

Phytosolutions for *Enterococcus faecalis* in Endodontics: An Update

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Abstract

Background: The key reason for failure of an endodontic treatment is incomplete debridement and sterilization because of complex root canal system anatomy which makes elimination of micro-organisms difficult. In spite of the chemical and mechanical debridement of root canals, studies have reported that some microbes like *Enterococcus faecalis* thrive in periapical lesions, triggering a failure of an endodontic treatment. Considering the vanity, adverse effects and toxicity issues of synthetic medications, the herbal alternatives have been sought for endodontic irrigation. **Objectives:** To review the current evidence on the efficacy of different plant derivatives against *Enterococcus faecalis*. **Materials and methods:** Studies were identified through systematic search of the following electronic databases: PubMed, Web of Science, Scopus, Google Scholar and Cochrane database of systematic reviews. The results from the relevant published literatures are discussed. **Summary and Conclusion:** The conclusion drawn from *in vitro* and *in vivo* studies seems encouraging and as proven in clinical studies, *Propolis* and *Salvadora persica* have been proven to be efficacious against *Enterococcus faecalis*. More laboratory and clinical research is required to assess the safety, efficacy and biocompatibility of other plant extracts, before finally recommending them as alternative endodontic irrigants.

Key Words: Endodontic pathogens, *Enterococcus faecalis*, Root canal irrigants, Endodontic failure, Plant extracts

Introduction

One of the key reasons behind the success of root canal treatment is the chemo-mechanical preparation which aids in removal of remaining tissue, various microbes and debris from the complex root canal areas and allow the canals to be obturated to achieve a hermetic seal which will prevent future ingress of microbes into the canals [1]. Although a plethora of microbes have been found to reside in oral cavity, the lower oxygen (O_2) potential inside root canals and nutrient availability leads to colony formation of facultative anaerobes predominantly. *Enterococcus faecalis*, a facultative anaerobe found in 4 to 40% of primary endodontic infections, survives unaided inside canals and periapical area and multiply by genetic polymorphism, hence triggering infection and local bone resorption [2]. *E. faecalis* due to its virulence factors like aggregation substance, cytolsin, lytic enzymes, can alter host responses and hence it is able to thrive better than other microbes and is the only strain isolated after unsuccessful endodontic treatment [2-9]. Moreover, they invade dentinal tubules and adhere to collagen due to their ability to form biofilm and therefore it may act as a nidus for recurrence of infection in failed root canal treated teeth [3,10]. Hence, to attain lasting successful root canal treatment, it necessitates a complete sterilization of root canal and limiting the recurrence of infection.

In chemo-mechanical preparation, chemicals are used along with mechanical instrumentation to decrease the bacterial load. Numerous chemical solutions are being used to sterilize the root canals and the most effective and commonly used is sodium hypochlorite (NaOCl) in concentrations varying from 1-6% [11]. Its unique ability to dissolve pulp tissue, and outstanding antimicrobial potency makes it the irrigant of choice over other irrigants like 2% solution of chlorhexidine (CHX) and calcium hydroxide $[Ca(OH)_2]$, which have a varying grade of antimicrobial action. The disadvantages with NaOCl include limited penetrability in complex canal system, toxicity, risk of emphysema, allergy, offensive smell and taste [1,11]; and also it fails in removing the smear layer which has

been suggested as a doorway for bacterial ingress and multiplication [11-13]. Recent studies show high concentrations of NaOCl can probably cause weakening of dentin by decreasing its hardness and structural reliability, thus making the tooth susceptible to a vertical fracture [12-14]. Although its efficacy is less than NaOCl, CHX has been used effectively as a possible alternative to NaOCl for irrigation of canals due to its broad spectrum antimicrobial action, biocompatibility but its disadvantage is that it can discolor the tooth and other reported concerns like it can cause dryness and burning sensation in oral mucosa [15]. In a recent Cochrane review, the authors also concluded that currently there is inadequate dependable evidence showing the efficacy of a particular irrigant over the other [16].

The safety concerns, side effects, constant increase in antibiotic resistance and ineffectiveness of conventional drug formulations has prompted investigators to shift to herbal alternatives recently [17-20]. The purpose of this review is to provide an update on the various plant extracts that are currently being researched as a possible alternative to conventional irrigants for more efficacious potential endodontic usage.

Methods

Search strategy

Studies were identified through systematic search of the following electronic databases: PubMed, Web of Science, Scopus and Google Scholar, Cochrane database of systematic reviews. The following terms were used: *Enterococcus faecalis*, root canal failure, endodontics, smear layer, biofilm, and antimicrobial activity. The literature was reviewed for past 25 years (1990-2015). Additional studies were recognized and included from reference lists of original research and review articles.

