Review Article

Azadirachta indica A. juss, *Morinda citrifolia* L. and *Triphala* as herbal endodontic irrigants: A scoping review

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Abstract

Background: The success of the root canal treatment depends on the complete elimination of the microflora, biofilms and smear layer from the pulp space. A wide variety of chemical endodontic irrigants are available to achieve disinfection and thorough debridement besides mechanical means. However, detrimental properties such as allergic potential, cytotoxicity, antimicrobial resistance and safety concerns have intrigued researchers over the years to look for safer options. **Aim:** The review is aimed at providing comprehensive information of the studies evaluating the efficacy of *Azadirachta indica* A. juss (*A. indica*), *Morinda citrifolia* L. (*M. citrifolia*) and *Triphala* (fruits of *Emblica officinalis* Gaertn., *Terminalia chebula* (Gaertn.) Roxb. and *Terminalia belerica* Retz.) as herbal endodontic irrigants. **Materials and methods:** The literature review was conducted using indexed databases (PubMed, Google Scholar, Cochrane) electronically for publications in peer-reviewed journals for relevant articles evaluating the efficacy of *A. indica*, *Triphala*, *M. citrifolia* as endodontic irrigant from the year 1985-March 2020. **Results:** A total of 58 studies were identified for full text reviewing after duplicate removal and screening title and abstracts. A total of 32 studies were included and processed for data extractions. **Conclusion:** Various in-vitro/in-vivo studies utilizing these herbal irrigants have documented promising results and hold the potential to replace chemical endodontic irrigants in routine practice but more preclinical and clinical trials are needed to substantiate these results before they can conclusively be recommended as intracanal irrigating solutions.

Keywords: *Azadirachta indica,* endodontic irrigants, Herbal, *Morinda citrifolia*, *Triphala*

Introduction

In recent years, dentistry has evolved from being sacrificial to a saviour. The proponents of the dental profession have emphasized on saving a tooth diagnosed with dental caries than to resort to extraction. Root canal therapy has been the ultimate game-changer. Microorganisms have been recognized since long as the primary etiologic factors in the development of pulp and periapical lesions.[1-3] Elimination of microorganisms from the root canal system is a challenging task. The process of endodontic therapy involves important steps of biomechanical preparation along with effective cleaning of the root canal space to free it from bacteria and debris to allow hermetic sealing of the root canal. Various *in-vitro* and clinical evidence have shown that mechanical instrumentation alone is inadequate for complete elimination of bacteria from the root canal as it cannot reach every portion of the root canal system due to its complex anatomy, therefore, the use of irrigation forms an important step in this protocol[4,5] Irrigants can augment mechanical debridement by flushing out debris, dissolving tissue and disinfecting the root canal system thus further reducing the bacterial count, bio-films and lubricating the root canal.[6] The ideal irrigant should be bactericidal, can dissolve necrotic tissue, remove the smear layer besides lubricating the canal and not irritate to healthy tissues.[7]

Studies have shown that the use of normal saline along with mechanical preparation of the root canal space does not provide predictable disinfection.[8,9] The most commonly used irrigants in dentistry are sodium hypochlorite (NaOCl), chlorhexidine (CHX), ethylenediaminetetracetic acid (EDTA),

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citric acid, maleic acid, etc. However, they have been found to be responsible for altering the root canal microbiota, causing allergic reactions, decrease in dentinal microhardness, dentinal erosions, and biocompatibility issues.[10-12] These drawbacks coupled with resistant strains have prompted researchers to look for herbal alternatives.

The ancient folk medicines have focused on the use of herbs in both eastern and western traditional medicine. Recently, dental treatment has seen a growing trend to seek natural remedies and this approach is termed phyto-therapeutics, phyto-dentistry, or ethno-pharmacology. Indian tradition has a rich heritage of medicinal plants and herbs which have been used since time immemorial. Herbal alternatives are easily available, cost-effective, have increased shelf-life, low toxicity, and exhibit lack of microbial resistance.[13] These medicinal plants and herbs are rich in phytochemicals and are known for their analgesic, anti-inflammatory, antioxidant, anxiolytic, sedative, and antibiotic properties and have been widely used as endodontic irrigants. Herbal irrigants have been found to be bio-friendly with negligible side effects and have shown promising results in the removal of the smear layer which acts as a deterrent in successful root canal therapy.[14,15] This paper aimed at summarizing the existing knowledge and providing a literature review of studies evaluating the efficacy of three herbs; *Azadirachta indica* A. juss*, Morinda Citrifolia,* and *Triphala* as herbal irrigating solutions.

Materials and methods

The literature review was started with a defined background to review the studies involving interventions using *A. indica* A. juss*, M. citrifolia,* and *Triphala* as herbal endodontic irrigants. The indexed databases PubMed, Google Scholar, and Cochrane were electronically searched for articles published in English in peer-reviewed scientific journals from the year 1985-March 2020.

Inclusion criteria

In-vitro, ex-vivo and *in-vivo* comparative studies evaluating antibacterial activity of *A. indica* A. juss, *M. citrifolia* L., *Triphala* (*Emblica officinalis* Gaertn., *Terminalia chebula* (Gaertn.) Roxb. and *Terminalia belerica* Retz.) as herbal root canal irrigants and chemical endodontic irrigants such as CHX and NaOCl.

