

Review Article

Herbal Medicines in Endodontics: An Overview

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Abstract

Natural products have been used since ancient times in folk medicine. Herbal medicines are the drugs of plant origin used to treat diseases and to attain or maintain a condition of improved health. Herbs with medicinal properties are a useful and effective source of treatment for various diseases. Many drugs used in Western medical science (called allopathic medicine) have their origin in medicinal plants. This review focuses on various natural drugs and products as well as their therapeutic applications when used as phytomedicine in endodontics.

Keywords: Endodontics; Herbal; Phytomedicine; Dental caries

Introduction

Herbal medicines (Botanical medicine, Phytomedicine, or Phytotherapy) refer to herbs, herbal materials, herbal preparations, and finished herbal products that contain parts of plants or other materials as active ingredients. Today the Herbal or natural products have become more popular due to their high antimicrobial activity, biocompatibility, anti-inflammatory and anti-oxidant properties [1]. As the incidence of increased resistance by pathogenic bacteria to currently used antibiotics and chemotherapeutics agents is more, the researchers are developing interest towards alternative treatment options and products for oral diseases. Hence, the natural phytochemicals isolated from plants used in traditional medicine are considered as good alternatives to synthetic chemicals.

According to the World Health Organization (WHO), as many as 80% of the world's people depend on traditional medicine (herbal) for their primary healthcare needs [2]. Herbal remedies have a long history of use for gum and tooth problems. In many traditional cultures, the use of herbal "chewing sticks" taken from plants, shrubs or trees with high anti-microbial activity are common. A herb may exhibit one or more following unique therapeutic properties like anti-bacterial, anti-inflammatory, astringents, anaesthetic, immune strengtheners, anticariogenic, anti plaque agents and tooth whitener [3]. Herbs may be good alternatives to current treatments for oral health problems but there is lack of information about the effect of herbs in oral tissues, mechanism of effect, and side effects. So the more research is required to explore these traditional medicines [3]. Dental caries are still one of the most common diseases in the world. *Streptococcus mutans* has the central role in the initiation of caries on tooth surfaces [4]. Today, herbal medicines are introduced into the tooth pastes to prevent dental caries. The anti-cariogenic property of polyphenols is mainly due to a direct effect against *S. mutans*. It inhibits the adherence of bacterial cells to the tooth surface by interacting with the microbial membrane proteins [5]. In endodontics herbs are mainly used for the disinfection of the root canal. There is increased research towards the herbal irrigants due to the some adverse effects of the most of synthetic intracanal medicaments. *E. Faecalis* is most common bacteria responsible for root canal treatment failure cases [6]. Sodium hypochlorite is used to eliminate *E. faecalis* from the root canal but there are several disadvantages of sodium hypochlorite

like unpleasant taste, toxicity, and potential weakening of the tooth structure by decreasing the hardness and structural integrity of the dentin within the root canal [7]. Thus the aim of this review is to enlist and describe the various herbal alternatives available today for use as effective endodontic medicaments and caries control agents. Articles were collected using PubMed and Google Scholar search engine in relation to herbal medicine, dentistry and endodontics.

Aloe Barbadensis (Aloe vera gel)

Green leaf of Aloe vera leaves contains clear gel that is used to produce juice. It contains aloins and barbadoins as main chemical constituents. In dentistry, Aloe vera is used in cases of apthous ulcers, lichen planus, alveolar osteitis [8]. Gel has inhibitory effects on *S. pyogens* and *E. faecalis* because of anthraquinone [8]. Aloe vera gel was used effectively for the disinfection of gutta-percha cones from *E. coli*, *E. faecalis* and *S. aureus* within a short duration [9]. Endodontic treatment using a mixture of zinc oxide powder and aloe vera gel in primary teeth has shown good clinical and radiographic success [10].

