

Role of Herbal Extract in Intracanal Medicament: An Update Review

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Abstract

Antimicrobial drug resistance is a major problem in the medical and dental fields. Because of these health professionals are inventing or looking for alternatives such as herbal products, which are safe and provides the significant antibacterial properties. Among many, herbal products, some herbs are rich in phytochemical compounds. These phytochemicals are used in producing phytomedicines which affects the human body. In dentistry, especially in the field of endodontics, extract of phytomedicines are very effective in various research. The purpose of endodontic treatments is to eliminate the bacteria from the root canal system and prevent its recontamination. Intracanal medicaments are used in a root canal to eliminate the remaining bacteria after instrumentation and irrigation, to reduce the inflammation of periapical tissues and to prevent from reinfection of the root canal system. Various herbal products have been widely used as analgesic, anti-inflammatory, sedatives, and antibiotics. Thus, this review aims to provide an update of the various herbal agents that can be used as intracanal medicaments.

Keywords: Herbs; Intracanal medicament; Root canal system.

Introduction

It is very difficult to disinfect the complex anatomy of the root canal system. The progression of periapical lesion, endodontically is clearly indicated by the presence of micro-organisms in the root canal system.¹ Bacteria are capable of invading and residing deeply within dentin, cementum around the periapex in infected root canal. Their control and elimination are the goal of endodontic therapy.

Endodontic therapy includes instrumentation and irrigation to remove microbial pathogens and debris from the root canal system. The use of interappointment medication has been widely used which helps in reducing the bacteria remaining after root canal preparation and providing a favourable

environment for periapical tissue. Hence, it reduces periapical inflammation, pain and induces healing. Intracanal medicament such as calcium hydroxide cause weakening of radicular dentin because it breakdowns the collagen.² TAP using minocycline, ciprofloxacin and metronidazole causes demineralization of dentin and discoloration of tooth.³ These also include the developing antibiotic resistance in certain strains of root canal bacteria⁴ and allergic reaction in sensitive patients.⁵

Therefore, herbs are better alternatives⁶⁻⁸ to disinfect the canal as intra canal medicament because of their more biofriendly nature. They are rich in antioxidant, sedative, antimicrobial activity, anxiolytic and anti-inflammatory properties which make them ideal for root canal disinfection.²

Various kind of herbs used in endodontic therapy as root canal medicaments

Spilanthes acmella

Spilanthes acmella is an important medicinal plant also known as antitoothache plant or Karkara. Due to high medicinal usage, its demand has increased worldwide. *Spilanthes acmella* plant contains a diverse group of highly valuable bioactive metabolites such as alkaloids, tannins, essential oil and flavonoids.⁹ *Spilanthes* (Compositae or Asteraceae) is a genus comprising of over 60 species that are widely distributed. Flower head of *Spilanthes acmella* have shown strong antimicrobial activity against common pathogens such as *Streptococcus mutans*, *E. faecalis*, *Staphylococcus aureus*, *Escherichia Coli*, *C. albicans*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Proteus vulgaris*, *Staphylococcus albus* and *Bacillus subtilis*.¹⁰ Rosas-Pinon et. al. in 2012^[11] showed that *S. Mutans* was the most sensitive to plant extracts. Another study was done in-vitro by S. Satyaprasad et. al. in 2015; it concluded that *Spilanthes acmella* possesses remarkable antibacterial and antifungal activity against root canal pathogens such as *E. faecalis* and *C. albicans* in endodontic failures cases when compared with calcium hydroxide medicaments.^[12]

Propolis

Now days, Propolis (Bee glue) has been widely used as popular medicine which is produced by honey bees. It has a property of antimicrobial, anti-inflammatory and antioxidant. In propolis, flavonoids and cinnamic acid derivatives are the two major active components. An ethanol extract of propolis can promote the bone regeneration and also induce the formation of hard tissue bridge.¹³

Madhubala et. al.¹⁴ showed that TA mixture and propolis as intracanal medicaments against *E. faecalis* had equal antibacterial effect on the seventh day. Another study which was conducted by Abhishek Parolia et. al. in 2010 also showed that propolis could be used as an alternative intracanal medicament because it has significant antibacterial activity against *E. faecalis* present in the root canal when compared with three intracanal medicaments.^[15] Awawdel et. al. found that propolis is very effective in rapidly eliminating *E. faecalis*.^[16]

Turmeric

The Indian golden spices ‘Turmeric’ is used since ancient times in beauty enhancement and to cure diseases. Scientific name of turmeric is *Curcuma longa*, which

belongs to ginger family *Zingiberaceae*. The Latin name is derived from ‘Kikum’ which means ‘saffron’.¹⁷ Turmeric is a perennial plant with orange oblong tubers 2 or 3 inches in length, one inch in diameter and pointed or tapering at one end. Dried form of it is yellow powder which is similar to ginger and having bitter, slightly acrid, yet sweet taste.