The studies were selected using the above-described protocol, titles, and abstracts. Reference lists of relevant studies were hand-searched to identify studies that might have been missed in the previous step. After screening title and abstract and duplicate removal a total of 58 articles were selected for full-text screening. Full-texts of pertinent studies were read independently of which 26 were excluded because they did not correspond with the inclusion criteria. Some articles were categorized as review articles [search strategy Flowchart 1].

Results

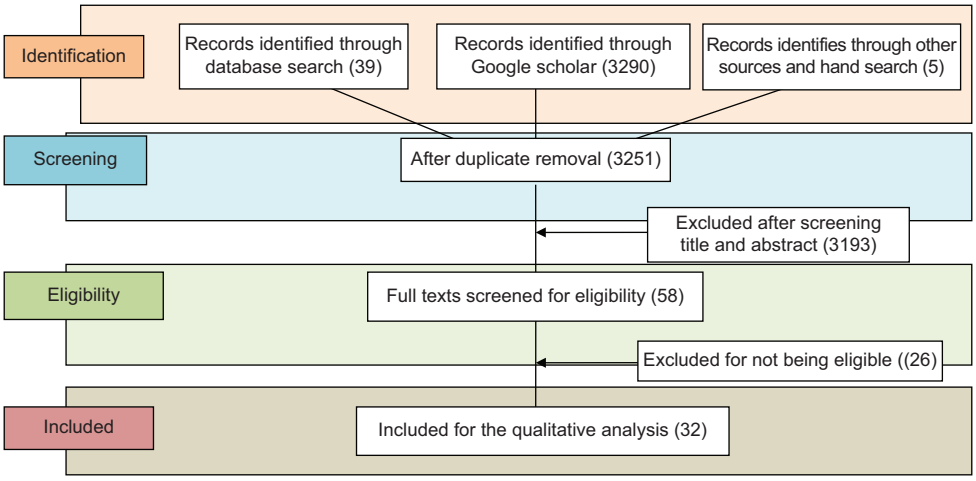
Study selection

After the screening of title and abstracts and duplicate removal, a total of 58 studies were identified for full-text reviewing and assessed for eligibility. Twenty-six studies did not meet the inclusion criteria and were excluded after full-text reviewing. Thirty-two studies (13 *in-vitro* and 15 *ex-vivo* and 4 *in-vivo* studies) were identified for inclusion in the review.

The collected information was tabulated based on:

1. *In-vitro* studies, *ex-vivo* studies, *in-vivo* studies on *A. indica* A. juss
2. Studies evaluating *Triphala* and *M. citrifolia* as endodontic irrigant
3. Studies evaluating the effect of herbal irrigants on smear layer
4. Studies evaluating the effect of herbal irrigants on biofilms.

The studies on the comparative evaluation of methanolic and ethanolic extracts of *A. indica* A. juss (*Neem*), NaOCl and CHX as root canal irrigants were tabulated [Table 1] The *in-vitro* studies[16-25] compared the antimicrobial activity of ethanolic and methanolic extracts of *A. indica A. juss*



Flowchart 1: Search Strategy

Table 1: *In vitro* studies on irrigant *Azadirachta indica*

Author	Year	Test/control/flora	Zone of inhibition (mm)			Results/conclusions
Híjar *et al*.[16]	2018	*A. indica*/CHX/ saline/*E. faecalis*	**Irrigant**	24 h	48 h	*A. indica* demonstrated an antibacterial effect against *E. faecalis* without any toxicity when used at low concentration
			A. indica (25 µg/ml methanolic extract)	32-34 mm	35-42 mm	
			2% CHX	17-20 mm	44-46 mm	
			Saline	0	0	
			P	<0.01		
Sinha *et al*.[17]	2017	*A. indica*/CHX/ saline/NaOCl/*E. faecalis*	*A. indica* (25 µg/ml ethanolic extract)	14.42 mm		*A. indica* yielded antibacterial activity equivalent to 2% CHX or 5% NaOCl against *E. faecalis*
			2% CHX	14.37 mm		
			5% NaOCl	14.5 mm		
			Saline	0 mm		
			P	<0.05		
Chandrappa *et al*.[18]	2015	*A. indica*/CHX/ saline/*E. faecalis*	*A. indica* (25 µg/ml ethanolic extract)	26.4 mm		*A. indica* extract has shown significant inhibitory effect against *E. faecalis* compared to CHX
			2% CHX	16.9 mm		
			Saline	0 mm		
			P	0.001		
Hegde *et al*.[19]	2013	*A. indica*/CHX/ saline/NaOCl/*E. faecalis*/*C. albicans*	**Irrigant**	***E. faecalis***	***C. albicans***	Efficacy of *A. indica* extract and NaOCl was compared against *E. faecalis* and *C. albicans* and it was concluded that neem extract had significant antimicrobial activity against these organisms
			A. indica (25 µ g/ml ethanolic extract)	21.33 mm	15.33 mm	
			5% NaOCl	17.67 mm	12.67 mm	
			Ethanol	0	0	
			P	<0.05		
Mustafa *et al*.[20]	2016	*A. indica*/CHX/ saline/*E. faecalis*	**Irrigant**	***E. faecalis***		*A. indica* leaf extract shows comparable zones of inhibition with that of CHX and NaOCl
			A. indica (25 µg/ml ethanolic extract)	17.19 mm		
			3% NaOCl	19.22 mm		
			2% CHX	20.45 mm		
			Saline	0		
			P	<0.05		
Srinidhi *et al*.[21]	2014	*A. indica*/CHX/ saline/NaOCl/*E. faecalis*/*C. albicans*	*A. indica* (25 µg/ml ethanolic extract)	16.33 mm		Efficacy of *A. indica* leaf extract against *C. albicans* is comparable to 3% NaOCl. Further, the action of neem extract was significantly better than that of 2% CHX
			3% NaOCl	19.66 mm		
			2% CHX	8.66 mm		
			Saline	0		
			Ethanol	8.33 mm		
			P	<0.011		
Ghonmode *et al*.[22]	2013	*A. indica*/NaOCl/ saline/*E. faecalis*	*A. indica* (25 µg/ml ethanolic extract)	19.57 mm		*A. indica* leaf extract has a significant antimicrobial effect against *E. faecalis*
			3% NaOCl	16.34 mm		
			Saline	0 mm		
			Ethanol	0		
			P	<0.05		
Bohora *et al*.[23]	2010	*A. indica*/CHX/ saline/ethanol/*E. faecalis*	**Irrigant**	***E. faecalis***	***C. albicans***	*A. indica* leaf extract has a significant antimicrobial effect against *E. faecalis* and *C. albicans*
			A. indica (25 µg/ml ethanolic extract)	20.0 mm	7.1 mm	
			2% NaOCl	17.0 mm	6.0 mm	
			Ethanol	0	0	
			P	<0.05	>0.05	
Jose *et al*.[24]	2015	*A. indica*/ NaOCl/*E. faecalis*/*C. albicans*	**Irrigant**	***E. faecalis***	***C. albicans***	*A. indica* leaf extract was found to be less effective against *Candida* and *E. faecalis* as compared to NaOCl but are less tissue toxic when compared with NaOCl
			A. indica (25 µg/ml ethanolic extract)	0.25 mm	0.76 mm	
			2.5% NaOCl	4.3 mm	4.2 mm	
			P	<0.01	<0.01	
Damre *et al*.[25]	2015	*A. indica*/ NaOCl/*E. faecalis*	**Irrigant**	***E. faecalis***		*A. indica* showed highest zone of inhibition against *E. faecalis* followed by NaOCl
			A. indica (25 µg/ml ethanolic extract)	4 mm		
			5% NaOCl	3 mm		
			Ethanol	0 mm		

