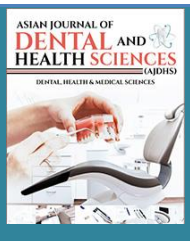

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Exploring the Efficacy of Natural Biomaterials in Endodontics

Dr Elizabeth Thomas *[1], Dr H Murali Rao [2], Dr B S Keshava Prasad [3], Dr. Suman C [4]

[1] Post Graduates, MDS, Department of Conservative Dentistry and Endodontics, DAPM RV Dental College, 1st Phase, J. P. Nagar, Bengaluru, Karnataka 560078

[2] MDS, Professor, Department of Conservative Dentistry and Endodontics, DAPM RV Dental College, 1st Phase, J. P. Nagar, Bengaluru, Karnataka 560078

[3] Professor and Head of the Department, Department of Conservative Dentistry and Endodontics, DAPM RV Dental College, 1st Phase, J. P. Nagar, Bengaluru, Karnataka 560078

[4] Lecturer, Department of Conservative Dentistry and Endodontics, DAPM RV Dental College, 1st Phase, J. P. Nagar, Bengaluru, Karnataka 560078

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Abstract

Endodontic therapy aims for thorough disinfection and three-dimensional filling of the root canal system, a goal often challenged by the complexity of root canal morphology. Traditional chemical irrigants and intracanal medicaments, such as sodium hypochlorite (NaOCl) and calcium hydroxide (CaOH2), are effective but can be cytotoxic and cause detrimental effects on periapical tissues and radicular dentin. Increasing antibiotic resistance and the adverse effects of synthetic agents have spurred interest in natural phytochemicals as alternatives. These phytochemicals exhibit promising antimicrobial, anti-inflammatory, and chelating properties, making them viable candidates for root canal irrigation, intracanal medicaments, and smear layer removal. The agents reviewed include Terminalia chebula [Triphala], Camellia sinensis [Green Tea] , Curcuma longa [Turmeric], Glycyrrhiza glabra [Liquorice], Propolis, Melaleuca alternifolia [Tea Tree Oil], Azadirachta indica [Neem] etc. These biomaterials have been studied in various combinations and against a variety of common intraoral bacteria like Enterococcus Faecalis. However, most of the conducted researches are in-vitro studies such as agar diffusion test. Despite their potential, there is a need for further comprehensive clinical and experimental studies to fully evaluate their biocompatibility, safety, and effectiveness compared to conventional treatments. This review aims to underscores the necessity of rigorous research and standardization protocols to confidently employ herbal extracts in endodontic practice.

Keywords: Endodntic irrigants, Herbal irrigants, Intracanal medicaments, antibacterial, Glycyrrhiza glabra, Azadirachta indica, Aloe vera

*Address for Correspondence:

Dr Elizabeth Thomas, DAPM RV Dental College, 1st Phase, J. P. Nagar, Bengaluru, Karnataka 560078

