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Ethnopharmacological approach in Endodontic Treatment: A Focused Review

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Abstract

Endodontic or root canal treatment involved removal of infected tissue and microorganisms from within the root canal space to prevent further infection of the periradicular tissues as well as to allow healing of these tissues. This critical process involves the use of some chemical substances for disinfection of the root canal space. Several studies have shown that contemporary chemical agents [both proteolytic and acidic] do not achieve complete disinfection, and have other disadvantages like weakening of the tooth structure, predisposing to fracture of the tooth. Recently, there has been a growing trend to seek natural remedies as part of dental treatment. This may be termed as ethnopharmacology or phytotherapy. This paper aims at providing a comprehensive review that focuses on the herbal agents that have been evaluated in endodontics. It also briefly reviews the agents with potential applications in root canal disinfection. The agents reviewed include Morinda citrofolia [Indian Noni], Terminalia chebula [Triphala], Curcuma longa [Turmeric], Glycyrrhiza glabra [Liquorice], Propolis, Melaleuca alternifolia [Tea Tree Oil] and Azadirachta indica A. Juss [Neem].

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INTRODUCTION

The prime objective of root canal treatment is to clean the root canal system thoroughly, free of microbiota and debris, so that it can be sealed with a microbial-tight filling. This process mainly revolves around a process called "chemomechanical preparation", wherein chemically active solutions are used along with mechanical instrumentation of the

root canal space [1]. The most commonly used chemical for this process is sodium hypochlorite [NaOCl] in concentrations ranging from 1-6%. The preference for this chemical over other irrigants stems from its unique ability to dissolve pulp tissue, and its excellent antimicrobial potency [2]. In addition to NaOCl, other acidic substances are used to to rid the root canal system of the so-called smear layer consisting of dentin particles embedded in an amorphous mass of organic material that forms on the canal walls during the instrumentation procedure [3]. Removing this layer can dissolve attached microbiota and their toxins from root canal walls and reduce the potential for bacterial survival and reproduction [4]. Calcium-chelating agents such as ethylenediaminetetraacetic acid [EDTA] or citric acid are used for the aforementioned purpose.

The weaknesses of NaOCl include the unpleasant taste, toxicity, and its inability to remove the smear layer by itself, as it dissolves only organic material. However, the limited antimicrobial effectiveness of NaOCl in vivo is also disappointing. This may be attributed to problems in penetration to the most peripheral parts of the root-canal system such as fins, anastomoses, apical canal, lateral canals, and dentin canals. Recently, it has been shown by in vitro studies that long-term exposure of dentin to high concentrations of sodium hypochlorite can have a detrimental effect on dentin elasticity and flexural strength, thereby predisposing the tooth to vertical fracture, which has a hopeless prognosis [5,6]. The constant increase in antibiotic resistant strains and side effects caused by synthetic drugs has prompted researchers to look for herbal alternatives.

Recently, there has been a growing trend to seek natural remedies as part of dental treatment [7] and this approach may be termed phytotherapeutics or ethnopharmacology. This paper will provide a brief review of the various herbal alternatives that are being researched for potential endodontic applications.

MORINDA CITROFOLIA [MC]

Among the medicinal plants discovered by the ancestors of Polynesians, Morinda citrifolia [Noni] is one of the traditional folk medicinal plants that has been used for over 2000 years in Polynesia [8]. It has been reported to have a broad range of therapeutic and nutritional value. Noni is the common name for Morinda citrifolia and is also called Indian Mulberry, Ba Ji Tian, Nono or Nonu, Cheese Fruit, and Nhau in various cultures throughout the world. It has been reported to have a broad range of health benefits for cancer, infection, arthritis, diabetes, asthma, hypertension, and pain. The Polynesians utilized the whole Noni plant in their medicinal remedies and dye for some of their traditional clothes. The roots, stems, bark, leaves, flowers, and fruits of the Noni plant are all involved in various combinations in almost 40 known and recorded herbal remedies [9].

Figure 1: Morinda citrofolia

A number of major components have been identified in the Noni plant such as scopoletin, octoanoic acid, potassium, vitamin C, terpenoids, alkaloids, anthraquinones [such as nordamnacanthal, morindone, rubiadin, and rubiadin-1-methyl ether, anthraquinone glycoside], β-sitosterol, carotene, vitamin A, flavone glycosides, linoleic acid, Alizarin, amino acids, acubin, L-asperuloside, caproic acid, caprylic acid, ursolic acid, rutin, and a putative proxer onine [10]. Antibacterial activity Acubin, L-

asperuloside, and alizarin in the Noni fruit, as well as some other anthraquinone compounds in Noni roots, are all proven antibacterial agents.These compounds have been shown to fight against infectious bacteria strains such as Pseudomonas aeruginosa, Proteus morgaii, Staphylococcus aureus, Baciillis subtilis, Escherichia coli, Salmonella, and Shigela. These antibacterial elements within Noni are responsible for the treatment of skin infections, colds, fevers, and other bacterial-caused health problems [11,12].

