

The Effect of Using Herbal Extracts as Irrigant Solution in Disinfecting Root Canals of Endodontically Treated Teeth: A Narrative Review

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Abstract

Objectives: The use of herbal medicine continues to grow worldwide in all fields including dentistry. The constant use of chemical products in the root canal treatment process has prompted researchers to look for herbal alternatives due to the side effects and the relatively high resistant microbial strains available in the root canal that can contribute to the refractory infection. Therefore, the aim of this narrative review is to evaluate the effectiveness of using selected herbal extracts in disinfecting the root canals and removing the smear layer of the endodontically treated teeth.

Design: Systematic search from 1999-2019 was performed using four electronic databases. The level of evidence of eligible studies was assessed using Critical Appraisal Skills Programme and Cochrane risk of bias tools.

Results: A total of 44 eligible experimental studies that assessed aloe vera, turmeric, *Peganum harmala*, green tea, garlic and chamomile extracts were retrieved electronically. Potent disinfectant properties provided by the herbal extract of the six selected plants were demonstrated. Among these herbal extracts, garlic and chamomile extracts were found to have better properties in removing the smear layer from the root canal compared to the other herbal extracts.

Conclusion: The results of the present review support the use of the examined herbal extracts in disinfecting the root canal; however, these findings need to be assessed clinically to determine the possibility of using herbal products as a successful alternative for chemical products within the process of root canal treatment.

Keywords: Irrigant solution; Herbal extract; Garlic; Chamomile; Green tea; *Peganum harmala*; Turmeric; Aloe vera

Introduction

Successful endodontic treatment can benefit from effective irrigation that can disinfect the root canal, help in removing of the smear layer and microbial biofilms, reduce the microbial counts and neutralise their by-products [1].

An irrigant solution is ideal when it is biocompatible, non-toxic active anti-microbial disinfectant that can prevent the formation of the smear layer and provide mechanical flushing properties [2,3]. Endodontic disinfectant solutions were categorised into chemical and herbal, where the latter has been widely used lately due to the effectiveness in disinfecting the root canal system with less side effects compared with the chemical solutions [4,5]. There are, however, microorganisms such as *E. faecalis* that associate with refractory endodontic infection due to the resistance to intracanal medicaments such as sodium hypochlorite (NaOCl) [6]. Hence, these microorganisms are susceptible to survive in a low nutrient environment [7,8].

Furthermore, *E. faecalis* and *C. albicans* were found prevalent in the root canal system and can participate in the periapical infections and using effective irrigant solutions against these microorganisms is important to prevent failure of the endodontic treatment [9].

The use of herbal products and supplements in medicine has been growing significantly over the past three decades. Consumers believe that herbal medicines are safer due to the natural components and therefore can possibly be used as alternatives to conventional chemical medicines [10].

Natural products contain essential oils, glycosides and alkaloids that can exhibit therapeutic properties such as antibacterial, anti-plaque, anti-fungal and anti-viral effect in addition to the wound healing properties [11,12]. The literature has shown that aloe vera, turmeric, *Peganum harmala*, green tea, garlic and chamomile have powerful antimicrobial activity that is comparable to NaOCl with a notable therapeutic characteristic that can activate the immune system

[13-18]. Therefore, using the extract of these herbs as irrigant solution during the root canal treatment can be beneficial to the disinfection and healing process.

The smear layer is a complex of organic and inorganic substances that can act as a potential leakage and passage for microorganisms between the dentinal canal walls and the root canal filling material, can also be a barrier that compromises the seal integrity in the root canal [19-21]. Therefore, the smear layer removal is important in achieving rigorous disinfection and satisfactory seal of the root canal filling. The aim of this narrative review was to summarise the literature of the antimicrobial efficacy and the smear layer removal properties of using herbal extracts of green tea, garlic, chamomile, aloe vera, turmeric or *Peganum harmala* as irrigant solution in the endodontically treated teeth.

Methodology

This is a narrative review to summarise the published articles that answered the following research question: Can herbal extracts be used as effective irrigant solution in disinfecting the root canals of endodontically treated teeth? An electronic systematic search of the database was used on PubMed, Google Scholar, Medline and Science Direct.

Objectives

1. To search the literature of the studies that assessed the antimicrobial properties of the selected herbal extracts as irrigant solution in disinfecting the root canals of endodontically treated teeth.
2. To search the literature of the studies that assessed the the smear layer removal properties of the above selected herbal extracts during intra canal irrigation.
3. To assess the relevant studies for eligibility and critically appraise the final selection of the studies to help draw a conclusion.

Search strategy

A systematic literature search was conducted on the aforementioned databases using the following key words: dental treatment, root canal, endodontic, lesion, pus, infection, pulp pathology, irreversible pulpitis, pulp abscess, periapical abscess, pulp disease, *Peganum harmala*, turmeric, harmala, aloe vera, curcuma longa, microbicidal, fungicidal, anti-bacterial effect, microbial survival rate, anti-microbial effect, irrigation, disinfection, green tea, extract, *Camellia sinensis*, garlic, *Allium sativum*, chamomile, matricariarecutita, antimicrobial, microbicidal, antibacterial, bactericidal, antifungal, fungicidal, disinfection, sterilization, smear layer. Manual search for the bibliography of eligible studies was conducted to ensure including all relevant articles that answer the research question. The search results were imported into "Endnote", a bibliographic management program, and duplicate items were removed.

Eligibility criteria

Inclusion criteria: 1. Studies published between 1999-2019. 2. Randomised clinical trials (human and animals) and experimental comparative studies. 3. Articles published in English.

Exclusion criteria: 1. Data from case reports, case series, literature reviews and unpublished studies.

Data extraction and quality assessment

All titles and abstracts for relevant studies were screened and full texts of eligible studies were independently read and data were extracted by two reviewers (NA) and (RH). The following data was

extracted: authors, year of publication, plant extract, study design, comparison substance, microorganisms, type of sample and the outcome. The level of evidence of eligible studies was graded using the Critical Appraisal Skills Programme (CASP) tools [14] and Cochrane risk of bias tool.

Results and Discussion

A total of 44 studies were eligible in this review including the following: Studies of the antimicrobial effect of aloe vera in 12 articles [5,22-31]. Studies that focused on the turmeric extract in 13 articles [11,17,32-37]. Studies that investigated *Peganum harmala* extract in three reports [18,38,39].