INTRODUCTION

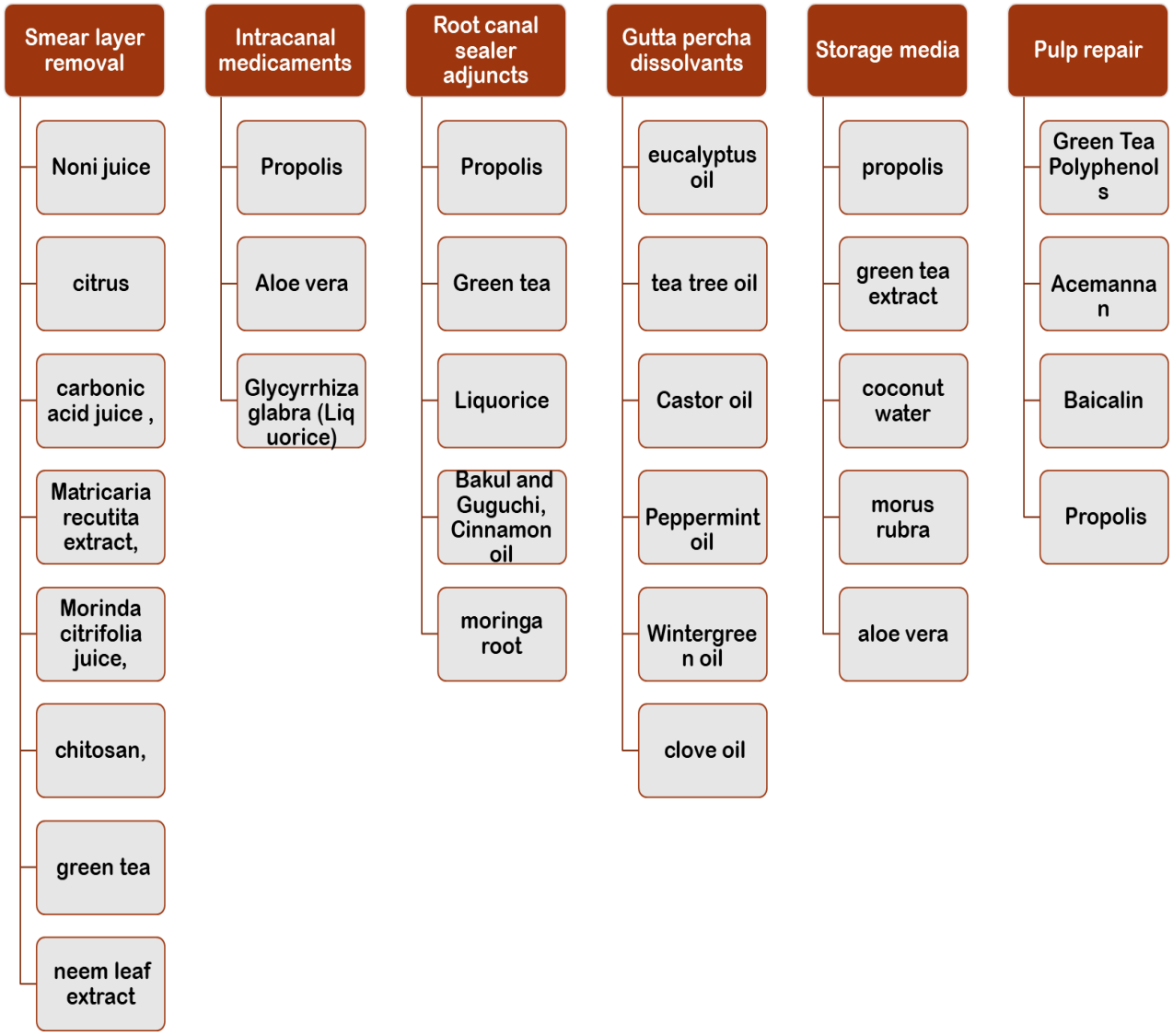
The paramount goal of endodontic therapy is the thorough disinfection and three-dimensional filling of the root canal system. The conjoint utilization of mechanical instrumentation, copious use of various irrigants and intracanal medicaments are important for the highest possible disinfection of root canals. However, the complexity of the root canal morphology poses a great challenge for disinfection till date[1].

The routinely used chemical irrigants such as sodium hypochlorite (NaOCl), ethylenediaminetetraacetic acid (EDTA) etc are documented to be cytotoxic and irritative to periapical tissues on extrusion. Certain Intracanal medicaments such as calcium hydroxide (CaOH2), Triple antibiotic paste, can weaken the radicular dentin by collagen breakdown, tooth discoloration, demineralisation of dentin etc[2].

The escalating resistance of pathogenic bacteria to antibiotics and chemotherapeutic agents has sparked a growing interest among researchers in exploring alternative products and treatment modalities for oral diseases[2]. Consequently, natural chemicals derived from plants and animals employed in traditional medicine are being considered as viable substitutes for synthetic chemicals. While herbs may offer a promising alternative to conventional treatments for oral health issues, there remains a research gap regarding their impact on oral tissues, mechanisms of action, and potential side effects. Thus, further research is warranted to investigate the efficacy of these traditional medicines[3].

CLASSIFICATION

The traditional medicines can be classified as[3] :(fig1)