Azadirachta indica (Neem)

It is known as Indian neem tree having medicinal property by each part of the tree. It has anti viral, anti fungal, anti bacterial and anti carcinogenic activity [11]. Nimbidin is a major active component isolated from seed of *A. indica*. From nimbidin other constituents like nimbin, nimbinin, nimbidinin, nimbolide and nimbidic acid has been isolated which are responsible for its biological activities [12]. The dental gel containing Neem extract was responsible to reduce plaque index and bacterial count significantly [13]. The antimicrobial effects of Neem have been reported against *S. mutans*, *E. faecalis* and *C. albicans* [14]. The Minimum Inhibitory Concentration (MIC) of the aqueous neem extract were 1.88%, 7.5% and 3.75 % for *E. Faecalis*, *S. Mutans*, *C. albicans* respectively [14]. Leaf extract has significant antimicrobial effect against *E. faecalis* derived from infected root canal samples thus can be used as an alternative to sodium hypochlorite [15].

Acacia nilotica (Babool)

Acacia nilotica also known as the gum Arabic tree, possesses good anti microbial, anti oxidant, anti fungal, anti viral and antibiotic activity [16,17]. It contains tannins, phenolic compounds, essential oil, and flavonoids which are responsible for antimicrobial activity

[18]. Babul plant has medicinal used as anticancer, anti tumours, antiscorbutic, astringent, anti-oxidant, natriuretic, antispasmodial, diuretic, diarrhea, malaria, sore throat and toothache [18]. Babool has antibacterial activity against *S. mutans* and *E. faecalis* [19]. It was found that babool at a concentration of 50% had the highest activity against *E. faecalis* [19].

Arctium lappa

Arctium lappa is widely used in popular medicine all over the world for its well-known therapeutic applications. *A. lappa* showed the significant antimicrobial activity against microorganisms specifically found in endodontic infections [20]. It was used as intra-canal medicament in teeth infected with *C. albicans*, *S. mutans*, *E. coli*, *P. aeruginosa* and *L. acidophilus*, was showed inhibition of microbial growth after 14 days [20]. Similarly the phytotherapeutic agent extracted from *A. lappa* inhibited the growth of *S. mutans*, *C. albicans*, *E. coli*, *P. aeruginosa* and *L. acidophilus*, [21].

Aroeira-da-praia

In an *in vitro* study conducted to evaluate the anti microbial activity and root canal cleaning potential of *Aroeira-da-praia* against *E. faecalis*. It was found that *Aroeira-da-praia* showed anti microbial activity at all concentrations [22]. Martinez Guerra et al. evaluated the activity of *aroeira-da-praia* extract at 100% and 50% concentrations and it is effective against Gram+ , Gram- bacteria, as well as against *Candida albicans*, at all concentrations [23].

Carvacrol

Carvacrol (Thymol isomer) is present in the essential oil of *Origanum vulgare*. It has a broad spectrum of antibacterial activity; it works by inhibiting ATPase activity and increasing the nonselective permeability of bacterial cell membranes [24]. Therefore, it not only inhibits microbial colonization, but also makes microbes more sensitive to antibacterial agents [24]. Carvacrol also has the anti-inflammatory effect. It can restrain neutrophilic elastase enzyme and suppresses prostaglandin production [25]. Carvacrol has antibacterial action on *E. coli*, *Salmonella enteritidis* and *Salmonella Essen*, *P. aeruginosa* and *E. faecalis* [26]. The 0.6% of Carvacrol was used effectively for disinfection of root canals [27]. It stimulates the pulpal fibres and helps in repair of periapical tissues due to the presence of phenolic component [27,28].

Casearia sylvestris (Gulkhair-wild coffee)

This plant species has been widely used in popular medicine as an antiseptic, topical anaesthetic, anti-tumor, anti-ulcer and anti-ophidian agent [29]. Alcoholic extract of *C. sylvestris* is a rich source of phospholipase A2 inhibitors, which reduce the acute phase of the inflammatory process and prolongs the regenerative phase [29]. Stamatis et al. in their study showed the antimicrobial efficacy of *C. sylvestris* extract against bacteria and fungi associated with oral diseases, such as dental caries, periodontitis and candidosis [30]. It can be used as an alternative short term intracanal medicament [31].