Turmeric is used in dentistry in a variety of ways such as plaque detection system, pit and fissure sealant, subgingival irrigant, therapy for pre-cancerous lesion and intracanal medicament.¹⁷ In 2014, Jay Chamele and Chetan Bhat concluded that calcium hydroxide can be substituted with curcumin as an intracanal medicament.¹⁸ Hemanshi Kumar in 2013, evaluated the antimicrobial efficiency of *Curcuma longa*, *Tachyspermum ammi*, chlorhexidine gluconate, and calcium hydroxide on *Enterococcus faecalis*. He concluded that turmeric can be used as intracanal medicament in endodontic failure cases.¹⁹

Neem

Neem has been broadly used in various alternative medical specialities.²⁰ Neem (*Azadirachta indica*, A. Juss) considered as holy medicinal tree of India. It is also known as “Indian neem/ margosa tree” or “Indian Lilac” and “Persian Lilac”.²¹ It belongs to the *Meliaceae* family. It has a wide range of biological activities, such as anti-inflammatory, antimicrobial, antimalarial, antifungal, antiviral, antioxidant, analgesic, antipyretic, immunestimulant, anti-acne, anti-fertility, anti-hypoglycemic, nematocidal and anti-cancer properties.^{22,23} Every part of the tree has medicinal properties including the leaves, bark, and seeds.²⁴

In 2013 Hegde et. al.²⁵ concluded that neem leaf extract showed the highest zone of inhibition against *C. albicans* and *E. faecalis*, using the agar diffusion method when compared with the antibacterial efficacy of 2% sodium hypochlorite, propolis, turmeric, and liquorice. Another study was done by C.S. Kusuma et. al., found that 2% chlorhexidine was the best Intracanal Medicament which consistently decreased the colony forming unit count of *E. faecalis* at days 1, 3 and 5 at both depths of 200µm and 400µm and neem showed similar activity compared to chlorhexidine and better activity than calcium hydroxide and alovera.²⁶ The study of Mohammed Mustafa, concluded that neem leaf extract has significant antimicrobial activity against *E. faecalis* and it can be used as an intracanal medication.²⁷

Allium Sativum

It is also called garlic. It has been known to have broad spectrum of antimicrobial properties for both bacteriostatic and bactericidal activities because of the presence of allicin as main active component of garlic. Allicin destroys cell wall and cell membrane of root

canal bacteria. It also has immune regulatory function.²⁸ Ourvind J. S. Birring et. al. in February 2020,²⁹ assessed the anti-microbial efficacy of garlic extract against *Enterococcus faecalis* biofilm and its penetration ability into root dentin. They found that garlic is an effective and biocompatible anti-microbial agent with good dentinal penetration property. In an in-vitro study, Iwaiokun BA et. al. showed the antimicrobial efficacy of aqueous garlic extract and use of garlic in health and herbal remedies.^[30] Thus, it could be an effective intracanal medicament but further studies are needed for confirmation its concentration as an intra canal medicament.

Rhus plant

The Rhus plant is enriched with tannins and gallic acid which have antibacterial, antimicrobial, antifungal, antioxidant properties. It also reduces periapical inflammation and has bactericidal properties. Water extracts from Rhus plants help in unblocking the dentinal tubules.³¹