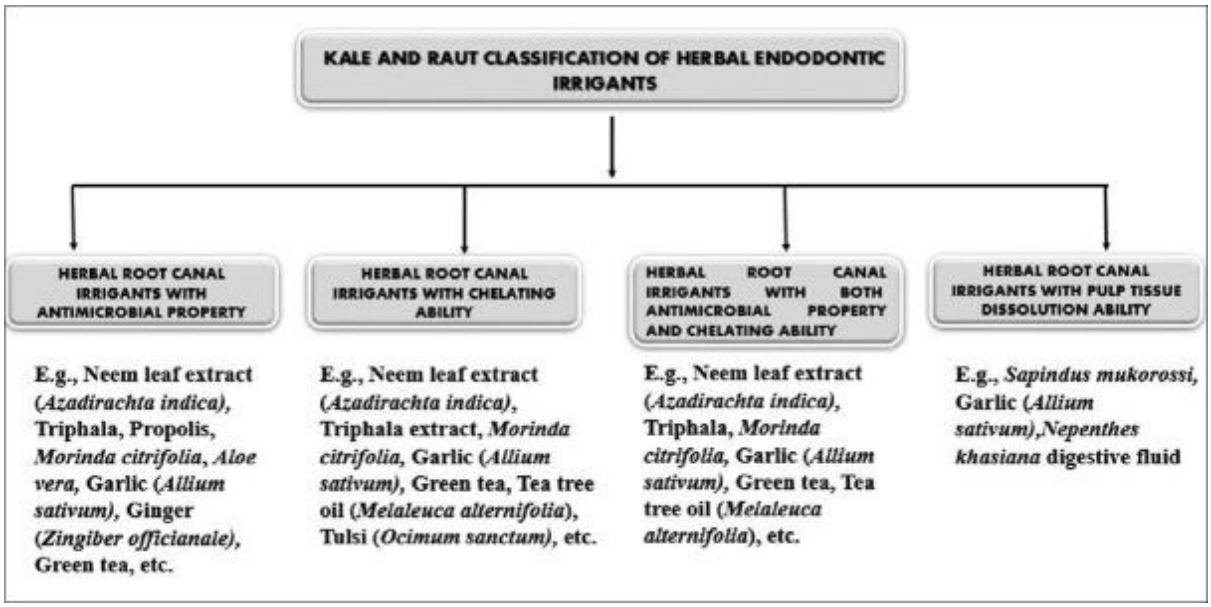


- **Smear layer removal**- Noni juice, citrus and carbonic acid juice , Matricaria recutita extract, Morinda citrifolia juice, chitosan, green tea and neem leaf extract
- **Intracanal medicaments**-Propolis, Aloe vera, Glycyrrhiza glabra (Liquorice)
- **Root canal sealer adjuncts**- Propolis and Green tea, Liquorice, Bakul and Guguchi, Cinnamon oil, moringa root
- **Gutta percha dissolvants**-eucalyptus oil, tea tree oil, Castor oil, Peppermint oil and Wintergreen oil, clove oil
- **Storage media-**propolis, green tea extract, coconut water, morus rubra, aloe vera
- **Pulp repair**- Green Tea Polyphenols, Acemannan, Baicalin, Propolis[3]

Kale and Raut's Proposed Classification of Herbal Endodontic Irrigants[4]

Based on properties(fig.2)

1. Herbal root canal irrigants with antimicrobial property
2. Herbal root canal irrigants with chelating ability
3. Herbal root canal irrigants with both antimicrobial property and chelating ability
4. Herbal root canal irrigants with pulp tissue dissolution [4]



SOME HERBAL EXTRACTS USED IN ENDODONTICS

Green Tea (*Camellia sinensis*)

Green tea, found commonly in semitropical environment of Southeast Asian platations,is derived from Camellia sinensis leaves. The catechins and the flavins are the microbiologically active ingredients in green tea. Phenolic acids such as chlorogenic acid, caffeic acid and flavonoids such as myricetin, kaempferol and quercetin are present in green tea. It also contains Gallic acid as a major component[5].

Tea polyphenol galloylated catechins, particularly Epigallocatechin-3-gallate (EGCG), have demonstrated remarkable antimicrobial and anti-cariogenic properties. Studies have shown that EGCG can effectively disrupt Gram-positive and Gram-negative bacterial membranes. Additionally, it can inhibit bacterial DNA gyrase by binding to the Adenosine triphosphate B subunit, thus preventing DNA supercoiling and ultimately leading to the demise of bacterial cells. [5,6].

Catechins have been discovered to act as an inhibitor against Streptococcus mutans and Streptococcus sobrinus at a minimum inhibitory concentration. The fluoride present in green tea may also play a role in enhancing the cariostatic action along with other tea components[5].

