

Phytotherapy- A Drive towards Green and Clean Dentistry!

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ABSTRACT

The term “Phytotherapy” refers to the direct or indirect treatment of disease through the use of plants and plant-derived products. Since the dawn of time, people have employed herbs as a type of traditional medicine. Natural remedies obtained from therapeutic plants have shown an abundant supply of biologically active ingredients, several of which have served as the inspiration for creation of novel molecules for different medications. A single herb exhibits multiple benefits, such as anti-inflammatory, antibacterial, and antifungal activity, and its use in dental treatment proves to be an effective adjuvant. The applications of medicinal plants in endodontics are varied ranging from intracanal medicaments to irrigants and retreatment agents. Various synthetic chemicals play a significant role in disinfection in endodontics but also have undesirable properties such as allergic potential, increased microbial resistance, toxicity, safety concerns and bitter taste. Due to their widespread availability, low toxicity, and cost-effectiveness, herbal remedies are now being used more frequently as part of dental treatment and have experienced an exceptional surge in popularity in recent years. Therefore, this article aims to provide a comprehensive review of various phytochemicals and its endodontic applications, standardisation, possible side-effects and its benefits as an adjunctive therapy.

Keywords: Antimicrobial efficacy, Herbal medicine, Phytochemicals, Standardisation

INTRODUCTION

“The essence of all beings is earth, the essence of earth is water, the essence of water is plants, and the essence of plants is human being” [1]. Medical sciences in India dates back to the time of Vedas and Puranas. Ayurveda, the conventional Indian medicinal system is the most ancient yet widely practised science with sound analytical and experimental basis [2]. It is the science by virtue of which prospective of life can be increased or its nature is comprehended. There are over 1,250 Indian therapeutic herbs that are employed in Ayurvedic or other ethnic remedies [3].

Many of the physiologically active components found in medicinal plants serve as the foundation for the creation of novel medications. An estimated 25% of contemporary medications come either directly or indirectly from plants [4]. Phytotherapy implies the use of plants and their products either to treat various diseases or as health promoting agents [5].

The World Health Organisation (WHO) defines “herbal medicine as a practice which includes herbs, herbal materials, herbal preparations and finished herbal products that contain as active ingredients parts of plants, or other plant materials, or combinations” [6]. It is an integrated approach that employs a variety of treatments obtained from medicinal herbs and their extracts to cure ailments and uphold one’s health [6].

In recent years, there has been an increasing trend to seek herbal alternatives due to their beneficial properties in a single herb, lesser side-effects when compared to synthetic chemicals used for disinfection, ease of availability as well as cost-effectiveness and therefore incorporation of these herbs in dental practice could pave the way to a more “Natural and Green Dental Practice” [5]. Hence, this article aims to review the advantages of this comprehensive treatment approach as an auxiliary therapy in endodontic procedures.

CLASSIFICATION

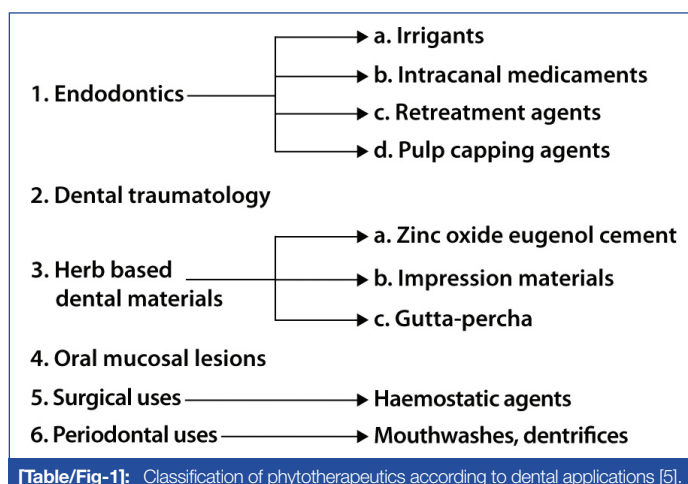
A. According to Phytotherapeutic Effects

- 1. Antimicrobial-** *Matricaria chamomile*, *Salvadora percaica*, *Azadirachta indica*.
- 2. Anti-inflammatory-** *Plumeria acuminata*, *Kalanchoe Brasiliensis*, Guaco, Propolis.

- 3. Sedative and anxiolytics-** *Melissa officinalis*, *Passiflora incarnale*, *Piper meythsticum*.
- 4. Miscellaneous-** Endodontic irrigants, medicaments and endodontic retreatment [7].

B. According to its Dental Applications

Classification of phytotherapeutics according to dental applications given in [Table/Fig-1].



[Table/Fig-1]: Classification of phytotherapeutics according to dental applications [5].

