USES OF HERBAL EXTRACTS IN ENDODONTOLOGY: A LITERATURE REVIEW

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1. INTRODUCTION:

The main objective of endodontic treatment is to prevent and eliminate infection, seize invasion of microorganisms to periradicular tissues and preserve the natural dentition. Furthermore, the success of endodontic treatment of the tooth increases its life span. The success of the treatment depends on the accuracy of diagnosis, treatment plan, instrumentation, proper disinfection, and filling procedures (antimicrobial material, coronal, and apical seal) (Torabinejad M. et al., 2002).

Endodontic treatment starts with removing the diseased tissue, eliminating bacteria, and prevent its recontamination, for this purpose, irrigation play a significant role in reducing bacteria in the root canal, and control the periapical disease (Iqbal, 2012). The most popular irrigating solution used is sodium hypochlorite, according to its toxic effect on periapical tissues, inability to remove the smear layer, disagreeable taste, and short shelf life, researchers looking for natural and biocompatible irrigants in fact to reduce unpleasant effects (Deshmukh S. et al., 2022).

Herbal and natural products were used in dental and medical practice for thousands of years and became popular due to their antimicrobial, anti-inflammatory, antioxidant, and biocompatibility properties. According to WHO (World Health Organization), herbal medicine is defined as plant derived material or preparation that contains raw or processed ingredients from one or more plants with therapeutic values (Agrawal V. et al., 2017).

Therefore, herbs are biocompatible and safer to use as an alternative to varied materials in endodontology. They are effective in root canal treatment as antibacterial, anti-inflammatory, and antioxidant, and removing smear layer and tissue dissolutions. Furthermore, studies showed that herbs play a bearable role as a medium in dental pulp stem regeneration. The literature review's purpose is to identify the effect of different herbs used in endodontology.

2. METHODOLOGY:

An electronic search through PubMed, EBSCO, ScienceDirect, PMC, and Google Scholar was conducted. English is the main language. The keywords were: endodontology, herbs, natural extracts, antibacterial, smear layer removal, tissue dissolution action, antioxidant effect, anti-inflammatory, and tissue regeneration. 2429 articles were collected. Articles related to herbs used in endodontology assembled. After the removal of duplication, 2105 articles were left. Then screening was done, and 1391 articles were excluded due to their irrelevance to the effect of herbs on endodontology. 538 full-text studies remained. Followed by eligibility assessment, 350 articles were excluded and 180 were left, correlated to the effect of herbs in endodontology.

3. RESULTS:

Herbs mentioned in the literature are widely used in medicinal and dental treatments. Their effects are illustrated in table 1. They are characterized by their active components that exert variable effects on tooth structures and/or microorganisms. Furthermore, some of these herbs create a conductive medium for tissue regeneration. Among the included studies within this review, many herbs were reported to have several effects and used as antimicrobial agents (antibacterial, antifungal, and antiviral), removing smear layer, tissue dissolution action, antioxidant, and anti-inflammatory sources, and in stem cell regeneration.
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<th>Antibacterial Activity</th>
<th>Smear Layer Removal</th>
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4. DISCUSSION:

In recent years, herbs used in endodontics have undergone rapid growth due to their beneficial effects, accessibility, and a notable absence of side effects. Based on the search, several herbs were found with different properties, such as antimicrobial effect, smear layer removal, tissue dissolution action, tissue regeneration, antioxidant, and anti-inflammatory properties

4.1. Antimicrobial Effect:

A wide range of approximately 700 bacterial species exists in the oral environment, a limited number colonize the root canal system, belonging to Firmicutes, Bacteroidetes, Actinobacteria, and Proteobacteria (Nagy-Bota CM et al., 2021). Microorganisms can exist in various parts of the root canal system, dentinal tubules, accessory canals, canal ramifications, apical deltas, fins, and transverse anastomoses (Cosan G. et al., 2022). These microorganisms can be present within biofilms, structured communities enclosed in a self-formed polymeric matrix and adhered to the root surface, or in a planktonic form, floating within a fluid medium (Iqbal A., 2012). Procedures like instrumentation and irrigation play a significant role in the success of root canal treatment (Cosan G et al., 2022). Sodium hypochlorite is the predominant choice for endodontic irrigation owing to its strong bactericidal properties and its effectiveness in eliminating both vital and necrotic organic tissues. Nonetheless, the use of NaOCl comes with certain drawbacks that have prompted researchers to seek alternative solutions that offer similar benefits. Herbal extracts became popular due to their antimicrobial properties and biocompatibility (Shukla N. et al., 2016). Aloe Vera is considered an antibacterial, antiviral, and antifungal agent. A stock solution obtained from leaves along with gel is significantly effective against E. Faecalis and Candida Albicans (Prasad DS et al., 2016). Aloin and aloe-emodin are the active constituents, that act on the protein synthesis in the bacterial cells. Aloe vera in minimal inhibitory concentration (MIC) is effective superiorly to calcium hydroxide against E. Faecalis and its antibacterial activity increases with time (Vishnuvardhini S et al., 2018). The direct effect of aloe-emodin makes the virus nonfunctional (Sajjad A. & Sajjad SS., 2014). Andrographis Paniculata is an annual herbaceous plant cultivated in southern Asia, China, and part of southeast Asia. It is considered an antibacterial, antifungal, and antiviral agent, with a broad spectrum of pharmacological effects (Abu Bin Nyeem M. et al., 2017). Dehdia et al. in their study concluded that A. paniculata against S. aureus and C. albicans is an effective endodontic irrigant due to its antimicrobial activity (Dehdia J. et al., 2018).