Curcuma longa (Turmeric)

The active constituents of turmeric are the flavonoid curcumin (diferuloylmethane) and various volatile oils, including tumerone, atlantone, and zingiberone. It possess good antioxidant, hepatoprotective, antimicrobial, anti-inflammatory and anticancer

activity [32,33]. It has been hypothesized that curcumin inhibits the assembly of a Protein - Filamenting Temperature Sensitive Mutant Z [FtsZ] protofilaments and also increases the GTPase activity of FtsZ. The perturbation of the GTPase activity of FtsZ assembly is lethal to bacteria [34]. For an irrigant to be effective against biofilms, the action on biofilms should involve the elimination of the extracellular polysaccharide matrix as well as the bacteria [35]. Curcumin in surfactant preparations showed its potential as a photosensitizer in antibacterial photodynamic therapy [36]. The exact mechanism by which curcumin causes light induced cell death has not yet been established, but it is generally accepted that a prerequisite for photosensitization of a microbial cell is the binding of the photosensitizer to the outer membrane [36]. Curcumin in aqueous preparations exhibits phototoxic effect against gram positive and gram negative bacteria [37]. It had significant antibacterial activity against *E. faecalis* [32,33]. It was effective against 2 day and 2 week biofilms of *E. faecalis* similar to that of 3% NaOCl and thus can be used in endodontics for root canal failure cases [38].

Cranberry

Cranberries contain numerous biologically active compounds including phenolic acids, anthocyanins, condensed tannins, and flavonoids which have antimicrobial activity [39]. It prevents the formation of dental plaque by inhibiting the enzymes responsible for the formation of the dental plaque polysaccharide matrix film, and also stops the bacteria sticking to the tooth surfaces [40]. The compounds prevent acid formation and reduce the acid tolerance of the bacteria that cause decay hence prevent tooth decay and gum disease [41]. Yamanaka et al. assessed the effect of cranberry juice on the ability of several oral species of *Streptococcus* to adhere to hydroxyapatite pellets. When the bacteria were exposed to cranberry juice, their adhesion to the pellets decreased significantly [42].

Marticaria recutitia (German chamomile)

It is used as table tea. Flower of chamomile plant contains a wide variety of active chemical components like chamazulene, capric acid, caprylic and chlorgenic acid. It is effectively used for removal of smear layer [43]. Chamomile was found to be effective when used as a mouthwash to treat irritations and minor infections of the mouth and gingiva [44].

Allium sativum (Garlic)

The main active component of garlic is allicin which is equivalent to that of penicillin (1mg of allicin is equated to that of 15 IU of penicillin) [45]. It has been shown to have wide range of antibacterial activity and more specific against the Gram-negative oral pathogens [46]. Extracts of garlic are bactericidal and are effective against *E. coli*, *S. aureus*, *B. cereus*, *Salmonella*, *listeria*, *Proteus* and *Streptococcal species* [47]. This compound has an inhibitory effect upon the key enzymes involved in cholesterol biosynthesis, such as 3-hydroxy-3-methyl-glutaryl-CoA reductase [48]. Allicin destroys the cell wall and cell membrane of root canal bacteria [49]. Fanni et al. revealed that garlic extract had significantly inhibited the growth of MDR *S. mutans* at MIC range of 4-32 mg/ml [50]. Houshmand et al. found that the 5%, 10%, 20%, and 100% concentrations of garlic extracts had similar antibacterial effects on dental plaque bacteria [51]. Thus the tooth paste or the mouth wash containing optimum concentration of garlic extract might be useful for prevention of dental caries.

Green Tea

It is a tea solely from the leaves of *Camellia sinensis*. The main flavonoids in tea are the catechins, making up 30–40% of the water-soluble solids in green tea [52]. Catechins bind to the bacterial lipid bilayer cell membrane and cause the membrane destruction [53]. It exhibits antibacterial activity against *E. Faecalis* as well as act as a good chelating agent [54]. Green and black teas both contain flavonoids that inhibit the growth and activity of the bacteria associated with tooth decay [55]. Tea also contains natural fluoride, which may be helpful in preventing dental caries [56]. Studies of Green tea polyphenols has significant anti microbial activity on *E.faecalis* biofilm formed in tooth substrate [54,57].