An in vitro study compared the effectiveness of the juice of MC with NaOCl and Chlorhexidine to remove the smear layer from root canal walls of instrumented teeth. It was concluded that the efficacy of Morinda Citrifolia was similar to NaOCl in conjunction with EDTA as an intracanal irrigant [13]. The antimicrobial activity of 2% CHX gel, propolis, Morinda Citrifolia juice and calcium hydroxide has been compared on E.faecalis infected root canal dentin at two different depths and three intervals. It was concluded that Propolis and Morinda Citrifolia were effective against E. faecalis in dentin on extracted teeth [14]. Morinda Citrifolia appears to be the first juice to be identified as a possible alternative to the use of NaOCl as an intracanal irrigant.

TRIPHALA

Triphala is an Indian ayurvedic herbal formulation consisting of dried and powdered fruits of three medicinal plants Terminalia bellerica, Terminalia chebula, and Emblica officinalis. Triphala has been proven to be safe, containing active constituents that have beneficial physiologic effect apart from its curative property such as antioxidant, anti-inflammatory, and radical scavenging activity [15], and may have an added advantage over the traditional root canal irrigants.

Figure 2: The three plants that constitute Triphala -Terminalia bellerica, Terminalia chebula, and Emblica officinalis

A recent study showed that Triphala was as effective as NaOCl and a doxycycline based irrigant on root canal biofilms that were 3 weeks old. It brought about a 8 log reduction in E.fecalis counts, when compared to saline. Moreover, Triphala is also a very good chelating agent because of the fruits that are rich in citric acid, and holds promise in the removal of smear layer [16].

TURMERIC

Turmeric [Curcuma longa] is extensively used as a spice, food preservative and coloring material in India, China and South East Asia. It has been used in traditional medicine for the treatment of numerous diseases. C. longa, botanically related to ginger [Zingiberaceae family], is a perennial plant having a short stem with large oblong leaves and bears ovate, pyriform or oblong rhizomes, which are often branched and brownish-yellow in colour. Turmeric is used as a food additive [spice], preservative and colouring agent in Asian countries, including China and South East Asia. It is also considered as auspicious and is a part of religious rituals. In old Hindu medicine, it is extensively used for the

treatment of sprains and swelling caused by injury [17]. In recent times, traditional Indian medicine uses turmeric powder for the treatment of biliary disorders, anorexia, coryza, cough, diabetic wounds, hepatic disorders, rheumatism and sinusitis. The colouring principle of turmeric is the main component of this plant and is responsible for the anti-inflammatory property [18].

Figure 3: Curcuma longa and its powder

Curcumin [diferuloylmethane], the main yellow bioactive component of turmeric has been shown to have a wide spectrum of biological actions, including antimicrobial, anti-inflammatory and antioxidant activities [19]. Many studies have attributed a wide spectrum of activities to this compound, and this provides a suitable basis for exploring its endodontic applications. Components of turmeric are named curcuminoids [curcumin [diferuloyl methane], demethoxycurcumin, and bisdemethoxycurcumin]. These components are polyphenols with a strong antioxidant function [20]. Curcumin, the most important fraction, is responsible for the biological activities of turmeric. It has been hypothesized that curcumin inhibits the assembly of a protein - filamenting temperature-sensitive mutant Z [FtsZ] protofilaments and also increases the GTPase activity of FtsZ. The perturbation of the GTPase activity of FtsZ assembly is lethal to bacteria [21]. For an irrigant to be effective against biofilms, the action on biofilms should involve the elimination of the EPS matrix as well as the bacteria because this matrix could act as an additional source of nutrients and/or as a suitable surface for further cell growth [22].

A recent report suggested that curcumin in aqueous preparations exhibits phototoxic effect against gram positive and gram negative bacteria [23]. This opens up avenues for further research on the use of turmeric in photodynamic therapy of root canal systems. Previous studies have focused on the in vitro phototoxic effect of curcumin in various aqueous preparations against gram-positive Enterococcus faecalis and gram-negative Escherichia coli bacteria [24]. Curcumin in surfactant preparations showed its potential as a photosensitiser [PS] in antibacterial photodynamic therapy [aPDT] in vitro. The killing effect was shown to be dependent on curcumin concentration, radiant exposure, post-irradiation incubation time, bacteria species and pharmaceutical preparation. The exact mechanism by which curcumin causes light induced cell death has not yet been established, but it is generally accepted that a prerequisite for photosensitisation of a microbial cell is the binding of the PS to the outer membrane [25].