Apple Cider Vinegar is a highly biocompatible material, had bactericidal activity against E. faecalis, making it a promising option as an endodontic irrigating solution. It had bactericidal effects against microorganisms commonly associated with endodontic infections, including Staphylococcus aureus and Enterococcus faecalis (Tekin B. & Demirkaya K., 2020). Apple cider vinegar has antibacterial, antiviral, and antifungal properties (Yagnik D. et al., 2018). Actium Lappa-Burdock a plant found in Japan and acclimated in Brazil, is used in popular medicine due to its therapeutical properties. It acts as an antifungal, and antibacterial source (Badole GP et al., 2016). It contains sterols, tannins, and polysaccharides (Sinha JD. & Sinha A. 2014). In vitro study showed that Actium Lappa inhibited the growth of Mutans. E. coli, P. aeruginosa, and L. acidophilus (Chikkama M. et al., 2014) Azadirachta Ismendia-Neem an Indian plant considered by the US National Academy of Sciences a tree for solving global problems (Vishnuvardhini S. et al., 2018). Each part of Neem as flowers, roots, seeds, leaves, and bark has medicinal properties. It showed antifungal, antiviral, and antibacterial action against gram-positive and gram-negative such as Streptococcus mutans, M. tuberculosis, M. Tuberculosis, Vibrio cholera, and Klebsiella pneumonia (Vishnuvardhini S et al., 2018). Studies revealed that Neem can be used as an alternative to Sodium Hypochlorite due to its effectiveness against E. faecalis and reducing sodium hypochlorite accidents (Yadav RB et al., 2021). Babool-Acacia Nilotica is known as the Gum Arabic tree. Babool has antibacterial activity against Streptococcus Mutans and E. Faecalis (Agrawal V. et al., 2017). Babool at 50% concentration was the most efficacy extract against E. Faecalis than Liquorice, Clove, and Cinnamon (Jain P. & Ranjan M., 2014). Babool has antiviral and antifungal activity (Yadav RB et al., 2021). Camellia Sinensis-Green Tea contains flavonoids, able to inhibit the growth activity of bacteria, fungi, and viruses (Penumudi MS. et al., 2015). Catechins, the components of Green Tea bind to the bacterial lipid bilayer cell membrane and cause its destruction (Badole GP et al., 2016). Carvacrol an oil found in Origanum Vulgare, is used in food products. It is a thymol isomer, has antibacterial activity, reduces microbial colonization, and increases the permeability of bacterial cell membranes which makes them more sensitive to antibacterial agents.
Carvacrol is effective against E. faecalis and Pseudomonas aeruginosa (Sinha JD. & Sinha AA. 2014). *Citrus Limonium* - *Lemon* known as lemon solution is considered an acidic agent with lower ph. 2.21. It is considered an antibacterial agent. It is effective against E. faecalis (Vishnudevadihin S et al., 2018), and can be used as intracanal medication and in endodontic retreatment (Sinha JD. & Sinha AA. 2014). *Clove Oil* - *Syzigium Aromaticum* contains eugenol, isoeugenol, and anillin. Clove oil has antibacterial, antifungal, and antiviral properties. It is effective against E. faecalis (Munaga S et al., 2022). *Curcumin* - *Vaccinium Macrocarpon* is naturally acidic, and contains biologically active ingredients such as flavonoids, phenols, anthocyanins, and condensed tannins. These components prevent acid formation and reduce dental caries. It is considered an antibacterial, antifungal and antiviral agent (Jain P. & Ranjan M., 2014). *Cumin or Cuminum Cymnun* from apiece family, a medicinal herb native to the Mediterranean region. It has antibacterial, and antifungal properties (Jain P. & Ranjan M., 2014). In vitro study done by Abbaszadegan A. et al., in 2016, showed that cumin is an antimicrobial agent against microbial flora with lower toxicity compared to 2% CHX (Abbaszadegan A. et al., 2016). *Curcumin Longa*- *Turmeric* is an ancient popular Indian herb used as food preservative material and treatment of swelling and sprains. Turmeric has antifungal and antibacterial properties. It contains polyphenols, and various volatile oils like turmerone, atlantone, and zingiberene. It is effective against gram-positive bacteria such as E. faecalis, and Streptococcus intermedius, and gram-negative bacteria such as E. coli (Neelakantan P. et al., 2013). A study by Tewari KR. et al. in 2016 showed that Curcumin in comparison with sodium hypochlorite is effective as NaOCl, and inhibits larger zones of anaerobes such as E. Faecalis (Tewari KR. et al., 2016). *Curry* is a tropical tree with long aromatic leaves with antifungal and antibacterial properties. A Study by Sewan S. and Qureshi M. in 2016 evaluated the antimicrobial activity of Neem, Clove, Curry leaves, Cardamom, Tulsi stem, and Tulsi leaves. They concluded that Curry has a maximum zone of inhibition