Likewise, the antimicrobial effect of green tea extract in disinfecting root canals was studied in nine articles [40-45]. Five studies had assessed garlic extract [29,46-49], and two studies investigated the chamomile extract [50,51] (Figure 1).

Aloe vera

This plant has a long history of a popular and traditional use in medicine. More than 75 active ingredients including vitamins, folic acid, minerals, enzymes, saponins, salicylic acid and amino acids that can help to enhance immunity, antiseptic and antimicrobial activity were found in the leaf pulp and exudate of this plant [52].

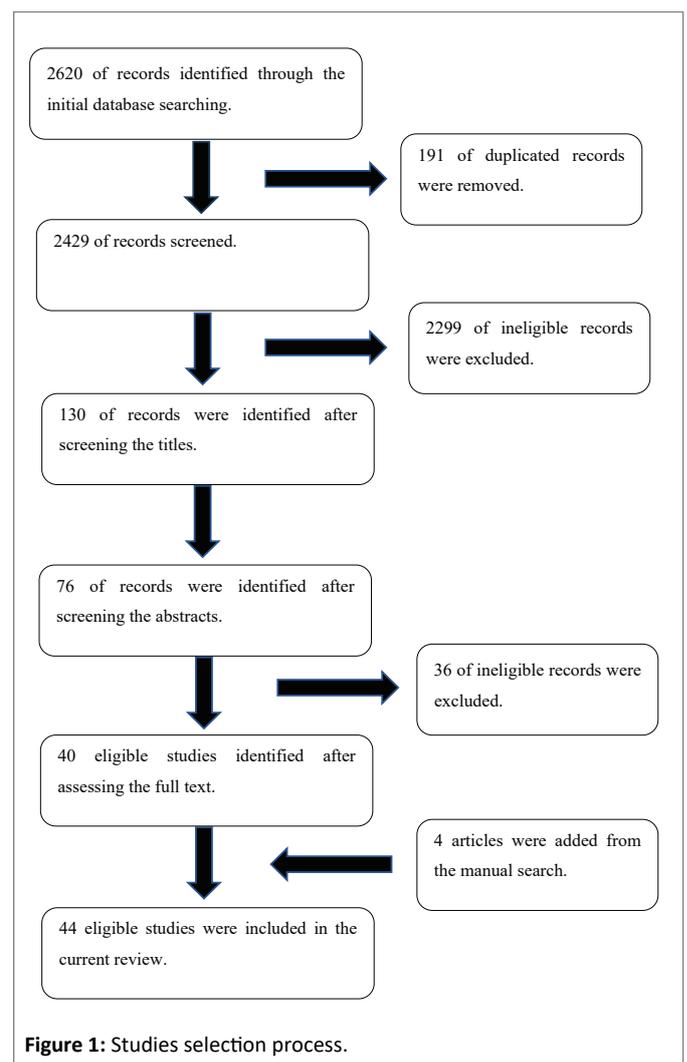


Figure 1: Studies selection process.

In dental uses, this plant is an effective antifungal that can also help treating conditions such as lichen planus, burning mouth syndrome, dry socket, oral sub mucous fibrosis and aphthous stomatitis. Sahebi S, et al. [5] conducted an experimental study on 60 extracted human teeth that were randomly subdivided into three groups, in which different disinfectant solutions of 2.5% NaOCl, normal saline and aloe vera extract were used. Aloe vera extract was not recommended as an endodontic disinfectant where the antimicrobial activity of NaOCl on *E. faecalis* bacteria was greater than both aloe vera and normal saline.

The results of this study could have been more reliable if the sample size was larger and tested against a wider range of microorganisms. These results were also supported by Babaji P, et al. [23], who concluded that the average inhibition zone formed around the methanolic aloe vera extract was 14.7mm against *E. faecalis* (ATCC 29212) compared with 28.6mm of the 3% NaOCl. The study reported that aloe vera extract can be used as endodontic disinfectants. However, these results need to be tested clinically to confirm the effectiveness of the extract.

In a study of 90 extracted single rooted teeth that was conducted to determine the antimicrobial activity of aloe vera compared to propolis and chlorhexidine gel, the aloe vera extract showed antimicrobial activity against *E. faecalis* but was less effective than the other two types of irrigants used [24]. This was supported by other studies that tested non-vital teeth using colony counter and turbid metric analysis, where aloe vera extract was proven to show anti-microbial activity against *E. faecalis* [27,30]. Therefore, this extract can be used as an antimicrobial solution for bacterial infections.

Bhardwaj A, et al. [25] conducted an experimental study to identify the antimicrobial effect of aloe vera extracts compared with morindacitrifolia juice (MCJ), propolis and NaOCl in removing the intraradicular biofilm of *E. faecalis* (ATCC 29212), that was found in extracted single rooted human teeth using a passive ultrasonic irrigation method. According to the study, aloe vera extract was not effective in the removal of the *E. faecalis* (ATCC 29212) biofilm. In the meantime, 1% of NaOCl with passive ultrasonic irrigation was the most effective substance in eliminating bacterial biofilm compared to the other three natural disinfectants ($P < 0.001$).

Valera MC, et al. [31] conducted an experimental study to assess the anti-microbial activity of aloe vera extract compared to castor oil, ginger extract, 2.5% NaOCl and 2% chlorhexidine. These agents were tested on human teeth ($n=72$) contaminated with *C. albicans* (ATCC 18804) and *E. faecalis* (ATCC 29212). The *E. faecalis* (ATCC 29212) was cultivated on Brain Heart Infusion agar while Sabouraud Dextrose Agar was used to cultivate *C. albicans* (ATCC 18804). According to the study, the authors reported that glycolic aloe vera extract had no antimicrobial activity against both microorganisms. Whilst the other two natural extracts (castor oil and glycolic ginger extract) showed slight reduction in the colony counts of the tested microorganisms compared to the significant antimicrobial activity of NaOCl and chlorhexidine. Therefore, the study concluded that aloe vera solution is not recommended as root canal disinfectant and future studies are required to investigate the effect of long duration use of aloe vera solution on bacteria. In agreement with Sahebi S, et al. [5].