Aloevera gel

The green part of the aloe-vera leaf and clear gel is used to produce juice or dried substance. It contains aloins and aloe-emodin as main active constituents of the gel. Leaf extracts of aloevera contain anthrax quinone which has antibacterial properties^{32,33} and especially effective agent against the formation of *Streptococcus pyogenes* and *E. faecalis*.³⁴ It is rich in vitamins, enzymes, minerals, lignin, sugars, saponins, salicylic acids, and amino acids. It synthesizes protein in bacterial cells which acts as antibacterial property. Bhardwaj et.al. in 2012 had also reported that aloe-vera gel has antimicrobial properties against various species of microorganisms, including *E. faecalis*.³⁵ Aloevera extract can also be used for lubrication of root canal. In 2019, RupamTripathi et. al. compared the antimicrobial efficacy of 2% chlorhexidine gel, calcium hydroxide and aloe-vera extracts as an intracanal medicament against *Enterococcus faecalis* in their in-vitro study. They found that antimicrobial efficacy of Aloe-vera was comparable to 2% chlorhexidine gel for shorter duration as mean CFU were lowest for both medicaments in 24 hrs and highest in 7 days.³⁶ In 2016, Bijo Kurian et. al. concluded that mushroom and Aloevera extracts can be used as an alternative intracanal medicament for resistant and retreatment cases.³⁷

Lemon paste

Lime is a natural source of citric acid (Ph=1.68) with lower acidity. Citric acid acts as a chelating agent by removing the smear layer. A chemical product of citric acid has some irritating effect when compared to natural lemon solution. In their study, Abuzied ST, Eissa SA showed that fresh lemon solution has wide antibacterial

properties which make it an ideal root canal medicament without any side effect.³⁸ In 2019, Ramamurthy Varshini et. al. evaluated the antimicrobial efficacy of aloe vera, lemon, ricinus communis, and calcium hydroxide as intracanal medicaments against *Enterococcus faecalis* using a confocal microscopy. In their experiment, complete elimination of *E. faecalis* was not achieved in any of the groups but calcium hydroxide showed more effective reduction of *E. faecalis* followed by aloe vera, lemon and ricinus communis.³⁹

Triphala

Triphala means 'three' (tri) 'fruits' (phala). It is an ayurvedic rasayana which contains dried and powdered fruits of three different medicinal plants-*Emblica officinalis* (Amalaki), *Terminalia chebula* (Halituki) and *Terminalia bellirica* (Bibhitaki).⁴⁰ It is also known as 'three myrobalan'. Due to the strong antioxidant activity of Triphala, it may have many of the biological properties. It has a potential of anti-bacterial and anti-inflammatory activity.⁴¹ *Terminalia bellirica* was the best antioxidant followed by *Emblica officinalis* and *Terminalia chebula*. Ellagic and gallic acid are major components of *terminalia bellirica* and *emblica officinalis* also has several gallic acid derivatives. Due to the phenolic nature of these active ingredients, it may be responsible for free radical scavenging which is generated by the bacteria and antimicrobial properties which prevent the formation of biofilm. Tannic acid is the major ingredient product of the ripe fruit of *Terminalia chebula*, *Terminalia bellirica* and *Emblica officinalis*.⁴² Triphala has the constituents of tannins, quinones, flavonoids, gallic acid, and Vitamin C which makes it an ideal chelating agent to remove the smear layer. It is used as an alternative to NaOCl for root canal irrigation.⁴³ S. Swapnil et. al. evaluated in an in-vitro study, the antimicrobial efficacy of Triphala and Curcumin extract in comparison with Calcium hydroxide against *E. Faecalis* as an intracanal medicament in 2017. According to them, all the tested medicaments have antibacterial activity but curcumin revealed the least antibacterial activity as compared with triphala and calcium hydroxide. Calcium hydroxide exhibited highest zone of inhibition in 24 hrs.⁴²

Liquorice

Liquorice is the root of *Glycyrrhiza glabra* and is also called as sweet wood. It is more biocompatible material and used in the treatment of eye diseases, peptic ulcers, liver diseases, and throat infections.⁴⁴

Badr AE et al, evaluated the antibacterial and cytotoxic effects of liquorice when used as an intra canal medicament. They found that liquorice had a potent bactericidal effect on *E. faecalis* and compatible with fibroblasts in tissue culture when compared with calcium hydroxide.⁴⁵ In 2019, an in-vitro study

was done by M. Chittrarasu et. al. In their study, they evaluated the antimicrobial efficacy of liquorice at various concentrations against *Enterococcus faecalis* biofilm at time-dependent variables in 24 h, 48 h, 72 h, 120 h, and 168 h. They found that at 24 h and 48 h *E. faecalis* biofilms were highly susceptible to liquorice at concentration of 3 and 4 g and concluded that liquorice extract can be used as an intracanal irrigant and root canal medicament.⁴⁴ Liquorice shows effective bacteriocidal activity against *E. faecalis* and is used as an effective root canal disinfectant.⁴⁶ In 2019, IB Geeta et. al. found that combination of licorice and calcium hydroxide completely inhibited the growth of *E. faecalis* and this combination showed best result in both microbial inhibition concentration and in docking mechanism.⁴⁷