A. indica: Azadirachta indica, E. faecalis: Enterococcus faecalis, C. albicans: Candida albicans, NaOCl: Sodium hypochlorite, CHX: Chlorhexidine

(Neem) to varying concentrations of NaOCl (2%, 2.5%, 3%, 5%) and CHX (0.25%, 0.5%, 2%) against *Enterococcus faecalis* (*E. faecalis*) and *Candida albicans* (*C. albicans*). In all of these studies, *Neem* performed equally well as NaOCl without showing any toxicity as compared to NaOCl when used at lower concentrations. One study by Jose *et al*.[24] however differed and concluded that 2.5% NaOCl was more effective against *C. albicans* as compared to ethanolic extract of *Neem*

(25 µg/ml), but the toxicity of NaOCl was found to be higher. Table 2a and b summarizes the *ex-vivo* and *in-vivo* studies evaluating *A. indica* A. juss as an endodontic irrigant.

Majority of *ex-vivo* studies evaluating the antimicrobial efficacy of *A. indica* A. juss in different solvents (ethanolic extract and 10% dimethyl sulfoxide [DMSO]) showed significant antimicrobial effect against *E. faecalis* and *C. albicans* besides being biocompatible to oral and periapical tissues.[26,28] Although a single study by Sundaram *et al.*[27] marked 5.25% NaOCl significantly more effective than ethanolic extract of *A. indica* against *E. faecalis*. Three *in-vivo* studies[29-31]

Table 2a: *Ex vivo* studies on *Azadirachta indica*

Author	Irrigant	Sample	Zone of inhibition (mm)				Results/conclusions
Bhargava *et al*., 2015[26]	*A. indica*/ Triphala/ NaOCl/ saline	60 infected pulp of primary molar from children aged 5-7 years	**Quantity of irrigant**	***A. indica* (Neem)**	**3% NaOCl**	**Triphala 60 mg/ ml in 10% DMSO**	3% NaOCl and *A. indica* showed maximum antibacterial activity against the endodontic microflora (P>0.05) followed by *Triphala*
			50 µl	13.8	15.8	4.6	
			100 µl	15.4	17	5	
			150 µl	16.6	19	6.8	
Sundaram *et al*. 2016[27]	*A. indica*/ NaOCl/*E. faecalis*/*C. albicans*	60 primary molars (5-7 years) indicated for pulpectomy	**Irrigants**		***E. faecalis***	***C. albicans***	NaOCl has maximum antimicrobial activity when compared with *A. indica* P<0.001
			5.25% NaOCl		19.37	19.17	
			A. indica (25 µg/ml ethanolic extract)		1.6	0	
Ambhore *et al*., 2017[28]	*A. indica*/ NaOCl/*E. faecalis*/*C. albicans*	*E. faecalis*/*C. albicans* isolated from patients with chronic periapical infection	**Irrigants**		***E. faecalis***	***C. albicans***	5% NaOCl solution and *A. indica* leaves extract has significant antimicrobial effect against *E. faecalis* and *C. albicans* with neem being possessing a significant property of biocompatibility to oral and periapical tissues
			A. indica 10% ethanolic extract		7.2	6.5	
			5% NaOCl		8.8	7.2	
			Saline		0	0	
			P		<0.001	<0.001	

