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INVITED REVIEW

Potential applications of medicinal herbs and phytochemicals in oral and dental health: Status quo and future perspectives

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Abstract

Objective: Herbal therapies are utilized to treat a broad diversity of diseases all over the globe. Although no clinical studies have been conducted to demonstrate the antibacterial, antimicrobial, and antiplaque characteristics of these plants, this does not imply that they are ineffectual as periodontal treatments or anti-cariogenic drugs. However, there is a scarcity of research confirming their efficacy and worth.

Subject: Herbs are utilized in dentistry as antimicrobial, antineoplastic, antiseptic, antioxidant, and analgesics agents as well as for the elimination of bad breath. In addition, the application of herbal agents in tissue engineering improved the regeneration of oral and dental tissues. This study reviews the application of medicinal herbs for the treatment of dental and oral diseases in different aspects.

Methods: This article focuses on current developments in the use of medicinal herbs and phytochemicals in oral and dental health. An extensive literature review was conducted via an Internet database, mostly PubMed. The articles included full-text publications written in English without any restrictions on a date.

Conclusion: Plants have been suggested, as an alternate remedy for oral–dental problems, and this vocation needs long-term dependability. More research on herbal medicine potential as pharmaceutical sources and/or therapies is needed.

KEYWORDS
herbal therapy, dentistry, oral diseases

1 | INTRODUCTION

Everything that threatens oral health, directly or indirectly, affects the quality of life, well-being, dietary choices, and the psychosocial elements of life (Modgi & Radke, 2021). Oro-dental diseases and anomalies affect people and society, which are classified as major public health threats because of their widespread occurrence and severity. It is well accepted that oro-dental diseases and anomalies pose a substantial public health problem because of their effect on people and society (Petruzzi et al., 2021).

In recent years, herbal compounds have been widely involved in oral care crops in addition to traditional treatment procedures. Their medicinal and physical properties make these substances intriguing. Several companies are increasing including herbal compounds in goods as a means of enhancing their medicinal properties (Mojtahedzadeh et al., 2021; Telrandhe et al., 2021). Complementary and alternative medicine (CAM) practitioners and patients are no longer on the fringes of conventional care. Plants that have been grown for their medicinal or fragrant characteristics are known as medicinal herbs. Herbs having medicinal characteristics are a valuable and useful resource for a broad variety of diseases. Many of the medications utilized in medical research are derived from medicinal plants, a practice known as "allopathy" (Rotblatt & Ziment, 2002).

The oldest type of health care in the world is the traditional medicine that is applied in the prevention and treatment of physical and mental illnesses (Payyappallimana, 2010). Historically, different societies developed different treatments to combat a variety of health- and life-threatening diseases. Types of medicine such as traditional Chinese medicine, Kampo, Ayurveda, Korean traditional medicine, and Unani medicine use natural products, have been used around the world for hundreds or even thousands of years, and have blossomed into orderly-regulated medicine systems (Pan et al., 2014). In various forms, they may have some flaws, but they are still an invaluable repository of human knowledge (Alves & Rosa, 2007; Fabricant & Farnsworth, 2001). Traditional medicine is also known as alternative or complementary medicine or ethnic medicine and still plays an important role in several countries today (Abdullahi, 2011; World Health Organization, 2000). Since ancient times, "clinical trials" have been performed in traditional medicine. Significant amounts of data have been obtained through clinical trials, and through this traditional medicine has assisted in the development of modern drugs (Yuan et al., 2016).

Due to the vast range of natural bio-characteristics, cheaper prices, greater accessibility, and higher safety margins of herbal medicines, these alternative treatments might sometimes be favored over conventional ones. Based on the World Health Organization's report, about 80% of the world's population today relies on herbal medicines to treat a variety of health issues (Siddeeqh et al., 2016).

Herbal qualities in dentistry are currently being used to alleviate tooth pain, gum irritation, and canker sores (Kumar et al., 2013).

Though understanding the interactions between plants and other medications is important in dental care because many medicinal plants have anti-inflammatory properties and minimize bleeding, understanding the interactions between plants and other drugs is essential (Taheri et al., 2011). Analgesics and antiseptics are two plant-derived compounds that are utilized in dentistry for several objectives (Sinha & Sinha, 2014). Plant extracts such as propolis, neem leaf, burdock root, and noni fruit, for example, have been utilized effectively as intracanal medications in periodontics and endodontics, opening up a new role for herbal agents in dental therapy across the globe (Pujar & Makandar, 2011; Shah et al., 2015). Clove oil, for example, may help reduce toothache pain (Uju & Obioma, 2011). In addition to relieving toothache, herbs can control tooth decay caused by various bacterial species due to their antibacterial properties. In review, first, we have reviewed the therapeutic effects of medicinal plants on the mouth, and then, we have discussed the effects of these plants on endodontic treatments and the regeneration of living tooth pulp.

2 | ROLE OF MEDICINAL HERBS IN ORAL DISEASES

Medicinal plants have various therapeutic properties, including Bad Breath Elimination, Analgesic properties, Anti-inflammatory can be beneficial for use in oral diseases.

2.1 | Bad breath elimination

The term "halitosis" refers to an unpleasant smell coming from the mouth or breath. More than a third of people suffer from bad breath (halitosis; Silva et al., 2018). Volatile molecules (such as sulfur, aromatic, and nitrogen-containing ones) are the cause of this condition, which may be caused by pathological or non-pathological reasons (Aylikci & Çolak, 2013; Maleki Dizaj et al., 2019). Either *Clonorchis sinensis* extract or EGCG may effectively kill *Solobacterium moorei* and reduce the bacterial adhesion to oral epithelial cells, according to the findings of this study (Morin et al., 2015). Compared to 0.012% chlorhexidine, clinical trials suggest that *C. sinensis* mouthwash may decrease oral malodor-causing volatile sulfur compounds (VSCs) (Farina et al., 2012; Rassameemasmaung et al., 2013). Plectranthus amboinicus species contain antibacterial essential oils such as β-caryophyllene, p-cymene, and γ-terpinenecan. Antibacterial action was shown for *P. amboinicus* mouthwash by Nazliniwaty and Laila (2019) against *Staphylococcus aureus*, a bacterium that causes bacterial-induced halitosis, in a study. A salivary sediment model indicated that *Punica granatum* extract inhibited the production of VSCs by *Parvimonas micra*, *Porphyromonas gingivalis*, and *Fusobacterium nucleatum* bacteria (Veloso et al., 2020). VSCs were substantially decreased and odor ratings improved in individuals with halitosis who were given *Echinacea augustifolia*, *Pistacia lentiscus*, *Lavender augustifolia*, and *Salvia officinal* is tablets for 9 h following product application, compared to placebo tablets (Sterer et al., 2013).

2.2 | Analgesic properties

Oral pain is a frequent symptom in a wide range of dental conditions and diagnoses (Hargitai, 2018). Bromelain has been discovered in *Ananas comosusis* an enzyme extract that has anti-inflammatory properties (Onken et al., 2008). Following third molar removal procedures, a triple-blind, placebo-controlled, randomized clinical trial by Isola et al. (2019) reported that a mixture of baicalin (*Scutellaria baicalenesis*), bromelain, and escin (*Aesculus hippocastanum*) was more effective at relieving pain than Ibuprofen and placebo (Isola et al., 2019). Analgesic qualities of *Zingiber officinale* are well-known, and the plant has a low risk of side effects (Lobina et al., 2021). Prostaglandin synthesis is inhibited by natural elements in the plant *Z. officinale* was shown to be equally effective as Ibuprofen in relieving postoperative pain after third molar removal surgery in another clinical research (Rayati et al., 2017). *Clonorchis sinensis* has been shown to have antibacterial activity against involved bacteria in caries and periodontal disease (Hirasawa et al., 2002; Jenabian et al., 2012; Otake et al., 1991).

Therefore, the effectiveness of *C. sinensis* mouthwash in controlling pain and trismus of acute pericoronitis can be related to its antibacterial activity as well as its anti-inflammatory effect. *Clonorchis sinensis* mouthwash 5%, compared to chlorhexidine 0.12%, meaningfully decreased pain ratings and the number of medicines required in patients with acute pericoronitis following

a 7-day follow-up (Shahakbari et al., 2014). Postoperative pain after third molar removal surgery may be reduced by using *C. sinensis* mouthwash rather than placebo mouthwash (Eshghpour et al., 2013).

For the treatment of aphthous stomatitis, *Guaiacum officinale* extract has been studied in a clinical trial. No clinically significant differences were seen in ulcer diameter reduction between the *G. officinale* extract-based herbal mucoadhesive paste group and the placebo group after 10 days of monitoring (Haghpanah et al., 2015). Promising outcomes were seen in pain reduction during healing of an aphthous ulceration lesion using *P. granatum* gel, compared to placebo (Tavangar et al., 2019).

Oral lichen planus is a chronic inflammatory mucocutaneous disease that causes intense burning, erythema, and ulcerative lesions in the oral cavity, among other symptoms (Cheng et al., 2016). Curcumin gel from the Curcuma longa plant has anti-inflammatory and antioxidant properties (Anuradha et al., 2015). After an initial course of corticosteroid treatment, curcumin gel has been shown to reduce pain and burning sensations in oral lichen planus and may be taken as a maintenance herbal medication (Negahdari et al., 2021; Thomas et al., 2017). The major bioactive chemicals identified in the herbal remedy Hangeshashinto are gingerol and shogaol, which are used in combination products. These two components diminish the production of substance P, a key modulator of nociceptive signal transmission in sensory neurons, by inhibiting the operation of voltage-dependent sodium cellular channels (Abdel-Aziz et al., 2006). In patients with oral mucositis, hangeshashinto may be used as an effective topical analgesic treatment (Hitomi et al., 2019; Zieglgänsberger, 2019).

2.3 | Anti-inflammation

For centuries, herbal treatments have been used for their calming properties. Dentistry has profited greatly from these possibilities. In recent years, a slew of plant-based anti-inflammatory medications has been approved for sale. Researchers have employed both simple and complicated formulations, including both single-ingredient and multi-ingredient compounds. The anti-inflammatory activities of *Chisandra chinensis* and Schisandrin C, a key lignan in the plant, are due to a decrease in the expression of interleukin-1 and tumor necrosis factor-α. Dental pulp cells also produce less nitric oxide when exposed to bacterial lipopolysaccharides (LPS), which may help alleviate dental inflammations such as pulpitis(Takanche et al., 2018). When *C. sinensis* extract was administered as a therapy, nicotine-induced mucosal inflammation was dramatically decreased in animals (Shahbaz et al., 2017). Prostaglandin E2 and COX-2 inhibitory properties of *Matricaria recutita* (chamomile) are effective in the treatment of oral mucositis (Gomes et al., 2016). A systematic review was conducted to study chamomile action in radio-chemotherapy oral mucositis management. The results displayed that the topical application of chamomile was effective in the treatment and/or prevention of oral mucositis in 4 of the 6 studies (de Lima Dantas et al., 2022). The topical administration of *Aloe vera* to the extraction site dramatically improves wound healing, perhaps owing to increased collagen and proteoglycan synthesis by fibroblasts and wound tensile strength (Nimma et al., 2017). Radiation-induced oral mucositis may be reduced by Isatis indigotica extract (Baharvand et al., 2017). In the context of cancer research, this is a huge deal. Curcumin mouth rinse was shown to be superior to chlorhexidine mouthwash in improving the oral mucositis assessment scale in individuals with oral mucositis after radio-chemotherapy (Patil et al., 2015).