against E. coli (Sewari S. & Qureshi M. 2016). *German Camomile* an annual plant belongs to the Asteraceae family. Camomile has antibacterial, and cancer prevention (Yousief AS., et al., 2023). *Glycyrrhiza glabra-liquorice* contains a tritone compound known as Glycyrrhizin that gives the sweet taste of liquorice root and is effective against E. faecalis. Liquorice as an antibacterial and antiviral agent inhibits cariogenic bacteria, such as Streptococcus mutans (Vishnudevadihin S et al., 2018). The flavonoids in Liquorice are strong inhibitors of oxygen consumption in bacterial cells (Fresno VR. et al., 2019). *Garlic-Allium Saliva* originated from the Liliaceae family, a bulbous perennial plant, used medicinally as an antimicrobial, antiviral, and antifungal agent for centuries (Vishnudevadihin S et al., 2018). The allicin active components in garlic destroy the cell wall and cell membrane of root canal bacteria. It is considered a bacteriostatic and bactericidal agent, effective against Staphylococcus aureus(Sinha JD. & Sinha AA. 2014). *Grape Seed* extracts contains proanthocyanins essential for antibacterial, antifungal and antiviral properties. D’adiz SF. et al. in 2020 compared the antibacterial effect of grape seed as an irrigant in root canal treatment. They showed that grape extracts have a lower capacity to eliminate E. Faecalis than sodium hypochlorite and chlorhexidine gel (D’Aviz SF. et al., 2020). *Marjoram or Origanum Marjorom*, known as sweet marjoram, is derived from the Lamiaceae plant. It is claimed that essential oil in sweet marjoram is more active against lactic acid bacteria and yeasts (Fresno VR. et al., 2019). *Miswak-Salvadora Persica* a medical plant, used for oral hygiene all over the world and particularly in Saudi Arabia. Miswak rich in trimethyl amine, salvadorian chloride, and fluoride, responsible for its antiviral and antifungal properties (Chikkama M. et al., 2014). Studies showed that alcoholic extracts of miswak prevent the formation of biofilm. It can be used as an alternative to NaOCl and chlorhexidine in root canal irrigation (Tewari KR. et al., 2016). *Morinda Citrifolia-Noni* a fruit juice is in demand due to its medicinal effects. Morinda Citrifolia contains potassium, vitamin C alkaloids, vitamin A, linoleic acid, Alizarin, and L-asperuloside. Analgesic noni extracts are as strong as 75% of morphine and have no side effects (Jain P. & Ranjan M., 2014). Morinda Citrifolia has various activities such as antibacterial, antiviral and antifungal action. Hence, it is the juice that can be used as an alternative to NaOCl as an intracanal irrigant (Tewari KR.et al., 2016). *Myrrh-Commiphora Myrrha* is a gum resin extracted from several small, thorny tree species of the genus Commiphora. The Commiphora genus is distributed around the red sea in east Africa, Arabia, and India. Myrrh used as an analgesic and antiseptic in mouthwashes, gargles, and toothpaste. It acts as an antiviral, antifungal and antibacterial agent (El EID AR, 2021). Studies revealed that myrrh inhibits bacterial pathogens such as Escherichia Coli, Staphylococcus aureus, and pseudomonas aeruginosa(Suresh Aet al., 2019). *Myrtus communis* is a species of flowering plant originated from the Myrtle family. Myrtaceous native to southern Europe,
North Africa, Western Asia, and the Indi subcontinent. The essential oil of Myrtus communis contains 8-Cineole, a-pinene, and linalool (Sulieman T.R., 2009). The essential oil in Myrtus communis responsible for its antiviral and antibacterial activity against persistent endodontic microorganisms (Almadi ME. & Almohaimede AA., 2018). *Nigella Sativa-Black Seed*, a miracle herb originated from the Ranunculaceae family. It is characterized by a wide spectrum of activities such as antimicrobial, antifungal, analgesic, anti-diabetic, anti-hypertensive, anticancer, and immunomodulatory. The constituents of nigella sativa are thymohydroquinone, dithymoquinione, thymol, carvacrol, nigellimine-N-oxide, nigellicine, nigelledine, alphahederin, and thymoquinone (TQ) is the major bioactive component. The TQ reduced the metabolic activity of E. faecalis which inhibits the biofilm formation and cell adhesion to host tissues. Jain N. et al. in 2019 announced that nigella sativa was more effective than 2.5% sodium hypochlorite against E. Faecalis (Jain N. et al., 2019). *Nutmeg-Myristica Fragrans* an evergreen tree native to Indonesia, used in Indian traditional medicine to treat diseases. Myristic acid is the component responsible for its antibacterial activity (Tewari KR. et al., 2016). *Melaleuca Alternifoli-Tea Tree Oil* is a tree native to wet lowlands in Australia and has a papery white bark with dark green needle-like leaves and colorful blossoms. The Trepenin-4-ol (30-40%) active