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PHARMACOLOGICAL ACTION OF DIFFERENT HERBAL ENDODONTIC IRRIGANTS AND THEIR EFFICACY AS IRRIGANTS IN PULPECTOMY OF PRIMARY TEETH: A LITERATURE REVIEW.

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ABSTRACT

For millennia, humans have been using traditional medicine to cure & prevent various illnesses. Different herbal products & their numerous beneficial properties have been promoted use in both the medical & dental fields. The pulpectomy procedure is directed to eliminate microorganisms from the primary teeth' root canal space, which ultimately carries out the associated healing of apical tissue. Complex root canal morphology, presence of lateral & accessory canals, continuously resorbing root, and primary teeth demand particular attention. Conventional irrigants are synthetically made chemical substances that pose some difficulty during the procedure as the physical & chemical properties of irrigants are less tolerated by pediatric patients. Post-treatment complications & certain adverse reactions are also well-documented with conventional irrigants. An irrigation solution has been chosen considering its antimicrobial efficacy, ability to remove smear layer & ability to dissolve pulp tissue. In this regard, Kaul & Raut instituted a classification of herbal endodontic irrigants. Different bioactive components in herbal agents and their mechanism of action inside the root canals are the potential for their use in pulpectomy procedures. In this context, this narrative review aims to discuss the pharmacodynamics of different herbal irrigants & their efficacy as root canal irrigants in the field of pediatric dentistry.

Keywords: Antimicrobial efficacy, chelating ability, herbal endodontic irrigants, pulp tissue dissolution capability.

INTRODUCTION

The knowledge of basic microbiology & dental pharmacology are interrelated & base of modern endodontics. Recently, natural irrigants have been given attention. literature searched following herbal irrigants and their efficacy as irrigants in primary teeth pulpectomy treatment & endorsed in this current narrative synthesis.[1] The success of the pulpectomy procedure is multifactorial, which builds upon the adequate access preparation and removal of necrotic pulp tissues, microorganisms, and their toxins from the root canal spaces in the hope of achieving an infection-free environment & to produce a hermetic seal.[2] Cleaning & shaping is the term connected with the endodontic procedure & is responsible for pulpectomy's ultimate success.[3] Polymicrobial nature of root canal infection, complex anatomy & continuously resorbing primary tooth root should be in consideration during the treatment.[4] Besides, instruments work in moist environments. So, medicated solutions are used to allow instruments to work properly & to deal with the previously mentioned issues. Furthermore, instruments cannot reach inaccessible areas where medicated solutions can be reached owing to their physical properties [5, 6]. Different chemical irrigants have currently been used as long as their properties meet all desired requirements. However, concerning pediatric patients' comfort, pedodontists cannot stay away from the undesirable side effects of conventional irrigants [7,8].

NaOCl is the irrigation solution of choice in routine endodontic practice. NaOCl is satisfying because of its wide range of antimicrobial activity, excellent tissue dissolution capability, accessibility & relatively lower cost. Certain downsides are to fail in the removal of the smear layer, strong bleach odor, and allergic reactions to the ocular & nasal mucosa. Baby's teeth are continuously resorbing as soon they erupt in the oral cavity, when NaOCl is extruded beyond the apex, it causes severe inflammatory responses, which ultimately destroys apical essential tissues. In addition, it has a detrimental impact on root dentin elasticity & bending resistance. Patients reported allergic reactions with NaOCl, IKI is recommended as an irrigants but severe staining of dentine also commenced with this [8,9].

CHX is an efficient irrigant against *E. faecalis* & *C. albicans*, the most culprit organisms for treatment failure. However, its efficacy is concentration-dependent. CHX removes an organic portion of the smear layer, but the inorganic portion still interferes with root dentin. Besides, tooth discoloration has no impact on pulp tissue dissolution, so it seems CHX is an incomplete task as an irrigant [9,10].

EDTA and citric acid are used as chelating agents in endodontics to remove the smear layer & also allow instrumentation in calcified & narrow canals and are not an effective bacteriocide[11].

