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PHARMACOKINETICS 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, human have been using traditional medicine to cure & prevent various illness. Different herbal products & their numerous beneficial properties which have been promoted its use in both medical & dental field. Pulpectomy procedure directed to eliminate microorganisms from the root canal space of primary teeth which ultimately carried out associated healing of apical tissue. Complex root canal morphology, presence of lateral & accessory canals, continuously resorbing root, primary teeth demand particular attention. Conventional irrigants are synthetically made chemical substances, pose some difficulty during procedure as physical & chemical properties of irrigants are less tolerated to the pediatric patients. Post treatment complication & certain adverse reactions are also well documented with conventional irrigants. An irrigation solution has been chosen considering antimicrobial efficacy, ability to remove smear layer & the ability to dissolve pulp tissue. In this regards, 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 potential for their use in pulpectomy procedure. In this context, this narrative review aims to discuss pharmacokinetics of different herbal irrigants & their efficacy as root canal irrigants in the field of pediatric dentistry.

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

INTRODUCTION

The knowledge of basic microbiology & dental pharmacology, interrelated & base of modern endodontics. Recently natural irrigants took the attention .literature searched in accordance with herbal irrigants and their efficacy as irrigants in primary teeth pulpectomy treatment & endorsed in this current narrative synthesis.[1] The success of pulpectomy procedure is multifactorial, which builds upon from the adequate access preparation, removal of necrotic pulp tissues, microorganisms and their toxins from the root canal spaces, in the hope of to achieve 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 environment. So, medicated solutions are used in order to allow instruments work properly & to deal with the previously mentioned issues. Furthermore, instruments cannot reach to the inaccessible areas where medicated solution can be reached owing to their physical properties [5, 6].Different chemical irrigants have currently been used as long as their properties met all desired requirements. But in respect of 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 satisfying by their wide range of antimicrobial activity, excellent tissue dissolution capability, accessibility & relatively lower cost. Certain downside is to failing in removal of smear layer, strong bleach odor, allergic reactions to the ocular & nasal mucosa. Baby's teeth are continuously resorbing as soon they erupt in the oral cavity, when NaOCl extruded beyond the apex they cause severe inflammatory responses which ultimately causes destruction of apical essential tissues. In addition, it has detrimental impact on root dentin elasticity & bending resistance. Patients reported with allergic reactions with NaOCl, IKI is recommended as irrigants but severe staining of dentine also commenced with this [8 ,9].

CHX is an efficient irrigants against *E. faecalis* & *C. albicans*, the most culprit organisms for treatment failure. But its efficacy is concentration dependent. CHX remove organic portion of smear layer but inorganic portion still interfering at root dentin. Besides, tooth discoloration, no impact on pulp tissue dissolution, seems CHX is an incomplete task as an irrigants [9 ,10].

EDTA and citric acid used as chelating agent in endodontics in order to remove smear layer & also allow instrumentation in calcified & narrow canal and is not an effective bacteriocide[11].