A. indica: Azadirachta indica, E. faecalis: Enterococcus faecalis, C. albicans: Candida albicans, NaOCl: Sodium hypochlorite, CHX: Chlorhexidine, DMSO: Dimethyl sulfoxide

Table 2b: *In vivo* studies on *Azadirachta indica* (*Neem*)

Author/ Year	irrigant	Sample	Result				Result
Dutta and Kundabala 2014[29]	*A. indica*/ NaOCl/ CHX/ endodontic flora	36 anterior single-rooted teeth with periapical radiolucency indicated for root canal treatment	**Irrigants**	**Percentage reduction in microorganisms**			Neem irrigant has demonstrable anti-microbial efficacy and can be considered for endodontic use. A combination of NaOCl and ethanolic neem leaf extract is synergistic antimicrobially
			2.5% NaOCl	84.86			
			0.2% CHX	69.17			
			A. indica (ethanolic extract)	74.09			
			NaOCl+*A. indica*	100			
			CHX+*A. indica*	86.83			
			Saline	4.55			
Podar *et al*., 2015[30]	MCJ/ NaOCl/*A. indica*	32 permanent maxillary incisors, canines with aymptomatic apical periodontitis and pulpal necrosis	**Irrigants**	**Preaerobic CFU's**	**Preanaerobic CFU's**	**Postaerobic CFU's**	**Postanaerobic CFU's**	No difference in antimicrobial efficacy of *M. citrifolia*, *A. indica* and 3% NaOCl. P>0.05 All the test irrigants caused a significant reduction in the mean CFU counts of aerobic and anaerobic bacteria versus control P<0.05
			6% *M. citrifolia*	59	58.9	18.6	14.0	
			A. indica (C preparation GMP Krishna)	74	62.4	43	24.2	
			3% NaOCl	105.8	84.7	81.6	57.3	
			Control	128	69.7	124.5	82.0	
Kaur *et al*., 2018[31]	*A. indica*/ NaOCl/ CHX/ endodontic flora	125 patients 18-45 years with definite periapical radiolucency	**Irrigants**	**Preaerobic CFU's**	**Postaerobic CFU's**	**Preanaerobic CFU's**	**Postanaerobic CFU's**	*A. indica* was better than NaOCl but it was statistically nonsignificant AI showed better results than CHX gluconate which was statistically significant
			A. indica	60.18	1.71	75.57	1.44	
			3% NaOCl	79.86	0.51	83.72	0.39	
			2% CHX	78.36	20.91	108.38	28.71	
			Distilled water	124.86	105.21	107.10	96.48	
			P	<0.001	<0.001	<0.052	<0.01	

M. citrifolia: *Morinda citrifolia*, AI: Artificial intelligence, *A. indica*: *Azadirachta indica*, NaOCl: Sodium hypochlorite, CHX: Chlorhexidine, GMP: Good Manufacturing Practice. CFU's: Colony Forming Units

investigating the antimicrobial efficacy of ethanolic extract and commercial preparations of *A. indica* A. juss (GMP Krishna, India) against endodontic aerobic and anaerobic bacteria concluded that *A. indica* had significant antimicrobial efficacy against endodontic microflora and was equally efficacious or better than 2.5%, 3% NaOCl and 2% CHX. Furthermore, the combination of NaOCl and ethanolic *A. indica* leaf extract was found to be anti-microbially synergistic.

Table 3 summarizes the *in-vitro*, *ex-vivo* and *in-vivo* studies evaluating the comparative efficacy of *M. citrifolia* and *Triphala* with NaOCl, CHX and *A. indica* A. juss. In the majority of these studies, *Triphala* and *M. citrifolia* had shown significant antibacterial effects against *E. faecalis* and *C. albicans*. Various studies showed *M. citrifolia* juice (MCJ) to have antimicrobial efficacy equivalent to that of 1% NaOCl and also *Triphala* in DMSO comparable to that of 2.5% and 5% NaOCl.[32-36] Although in studies by Chaitanya *et al*.[37] 3% NaOCl scored better than 6% MCJ and Saxena *et al*.[38] mean zone of inhibition was found to be higher for 2.5% NaOCl than the ethanolic extract of *Triphala*.

The study by Thomas *et al*.[39] compared effectiveness of Diode laser in primary teeth as compared to 3% NaOCl and *Triphala* in 10% DMSO; in this randomized controlled trial, laser was found to be the most effective followed by *Triphala* which showed better antibacterial efficacy than NaOCl.

Table 4 summarizes the efficacy of herbal irrigants in removing the smear layer. Sebatni and Kumar[40] in their study is proved that the aqueous extract of *A. indica* A. juss was an effective irrigating solution for the removal of the smear layer. Sowjanyaa *et al*.[42] concluded that *Triphala* in DMSO (1:1) could be used as an adjunct to EDTA as final rinse for better removal of the smear layer. Susan *et al*.[41] observed that combination of aqueous extract of *Triphala* and 5% NaOCl with ultrasonic activation and 10% *Triphala* in 10% DMSO were as effective as 17% EDTA and 5% NaOCl when used in combination as irrigating solutions for the removal of the smear layer. Murray *et al*.[43] found that when used in combination with 17% EDTA 6% MCJ was as effective as 6% NaOCl and more effective than 2% CHX in the removal of *E. faecalis* smear layer.