The antibacterial effect of aloe vera gel compared with propolis extract and 2% chlorhexidine on *E. faecalis* bacteria (PTCC 1394), *S. aureus* (ATCC 25923) and *S. mutans* (ATCC 1601) was investigated. Distilled water and ethanol (15% and 40%) were used as negative controls and the standard strain samples of *E. faecalis* (PTCC 1394), *S. aureus* (ATCC 25923) and *S. mutans* (ATCC 1601) were incubated in Brain Heart Infusion culture. Aloe vera extract showed weak or no antimicrobial activity against the studied bacteria [26].

Karkare SR, et al. [29] conducted experimental study to compare the antimicrobial effect of saturated and diluted hydro-alcoholic extracts of aloe vera compared with 5% NaOCl, saturated and diluted hydro-alcoholic extract of garlic against *E. faecalis* bacteria (ATCC 11420). The study reported that the best antibacterial solution was 5% NaOCl followed by saturated hydro alcoholic aloe vera solution.

Jose J, et al. [28] compared the anti-microbial activity of the aqueous extract of aloe vera with guava leaf extract, 2.5% NaOCl, 2% chlorhexidine gluconate and QMiX against *C. albicans* (ATCC 10231) and *E. faecalis* (ATCC 29212) strains. The QMiX is a mixed solution containing 2% chlorhexidine, a surfactant and 17% EDTA. The authors of the study concluded that the aqueous extract of aloe vera had the weakest anti-microbial effect against *E. faecalis* (ATCC 29212) and *C. albicans* (ATCC 10231) compared with the other tested solutions while the QMiX showed the strongest anti-microbial activity. Marwah, et al. (2017) compared the 80% of A. vera with 2.5% NaOCl and saline against *E. faecalis*. The results showed that NaOCl is more suitable for root canal irrigation infected with *E. faecalis* compared with aloe vera extract solution. Table 1 summarises the studies' characteristics that examined aloe vera extract as an irrigant endodontic solution.

Turmeric

Turmeric, also known as curcuma longa, which is part of the ginger family, and is widely used in East Asia for food seasoning [53]. Turmeric consists of volatile oils such as zingiberen and turmerone, in addition to other components such as protein, sugar and resins which are known as anti-microbial and antioxidant substance [17]. A number of medical uses of turmeric extract has been reported. These were to protect the body from toxic reactions, platelets formation, joints stiffness, stone formation in the gallbladder [54]. While turmeric showed significant influence against prostatic cancer and other types of cancers, it can also help in slowing the progression of multiple sclerosis, prevent the spreading of breast cancer, help in weight control, food poisoning and poor circulation [54].

Neelakantan P, et al. [17] concurred Panpatil VV, et al. [55] in reporting that turmeric extract was comparable to NaOCl (3%) and achieved 100% microorganism clearance at different time intervals.

One study by Chaitanya BV, et al. [16] showed that turmeric extract (50%) was not as effective as 3% NaOCl against *E. faecalis* and *S. aureus*. The antimicrobial activity was measured by using agar diffusion method and the turmeric extract demonstrated weakness against the tested microorganisms. However, agar diffusion test does not reflect a true microbiostatic and microbicidal properties of dental materials and the use of herbal alternatives in endodontics might be proven to be of benefit in future. Similarly, Vinothkumar, et al. (2013) and Dedhia J, et al. [33] showed that turmeric extract has weak antimicrobial effect against *C. albicans* and *S. aureus*. The antimicrobial activity was assessed using agar diffusion method and the results were compared with methanol extracts of the andrographis paniculate, azadirachta indica and NaOCl.

Joy Sinha D, et al. [36] conducted an *in-vitro* experimental study to compare the antibacterial activity of ethanolic turmeric solution (*C. longa*) with three other tested solutions such as; neem extracts, 5% NaOCl and 2% chlorhexidine against *E. faecalis* (ATCC 29212) bacterial strain used as endodontic disinfectant. The method used to measure the effect was the agar disk diffusion test. The study reported that the ethanolic extract of turmeric in showed limited antibacterial activity against *E. faecalis* (ATCC 29212) which was less effective than the other three tested disinfectants.

Table 1: Summary of findings of experimental studies of the effect of aloe vera extracts.

Author/Year	Plant's extract	Comparison substance	Microorganism	Type of sample	Outcome
Bhardwaj A, et al. [25]	A. vera, Morindacitrifolia-papain	calcium hydroxide-2% CHX	<i>E. faecalis</i> (ATCC 29212)	180 freshly extracted single rooted teeth	CHX gel showed the maximum antimicrobial activity against <i>E. faecalis</i> , calcium hydroxide showed the least. <i>M. citrifolia</i> gel exhibited good inhibition up to the 5th day followed by aloe vera gel and papain gel.
Bhardwaj A, et al. [25]	A. vera extract, MCI, Propolis.	1% NaOCl, Normal saline	<i>E. faecalis</i> strain (ATCC 29212)	60 extracted single-rooted teeth	Not as effective in removing <i>E. faecalis</i> biofilm compared with 1% NaOCl+ passive ultrasonic irrigation.
Ehsani M, et al. [26]	A. vera in gel form, Propolis alcohol (15% & 40%), Propolis aqueous extract.	2% CHX, distilled water	<i>E. faecalis</i> (PTCC1349), <i>S aureus</i> (ATCC25923), <i>S. mutans</i> (ATCC160) strains	Bacterial culture medium	Mild anti-bacterial effect against three bacteria.
Valera MC, et al. [31]	Glycolic a. vera extracts, Glycolic ginger extract, Castor oil	2.5% NaOCl, 2% CHX, normal saline	<i>C. albicans</i> (ATCC 18804) and <i>E. faecalis</i> (ATCC29212) strains	Extracted single rooted teeth	No anti-microbial effect
Bazvand L. et al. [24]	A. vera	propolis - 0.2% CHX - triantibiotic paste -	<i>E. faecalis</i> (ATCC 29212)	90 single-root canal teeth	Aloe vera had antibacterial effects on <i>E. faecalis</i> , but in comparison with other medicaments, it was less effective ($P < 0.05$).
Sahebi S, et al. [5]	80% a. vera aqueous extract	2.5% NaOCl, normal saline	<i>E. faecalis</i> (ATCC11700) strain	Extracted single rooted teeth	Mild antibacterial effect
Karkare SR, et al. [29]	Saturated and diluted hydroalcoholic extracts of a. vera and garlic	5% NaOCl,	<i>E. faecalis</i> bacteria(ATCC 11420)	Bacterial culture medium	Good anti-bacterial effect of saturated hydro alcoholic A. vera (13mm inhibition zone) whiles the diluted A. vera extracts inhibition zone was (9.6667 mm).
Prasad S, et al. [30]	A. vera leaf extract alcoholic neem	3% Naocl-2% CHX	<i>E. faecalis</i> (ATCC29212) <i>C. albicans</i> (ATCC14053)	Bacterial culture medium	The antimicrobial activity of both neem and Aloe vera leaf extracts against <i>E. faecalis</i> and <i>C. albicans</i> is quite effective.
Babaji P, et al. [23]	Alcoholic extract (Methanol) of neem, morindacitrifolia and a. vera	3% NaOCl, distilled water	<i>E. faecalis</i> bacteria(ATCC 29212)	Bacterial culture medium	These irrigants showed antibacterial activity against <i>E. faecalis</i> .
Jose J, et al. [28]	A. vera aqueous extract, QMiX, guava leaf extract	2.5% NaOCl, 2% CHX	<i>E. faecalis</i> (ATCC 29212) , <i>C. albicans</i> (ATCC 10231)	Culture medium	Slight effect on both microorganisms
Marwah, et al. 2017	80% A. vera	2.5% Naocl -saline	<i>E. faecalis</i> (ATCC)	30 extracted single rooted teeth	2.5% naocl is best suited for irrigating root canal with <i>E. faecalis</i> infection in comparison to aloe vera solution.
Goud S, et al. [27]	A. vera	3% Naocl- 2% CHX -saline	<i>E. faecalis</i> ATCC 29212	80 freshly extracted, single-rooted	Three percent NaOCl and aloe vera showed a similar antimicrobial efficacy against <i>E. faecalis</i> . Two percent chlorhexidine exhibited good antimicrobial efficacy against <i>E. faecalis</i> .