Coptis rhizome, ginseng, *Glycyrrhiza glabra*, jujube, *Pinellia ternata*, processed ginger, and Scutellaria root make up the traditional Japanese herbal remedy Hangeshashinto. An anti-inflammatory substance called Glycyrrhizin is present in *G. glabra* and is the most often recommended traditional Japanese medication for stomatitis in Japanese hospitals (Hara et al., 2019). *Glycyrrhiza glabra*'s ability to alleviate symptoms of oral mucositis after head and neck radiation therapy has been shown (Najafi et al., 2017). To promote the production of granulation tissue, this herbal drug enhances cell proliferation and migration in epidermal keratinocytes and fibroblasts (Ozawa et al., 2020). Ingredients in Hangeshashinto decrease the expression of cyclooxygenase-2 in human oral keratinocytes, which reduces interleukin-1-induced prostaglandin E2 synthesis (Kato et al., 2016; Miyano et al., 2020; Sunagawa et al., 2018). As a result, anti-tumor drugs and radiation therapy both produce stomatitis, and Hangeshashinto may cure it (Ara et al., 2018).

2.4 | Antineoplastic properties

In 2017, 4.84 out of every 100,000 people were diagnosed with head and neck cancer, making it one of the world's 10 most prevalent cancers (Ren et al., 2020). Researchers confront several challenges in the fight against oral cancer, including delayed clinical diagnosis, a poor prognosis, and a lack of effective and affordable treatment options (Ahmadian et al., 2019; Rivera, 2015). Currently, patients with oral squamous cell carcinoma (OSCC) are treated using standard methods such as radiation therapy, chemotherapy, and surgical resection. However, OSCC still has a high death rate (Ren et al., 2020); thus, new therapeutic techniques and pharmaceuticals are needed (Fathi et al., 2020). One of the most promising antineoplastic therapy strategies is the administration of herbal medicines (Armat et al., 2016; Bakhshaiesh et al., 2015; Lee et al., 2017; Mohseni et al., 2016). STAT3 (signal transducer and activator of transcription 3) is a transcription factor that enhances tumor development and metastasis in patients with OSCC (Masuda et al., 2010). Inhibiting active janus tyrosine kinase (JAK)/STAT signaling is an essential therapeutic target to investigate in cancer treatment. 8-tigloyloxyhirsutinolide-13-O-acetate (8TGH), a bioactive molecule discovered in Vernonia cinerea species, has been shown to decrease STAT3 phosphorylation in OSCC and control cancer progression (Pouyfung et al., 2019).

3 | ROLE OF MEDICINAL HERBS IN DENTISTRY AND TOOTH REGENERATION

The role of herbs in dentistry and tooth reconstruction in three different aspects of periodontal health, endodontic treatments, and vital pulp therapy can be evaluated.

3.1 | Periodontal health

Periodontal disorders are developed once the bacteria in dental plaque infect the gums and bones (Ananthathavam & Ramamurthy, 2014). Periodontal disorders are divided into two categories: aggressive and chronic periodontitis (Armitage, 1999). Chronic type is widespread, although aggressive kind is more frequent in those under the age of 30. In mild to moderate periodontitis, non-surgical therapy is beneficial, but surgical treatment is beneficial in advanced instances. Antimicrobial drugs are distributed through confined drug delivery methods such as irrigating solutions, mouth rinses, and sustained release strategies (Ananthathavam & Ramamurthy, 2014; Highfield, 2009). Antimicrobial resistance has been demonstrated to be caused by artificial antimicrobial agents and medicines (Zhu et al., 2005). In combination with the use of an adjuvant antimicrobial mediator, scaling and root planing have been shown to improve patient outcomes over time in individuals with chronic periodontitis (Bonito et al., 2005). Modern chemotherapeutic drugs have shown to be effective in restoring periodontal health, but they come with a slew of negative side effects, including tooth discoloration, altered taste, and a high price tag (Hotwani et al., 2014; Pandita et al., 2014). Turmeric has been one of the most often utilized herbal medicines in recent clinical trials on periodontal diseases. Curcumin's analgesic, anti-inflammatory, antimicrobial, and anticarcinogenic effects have made it a mainstay in the natural system of medicine for thousands of years (Behal et al., 2011; Khezri et al., 2021; Samiei et al., 2021; Sharifi et al., 2019). Several recent studies have revealed that Curcuma extract is an effective supplement for root planning and scaling (Gadagi et al., 2013). Recent research has shown that this medication's gel and powder forms were shown to be equally effective (Pradeep et al., 2012). According to clinical research, Acacia Arabica (Kikar) has the same anti-gingivitis effectiveness as chlorhexidine (Pradeep et al., 2010). Acacia Arabica has also been demonstrated to be useful in avoiding early plaque development, while its long-term influence is unknown (Vennila et al., 2016). In culture media, neem extract was exposed to be efficient against Gram-positive and Gram-negative bacteria and was proven more effective in clinical studies. Green tea is also effective against Gram-negative anaerobic bacteria (Kudva et al., 2011). Another Indian research suggested that green tea extract might be utilized to help treat chronic periodontitis, particularly in diabetics, by delivering medication straight to the tissues (Hotwani et al., 2014). *Actinomyces lundii* and *Porphyromonas gingivalis* are known to be resistant to many contemporary therapies; however, the plant is very efficient against these strains (Cruz Martínez et al., 2017). Gum and plaque indices were considerably lower in research participants who used a 0.25 percent lemongrass mouthwash (Akula et al., 2021). In recent research, *Ocimum sanctum* was demonstrated to be as beneficial as chlorhexidine in the treatment of periodontitis. The research also revealed an anti-gingivitis and anti-inflammatory mouthwash made from *Ocimum sanctum* extract (Gupta et al., 2014). Antibacterial characteristics were also discovered as a consequence of the inquiry. In the research, a 4% concentration of Ocimum sanctum extract was shown to be the most efficient in combating oral bacterial microflora. In Iran, a *Coriandrum sativum* and *Quercus brantii* oral gel were recently explored (Yaghini et al., 2014). The clinical experiment used a combination of *Coriandrum sativum* and *Quercus brantii* because both plants contained tannins that may restrict bacterial activity in the

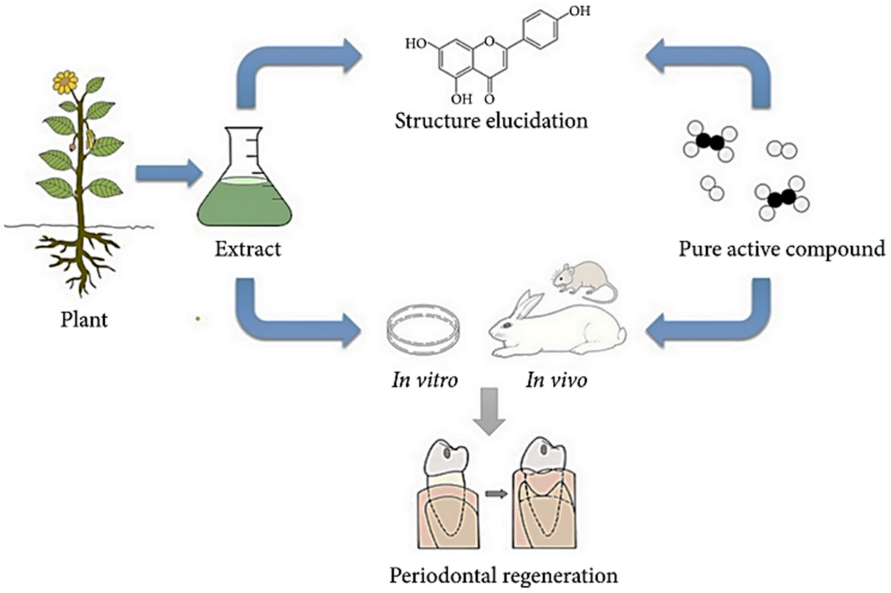

FIGURE 1 Procedure of studying herbal medicine for periodontal regeneration by hyphenated techniques (Xue et al., 2018; under the Creative Commons Attribution License)

periodontium. Meswak extract is used in a variety of commercial dentifrices because of its substantial antiplaque and antibacterial properties.

Stem cells can be treated with pure herbal bioactive compounds and herbal extracts (Xue et al., 2018). The application of phytochemicals as loading agents for periodontal regeneration is more possible compare with directly used plant products because the dose of phytochemicals can be easily calculated (Xue et al., 2018). In addition, once standardized, the cost of herbal extracts made from individual plants and herbal mixtures is reduced when they enter commercial production (Uhlenbrock et al., 2018). Plant product therapeutic examination requests to go over sequences of processes (Figure 1). Some of the herbal agents incorporated in scaffolds to be used in tissue engineering are shown in Table 1.

3.2 | Regenerative endodontics

Regenerative endodontics embraces biological processes to substitute damaged dentin or root structures as well as pulp-dentin

TABLE 1 Herbal derivatives in scaffolds for application in tissue engineering

Plant-derived agent	Delivery system	Study design	Cell line/Animal model	Results	Ref
Curcumin	Nanofibers with curcumin/collagen membrane comprising aspirin-loaded PLGA for guided bone regeneration	In vitro in vivo	DPSCs Dog	Curcumin in the membrane improved osteogenic differentiation. The animal test showed the formation of new bone in the tested area	Ghavimi et al. (2020)
Aloe vera	Acemannan containing sponges	In vivo	Mongrels	Acemannan showed an osteoinductive effect that can be used for periodontal regeneration	Chantarawaratit et al. (2014)
Agarose	Agarose gel combined with adenovirus-mediated human BMP-2 gene transduced bone marrow stromal cells	In vivo	Athymic mice	The gel of agarose-gene-transduced BMSC contained more hyaline cartilage compared with the collagen and alginate gel	Xu et al. (2005)
Cissus quadrangularis extracts with alginate	Alginate/O -carboxymethyl chitosan/ *Cissus quadrangularis* scaffold	In vitro	hMSCs	The hybrid scaffold possessed a significantly osteoinductive capacity, which could be used as a suitable agent for bone tissue engineering	Soumya et al. (2012)
Soybean	Soybean granules	In vivo	New Zealand rabbits	Soybean-based material can be a potent active osteoinductive agent for periodontal regeneration	Merolli et al. (2010)
Genipin	Genipin-crosslinked chitosan in hydrogel form	In vitro	Osteosarcoma (MG-63) cells, hMSCs	Genipin-crosslinked chitosan scaffolds are appropriate for bone tissue engineering. Different concentrations of genipin efficiently alter the mechanical and structural properties as well as the degradation profile of the scaffolds	Dimida et al., 2017)
Genipin	Electrospun from chitosan crosslinked with genipin	In vitro in vivo	Murine mesenchymal stem cells/CD1 female mice	The attendance of HA in the CTS-GP scaffold considerably improved their osseointegration effect and made it an exceptional material for the regeneration of bone defects	Frohbergh et al., 2015)
Alginate	Ceramic composite of alginate/nano bioactive glass	In vitro	MG-63 cells, human periodontal ligament fibroblasts	The prepared scaffolds exhibited the potential for periodontal tissue regeneration	Srinivasan et al. (2012)

complex cells (Moghadam et al., 2021; Murray et al., 2007). Recent natural-based approaches for dentin regeneration and capping of pulp have remarkable results. The main disadvantage of this methodology is severe inflammations stimulated by synthetic capping materials that can fail therapy (Schmalz & Smith, 2014; Shahi et al., 2019). In this part, it is reviewed current investigations including the application of herbal bioactive agents in the regeneration of tooth structure.

