate herbal remedies into oral health care. LMICs with limited access to oral healthcare facilities stand to benefit significantly from evidence supporting the use of herbal products in preventing dental caries, especially during situations such as pandemics when access to health care becomes particularly challenging.

OBJECTIVES

To assess the effects of herbs/herbal extracts to prevent or minimise tooth decay in children and adults.

METHODS

Criteria for considering studies for this review

Types of studies

We will include RCTs with parallel arm (randomized at the level of participant) or cluster-RCT design (randomized at the cluster level). We do not expect to find cross-over trials on this review topic. We will exclude quasi-RCTs, split-mouth studies, controlled clinical trials, and experimental studies conducted in a laboratory environment.

Types of participants

We will include participants of any age or gender who are exposed to herbal intervention strategies that aim to prevent dental caries.

We will include participants who have undergone radiotherapy in the head and neck region, diagnosed with xerostomia, dental anomalies such as Turner's hypoplasia, dental fluorosis, and studies that have included people with behavioural, physical, emotional, or learning difficulties.

We will include studies that have assessed the outcomes in deciduous dentition, mixed dentition, permanent dentition, or combinations of these.

Types of interventions

- **Experimental interventions:** we will include all types of herbal interventions (e.g. Miswak, erythritol, grape seed, fennel seed, oil pulling/swishing, turmeric/curcumin, stevia rebaudina, cardamom, liquorice, sorbitol, magnoliae cortex, xanthorrhizol, bauhinia forfitica, propolis, pomegranate, triphala, rice husk, cacao, clove, thulasi).
- **Control interventions:** we will include all types of control interventions such as routine toothbrushing using toothpaste/powder or use of herbal/non-herbal mouthwash.

We will include studies that have any herbal intervention with or without routine toothbrushing once or twice per day ('herbal intervention A' versus 'usual care (toothpaste or tooth powder)' or 'herbal intervention A plus usual care (toothpaste or tooth powder)' versus 'herbal intervention B plus usual care (toothpaste or tooth powder))'.

We will include studies that have used herbal interventions as a component of toothpaste/tooth powder/mouthwash or as a stand-alone intervention.

In multiple arm studies, we will list the details of all treatment arms in the 'Characteristics of included studies' table.

Types of outcome measures

We could not find any core outcomes reported in the literature. We have tentatively listed all the primary and secondary outcomes based on the available literature and consensus between the review authors. We will not exclude any study solely based on the reported outcomes.

Primary outcomes

- **Caries increment** measured by dentist/dental auxiliaries using DMFT/DMFS (permanent teeth), dmft/dmfs (deciduous teeth), or International Caries Detection and Assessment System (ICDAS) (clinical and radiographic scoring) (continuous data or dichotomous data) (for definitions, see Table 1). We will follow the time points of high caries risk: three months; moderate caries risk: six months; low caries risk: six to 12 months for children and adults (as described by AAPD 2022 and Brown 2008).
- **Adverse effects** (descriptive) measured by dentist/dental auxiliaries for up to one year.

Secondary outcomes

- **Quality of life** measured using the Oral Health-Related Quality of Life (OHRQOL) or any other validated tool (continuous data).
- **Plaque scores** (continuous data) using any of the indices such as Plaque Index, Turesky Index, Patient Hygiene Performance Index
- **Bacterial count** (continuous data) using colony forming units (CFU)
- **Salivary pH** (continuous data)

We will use the longest time point (six months or greater) reported in the included studies for the quality of life outcome. We will use short-term (one to 15 days) time points for plaque scores, bacterial count, and salivary pH data.

If multiple outcome measures are reported in an included study, we will use the following.

- Caries increment: DMFT/DMFS and dmft/dmfs
- Quality of life: OHRQOL
- Plaque scores: Plaque Index

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We do not expect studies to report on the economic data and, therefore, do not plan to include this as an outcome in this review.

We understand that herbal medicines used in traditional medicine emphasises the overall health of an individual rather than an ailment (Wachtel-Galor 2011), it might be challenging to document and measure such outcomes. For example, system effects of tooth decay on the well-being of an individual and loss of teeth may not be reported in the included studies as the study outcomes. However, wherever the data are available regarding such mode of action and outcomes, we will describe them qualitatively.

Search methods for identification of studies

We will conduct systematic searches for RCTs.