ingredient is essential to its antibacterial and antifungal activity (Vishnuvardhini S et al. 2018). The concentration of 2.5 to 5% tea tree oil has no toxic effect (Badole GP., 2016). *Oregano or Origanum Minutiflorum* is a flowering plant belonging to the Lamiaceae family, found in the Mediterranean region. It was identified that oregano has strong antibacterial properties (Karobari IM. et al., 2022). Oregano at concentration 2 or 5% is more effective against E. faecalis than NaOCl (Janani K. et al., 2019). *Pomegranate- Punica granatum* is a source of nutrients and is used for medicinal purposes. It is considered an antifungal and antibacterial agent effective against resistant bacteria. Hydrolyze tannin is a complex high molecular weight form of Pomegranate with proteins that increased bacterial lysis and interfered with the bacteria in the tooth surfaces (Zarina R. et al., 2016). *Propolis (Chitosan)-Bee Glue* is a resinous material assembled by bees from the trees of poplars or conifers or from flowers. It is a sticky substance, in low temperatures, propolis becomes hard and brittle. The active constituents of propolis are flavonoids and cinnamic acids are essential to their antibacterial activity (Chikkama M. et al., 2014). Propolis has antifungal and antibacterial properties. It acts against the bacteria present in dental abscesses and osteomyelitis (Badole GP, 2016). *Psidium Guajava-Guava* rich in essential oil contains cineol, tannins, flavonoids, and tripenents. The active ingredients are liable for the effects of guava. The ethanol extracts from guava have antifungal, antiviral and a higher antibacterial activity against E. faecalis (Singha JD & Sinha AA., 2014). *Rosemary- Rosmarinus Officinalis* a herb originates from the Lamiaceae plant, has antifungal and antibacterial properties. In vitro study evaluating the disinfection activity of Rosemary compared with NaOCl 2.5% and CHX 2%, showed that the hydroalcoholic extract of Rosemary is effective against E.Faecalis and able to be used to disinfect the gutta percha (Almadi ME. & Almohaimede AA., 2018). *Rhus Lancia-African Sumac* contains gallic tannins and gallic acids, acts as antifungal and antibacterial agents. Tannins have antibacterial properties and gallic acid is a bactericidal factor (Tewari KR. et al., 2016). *Sapindus Mukorossi* is a deciduous tree grown in tropical and subtropical regions of Asia. S.mukorosi used as a medicinal plant in epilepsy, sclerosis, migraines, eczema, and psoriasis. It is considered as an antibacterial and antifungal sources. Sağlık I. et al. in 2020 showed that Sapindus Mukorossi has an antibacterial effect against anaerobic facultative, and aerobic bacteria such as P. gingivitis, A. odontolyticus, F. nucleatum ( Sağlık I. et al., 2020). *Triphala* is a traditional Ayurvedic herbal. It contains phenolic chemical constituents such as syringic acid, gallic acid, tannic acid and epicatechin along with ascorbic acid (Tekin B & Demirkaya K., 2020). In dental practice, it treats diseases of the mouth such as dental caries, gingivitis, and stomatitis (Zarina R. et al., 2016). Triphala showed effectiveness against E. faecalis (Badole GP, 2016). *Tulsi- Ocimum Sanctum* a small herb found in India, known as the queen of herbs due to its popular medicinal uses(Zarina R. et al. 2016). The leaves of tulsi contain 0.7% volatile oil and consist of 71% eugenol and 20% methyl eugenol. The essential oil of tulsi is responsible for the antifungal and antibacterial properties. The action increased with concentration and contact period (Badole GP, 2016). Tulsi inhibited E.faecalis, and it is recommended to be used as an alternative to endodontic irrigants and medicaments (Munaga S. et al., 2022). *Zingiber Officinale-Ginger* is a constituent used across the world in foods and beverages. The components such as ethanol and n-hexane in ginger are essential for antibacterial, antiviral, and antifungal properties. It was suggested that ethanolic extracts of ginger have a higher antibacterial effect against E. faecalis. The gingerol in ginger inhibits the growth of gran-
negative bacteria (Vishnuvardhini S. et al., 2018). **Passion Fruit** is a creeper plant, nontoxic, and tastes better. It contains flavonoids, alkaloids, cyanogenic compounds, glucosides, vitamins, minerals, and terpenoids that flourish their antibacterial and antiviral properties (Deshmukh S. et al., 2022). **Thymus Masticina** is an endemic species of the Iberian Peninsula in Spain and Portugal, known as Spanish Marjoram. Gupta D et al. evaluated the antibacterial, antifungal, and antiviral effect of Thymus Masticina against E. faecalis in comparison with 5% of NaOCl, and they concluded that Thymus has effectiveness but less than NaOCl (Gupta D. et al, 2020)