LIQUORICE

Liquorice is the most commonly used crude drug and flavouring agent in kampo medicines [traditional Chinese medicines modified in Japan] [26]. A number of pharmaceutical effects of Liquorice are known - anti-inflammatory, antiviral and anticarcinogenic [27]. Liquorice has been found that growth and adherence [plaque formation] of the cariogenic bacteria Streptococcus mutans was markedly inhibited [28]. Liquorice has been evaluated for the management of oral lichen planus. The study reported that Liquorice extract was as effective as triamcinolone acetonide but safer and may be used as an alternative treatment

for lichen planus [29]. The antibacterial activity of Liquorice and glycyrrhizin on different strains of S. mutans was also studied and their effects on the adherence of S. mutans to glass. Liquorice extract exhibited a more profound activity in both adherence and anti-bacterial assays than that of glycyrrhizin [30].

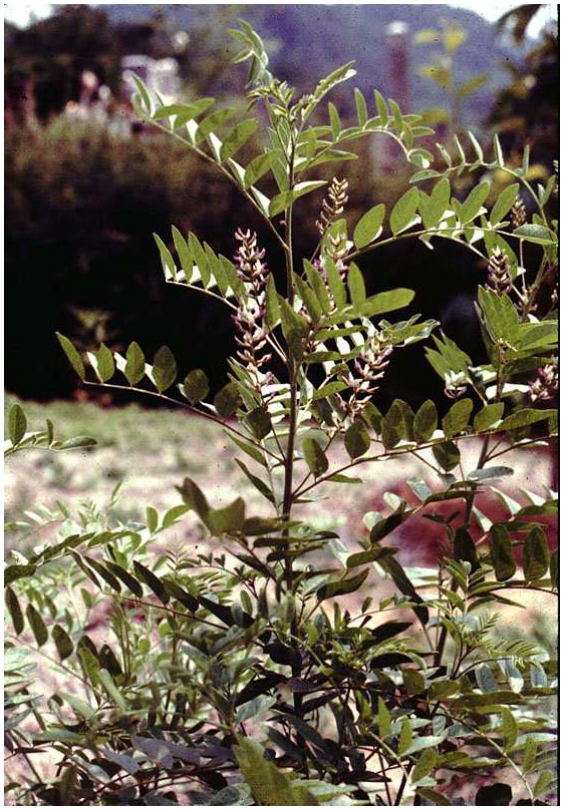

Figure 4: Liquorice [Glycyrrhiza glabra]

Glycyrrhizin, a triterpenoid compound, accounts for the sweet taste of Liquorice root. This compound represents a mixture of potassium-calcium magnesium salts of glycyrrhizic acid that varies within a 2–25% range. Amongst the natural saponins, glycyrrhizic acid is a molecule composed of a hydrophilic part, two molecules of glucuronic acid and a hydrophobic fragment, glycyrrhetic acid [31]. 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, rather than simply altering the surface tension of the extracellular medium, thus being influenced by microbial population density [32]. The flavonoid content of Liquorice extract is also a strong inhibitor of oxygen consumption in bacterial cells; the site of inhibition is thought to be between CoQ and cytochrome C in the bacterial respiratory electron transport chain [33].

Liquorice has also shown greater biocompatibility with fibroblasts cells compared to calcium hydroxide, which was severely toxic to the cells. A mixture of Liquorice and calcium hydroxide showed moderate cytotoxicity. The test implied a relative tolerability of Liquorice to fibroblasts at a relatively high concentration. This may be explained on the basis of the pentacyclic triterpenoid structure, which may resemble the phospholipid bilayer of the cell in containing polar [hydrophilic moiety] and non-polar [hydrophobic moiety] components. The Liquorice extract retains a slight acidic pH 6, whilst calcium hydroxide is a very polar and strong alkali [pH 12] [34].

PROPOLIS

Propolis is a resin widely used in folk medicine for centuries. Propolis is a resinous material that honeybees [Apis mellifera L.] collect from various plant species and mix with wax and other substances. Scientific research has revealed its antioxidant, antibacterial, anti- fungal, antiviral, anti-inflammatory, anti-tumor and immunomodulating properties [35]. Studies on propolis applications have increased because of its therapeutic and biological properties. Current research involving propolis in dentistry spans many fields and highlights its antimicrobial and antiinflammatory activities, particularly in cariology, oral surgery, pathology, periodontics and endodontics [36,37].