Arctium Lappa

Arctium lappa is a herbal plant which is acclimatized in Brazil and obtained from Japan. It is prepared from ethyl acetate and has been widely used in therapeutic applications. It has anti bacterial, anti fungal and anti oxidant properties including platelet anti-aggregating effect, and also used in human immunodeficiency virus-inhibitory treatment. It is used for intracanal medicament due to the presence of ethyl acetate. Julaina Vianna et. al.⁴⁸ observed that when *Arctium lappa* is used as an intracanal medicament, it exhibited a great microbial inhibition potential. In other in vitro study, Gentil Marcelo et. al. found that the plant of *Arctium lappa* has antimicrobial property which prevents the formation of biofilm and is also effective against harmful pathogens. They tested on mixed bacterial suspension of *Escherichia coli*, *Pseudomonas aeruginosa*, *Streptococcus mutans*, *Lactobacillus acidophilus*, and *Candida albicans*. It was found to inhibit the growth of all microorganisms and hence it can be primarily used in the treatment of root canal infections.⁴⁹ Andrada Tanea et. al. concluded that mix extract of *Arctium lappa* root powder and Aloe vera gel is able to inhibit very resistant microorganisms, like *Enterococcus faecalis* and *Candida albicans*.⁵⁰

Morinda citrifolia

It is also called as Indian Mulberry. It is used in a wide range due to its biocompatibility, anti bacterial, anti-inflammatory, anti viral, anti oxidant and analgesic effects. L-asperuloside and alizarin are the primary components of *Morinda citrifolia*.⁵¹ Other phytochemicals are present in it such as lignans, flavonoids, oligopolysaccharides, and catechins. It also exhibits antitumor, anthelmintic, hypotensive, analgesic, anti-inflammatory, and immune enhancing properties. It can inhibit carcinogen-DNA adduct formation and have the property of effective chelating agent.^{52,53} In an in vitro study by Anuj Bhardwaj et. al. compared the antimicrobial activity of natural extracts of *Morinda citrifolia*, Papain

and Aloevera (all in gel formulation), 2% Chlorhexidine and Calcium hydroxide against *E. faecalis*. It showed that Chlorhexidine has 100% inhibition from day 1-5 followed by *Morinda citrifolia* which showed 86.02% inhibition from day 1-5 and calcium hydroxide had the least antimicrobial activity against *E. faecalis*. Thus it was concluded from the study that *Morinda citrifolia* could be used as an effective intra canal medicament.⁵⁴

Agaricusbisporus – Mushroom

Mushrooms contain low molecular weight (LMW) and high molecular weight (HMW) active compounds which possess medicinal properties such as immune modulatory, anti-inflammatory, antiviral, antioxidant, and antimicrobial properties with higher antimicrobial activity against Gram-positive bacteria.⁵⁵

According to Lipinski's rule of active drug, the low molecular weight compounds (plectasin, confuentin, grifolin, and neogrifolin) show antibacterial activity against potential oral pathogens.⁵⁶ Low molecular weight fraction of mushroom extract (molecular weight around 12 kDa) may have the capacity to penetrate deep into dentinal tubules and hence better antibacterial property.^{56,57}

Abidin et. al. described their mechanism of action was predominantly on the cell membrane by disrupting its structure, blocking membrane synthesis, and inhibition of cellular respiration thereby causing cell leakage and cell death.⁵⁸

In a study conducted by Kurian et. al.⁵⁹ Mushroom demonstrated a better antimicrobial efficacy followed by A. vera and calcium hydroxide. Mushroom can be considered in situations where there is a limitation of time and the gel form of extract increases the contact time, which enhances its performance and can be considered as an intracanal medicament in resistant cases.⁶⁰