Electronic searches

We will search the following electronic databases.

- Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Register of Studies (latest issue; Appendix 1)
- MEDLINE Ovid (1946 to current; Appendix 2)
- Embase Ovid (1974 to current; Appendix 3)
- AMED EBSCOhost (1985 to current; Appendix 4)

Subject strategies will be modelled on the search strategy designed for MEDLINE Ovid. Where appropriate, they will be combined with subject strategy adaptations of the highly sensitive search strategies designed by Cochrane for identifying RCTs, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Lefebvre 2022).

Searching other resources

We will search the following trial registries.

- US National Institutes of Health Ongoing Trials Register ClinicalTrials.gov (clinicaltrials.gov; Appendix 5).
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch; Appendix 6).

We will search the reference lists of included studies and relevant systematic reviews for further studies.

We will check that none of the included studies in this review were retracted due to error or fraud.

We do not intend to perform a separate search for adverse effects of interventions used, considering only the adverse effects described in included studies.

Data collection and analysis

Selection of studies

We will merge search results from all the sources using Rayyan (Rayyan 2016), and remove duplicate records of the same report. Two review authors (SSR and MA) will independently screen the titles and abstracts using Rayyan software. We will code the potential studies as 'retrieve' for eligible or potentially eligible/unclear records or 'do not retrieve'. We will resolve any conflicts during the screening process by discussion. If this is not possible, we will consult a third review author (SKN) and reach a consensus through discussion. Two review authors (TAR and KK) will independently screen the full-text articles. We will resolve any conflicts during the screening process by discussion. If this is not possible, we will consult a third review author (SKN) and reach a consensus through discussion.

The unit of interest for the review will be the study and if there are multiple reports and papers related to a single study, we will group them under a single study ID (Liberati 2009).

We plan to record the selection process in sufficient detail to complete the PRISMA flow diagram according to the PRISMA 2021 reporting standards (Page 2021).

Data extraction and management

Use of a data extraction form

For included studies, two pairs of review authors (PP and KK, TAR and MA) will independently extract the useful information and data from the full-text articles on to a customized data extraction sheet. We will resolve any conflicts during the data extraction process by discussion. If this is not possible, we will consult a third review author (SKN) and reach consensus through discussion. We will present these details in the 'Characteristics of included studies' table. We will present the reasons for excluding studies at this stage in the 'Characteristics of excluded studies' table.

We will draft an electronic data extraction form, and will pilot it on three included studies. Based on this, the final data extraction form will be prepared. One review author (PP) will transfer the extracted data to Review Manager, which another review author (SSR) will cross-verify (RevMan 2022).

We will contact the study authors for any missing data through e-mails. If the primary studies are old and do not have contact author email address, we will try to search their profiles in their affiliations and websites (e.g. ResearchGate, Academia, or Google Scholar) to obtain their recent contact details. We will try to contact such authors three times and if we receive no response, we will document the efforts and list such articles under 'studies awaiting classification'.

We will extract the following data from each included study.

- Methods: study design, trial registration, total duration of study, details of any 'run-in' period (if applicable), number of study centres and location, study setting, and date of study
- Participants: number randomized, number lost to follow-up/ withdrawn, number analysed, mean age, age range, gender, severity of condition, diagnostic criteria, type of dentition, caries risk, disability (if any), inclusion criteria and exclusion criteria
- Interventions: intervention, comparison, concomitant medications, and excluded medications
- Outcomes: outcomes specified and collected, and time points
- Notes: funding for trial and notable conflicts of interest of trial authors
- Information needed to assess bias (e.g. any deviations from intended interventions, imputed data for key outcomes, etc.)
- Information needed to assess GRADE (e.g. baseline risk in the control group for key outcomes)

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We will meta-analyse the following outcomes: caries increments, adverse effects, quality of life, Plaque Index, bacterial count, and salivary pH.

If the meta-analysis for any of the outcomes is not appropriate clinically and methodologically, then we will present the outcomes descriptively. If the progression of lesions and quality of life data are presented as ordinal scales, we will consider the possibility of converting the scale into dichotomous data. If this is not possible, then we will analyse it following the methods used for continuous data.

Assessment of risk of bias in included studies

Two pairs of review authors (PP and KK, TAR and MA) will independently assess the risk of bias from the full-text articles in a customized data extraction sheet. We will resolve any conflicts during the data extraction process by discussion. If this is not possible, we will consult a third review author (SKN) and reach consensus through discussion.