Acemannan (polysaccharide in *Aloe Vera*) is as effective as mineral trioxide aggregate (MTA) as a material of pulp capping used on top of the exposed dental pulp. Acemannan induced the formation of a mineralized dentin bond with normal pulp tissue without stimulation of inflammation (Songsiripradubboon et al., 2017). It can stimulate the proliferation of primary dental pulp, the activity of ALP, BMP 2 & 4, type I collagen, vascular endothelial growth factor, and dentin sialoprotein expression and mineralization (Vu et al., 2020).

EGCG improves the antibacterial and mechanical properties of collagen scaffolds (Kwon et al., 2017). EGCG could modulate the secretion of numerous mediators of inflammation and anti-inflammation from odontoblastic cells (Forouzideh et al., 2020; Sharifi et al., 2020; Stavroullakis et al., 2018). In a study, after direct pulp capping with propolis, all cases in the propolis group had regenerative tubular dentin bridge under the capping material (Ahangari et al., 2012). Tu et al. (2020) showed that the addition of caffeic acid to MTA meaningfully increases its biological and physicochemical properties and enhances the angiogenic, odontogenic, and immunosuppressive response of hDPSCs. Similar odontogenic and immunemodulatory results were shown by calcium silicate cement modified by hinokitiol (Huang et al., 2016).

Berberine, Baicalein, and Wedelolactone are three herbal bioactive agents with the capability to act as an inducer of odontoblastic differentiation and expression of BMP-2 by stimulating the Wnt/b-catenin pathway in dental pulp stem cells (DPSCs; Lee et al., 2016; Samiei et al., 2020; Wang et al., 2018; Wu et al., 2019).

Shikonin can stimulate odontoblastic differentiation of DPSCs by CD44-related mechanisms and AKT–mTOR signaling pathways (Kajiura et al., 2021). Curcumin and Astragaloside IV exert modulatory influence on inflammation cascades and display pro-differentiation properties on dental pulp cells (Ding et al., 2019; Sinjari et al., 2019). Total polyphenols extracted from the plant *Drynaria fortune* and *Sapindus mukorossi* seed oil increased ALP activity and proliferation of DPSCs that can be correlated to the promotion of the S phase and shortening of the G0/G1 phase in stem cells (X.-F. Huang et al., 2012; Shiu et al., 2020).

When administered to human dental pulp cells, baicalein, a flavonoid derived from the root of the *Scutellaria baicalensis* plant, was shown to exhibit osteoblastic and angiogenic activities (HDPCs). Baicalein (1–10 μM) enhanced ALP activity and morphogenetic protein expression in HDPCs, promoting odontoblastic differentiation and angiogenesis (BMP). Baicalein has been shown to have promise as a dental pulp repair agent (Lee et al., 2016). Researchers examined the capacity of genipin to stimulate odontogenic differentiation in human dental pulp cells (hDPCs) using gardenia fruit extract as the source of the chemical. According to the results of the investigation, genipin enhanced alkaline phosphatase activity, odontogenic marker expression, and the production of mineralized nodules, indicating that genipin may promote hDPC odontogenic differentiation (Kwon et al., 2015). Omar et al. (2012) compared Nigella Sativa (NS) oil to formocresol. Nigella Sativa (NS) oil is produced by a Ranunculaceae family plant native to South and Southwest Asia. Both chemicals are used as pulpotomy medicaments on forty male dogs' premolars. The animals were slaughtered four weeks after being treated. Vasodilation was mild to moderate in the NS group specimens. A few samples included inflammatory cells and a persistent odontoblastic layer. In addition to its anti-inflammatory properties, the researchers discovered that NS might aid in the preservation of pulp viability.

3.3 | Dental caries

Herbal medicines have long been used to heal gum and tooth diseases. Many ancient cultures make use of herbal "chewing sticks" made from herbs, bushes, or trees that have potent antibacterial properties. A plant's medicinal properties may include the following: antibacterial, anti-inflammatory, astringent, antiplaque agents and tooth whitener, and so on. There is a dearth of awareness regarding the effects of herbs on oral tissues, their mechanism of action, and their negative effects, which might make them a viable alternative to presently existing therapies for oral health concerns. As a result, further investigation into these age-old therapies is needed (Taheri et al., 2011). Dental caries, one of the most frequent diseases on the planet, affects a large number of individuals. *Streptococcus mutans* shows a vital part in the development of tooth decay (Burne, 1998). Herbal medications are increasingly being used in toothpaste to help in the prevention of dental cavities. The principal target of polyphenols' anti-cariogenic actions is *S. mutans*. It inhibits bacterial cell adhesion to the tooth surface by interacting with microbial membrane proteins (Ferrazzano et al., 2011). Herbs are often used in endodontics for root canal disinfection. Because of the detrimental effects of most synthetic intracanal medications, an investigation into herbal irrigants is underway (Stuart et al., 2006). The most prevalent cause of root canal treatment failure has been identified as *Enterococcus faecalis*. Root canal disinfection using sodium hypochlorite has some drawbacks, including unpleasant taste, toxicity, and the possibility of tooth structure weakening by diminishing the hardness and structural integrity of dentin in the root canal, which may lead to tooth loss (Davis et al., 2007). The following table shows the therapeutic effects of the herb concerning dental treatment (Table 2).

4 | PRECAUTION IN THE APPLICATION OF HERBS

Herbal-based treatments are mostly better tolerated than synthetic drugs. However, some serious side effects, including herb-drug interactions, may be happened (Izzo et al., 2016). It is suggested that

TABLE 2 The medicinal herbs used in dental caries treatments

Medicinal herb	Chemical constituents	Inhibitory effects on	Application	References
Aloe Barbadensis (Aloe vera gel)	Alloins and barbadoins	*Streptococcus pyogens* *Enterococcus faecalis*	The combination of zinc oxide powder and aloe vera gel has been found in clinical and radiological studies to be an effective therapy for primary teeth	Athiban et al. (2012), Khairwa et al. (2014), Wynn (2005)
Azadirachta aindica (Neem)	Nimbidin, nimbin, nimbinin, nimbidinin, nimbolide, and nimbidic acid	*S. mutans* *E. faecalis* *Candida albicans*	Reduction of plaque index and bacterial count/antiviral, antifungal, antibacterial, and anticarcinogenic activity	Eid et al. (2017), Tyagi et al. (2013)
Acacia nilotica (Babool)	Tannins, phenolic compounds, essential oil, and flavonoids	*S. mutans* *E. faecalis*	Anticancer, anti-tumors, antiscorbutic, astringent, antioxidant, natriuretic, antispasmodial, diuretic, diarrhea, malaria, sore throat, and toothache	Khan et al. (2009), Saini et al. (2008)
Arctium lappa	Mucilage, sulfurous acetylene compounds	*C. albicans* *S. mutans* *Escherichia coli* *P. aeruginosa* *L. acidophilus*	Antimicrobial activity	Miraj (2016)
Origanum vulgare	Carvacrol	*E. coli* *Salmonella enteritidis* *Salmonella Essen* *P. aeruginosa* *E. faecalis*	Antibacterial activity, inhibiting ATPase activity, and increasing the nonselective permeability of bacterial cell membranes/Pulpal fibers are stimulated and periapical tissues are repaired due to the presence of phenolic components in this product	De Vincenzi et al. (2004), Nosrat et al. (2009), Peñalver et al. (2005)
Casearia sylvestris (Gulkhair-wild coffee)	Phospholipase A2 inhibitors	*E. coli* *S. enteritidis* *S. Essen* *P. aeruginosa* *E. faecalis*	Because of its phenolic components, it activates pulpal fibers and aids in the repair of periapical tissues	Basile et al. (1990), Stamatis et al. (2003)
Curcuma longa (Turmeric)		*E. faecalis*	Tumerone, atlantone, and zingiberone. It possesses good antioxidant, hepatoprotective, antimicrobial, anti-inflammatory, and anticancer activity	Chaturvedi (2009), Haukvik et al. (2010)
Cranberry		*Several oral species of Streptococcus*	Phenolic acids, anthocyanins, condensed tannins, and flavonoids have antimicrobial activity	Koo et al. (2010), Sethi and Govila (2011), Yamanaka et al. (2004)
Marticaria recutitia (German chamomile)	Chamazolene, capric acid, caprylic, and chlorgenic acid		Mouthwash to treat irritations and minor infections of the mouth and gingiva	Pistorius et al. (2003)

TABLE 2 (Continued)

Medicinal herb	Chemical constituents	Inhibitory effects on	Application	References
Allium sativum (Garlic)	Enzymes involved in the production of cholesterol, such as 3-hydroxy-3-methylglutaryl-coa reductase and others, are rendered inactive.	*Gram-negative oral pathogens* *E. coli* *Staphylococcus aureus* *Bacillus cereus* *Salmonella* *Listeria* *Proteus* *Streptococcal species*	The toothpaste or the mouthwash containing an optimum concentration of garlic extract might be useful for the prevention of dental caries	Lu et al. (2011)
Green Tea	Catechins	*E. faecalis*	Natural fluoride, which may help prevent dental caries	Araghizadeh et al. (2013), Pujar and Makandar (2011)
Glycyrrhiza glabra (Yashtimadhu -liquorice)		*S. mutans*	Anti-inflammatory, antiviral, and anticarcinogenic/ Liquorice extract prevent the plaque formation	Segal et al. (1985)
Morinda citrifolia (Indian Mulberry- Noni)		*P. aeruginosa* *Proteus morgaii* *S. aureus* *Bacillus subtilis* *E. coli* *Salmonella* *Shigella* *E. feacalis* *C. albicans*	Cancer, infection, arthritis, diabetes, asthma, hypertension, and pain	Morton (1992), Murray et al. (2008)
Mimusops Elengi (Bakul)	Glycosides, alkaloids, phenols, tannins, and saponins	*E. faecalis*	Anti-inflammatory, analgesic, and antipyretic activity/ *Streptococci* isolated from dental tartar may be beneficial as a gargle for inflamed and bleeding gums	Mistry et al. (2014)
Melaleuca Alternifolia (Tea Tree Oil)	Terpinen-4-ol	*E. faecalis* *S. aureus* *C. albicans* *E. coli*	Antibacterial and antifungal activity/ In dentistry, tea tree oil has been used to destroy microorganisms in the mouth before dental surgery, remove of smear layer, and relieve mouth soreness	Sharaf et al. (2012), Soukoulis and Hirsch (2004), Thosar et al. (2013)
Myristica fragrans (Nutmeg) and *Terminalia chebula*	Chebulinic acid, tannic acid, and ellagic acid	*S. mutans* *Streptococcus sanguinis* *Actinomyces viscosus*	The capacity of phenolic compounds to scavenge and neutralize free radicals is linked to their antioxidant properties. Macelignan produced from nutmeg has an antibacterial action in the mouth	Rukayadi et al. (2008), Saleem et al. (2002)
Myrtus communis	1, 8-cineole, a-pinene, and linalool	*Persistent endodontic microorganisms*	Antifungal, antibacterial, and antioxidant activities	Nabavizadeh et al. (2014), Sulieman (2009), Zomorodian et al. (2013)