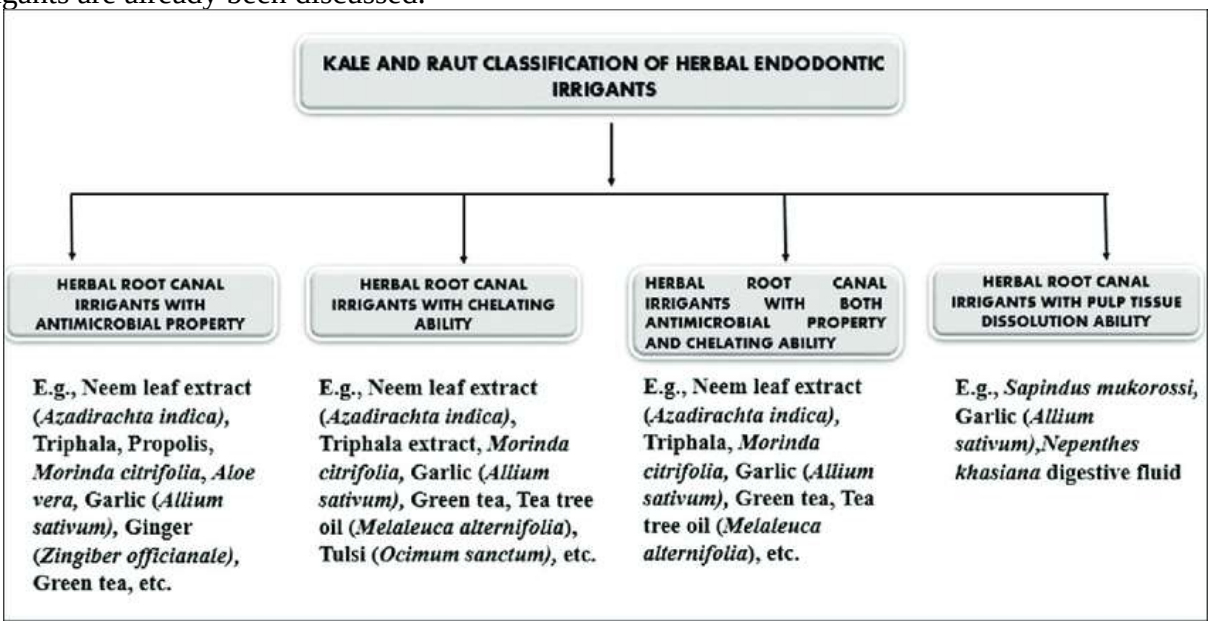
MTAD, an irrigation solution which is capable of disinfecting the root canals & at the same time ensuring removal of smear layer. Reportedly MTAD causes Discoloration of tooth & also not cost effective.[12] Tetraclean and QMIX possess adequate antimicrobial efficacy. But they aren't cost effective, nor 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 the baby's teeth, avoiding side effects along with proper disinfection is the prime target [16]. The dilemma associated with the chemical irrigants lifts the attention towards medicinal plants from 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 for the antimicrobial property of plant derived endodontic irrigants[17],[18].These bioactive components provided desirable disinfection of the primary root canals without any side effects of the apical main tissues. Herbal endodontic irrigants possess some advantages over chemical irrigants such as 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].

On the basis of previous research work & highlighting the property 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 the herbal endodontic irrigants and is welcomed in the field of pediatric endodontics [21].

So, this review article express a combination of data about efficacy of herbal irrigants besides conventional irrigants applied in pulpectomy of primary teeth. This review also suggested to discuss pharmacokinetics of herbal irrigants in the text book of dental pharmacology, where conventional irrigants are 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 identified in infected deciduous root canals. *Enterococcus faecalis, Porphyromonas gingivalis* & *Treponema denticola* reportedly most prevalent species isolated from deciduous root canals [23]. Facultative organisms are the main culprit for the pathogenesis of the diseases process & later on infected areas predominated by anaerobic organisms. From 22 infected primary root canals about 240 strains of bacteria 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 an endodontic irrigants. Methanol, ethanol, butathenol, acetone, 10% DMSO are the preferred solvent for herbal extracts. Ethanol is more familiar & more studied solvent. It has long history of being in our food & is preferred solvent for many flavoured compounds, coloring agents & bioactive or medicinal components. High biocompatibility, environmentally friendly & low toxicity, ethanol termed as 'green solvent'[26]. Next to ethanol is10% DMSO, an aprotic, relatively inert, stable at high temperature & nontoxic. It can maintain all pure properties of herbal agent being dissolved [27]. Other mentioned solvents are also preferred.