We will use the Cochrane RoB 2 tool as described in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022).

The RoB 2 tool will assess risk of bias for each of the primary outcomes across different studies for the following domains:

- bias arising from the randomization process;
- bias due to deviations from intended interventions;
- bias due to missing outcome data;
- bias in measurement of the outcome;
- bias in selection of the reported result

We will use signalling questions in the RoB 2 tool to rate each domain as 'low risk of bias', 'some concerns', or 'high risk of bias' (Sterne 2019). We will use Microsoft Excel to assess the risk of bias and will upload it to an open data repository website (such as OSF or Figshare).

We will use the risk of bias assessments to perform sensitivity analyses and subgroup analyses by removing studies at high risk of bias and will present the results if there are changes in the direction of summary effect estimates.

If there are any deviations in the intended interventions, we will follow the per-protocol method for the calculation of effect estimates.

For Domain 2, the potential 'non-protocol interventions' could be the use of topical fluoride therapy, pit and fissure sealants or new restorations for carious lesions during the study period or getting scaling or oral prophylaxis, using an electric toothbrush or using fluoride mouth rinses. For the control group, potential non-protocol deviations would be the use of herbal home remedies (e.g. clove oil).

For Domain 5, all the listed outcomes in the clinical trial protocol should be reported for all the intended timelines. If the trial protocol is not available or registered retrospectively, we will assess the domain at 'high risk of bias'.

In this review, we consider that the estimated effect of adhering to the intervention as specified in the trial protocol would be the most appropriate to inform a care decision by an individual patient. We will follow the 'per protocol' approach in the case of deviations to the interventions in the included studies where we will only analyze data from those who strictly adhered to the study protocol (Higgins 2022).

Assessment of risk of bias in cluster-randomized controlled trials

For cluster-RCTs, we will follow the methods described in Sections 23.1.2 and 23.2.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022). We will also refer to the risk of bias variant tool for cluster-RCTS (RoB 2). In addition to the above-listed domains, for cluster-RCTs, we will also assess bias arising from the timing and recruitment of participants.

Measures of treatment effect

We will analyse dichotomous data as risk ratios with 95% confidence intervals (CI) and continuous data as mean difference (MD) or standardized mean difference (SMD) (if studies use different scales) with 95% CIs. We will enter data presented as a scale with a consistent direction of effect.

We anticipate that caries increments, quality of life, and Plaque Index will be expressed using different scales and hence we will use SMDs to measure these outcomes. We will follow the methods described in Section 15.5 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Schünemann 2022).

If data are not reported in an RCT in a format that we can enter directly into a meta-analysis, we will convert them to the required format using the information in Chapter 6 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022).

For cluster-RCTs that appropriately account for correlations within clusters, we will use the reported results in the analysis. Otherwise, we will adjust trial results by the design effect to calculate an effective sample size using either the intraclass correlation coefficient reported in the trial or, if one is not reported, an intraclass correlation coefficient from a similar trial (Higgins 2022).

Unit of analysis issues

If we identify multiple arm trials, we will select the relevant arms for inclusion in our analyses. If more than two arms are relevant to this review, we will split the control group between multiple comparisons so that participants are not double-counted in a meta-analysis.

If the trials report multiple timelines of outcome assessment in children, we will use the timelines as recommended by the American Academy of Pediatric Dentistry (AAPD 2022). For adults, we intend to use the median timeline or the most common timeline reported in the included studies.

We expect two types of non-standard study designs in this review.

- Repeated observations on participants
- Cluster-RCTs

In cases of repeated observations on participants for our primary outcomes, we will follow the method described in Section 9.3.4 of the *Cochrane Handbook for Systematic Reviews of Interventions* (McKenzie 2022).

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In cluster-RCTs, we will handle the data following the method described in Section 6.3 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2022). In cluster-RCTs, the unit of analysis will be the cluster.

Dealing with missing data

If we encounter trials with missing data, we will contact the investigators or sponsors of these studies if the contact author's email address is available. We will calculate missing data from other data, such as standard deviations (SDs) from P values if needed. We will reanalyse the data according to the intention-to-treat (ITT) principle whenever possible.

We will contact the trial authors to obtain the missing intracluster correlation coefficient. If not available, then we will use the intracluster correlation coefficient values from relatively (in terms of population) similar trials.