Glycyrrhiza glabra (Yashtimadhu -liquorice)

A number of pharmaceutical effects of liquorice are known anti-inflammatory, antiviral and anticarcinogenic [58]. The study reported that liquorice extract was as effective as triamcinolone acetonide, but safer and may be used as an alternative treatment for lichen planus [59]. Liquorice extract prevent the plaque formation by inhibiting the growth and adherence of *S. Mutans* [60]. The flavonoid content of liquorice extract is also a strong inhibitor of oxygen consumption in bacterial cells; the site of inhibition is thought to be between CoQ and cytochrome C in the bacterial respiratory electron transport chain [61]. Glycyrrhizin, a triterpenoid compound, accounts for the sweet taste of liquorice root. This compound represents a mixture of potassium-calcium-magnesium salts of glycyrrhizic acid that varies within a 2–25% range [62]. Glycyrrhizin act by altering the surface tension of the extracellular medium and has membranolytic properties [63].

Morinda citrifolia (Indian Mulberry- Noni)

M. Citrifolia has been reported to have a broad range of health benefits for cancer, infection, arthritis, diabetes, asthma, hypertension and pain [64]. Antibacterial action of *Morinda Citrifolia* Juice (MCJ) is mainly due to the presence of L-asperuloside and alizarin [65]. It has antimicrobial action against *P. aeruginosa*, *Proteus morgaii*, *S. aureus*, *Bacillus subtilis*, *E. coli*, *Salmonella*, *Shigella*, *E. Faecalis* and *C. Albicans* [66]. In the studies conducted to evaluate *M. Citrifolia* as an endodontic irrigant, it was concluded that MCJ was more effective than CHX and was similar in efficacy to NaOCl [67,68]. MCJ was more effective than calcium hydroxide against *E. faecalis* at different depth in dentin [67]. It has an inhibitory effect on caries causing oral streptococci [69]. MCJ is a biocompatible irrigant that promotes dental pulp stem cell attachment to root canal dentin, which is essential to accomplish regenerative endodontic treatment [70].

Mimusops Elengi (Bakul)

Bakul is a small to large tree found all over India. It has shown significant anti-inflammatory, analgesic and antipyretic activity [71]. The bark of *M. elengi* is used as a gargle for inflammatory and bleeding gums [72]. The tender stems are used as tooth brushes [73]. Different types of glycosides, alkaloids, phenols, tannins and saponins have been screened in the methanolic extract of this plant [74]. *M. elengi* was most effective agent against *E. faecalis* at 3 mg concentration [75]. The extract of *M. elengi* was found to be effective against Streptococci isolated from tooth tartar [76].

Melaleuca Alternifolia (Tea Tree Oil)

It contains terpinen-4-ol [typically 30- 40%] as a major component responsible for antibacterial and antifungal activity [56]. Tea tree oil causes lysis and the loss of membrane integrity of bacteria by the leakage of ions and the inhibition of respiration [77]. In dentistry, tea tree oil has been used to destroy microorganisms in the mouth before dental surgery, removal of smear layer and to relieve mouth soreness [78]. Tea tree oil removed the smear layer and showed comparable inhibition of bacterial growth with sodium hypochlorite when used as root canal irrigant [43,79]. An *in vitro* study, antimicrobial effect of tea tree oil for *C. albicans* (MIC: 0.5 µl/ml) was found at the lowest concentration followed by *S. aureus* (MIC: 1 µl/ml) and *E. coli* (MIC: 2 µl/ml), lastly *E. faecalis* (MIC: 64 µl/ml) [80]. The recommended therapeutic concentration for tea tree oil is 2.5 to 5 %, in which it can retain its antimicrobial property without any toxic effects [81].