NEEM (Azadiracta indica A. Juss)

Also known as margosa, nimtree or Indian lilac. Neem tree is native to the Indian subcontinent & to the part of southeast Asia, but it is naturalized & grown around the world in tropical & subtropical areas [28]. Every part of neem tree has medicinal value. Hence, neem tree considered as "Village Dispensary" [29]. In 1992, 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] . Non-isoprenoid group are polyphenolic flavonoid, known for bactericidal & fungicidal action → causes lysis of the cell wall of root canal orgamisms, changing in cellular permeability, inhibiting enzyme activity, affecting protein synthesis & gene expression, inhibits neucleic 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]. 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 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 found superior to 2% NaOCl against *E. faecalis, C. albicans* & mixed culture [39]. Non- isoprenoid group inhibite glucan & some other virulence factor necessary for plaque & smear layer formation. Aquous extract of neem prevents smear layer formation by interfering microbial aggregation, growth, adhesion to hydroxyapaite & production of insoluble glucan [40]. Neem showed the highest smear layer removal efficacy than green tea extract & orange oil. Owing to low viscosity & better penetration to the canal irregularities It is efficacious in removing smear from apical third of the root canals [41]. Ethanolic extract of neem has better chelating capability without affecting microhardness of root dentin & on SEM observation there was all dentinal tubules found open in coronal, middle & apical third of the root canals , the efficacy of neem found to be superior than orange oil & propolis[42]. Chelating ability of neem supposed to its acid metabolites-gallic acid, caffeic acid, ferulic acid, nimbin. These organic compounds binds to the inorganic ions of smear layer like a 'claws of a crab' & assisted their removal [39]. Different vivo& vitro investigations were carried out between different herbal irrigants, where neem found superior to other irrigants in terms of antimicrobial efficacy & chealating ability. High biocompatibility due to neutral P^H (7.4), seems neem can be very efficient irrigation solution for primary teeth pulpectomy procedure. Its bitter taste is a barrier for its compliance & acceptance by the kido which can be easily overcome by adding sweeteners & flavors [32].

TRIPHALA

Word triphala Comes from 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 dissolve in 10% DMSO at a concentration of 125mg/ ml to make irrigation solution which has broad range of antimicrobial activity and is very effective in removal of smear layer [43]. Different bioactive ingredients and their action against root canal bacteria received particular attention about triphala. The antibacterial efficacy of tannic acid is described as their ability to pass through the cell wall upto the internal membrane & interfere with the sugar, amino acid uptake by bacteria what limits the growth of bacteria. inhibiting cell envelop transport proteins & enzymes. Tannic acid also interfere bacterial adhesion to the living surface resulting in bacterial cell death. It acts as an astringent also. Flavonoids acts by interacting with cell wall & proteins of bacteria & lipophilic flavonoids act by disrupting microbial membrane. Bioflavonoids & vitamin C speeded up the healing process through fibroblastic activity[44, 45]. Triphala contains citric acid which is mild organic chelant,binding to the inorganic ions of the smear layer & making them soluble. Hence, triphala holds promise to remove smear layer without affecting microhardness of root dentin[46,47]. Chelating ability of triphala is superior to sodium hypochlorite[47]. An In vitro investigation, triphala reveals hightest 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 while used as an irrigant in infecyed primary root canals[50]. In an in vivo investigation triphala demonstrating 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 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 produced by Apis mellifera bees, which is an adhesive resinous mixture. The mixture consisted of saliva, wax & exudates of bees that are used to seal the gaps in the hive & protects it from light, moisture, invaders & external factors[54]. Propolis' composition varies depending on the location, what tree & flowers bees are access to. Seasonal variation in 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 reduces E. faecalis (52.3%) count in post microbial sample. The author concluded that 25% propolis extract contains active ingredients & can be an efficient endodontic irrigants. Caffeic acid & flavonoids are the bioactive components responsible for antibacterial property of propolis. They induce the synthesis of insoluble glycan by inhibiting the enzyme glycosyltransferase[57]. Pinocembrin, a flavoinoid in propolis that possess antifungal activity by preventing fungal cell division & breaks down fungal cell wall & cytoplasm. Propolis has similar level of effectiveness while 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 macrophases. Propolis also inhibit production of prostaglandin by inhibiting lipoxygenase enzymes[59].