Table 5 summarizes the studies on the use of herbal irrigants and their effect on biofilms. Tyagi *et al*.[44] investigated the antimicrobial efficacy of MCJ, ethanolic extracts of *A. indica* A. juss and propolis as compared to 5% NaOCl and found propolis to be equally effective as NaOCl against *C. albicans* biofilm followed by *A. indica* A. juss and MCJ. Garg *et al*.[45] in an *ex-vivo* study evaluating *Triphala* in 10% DMSO, 6% MCJ and *A. indica* A. juss (aqueous extract) found *Triphala* to be as efficacious as 5.25% NaOCl followed by *A. indica* and MCJ against *E. faecalis* biofilm. Rosaline *et al*.[46] found that ethanolic extract of *A. indica* A. juss achieved maximum reduction in adherence of *E. faecalis* to dentin (9.30%) followed by 5.25% NaOCl (12.50%) and least by MCJ (44.2%) and saline (86.7%). VinothKumar *et al*.[47] found ethanolic extract of *A. indica* (1:1) to provide promising results against both *E. faecalis* and *C. albicans* biofilms when compared to 5.25% NaOCl.

Discussion

The major objective of root canal treatment is to disinfect the entire root canal system. Cleaning, shaping, and use of antimicrobial medicaments are effective in reducing the bacterial load to some extent, but some bacteria do remain behind and multiply causing reinfection. Taking the ineffectiveness, potential side-effects and safety concerns of synthetic drugs into consideration, herbal alternatives for endodontic usage might prove to be advantageous. Over the past decade, interest in drugs derived from medicinal plants has markedly increased. This review aimed at compiling the studies evaluating the efficacy of irrigants utilizing herbs in cleaning root canal of its debris in the form of bacterial biofilm and smear layer.

A. indica A. juss (*Neem*) has been described for its value in traditional Indian medicinal texts.[48] *Neem* tree is also named as "village dispensary" as every part including the seeds, leaves and bark has a medicinal value.[49] In majority of studies reviewed, the *A. indica* extract used was prepared from the leaf part of the plant utilizing various solvents including ethanol, distilled water, and methanol. Several techniques are used for making the neem leaf extract utilizing different solvents.[50] Our search screened several studies that evaluated the antimicrobial properties of neem extract as an irrigant during root canal treatment and compared it with NaOCl and CHX irrigants. *E. faecalis* was chosen as one of the test microorganisms in most of these experiments due to its persistence in endodontically treated teeth with apical periodontics, its resistance to NaOCl and its rapid growth along the entire wall of the dentinal tubules.[51-53] In majority of *in vitro* studies, *A. indica* A. juss demonstrated significant efficacy against *E. faecalis* and *C. albicans* and proved to be as efficacious as NaOCl at various concentrations (2.5%, 3%, 5%).[26-31]

Ex-vivo studies also showed biocompatibility with oral tissues and significant antimicrobial efficacy against *E. faecalis* and *C. albicans* equivalent to that of NaOCl. In comparative clinical studies evaluating of *A. indica* A. juss demonstrable reduction of aerobic and anaerobic flora was seen equivalent to that of CHX and NaOCl.

Dutta and Kundabala *et al*.[29] investigated the synergistic action between the herbal and chemical irrigants, which potezntiated their individual anti-microbial efficacy and they hypothesized that using the NaOCl and ethanolic *A. indica* leaf extract combination as an endodontic irrigant would prove beneficial. Sebatni and Kumar[40] found *A. indica* leaf extract in distilled water to have significant smear layer removal followed by NaOCl. The biocompatibility, antioxidant, antimicrobial properties, effective removal of smear layer and *E. faecalis* biofilm make it a potential agent for root canal irrigation as an alternative to NaOCl.[23]