(Continues)

TABLE 2 (Continued)

Medicinal herb	Chemical constituents	Inhibitory effects on	Application	References
Propolis (Propolis resin)	Flavonoids and cinnamic acid	*E. faecalis*	Direct pulp capping with propolis in rats may delay dental pulp inflammation and stimulate reparative dentin/ Its dental applications include intraoral medicament, intracanal irrigant, and mouth rinse; cariostatic agent; storage medium for avulsed teeth; treatment of periodontitis and denture stomatitis; and pulp capping agent	Kosalec et al. (2005), Oncag et al. (2006), Ozan et al. (2007), Sabir et al. (2005)
Salvadora persica (Miswak)	Trimethyl amine, salvadorime chloride, and fluoride in large amounts	*E. feacalis* *C. albicans*	It is an excellent antibacterial agent for necrotic pulp when used as a root canal irrigant	Almas (1999), Naseem et al. (2014)
Triphala			A potent antiplaque medicine that reduced sucrose-induced adhesion and glucan-induced aggregation—two mechanisms that promote bacterial colonization of the tooth surface	Prakash and Shelke (2014)

care in the application of herbal medicines, especially in the pediatric population and during pregnancy.

For example, *Allium sativum* compounds have the potential to prevent dental caries. However, this plant has the potential to cause chemical burns to the skin and mucousa. A case report presents a burn on the palate of a 57-year-old woman who placed *Allium sativum* on her palate to relieve the pain of trigeminal neuralgia. This case shows the potential of *Allium sativum* for chemical burns in the oral mucosa and warns oral health professionals about inappropriate self-medication methods (Tomo et al., 2022).

Furthermore, Health professionals have an important role to alert and educate of people about the folk use of herbs and their effects.

5 | CONCLUSION AND FUTURE PROSPECTS

It is crucial to approach herbal medicine with an open mind and critical skepticism. More research on their potential as pharmaceutical sources and/or therapies is needed. The marketing of herbal medicines must be done with caution since, in addition to the medicinal advantages that they may give; there is a risk of overuse or adulteration. The benefits of herbal therapy can only be maximized if the source and quality of the plants are adequately managed.

Plants have been suggested, as an alternate remedy for oral–dental problems, and this vocation needs long-term dependability. New medical professionals must be able to obtain public knowledge, update it, and incorporate it into current medicine for the benefit of society.

Herbal extracts are utilized in dentistry as antimicrobial plaque agents that reduce inflammation and histamine production, as well as antiseptic, antioxidant, and analgesics. Patients with gingivitis and periodontitis benefit from their immune systems' capacity to manage microbial plaque.

AUTHOR CONTRIBUTIONS

Elaheh Dalir Abdolahinia: Conceptualization; investigation; methodology; resources; validation; writing – original draft. **Samira Hajisadeghi:** Investigation; writing – original draft. **Zahra Moayedi Banan:** Investigation; writing – original draft. **Esmaeel Dadgar:** Investigation; writing – original draft. **Amin Delaramifar:** Investigation; writing – original draft. **Sepideh Izadian:** Investigation; writing – original draft. **Simin Sharifi:** Conceptualization; funding acquisition; methodology; supervision; writing – review and editing. **Solmaz Maleki Dizaj:** Conceptualization; data curation; investigation; methodology; resources; supervision; writing – review and editing.

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CONFLICT OF INTEREST

The authors do not have any conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the results of this work are available on request from the corresponding authors.

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REFERENCES

Abdel-Aziz, H., Windeck, T., Ploch, M., & Verspohl, E. J. (2006). Mode of action of gingerols and shogaols on 5-HT3 receptors: Binding studies, cation uptake by the receptor channel and contraction of isolated guinea-pig ileum. *European Journal of Pharmacology*, *530*(1-2), 136–143. https://doi.org/10.1016/j.ejphar.2005.10.049

Abdullahi, A. A. (2011). Trends and challenges of traditional medicine in Africa. *The African Journal of Traditional, Complementary and Alternative Medicines*, *8*(5 Suppl), 115–123. https://doi.org/10.4314/ajtcam.v8i5S.5

Ahangari, Z., Naseri, M., Jalili, M., Mansouri, Y., Mashhadiabbas, F., & Torkaman, A. (2012). Effect of propolis on dentin regeneration and the potential role of dental pulp stem cell in Guinea pigs. *Cell Journal*, *13*(4), 223.

Ahmadian, E., Dizaj, S. M., Sharifi, S., Shahi, S., Khalilov, R., Eftekhari, A., & Hasanzadeh, M. (2019). The potential of nanomaterials in theranostics of oral squamous cell carcinoma: Recent progress. *Trends in Analytical Chemistry*, *116*, 167–176.

Akula, S., Nagarathna, J., & Srinath, S. K. (2021). Anti-plaque and anti-gingivitis efficacy of 0.25% Lemongrass oil and 0.2% chlorhexidine mouthwash in children. *Frontiers in Dentistry*, *18*. https://doi.org/10.18502/fid.v18i32.7237

Almas, K. (1999). The antimicrobial effects of extracts of *Azadirachta indica* (Neem) and *Salvadora persica* (Arak) chewing sticks. *Indian Journal of Dental Research*, *10*(1), 23–26.

Alves, R. R., & Rosa, I. M. (2007). Biodiversity, traditional medicine and public health: Where do they meet? *Journal of Ethnobiology and Ethnomedicine*, *3*, 14. https://doi.org/10.1186/1746-4269-3-14

Ananthathavam, K., & Ramamurthy, J. (2014). Treating periodontitis with the use of essential oil and herbs. *Journal of Pharmacy and Pharmacology*, *4*(1), 39–42.

Anuradha, B. R., Bai, Y. D., Sailaja, S., Sudhakar, J., Priyanka, M., & Deepika, V. (2015). Evaluation of anti-inflammatory effects of curcumin gel as an adjunct to scaling and root planing: A clinical study. *Journal of International Oral Health*, *7*(7), 90–93.

Ara, T., Nakatani, S., Kobata, K., Sogawa, N., & Sogawa, C. (2018). The biological efficacy of natural products against acute and chronic inflammatory diseases in the oral region. *Medicines*, *5*(4), 122.

Araghizadeh, A., Kohanteb, J., & Fani, M. M. (2013). Inhibitory activity of green tea (*Camellia sinensis*) extract on some clinically isolated cariogenic and periodontopathic bacteria. *Medical Principles and Practice*, *22*(4), 368–372. https://doi.org/10.1159/000348299

Armat, M., Bakhshaiesh, T. O., Sabzichi, M., Shanehbandi, D., Sharifi, S., Molavi, O., Mohammadian, J., Saeid Hejazi, M., & Samadi, N. (2016). The role of Six1 signaling in paclitaxel-dependent apoptosis in MCF-7 cell line. *Bosnian Journal of Basic Medical Sciences*, *16*(1), 28.

Armitage, G. C. (1999). Development of a classification system for periodontal diseases and conditions. *Annals of Periodontology*, *4*(1), 1–6. https://doi.org/10.1902/annals.1999.4.1.1

Athiban, P. P., Borthakur, B. J., Ganesan, S., & Swathika, B. (2012). Evaluation of antimicrobial efficacy of Aloe vera and its effectiveness in decontaminating gutta percha cones. *Journal of Conservative Dentistry*, *15*(3), 246–248. https://doi.org/10.4103/0972-0707.97949

Aylikci, B., & Çolak, H. (2013). Halitosis: From diagnosis to management. *Journal of Natural Science, Biology and Medicine*, *4*(1), 14–23. https://doi.org/10.4103/0976-9668.107255

Baharvand, M., Jafari, S., & Mortazavi, H. (2017). Herbs in oral mucositis. *Journal of Clinical and Diagnostic Research*, *11*(3), ZE05.

Bakhshaiesh, T. O., Armat, M., Shanehbandi, D., Sharifi, S., Baradaran, B., Hejazi, M. S., & Samadi, N. (2015). Arsenic trioxide promotes paclitaxel cytotoxicity in resistant breast cancer cells. *Asian Pacific Journal of Cancer Prevention*, *16*(13), 5191–5197.

Basile, A. C., Sertié, J. A., Panizza, S., Oshiro, T. T., & Azzolini, C. A. (1990). Pharmacological assay of Casearia sylvestris. I: Preventive anti-ulcer activity and toxicity of the leaf crude extract. *Journal of Ethnopharmacology*, *30*(2), 185–197. https://doi.org/10.1016/0378-8741(90)90007-g

Behal, R., Mali, A. M., Gilda, S. S., & Paradkar, A. R. (2011). Evaluation of local drug-delivery system containing 2% whole turmeric gel used as an adjunct to scaling and root planing in chronic periodontitis: A clinical and microbiological study. *Journal of Indian Society of Periodontology*, *15*(1), 35–38. https://doi.org/10.4103/0972-124x.82264

Bonito, A. J., Lux, L., & Lohr, K. N. (2005). Impact of local adjuncts to scaling and root planing in periodontal disease therapy: A systematic review. *Journal of Periodontology*, *76*(8), 1227–1236. https://doi.org/10.1902/jop.2005.76.8.1227

Burne, R. A. (1998). Oral streptococci… products of their environment. *Journal of Dental Research*, *77*(3), 445–452. https://doi.org/10.1177/00220345980770030301

Chantarawaratit, P., Sangvanich, P., Banlunara, W., Soontornvipart, K., & Thunyakitpisal, P. (2014). Acemannan sponges stimulate alveolar bone, cementum and periodontal ligament regeneration in a canine class II furcation defect model. *Journal of Periodontal Research*, *49*(2), 164–178.