### 4.2. Smear Layer Removal:

Root canal treatment requires the elimination of infected pulp tissues, bacteria, and toxins to create a sterile and sealed environment. This is achieved through chemo-mechanical preparation, using a chemical solution along with mechanical instruments to clean the root canal system (Borzini L. et al., 2016). During the instrumentation process, a smear layer is formed on the root canal walls, consisting of dentin fragments, bacteria, odontoblastic processes, and necrotic pulp tissues. The elimination of this smear layer is crucial for the success of root canal therapy, as it contains microorganisms and toxins that can lead to persistent infections and treatment failures (Torabinejad M. et al., 2002). As a result, irrigation plays a significant role in root canal debridement. In addition to disinfection, irrigants help eliminate the smear layer from the root canal wall (Deshmukh S. et al., 2022). **Apple Cider Vinegar** can remove the smear layer consisting of organic and inorganic components that obstruct dentinal tubules (Tekin B & Demirkaya K, 2020). It was found that Apple Cider Vinegar used for one minute as a final rinse is more successful in removing the smear layer without changing the calcium level in the canals (Deshmukh S. et al., 2022). Abu Zed ST and Bastawy HA in 2021 announced that the combined irrigation of EDTA and apple cider vinegar was more effective in removing the smear layer in the middle third of the root canal compared to the group treated with NaOCl (Abu Zeid ST, Bastawy HA, 2021). The citric acid component in **Citrus Limonum** acts as a chelating agent and shows effectiveness in removing the smear layer (Tewari KR. et al., 2016). Studies showed that 1 mol L-1 of citric acid is effective as EDTA in removing the smear layer (Deshmukh S. et al., 2022). The components of **German Camomile** are chamazulene, caprylic acid, caprylic acid, and chlorogenic acid, alone can remove the smear layer superiorly to NaOCl, but less than NaOCl with EDTA (Tewari KR. et al., 2016) Balto H. et al. in 2012, in their study, observed that the stearic acid in **Salvadora Persica** extract solution with a concentration of 5 mg/ml demonstrated a notably higher efficacy compared to the 1 mg/ml solution in the coronal and middle thirds. 5 mg/ml of S. Persica solution has similar effectiveness to a 17% EDTA solution in eliminating the smear layer from the coronal third. Both concentrations of S. Persica showed similar effects and were found to be less effective than EDTA in removing the smear layer at the apical third (Balto H. et al., 2012) A study showed that **Oregano** at concentrations 2 and 5% was not able to eliminate the smear layer, while in combination with 17% of EDTA, removal of the smear layer was successful without dentin erosion (Almadi & Almohamede, 2018). **Camellia Sinensis-Green Tea** polyphenol is a good chelating agent with a lower capacity to remove the smear layer due to the lack of acid metabolites (Deshmukh S. et al., 2022). A study by Sebatni MA and Kumar AA showed that green tea was able to remove the smear layer, but less than neem leaf, orange oil, and sodium hypochlorite used (Sebatni MA. & Kumar AA., 2017). **Tea tree oil or Melaleuca Alternifolia** removed the smear layer from the coronal and middle third, less than EDTA while more than saline was used. Hence it is not effective in the apical third due to surface higher tension. It is recommended to use as a non-oily solution or an emulsion of Tea Tree Oil to reduce its surface tension (Mallika et al., 2019). **Tumeric or Curcumin Longa**, an aqueous extract, can reduce the smear layer and be used as an alternative to chemical irrigants due to its biocompatibility (Vishnuvardhini S. et al., 2018). The citric acid in **Triphala** leads to eliminating the smear layer and acts as a chelating agent (Sahni A. & Chandak GM., 2015). **Tulsi** showed the efficiency of removing the smear layer due to the presence of acid metabolites and can be used as irrigants in primary teeth. **Passion Fruit** use at a concentration of 30% reduces the smear layer from the coronal and middle third, while in combination with 17% EDTA show effectiveness in removing the smear layer from all the canal (Deshmukh S. et al., 2022). **Clove oil or Syzigium Aromaticum** with EDTA showed effectiveness in removing the smear layer, and sedative agent when used in inflamed pulp (Vishnuvardhini S. et al., 2018) **Rhus Lancia-African Sumac** rich in acids and tannins unblocked the dentinal tubules, due to its capability to decrease the endogenous matrix metalloproteinase (MMP-2, 8 and 9) activity of demineralized dentin matrix (Alsamri H. et al., 2021). Sharma K and Dhawan discovered in their study that **Neem Leaf** extract was more effective in removing
the smear layer than the Tulsi and Green Tea solution used (Sharma K & Dhawan R, 2021). Deshmukh S. et al in 2022 announced that Neem extract was efficient in removing the smear layer in the apical third of the root canal (Deshmukh S., et al., 2022). Murray EP. et al in 2008 evaluated the effect of *Morinda Citrifolia* as an endodontic irrigant. They concluded that M. Citrifolia showed more effectiveness in removing the smear layer than CHX and similar effects as NaOCl with EDTA. They suggested that an increased concentration of M. Citrifolia above 6% leads to a higher effect in removing the smear layer (Murray EP. et al., 2008).