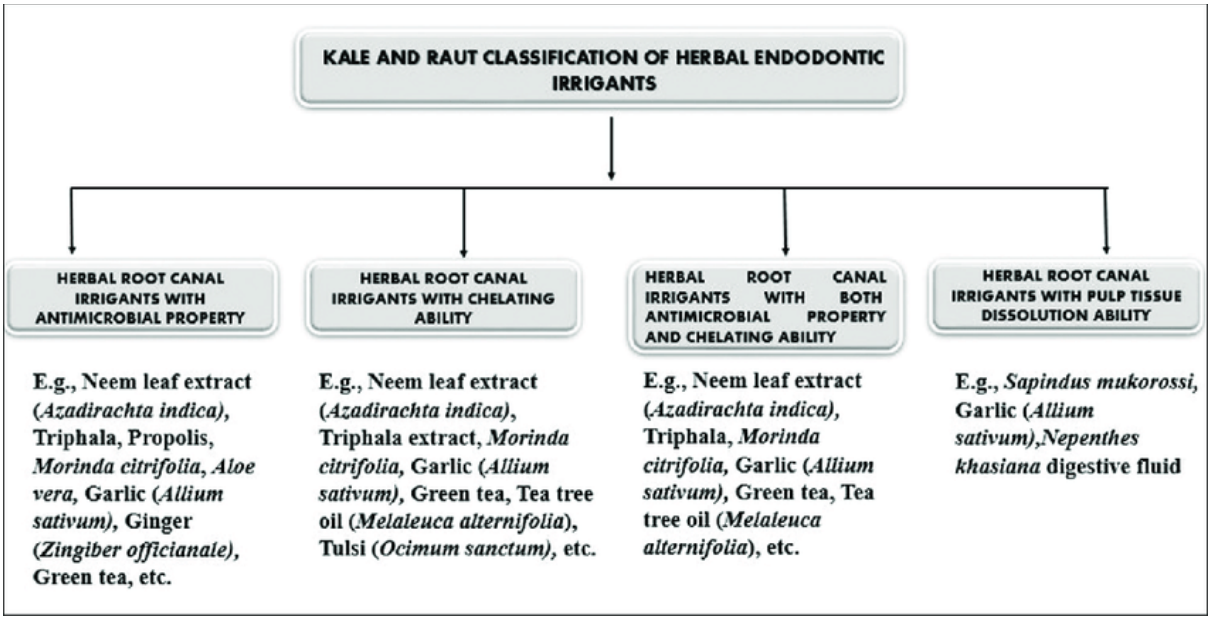
MTAD, is an irrigation solution that is capable of disinfecting the root canals & at the same time, ensuring the removal of the smear layer. Reportedly, MTAD causes Discoloration of the teeth & also not cost-effective. [12] Tetraclean and QMIX possess adequate antimicrobial efficacy. But they aren't cost-effective, nor easily available.[13]

H_2O_2 produces nascent oxygen[o] when used in combination with NaOCl & associated with severe post-operative pain if not handled properly during treatment [9,14,15].

When the term is to deal with the baby's teeth, avoiding side effects along with proper disinfection is the prime target [16]. The dilemma associated with chemical irrigants has lifted the attention towards medicinal plants for a few decades. The therapeutic potential of plant extracts like detergent & their action inside the root canals received particular attention. Phenolic & polyphenols (flavonoids, quinones, tannins, coumarins), terpenoids, alkaloids, lectins& polypeptides are the major groups of phytochemicals attributed to the antimicrobial properties of plant-derived endodontic irrigants[17],[18]. These bioactive components provided desirable disinfection of the primary root canals without any side effects on the apical main tissues. Herbal endodontic irrigants possess some advantages over chemical irrigants, such as a wide range of antimicrobial coverage, anti-inflammatory, antiseptic, and antioxidant properties, high biocompatibility, easy availability, cost effectivity, less or no cytotoxicity, minimal or no discoloration of teeth [19,20].

Based on previous research work & highlighting the properties of plant extracts in terms of antimicrobial coverage, chelating ability & pulp tissue dissolving capability, Dr. Purva Parvin Kale & Dr. Ambar W Raut instituted a classification system in 2021, known as KALE& RAUT classification of herbal endodontic irrigants. The classification gives a detailed overview of the diversity of herbal endodontic irrigants and is welcomed in the field of pediatric endodontics [21].

So, this review article expresses a combination of data about the efficacy of herbal irrigants besides conventional irrigants applied in the pulpectomy of primary teeth. This review also suggested discussing the mechanism of action of herbal irrigants in the textbook of dental pharmacology, where conventional irrigants have already been discussed.