(*M. citrifolia*) =*Morinda citrifolia*; (*A. indica*) =*Azadirachta indica*; (MCI)= *Morinda citrifolia* juice; (NaOCl)= sodium hypochlorite; (*E. faecalis*) =*Enterococcus faecalis*; (A. Vera) =Aloe Vera; (*S. aureus*) =*Staphylococcus aureus*; (*S. mutans*) = *Streptococcus mutans*; (CHX)=Chlorhexidine; (NR)=Not reported; (QMiX)= mixed of 2% CHX, a surfactant and 17% EDTA; (*C.albicans*=*Candida albicans*).

Furthermore, Puspita, et al. (2019) and Lokhande, et al. (2018) concluded that the microbial inhibition activity of turmeric extract that was observed in this study, has the potential to be used as a root canal irrigant solution in future.

However, further *in-vivo* experimental studies recommended investigating the long-term effect of the herbal irrigants. The study also concluded that the 2% chlorhexidine and neem extracts showed strong antibacterial before and after dilution while the 5% NaOCl showed good antibacterial effect on dilution.

Dhariwal NS, et al. [34] conducted an *in-vitro* experimental study to compare the antibacterial effect of 20% ethanol extract of turmeric and green tea compared with 3% NaOCl as endodontic irrigants against anaerobic bacteria in the root canals of primary teeth. The sample was infected root canals (n=30) selected according to the standard inclusion and exclusion criteria. The authors concluded that the 20% ethanolic turmeric solution and 3% NaOCl showed the same antibacterial sensitivity in 85% of the cases. The comparison between the three irrigants showed no significant difference between 3% NaOCl and turmeric extract and the isolated obligatory anaerobes showed higher sensitivity of the isolated bacteria (*P. intermedia*, *Porphyromonas gingivalis* and *Bacteroides fragilis*). Meanwhile, the *E. faecalis*, Streptococci and Peptostreptococci are the facultative anaerobes bacteria which showed anti-bacterial susceptibility against both ethanolic turmeric solution and 3%NaOCl. The ethanol extract of turmeric showed potent antibacterial activity against *E. faecalis*, *Porphyromonas species*, *P.intermedia* and Peptostreptococci which is promising for future clinical studies. However, if there is a difference in the response of microorganisms to the extract, it can be referred to the part of the plant, collection time or concentration of the extract.

Sinha DJ, et al. [37] conducted an *in-vitro* experimental study on 120 single rooted teeth to compare the antimicrobial activity of alcoholic turmeric solution with other irrigant solutions such as; tea tree oil (*M. alternifolia*), neem extracts (*A. india*), propolis and 5% NaOCl against *C. albicans* (MTCC 3017). The teeth were sectioned to standardise tooth length at 8 mm. Fractured and decayed teeth were excluded from the study. The study concluded that alcoholic solution of turmeric extract showed good antifungal activity against *C. albicans* (MTCC 3017) compared with the other tested solutions. The antifungal effect of the alcoholic extract opens new perspectives for its use as an endodontic disinfectant. Therefore, we suggest investigating the effectiveness of alcoholic extract of turmeric in a clinical trial to evaluate its biocompatibility and the antimicrobial effect in preventing dental caries.

Hedge, et al. (2013) examined the effect of the aqueous extract of turmeric against *C. albicans* and *E. faecalis* microorganisms. The results showed that the aqueous extract of turmeric has a powerful antifungal activity against *C. albicans* but not *E. faecalis*, in agreement with another previous study which concluded that the aqueous extract of turmeric has effective inhibitory activity against *C. albicans*.

Turmeric extract showed medicinal interactions with drugs such as non-steroidal anti-inflammatory drugs (NSAIDs) that can cause bleeding and clotting disorders [56]. Additionally, turmeric solution can stimulate releasing hydrocortisone, but can also inhibit the release of prostaglandin [57]. Little information is available to define the safety of turmeric extracts when applied in higher doses. Therefore, further research is required to identify the optimal dosage, bio-efficacy and bioavailability of turmeric extracts. Table 2 summarises the studies' characteristics that examined turmeric extract as an irrigant endodontic solution.

Peganum harmala

Peganum harmala is known as "Harmel" or "Syrian rue" and is considered as a member of zygothyllaceous family of plants. It is one of the most popular and traditional plants that is widely used for medical purposes. The plant is 0.3-0.8m height, and the roots can reach up to 6.1 meter length. The plant has three chambers which can incubate more than 50 seeds [58]. The southern states of America and central Asia were the first places that this plant was discovered due to the dry environment that *Peganum harmala* growth prefers.