### 4.3. Tissue Dissolution:

The main objectives of endodontic treatment are cleaning and shaping the pulp space, the root canal system is complex, with branching and dividing canals. Anatomical variations like fins, isthmus, and C-shaped canals can be present. About 35-40% of canal walls remain non-instrumented due to these complexities. Traditional symmetrical instruments cannot reach these inaccessible areas. To address this, chemical irrigation is used alongside mechanical preparation (Dioguardi M et al., 2018). The ideal endodontic irrigant should have antimicrobial properties, dissolve tissue remnants, and remove the smear layer (Kandaswamy D & Venkateshbabu N. 2010). It should also be non-irritating, non-antigenic, non-toxic, and non-carcinogenic. Many herbs were found effective as tissue-dissolving agents due to their biocompatibility and not toxic.

The *Cranberry-Vaccinium Macrocarpon* naturally acidic juice contains active ingredients such as flavonoids, phenols, anthocyanins, and condensed tannins. These components prevent acid formation and play a role in the reduction of dental caries. As cranberry is considered acidic juice, consuming too often can cause erosion, and lead to pain and sensitivity in the teeth (Vishnuvardhini S. et al., 2018). *Curcumin longa-Tumeric* the Indian herb, used as an irrigant prevents the formation of biofilm by eliminating the extracellular polymeric substance matrix that is considered a nutrient for the cell growth of bacteria (Karobari IM. et al., 2022). The allicin-active components in *Garlic* are responsible for its tissue dissolution action (Sinha JD & Sinha AA, 2014). *Salvadora Persica* is rich in trimethyl amine, salvadorime chloride, and fluoride, effective in preventing tooth decay, the stearic acid in S.persica acts as a chelating agent and can bind to the calcium in dentin (Deshmukh S., et al., 2022). *Pomegranate* with soluble proteins forms a complex with high molecular weight, interfering with bacterial adherence to the tooth surface (Zarina R et al., 2016). The *Psidium Guava* contains gujaverin an active flavonoid compound that inhibits growth, adherence, and co-aggregation of dental plaque material (Badole Gp. et al., 2016). The *Rhus Plant* increased the intra and inter-fibrillar crosslinking density of the dentin collagen matrix (Alsamri H. et al., 2021). *Sapindus Mukorossi* contains saponin essential for its surfactant action. The emulsification action of the biosurfactant of S. mukorossi dissolves water-insoluble substance/hydrocarbon (Karobari IM. et al., 2022). *Tea Tree Oil* is considered a mild solvent used for dissolving necrotic pulp tissue (Vishnuvardhini S. et al., 2018). *Triphala* is a chelating agent due to the presence of citric acid, and its free radical scavenging prevents biofilm formation (Badole Gp et al., 2016).

### 4.4. Antioxidant and Anti-Inflammatory Properties:

Oxygen is essential for life, but it can have both positive and negative effects on the body's health. The toxic effects of oxygen were discovered through Gershman's free radical theory of oxygen toxicity in 1954. This theory explains that oxygen toxicity is caused by partially reduced forms of oxygen. When cells use oxygen to generate adenosine triphosphate (ATP) energy in the mitochondria, free radicals are produced. Free radicals are chemically active atoms with unpaired electrons, known as reactive oxygen species (ROS) or reactive nitrogen species (RNS). ROS and RNS have dual roles, being both harmful and beneficial. ROS, derived from oxygen metabolism, has constructive functions in cell physiology but can also cause damage to cell membranes and DNA. During oxidative stress, ROS levels increase significantly, leading to substantial damage to cellular structures. To prevent and manage human diseases, it is crucial to use ROS scavengers or antioxidants that react with oxygen and help counteract ROS formation. Antioxidants play a vital role in preventing the harmful effects of ROS and maintaining cellular health (Patel S. et al., 2015). On the other hand, endodontic infections release cytokines and other inflammatory mediators, which are then recruited and retained until the infection is eliminated, hence, root canal therapy is performed to stop the spreading of infection (Soh AJ. et al. 2019).