Primary Endodontic Microbiology

Primary endodontic infection comprises a mixed community of bacterial species. Microbiota isolated from clinically asymptomatic teeth is completely different from microbiota isolated from clinically symptomatic teeth [22]. Aerobic, facultative organisms & anaerobic microbes were identified in infected deciduous root canals. *Enterococcus faecalis, Porphyromonas gingivalis* & *Treponema denticola are* reportedly the most prevalent species isolated from deciduous root canals [23]. Facultative organisms are the main culprit for the pathogenesis of the disease process & later on, infected areas are predominated by anaerobic organisms. From 22 infected primary root canals about 240 strains of bacteria were isolated where 200 strains were found obligate anaerobes [24]. *Peptostreptococcus, Actinomyces, Fusobacterium, Veillonella, Eubacterium, Propionibacterium, Bacteroids, Treponema denticola, Parvineonas micra, Tannerlla frosythensis* were isolated from teeth with acute periapical inflammation & *Veillonella parvula* found in association to chronic periapical inflammation of primary teeth [25].

Solvent for herbal endodontic irrigants

Extracts from herbs dissolved into an appropriate solvent in an appropriate quantity to make endodontic irrigants. Methanol, ethanol, butathenol, acetone, and 10% DMSO are the preferred solvents for herbal extracts. Ethanol is a more familiar & more studied solvent. It has a long history of being in our food & is the preferred solvent for many flavored compounds, coloring agents & bioactive or medicinal components. With high biocompatibility, environmentally friendly & low toxicity, ethanol is termed a 'green solvent'[26]. Next to ethanol is 10% DMSO, an aprotic, relatively

inert, stable at high temperatures & nontoxic. It can maintain all pure properties of a herbal agent being dissolved [27]. Other mentioned solvents are also preferred.

NEEM (Azadiracta indica A. Juss)

Also known as margosa, nimtree, or Indian lilac. The neem tree is native to the Indian subcontinent & to part of Southeast Asia, but it is naturalized & grown around the world in tropical & subtropical areas [28]. Every part of the neem tree has medicinal value. Hence, the neem tree is considered a "Village Dispensary" [29]. In 1992, The US National Academy of Sciences named neem as "a tree for solving global problems" [30, 31]. The isoprenoid group (nimbin, nimbinin, nimbidin, nimbolide, nimbidic acid) & non-isoprenoid group (Quercetin & beta-sitosterol) are responsible for antibacterial, antifungal, anti-inflammatory properties of neem [31,32, 33]. The non-isoprenoid group is polyphenolic flavonoids, known for bactericidal & fungicidal action → causes lysis of the cell wall of root canal organisms, changing in cellular permeability, inhibiting enzyme activity, affecting protein synthesis & gene expression, inhibits nucleic acid synthesis gradually protoplasmic content disappears, microbial cell death due to deprivation of essential nutrients. [34] Neem has better efficacy than 0.2% CHX against *C. albicans* colony [35]. In an in vitro investigation by using quantitative PCR, neem was highly efficacious to 5.25% NaOCl & 5 other herbal irrigants in reducing *E. faecalis* & *C. albicans* [36]. Neem leaf extract showed the highest zone of inhibition against root canal organisms than 2% NaOCl, propolis, turmeric & liquoorice [37]. In an in vitro investigation, neem leaf extract showed a significantly greater zone of inhibition of common root canal pathogen (agar diffusion test) compared to test materials.[38]. The antibacterial efficacy of neem leaf extract was found superior to 2% NaOCl against *E. faecalis*, *C. albicans* & mixed culture [39]. Non-isoprenoid group inhibits glucan & some other virulence factors necessary for plaque & smear layer formation. Aqueous extract of neem prevents smear layer formation by interfering with microbial aggregation, growth, adhesion to hydroxyapatite & production of insoluble glucan [40]. Neem showed the highest smear layer removal efficacy compared to green tea extract & orange oil. Owing to low viscosity & better penetration to the canal irregularities, It is efficacious in removing smears from the apical third of the root canals [41]. Ethanolic extract of neem has better chelating capability without affecting the microhardness of root dentin & on SEM observation there was all dentinal tubules were found open in the coronal, middle & apical third of the root canals, the efficacy of neem was found to be superior to orange oil & propolis[42]. The chelating ability of neem is supposed to its acid metabolites-gallic acid, caffeic acid, ferulic acid, and nimbin. These organic compounds bind to the inorganic ions of the smear layer like the 'claws of a crab' & assist their removal [39]. Different vivo& vitro investigations were carried out between different herbal irrigants, where neem was found superior to other irrigants in terms of antimicrobial efficacy & chelating ability. With high biocompatibility due to neutral P^H (7.4), it seems neem can be a very efficient irrigation solution for primary teeth pulpectomy procedures. Its bitter taste is a barrier to its compliance & acceptance by the Kido which can be easily overcome by adding sweeteners & flavors [32].