Chaturvedi, T. P. (2009). Uses of turmeric in dentistry: An update. *Indian Journal of Dental Research*, *20*(1), 107–109. https://doi.org/10.4103/0970-9290.49065

Cheng, Y. S., Gould, A., Kurago, Z., Fantasia, J., & Muller, S. (2016). Diagnosis of oral lichen planus: A position paper of the American Academy of Oral and Maxillofacial Pathology. *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology*, *122*(3), 332–354. https://doi.org/10.1016/j.oooo.2016.05.004

Cruz Martínez, C., Diaz Gómez, M., & Oh, M. S. (2017). Use of traditional herbal medicine as an alternative in dental treatment in Mexican dentistry: A review. *Pharmaceutical Biology*, *55*(1), 1992–1998. https://doi.org/10.1080/13880209.2017.1347188

Davis, J. M., Maki, J., & Bahcall, J. K. (2007). An in vitro comparison of the antimicrobial effects of various endodontic medicaments on *Enterococcus faecalis*. *Journal of Endodontia*, *33*(5), 567–569. https://doi.org/10.1016/j.joen.2007.01.015

de Lima Dantas, J. B., Freire, T. F. C., Sanches, A. C. B., Julião, E. L. D., Medrado, A. R. A. P., & Martins, G. B. (2022). Action of *Matricaria recutita* (chamomile) in the management of radiochemotherapy oral mucositis: A systematic review. *Phytotherapy Research*, *36*(3), 1115–1125. https://doi.org/10.1002/ptr.7378

De Vincenzi, M., Stammati, A., De Vincenzi, A., & Silano, M. (2004). Constituents of aromatic plants: Carvacrol. *Fitoterapia*, *75*(7-8), 801–804. https://doi.org/10.1016/j.fitote.2004.05.002

Dimida, S., Barca, A., Cancelli, N., De Benedictis, V., Raucci, M. G., & Demitri, C. (2017). Effects of genipin concentration on cross-linked

chitosan scaffolds for bone tissue engineering: Structural characterization and evidence of biocompatibility features. *International Journal of Polymer Science*. https://doi.org/10.1155/2017/8410750

Ding, Q., Gao, J., Zheng, J., Wang, A., & Jing, S. (2019). Astragaloside IV attenuates inflammatory injury and promotes odontoblastic differentiation in lipopolysaccharide-stimulated MDPC-23 cells and rat pulpitis. *Journal of Oral Pathology & Medicine*, *48*(10), 951–958.

Eid, A., Jaradat, N., & Elmarzugi, N. (2017). A Review of chemical constituents and traditional usage of Neem plant (*Azadirachta indica*). *Palestinian Medical and Pharmaceutical Journal*, *2*(2), 75–81.

Eshghpour, M., Mortazavi, H., Mohammadzadeh Rezaei, N., & Nejat, A. (2013). Effectiveness of green tea mouthwash in postoperative pain control following surgical removal of impacted third molars: Double blind randomized clinical trial. *DARU: Journal of Pharmaceutical Sciences*, *21*(1), 59. https://doi.org/10.1186/2008-2231-21-59

Fabricant, D. S., & Farnsworth, N. R. (2001). The value of plants used in traditional medicine for drug discovery. *Environmental Health Perspectives*, *109*(Suppl 1), 69–75. https://doi.org/10.1289/ehp.01109s169

Farina, V. H., Lima, A. P., Balducci, I., & Brandão, A. A. H. (2012). Effects of the medicinal plants curcuma zedoaria and camellia sinensis on halitosis control. *Brazilian Oral Research*, *26*(6), 523–529. https://doi.org/10.1590/S1806-83242012005000022

Fathi, M., Abdolahinia, E. D., Barar, J., & Omidi, Y. (2020). Smart stimuli-responsive biopolymeric nanomedicines for targeted therapy of solid tumors. *Nanomedicine*, *15*(22), 2171–2200.

Ferrazzano, G. F., Amato, I., Ingenito, A., Zarrelli, A., Pinto, G., & Pollio, A. (2011). Plant polyphenols and their anti-cariogenic properties: a review. *Molecules*, *16*(2), 1486–1507. https://doi.org/10.3390/molecules16021486

Forouzideh, N., Nadri, S., Fattahi, A., Abdolahinia, E. D., Habibizadeh, M., Rostamizadeh, K., Baradaran-Rafii, A., & Bakhshandeh, H. (2020). Epigallocatechin gallate loaded electrospun silk fibroin scaffold with anti-angiogenic properties for corneal tissue engineering. *Journal of Drug Delivery Science and Technology*, *56*, 101498. https://doi.org/10.1016/j.jddst.2020.101498

Frohbergh, M. E., Katsman, A., Mondrinos, M. J., Stabler, C. T., Hankenson, K. D., Oristaglio, J. T., & Lelkes, P. I. (2015). Osseointegrative properties of electrospun hydroxyapatite-containing nanofibrous chitosan scaffolds. *Tissue Engineering Part A*, *21*(5-6), 970–981.

Gadagi, J. S., Chava, V. K., & Reddy, V. R. (2013). Green tea extract as a local drug therapy on periodontitis patients with diabetes mellitus: A randomized case-control study. *Journal of Indian Society of Periodontology*, *17*(2), 198–203. https://doi.org/10.4103/0972-124x.113069

Ghavimi, M. A., Bani Shahabadi, A., Jarolmasjed, S., Memar, M. Y., Maleki Dizaj, S., & Sharifi, S. (2020). Nanofibrous asymmetric collagen/curcumin membrane containing aspirin-loaded PLGA nanoparticles for guided bone regeneration. *Scientific Reports*, *10*(1), 1–15.

Gomes, C. E. B., Cavalcante, D. G., Filho, J. E. G., Da Costa, F. N., & Da Silva Pereira, S. L. (2016). Clinical effect of a mouthwash containing *Anacardium occidentale* Linn. on plaque and gingivitis control: A randomized controlled trial. *Indian Journal of Dental Research*, *27*(4), 364–369. https://doi.org/10.4103/0970-9290.191883

Gupta, D., Bhaskar, D. J., Gupta, R. K., Karim, B., Jain, A., Singh, R., & Karim, W. (2014). A randomized controlled clinical trial of *Ocimum sanctum* and chlorhexidine mouthwash on dental plaque and gingival inflammation. *Journal of Ayurveda and Integrative Medicine*, *5*(2), 109–116. https://doi.org/10.4103/0975-9476.131727

Haghpanah, P., Moghadamnia, A. A., Zarghami, A., & Motallebnejad, M. (2015). Muco-bioadhesive containing ginger officinale extract in the management of recurrent aphthous stomatitis: A randomized clinical study. *Caspian Journal of Internal Medicine*, *6*(1), 3–8.

Hara, Y., Shiratuchi, H., Kaneko, T., & Sakagami, H. (2019). Search for drugs used in hospitals to treat stomatitis. *Medicines (Basel)*, *6*(1), 19.

Hargitai, I. A. (2018). Painful oral lesions. *Dental Clinics of North America*, *62*(4), 597–609. https://doi.org/10.1016/j.cden.2018.06.002

Haukvik, T., Bruzell, E., Kristensen, S., & Tønnesen, H. H. (2010). Photokilling of bacteria by curcumin in selected polyethylene glycol 400 (PEG 400) preparations. Studies on curcumin and curcuminoids, XLI. *Pharmazie*, *65*(8), 600–606.

Highfield, J. (2009). Diagnosis and classification of periodontal disease. *Australian Dental Journal*, *54*(s1), S11–S26. https://doi.org/10.1111/j.1834-7819.2009.01140.x

Hirasawa, M., Takada, K., Makimura, M., & Otake, S. (2002). Improvement of periodontal status by green tea catechin using a local delivery system: A clinical pilot study. *Journal of Periodontal Research*, *37*(6), 433–438. https://doi.org/10.1034/j.1600-0765.2002.01640.x

Hitomi, S., Ujihara, I., & Ono, K. (2019). Pain mechanism of oral ulcerative mucositis and the therapeutic traditional herbal medicine hangeshashinto. *Journal of Oral Biosciences*, *61*(1), 12–15. https://doi.org/10.1016/j.job.2019.01.004

Hotwani, K., Baliga, S., & Sharma, K. (2014). Phytodentistry: Use of medicinal plants. *Journal of Complementary and Integrative Medicine*, *11*(4), 233–251. https://doi.org/10.1515/jcim-2013-0015

Huang, M.-H., Shen, Y.-F., Hsu, T.-T., Huang, T.-H., & Shie, M.-Y. (2016). Physical characteristics, antimicrobial and odontogenesis potentials of calcium silicate cement containing hinokitiol. *Materials Science and Engineering: C*, *65*, 1–8.

Huang, X.-F., Yuan, S.-J., & Yang, C. (2012). Effects of total flavonoids from *Drynaria fortunei* on the proliferation and osteogenic differentiation of rat dental pulp stem cells. *Molecular Medicine Reports*, *6*(3), 547–552.

Isola, G., Matarese, M., Ramaglia, L., Iorio-Siciliano, V., Cordasco, G., & Matarese, G. (2019). Efficacy of a drug composed of herbal extracts on postoperative discomfort after surgical removal of impacted mandibular third molar: A randomized, triple-blind, controlled clinical trial. *Clinical Oral Investigations*, *23*(5), 2443–2453. https://doi.org/10.1007/s00784-018-2690-9

Izzo, A. A., Hoon-Kim, S., Radhakrishnan, R., & Williamson, E. M. (2016). A critical approach to evaluating clinical efficacy, adverse events and drug interactions of herbal remedies. *Phytotherapy Research*, *30*(5), 691–700.

Jenabian, N., Moghadamnia, A. A., Karami, E., & Mir, A. P. (2012). The effect of Camellia Sinensis (green tea) mouthwash on plaque-induced gingivitis: A single-blinded randomized controlled clinical trial. *Daru: Journal of Faculty of Pharmacy*, *20*(1), 39. https://doi.org/10.1186/2008-2231-20-39

Kajiura, K., Umemura, N., Ohkoshi, E., Ohta, T., Kondoh, N., & Kawano, S. (2021). Shikonin induces odontoblastic differentiation of dental pulp stem cells via AKT–mTOR signaling in the presence of CD44. *Connective Tissue Research*, *62*(6), 1–9.

Kato, T., Segami, N., & Sakagami, H. (2016). Anti-inflammatory activity of Hangeshashinto in IL-1β-stimulated gingival and periodontal ligament fibroblasts. *In vivo (Athens, Greece)*, *30*(3), 257–263.

Khairwa, A., Bhat, M., Sharma, R., Satish, V., Maganur, P., & Goyal, A. K. (2014). Clinical and radiographic evaluation of zinc oxide with aloe vera as an obturating material in pulpectomy: An in vivo study. *Journal of the Indian Society of Pedodontics and Preventive Dentistry*, *32*(1), 33–38. https://doi.org/10.4103/0970-4388.127051

Khan, R., Islam, B., Akram, M., Shakil, S., Ahmad, A., Ali, S. M., Siddiqui, M., & Khan, A. U. (2009). Antimicrobial activity of five herbal extracts against multi drug resistant (MDR) strains of bacteria and fungus of clinical origin. *Molecules*, *14*(2), 586–597. https://doi.org/10.3390/molecules14020586

Khezri, K., Maleki Dizaj, S., Rahbar Saadat, Y., Sharifi, S., Shahi, S., Ahmadian, E., Eftekhari, A., Dalir Abdolahinia, E., & Lotfipour, F. (2021). Osteogenic differentiation of mesenchymal stem cells via curcumin-containing nanoscaffolds. *Stem Cells International*, *2021*, 1520052.