Ricinuscommunis

It is rich in ricinoleic acid, also known as castor acid, is an unsaturated fatty acid and the main bioproduct obtained from the *Ricinus communis* and can be used as a root canal irrigant as well as an intracanal medicament.⁶¹ It also shows high repairing and osteogenic potential^{62,63} and anti-inflammatory action.⁶⁴ The natural polyol derived from the castor oil plant or tropical castor bean (*Ricinus communis*) has emerged as a potential graft material for dental application as a bone substitute.⁶⁵

In a study conducted by Marcia Carneiro Valera et al, the antimicrobial activity of auxillary chemical substances and natural extracts against *Candida albicans* and *Enterococcus faecalis* in root canals was evaluated in vitro. It was found that *Ricinus*

communis extract was able to completely eliminate *Candida.albicans* and it was also able to significantly reduce the amount of *Enterococcus faecalis*.⁶⁶

In another study by Lucas da Fonseca Roberti Garcia et al, it was observed that calcium hydroxide and Ricinus communis oil paste had better activity than calcium hydroxide and propylene glycol paste against microorganisms commonly found in endodontic infections.⁶¹ Therefore, the association of ricinoleic oil with calcium hydroxide could be a viable alternative intracanal medication.

Casearia Sylvestris (*Gulkhair – Wild Coffee*)

Casearia Sylvestris also known as guacatonga is a medicinal plant commonly found in tropical America and Brazil that offers a wide range of uses: antiseptic, healing and antimicrobial activity. It is rich in phospholipase A2 inhibitors making it an ideal anti-inflammatory drug to be used for the intracanal medicament.⁶⁷ This reduces the acute phase of inflammatory process and prolongs the regenerative phase.⁶⁸ The C. sylvestris extract is effective in inhibiting isolated class I and II phospholipases A2, and the extract is partially effective against edema formation⁶⁹ and has lower irritant potential.⁶⁷

In a study by Silva FB et al it was found that propolis showed the least anti-inflammatory exudates followed by Casearia sylvestris extract when compared to Otosporin, a corticosteroid-antibiotic solution. Thus, Casearia sylvestris could be a valid alternative for a short term intra canal medicament in cases of pulp and periapical inflammatory processes.⁶⁷

Psoralea corylifolia Linn (*Bakuchi-Psoralea seeds*)

P. corylifolia extract contains a number of bioactive compounds including flavonoids, coumarins, meroterpenes and benzofuran glycosides that are the molecular basis of its action.

Neobavaisoflavone is isolated from fruits and seeds of *P. corylifolia*.⁷⁰ It has properties to injure the cell membrane and inhibit DNA polymerase. Thus, is used as an effective treatment for *E. faecalis*.⁷¹ Bakuchiol was isolated from the seeds of *Psoralea corylifolia* and possesses antioxidant, antimicrobial and anti-inflammatory properties. It showed bacteriocidal effects against all bacteria tested, including *Streptococcus mutans* (Growth was inhibited in a bakuchiol concentration-dependent manner), *Streptococcus sanguis*, *Streptococcus salivarius*, *Streptococcus sobrinus*, *E. faecalis*, *Enterococcus faecium*, *Lactobacillus acidophilus*, *Lactobacillus casei*, *Lactobacillus plantarum*, *Actinomyces viscosus*, and

Porphyromonas gingivalis, with minimum inhibitory concentrations ranging from 1 to 4 µg/mL and the sterilizing concentration for 15 min ranging from 5 to 20 µg/mL.⁷²

Vaccinium macrocarpon – Cranberry

Cranberry or *Vaccinium macrocarpon* is a shrub which was used in the 17th century mainly as a remedy to solve stomach and liver problems and also to relieve scurvy. Cranberry extracts are a rich source of numerous biologically active ingredients such as flavonoids, polyphenols, anthocyanins and condensed tannins. They have antibacterial, antimicrobial and antiadhesive properties, thereby preventing inhibition of many pathogens and biofilms.⁷³ These are thought to prevent dental caries by inhibiting the colonization of dental structures and inhibiting the production of acids by cariogenic bacteria such as *Streptococcus mutans*. They inhibit the activity of proteolytic enzymes, which are responsible for periodontal destruction and thus, reduce the inflammatory processes. It also inhibits coaggregation of periodontal pathogens and adherence of *Porphyromonas gingivalis*.⁷⁴