TRIPHALA

The word Triphala Comes from the Sanskrit words tri-three, phala- fruits, a polyherbal medicine consisting of an equi proportional mixture of powder of 3 medicinal fruits, namely *Emblica officinalis*, *Terminalia chebula*, *Terminalia belerica*. Triphala powder dissolves in 10% DMSO at a concentration of 125mg/ ml to make an irrigation solution that has a broad range of antimicrobial activity and is very effective in the removal of smear layer [43]. Different bioactive ingredients and their action against root canal bacteria received particular attention from Triphala. The antibacterial efficacy of tannic acid is described as its ability to pass through the cell wall up to the internal membrane & interfere with the sugar and amino acid uptake by bacteria, which limits the growth of bacteria. inhibiting cell envelop transport proteins & enzymes. Tannic acid also interferes with bacterial adhesion to the living surface, resulting in bacterial cell death. It acts as an astringent also. Flavonoids act by interacting with the cell wall & proteins of bacteria & lipophilic flavonoids act by

disrupting microbial membranes. Bioflavonoids & vitamin C speeded up the healing process through fibroblastic activity[44, 45]. Triphala contains citric acid, which is a mild organic chelate that binds to the inorganic ions of the smear layer & making them soluble. Hence, Triphala holds promise to remove the smear layer without affecting the microhardness of root dentin[46,47]. The chelating ability of Triphala is superior to sodium hypochlorite[47]. An In vitro investigation, triphala reveals the highest smear layer removing capability than 17% EDTA & neem irrigation solution[48]. Triphala has superior antimicrobial efficacy than 0.5% & 1% NaOCl. Its antimicrobial effectiveness is comparable to 2.5% & 5.25% NaOCl[49].Triphala shows better antimicrobial efficacy than 0.5% NaOCl when used as an irrigant in infected primary root canals[50]. In an in vivo investigation, Triphala demonstrated desirable efficacy in reducing CFU/ml. The study also depicted the comparison of clinical outcomes between Triphala & 2.5% NaOCl; the result was outstanding. The antimicrobial efficacy & clinical outcomes were found satisfactory in that study[51]. Triphala also has significant antifungal activity against *C. albicans*. Triphala is equally as effective as NaOCl against both C. albicans and E. faecalis[52]. Triphala found more biofriendly in cototoxicity assessment (using Almer Blue Assay) result[53].

PROPOLIS

Propolis is produced by Apis mellifera bees, which is an adhesive resinous mixture. The mixture consists of saliva, wax & exudates of bees that are used to seal the gaps in the hive & protect it from light, moisture, invaders & external factors[54]. Propolis' composition varies depending on the location of what tree & flower bees have access to. Seasonal variations in the composition of propolis are highly recognizable. High contents of its ingredients & antimicrobial activity reported during rainy season[55,56]. 25% propolis without wax & resins are used as endodontic irrigants. An in vivo investigation showed that 25% water-soluble derivatives of propolis reduce E. faecalis (52.3%) count in the post-microbial sample. The author concluded that 25% propolis extract contains active ingredients & can be an efficient endodontic irrigant. Caffeic acid & flavonoids are the bioactive components responsible for the antibacterial properties of propolis. They induce the synthesis of insoluble glycan by inhibiting the enzyme glycosyltransferase[57]. Pinocembrin is a flavonoid in propolis that possesses antifungal activity by preventing fungal cell division & breaking down fungal cell walls & cytoplasm. Propolis has a similar level of effectiveness when compared with 2% CHX & 3%NaOCl against C. albicans[58]. Anti-inflammatory & analgesic activity through inhibiting the production of IL-10, lowering the release of inflammatory cytokines & by the metabolic reprogramming of LPS activity in macrophages. Propolis also inhibits the production of prostaglandin by inhibiting lipoxygenase enzymes[59].