Koo, H., Duarte, S., Murata, R. M., Scott-Anne, K., Gregoire, S., Watson, G. E., Singh, A. P., & Vorsa, N. (2010). Influence of cranberry proanthocyanidins on formation of biofilms by *Streptococcus*

mutans on saliva-coated apatitic surface and on dental caries development in vivo. *Caries Research*, *44*(2), 116–126. https://doi.org/10.1159/000296306

Kosalec, I., Pepeljnjak, S., Bakmaz, M., & Vladimir-Knežević, S. (2005). Flavonoid analysis and antimicrobial activity of commercially available propolis products. *Acta Pharmaceutica*, *55*(4), 423–430.

Kudva, P., Tabasum, S. T., & Shekhawat, N. K. (2011). Effect of green tea catechin, a local drug delivery system as an adjunct to scaling and root planing in chronic periodontitis patients: A clinicomicrobiological study. *Journal of Indian Society of Periodontology*, *15*(1), 39–45. https://doi.org/10.4103/0972-124x.82269

Kumar, G., Jalaluddin, M., Rout, P., Mohanty, R., & Dileep, C. L. (2013). Emerging trends of herbal care in dentistry. *Journal of Clinical and Diagnostic Research*, *7*(8), 1827–1829. https://doi.org/10.7860/jcdr/2013/6339.3282

Kwon, Y.-S., Kim, H.-J., Hwang, Y.-C., Rosa, V., Yu, M.-K., & Min, K.-S. (2017). Effects of epigallocatechin gallate, an antibacterial cross-linking agent, on proliferation and differentiation of human dental pulp cells cultured in collagen scaffolds. *Journal of Endodontics*, *43*(2), 289–296.

Kwon, Y. S., Lim, E. S., Kim, H. M., Hwang, Y. C., Lee, K. W., & Min, K. S. (2015). Genipin, a cross-linking agent, promotes odontogenic differentiation of human dental pulp cells. *Journal of Endodontia*, *41*(4), 501–507. https://doi.org/10.1016/j.joen.2014.12.002

Lee, S.-I., Kim, S.-Y., Park, K.-R., & Kim, E.-C. (2016). Baicalein promotes angiogenesis and odontoblastic differentiation via the BMP and Wnt pathways in human dental pulp cells. *The American Journal of Chinese Medicine*, *44*(7), 1457–1472. https://doi.org/10.1142/s0192415x16500816

Lee, Y. J., Park, B. S., Park, H. R., Yu, S. B., Kang, H. M., & Kim, I. R. (2017). XIAP inhibitor embelin induces autophagic and apoptotic cell death in human oral squamous cell carcinoma cells. *Environmental Toxicology*, *32*(11), 2371–2378. https://doi.org/10.1002/tox.22450

Lobina, C., Sau, R., Fara, F., Maccioni, P., Carai, M. A., & Colombo, G. (2021). Analgesic properties of a food grade lecithin delivery system of *Zingiber officinale* and *Acmella oleracea* standardized extracts in rats. *Natural Product Research*, *35*(18), 3078–3082.

Lu, X., Rasco, B. A., Jabal, J. M. F., Aston, D. E., Lin, M., & Konkel, M. E. (2011). Investigating antibacterial effects of garlic (*Allium sativum*) concentrate and garlic-derived organosulfur compounds on *Campylobacter jejuni* by using Fourier transform infrared spectroscopy, Raman spectroscopy, and electron microscopy. *Applied and Environmental Microbiology*, *77*(15), 5257–5269. https://doi.org/10.1128/AEM.02845-10

Maleki Dizaj, S., Sharifi, S., & Jahangiri, A. (2019). Electrospun nanofibers as versatile platform in antimicrobial delivery: Current state and perspectives. *Pharmaceutical Development and Technology*, *24*(10), 1187–1199.

Masuda, M., Wakasaki, T., Suzui, M., Toh, S., Joe, A. K., & Weinstein, I. B. (2010). Stat3 orchestrates tumor development and progression: The Achilles' heel of head and neck cancers? *Current Cancer Drug Targets*, *10*(1), 117–126. https://doi.org/10.2174/156800910790980197

Merolli, A., Nicolais, L., Ambrosio, L., & Santin, M. (2010). A degradable soybean-based biomaterial used effectively as a bone filler in vivo in a rabbit. *Biomedical Materials*, *5*(1), 15008.

Miraj, S. (2016). Pharmacological effect of Actiumlappa: A review study. *Der Pharmacia Lettre*, *8*(9), 102–106.

Mistry, K. S., Sanghvi, Z., Parmar, G., & Shah, S. (2014). The antimicrobial activity of *Azadirachta indica*, *Mimusops elengi*, *Tinospora cardifolia*, *Ocimum sanctum* and 2% chlorhexidine gluconate on common endodontic pathogens: An in vitro study. *European Journal of Dentistry*, *8*(2), 172–177. https://doi.org/10.4103/1305-7456.130591

Miyano, K., Eto, M., Hitomi, S., Matsumoto, T., Hasegawa, S., Hirano, A., Nagabuchi, K., Asai, N., Uzu, M., Nonaka, M., Omiya, Y., Kaneko, A., Ono, K., Fujii, H., Higami, Y., Kono, T., & Uezono, Y. (2020). The Japanese herbal medicine Hangeshashinto enhances oral keratinocyte migration to facilitate healing of chemotherapy-induced oral ulcerative mucositis. *Scientific Reports*, *10*(1), 1–13. https://doi.org/10.1038/s41598-019-57192-2

Modgi, C., & Radke, U. (2021). Oral health related quality of life in geriatric patients-A review. *Journal of Orofacial Research*, *10*(3), 33–37.

Moghadam, E. T., Yazdanian, M., Alam, M., Tebyanian, H., Tafazoli, A., Tahmasebi, E., Ranjbar, R., Yazdanian, A., & Seifalian, A. (2021). Current natural bioactive materials in bone and tooth regeneration in dentistry: A comprehensive overview. *Journal of Materials Research and Technology*, *13*, 2078–2114.

Mohseni, M., Samadi, N., Ghanbari, P., Yousefi, B., Tabasinezhad, M., Sharifi, S., & Nazemiyeh, H. (2016). Co-treatment by docetaxel and vinblastine breaks down P-glycoprotein mediated chemoresistance. *Iranian Journal of Basic Medical Sciences*, *19*(3), 300.

Mojtahedzadeh, M., Mashhadi Akbar Boojar, M., Habtemariam, S., Nabavi, S. M., Najafi, A., Ghahremanian, A., Baktash, M., Aghaabdollahian, S., Sureda, A., & Bagheri, M. (2021). Systematic review: Effectiveness of herbal oral care products on ventilator-associated pneumonia. *Phytotherapy Research*, *35*(7), 3665–3672.

Morin, M.-P., Bedran, T. B. L., Fournier-Larente, J., Haas, B., Azelmat, J., & Grenier, D. (2015). Green tea extract and its major constituent epigallocatechin-3-gallate inhibit growth and halitosis-related properties of *Solobacterium moorei*. *BMC Complementary and Alternative Medicine*, *15*(1), 1–11.

Morton, J. F. (1992). The ocean-going noni, or Indian Mulberry (*Morinda citrifolia*, Rubiaceae) and some of its "colorful" relatives. *Economic Botany*, *46*(3), 241–256. https://doi.org/10.1007/BF02866623

Murray, P. E., Farber, R. M., Namerow, K. N., Kuttler, S., & Garcia-Godoy, F. (2008). Evaluation of *Morinda citrifolia* as an endodontic irrigant. *Journal of Endodontia*, *34*(1), 66–70. https://doi.org/10.1016/j.joen.2007.09.016

Murray, P. E., Garcia-Godoy, F., & Hargreaves, K. M. (2007). Regenerative endodontics: A review of current status and a call for action. *Journal of Endodontics*, *33*(4), 377–390.

Nabavizadeh, M., Abbaszadegan, A., Gholami, A., Sheikhiani, R., Shokouhi, M., Shams, M. S., & Ghasemi, Y. (2014). Chemical constituent and antimicrobial effect of essential oil from *Myrtus communis* leaves on microorganisms involved in persistent endodontic infection compared to two common endodontic irrigants: An in vitro study. *Journal of Conservative Dentistry*, *17*(5), 449–453. https://doi.org/10.4103/0972-0707.139836

Najafi, S., Koujan, S. E., Manifar, S., Kharazifard, M. J., Kidi, S., & Hajheidary, S. (2017). Preventive effect of *Glycyrrhiza glabra* extract on oral mucositis in patients under head and neck radiotherapy: A randomized clinical trial. *Journal of Dentistry (Tehran, Iran)*, *14*(5), 267–274.

Naseem, S., Hashmi, K., Fasih, F., Sharafat, S., & Khanani, R. (2014). In vitro evaluation of antimicrobial effect of miswak against common oral pathogens. *Pakistan Journal of Medical Sciences*, *30*(2), 398–403. https://doi.org/10.12669/pjms.302.4284

Nazliniwaty, N., & Laila, L. (2019). Formulation and antibacterial activity of plectranthus amboinicus (Lour.) spreng leaves ethanolic extract as herbal mouthwash against halitosis caused bacteria. *Open Access Macedonian Journal of Medical Sciences*, *7*(22), 3900–3903. https://doi.org/10.3889/oamjms.2019.529

Negahdari, R., Ghavimi, M. A., Barzegar, A., Memar, M. Y., Balazadeh, L., Bohlouli, S., Sharifi, S., & Maleki Dizaj, S. (2021). Antibacterial effect of nanocurcumin inside the implant fixture: An in vitro study. *Clinical and Experimental Dental Research*, *7*(2), 163–169.

Nimma, V. L., Talla, H. V., Bairi, J. K., Gopaldas, M., Bathula, H., & Vangdoth, S. (2017). Holistic healing through herbs: Effectiveness of aloe vera on post extraction socket healing. *Journal of Clinical and Diagnostic Research*, *11*(3), ZC83.

Nosrat, A., Bolhari, B., Sharifian, M. R., Aligholi, M., & Mortazavi, M. S. (2009). The effect of Carvacrol on *Enterococcus faecalis* as a final irrigant. *Iranian Endodontic Journal*, *4*(3), 96–100.

Omar, O. M., Khattab, N. M., & Khater, D. S. (2012). Nigella sativa oil as a pulp medicament for pulpotomized teeth: A histopathological evaluation. *The Journal of Clinical Pediatric Dentistry*, *36*(4), 335–341. https://doi.org/10.17796/jcpd.36.4.n6674435856q86w8

Oncag, O., Cogulu, D., Uzel, A., & Sorkun, K. (2006). Efficacy of propolis as an intracanal medicament against *Enterococcus faecalis*. *General Dentistry*, *54*(5), 319–322.