Our previous findings of the antimicrobial effects of the aqueous and alcoholic extract of *Peganum harmala* seeds against Lactobacilli and Candida (n=10), suggested that all three tested concentrations (20%, 30% and 50%) of the seeds were more effective than 0.2% chlorhexidine against the examined microorganisms [38]. Darabpour E, et al. [39] had also investigated the potency of *Peganum harmala* that is extracted from different parts of the plant (stem, root, leaf, seeds and flower) against gram positive and negative bacteria (a total of 13 bacterial isolates) including *Listeria monocytogenes*, *S. aureus*, *S. pyogenes*, *Bacillus cereus*, *Bacillus anthracis*, *Bacillus pumilus* and *S. epidermidis* as gram positive bacteria. Whilst *Salmonella typhi*, *E.coli*, *Brucella melitensis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Proteus mirabilis* as gram negative bacteria. The disc diffusion method was used to assess the antibacterial activity of *Peganum harmala* methanolic solution. The authors concluded that among different parts of the plant, the roots and seeds showed stronger antibacterial activity against the examined bacterial pathogen while the leaf, flower and stem showed poor antibacterial activity.

Tabrizzadeh M, et al. [18] conducted a study to determine the anti-microbial activity of the *Peganum harmala* seeds (aqueous and alcoholic) compared with 5.25% NaOCl used as endodontic disinfectant solution against *E. faecalis* bacteria (ATCC 29212). The authors reported that the aqueous ethanolic extracts of *Peganum harmala* seeds showed antimicrobial activity against *E. faecalis* (ATCC 29212) and there was no significant difference between the antimicrobial activity of 5.25% NaOCl and the *Peganum harmala* extract (p > .05; MIC 4 mg/milliliter). Moreover, *peganum harmala* seeds extract showed lower cytotoxic effect in comparison to 5.25% NaOCl (p < .05). The lowest cytotoxicity belonged to *peganum harmala* seeds extract at 72 hours and the highest cytotoxicity belonged to 5.25% NaOCl at 24 hours. Table 3 summarises the studies' characteristics that examined *Peganum harmala* extract as an irrigant endodontic solution.

Green Tea

Tea leaves belong to a species of evergreen shrubs or small trees in the flowering plant family Theaceae whose leaves and leaf buds are used to produce tea. The plant is characterised with varied components of polyphenolic catechins, mainly Epigallocatechin-3-Gallate (EGCG), which is the most concentrated and powerful catechin (50%-80% of catechins) [59]. The catechins components are responsible for the anti-inflammatory, antioxidant as well as antibacterial activity, especially against *E. faecalis* [15,16,43,60,61]. The antibacterial mechanism of EGCG is observed by its direct binding to the layers of peptidoglycans that are found on the surface of Gram-positive bacteria, which in turn leads to cell death. However, it has been found that EGCG displays antibacterial activity by developing oxidative action through producing hydrogen peroxide radicals (H₂O₂) [40,61]. Lee and Tan, [15] found that EGCG is effective in eradicating *E. faecalis* biofilm that was found on the walls of root canals and weakening its major virulence genes expression. Green tea extract was exhibited significant antibacterial

Table 2: Summary of findings of the experimental studies of the effect of turmeric extract.

Author/Year	Plant's extract	Comparison substance	Microorganism	Type of samples	Outcome
Hegde V, et al. [35]	Aqueous TE, Propolis tablets, Neem, Liquorice powder	5% NaOCl	<i>C. albicans</i> <i>E. faecalis</i>	Culture media	Good anti-microbial effect against <i>C. albicans</i> only (12.5 mm).
Neelakantan P, et al. [17]	Turmeric	NaOCl CHX	<i>E. faecalis</i>	96 extracted human teeth	Strong antimicrobial agent.
Panpatil VV, et al. [55]	Ginger, turmeric and garlic	Ginger, turmeric and garlic	<i>E. coli</i> , <i>S. typhi</i> and <i>S. aureus</i>	Culture media	Good antimicrobial and antioxidant activity
Vinothkuma, et al. (2013)	A.vera ,turmeric - <i>Terminalia chebula</i> , <i>Myristica fragrans</i> , <i>Azadiracta indica</i>	5.25% NaOCl	<i>E. faecalis</i> (ATCC 29212) <i>C. albicans</i> (c 24433)	Neem was highly efficient to 5.25% NaOCl in reducing <i>Enterococcus faecalis</i> and <i>Candida albicans</i> within the root canals when compared with other extracts.	Eighty-four teeth were extracted
Sinha DJ, et al. [37]	Alcoholic turmeric extract, Propolis extracts, <i>A. indica</i> , Tea tree or (<i>M. alternifolia</i>),	5% NaOCl, Sterile saline	<i>C. albicans</i> (MTCC 3017)	Extracted single rooted teeth	Good anti-fungal activity
Saxena, et al. (2015)	<i>Azadirachta indica</i> (AI), <i>Triphala</i> , <i>Curcuma longa</i> , and <i>Morinda citrifolia</i> (MC)	2.5% Naocl,	<i>E. faecalis</i> (ATCC 29212)	Propolis showed highest zone of inhibition among all the herbal extracts	Bacterial Culture Medium
Joy Sinha D, et al. [36]	Alcoholic extract of each of curcuma and Neem	5% NaOCl, 2% CHX, Normal saline	<i>E. faecalis</i> bacteria (ATCC 29212).	Bacterial culture media	Limited anti-bacterial activity
Chaitanya BV, et al. [32]	Turmeric extract, <i>Morinda citrifolia</i>	3% NaOCl	<i>E. faecalis</i> (ATCC 21224) <i>S. aureus</i> (no strains mentioned)	3% naocl showed maximum antibacterial activity against <i>E. faecalis</i> , followed by <i>Morinda citrifolia</i> and turmeric extracts.	Bacterial culture medium
Dhariwal NS , et al. [34]	Alcoholic curcuma extract, ethanolic extract of <i>Camellia sinens</i>	3% NaOCl	<i>Bacteroids fragilis</i> , <i>E. faecalis</i> , <i>Fusobacterium spp</i> , <i>Peptostreptococcus</i> , <i>P.intermedia</i> , <i>Porphyromonas spp</i> , <i>S.pyogenes</i> , <i>S.mutans</i> , <i>S.aureus</i> . <i>Pyophilia</i> .	Extracted primary teeth from 30 patients.	Showed a wide spectrum of anti-bacterial activity against <i>E. faecalis</i> , <i>Porphyromonas species</i> , <i>P. intermedia</i> and <i>Peptostreptococci</i> except a few G+ve Bacilli obligate and G-ve Gram negative Bacilli obligate anaerobes.
Dedhia J, et al. [33]	<i>Andrographis paniculata</i> - <i>Azadirachta indica</i> (neem), Curcumin	Naocl	<i>Staphylococcus aureus</i> , <i>Candida albicans</i>	Zones of inhibition exhibited by novel herbal agent <i>A. paniculata</i> were higer against <i>C. albicans</i> and similar against <i>S. aureus</i> , when compared to NaOCl.	Bacterial Culture Medium
Lokhande, et al. (2018)	Turmeric	2% Naocl -2% CHX -ozone gas	<i>E. faecalis</i>	2% of CHX has a significant antimicrobial effect against <i>E. faecalis</i> . Microbial inhibition potential of turmeric extract and ozonated water observed in this study opens perspectives for its use as a root canal irrigant.	Bacterial culture medium
Brar, et al. (2019)	Turmeric, triphala	2% CHX	<i>E. faecalis</i> MTCC 439	Triphala and Turmeric did show antibacterial activity against the organism but at significantly reduced levels	Bacterial culture medium
Puspita, et al. (2019)	100%, 50%, 25%, 12.5% of Turmeric extract	2% CHX Distilled water	<i>Streptococcus viridans</i>	White turmeric extracts can inhibit the growth of <i>Streptococcus viridans</i> .	Bacterial culture medium