Morinda Citrofolia (NONI)

Morinfa citrofolia (Rubiaceae), belongs to the coffee family, native to southern Asia & Australasia, known as noni. Polynesians have been using noni as traditional medicine for over 2000 years[60]. With a wide range of therapeutic properties of *Morinda citrofolia* because of its bioactive components. Phenolic compounds (Scopolatin, alizarin, rutin), Anthraquinones (morindone, rubiadin, nordamnacanthal, rubiadin-1-methyl ether, anthraquinone glycoside), scopoletin, terpenoids are responsible for its antibacterial & antifungal activity[61]. MCJ acts by depolarization of hydrosoluble pectins, pectins & hemicelluloses in MCJ, leading to differential disassembly of bacterial cell wall polymers. Thus, there is a breakdown of cellular integrity, which results in cell death. MCJ also exerted a cytotoxic effect on *C. albicans.* An in vitro comparison concluded that *M. citrofolia* extract could effectively inhibit the growth of C. albicans (16.6±0.3) while Amphotericin B (20.6±0.6) was a positive control. However, the antifungal action of *M. citrofolia* varied with concentration & contact time[62]. 6% MCJ effectively inhibits E. faecalis count[63]. An in vivo comparison showed that MCJ irrigation solution is as effective as 1% sodium hypochlorite & can be used as a primary tooth pulpectomy procedure[64]. Low P^H (3.5) & acid metabolites (caproic acid, ursolic acid, caprylic acid) of 6% *M. citrofolia* extract have chelating ability without hampering microhardness of root dentin

(Vickers microhardness test) & all dentinal tubules were opened after irrigation, showed a hopeful outcome, concluded an in vitro investigation[65].

ALOEVERA

Aloe vera is a perennial succulent plant with long & pointed leaves that belongs to the Liliaceal family. More than 400 species of Aloe have been reported. Among them *Aloe barbadensis* Miller, which is commonly referred to as Aloe vera. About 75 ingredients have been identified. Of them, alloin & barbadoins are the main active ingredients responsible for different beneficial activities[66]. Anthraquinones are the bioactive component that shows antibacterial activity against *E. faecalis* when used as root canal irrigants. Anthraquinone inhibits the Krebs cycle of oxidation of sugar & hampered synthesis of ATP and NADH in cells; the respiratory metabolism of bacteria is affected, leading to cell death. Different in vitro investigations showed that the antimicrobial efficacy of aloe vera is similar to normal saline & is far less compared with 2.5% sodium hypochlorite and 2%chlorhexidine. Aloe vera expressed its antimicrobial potential after a long time of contact through the root canal. No studies are available to suggest a specific duration or concentration for aloe vera to act as a root canal irrigants. Furthermore, the limited flow of the substances through the canal irregularities is considered a weak irrigation solution[67]. Aloe vera shows the same level of antimicrobial activity with Ca $(OH)_2$ against *E. faecalis* [68].