Assessment of heterogeneity

We will investigate heterogeneity based on the clinical diversity at population level, such as caries risk of participants (high, moderate, and low risk), water (or milk) fluoridation status of the population, and smokers or non-smokers. At interventions level, we will investigate heterogeneity based on the oral hygiene habits (brushing twice a day and once a day, using dental floss or interdental cleaning aids, using fluoride mouth rinses). Data on these variables will be detailed in the 'Characteristics of included studies' table.

We will assess heterogeneity by visually inspecting the forest plots to determine closeness of point estimates with each other and overlap of CIs. We will use the Chi^2 test with a P value of 0.1 to indicate statistical significance. We will use the I^2 statistic to quantify inconsistency amongst the trials in each analysis. If we identify substantial heterogeneity, we will report it and explore possible causes using prespecified subgroup analysis. If there are fewer included studies, we will avoid using simple thresholds to interpret statistical heterogeneity because of the uncertainty around measures such as the I^2 statistic and Tau^2.

We will use the following approximate guide to interpretation (e.g. Deeks 2022).

- 0% to 40%: might not be important
- 30% to 60%: may represent moderate heterogeneity[a]
- 50% to 90%: may represent substantial heterogeneity[a]
- 75% to 100%: considerable heterogeneity[a]

[a]The importance of the observed value of the I^2 statistic depends on 1. the magnitude and direction of effects, and 2. strength of evidence for heterogeneity (e.g. P value from the Chi^2 test, or a CI for the I^2 statistic: uncertainty in the value of the I^2 statistic is substantial when the number of studies is small).

Assessment of reporting biases

If we include 10 or more studies, we will construct a funnel plot to investigate any potential reporting bias.

Data synthesis

Meta-analysis of numerical data

We will analyse the data using Review Manager (RevMan 2022). In the absence of substantial clinical or methodological heterogeneity, we will perform a meta-analysis using a random-effects model. If there is substantial or considerable heterogeneity, we will investigate this using a subgroup analysis.

Synthesis using other methods

Where a meta-analysis is not appropriate, we will present the synthesis following the SWiM (Synthesis Without Meta-analysis) reporting guidelines (Campbell 2020).

Subgroup analysis and investigation of heterogeneity

We will run the subgroup analyses for the following variables.

- **High, moderate, and low risk of caries** as the type of risk of caries can affect the outcome. For example, people with high risk due to radiation-induced xerostomia might need more frequent interventions compared to people with low risk of caries.
- **Multiple intervention versus single intervention** (e.g. herbal toothpaste plus herbal mouthrinse versus herbal toothpaste alone). If studies are conducted wherein herbal interventions are combined with herbal mouthrinses, subgroup analysis will help us to differentiate the effects.
- **A herb as one of the ingredients in the intervention versus a herb as the only ingredient** (e.g. herbal oil as one of the ingredients in mouthrinse versus herbal extract application). Differentiation of the effects of a herb alone as the ingredient and a herb as one of the ingredients would be useful.
- **Type of intervention** (e.g. mouthwash or toothpaste) as this determines the contact of the herbal agents to the tooth surface. For example, toothpaste has comparatively higher contact time on the tooth surface compared to mouthwash.

However, we are aware of the limitations of subgroup analyses that require consideration when interpreting results, including their observational nature.

Sensitivity analysis

To explore the possible effect of losses to follow-up on the effect estimates for the primary outcomes, we will perform sensitivity analyses. We will perform sensitivity analyses for those comparisons that have studies with imputed data or any such assumptions that we have made in our analyses. We will restrict the primary analyses to studies judged at an overall low risk of bias or low risk of bias and some concerns. We will report any significant difference between the results of these analyses. We will not compare changes in P values to judge whether there is a difference between the main analysis and sensitivity analysis.

Summary of findings and assessment of the certainty of the evidence

We will report the summary of findings for the primary outcomes of the following comparisons using GRADE approach as we consider these five herbal products are important to patients.