Extensive research has focused on the potential uses of green tea extract in restorative and endodontic dentistry. Studies have yielded promising findings, suggesting that green tea extract can effectively serve as a storage medium to minimize infections after tooth replantation. It can preserve PDL cell viability, and reduce root resorption and ankylosis. The study found that 90 percent cell viability was maintained for up to 24 hours[3]. However, comparative studies have also revealed limitations of green tea extract, particularly in its antimicrobial activity when compared to other agents such as propolis, triphala, and orange oil. Divia et al, found that green tea extract showed a greater reduction of E. faecalis colonies compared to Triphala and morinda. Furthermore, Sebatni et al's research in 2017 indicated that green tea extract exhibited relatively lower efficacy in removing smear layer compared to Neem leaf extract, Orange peel extracts, and Sodium hypochlorite (NaOCl)[7]. These findings suggest that while green tea extract holds promise in certain applications, further research and comparative studies are necessary to fully understand its potential benefits and limitations in restorative and endodontic dentistry.

Neem (*Azadirachta indica*)

Neem is widely recognized as a potent therapeutic herb in naturopathy due to its strong antioxidant and antibacterial properties, making it a highly effective alternative to sodium hypochlorite for root canal irrigation.[8].

The active compounds in neem, such as Nimbidin, Azadirachtin, and nimbinin, are responsible for its antibacterial properties[9]. The aqueous extract of neem stick and the gallotannin-enriched extract from Melaphis chinensis hinder the synthesis of insoluble glucans, leading to bacterial aggregation, and reducing the capacity of streptococci to colonize enamel surfaces. Both aqueous and ethanolic extracts of neem leaf inhibit S. mutans and E. faecalis. According to literature, neem leaf extract has significant antimicrobial activity against E. faecalis derived from inflamed root canal samples, demonstrating efficacy compared to 2% sodium hypochlorite[10].

The established biocompatibility of neem supports its application as an intracanal irrigant in endodontics. However, the inherent bitter taste attributed to nimbidin presents an undesirable attribute. This limitation can be addressed by integrating sweeteners into the neem extract.

Aloe vera (*Aloe barbadensis*)

Aloe vera extract is known for its potent antibacterial, antifungal, and anti-inflammatory properties. The active constituents of the gel, aloin, and aloe-emodin, contribute to its therapeutic effects[9].Widely used in Endodontics, Aloe vera serves as both a medicament and an irrigant due to its effectiveness against S. pyogenes and E. faecalis, attributed to the presence of anthraquinone which inhibits the formation of these organisms[11].

In a 2015 study conducted by Swati et al, compared the antimicrobial activity of hydroalcoholic extract of Aloe vera, garlic, and 5% NaOCl against E. faecalis. The results showed that the saturated hydroalcoholic extract of Aloe vera exhibited the highest zone of inhibition against E. faecalis[12].

The ability of Aloe vera to inhibit the COX pathway and reduce prostaglandin E2 production makes it a robust anti-inflammatory agent. Notably, Aloe vera has been recognized for its ability to penetrate deeper layers of the epidermis when applied topically[10].Another study by Seth et al. in 2016 indicated that compared to tea tree oil and NaOCl ,Aloe vera demonstrated the highest zone of inhibition against E. faecalis

[7]. Additionally, Aloe vera exhibits wide spectrum of antibacterial activity compared to other natural extracts, against various oral pathogens[13].

Triphala (*Terminalia Chebula*)

Triphala, a herbal blend originating from India, consists of dried and powdered fruits from three medicinal plants. Terminalia bellerica, Terminalia chebula, and Emblica officinalis. It is found to be safe and contains active components such as Gallic acid and Tannic acid that provide beneficial physiological effects beyond its healing properties, including antioxidant, anti-inflammatory, and radical scavenging activities[14]. Triphala acts by inhibiting the cell division or by causing damage to the cell walls of the bacterium[7].

Triphala has excellent antimicrobial action towards gram positive and gram negative micro organism particularly Staphylococcus aureus, Staphylococcus epidermidis, Bacillus subtilis, Escherichia coli and Pseudomonas aeruginosa. This is due to presence of various chemical parts like flavonoids, terpenes and alkaloids. Triphala demonstrates remarkable bacteriostatic and bactericidal activities at an exceptionally low concentration of 50 µg/ml. Moreover, a 5% solution of Triphala exhibits an inhibition of approximately 83% against Streptococcus mutans[10,15].

Chitosan

Chitosan, a biopolymer resulting from the partial deacetylation of chitin sourced from crustacean exoskeletons, serves as an efficacious drug carrier, facilitating a gradual and controlled release of intracanal medicament. It also exhibits bio-adhesive properties and minimal toxicity[16]. Chitosan as a vehicle can enhance the antibacterial properties of an intracanal medicament. It has been linked to antibacterial effects on Streptococcus mutans, Actinomyces actinomycetemcomitans, and Porphyromonas gingivalis[17]. Chitosan has a broad spectrum of antibacterial properties, high chelating ability in acidic conditions, biocompatibility, and biodegradability. Studies have demonstrated that chitosan-based scaffolds promote pulp regeneration and dentin formation by inducing mineralization. Chitosan-based scaffolds contain tricalcium phosphate that promotes high expression of mineralization markers, such as osteopontin and alkaline phosphatase, and dentin formation by human periodontal ligament cells (HPLCs)[16].