(*A. indica*)=*Azadirachta indica*; (*C. longa*)=*Curcuma longa*; (*M. alternifolia*)=*Melaleuca alternifolia*; (NaOCl)=Sodium hypochlorite; (CHX)=Chlorohexidine; (*C. longa*)=*Curcuma longa*; (TE)=Turmeric extract; (*E. faecalis*)=*Enterococcus faecalis*; (*P. intermedia*)=*Prevotella intermedia*; (*S. pyogenes*)=*Streptococcus pyogenes*; (*S. mutans*)=*Streptococcus mutans*; (*S. aureus*)=*Staphylococcus aureus*; (NR)=Not reported; G+ve=Gram positive; G-ve=Gram negative.

Table 3: Summary of the findings of the experimental studies of the effect of *Peganum harmala* extract.

Author/Year	Plant's extract	Comparison substance	Microorganism	Type of samples	Outcome
Al-Izzy MY, et al. [29]	Aqueous and alcoholic extract (methanol)	0.2% CHX	<i>Lactobacilli</i> and <i>C. albicans</i>	Saliva samples from 20 students.	Both extracts showed anti-microbial activity against both microorganisms.
Darabpour E, et al. [59]	Alcoholic (methanol) extract of root, stem, leaf, flower and seeds of <i>P. harmala</i>	Novobiocin, colistin and carbenicillin	<i>Bacillus anthracis</i> , <i>Bacillus cereus</i> , <i>Bacillus pumilus</i> , <i>S. aureus</i> , <i>S. epidermidis</i> , <i>Listeria monocytogenes</i> and <i>S. pyogenes</i> , <i>P. aeruginosa</i> , <i>Brucella melitensis</i> , <i>Proteus mirabilis</i> , <i>Salmonella typhi</i> , <i>Escherichia coli</i> and <i>Klebsiella pneumoniae</i> .	Bacterial culture medium.	The roots and seeds showed significant strong anti-bacterial activity. The leaf, flower and stem showed poor anti-bacterial activity.
Tabrizzadeh M, et al. [62]	Aqueous and alcoholic (ethanol) extract of <i>P. harmala</i>	5.25% NaOCl	<i>E. faecalis</i> bacteria (ATCC 29212)	Bacterial culture medium.	<i>P. harmala</i> seeds showed anti-microbial activity.

(G+ve bacteria)=Gram positive bacteria; (G-ve bacteria)=Gram negative bacteria; (*S. aureus*)=*Staphylococcus aureus*; (*S. pyogenes*)=*Streptococcus pyogenes*; (*S. epidermidis*)=*Staphylococcus epidermidis*; (*P. harmala*)=*Peganum harmala*; (NaOCl)=Sodium hypochlorite; (*E. faecalis*)=*Enterococcus faecalis*; (CHX)=Chlorohexidine; (*P. aeruginosa*)=*Pseudomonas aeruginosa*; (NR)=Not reported.

effects but weak cleaning properties for the smear layer when used as an irrigant solution in endodontically treated teeth [44]. Moreover, it was found that green tea catechins demonstrated antifungal activity against *C. albicans* and this activity was pH dependent [5].

Divia AR, et al. [41] conducted an *in-vitro* experimental study to evaluate the antimicrobial efficacy of several herbal extracts including green tea compared with 5% NaOCl as an irrigant solution in human premolar teeth (n=60) treated with *E. faecalis*. The authors concluded that green tea extract showed significant and more effective antibacterial activity as an irrigant solution compared with NaOCl. Martina L, et al. [42] concluded that green tea extract has a powerful antimicrobial activity against *E. faecalis* compared with chlorhexidine. Nevertheless, Farhad Mollashahi N, et al. [43] reported that the antifungal activity of the green tea extract against *C. albicans* (PTCC 5027) was time-dependant when compared to NaOCl and that the inhibitory action on the culture media was not significant over time.

Even though NaOCl recorded better antibacterial activity against *E. faecalis* biofilms on tooth substrate, Ramezani F, et al. [45] and Prabhakar J, et al. [44] agreed that green tea extract had significant bacterial growth reduction against *E. faecalis* biofilms, which can be a useful replacement for the commonly used chemical agents when the side effects are considered. Moreover, the availability of green tea and its long shelf life beside its biocompatibility are favorable as an irrigant agent in endodontics [45]. Table 4 summarises the studies' characteristics that examined green tea extract as an irrigant endodontic solution.