- Neem extract as a main component of toothpaste/tooth powder/ mouthwash versus 'usual care (toothpaste or tooth powder)'

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- Miswak extract as a main component of toothpaste/tooth powder/mouthwash versus 'usual care (toothpaste or tooth powder)'
- Clove extract as a main component of toothpaste/tooth powder/mouthwash versus 'usual care (toothpaste or tooth powder)'
- Tea leaves extract as a main component of toothpaste/tooth powder/mouthwash versus 'usual care (toothpaste or tooth powder)'
- Tulasi extract as a main component of toothpaste/tooth powder/mouthwash versus 'usual care (toothpaste or tooth powder)'

We will present the summary of findings for the remaining comparisons as additional tables.

We will use GRADE (overall risk of bias, consistency of effect, imprecision, indirectness, and publication bias) to evaluate the certainty of evidence for each outcome as high, moderate, low, or very low, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (GRADEpro GDT; Higgins 2022). We will justify all decisions to downgrade the certainty of the evidence using footnotes and will provide comments to aid readers' understanding where necessary.

Two review authors (PP and TAR) will independently make the judgements about evidence certainty. We will resolve any conflicts during the GRADE assessment process by discussion. If this is not possible, we will consult a third review author (SKN) and reach consensus through discussion.

We will report the results of the analyses in summary of findings tables for the primary outcomes.

- Caries increment measured using DMFT/DMFS (permanent teeth), dmft/dmfs (deciduous teeth), or ICDAS (clinical and radiographic scoring) (continuous data or dichotomous data) at six months or greater
- Adverse effects (descriptive) at one year

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Editorial and peer-reviewer contributions

The following people conducted the editorial process for this article.

- Sign-off Editor (final editorial decision): Fang Hua, Centre for Evidence-Based Stomatology, School and Hospital of Stomatology, Wuhan University
- Managing Editor (selected peer reviewers, provided editorial guidance to authors, edited the article): Anupa Shah, Cochrane Central Editorial Service
- Assistant Editor (conducted editorial policy checks, collated peer-reviewer comments and supported editorial team): Justin Mann, Cochrane Central Editorial Service
- Copy Editor (copy editing and production): Anne Lawson, Cochrane Central Production Service
- Peer-reviewers (provided comments and recommended an editorial decision): Jennifer S Hilgart, Cochrane Evidence Production and Methods Directorate (methods), Joanne Platt, Cochrane Central Editorial Service (search), Dr Swapnil B Shankargouda, Department of Prosthodontics, KLE Academy of Higher Education and Research's VK Institute of Dental Sciences, Belgaum, Karnataka, India (clinical), Dr Srikanth S, MD, Scientist-B, ICMR-Vector Control Research Centre, Puducherry, India (clinical), and Bhaswati Bhattacharya MPH MD PhD, Weill Cornell Medical College, New York, USA (clinical)

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ADDITIONAL TABLES

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Table 1. Glossary of terms used in the review

Terms	Definitions
DMFT/DMFS (Decayed, Missing, Filled Teeth/Surfaces in Permanent Teeth)	This index represents the total number of decayed (D), missing due to decay (M), and filled (F) teeth (T) or surfaces (S) in the permanent dentition (WHO 2013).
dmft/dmfs (Decayed, Missing, Filled Teeth/Surfaces in Deciduous Teeth)	This index represents the total number of decayed (d), missing due to decay (m), and filled (f) teeth (t) or surfaces (s) in the deciduous (primary) dentition (WHO 2013).
ICDAS (International Caries Detection and Assessment System)	ICDAS is a clinical scoring system for use in dental education, clinical practice, and research. It provides a common language for describing and assessing caries in its various stages, from the earliest visual signs to extensive cavitated lesions (Ismail 2007).
Caries Increment	The change in caries status over a specific period of time, calculated by counting the number of surfaces that changed from "sound" to "decayed" or "filled" over the study period, as well as the progression of an existing caries lesion to a more advanced stage or filling (Petersson 2019).
Plaque Index	An index developed to assess the thickness of plaque on the gingival third of the tooth surface. It is a common method for assessing an individual's oral hygiene status (Silness 1964).
Turesky Index	A modification of the Quigley-Hein Plaque Index, this index assesses the thickness of dental plaque on specific areas of teeth. It provides a more detailed scoring system than the original Quigley-Hein index (Turesky 1970).
Patient Hygiene Performance Index	This index assesses the status of oral hygiene by measuring the debris and calculus on selected tooth surfaces. It provides a comprehensive view of an individual's oral hygiene by considering both soft debris and mineralized deposits (Podshadley 1968).