Onken, J. E., Greer, P. K., Calingaert, B., & Hale, L. P. (2008). Bromelain treatment decreases secretion of pro-inflammatory cytokines and chemokines by colon biopsies in vitro. *Clinical Immunology*, *126*(3), 345–352. https://doi.org/10.1016/j.clim.2007.11.002

Otake, S., Makimura, M., Kuroki, T., Nishihara, Y., & Hirasawa, M. (1991). Anticaries effects of polyphenolic compounds from Japanese green tea. *Caries Research*, *25*(6), 438–443. https://doi.org/10.1159/000261407

Ozan, F., Sümer, Z., Polat, Z. A., Er, K., Ozan, U., & Deger, O. (2007). Effect of mouthrinse containing propolis on oral microorganisms and human gingival fibroblasts. *European Journal of Dentistry*, *1*(4), 195–201.

Ozawa, N., Onda, T., Hayashi, K., Honda, H., & Shibahara, T. (2020). Effects of topical hangeshashinto (Tj-14) on chemotherapy-induced oral mucositis. *Cancer Management and Research*, *12*, 1069–1078. https://doi.org/10.2147/CMAR.S238306

Pan, S.-Y., Litscher, G., Gao, S.-H., Zhou, S.-F., Yu, Z.-L., Chen, H.-Q., Zhang, S. F., Tang, M. K., Sun, J. N., & Ko, K.-M. (2014). Historical perspective of traditional indigenous medical practices: The current renaissance and conservation of herbal resources. *Evidence-based Complementary and Alternative Medicine*, 2014. https://doi.org/10.1155/2014/525340

Pandita, V., Patthi, B., Singla, A., Singh, S., Malhi, R., & Vashishtha, V. (2014). Dentistry meets nature-role of herbs in periodontal care: A systematic review. *Journal of Indian Association of Public Health Dentistry*, *12*(3), 148.

Patil, K., Guledgud, M. V., Kulkarni, P., Keshari, D., & Tayal, S. (2015). Use of curcumin mouthrinse in radio-chemotherapy induced oral mucositis patients: A pilot study. *Journal of Clinical and Diagnostic Research*, *9*(8), ZC59.

Payyappallimana, U. (2010). Role of traditional medicine in primary health care: An overview of perspectives and challenging. *Yokohama Journal of Social Sciences*, *14*, 57–77.

Peñalver, P., Huerta, B., Borge, C., Astorga, R., Romero, R., & Perea, A. (2005). Antimicrobial activity of five essential oils against origin strains of the Enterobacteriaceae family. *APMIS*, *113*(1), 1–6. https://doi.org/10.1111/j.1600-0463.2005.apm1130101.x

Petruzzi, M., Stella, A., Capra, V., Contaldo, M., & Della Vella, F. (2021). Oro-dental manifestations in a pediatric patient affected by Helsmoortel-Van der Aa Syndrome. *International Journal of Environmental Research and Public Health*, *18*(17), 8957.

Pistorius, A., Willershausen, B., Steinmeier, E. M., & Kreislert, M. (2003). Efficacy of subgingival irrigation using herbal extracts on gingival inflammation. *Journal of Periodontology*, *74*(5), 616–622. https://doi.org/10.1902/jop.2003.74.5.616

Pouyfung, P., Choonate, S., Wongnoppavich, A., Rongnoparut, P., & Chairatvit, K. (2019). Anti-proliferative effect of 8α-tigloyloxyhirsutinolide-13-O-acetate (8αTGH) isolated from Vernonia cinerea on oral squamous cell carcinoma through inhibition of STAT3 and STAT2 phosphorylation. *Phytomedicine*, *52*, 238–246. https://doi.org/10.1016/j.phymed.2018.09.211

Pradeep, A. R., Agarwal, E., Bajaj, P., Naik, S. B., Shanbhag, N., & Uma, S. R. (2012). Clinical and microbiologic effects of commercially available gel and powder containing *Acacia arabica* on gingivitis. *Australian Dental Journal*, *57*(3), 312–318. https://doi.org/10.1111/j.1834-7819.2012.01714.x

Pradeep, A. R., Happy, D., & Garg, G. (2010). Short-term clinical effects of commercially available gel containing Acacia arabica: A randomized controlled clinical trial. *Australian Dental Journal*, *55*(1), 65–69. https://doi.org/10.1111/j.1834-7819.2009.01180.x

Prakash, S., & Shelke, A. U. (2014). Role of Triphala in dentistry. *Journal of Indian Society of Periodontology*, *18*(2), 132–135. https://doi.org/10.4103/0972-124X.131299

Pujar, M., & Makandar, S. D. (2011). Herbal usage in endodontics-A review. *International Journal of Contemporary Dentistry*, *2*(1), 34–37.

Rassameemasmaung, S., Phusudsawang, P., & Sangalungkarn, V. (2013). Effect of green tea mouthwash on oral malodor. *International Scholarly Research Notices*, *2013*. https://doi.org/10.5402/2013/975148

Rayati, F., Hajmanouchehri, F., & Najafi, E. (2017). Comparison of anti-inflammatory and analgesic effects of Ginger powder and Ibuprofen in postsurgical pain model: A randomized, double-blind, case-control clinical trial. *Dental Research Journal*, *14*(1), 1–7. https://doi.org/10.4103/1735-3327.201135

Ren, Z. H., Hu, C. Y., He, H. R., Li, Y. J., & Lyu, J. (2020). Global and regional burdens of oral cancer from 1990 to 2017: Results from the global burden of disease study. *Cancer Communications*, *40*(2-3), 81–92. https://doi.org/10.1002/cac2.12009

Rivera, C. (2015). Essentials of oral cancer. *International journal of clinical and experimental pathology*, *8*(9), 11884–94.

Rotblatt, M., & Ziment, I. (2002). *Evidence-based herbal medicine*. Hanley & Belfus.

Rukayadi, Y., Kim, K. H., & Hwang, J. K. (2008). In vitro anti-biofilm activity of macelignan isolated from Myristica fragrans Houtt. against oral primary colonizer bacteria. *Phytotherapy Research*, *22*(3), 308–312. https://doi.org/10.1002/ptr.2312

Sabir, A., Tabbu, C. R., Agustiono, P., & Sosroseno, W. (2005). Histological analysis of rat dental pulp tissue capped with propolis. *Journal of Oral Science*, *47*(3), 135–138.

Saini, M. L., Saini, R., Roy, S., & Kumar, A. (2008). Comparative pharmacognostical and antimicrobial studies of Acacia species (Mimosaceae). *Journal of Medicinal Plants Research*, *2*(12), 378–386.

Saleem, A., Husheem, M., Härkönen, P., & Pihlaja, K. (2002). Inhibition of cancer cell growth by crude extract and the phenolics of *Terminalia chebula* retz. fruit. *Journal of Ethnopharmacology*, *81*(3), 327–336. https://doi.org/10.1016/s0378-8741(02)00099-5

Samiei, M., Abedi, A., Sharifi, S., & Maleki Dizaj, S. (2021). Early osteogenic differentiation stimulation of dental pulp stem cells by calcitriol and curcumin. *Stem Cells International*, *2021*. https://doi.org/10.1155/2021/9980137

Samiei, M., Aghazadeh, Z., Abdolahinia, E. D., Vahdati, A., Daneshvar, S., & Noghani, A. (2020). The effect of electromagnetic fields on survival and proliferation rate of dental pulp stem cells. *Acta Odontologica Scandinavica*, *78*(7), 494–500.

Schmalz, G., & Smith, A. J. (2014). Pulp development, repair, and regeneration: Challenges of the transition from traditional dentistry to biologically based therapies. *Journal of Endodontics*, *40*(4), S2–S5.

Segal, R., Pisanty, S., Wormser, R., Azaz, E., & Sela, M. N. (1985). Anticariogenic activity of licorice and glycyrrhizine I: Inhibition of in vitro plaque formation by *Streptococcus mutans*. *Journal of Pharmaceutical Sciences*, *74*(1), 79–81. https://doi.org/10.1002/jps.2600740121

Sethi, R., & Govila, V. (2011). Inhibitory effect of cranberry juice on the colonization of *Streptococci* species: An in vitro study. *Journal of Indian Society of Periodontology*, *15*(1), 46–50. https://doi.org/10.4103/0972-124x.82271

Shah, R., Gayathri, G., & Mehta, D. S. (2015). Application of herbal products in management of periodontal diseases: A mini review. *International Journal of Oral Health Sciences*, *5*(1), 38.

Shahakbari, R., Eshghpour, M., Rajaei, A., Rezaei, N. M., Golfakhrabadi, P., & Nejat, A. (2014). Effectiveness of green tea mouthwash in comparison to chlorhexidine mouthwash in patients with acute

pericoronitis: A randomized clinical trial. *International Journal of Oral and Maxillofacial Surgery*, *43*(11), 1394–1398. https://doi.org/10.1016/j.ijom.2014.05.017

Shahbaz, M., Zaheer, N., Sagheer, A., Arshad, A. I., Zaheer, U., & Alam, M. K. (2017). Role of green tea extract (*Camellia sinensis*) in prevention of nicotine-induced inflammatory and epithelial changes in buccal mucosa of albino rats. *International Medical Journal*, *24*(2), 230–233.

Shahi, S., Özcan, M., Maleki Dizaj, S., Sharifi, S., Al-Haj Husain, N., Eftekhari, A., & Ahmadian, E. (2019). A review on potential toxicity of dental material and screening their biocompatibility. *Toxicology Mechanisms and Methods*, *29*(5), 368–377.

Sharaf, N., Aboul-Enein, N., Hassan, M., Ayad, M., Zaazou, M., & Farrag, A. (2012). Effect of MTAD and tea tree oil irrigation before pulp capping on healing of exposed dental pulp. *Australian Journal of Basic and Applied Sciences*, *6*(7), 553–557.

Sharifi, S., Moghaddam, F. A., Abedi, A., Maleki Dizaj, S., Ahmadian, S., Abdolahinia, E. D., SMH, K., & Samiei, M. (2020). Phytochemicals impact on osteogenic differentiation of mesenchymal stem cells. *BioFactors*, *46*(6), 874–893.

Sharifi, S., Zununi Vahed, S., Ahmadian, E., Maleki Dizaj, S., Abedi, A., Hosseiniyan Khatibi, S. M., & Samiei, M. (2019). Stem cell therapy: Curcumin does the trick. *Phytotherapy Research*, *33*(11), 2927–2937.

Shiu, S.-T., Lew, W.-Z., Lee, S.-Y., Feng, S.-W., & Huang, H.-M. (2020). Effects of sapindus mukorossi seed oil on proliferation, osteogenetic/odontogenetic differentiation and matrix vesicle secretion of human dental pulp mesenchymal stem cells. *Materials*, *13*(18), 4063.

Siddeeqh, S., Parida, A., Jose, M., & Pai, V. (2016). Estimation of Antimicrobial Properties of Aqueous and Alcoholic Extracts of Salvadora Persica (Miswak) on Oral Microbial Pathogens - An Invitro Study. *J Clin Diagn Res*, *10*(9), FC13–FC16. https://doi.org/10.7860/JCDR/2016/22213.8524

Silva, M. F., Leite, F. R. M., Ferreira, L. B., Pola, N. M., Scannapieco, F. A., Demarco, F. F., & Nascimento, G. G. (2018). Estimated prevalence of halitosis: A systematic review and meta-regression analysis. *Clinical Oral Investigations*, *22*(1), 47–55. https://doi.org/10.1007/s00784-017-2164-5

Sinha, D. J., & Sinha, A. A. (2014). Natural medicaments in dentistry. *Ayu*, *35*(2), 113–118. https://doi.org/10.4103/0974-8520.146198

Sinjari, B., Pizzicannella, J., D'Aurora, M., Zappacosta, R., Gatta, V., Fontana, A., Trubiani, O., & Diomede, F. (2019). Curcumin/liposome nanotechnology as delivery platform for anti-inflammatory activities via NFkB/ERK/pERK pathway in human dental pulp treated with 2-hydroxyethyl methacrylate (HEMA). *Frontiers in Physiology*, *10*, 633.