Turmeric[*Curcuma longa*]

Turmeric plays a significant role as a spice, food preservative, and coloring agent in the culinary traditions of India, China, and Southeast Asia. It has a rich traditional medicinal history for addressing various health concerns. Curcumin, the primary yellow bioactive compound in turmeric, has demonstrated a diverse array of biological effects, including antimicrobial, anti-inflammatory, and antioxidant properties. Numerous studies have established strong connections between these activities and curcumin, laying a solid foundation for exploring its potential applications in endodontics[14].

The antimicrobial properties of turmeric stem from curcumin's ability to disrupt the assembly of a protein- Filamenting Temperature-Sensitive Mutant Z (FTSZ) profilaments and enhance the GTPase activity of FTSZ, which are harmful to bacteria. When used as an irrigating solution, turmeric prevents the formation of biofilms by eliminating the extracellular polymeric substance matrix, which serves as a source of nutrients for further bacterial growth[11].

In 2013, Neelakantan et al. examined the antimicrobial effectiveness of curcumin against Enterococcus faecalis biofilm formed on tooth substrate in vitro, comparing it to chlorhexidine and sodium hypochlorite[18]. The findings revealed that sodium hypochlorite displayed the highest antibacterial activity, followed by curcumin and CHX[9].

A recent report indicated that aqueous preparations of curcumin exhibit a phototoxic effect against both gram-positive and gram-negative bacteria. This discovery paves the way for further research into the use of turmeric in the photodynamic therapy of root canal systems[14].

Tea Tree oil (*Melaleuca alternifolia*)

Tea tree, an indigenous Australian plant, produces oil with notable antiseptic and antifungal properties, along with a mild solvent action, rendering it a promising candidate for implementation in dental care. Moreover, its principal active constituent, terpinen-4-ol, typically accounting for 30-40% of the oil, suggests potential utility in dissolving necrotic pulp tissue, particularly in the context of root canal treatment[14]. Based on a study by Seth et al, tea tree oil exhibited a higher zone of inhibition against C. albicans compared to Aloe vera and NaOCl. However, it had a lower zone of inhibition against E. faecalis compared to Aloe vera and NaOCl. In addition, it showed a higher zone of inhibition against a mixed culture compared to Aloe vera, but lower than NaOCl[7].

Clove (*Syzygium aromaticum*)

Both Indian and Chinese traditional medicine have historically utilized clove flowers and oil to address a variety of health issues. It is an evergreen plant with strong phenolic smell and pungant taste[19]. Active constituents are Acetyl eugenol, betacaryophylle, vanillin, crategolic acid, and tannins[7]. It destroys the integrity and reduces biofilm quality, disrupts the bacterial membrane, cause cytoplasm leakage, and form vesicles on the surface of cytoplasmic membrane[19].

In their study, Madhavan et al. investigated the potential of clove oil to amplify the antibacterial efficacy of intracanal medicaments. The findings reveal that when combined with other intracanal medicaments such as triple antibiotic paste and calcium hydroxide, clove oil exhibits enhanced antibacterial activity against E. faecalis[7].

Propolis

Propolis is a resinous material collected by honeybees from various plant species and blended with wax and other substances. Scientific research has revealed its antioxidant, antibacterial, anti-fungal, antiviral, anti-inflammatory, anti-tumor, and immunomodulating properties. Current research involving propolis in dentistry spans many fields and highlights its antimicrobial and anti-inflammatory activities, particularly in cariology, oral surgery, pathology, periodontics, and endodontics[14].

Propolis is known for its antimicrobial properties, which are attributed to flavonoids and esters of caffeine. Additionally, it contains an unidentified, water-soluble component that absorbs ultraviolet light and hinders bacterial DNA-dependent RNA polymerases[20].