Garlic

Garlic or *Allium sativum*, is a well-known plant in which its medicinal use was advocated hundreds of years ago. Garlic extract has fungicidal and a wide spectrum of antibacterial activities against Gram-positive and Gram-negative bacteria [63-65]. One of its active ingredients is allicin which is a water-soluble sulfur-containing compound that is effective antibacterial substance [66]. The chemical action mode of garlic against bacteria is poorly understood. However, it was assumed that allicin and other thiosulfonates that react with

thiol groups of thiol-containing enzymes of bacteria is the main antibacterial mechanism of allicin, which consequently is able to destroy the bacterial cell wall and membrane [14,67]. Furthermore, it was reported that allicin antibacterial mode of action can partially suppress the DNA and fully suppress RNA synthesis in bacteria [66,67]. The antifungal action of allicin has not been investigated yet, however, it was assumed to be similar to the antibacterial activity [68]. It was also proved that garlic extract can remove inorganic materials of the smear layer precipitated in root canals [49,69].

Birring OJ, et al. [46] conducted an *in vitro* study to evaluate the antibacterial efficacy of garlic extract against *E. faecalis* and to assess its root dentin penetration ability. The study concluded that garlic extract can be effectively used as an alternative irrigant agent to NaOCl due to its high antibacterial efficacy and dentin penetration. The same study used extract of raw garlic that has not been exposed to high temperatures to maintain the active ingredients from denaturation, and hence, there was no significant difference in the antimicrobial activity between NaOCl and garlic. The efficacy of garlic extract in disinfecting the dentinal tubules against *E. faecalis* was evaluated in an experimental study by Eswar K, et al. [47], and was compared with 2% chlorhexidine and Ca(OH)₂ using the real-time polymerase chain reaction analysis method. The study showed that even though chlorhexidine was the most effective agent against the examined bacteria, garlic extract demonstrated the following effective antimicrobial agent after chlorhexidine which is a promising result. However, the active ingredients in garlic can take several hours to act effectively against microorganisms in room temperature, therefore, there needs to find a technique to speed up the effectivity of garlic extract. In a study by Gopalakrishnan S, et al. [48] who assessed the antibacterial activity of garlic compared to 2% chlorhexidine and 5.25% NaOCl in inoculated dentinal tubules with *E. faecalis* concluded that NaOCl and chlorhexidine remain the most potent irrigant solutions. However, garlic had also showed effective antimicrobial properties considering the potency of the natural products, but the inhibitory action of dentine in the dentinal tubules could have affected the results. The saturated vs diluted hydroalcoholic extract of garlic compared to 5% NaOCl was assessed by Karkare *et al.* (2015) who

Table 4: Summary of findings of experimental studies of green tea extract.

Author/year	Plant's extract	Comparison substance	Microorganisms	Type of sample	Outcome
Hirasawa and Takada, (2004)	GT catechins.	EGCG + Amphotericin B. EGCG + Fluconazole.	<i>C. albicans</i> .	Agar plates.	Green tea catechins have antifungal activity against <i>C. albicans</i> . The addition of EGCG to amphotericin B and fluconazole enhanced the antifungal activity of these antimycotics against <i>C. albicans</i> and were more effective than using them alone.
Prabhakar J, et al [44]	Triphala. GT polyphenols.	Normal saline, 5% NaOCl, MTAD	<i>E. faecalis</i> .	Single-rooted mandibular premolars were vertically sectioned and divided into the five groups with 30 sections in each group.	Triphala, GT polyphenols and MTAD showed statistically significant antibacterial activity.
Martina L, et al. [42]	1%, 1.5%, 2%, 2.5%, 3% GT	Distilled water, 2% CHX	<i>E. faecalis</i> .	Agar plates and test tubes	3% GT extract showed an antibacterial activity equivalent to 2% CHX against <i>E. faecalis</i> .
Farhad Mollashahi N, et al. [43]	1% GT.	Normal saline 5% NaOCl.	<i>C. albicans</i> .	45 extracted single rooted premolars were vertically sectioned to give 90 samples.	Antifungal activity of green tea extract was time-dependent and its inhibitory action did not decrease significantly over time
Prabhakar J, et al. [44]	GT Polyphenol, Triphala.	2.5% NaOCl + 17% EDTA. 2.5% NaOCl. sterile distilled water	---	40 teeth	Green tea polyphenol was not effective in smear layer removal. Smear layer was effectively removed by NaOCl when combined with EDTA.
Lee P, Tan KS, et al. [15]	GT Polyphenol (EGCG).	---	<i>E. faecalis</i> .	Dentin disc on agar plates.	Green tea polyphenol (EGCG) was effective in eradicating and inhibiting the bacterial growth. It was also effective in suppressing the <i>E. faecalis</i> virulence and formation of biofilm.
Prabhakar J, et al. [44]	Triphala. GT polyphenols	17% EDTA, 2.5 NaOCl, distilled water	---	40 maxillary and mandibular teeth	A less effective cleaning effect was found in groups in which either distilled water or GTP was used as irrigants.
Ramezani F, et al. [45]	GT.	Normal saline, 2.5% NaOCl.	<i>E. faecalis</i> .	30 freshly extracted mandibular premolars were vertically sectioned to give 60 samples.	Green tea showed acceptable antibacterial effect on the biofilm of <i>E. faecalis</i> .
Divia AR, et al. [41]	- <i>Morinda citrifolia</i> , -Triphala, -95%GT polyphenols.	-5% NaOCl -Distilled water	<i>E. faecalis</i>	60 extracted single-rooted premolars	Significant reduction in bacterial colony count using GT extract compared to the other substances used.

found that garlic extract has potent antibacterial activity against *E. faecalis* which further supports the fact that garlic has great potential in the treatment of many microbial diseases. However, garlic in this study was not as effective as NaOCl which could possibly be referred to the impact of the preservatives in the dried commercially available preparations of garlic that was used in the study instead of the freshly prepared extract, where the latter showed better results as it was presented in the aforementioned study by Birring OJ, et al. [46].

Moreover, garlic extract was not as effective in removing the smear layer in root canals as NaOCl, when scanning electron microscope analysis method was used [49]. The authors concluded that even though plain garlic extract was less potent than NaOCl in clearing the root canal from the smear layer, its strong natural properties cannot be denied.

All the aforementioned studies recommended the use of garlic extract as an endodontic irrigant due to its effective antibacterial activity. However, the complexity of the extract preparation method,

controlling the odour of garlic extract and the possible toxicity should be taken into account for successful natural product alternative. Table 5 summarises the studies' characteristics that examined garlic extract as an irrigant endodontic solution.