GARLIC (*Allium sativum)*

Garlic is a bulbous flowering plant and belongs to the Alliaceae family. It is a horticultural crop and one of the oldest common cultivated herbs originating particularly from central Asia[69]. Garlic is popularly used as a culinary ingredient. Its therapeutic properties are also well known. Organic sulphides, different phenolic compounds, tannins, flavonoids, and alkaloids are responsible for their antimicrobial activity. The most abundant organic sulphid in garlic is diallyl thiosulphinate (DAS), which is Allicin[70]. Allicin is called a natural antibiotic and just acts like Penicillin (1mg Allicin=15 IU penicillin). Antibacterial action of Allicin involves– I) destruction of the cell wall & cell membrane of bacteria II) RNA is the primary target of Allicin, causing total inhibition of synthesis of RNA III) inhibit DNA gyrase activity III) Prevent the ability of germination of spore & growth of hyphae. The inhibitory function of Allicin on thiol enzymes resulting in the activation of microbial apoptosis has been reported with *Candida albicans*. The chemical reaction of Allicin with thiol groups of various enzymes (alcohol dehydrogenase, thioredoxin reductase, RNA polymerase) affects the metabolism of cysteine proteinase activity, which involves the virulence of the root canal organisms[71]. Anti-inflammatory activity of Allicin through inhibiting nuclear factor-kB (NF – κB). Garlic is rich in ascorbic acid & vitamin B complex (B_1,B_2, B_3,B_5,B_6,B_9) & is associated with the healing process through fibroblastic proliferation[72]. With a broad spectrum of antimicrobial coverage as well as a bio-friendly nature, garlic is a good choice in primary teeth pulpectomy procedures. Garlic is equally efficacious with sodium hypochlorite[73] & garlic's antimicrobial efficacy is better than calcium hydroxide[74]. The ethanolic extract of garlic contains ferrous iron, associated with the chelating ability by binding with the inorganic ions of the smear layer. 64mg/ml of ethanolic extract of garlic can remove the smear layer & on SEM evaluation, the integrity of intertubular dentin was maintained at the coronal & middle third of root dentin[75]. P^H of ASE is very low (5.3-6.3), which is not advantageous for pulp tissue dissolution. Allin is converted to Allicin by the enzyme allicinase, immediately after it is crushed. Allicin takes part in the metabolism of cysteine in protein, disrupting the epidermal junction and resulting in coagulation necrosis of tissues. This mechanism of garlic represents the pulp tissue dissolution capability[76]. 30mg/ml concentration of ASE has little effect on dissolution of human pulp tissue at 90 minutes[77].

GINGER

Zingiber officinalae is a flowering plant belonging to the Zingiberaceae family. Rhizome, ginger root or ginger, is widely used as a spice and a folk medicine[78]. For centuries, China, India& Japan used

ginger as a traditional medicine & as a dietary supplement[78,79]. Carbohydrates (50%-70%) as starch are the major constituents of ginger rhizome. Gingerols, shogaols, paradols, and terpene compounds are bioactive compounds and are responsible for several biological activities. Gingerol & shogaol are lipid-soluble phenolic compounds, responsible for antimicrobial activity and act as a detergent. They break the phospholipid membrane of root canal bacteria & cell walls of fungi. The cell becomes permeable and decreases the efflux, releasing its cytoplasmic contents, resulting in functional loss[80]. 15.625 mg/ ml concentration of ethanolic extract of ginger showed bactericidal action against *E. faecalis* and concluded as more potent than 2%chlorhexidine[81]. Ethanol itself has antifungal activity, adding the ginger powder to the ethanol produces synergistic action against *C. albicans*[82]. 10% ethanolic extract of ginger showed comparable results to 2.5%. NaOCl. With low risk, great wettability, and pharmacokinetics of active compounds, ginger can be a risk-free irrigant for pulpectomy procedure [83].

GREEN TEA

Camellia sinesis, is an evergreen shrub that is a flowering plant belonging to the family of Theaceae, known as *the* tea plant. Leaves & buds of *C. sinesis* plant are used as a tea, which is the 2nd most popular drink in the world after water [84]. Several bioactive components are associated with its different health benefits—Polyphenols (Flavonols, flavandiols, flavonoids) & phenolic acid, L-theanine, caffeine, theobromines& volatile organic substances. The most abundant polyphenols are flavonols, commonly known as catechins. EGCG (Epigallocatechin Gallate) is a catechine responsible for its antibacterial & antifungal activity by binding to the ATP site of the DNA gyrase Subunit B of bacteria thereby reducing the activity of the gyrase enzyme. Catechin generates hydrogen peroxide which causes damage to the bacterial cell membrane. There is cellular death due to loss of function & structural integrity[85]. Catechins affect the absorption & metabolism of ions by interacting with metal ions and, hence, act as a chelating agent. The P^H of green tea is 7-10. Thus, it is a weak chelator. 3.5% green tea solution (Distilled water was a solvent) possesses better antimicrobial activity against aerobic & anaerobic bacteria than normal saline[86]. The antifungal activity of green tea is time-dependent and not much pronounced[87]. Smear layer removing capability of different irrigants where DMSO was a solvent for green tea. Green tea shows smear layer removing capability better than sterile distilled water and far less compared to 17% EDTA, Triphala & 3% NaOCl. Green tea is a weak chelator because it lacks acid components & high P^H [88].