Study selection

According to selection criteria, studies were required to: (a) be published in peer reviewed journals in the English

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language (b) provide original data and (c) explicitly report on antimicrobial efficacy of phytochemicals on *Enterococcus faecalis* from root canals. Articles published as abstracts only, were excluded.

Plant extract as endodontic irrigants

A herbal medicine is defined as a plant extract or a preparation which contains raw or processed ingredients from one or more plants with therapeutic values [17]. Owing to the safety concerns, side effects, constant increase in antibiotic resistance and ineffectiveness of conventional drug formulations, investigators are interested in herbal alternatives

which have been extensively used in medical practice since many centuries and have become even more popular today due to their biocompatibility, high , anti-inflammatory, antimicrobial properties, anti-oxidant properties and least toxicity and antimicrobial resistance issues [17-20]. With this recent paradigm shift from allopathic conventional drugs to plant extracts gaining more acceptance nowadays, current research is focused on to explore these herbal products and their implications on various clinical conditions. The most commonly tested plant extracts for endodontic irrigation have been summarized in Table 1.

Table 1. Plant extracts efficacious against *Enterococcus faecalis*.

Sl. No.	Scientific name	Common name	Pharmacological active components	Type of extract	References
1	<i>Curcuma longa</i>	Turmeric, Indian saffron, Yellow ginger	Zingiberene, curcumin, α and β turmerone	Ethyl acetate, methanol and water extracts	Marickar et al., Neelakantan et al.
2	Propolis	Beeswax	Flavonoids, Aromatic acids, Esters present in Resins, Galangin, Pinocembrin	Ethanol, chloroform, methanol, propylene glycol	Oncag O et al., Al-Qathami H et al., Kandaswamy et al.
3	<i>Aloe vera</i>	Star cactus, Barbados	Latex, Glucomannan, mannose derivatives, hemicellulose, calcium oxalate	Aqueous, Ethanol and methanolic extracts	George et al., Karkare et al., Sureshchandra et al.
4	<i>Azadirachta indica</i>	Neem, Holy tree	Azadirachtin, nimbin, gallic acid, catechin	Aqueous, Ethanol and methanolic extracts from seeds, leaves and roots	Nayak et al.
5	<i>Morinda citrifolia</i>	Indian mulberry, Painkiller bush, Cheese fruit, Beach mulberry	L-asperuloside, Acubin, Alizarin kaempferol, Octanoic acid, Ascorbic acid, Ricinoleic acid	Aqueous, Ethanol, chloroform and methanolic extracts from seeds, leaves, fruits and roots	Murray et al., Prabhakar et al.
6	<i>Salvadora persica</i>	Miswak, Arak tree, Toothbrush tree	Trimethylamine, Salvadorine, Resins, Flavodine, Saponins, Sterol, And Fluoride	Aqueous, Ethanol and methanolic extracts	Balto et al., Shingare et al.

Curcuma longa (Turmeric)

Curcumin, a member of a ginger family has been widely reported to possess anti-inflammatory, antioxidant, antimicrobial and anti-cancer activity [21-23,25]. *In vitro* studies have revealed that curcumin has noteworthy antibacterial action against *E. faecalis* and can be used as a substitute to NaOCl for endodontic irrigation [23,24].

Propolis

Propolis possesses antibacterial activities against *S. sobrinus* and *S. mutans*. It also possesses good antioxidant and anti-inflammatory actions [26-28]. It has been used as a, cariostatic agent [27] and in the treatment of periodontitis [29]. Ethanolic extract of propolis can promote bone regeneration and induce formation of hard tissue bridge in pulpotomies or pulp capping [30]. Recent studies have concluded that antimicrobial activity of propolis is equivalent to that of sodium hypochlorite [26,29,31,32]. In a clinical study comparing the antimicrobial activity of 25% propolis extract with 0.9% isotonic saline, it was found that there was significant difference in reduction of bacterial colony counts and the authors concluded that due to low toxicity concerns and antibacterial effectiveness, water-soluble extract of 25% propolis can be promoted as a endodontic irrigant in primary teeth [33].

Acacia nilotica (Babool)

A. nilotica as reported in literature possesses good antimicrobial, antioxidant, antifungal, antiviral and antibiotic activity. Khan et al. [34] in their study have proved the antibacterial action of extract of babool against *S. mutans* and *E. faecalis*. In another study, the authors reported that *A. nilotica* at a 50% concentration, had the highest activity against *E. faecalis* [35].