Songsiripradubboon, S., Kladkaew, S., Trairatvorakul, C., Sangvanich, P., Soontornvipart, K., Banlunara, W., & Thunyakitpisal, P. (2017). Stimulation of dentin regeneration by using acemannan in teeth with lipopolysaccharide-induced pulp inflammation. *Journal of Endodontics*, *43*(7), 1097–1103.

Soukoulis, S., & Hirsch, R. (2004). The effects of a tea tree oil-containing gel on plaque and chronic gingivitis. *Australian Dental Journal*, *49*(2), 78–83. https://doi.org/10.1111/j.1834-7819.2004.tb00054.x

Soumya, S., Sajesh, K., Jayakumar, R., Nair, S., & Chennazhi, K. (2012). Development of a phytochemical scaffold for bone tissue engineering using *Cissus quadrangularis* extract. *Carbohydrate Polymers*, *87*(2), 1787–1795.

Srinivasan, S., Jayasree, R., Chennazhi, K., Nair, S., & Jayakumar, R. (2012). Biocompatible alginate/nano bioactive glass ceramic composite scaffolds for periodontal tissue regeneration. *Carbohydrate Polymers*, *87*(1), 274–283.

Stamatis, G., Kyriazopoulos, P., Golegou, S., Basayiannis, A., Skaltsas, S., & Skaltsa, H. (2003). In vitro anti-*Helicobacter pylori* activity of Greek herbal medicines. *Journal of Ethnopharmacology*, *88*(2-3), 175–179. https://doi.org/10.1016/s0378-8741(03)00217-4

Stavroullakis, A. T., Carrilho, M. R., Levesque, C. M., & Prakki, A. (2018). Profiling cytokine levels in chlorhexidine and EGCG-treated odontoblast-like cells. *Dental Materials*, *34*(6), e107–e114.

Sterer, N., Ovadia, O., Weiss, E. I., & Perez Davidi, M. (2013). Day-long reduction of oral malodor by a palatal mucoadhesive tablet containing herbal formulation. *Journal of Breath Research*, *7*(2). https://doi.org/10.1088/1752-7155/7/2/026004

Stuart, C. H., Schwartz, S. A., Beeson, T. J., & Owatz, C. B. (2006). *Enterococcus faecalis*: Its role in root canal treatment failure and current concepts in retreatment. *Journal of Endodontia*, *32*(2), 93–98. https://doi.org/10.1016/j.joen.2005.10.049

Sulieman, R. T. (2009). The antibacterial effect of *Myrtus communis* as root canal irrigant: A comparative study. *Al-Rafidain Dental Journal*, *9*(2), 289–296.

Sunagawa, M., Yamaguchi, K., Tsukada, M., Ebihara, N., Ikemoto, H., & Hisamitsu, T. (2018). Kampo (traditional Japanese herbal) formulae for treatment of stomatitis and oral mucositis. *Medicines*, *5*(4), 130.

Taheri, J. B., Azimi, S., Rafieian, N., & Zanjani, H. A. (2011). Herbs in dentistry. *International Dental Journal*, *61*(6), 287–296. https://doi.org/10.1111/j.1875-595X.2011.00064.x

Takanche, J. S., Lee, Y. H., Kim, J. S., Kim, J. E., Han, S. H., Lee, S. W., & Yi, H. K. (2018). Anti-inflammatory and antioxidant properties of Schisandrin C promote mitochondrial biogenesis in human dental pulp cells. *International Endodontic Journal*, *51*(4), 438–447. https://doi.org/10.1111/iej.12861

Tavangar, A., Aslani, A., & Nikbakht, N. (2019). Comparative study of *Punica granatum* gel and triadent oral paste effect on recurrent aphthous stomatitis, a double blind clinical trial. *Journal of Dentistry*, *20*(3), 184.

Telrandhe, U. B., Lokhande, R. R., Lodhe, V. N., Kosalge, S. B., Parihar, S., & Sharma, D. (2021). Review on herbal drugs used in dental care management. *Asian Journal of Pharmaceutical Research and Development*, *9*(6), 71–79.

Thomas, A. E., Varma, B., Kurup, S., Jose, R., Chandy, M. L., Kumar, S. P., Aravind, M. S., & Ramadas, A. A. (2017). Evaluation of efficacy of 1% curcuminoids as local application in management of oral lichen planus–interventional study. *Journal of Clinical and Diagnostic Research*, *11*(4), ZC89.

Thosar, N., Basak, S., Bahadure, R. N., & Rajurkar, M. (2013). Antimicrobial efficacy of five essential oils against oral pathogens: An in vitro study. *European Journal of Dentistry*, *7*(Suppl 1), S071–S077. https://doi.org/10.4103/1305-7456.119078

Tomo, S., Santos, I., TMD, C., Miyahara, G. I., & Simonato, L. E. (2022). Garlic burn trauma of the oral mucosa in a patient with trigeminal neuralgia: A case report. *Dental Traumatology*. https://doi.org/10.1111/edt.12740

Tu, M.-G., Lee, A. K.-X., Lin, Y.-H., Huang, T.-H., Ho, C.-C., & Shie, M.-Y. (2020). Caffeic acid–coated nanolayer on mineral trioxide aggregate potentiates the host immune responses, angiogenesis, and odontogenesis. *Journal of Endodontics*, *46*(10), 1455–1464.

Tyagi, S. P., Sinha, D. J., Garg, P., Singh, U. P., Mishra, C. C., & Nagpal, R. (2013). Comparison of antimicrobial efficacy of propolis, *Morinda citrifolia*, *Azadirachta indica* (Neem) and 5% sodium hypochlorite on *Candida albicans* biofilm formed on tooth substrate: An in-vitro study. *Journal of Conservative Dentistry*, *16*(6), 532.

Uhlenbrock, L., Sixt, M., Tegtmeier, M., Schulz, H., Hagels, H., Ditz, R., & Strube, J. (2018). Natural products extraction of the future—sustainable manufacturing solutions for societal needs. *Processes*, *6*(10), 177. https://doi.org/10.3390/pr6100177

Uju, D. E., & Obioma, N. P. (2011). Anticariogenic potentials of clove, tobacco and bitter kola. *Asian Pacific Journal of Tropical Medicine*, *4*(10), 814–818. https://doi.org/10.1016/s1995-7645(11)60200-9

Veloso, D. J., Abrão, F., Martins, C. H. G., Bronzato, J. D., Gomes, B. P. F. A., Higino, J. S., & Sampaio, F. C. (2020). Potential antibacterial and anti-halitosis activity of medicinal plants against oral bacteria. *Archives of Oral Biology*, *110*, 104585. https://doi.org/10.1016/j.archoralbio.2019.104585

Vennila, K., Elanchezhiyan, S., & Ilavarasu, S. (2016). Efficacy of 10% whole *Azadirachta indica* (neem) chip as an adjunct to scaling and root planning in chronic periodontitis: A clinical and microbiological study. *Indian Journal of Dental Research*, *27*(1), 15–21. https://doi.org/10.4103/0970-9290.179808

Vu, T. T., Nguyen, M. T., Sangvanich, P., Nguyen, Q. N., & Thunyakitpisal, P. (2020). Acemannan used as an implantable biomaterial for vital pulp therapy of immature permanent teeth induced continued root formation. *Pharmaceutics*, *12*(7), 644.

Wang, C., Song, Y., Gu, Z., Lian, M., Huang, D., Lu, X., Feng, X., & Lu, Q. (2018). Wedelolactone enhances odontoblast differentiation by promoting Wnt/β-catenin signaling pathway and suppressing NF-κB signaling pathway. *Cellular Reprogramming*, *20*(4), 236–244.

World Health Organization (2000). *General guidelines for methodologies on research and evaluation of traditional medicine*. No. WHO/EDM/TRM/2000.1.

Wu, A., Bao, Y., Yu, H., Zhou, Y., & Lu, Q. (2019). Berberine accelerates odontoblast differentiation by Wnt/β-catenin activation. *Cellular Reprogramming*, *21*(2), 108–114.

Wynn, R. L. (2005). Aloe vera gel: Update for dentistry. *General Dentistry*, *53*(1), 6–9.

Xu, X. L., Lou, J., Tang, T., Ng, K. W., Zhang, J., Yu, C., & Dai, K. (2005). Evaluation of different scaffolds for BMP-2 genetic orthopedic tissue engineering. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, *75*(2), 289–303.

Xue, W., Yu, J., & Chen, W. (2018). Plants and their bioactive constituents in mesenchymal stem cell-based periodontal regeneration: A novel prospective. *BioMed Research International*, *2018*(2), 1–15.

Yaghini, J., Shahabooei, M., Aslani, A., Zadeh, M. R., Kiani, S., & Naghsh, N. (2014). Efficacy of a local-drug delivery gel containing extracts of *Quercus brantii* and *Coriandrum sativum* as an adjunct to scaling and root planing in moderate chronic periodontitis patients. *Journal of Research in Pharmacy Practice*, *3*(2), 67–71. https://doi.org/10.4103/2279-042x.137076

Yamanaka, A., Kimizuka, R., Kato, T., & Okuda, K. (2004). Inhibitory effects of cranberry juice on attachment of oral streptococci and biofilm formation. *Oral Microbiology and Immunology*, *19*(3), 150–154. https://doi.org/10.1111/j.0902-0055.2004.00130.x

Yuan, H., Ma, Q., Ye, L., & Piao, G. (2016). The Traditional Medicine and Modern Medicine from Natural Products. *Molecules*, *21*(5), 559.

Zhu, L., Petersen, P. E., Wang, H. Y., Bian, J. Y., & Zhang, B. X. (2005). Oral health knowledge, attitudes and behaviour of adults in China. *International Dental Journal*, *55*(4), 231–241. https://doi.org/10.1111/j.1875-595x.2005.tb00321.x

Zieglgänsberger, W. (2019). Substance P and pain chronicity. *Cell and Tissue Research*, *375*(1), 227–241. https://doi.org/10.1007/s00441-018-2922-y

Zomorodian, K., Moein, M., Lori, Z. G., Ghasemi, Y., Rahimi, M. J., Bandegani, A., Pakshir, K., Bazargani, A., Mirzamohammadi, S., & Abbasi, N. (2013). Chemical composition and antimicrobial activities of the essential oil from *Myrtus communis* leaves. *Journal of Essential Oil Bearing Plants*, *16*(1), 76–84. https://doi.org/10.1080/0972060X.2013.764183

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