TEA TREE OIL

Also known as melaleuca oil. *Melaleuca alternifolia, a* species of tree or tall shrub, belongs to the myrtle family, Myrtaceae. Tea tree oil obtained from the leaves of tea tree *Melaleuca alternifolia* native to southeast Queensland & the northeast coast of New South Wales, Australia[89]. Terpinen-4-ol, alpha-terpinolene, and terpinene are the principal bioactive components associated with antibacterial & antifungal activity. The therapeutic concentration of tea tree oil is 2.5 to 5%, showing its antibacterial properties without any toxic effects[90]. These active metabolites are attributed to their hydrocarbon structure & intrinsic lipophilicity. Tea tree oil destroys cell membrane structural integrity, hampers the respiration of microbes, and loss of intracellular ions leading to cell death. Tea tree oil can significantly reduce *E. faecalis* count which was comparable to 3% sodium hypochlorite & 2% chlorhexidine[91]. High surface tension & lack of acid metabolites (P^H – 5-7) tea tree oil is less favorable for smear layer removal from all the regions of root canals[92].

TULSI (Ocimum sanctum)

An aromatic perennial plant in the family Lamiaceae, native to India[93]. Eugenol, thymol, aerosol acid, caryophyllene, camphor, and germacrene are the main components. Eugenol (l-hydroxy2-methoxy-4-allylbenzene), discovered in O. *sanctum* L., is responsible for tulsi's smear layer removal & anti-inflammatory properties[94]. On SEM observation, almost all dentinal tubules were opened with the use of a Tulsi irrigant, where almost all tubules were covered with a smear layer while using a 2.5%

NaOCl irrigant. Acidic P^H (3.5) is also associated with its smear layer removing capability[95]. The Pharmacokinetic result of eugenol is exactly like $NSAID_s$ (Aspirin & Diclofenac). The biotransformation product of eugenol binds to COX-2 & LOX-5, inhibits the release of inflammatory mediators (Prostaglandin) thus a potent anti-inflammatory agent[96]

Sapindas mukorossi

Commonly known as Indian soapberry, washnut, ritha, or Chinese soapberry, it belongs to the Sapindacecae family. This deciduous tree is found mainly in the lower foothills & mid-hills of the Himalayas at the altitudes of 1200 meters (4000 ft)[97]. Saponin (10-11.5%), sugar (10%), mucilage (10%) & flavonoids are its main components. Triterpentine saponin is the main bioactive component & is responsible for the pulp tissue dissolution capability of SM. The glycoside of triterpentine saponin reduces cell surface tension, thus increasing membrane permeability. Furthermore, the attraction of aglycon moiety for membrane sterol, particularly cholesterol, causes irreversible damage to the lipid bilayer membrane allowing cellular macromolecules to leak out, which results in cellular lysis. An in vitro investigation of 50µg/ml of methanolic extract & 100µg/ml of butanolic extract of SM solution can dissolute 55% & 57% rate of human pulp tissue at 45 minutes[98].

Nepenthes Khasiana digestive fluid

Carnivorous or insectivorous plant endemic to the Khasi hills of Meghalaya by Which it is named. The modified specialized leaf, which has a bulbous trap at the bottom part, gives it the shape of a pitcher[99]. The pitcher containing digestive enzymes & the P^H of the fluid is explained as acidic (2 to 6 varies from species). Digestive enzymes and acidic P^H decompose the protein of insects when it is trapped inside the pitcher[100]. Fresh digestive secretion of pitcher plant P^H analyzed 4.4 & used as irrigants to dissolute human pulp tissue[101]. In an in vitro investigation, Khasina's digestive fluid can completely dissolve human pulp tissues in 7 hours[102]. Pulp tissue is loose connective tissue & the structural element of the cell is protein. Digestive fluid contains nepenthesin (pepsin) & its action is to split the structural protein into protease, peptone & polypeptides. Nepenthesiins are remarkably stable at or below 50ºC & are extremely stable over a wide range of P^H (3-10) for over 30 days. The existence of carbohydrate moieties also reduces the denaturation of nepenthesins & can be a potential irrigant for pulp dissolution[103,104].