Azadirachta indica (Neem)

Antimicrobial effects of neem extract against various microbes have been widely reviewed in literature [36,37]. In previous studies, aqueous and alcoholic extract of Neem leaf have been proved to inhibit *S. mutans* and also *E. faecalis* [37-40]. The minimum inhibitory concentration (MIC) of aqueous neem extract for *E. faecalis* was found to be 7.5% as against 1.88% for alcoholic neem extract [41]. In another study, the effects of herbal extracts such as *Morinda Citrifolia*, *Azadirachta indica* and green tea were studied and *Azadirachta indica* was found to be most effective irrigant [22]. The antioxidant and antimicrobial properties of neem extract makes it a potent irrigant for endodontics as a substitute to sodium hypochlorite.

Aloe barbadensis miller (Aloe vera)

Aloe vera is known to possess good antibacterial and antifungal activity [42]. Karkare et al. [43] found that chloroform extract of aloe vera had substantial antimicrobial effect against *E.faecalis*. In another study, *Aloe vera* tooth gel was found to inhibit the growth of *S. mutans*, *L. acidophilus*, *P. intermedia*, *C. albicans*, *E. faecalis*, and *P. anaerobius* [43].

***Morinda citrifolia* (Indian mulberry)**

Morinda Citrifolia is one of the first plant extracts to be tested as alternatives for an intra-canal irrigant [45]. *Morinda Citrifolia* has been found to have a significant antibacterial activity [32] which is attributed due to its contents alizarin, scopoletin, aucubin and asperuloside. However its antibacterial action is lower than 0.2% Chlorhexidine [32, 46].

Triphala and green tea polyphenols

Triphala and Green tea polyphenols can act as substitute for conventional endodontic irrigants due to their antimicrobial, anti-inflammatory and scavenging properties [47-49]. Various studies have found Triphala and Green tea polyphenols to have significant antimicrobial activity against *E. faecalis* [50,51].

Citric acid in Triphala has been reported to help in removing the smear layer and hence enhanced sterilization of canal system. Its chelating property makes it an effective substitute to NaOCl for endodontic irrigation [51].

German chamomile and tea tree oil (*Melaleuca alternifolia*)

Terpinen-4-ol, an active component in tea tree oil is responsible for its antiseptic, antifungal and antibacterial properties [18]. In a recent study comparing the antibacterial efficacy of tea tree oil, it was concluded that maximum antimicrobial activity was shown by 2% Chlorhexidine followed by tea tree oil and then 3% sodium hypochlorite [52]. German chamomile also has been reported to possess anti-inflammatory, analgesic and antimicrobial properties. Sadr et al. [53] in their SEM study, observed that chamomile when used as an irrigant was more effective in removing smear layer when compared to NaOCl used alone but less effective when NaOCl is used in combination with 17% Ethylenediaminetetraacetic acid (EDTA).

***Salvadora persica* solution (Miswak)**

Previous studies have proved the antimicrobial action of *S. Persica* [32,54,55] and have also found that 5 mg/ml solution of *S. persica* was as effective as 17% EDTA in eliminating the smear layer from the canal wall [54]. In a clinical study comparing the antimicrobial activity of *S. persica*, propolis, NaOCl and saline as root canal irrigants in primary teeth, it was concluded that 12.5% alcoholic extract of *S. persica* could be a good natural substitute to 3% sodium hypochlorite [56].

What this Review Contributes and Why This Paper is Important to Field of Phytomedicine and Phytotherapy

- This review provides the clinical update about the selective plant extracts.

- This update opens the avenues in the field of phytomedicine to investigate further for more alternative natural endodontic irrigants
- The importance of multidisciplinary treatment is highlighted taking into consideration the safety, cost effectiveness, accessibility and efficacy of plant extracts.

Conclusion

Plant extracts are safe when used with credible evidence and clinical judgement. The benefits like easy accessibility, cost-effective, minimal toxicity, improved shelf life and lack of microbial resistance, have made plant extracts a potential alternative to conventional endodontic irrigants.

The conclusion drawn from *in vitro* and *in vivo* studies seems encouraging and as proven in clinical studies, Propolis and *S. persica* have been proven to be efficacious against *E. faecalis*. More laboratory and clinical research is required to assess the safety, efficacy and biocompatibility of other plant extracts, before finally recommending them as alternative endodontic irrigants. Finally, clinically tested plant extracts should only be used for treatment procedures that have been established.

Declarations

List of abbreviations

CHX – Chlorhexidine; $[\text{Ca}(\text{OH})_2]$ – Calcium hydroxide; EDTA – Ethylene diamine tetra acetic acid; MIC – Minimum inhibitory concentration; NaOCl – Sodium hypochlorite

Conflict of interest

The authors declare that there are no known conflicts of interest associated with this publication and there has been no financial support for this work that could have influenced its outcome.

Author's Contributions

- ASA: contributed to the conception and design of the study, analysis and article writing
- SB: contributed to the design of the study, analysis of data for the work, drafting the article and submission
- KA: drafting and revising the article critically for important intellectual content

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