A highmolecular-weight fraction prepared from cranberry juice inhibits the coaggregation of many oral bacteria⁷⁵ and affects dental biofilm formation.⁷⁶ Cranberry non-dialyzable material (NDM) fraction was a potent inhibitor of the pro-inflammatory cytokine and chemokine responses induced by periodontopathogens and *E. coli*.⁷⁷

Teucrium polium

Teucrium plant belongs to the Labiatae family and is abundant in Southwest Asia, Europe and North Africa. Plants belonging to the genus *Teucrium* have been shown to contain different classes of compounds such as fatty acid, esters, terpenes, flavonoids and polyphenolics.⁷⁸ This plant is well known for its antinociceptive, antioxidant and anti-inflammatory activity.

It was reported that essential oils and alcoholic extracts of *T. polium* had antibacterial activities against both Gram negative and Gram positive bacteria. This is due to polyphenolic compounds which leak out intracellular constituents by altering cells walls and membranes, which increase cells permeability.⁷⁹

In a study conducted by Ben Othman M et al, all extracts exhibited an antibacterial activity against both Gram-negative and Gram-positive bacteria at different levels and *S. aureus* were the most sensitive.⁷⁹

Syzygium aromaticum-Lavang (cloves)

Cloves are the aromatic flower buds of a tree in the family Myrtaceae, *Syzygium aromaticum*. They are native to the Maluku Islands (or Moluccas) in Indonesia, and are commonly used as a spice. Clove is known to have antioxidant, antibacterial and antimicrobial properties. Clove oil has sedative action on the pulpal inflammation.⁸⁰ The clove oil from *S. aromaticum* and eugenol have been described as having useful antiseptic, analgesic and anodyne effects and are largely used in dental medicine.⁸¹

The main antifungal action of phenolic compounds, such as eugenol, appears to be exerted on the cellular membrane.⁸² In a study by *Syzygium aromaticum* demonstrated antimicrobial activity against planktonic and biofilm forms of *E. faecalis*.⁸³

Acacia nilotica – Babool

Acacia nilotica(Babool) is a tree native to Africa and is reported to have antimicrobial, antihyperglycemic and antiplasmodial properties. It is rich in tannins, phenolic compounds, essential oils and flavanoids. The bark of babool has proved to be effective in treatment of toothache.

Babool has shown to possess antibacterial activity against *Streptococcus mutans* and *E. faecalis*. Antimicrobial function is believed to be due to tannins, phenolic compounds, essential oil, and flavonoids, thus it is ideally used to treat *E. faecalis*.⁸⁴

In a study conducted by Rosina Khan et al to assess antimicrobial activity of five herbal extracts against multi drug resistant (MDR) strains of bacteria and fungus of clinical origin, *Acacia nilotica* was found to give the most potent antimicrobial extract followed by *Cinnamum zeylanicum* and *Syzygium aromaticum*.⁸⁴

Carvacrol

Carvacrol (thymol isomer) is present in the essential oil of *Origanum vulgare*, which is edible plant oil used in food products. It offers a wide range of uses: antimicrobial, healing and anti-inflammatory activity, thus making it ideal for endodontic usage. It has a broad spectrum of antibacterial activity; it works by inhibiting ATPase activity and increasing the nonselective permeability of bacterial cell membranes. Therefore, it not only inhibits microbial colonization, but also makes microbes more sensitive to antibacterial agents.⁸⁵

The prime use of carvacrol is inhibiting *Escherichia coli* and *Pseudomonas aeruginosa* which is attributed to action on several targets in bacterial cell and disruption of bacterial cell membrane. It also helps in repair of periapical tissues. This property is due to the presence of phenolic component, which stimulates pulpal fibers, a phenomenon known as hormesis.^{86,87}

Carvacrol also has anti-inflammatory effects. It can restrain neutrophilic elastase enzyme and suppress prostaglandin production.^[88]

Conclusion

Literature has pointed towards many plants with potential source for new therapies in endodontics. These herbs have major advantages in the root canal disinfection and intracanal medicaments are specially used as disinfecting agents in the root canal. These herbs have antibacterial, anti-inflammatory, and antioxidant properties which inhibit microbes greatly without affecting the dental tissues.

However there is limit information on the quality, safety and greater efficiency of these products for use in endodontics. So, more research and tests need to be done to get better treatments and usage of these herbs and also their side effects if any.

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