Year	Author	Irrigants used	Conclusion
2014	Dutta A.& Kundubala M. [32]	Neem NaOCl CHX	Neem showed superior antimicrobial activity among tested irrigants
2024	Akhanda MH et al. [51]	2.5% NaOCl Triphala	Both were equally significant regarding antimicrobial efficacy
2014	Agarwal J. Et al. [57]	25% Propolis 0.9% isotonic saline	Propolis showed antimicrobial activity
2017	Chandwani m. et al. [64]	MCJ 1% NaOCl	Both were equally effective
2019	Dr. Yavagal PC Dr. Sravanthi SV[67]	Aloevera 2.5% NaOCl 0.2% CHX	Aloevera showed potential antimicrobial activity but less pronounced than 2.5% NaOCl & CHX
2019	Elheeny AAH [73]	ASENaOCl	Both were equally efficacious regarding antimicrobial activity
2022	Mansoorkhani HRA et al. [86]	10% ethanolic ginger extract5.25% NaOCl 2.5% NaOCl 2% CHX	Ginger extract showed comparable efficacy with 2.5% NaOCl
2017	Mai Ramadan EI Sayed Salem et al. [86]	3.5% Green tea Physiologic saline	Green tea showed promising result

Table 1: Comparative evaluation of herbal & conventional irrigants in regard to antimicrobial efficacy in deciduous dentition (In Vivo)

Year	Author	Irrigants used	Method of Assessment	Conclusion
2023	Setia et al. [42]	Neem leaf extract Propolis Orange oil	SEM	Neem leaf extract was significantly better in removing smear layer at coronal, middle & apical third of root canal.
2024	Dr.Nitin Lokhande [48]	Neem Triphala 17% EDTA	SEM	Triphala was found superior than 17% EDTA & Neem
2012	Saghiri Ma et al [65]	6%MCJ 17% EDTA NaOCl MTAD	VMT	All dentinal tubele were opend after a final flush with 6%MCJ
2018	Prabhakaran P [75]	NaOCl Ethanolic extract of garlic 17%EDTA	SEM	Intertubular dentin of coronal & middle third were maintained with garlic extract but while combined with 17% EDTA better efficacy were observed at apical third.
2019	Mallika et al.[91]	Tea tree oil 17% EDTA Qmix Tea tree oil Saline	SEM	Tea tree oil was better than saline & result was significantly good while combined with 17% EDTA
2020	Malis et al. [94]	2.5% NaOCl Tulsi	SEM	Allmost all dentinal tubules were found opened after with tulsi irrigant & proven to be better than 2.5% NaOCl

Table 2: Comparative evaluation of herbal endodontic irrigants & conventional irrigants in regards to chelating capability (In Vitro)

Year	Author	Irrigants used	Conclusion
2017	Rao SA et al. [77]	2.5% NaOCl ASE	Shows some pulp dissolution capability but the efficacy is less than 2.5% NaOCl
2019	Tamilselvi R [102]	NaOCl, Ethanolic extract & NK digestive secretions	Total dissolution pf pulp tissue at 7 hours by NK digestive secretions
2020	Özunur Güçlüer et al [98]	Different extract of SM & NaOCl	SMM& SMB showed 55% & 57% dissolution of pulp tissue respectively at 15 minutes.

Table 3: Pulp tissue dissolution capability of herbal irrigants (In Vitro)

CONCLUSION

Biofriendly pharmacokinetic activity & efficacy of Herbal Endodontic Irrigants mentioned in the Kale & Raut classification are safe. Neem irrigation solution is remarkably good among all herbal endodontic irrigants in terms of antimicrobial activity. Triphala is a potent irrigant for primary teeth pulpectomy procedures and possesses maximum chelating ability. Allicin of garlic has antimicrobial activity, aiding in the removal of smear layer & possessing pulp tissue dissolution capability to some extent. Hence, it can be used in all phases of the pulpectomy procedure. Nimbin in neem, citric acid in Triphala, acidic p^H of noni, eugenol in tulsi, and catechin in green tea make them more prominent in chelating ability. The acidic p^H of herbal endodontic irrigants lacks dissolution of the pulp tissue. Some recent studies concluded that *S. mukorossi* irrigants (SMM, SMB) can significantly dissolve pulp tissue. Fresh secretion of *Nepenthes khashiana* can dissolve total pulp tissue but takes longer. There are lacunae of article found in regards to pulp tissue dissolution ability & demands further attention. The knowledge of plant-based pharmacology should be explored more & the implication of explored knowledge in clinical dentistry is highly encouraged.

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