Chamomile

Chamomile (*matricariacutita*) is rich with phytochemicals; however, the most effective bioactive components are phenols and flavonoids and apigenin [70]. The latter (*4',5,7-trihydroxyflavone*) is potently bioactive due to its low toxicity, anti-carcinogenesis, antibacterial, antioxidant and anti-inflammatory properties [16,71,72].

Chamomile was found effective in removing the smear layer from root canals due to its acidic compounds [50]. Therefore, chamomile extract is a promising natural alternative for root canal irrigation, however, the literature is limited in supporting its potential effectiveness and more studies are required to confirm the chamomile's activity as a potent natural endodontic irrigation solution.

Table 5: Summary of findings of the experimental studies of garlic extract.

Author/year	Plant's extract	Comparison substance	Microorganism	Type of samples	Outcome
Eswar k, et al. [47]	GE	Normal saline, CaOH ₂ , 2% CHX	<i>E. faecalis</i>	40 sample blocks (middle third of root)	Reduction in bacterial load in the GE group compared to the control groups.
Gopalakrishnan S, et al. [48]	Cinnamon, GE.	Normal Saline, 5.25% NaOCl, 2% CHX,	<i>E. faecalis</i> .	50 samples	GE better than cinnamon but weaker than NaOCl and CHX
Birring OJ, et al. [46]	10%, 40% and 70% GE.	Normal saline, 5.25% NaOCl.	<i>E. faecalis</i>	10 extracted single rooted teeth for dentin penetration test were divided into: Two groups to test GT and NaOCl.	GE has a potential to serve as an alternative herbal root canal irrigant, with considerable inhibition of <i>E. faecalis</i> growth.
Karkare SR, et al. [29]	-Aloe vera (saturated). -Aloe vera (diluted). -GE (saturated). -GE (diluted).	5% NaOCl	<i>E. faecalis</i> .	N/R	GE saturated and diluted showed better antimicrobial effects compared with aloe vera.
Prabhakaran P, et al. [49]	5% NaOCl + 17% EDTA without MES, 5% NaOCl + 17% EDTA with MES, GE + 17% EDTA without MES, GE + 17% EDTA with MES, GE without MES, GE with MES.	Normal Saline with and without MES.	68 single-rooted mandibular premolars.	68 teeth	All groups with MES showed better results.

MES - Modified Evacuation System.

Table 6: Summary of findings of the experimental studies of chamomile extract (CE).

Author/year	Plant extract	Comparison substance (CG)	Microorganisms	Type of samples	Outcome
Sadr Lahijani MS, et al. [50]	German CE, tea tree oil.	2.5% NaOCl + 17% EDTA. sterile distilled water. -2.5% NaOCl.		40 teeth	Smear layer was removed effectively by chamomile compared to NaOCl alone, but less effectively removed when NaOCl combined with EDTA.
Venkataram V, et al [51]	CE.	MTAD, 2.5% NaOCl		30 teeth	Smear layer was effectively removed by MTAD followed by CE. A 2.5 % solution of NaOCl alone did not produce any satisfactory results.

Sadr Lahijani MS, et al. [50] conducted experimental study to compare the smear layer removal properties of chamomile extract as an intracanal irrigant solutions compared with of 2.5% NaOCl, by using scanning electron microscope analysis. The study concluded that chamomile extract was effective in removing the smear layer and showed superiority to the activity of NaOCl. However, NaOCl was more effective when combined with a final rinse with 17% EDTA in the smear layer removal than chamomile alone.

In a randomised clinical trial by Venkataram V, et al. [51] the effectiveness of chamomile extract compared with MTAD (Biopure™ mixture of tetracycline, acid and detergent) and 2.5% NaOCl in removing the smear layer by using a scanning electron microscope

analysis method was studied. The authors concluded that chamomile extract was an effective agent in removing the smear layer and was superior to the effectiveness of NaOCl when used on its own without additives. However, MTAD was found significantly more effective in removing the smear layer than chamomile extract and this can be referred to the irrigation schemes used which was preceded with initial rinse of 1.3% NaOCl for a cumulated period of 20 minutes, whilst chamomile extract was used on its own. Therefore, the comparison between both agents in this study is biased as MTAD efficacy was supported with NaOCl [73]. Table 6 summarises the studies' characteristics that examined *Peganum haramal* extract as an irrigant endodontic solution.

Conclusion

The evidence of eligible studies in this review showed that aloe vera, turmeric, *Peganum harmala*, green tea, garlic and chamomile extracts are effective antimicrobial agents against several strains of *E. faecalis* and *C. albicans*. However, the antimicrobial effect of these extracts was less effective than that of NaOCl and chlorhexidine and can be concentration dependant. Garlic and chamomile extracts displayed effective smear layer removal properties which was comparable to NaOCl activity.

Limitations of the Study

This narrative review compiled the available published evidence of the herbal extract antimicrobial properties and the potential to replace the commonly used chemical agents to disinfect the root canals. However, the current review addresses limited types of herbal extracts available in the literature, and there is a need to review other popular plants' such as cinnamon zeylanicum or ginger extracts...etc. Also, the lack of systematic selection of studies in this review could have led to a biased interpretation of results. Additionally, the selected herbal extracts come from very different sources, such as leaves, seeds or roots; and they have differences in chemistry/phytochemical or the so-called active components. Solubility is a problem with these materials and the solvents used in the studies reported in this review have antimicrobial effects that could have biased the results. The different methods used to extract these plants throughout the studies, are additional limitations of the current review which made it difficult to perform meta-analysis. Due to the lack in the relevant clinical evidence, the recommendation to use herbal alternatives to disinfect the root canals in clinical settings is yet to be approved.

Suggestions for Future Studies

To consider investigating the antimicrobial effect of the herbal extracts on other types of endodontic microorganisms to help drawing a conclusion on the effectiveness of these extracts as natural product alternatives for root canal irrigation. Clinical studies that can examine preparation protocols of each herbal extract, and evaluate the most effective form and adverse effects, are required. We recommend standardising the concentration and time pattern of irrigation in using herbal extracts as root canal irrigant solution, to give clear idea of the most effective type.

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Conflict of Interest

Authors of this work declare no conflict of interest.

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