Liquorice(*Glycyrrhiza glabra*)

Liquorice has been traditionally used in Chinese medicine, owing to its anti-inflammatory, anticarcinogenic and antiviral properties. The sweet taste of liquorice root is due to glycyrrhizin, a triterpenoid compound[9]. This compound is a mix of potassium-calcium magnesium salts of glycyrrhizic acid and can range from 2–25%. Within natural saponins, glycyrrhizic acid is characterized by a hydrophilic segment consisting of two molecules of glucuronic acid and a hydrophobic fragment known as glycyrrhetic acid. The antimicrobial effect of Liquorice extract against E. faecalis, may be related to the Glycyrrhizin. The mode of action of antibacterial effects of saponins seems to involve membranolytic properties .It has

been studied for its action against S.Mutans[3]. Studies have demonstrated marked inhibition of adherence and growth of Streptococcus Mutans in plaque. Liquorice has demonstrated higher biocompatibility with fibroblast cells in comparison to calcium hydroxide, which caused severe toxicity to the cells[14].

Shikakai (*Acacia Concinna*)

Shikakai, a thorny plant prevalent in central and south India, has been traditionally utilized for hair care and as an oral rinse for addressing halitosis, dental caries, mouth ulcers, and gum bleeding. The methanol extract of the plant's bark has exhibited antibacterial activity against Staphylococcus aureus, gram-positive bacteria such as Streptococcus mutans, Lactobacillus casei, and Lactobacillus acidophilus. Active constituents encompass alkaloids, flavonoids, phytosterols, saponins, phenolic compounds, and tannins.[23]

A recent study conducted by Aravind et al. aimed to assess the cytotoxicity of shikakai on periodontal cells in comparison to sodium hypochlorite. The research findings indicated that the extract derived from acacia concinna demonstrated increased cell viability with periodontal cells when contrasted with sodium hypochlorite at both 1-hour and 24-hour intervals[24]. Thus far, there has been limited research investigating the properties of shikakai concerning its potential application in dentistry.

OTHER APPLICATIONS

One of the crucial requirements for an intra-canal medication is its stability and sustained release over an extended period. According to Digole VR et al , Aloe vera does not exhibit significant activity against Enterococcus Faecalis compared to synthetic alternatives. This could be due to its inferior molecule binding ability to E. faecalis and inferior potential to alter its membrane permeability and structural integrity to thus reduce its resistance. According to Patri et al, Propolis and curcumin showed considerable antibacterial property, but not as much as triple antibiotic paste[17].

A study compared the smear removal and antibacterial properties of chitosan nanoparticles (CNPs) to sodium hypochlorite(NaOCl) and Ethylenediaminetetraacetic acid (EDTA) which demonstrated that irrigation with CNP effectively removes the smear layer and inorganic contents from the dentin. Additionally, CNP demonstrates significantly greater resistance to biofilm formation compared to NaOCl and EDTA, while exhibiting a chelating effect similar to that of EDTA. A major drawback of EDTA is related to its dentin demineralization, unlike which chitosan showed remineralization capacity as well as resistance to bacterial adherence. These findings advocate the use of CNPs as a substitute for EDTA as a final root canal irrigant[16].

Numerous studies have demonstrated that extracts of Morinda citrifolia, German chamomile, Propolis, Tea tree, Triphala etc possess the capability to effectively eliminate the smear layer. 6% concentration of Morinda citrifolia (MC) has shown effective antimicrobial activity when used as an intracanal medicament as well as smear layer removal. A majority of studies suggest that Azadirachta indica (AI) is the most effective against E. faecalis, followed by propolis, then Morinda citrifolia (MC). There are contradictory results regarding the effect of Aloe vera on E. faecalis[9,21]. This could be due to the variation in isolation techniques as well as differences in chemical composition of aloe vera pulp acquired from different geographical sites[21].

The literature search shows that most of the studies conducted on the efficacy of herbal extracts are in vitro antimicrobial studies. It is important to determine the cytotoxicity of these agents for its effective use in clinical scenarios. Employment of these natural biomaterials in root canal disinfection requires more clinical trials, in-vivo studies, biocompatibility tests etc[22].

CONCLUSION

The study of herbal extracts for root canal disinfection has created new avenues for promising research. When used with proper knowledge, herbal extracts are generally safe; however, caution is warranted as their misuse can lead to adverse effects. While preliminary findings from laboratory studies suggest potential, it is crucial to prioritize comprehensive clinical, longitudinal, preclinical, and experimental studies to assess the biocompatibility and safety of herbal products before confidently endorsing their implementation in root canal disinfection. Notably, herbal extracts represent a valuable prospect for root canal disinfection, serving as effective irrigants, intra-canal medicaments, and agents for removing the smear layer[3,14,21].

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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