Table 3: Triphala and *Morinda citrifolia*

Author/year	Irrigant	Material and method	Irrigant		Results	conclusion
Satti *et al.* 2019[32]	*Triphala*/NaOCl/distilled water/*E. faecalis*/*Ex vivo*	Agar well diffusion method/M. Hilton Agar ×24 h	*Triphala* 50 mg/ml (aqueous extract)		20.33 mm	*Triphala* showed the highest antimicrobial efficacy followed by NaOCl. *Triphala* and showed no cytotoxic effect as compared to NaOCl mean difference of cell viability was 89.67 for human PDL fibroblasts
			NaOCl 3%		14.67 mm	
			Distilled water		0	
			P		<0.001	
Choudhary *et al.*[33]	*M. citrifolia*/*Triphala*/*E. faecalis*/*C. albicans*/*Ex vivo*	84 single-rooted teeth inoculated with *E. faecalis*/*C. albicans*/ irrigated with test solutions	**Percentage reduction CFU's after 72 h**	***E. faecalis***	***C. albicans***	The overall antimicrobial effects of different irrigants were maximum for CHX, whereas MCJ and *Triphala* juice also showed significant reductions. 1% NaOCl was not effective in completely removing the two tested organisms. The herbal irrigants hold the promise of becoming efficient irrigants and warrant further research
			MCJ (C. preparation basic Ayurveda GZD, India)	−73.7	−78.2	
			Triphala juice (C. prepararion basic Ayurveda GZD, India)	−77.7	−79.5	
			1% NaOCl	−87.05	−94.4	
			2% CHX	−88.2	−94.5	
			Distilled water	−76.9	−77.8	
			P	<0.001	<0.001	
Divia *et al.*[34]	*M. citrifolia*/triphala/ NaOCl/*Ex vivo*	60 extracted teeth inoculated with *E. faecalis* Irrigated with test solutions	**Irrigant**	**Pretreatment**	**Posttreatment**	*Triphala* and MC showed a significant antibacterial effect against *E. faecalis*. Among the tested agents, *Triphala* was found to be as efficacious as NaOCl
			6% *M. citrifolia*	940.5	158.17	
			5% NaOCl	939.17	0.67	
			Triphala (organic India ltd. commercial preparation)	940.92	15.92	
			Distilled water	948.3	944.5	
			P	<0.05	<0.001	
Chandwani *et al.*, 2017[35]	*M. citrifolia*/NaOCl/ *in vivo*	60 deciduous teeth indicated for endodontic treatment	**Irrigant**	**Preoperative**	**Postoperative**	There was no statistically significant difference observed in the antimicrobial efficacy between 1% NaOCl and MCJ
			7% MCJ	4.78	2.39	
			1% NaOCl	4.77	2.34	
			P		<0.001	
Shakouie *et al.*, 2014[36]	*Triphala* (IMPCOPS ltd. In 10% DMSO)/NaOCl/ *In vitro*	200 plates of BHI agar inoculated with *E. faecalis*×24 h	**Irrigants**		**Zone of inhibition**	*Triphala* exhibited better antimicrobial activity against *E. faecalis* compared to 0.5% and 1% NaOCl ($P<0.05$)
			0.5% NaOCl		4.6	
			1% NaOCl		6.3	
			2.5% NaOCl		7	
			5% NaOCl		7.6	
			5 mg/ml *Triphala*		7.3	
Chaitanya *et al.*, 2016[37]	*M. citrifolia*/NaOCl/*E. faecalis*/*In vitro*	Agar well diffusion method/M. Hilton Agar ×24 h	**Irrigants**		**Zone of inhibition**	NaOCl (3%) showed maximum antibacterial activity against *E. faecalis*, followed by *M. citrifolia* $P<0.05$
			6% MCJ		20.25mm	
			3% NaOCl		27.33 mm	
Saxena *et al.*, 2015[38]	*M. citrifolia* (Vestige india)/*triphala* (Vindhya herbals)/*A. indica* (Vindhya herbals/ NaOCl/*E. faecalis*/*In vitro*	Agar well diffusion method/ BHI agar incubated for 24 h	**Irrigants**		**Zone of inhibition**	Mean zone of inhibition in descending order was found as NaOCl > AI > *Triphala* > MC > ethanol $P>0.05$
			M. citrifolia (20 g/25 ml of ethanol)		02.2 mm	
			Triphala (20 g/25 ml of ethanol)		05.1 mm	
			A. indica (20 g/25ml of ethanol)		08.8 mm	
			2.5% NaOCl		22.0 mm	
			Ethanol		02.2 mm	

Contd...

Table 3: Contd...

Author/year	Irrigant	Material and method	Irrigant	Results	conclusion
Thomas *et al*., 2017[39]	*Triphala* (Nilogram India pvt)/NaOCl/Diode laser/ Randomised controlled trial/*Ex vivo*	49 single rooted human primary teeth reduced upto CEJ and prepared and inoculated with *E. faecalis*	Irrigant	CFU's/ml	Laser was most effective against *E. faecalis* and *Triphala* showed better antibacterial efficacy than NaOCl. NaOCl can be substituted with *triphala* due to its herbal properties $P<0.3$
			Diode laser	8.00±7.87 CFUs/ml	
			Triphala in 10% DMSO	58.60±16.63 CFU's/ml	
			3% NaOCl	69.80±19.57 CFU's/ml	

A. indica: *Azadirachta indica*, *E. faecalis*: *Enterococcus faecalis*, *C. albicans*: *Candida albicans*, NaOCl: Sodium hypochlorite, CHX: Chlorhexidine, *M. citrifolia*: Morinda citrifolia, AI: Artificial intelligence, MCJ: *M. citrifolia* juice, DMSO: Dimethyl sulfoxide, PDL: Periodontal ligament, BHI: Brain-heart infusion, CEJ: Cemento-enamel junction, CFU's: Colony forming unit

Triphala is an ayurvedic polyherbal medicine containing *Amalaki* (*E. officinalis* Gaertn.), *Bibhitaki* (*T. chebula* [Gaertn.] Roxb.) and *Haritaki* (*T. belerica* Retz.). In various classic Ayurvedic medicine literature *Triphala* is considered as multi-therapeutic and with cure-all properties, it is even labeled as panacea historically.[54,55]

*Tr*iphala has been used conventionally in Ayurvedic medicine as an antimicrobial agent.[56] The citric acids from the fruits aid in the removal of the smear layer and act as chelating agents. Different solvents have been used in the preparation of the *Triphala* extract such as distilled water, ethanol, DMSO; the latter being the most commonly used. Various *in-vitro* studies found *Triphala* (ethanolic extract) to be more effective than 0.5% and 1% NaOCl solution and also *Triphala* (10% DMSO) was marked equally effective as compared to 2.5% and 3% NaOCl solutions at eliminating *E. faecalis*.[36,39] Satti *et al*.[32] demonstrated higher antimicrobial efficacy of aqueous extract *Triphala* as compared 3% NaOCl whereas a study by Saxena *et al*.[38] revealed 2.5% NaOCl to be more effective than ethanolic extract of *Triphala*.