Myristica fragrans (Nutmeg) and Terminalia chebula

Myristica fragrans contains myristic acid which is responsible for its antibacterial activity [82]. Yanti et al. reported anti-biofilm activity of macelignan, isolated from nutmeg against oral bacteria. Macelignan activity at 10 µg/mL for 30 minutes exposure could remove more than half of each single oral biofilm formed by *S. mutans*, *S. sanguinis* and *A. viscosus* at 24 hrs [82]. *Terminalia* species are a rich source of flavonoids, tannins, and many phenolic derivatives, it also has antioxidant capabilities [83]. Chebulinic acid, tannic acid and ellagic acid are responsible for the anti bacterial action of *terminalia* *Chebula* [84]. The antioxidant property of phenolic compounds is attributed to their ability to absorb and neutralize free radicals [83]. It is evident *in vitro* study that *T.Chebula* showed a definite reduction in the microbial activity and an increase in the pH resulting in marked anticariogenic effect [85].

Myrtus communis

The main constituents of the essential oil are 1, 8-cineole (28.62%), α-pinene (17/8%), and linalool (17.53%) [86]. Essential oil from *M. Communis* leaves has exhibited satisfactory antifungal, antibacterial, and antioxidant activities [87]. This plant has anti bacterial activity against both gram positive and gram negative organisms. *M. communis* essential oil was an effective antimicrobial agent against persistent endodontic microorganisms with the minimum inhibitory concentration in the range of 0.032-32 µg/mL [86,87]. Suliman et al. showed that *M. communis* has the antimicrobial effect at different concentration and the best being at 35% concentration which is nearly similar to 5.25% sodium hypochlorite and 0.2% Chlorhexidine [88].

Ocimum sanctum (Tulsi)

Tulsi is a time-tested premier medicinal herb that is used in ayurvedic medicine since ancient times. Different parts of the plant have shown antimicrobial, anti-inflammatory, analgesic, antipyretic, antiulcer, antidiabetic, antioxidant and anticancer activity [89]. The leaves of Tulsi contain 0.7% volatile oil comprising about 71% eugenol and 20% methyl eugenol [89]. Eugenol is the most prominent phytoconstituents present in this plant which may be responsible for antimicrobial activity [90]. *O. Sanctum* was the most effective against *S. Mutans* at 3mg concentration [75]. The essential oil extract of *O. Sanctum* showed antibacterial efficacy against *E. Faecalis*, which improved with an increase in concentration and contact period [91]. It exhibited minimum bactericidal concentration at 40% [92].

Orange oil

Orange essence oil was composed 94% of d-limonene and 3% of myrcene [93]. It is suggested as an alternative to chloroform or xylene for gutta-percha softening and also in dissolving the endodontic sealers [94]. Rehman et al. in a *in vitro* study found that there was 5.19 mm of remaining gutta-percha in the orange oil group and 5.37 mm in the chloroform group [95]. Similar results were found with other investigators suggesting orange oil equally efficient in dissolving gutta-percha and biocompatible than chloroform and xylene [96,97]. Chloroform as gutta-percha solvents has an effect on the mineral contents of root dentin leading to transportation of root dentin. Orange oil showed less dentin transportation than chloroform [98].

Propolis (Propolis resin)