Therefore, several herbs are found to have antioxidant and anti-inflammatory properties and were listed as alternatives to endodontic irrigants, such as *Aloe Vera* contains active ingredients such as...
vitamins, minerals, enzymes, sugars, amino acids, organic and inorganic components that determine its antioxidant and anti-inflammatory effects (Rathee G. et al., 2020). The components of Babool-Acacia Nilotica-Gum Arabic such as phenolic and flavonoids are responsible for antioxidant and anti-inflammatory activity (Wong J. et al., 2021) The Essential oil in a Clove-Syzigium Aromaticum is eugenol, isoeugenol, and vanillin lead to its antioxidant effects. It is also considered an anti-inflammatory agent (Nagy-Bota CM et al., 2021). The diferuloylmethane, a yellow active ingredient in Curcumin leads to its antioxidant and anti-inflammatory properties (Fresno VR et al., 2019). Since ancient times, Garlic considered a dietary and medicinal agent with various actions such as antioxidant, anti-inflammatory, antihypertensive, anticarcinogenic, antiagulant, and detoxification effects (Vishnuvardhini S. et al., 2018) The proanthocyanidins in the Grape Seed extracts are responsible for his antioxidant and anti-inflammatory action (Fresno VR et al., 2019), Oregano, Marjoram, Rosemary, and Thymus Vulgaris are herbs derived from the Lamiaceae plant. Some essential oils are common ingredients in this family, rosmarinic acid is a specific polyphenol, considered a specific biomarker that leads to their antioxidant and anti-inflammatory properties (Fresno VR. et al., 2019) Miswak is characterized by higher antioxidant and anti-inflammatory effects due to the presence of aromatic oil (Deshmukh S., et al., 2022). The components in Morinda Citrifolia such as lignans,oligopolysaccharides, flavonoids, and catechins are principle to its anti-inflammatory and antioxidant properties (Khallaf EM. et al., 2020). Myrrh is used in dentistry, especially after extraction for wound healing due to its wide properties such as antioxidant and anti-inflammatory agents (El Eid AR, 2021). Myrtus Communis, rich in essential oil, exhibited its antioxidant properties. Pomegranate has various mechanisms such as reduction of oxidative stress in the oral cavity, direct antioxidant action, and anti-inflammatory effect due to the presence of active ingredients including polyphenol components (Zarina R et al., 2016). Apple Cider Vinegar exhibits anti-inflammatory activity, which is advantageous for periapical repair. It combats free radicals and supports the immune system due to its antioxidant properties (Tekin B & Demirkaya K, 2020). The Green Tea- Camellia Sinensis is considered an antioxidant agent due to the galloカテchins and inactive free radicals. The polyphenols in the leaves of Camellia Sinensis enhanced its anti-inflammatory properties (Sinha JD. & Sinha AA, 2014). Flavonoids, phenolic, anthocyanin, and condensed tannins in Cranberry are responsible for anti-inflammatory and antioxidant effects (Jain P., 2014). The terpinen-4-o1 active component in German Camomile leads to its anti-inflammatory effect (Yousief AS. et al., 2023). The active constituents of Curcuma longa-Tumeric are curcumin (diferuloylmethane) and volatile oils such asumorine, atlantone, and zingiberon are responsible for anti-inflammatory and antioxidant properties ((Badole GP, 2016) Glycerzihla Glabra-liquorice has anti-inflammatory properties due to triterpenoid compound and glycyrrhizin (Vishnuvardhini S. et al., 2018). Propolis is rich in flavonoids and cinnamic acid derivatives, the guaaverin in Psidium Guajava, tannins and gallic acids in Rhus Lancia, Triphala contains tannins, quinones, flavonoids, gallic acid, and vitamin C, Ginger rich in gingerone, gingerol and 6-shagoal, the chemical components of Curry leaves are linalool, elemol geranlylacetate, myrcene, auro-ocimene, α-terpiene, β-ocimene, and nerylacetate leads to their anti-inflammatory and antioxidant effect(Vishnuvardhini S. et al., 2018). Passion Fruit has anti-inflammatory and antioxidant properties due to flavonoids, alkaloids, and cyanogenic compounds (Munaga S. et al., 2022). Eugenol (1-hydroxy2-methoxy-4 allylbenezene) is the active ingredient in Turulsi essential for its anti-inflammatory and antioxidant effects (Deshmukh S., et al., 2022). Andographis Paniculita-Green Chirehta has an anti-inflammatory effect due to the active component andrographolide. The Hydroalcoholic extract from A. Paniculata is responsible for its antioxidant properties (Abu Bin Nyeem M. et al., 2017). The antioxidant and anti-inflammatory effects of Thymus Mastichina are caused by the essential oil, tannin, flavonoids, saponins, and tritepinic acid (Taghouiti M. et al., 2020). The antioxidant effect of Azadirachta Ismednia-Neem is caused by components such as nimbin, nimbimid, nimboide, and nimbidic acid (Kala SB. et al., 2015). The phenolic constituents in Nutmeg-Myristica Fragrans inhibit and absorb the free radicals, leading to their antioxidant properties (Tewari KR. et al., 2016). The essential oils in Nigella Sativa are responsible for antioxidant and anti-inflammatory effects (Jain N. et al., 2019). Sapindus Mukorossi acts as an antioxidant and anti-inflammatory agent due to the components such as saponins (10-11.5%), sugars (10%), and mucilage (Sağluka I. et al., 2020)