Significant removal of smear layer was observed by Thomas *et al*. when *Triphala* was used in combination with 17% EDTA and 5% NaOCl or 5% NaOCl and ultrasonic activation.[39] Another study also showed effective removal of smear layer by 17% NaOCl along with *Triphala*. It was concluded that its use as an adjunctive herbal root canal irrigating solution might prove to be advantageous. *Triphala* thus represents a potential therapy to eliminate *E. faecalis* as more side-effects and risks being associated with NaOCl although further clinical trials have been recommended to evaluate its potential use as a root canal irrigant.

MCJ has been relatively new to endodontics and recommended as an alternative to NaOCl because of its chelating ability to remove the smear layer and antimicrobial activities, especially against anaerobic bacteria such as *E. faecalis* and *C. albicans.* Murray *et al*., investigated the antimicrobial effectiveness of MCJ against *E. faecalis* and found its MIC to be 6%.[43] *Ex-vivo* studies evaluating the efficacy of *M. citrifolia* as root canal irrigant showed that MCJ to be effective against *E. faecalis* biofilms and also in the removal of smear layer, especially when used in combination with EDTA but not to the same extent as NaOCl.[44,45] Authors however have recommended the use of MCJ as an irrigant because of it is biocompatibility, antioxidant property, and safety profile as it is not likely to cause severe injuries to patients which might occur with the use of NaOCl accidents or if extruded out.

Herbal formulations are advantageous in many ways. They are safe, easily available, better shelf life, economical, and absence of microbial resistance so far. They are most effective when used with proper knowledge. Considering the low toxicity and antibacterial effectiveness, these herbs could be used as an adjunct to NaOCl thereby lowering its toxicity and also providing the added antioxidant advantage. Due to their high safety profile, these irrigants have the potential to

Table 4: Herbal irrigants and smear layer

Author/ year	Sample	Material & method	Irrigant		Results	Conclusion
Sebatni and Kumar 2017[40]	*A. indica*/NaOCl/ smear layer/SEM/ *Ex vivo*	40 healthy permanent extracted teeth due to orthodontic/periodontal reasons prepared and irrigated with test solutions sectioned and observed - SEM	Test solution NaOCl *A. indica* (aqueous extract 15 g/150 ml) *P*		Smear layer removal efficacy score 2.2 1.3 0.001	*A. indica* leaf extract showed significant smear layer removal followed by NaOCl
Sowjanyaa *et al*.[41]	*Triphala* (1:1 DMSO Imcops, Chennai)/EDTA/ SEM/*Ex vivo*	60 unhealthy due periodontal/prosthetic reasons prepared and irrigated with 2.5% NaOCl and saline followed by test irrigant; sectioned-SEM	**Irrigant** Coronal Middle Apical *P*	**17% EDTA** 1.1 2.0 2.9	**Triphala** 1.15 1.9 2.95 <0.005	*Triphala* showed good cleaning efficacy in removing the smear layer but EDTA was found to be more effective (P<0.005) The most effective removal of the smear layer occurred with the use 17% EDTA as a final rinse followed by the use of *Triphala*
Susan *et al*., 2019[42]	*Triphala*/EDTA/ NaOCl (SHC)/ SEM/*Ex vivo*	74 permanent molars with 25-35 degree root curvature prepared and irrigated with 5% SHC	Normal saline 5% NaOCl + 17% EDTA 5% NaOCl + *triphala* 5% NaOCl + *triphala* + sonic activation 5% NaOCl + *triphala* + ultrasonic activation 5% NaOCl + 3% *triphala* in 10% DMSO	5% NaOCl + 5% *triphala* in 10% DMSO 5% NaOCl + 10% *triphala* in 10% DMSO 10% citric acid in 10% DMSO 10% DMSO		*Triphala* was very effective and was nearly as efficient in the removal of smear when compared to groups II at the coronal and apical thirds whereas in the middle third it was comparable to groups II and IX. On statistical comparison and analysis, there was no significant difference between group II, V, and VIII (P>0.05)
Murray *et al*., 2008[43]	6% *M. citrifolia*/6% NaOCl/2% CHX/ smear layer/17% EDTA/0.9%saline/ SEM/*Ex vivo*	60 permanent single rooted teeth inoculated with *E. faecalis* for 30 days	**Irrigant** 6% MCJ (coronal) Middle Apical 2% CHX (coronal) Middle Apical 6% NaOCl (coronal) Middle Apical	**Percentage reduction in smear layer** 60 70 40 10 30 0 80 80 60		Both MCJ and NaOCl treatments were similarly effective with a rinse of 17% EDTA (P<0.2471) to completely remove up to 80% of the smear layer from some aspects of the root canal. MCJ was more effective than CHX for removing the smear layer (P<0.0085) and saline as the negative control (P<0.0001). The efficacy of MCJ was similar to NaOCl in conjunction with EDTA as an intracanal irrigant

SEM: Scanning electron microscopy, *A. indica*: *Azadirachta indica*, *E. faecalis*: *Enterococcus faecalis*, NaOCl: Sodium hypochlorite, CHX: Chlorhexidine, *M. citrifolia: Morinda citrifolia*, MCJ: M. citrifolia juice, EDTA: Ethylenediaminetetracetic acid, DMSO: Dimethyl sulfoxide, SHC: Sodium Hypochlorite

replace chemical irrigants in patients with a history of allergic reactions to NaOCl and also in pediatric patients where open apices limit the use of chemical irrigants. Many studies have concluded that herbal extracts produce promising results when used as endodontic irrigants. Further studies like quantitative real-time-polymerase chain reaction and confocal microscopic examination of the biofilms could provide better insight into the herbal irrigants. Combination of these herbal irrigants can also be tested for their synergistic action and also the possible interactions between the ingredients. This review has revealed that there is a paucity of comparative clinical trials utilizing these herbal endodontic irrigants despite having good baseline data showing promising results from *in-vitro* and *ex-vivo* studies.