It is prepared from resin collected by bees from the trees of poplars and conifers or from flowers of genera *clusia*. Pharmacologically active constituents in propolis are Flavonoids and cinnamic acid [99]. It exhibits various biologic activities, including antimicrobial, anti-inflammatory, antioxidant, anaesthetic and cytotoxic properties [100]. The anti-inflammatory property of propolis is due to the presence of caffeic acid and phenethyl ester in propolis [31]. In dental practice it is used as a pulp capping agent, intracanal medicament, intracanal irrigant, mouth rinse, cariostatic agent, storage media for avulsed tooth to maintain viability of periodontal ligaments, treatment of periodontitis and denture stomatitis [31,101-107]. Propolis was effective against the *E. faecalis* [101]. Ehsani M et al. suggested that the hydroalcoholic extract of propolis could be a good anti-microbial agent against *E. faecalis* especially following direct contact to this microorganism [108]. Propolis showed antimicrobial activity equal to that of sodium hypochlorite [109]. Awawdeh et al. also evaluated the effectiveness of propolis and calcium hydroxide in *Ex-vivo* as a short-term intracanal medicament against *E. faecalis* and found that the propolis is very effective in rapidly eliminating *E. faecalis* [110]. Natural honey showed antibacterial action against anaerobic bacteroides present in dental abscess and osteomyelitis [111]. Studies suggested that chewing "honey leather" can reduce gingival inflammation [112,106]. Direct pulp capping with propolis in rats may delay dental pulp inflammation and stimulate reparative dentin [104]. Another study conducted to evaluate the antimicrobial activity of two experimental pastes containing propolis extract associated with calcium hydroxide against polymicrobial cultures collected from 16 necrotic and fistulae root canals in primary molars. The association between propolis and calcium hydroxide was effective in controlling dental infections *in vitro* [113].

Psidium guajava (Guava)

The fruits and leaves of *P. Guajava* contain essential oil rich in cineol, tannins, triptenes and flavonoids. Ethanol extracts of it has higher antimicrobial activity, especially against *E. faecalis* [114]. The active flavonoid compound gujaverin isolated from the methanol leaf extract of *P. guajava* act as a potential antiplaque agent by inhibiting the growth, adherence and co-aggregation of dental plaque bacteria. Guava extracts may inhibit plaque development without disrupting homeostasis of the oral cavity [115].

Salvadora persica (Miswak)

Miswak is chewing stick commonly used as a brush to clean the teeth. Its chewing stick contains trimethyl amine, salvadorime

chloride, and fluoride in large amounts [116]. 10% water extraction of Miswak is an effective antimicrobial agent when utilized as root canal irrigant with necrotic pulps [117]. *S. Persica* extract stimulates parotid gland secretion and raise the plaque pH, suggesting a potential role in caries prevention [118]. *S. Persica* has good antimicrobial activity with a low level of cytotoxicity to the host cells at an optimal therapeutic concentration [119]. 20% *S. Persica* extract was completely effective in inhibiting the growth of *E. Faecalis* and *C. Albicans* after 6 and 24 hrs of exposure [120]. Almas et al. showed that *E. faecalis* is the most sensitive microorganism affected by the use of *S. Persica*, and noted no significant difference in the antimicrobial effects of freshly cut and 1-month-old *S. Persica* [121]. It can be used as substitute for sodium hypochlorite and chlorhexidine as root canal irrigant [122]. Baeshen et al. recommended the use of fresh miswak impregnated in 0.1% sodium fluoride (NaF) or a maximum of 0.5% NaF for a day for the prevention of dental caries [123].

Triphala

It is a mixer of Amulaki (*Emblica Officinalis*), Bibhitaki (*Terminalia bellirica*) and Halituki (*Terminalia chebula*). It can be used as an effective antiplaque agent as it inhibited the sucrose induced adherence and the glucan induced aggregation, the two processes which foster the colonization of the organism on the tooth surface [124]. It also showed complete eradication of 3-week *E. faecalis* biofilm [54,57]. Shakouie et al. compare the antimicrobial activity of Triphala with different concentrations of sodium hypochlorite and found that the Triphala exhibited better antimicrobial activity against *E. faecalis* compared to 0.5 and 1% NaOCl [125]. In another *in vitro* study Triphala was found to be as efficacious as sodium hypochlorite [126]. Its fruit is rich in citric acid thereby act as chelating agent [68].

Conclusion

Herbal medicines are the emerging trend in dental treatment. The major advantages of using herbal alternatives are easy availability, cost effectiveness, increased shelf life, low toxicity and lack of microbial resistance. Herbal extracts have been used in dentistry for reducing inflammation, as antimicrobial plaque agents, as antiseptics, antioxidants, antimicrobials, antifungals, antibacterial, antivirals and analgesics. The knowledge and understanding of natural approach of treatments is still the area of interest of researchers.

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