APPENDICES

Appendix 1. Cochrane Central Register of Controlled Clinical Trials (CENTRAL) search strategy

#1 MeSH descriptor: [Tooth Demineralization] explode all trees

#2 (teeth NEAR/5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))

#3 (enamel NEAR/5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))

#4 ((dentin or dental) NEAR/5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))

#5 (root NEAR/5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))

#6 "dental plaque"

#7 #1 OR #2 OR #3 OR #4 OR #5 OR #6

#8 MeSH descriptor: [Drugs, Chinese Herbal] explode all trees

#9 "medicinal plants"

#10 MeSH descriptor: [Herbal Medicine] explode all trees

#11 herbal* or herbs

#12 MeSH descriptor: [Medicine, Traditional] explode all trees

#13 "traditional medicine" OR "traditional medicines"

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#14 MeSH descriptor: [Plant Extracts] explode all trees

#15 (plant* NEAR/3 extract*)

#16 MeSH descriptor: [Teas, Herbal] explode all trees

#17 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16

#19 #7 AND #17

Appendix 2. MEDLINE (Ovid) search strategy

Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations <1946 to February 08, 2024>

1 exp Tooth Demineralization/

2 (teeth adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

3 (enamel adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

4 ((dentin or dental) adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

5 (root adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

6 dental plaque/

7 ((dental or tooth or teeth) and plaque).mp.

8 1 or 2 or 3 or 4 or 5 or 6 or 7

9 exp Drugs, Chinese Herbal/

10 Chinese Herbal Drugs.mp.

11 exp Herbal Medicine/

12 (Hawaiian Herbal Medicine or Herbal or Herbal Medicine or Herbal Medicines or Herbal Preparation or Herbal Preparations or Herbal Therapy).mp.

13 exp Teas, Herbal/

14 (Herbal Tea or Herbal Teas).mp.

15 exp Plants, Medicinal/

16 (Plants Medicinal or "Medicinal Herbs and Plants").mp.

17 exp Plant Extracts/

18 Plant Extracts.mp.

19 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18

20 8 and 19

The above subject search will be linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled

Trials and controlled clinical trials in MEDLINE (as described in Lefebvre 2022, box 3c).

1. randomised controlled trial.pt.

2. controlled clinical trial.pt.

3. randomized.ab.

4. placebo.ab.

5. drug therapy.fs.

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6. randomly.ab.

7. trial.ab.

8. groups.ab.

9. or/1-8

10. exp animals/ not humans.sh.

11. 9 not 10

Appendix 3. Embase (Ovid) search strategy

Embase <1974 to 2024 February 08>

1 exp tooth demineralization/

2 (teeth adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

3 (enamel adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

4 ((dentin or dental) adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

5 (root adj5 (cavit$ or caries or carious or decay$ or lesion$ or demineral$ or remineral$)).mp.

6 dental plaque.mp. or tooth plaque/

7 1 or 2 or 3 or 4 or 5 or 6

8 Medicinal plant/ or exp herbal medicine/

9 exp Chinese medicine/

10 exp traditional medicine/ or exp alternative medicine/

11 exp herbal tea/

12 exp medicinal plant/

13 exp plant extract/

14 (herbs or herbal*).mp.

15 Medicinal plants.mp.

16 (plant* adj3 extract*).mp.

17 traditional medicine*.mp.

18 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17

19 7 and 18

The above subject search will be linked with the highly sensitive search strategy designed by Cochrane for identifying randomised controlled

Trials and controlled clinical trials in Embase (as described in Lefebvre 2022, box 3e).

1. Randomised controlled trial/

2. Controlled clinical study/

3. random$.ti,ab.

4. randomisation/

5. inter method comparison/

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6. placebo.ti, ab.

7. (compare or compared or comparison).ti.

8. ((evaluated or evaluate or evaluating or assessed or assess) and (compare or compared or comparing or comparison)).ab.

9. (open adj label).ti, ab.

10.((double or single or doubly or singly) adj (blind or blinded or blindly)).ti, ab.

11.double-blind procedure/

12.parallel group$1.ti, ab.

13.(crossover or cross over).ti, ab.

14.((assign$ or match or matched or allocation) adj5 (alternate or group$1 or intervention$1 or patient$1 or subject$1 or participant $1)).ti, ab.

15.(assigned or allocated).ti, ab.

16.(controlled adj7 (study or design or trial)).ti, ab.