Morinda citrofolia (NONI)

Morinfa citrofolia (Rubiaceae), belongs to coffee family, native to southern Asia & Australasia, known as noni. Polynasian have been used noni as traditional medicine over 2000 years[60]. Wide range of therapeutic property 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 hydro soluble pectins, pectins & hemicelluloses in MCJ leads to differential disassembly of bacterial cell wall polymers. Thus, there is break down 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 can effectively inhibit the growth of C. albicans (16.6±0.3) while Amphotericin B (20.6±0.6) was a positive control. But the antifungal action of *M. citrofolia* varied with concentration & contact time[62]. 6% MCJ effectively inhibit E. faecalis count[63]. An in vivo comparison showed that MCJ irrigation solution as effective as 1% sodium hypochlorite & can be used as an primary tooth pulpectomy procedure[64].Low P^H (3.5) & acid metabolites (caproic acid, ursolic acid, caprylic acid) of 6% *M. citrofolia* extract has chealating 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, belongs to the Liliaceal family. More than 400 species of Aloe have been reported. Among them *Aloe barbadensis* Miller which

commonly referred 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 is the bioactive component 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 cell, respiratory metabolism of bacteria affected leading to cell death. Different in vitro investigations showed that 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 long time contact through the root canal. No studies available to suggest a specific duration or concentrations for aloe vera to act as a root canal irrigants. Furthermore, limited flow of the substances through the canal irregularities , it is considered as weak irrigation solution[67]. Aloe vera shows 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 Alliaceae family. It is a horticultural crop and one of the oldest common cultivated herbs originate particularly from central Asia[69]. Garlic popularly used as culinary ingredients. Its therapeutic property also well known. Organic sulphides, different phenolic compounds, tannins, flavonoids, alkaloids are responsible for its antimicrobial activity. Most abundant organic sulphid in garlic is diallyl thiosulphinate (DAS), that is Allicin[70]. Allicin is called natural antibiotic and just act 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. 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 metabolism of cysteine proteinase activity which involves in the virulence of the root canal organisms[71]. Anti -inflammatory activity of Allicin through inhibiting Neuclear 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 healing process through fibbroblastic proliferation[72]. Broad spectrum of antimicrobial coverage as well as biofriendly nature, garlic is a good choice in primary teeth pulpectomy procedure. Garlic is equally efficacious with sodium hypochlorite[73] & garlics' antimicrobial efficacy is better than calcium hydroxide[74]. Ethanolic extract of garlic contains ferrous iron, associated with the chelating ability by binding with the inorganic ions of smear layer. 64mg/ml of ethanolic extract of garlic can remove smear layer & on SEM evaluation the integrity of intertubular dentin was maintained at 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 converted to Allicin by enzyme allicinase, immediately after it is crushed. Allicin takes part in metabolism of cysteine in protein causing disruption in the epidermal junction 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 belongs to 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]. Carbohydrate (50%-70%) as starch is the major constituents of ginger rhizome. Gingerols, shogaols, paradols and terpene compounds are the bioactive compounds and are responsible for its several biological activities. Gingerol & shogaol are lipid soluble phenolic compound, responsible for antimicrobial activity and acts as a detergent. They break the phosoholipid membrane of root canal bacteria & cell wall of fungas. Cell become permeable and decrease the efflux, release 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 itshelf has antifungal activity, adding ginger powder to the ethanol produce synergestic action against *C. albicans*[82]. 10% ethanolic extract of ginger showed comparable result to 2.5%. NaOCl. Low risk, great wettability and pharmacokinetics of active compounds, ginger can be a risk-free irrigants for pulpectomy procedure[83].

GREEN TEA

Camellia sinesis, evergreen shrub which is a flowring plant belonging to the family of Theaceae, known as tea plant. Leaves & buds of *C. sinesis* plant used as tea which is a 2nd most popular drink in the world after water [84]. A number of bioactive components associated with its different health benifites—Polyphenols (Flavonols, flavandiols, flavonoids) & phenolic acid, L-theanine, caffeine, theobromines& volatile organic substances. Most aboundant 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 gyrase enzyme. Catechin generate hydrogen peroxide which causes damage to the bacterial cell membrane. There is cellular death due to loss of function & structural integrity[85]. Catechins affects absorption & metabolism of ions by interacting with metal ions and hence, act as a chealating agent. P^H of green tea is 7-10, thus it is a weak chealator. 3.5% green tea solution (Distilled water was a solvent) possess better antimicrobial activity against aerobic & anaerobic bacteria than normal saline[86]. 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 chealator because of it lacks acid component & high P^H [88].