The chemical composition of this atoxic natural substance is complex. Flavonoids and cinnamic acid derivatives have been considered as the main primary biologically active components [38]. It is known that propolis exhibits several pharmacological properties such as anti-microbial,

anti-inflammatory, healing, anesthetic, cytostatic and cariostatic properties. Ethanolic extract of propolis inhibits hyaluronidase activity and hence has great potential as an anti-inflammatory agent [39].

In Dentistry, propolis has been used for the treatment of aphthous ulcers, Candida albicans, acute necrotizing ulcerative gingivitis [ANUG], gingivitis and periodontitis, and recently as a storage medium for teeth that get avulsed from its socket, in order to maintain the viability of the periodontal ligament cells. The anti-inflammatory property of propolis is due to the presence of caffeic acid and phenethyl ester [CAPE] in propolis. Ethanol extract of propolis presents good properties for endodontic use, such as promoting bone regeneration and inducing hard tissue bridge formation in pulpotomies or pulp capping. Propolis is dispensed in various forms. Propolis being a good antimicrobial and anti-inflammatory agent, can serve as a better intracanal irrigant and intracanal medicament [40,41].

The antibacterial efficacy of three commonly used intracanal medicaments with propolis against Enterococcus faecalis has been compared. They concluded that propolis had good in-vitro antibacterial activity against Enterococcus faecalis in the root canals, suggesting that it could be used as an alternative intracanal medicament. The antimicrobial activity of propolis with calcium hydroxide as intracanal, medicament against Enterococcus faecalis found that propolis was effective in eliminating the microorganisms [14].

TEA TREE OIL

Tea tree [Melaleuca alternifolia] is a native Australian plant, the oil of which has many properties that favor its use in dentistry. It is an antiseptic as well as an antifungal agent. It also has mild solvent action, and hence could hold potential applications in root canal treatment for dissolving the necrotic pulp tissue. Tea tree oil's major active component is terpinen-4-ol [typically 30- 40%]. This compound is responsible for its antibacterial and antifungal properties. An in vitro study showed that tea tree oil which might disinfect the root canal system as effective as NaOCl. Further, the toxicity of tea tree oil is lesser than NaOCl [42,43].

Figure 5: Tea tree oil [Melaleuca alternifolia]

NEEM

Azadirachta indica A. Juss is a commonly seen medicinal tree in India, which is considered holy. Popularly known as "Indian neem/ Margosa tree" or "Indian lilac", is well known in India and its neighboring countries for more than 2000 years as one of the most versatile medicinal plants having a wide spectrum of biological activity. In Sanskrit, it is called "arishtha" meaning "reliever of sickness" and is regarded as the village dispensary of India. Importance of neem tree has been recognized by US National Academy of Sciences where neem is entitled as 'a tree for solving global problems' [44]. Each part of the neem tree has some medicinal property and is thus commercially exploitable. Biologic activities and pharmacologic actions of neem are very well established with crude extracts and their different

fractions from its leaf, bark, flowers, roots, seed and oil [45].

Neem has a broad range of therapeutic effects. Several pharmacological activities and medicinal applications of various parts of neem are well known. Interest on this substance is based on its properties like antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, antipyretic, analgesic and immunostimulant activity [46]. Furthermore, it also has an anti-adherence activity by altering bacterial adhesion and ability of organism to colonize [47]. It has been shown that neem is highly effective in the treatment of periodontal disease. Its biocompatibility to human periodontal ligament fibroblasts is an important factor favoring its clinical application [48].

Figure 6: Neem [Azadirachta indica A. Juss]

Use of neem as an endodontic irrigant might be advantageous because it is a biocompatible antioxidant and thus not likely to cause the severe injuries to patients that might occur via NaOCl accidents. Bitter taste associated with this plant can be altered by different formulations due to addition of sweeteners and flavors to increase the patient compliance and acceptability [49]. A study showed significant differences in the zone of inhibition of diameters of neem extract and 2% NaOCl against E.faecalis and mixed culture [50].

CONCLUSION

We are living in an age of evidence based medicine. Any material with potential clinical application must go through a series of tests to demonstrate biocompatibility to the tissues of the oral cavity as well as marked advantages in terms of efficacy in root canal disinfection, when compared to contemporary irrigants. In vivo studies will also be required for recommending ideal clinical protocols using these materials. Currently, the development and accessibility of information on phytopharmaceuticals and natural medications are gradually gaining the respect of some patients and health professionals. Besides, the exploitation of these substances has a socioeconomic impact. It will lead to an increase in cultivation fields and in the market of informal herbs, as well as in an expansion of small and medium national pharmaceutical laboratories dedicated to manufacturing medicaments of natural and vegetable origin.

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