4.5. Tissue Regeneration:
The dental pulp is a soft ecto-mesenchymal tissue that is highly vascularized and innervated (Nisha G. & Amit G., 2014). It is surrounded by dentin and consists of a heterogeneous population of cells.

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including fibroblastic cells, stem cells, capillary blood vessels, peripheral nerves, lymphatic elements, immune cells, and an extracellular matrix composed of fibers and fundamental substances, with a concentration of collagen fibers to support blood vessels and nerves (Demarco FF. et al., 2011). The dental pulp is considered a promising source of mesenchymal stem cells (MSCs) for regenerative medicine applications due to its availability and ease of isolation (Tatullo M. et al., 2015). It aims to restore normal physiological features and overcome issues associated with necrotic pulp. Three essential components for pulpal regeneration are dental stem cells, biomaterials, and growth factors (Xie Z. et al., 2021). Interest in medicinal plants as a source of regenerative drugs has increased in recent years (Dhoum S. et al., 2023).

The Aloe Vera 10, 30, and 50 % is considered a storage medium for avulsed teeth; it maintains the PDL cells. Furthermore, Tizard et al in 1994 suggested that aloe vera has a cell growth stimulatory activity, and Ramamoorthy and Tizard in 1998 announced that aloe vera has immunostimulatory activity (Sajjad A & Sajjad SS, 2014). Propolis can stimulate enzyme systems, cell metabolism, and collagen formation and contribute to hard tissue bridge formation. Honey rich in proteins, vital amino acids, vitamins, and minerals maintains the viability of PDL cells and increases their shelf life (Karobari IM. et al., 2022). A study on premolars treated by propolis for direct pulp capping showed effectiveness as calcium hydroxide (Sinha JD & Sinha AA., 2014). Nigella Sativa showed effectiveness as a pulp capping agent for deciduous teeth, retains the vitality of the pulp after application (Almadi ME. & Almohaimede AA., 2018), and promotes wound healing (Dhoum S. et al., 2023). Camellia Sinensis-Green Tea preserves the viability of cells and can be used as transfer media to the avulsed teeth (Karobari IM. et al., 2022). Dhoum et al in their study notify that camellia sinensis is effective in odontoblastic differentiation (Dhoum S. et al., 2023). Morinda Citrifolia is a biocompatible agent, promotes dental pulp stem cell attachment to root canal dentin and is successful in use in regenerative endodontic treatment (Dhoum S. et al., 2023). In vitro studies assessing the effect of ethanolic and water components of Salvadora Persica on cultured human dental pulp stem cells (HDPSCs) showed that water of SP causes significant proliferation and maintains the viability of DPGCs that Tabataabae SF. et al., 2015). Studies report that Sapindus mukorossi seed oil cultured with DPSCs increases cell viability and vesicle secretion of DPSCs (Shiu TS et al., 2020). Studies announced that Psidium Guayava 0.05-50 µg/ml concentration increases the viability of dental pulp stem cells DPSCs (Khodabandeh Z. et al., 2022). Anzoflophan Paniculita-Green Chiretta exhibits potential anticancer and immunomodulatory properties in human cells (Dedhia J. et al., 2018). Podar R. et al. suggested that Azadirachta Ismendia-Neem has immune-modulatory and anti-carcinogenic effects (Podar R. et al., 2015). A study announced that Carvacrol is beneficial in endodontic use, due to its capability to stimulate pulpal fibers and repair periapical tissue (Yadav RB et al., 2021). Grape Seed Extracts have immune-stimulating action, increase collagen cross-link, and strengthen collagen-based tissue (D’Aviz SF. et al., 2020).

5. CONCLUSION:

Studies concerning the use of herbs in endodontology show affordable effects, safer than sodium hypochlorite, less toxicity, and effective against bacterial, with antioxidant and anti-inflammatory properties. In addition, more in vitro as well as in vivo studies are needed to evaluate the effectiveness of herbs as alternatives irrigants to NaOCl and intra-canial medication, and to assess their effect on dental pulp regeneration.

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