TEA TREE OIL

Also known as melaleuca oil. *Melaleuca alternifolia,* 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, a- terpinene are the principle bioactive components associated with antibacterial & antifungal activity. The therapeutic concentration of tea tree oil is 2.5 to 5%, shows it's antibacterial property without any toxic effects[90]. These active metabolites attiributed to its hydrocarbon structure & intrinsic lipophilicity. Tea tree oil causes destruction of cell membrane structural integrity, hampers respiration of microbes, loss of intracellular ions leads 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 region of root canals[92].

TULSI (Ocimum sanctum)

Aromatic perennial plant in the family Lamiaceae, native to the India[93]. Eugenol, thymol, aerosol acid, caryophyliene, camphor, germacrene, are the main components. Eugenol (l-hydroxy2-methoxy-4-allylbenzene) discovered in O. *sanctum* L., has been found to be responsible for tulsi's smear layer removing & anti-inflammatory properties[94]. On SEM observation almost all dentinal tubules were opened with the use of tulsi irrigant where almost all tubules were covered with smear layer while using 2.5% NaOCl irrigant. Acidic P^H (3.5) also associated with its smear layer removing capability[95]. The Pharmacokinetic result of eugenol is exactly like $NSAID_s$ (Aspirin & Diclofenac). 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 and belongs to the Sapindacecae family. This deciduous tree found mainly in the lower foot hills & midhills of the Himalayas at the altitudes of 1200meters (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 pulp tissue dissolution capability of SM. Glycoside of triterpentine saponin reduces cell surface tension, thus increase membrane permeability. Furthermore, attraction of aglycon moiety for membrane sterol particularly cholesterol causing irreversible damage to the lipid bilayer membrane allowing cellular macromolecule to leak out which results in cellular lysis. An in vitro investigation 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 khasihills of Meghalaya by Which it is named. Modified specialized leaf which has a bulbous trap at the bottom part give it a shape of a pitcher[99]. The pitcher containing digestive enzymes & the P^H of the fluid is explained acidic (2 to 6 varies from species). Digestive enzymes and acidic P^H decompose the protein of insects when it 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 dissolved human pulp tissues at 7 hours[102]. Pulp tissue is loose connective tissue & the structural element of 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 50^{o}C & is extremely stable over a wide range of P^H (3-10) for over 30 days. The existance of carbohydrate moieties also reduces denaturation of nepenthesins & can be a potential irrigants 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 evaluation of herbal & conventiontional irrigants in regards 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	VMT	All dentinal tubele were opend after a final flush with 6%MCJ

		MTAD		
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 proven to be safe. Neem irrigation solution is remarkably good among all herbal endodontic irrigants in terms of antimicrobial activity. Triphala is a potent irrigants for primary teeth pulpectomy procedure and possess maximum chelating ability. Allicin of garlic has antimicrobial activity, aiding in removal of smear layer & possess pulp tissue dissolution capability to some extent. Hence can be used in all phases of pulpectomy procedure. Nimbin in neem, citric acid in triphala, acidic p^H of noni, eugenol in tulsi, catechin in green tea; make them more prominent in chelating ability. Acidic P^H of herbal endodontic irrigants lacks dissolution of pulp tissue. Some recent study concluded that *S. mukorossi* irrigants (SMM, SMB) can significantly dissolute a large volume of pulp tissue. Fresh secretion of *Nepenthes khashiana* can dissolve total pulp tissue but takes at a longer time period. There are lacunae of article found in regards of pulp tissue dissolution ability & demands further attention. The knowledge of plant- based pharmacology should be explore more & implication of explored knowledge in clinical dentistry is highly encouraged.

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