17.(volunteer or volunteers).ti, ab.

18.human experiment/

19.trial.ti.

20.or/1-19

21.random$ adj sampl$ adj7 ("cross section$" or questionnaire$1 or survey$ or database$1)).ti,ab. not (comparative study/ or controlled study/ or randomi?ed controlled.ti,ab. or randomly assigned.ti,ab.)

22.Cross-sectional study/ not (randomized controlled trial/ or controlled clinical study/ or controlled study/ or randomi?ed controlled.ti,ab. or control group$1.ti,ab.)

23.(((case adj control$) and random$) not randomi?ed controlled).ti,ab.

24.(Systematic review not (trial or study)).ti.

25.(nonrandom$ not random$).ti,ab.

26." Random field$".ti,ab.

27.(random cluster adj3 sampl$).ti,ab.

28.(review.ab. and review.pt.) not trial.ti.

29."we searched".ab. and (review.ti. or review.pt.)

30."update review".ab.

31.(databases adj4 searched).ab.

32.(rat or rats or mouse or mice or swine or porcine or murine or sheep or lambs or pigs or piglets or rabbit or rabbits or cat or cats or dog or dogs or cattle or bovine or monkey or monkeys or trout or marmoset$1).ti. and animal experiment/

33. Animal experiment/ not (human experiment/ or human/)

34.or/21-33

35.20 not 34

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Appendix 4. AMED (EBSCOhost) search strategy

	Database - AMED - The Allied and Complementary Medicine Database (EBSCOhost)
S1	(ZU "dental caries")
S2	(ZU "dental plaque")
S3	TI (teeth N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR AB (teeth N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR KW (teeth N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))
S4	TI (enamel N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR AB (enamel N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR KW (enamel N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))
S5	TI ((dentin or dental) N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR AB ((dentin or dental) N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR KW ((dentin or dental) N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))
S6	TI (root N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR AB (root N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*)) OR KW (root N5 (cavit* or caries or carious or decay* or lesion* or deminerali* or reminerali*))
S7	TI ((dental or tooth or teeth) and plaque) OR AB ((dental or tooth or teeth) and plaque) OR KW ((dental or tooth or teeth) and plaque)
S8	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7
S9	(ZU "chinese traditional medicine")
S10	(ZU "herbal drugs")
S11	(ZU "herbal medicine")
S12	(ZU "herbal preparations")
S13	(ZU "herbal tea")
S14	(ZU "herbalism")
S15	TI ("Chinese herbal drugs" or "Hawaiian Herbal Medicine" or Herbal or "Herbal Medicine" or "Herbal Medicines" or "Herbal Preparation" or "Herbal Preparations" or "Herbal Therapy") OR AB ("Chinese herbal drugs" or "Hawaiian Herbal Medicine" or Herbal or "Herbal Medicine" or "Herbal Medicines" or "Herbal Preparation" or "Herbal Preparations" or "Herbal Therapy") OR KW ("Chinese herbal drugs" or "Hawaiian Herbal Medicine" or Herbal or "Herbal Medicine" or "Herbal Medicines" or "Herbal Preparation" or "Herbal Preparations" or "Herbal Therapy")
S16	TI ("medicinal plants" or "medicinal herbs" or "plant extracts") OR AB ("medicinal plants" or "medicinal herbs" or "plant extracts") OR KW ("medicinal plants" or "medicinal herbs" or "plant extracts")
S17	S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16
S18	S8 AND S17

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Appendix 5. US National Institutes of Health Ongoing Trials Register (ClinicalTrials.gov) search strategy

Caries AND Herbal OR "Traditional Medicine" OR "Alternative Medicine"

Appendix 6. World Health Organization International Clinical Trials Registry Platform search strategy

dental caries AND herbal

CONTRIBUTIONS OF AUTHORS

PP: conception of the topic, drafting the protocol, contact author

TAR: drafting background section, objectives, references, and overall completion of the protocol

KK: drafting background section, objectives, and references

SSR: drafting background section, objectives, and references

MA: drafting objectives, additional tables, and references

AS: expert opinion on herbal interventions and drafting background section

SKN: drafting objectives, methods section, search strategy, and overall completion of the protocol

DECLARATIONS OF INTEREST

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MA: none

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SKN: is a Cochrane editor, and was not involved in the editorial process.

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