Randomized clinical controlled trials can be carried out to further substantiate the clinical efficacy of these herbal irrigants. However, this scoping review could not quantitatively assess and combine the research data and could only provide an overview of the literature pertaining to the use of *A. indica, M. citrifolia* and *Triphala* as herbal root canal irrigants.

Conclusion

The article reviewed studies utilizing *A. indica* A. juss, *Morinda Citrofolia,* and *Triphala* as endodontic irrigants. Various *in vitro* studies of herbal products have yielded promising results, but more clinical trials are needed to substantiate the results from *in-vitro* studies and evaluate the biocompatibility before they can conclusively be recommended as intracanal irrigating solutions. Clinical studies investigating synergistic action

Table 5: Studies on herbal irrigants and biofilms

Author/year	Sample	Material & method	Irrigant			Result
Tyagi *et al*., 2013[44]	*M. citrifolia*/*A. indica* (ethanolic extract)/11% propolis (ethanolic extract/NaOCl/ Saline/*C. albicans* biofilm/*Ex vivo*	50 extracted mandibular premolars incubated with *C. albicans* culture 2 days, treated with test solutions for 10 min	**Irrigant**	**CFU's**		NaOCl and propolis exhibited highest antimicrobial efficacy against *C. albicans*. It was followed by the *A. indica*. *M. citrifolia* had limited antifungal action followed by the negative control group of saline $P<0.001$
			6% *M. citrifolia*	92.0±0.82		
			A. indica Ethanolic extract 25 µg/ml	3.8±0.92		
			5% NaOCl	0.20±0.42		
			11% Propolis	0.20±0.42		
			Saline	133.2±1.03		
Garg *et al*., 2014[45]	*M. citrifolia*/*A. indica*/*Triphala*/ NaOCl/*E. faecalis* biofilm/*Ex vivo*	70 single rooted premolars with fully formed apex prepared and irrigated with5% NaOCl sectioned and placed in tissue culture ×6 weeks then immersed in test solution ×10 mins	**Irrigant**	**CFU's**		*Triphala* was found to be as efficacious as NaOCl. The use of herbal alternatives as root canal irrigation solutions might prove to be advantageous considering several unfavorable properties of NaOCl NaOCl ~_ *Triphala* > Neem > MCJ>Saline $P<0.001$
			6% *M. citrifolia*	64.6		
			A. indica (aqueous extract15 g/100 ml)	50.1		
			Triphala (60 mg/ml 10% DMSO	1.4		
			5.25% NaOCl	0.3		
			Saline	93.0		
Rosaline *et al*., 2013[46]	*A. indica* (ethanolic extract)/*M. citrifolia* (ethanolic extract)/NaOCl/ Saline/*E. faecalis*/ Confocal laser scanning microscope/*Ex vivo*	50 noncarious single rooted teeth specimens were treated with 5.25% NaOCl and 5 mmol EDTA followed by final irrigant	**Irrigant**	**Percentage of adherent *E. faecalis* to dentin**		AI treatment produced the maximum reduction in adherence of *E. faecalis* to dentin (9.30%) followed by NaOCl (12.50%), *M. citrifolia* (44.20%) and saline (86.70%) No statistical difference was seen between AI and NaOCl
			Saline	86.70		
			5.25% NaOCl	12.5		
			M. citrifolia (1.25 mg/ml)	44.20		
			A. indica (ethanolic extract 0.33 mg/ml)	9.3		
Vinothkumar *et al*., 2013[47]	*A. indica* (ethanolic extract 1:1)/ NaOCl/saline/*C. albicans*/*E. faecalis*/ Polymerase chain reaction/*Ex vivo*	84 extracted teeth single rooted mandibular premolars prepared and irrigated with 5.25% NaOCl and 17% EDTA followedby contamination by *E. facealis C. albicans* ×21 days, test irrigants, PCR	**Percentage of bacteria remaining**	***E. faecalis***	***C. albicans***	0.033% AI was equally efficient to 5.25% NaOCl in reducing *E. faecalis* within the root canals 0.033% AI was highly efficient to 5.25% NaOCl in reducing *C. albicans* within the root canals when compared with other extracts. $P<0.005$
			A. indica (ethanolic extract)	13.1	8.2	
			5.25% NaOCl	11.5	11.5	
			Saline	70.4	65.5	

A. indica: *Azadirachta indica*, *E. faecalis: Enterococcus faecalis*, *C. albicans: Candida albicans*, NaOCl: Sodium hypochlorite, *M. citrifolia*: *Morinda citrifolia,* AI: Artificial intelligence, MCJ: *M. citrifolia* juice, EDTA: Ethylenediaminetetracetic acid, PCR: Polymerase chain reaction, DMSO: Dimethyl sulfoxide, CFU's: Colony forming units

utilizing various combinations of herbal irrigants at different concentrations and solvents are recommended to bridge the gaps in preclinical and clinical research activities and promote green dentistry in clinical practice in the true sense.

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Conflicts of interest

There are no conflicts of interest.

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