SYNTHETIC DRUGS VS HERBAL MEDICINES

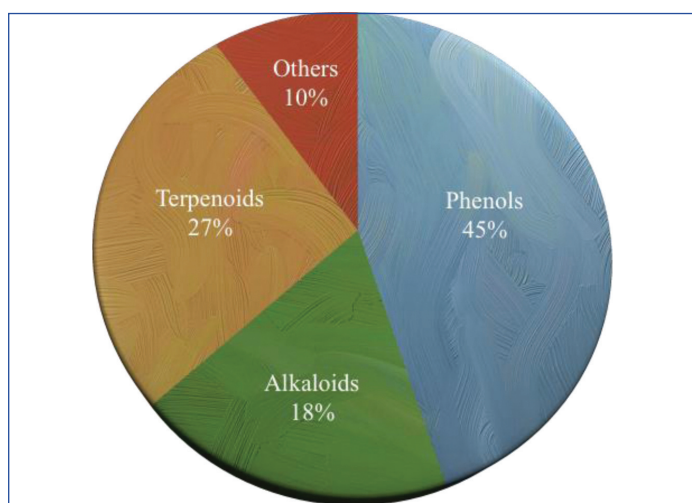
Herbal medicines exhibit some marked differences when compared to synthetic drugs, namely:

- Frequently unknown active constituents,
- Difficulty in standardisation, stabilisation and quality control,
- Less number of existing well-controlled randomised clinical trials to prove their efficacy and safety,
- Overcomes the problem of emerging resistance of pathogens to synthetic drugs,
- Availability and quality of raw materials are often problematic,
- Suitable for chronic treatments and possess a wide range of therapeutic actions,

- Lesser occurrence of undesirable side-effects and
- More economical [4].

PHYTOCHEMICALS AND ITS BIOLOGICAL ACTIVITIES

Phytochemicals are chemical constituents derived from medicinal herbs which are physiologically active and beneficent for human health [8]. The science of plant metabolites and their derivatives is known as Phytochemistry [9]. A plant's metabolic system can be thought of as being composed of controlled processes where biochemical transformations and mass transfer occur [10]. Primary metabolism and secondary metabolism are the two types of metabolic functions recognised in plants. Primary metabolites include common sugars, aminoacids, proteins, purines and pyrimidines of nucleic acids etc. Secondary metabolites include chemicals such as alkaloids, terpenes, flavonoids, lignans, phenolics and saponins [10]. Secondary metabolites constitute the majority of plant compounds that have been recognised to have therapeutic value and the major groups are illustrated in [Table/Fig-2]. According to a literature review, phenolics are the most prevalent and structurally diverse phytochemical [11].



[Table/Fig-2]: Major groups of phytochemicals.

The various plant metabolites and its potential value in medicine and dentistry are as follows:

Polyphenols

Phenols are among the largest group of secondary metabolites. A minimum of one aromatic ring and one or more hydroxyl groups are present in these molecules [11]. The three main types of polyphenols include tannins, catechins and flavonoids [5].

- Tannins** are high molecular weight polyphenols which exhibits multiple benefits as anti-inflammatory, antioxidant, antiseptic and haemostatic agents. It forms reversible and irreversible complexes with proteins and nucleic acid and produces antimicrobial action by inactivating bacterial enzymes. Examples- Common or great burdock (*Arctium Lappa*), Clove (*Syzygium aromaticum*) [5,11].
- Flavonoids** correspond to a wide range of substances which play a pivotal role in protecting physiological systems from the detrimental effects of reactive oxygen species on macromolecules like DNA, proteins, carbohydrates, and lipids [12]. They are water soluble polyphenols with numerous biotic properties, such as, anti-inflammatory, antibacterial, cytotoxic, and antitumour effects [11]. Examples- Propolis, Blue-gum tree (*Eucalyptus globules*) [5].
- Catechins** have been the subject of much research because of their appearance in oolong green tea. Catechins inactivate the bacterial glucosyltransferase in *S.mutans* and produces antimicrobial activity [5].

Alkaloids

Alkaloids are cyclic organic compounds containing nitrogen and are basic in nature [5]. Pharmaceutical significance of alkaloids includes antibacterial, antihypertensive, analgesic and antifungal activities [11]. Examples- Garlic (*Allium sativum*), Lemon (*Citrus limon*) [5].

Terpenoids and Essential Oils

Essential oils are responsible for imparting fragrance of plants. These oils are secondary metabolites which are highly rich in five carbon isoprene units called terpenes. Terpenoids are the name given to compounds when they include additional elements, typically oxygen [11]. Terpenenes or terpenoids have antibacterial, antifungal, and antiviral properties [5]. Examples- Camphor tree (*Cinnamomum camphora*), Coriander (*Coriandrum sativum*), Neem tree (*Azadirachta indica*) [5].

DENTAL APPLICATIONS OF PHYTOMEDICINE

As a single herb can perform a number of different functions, the use of phytomedicine for endodontic procedures has become increasingly popular. Medicinal plants have been employed as antibacterial agents to combat several endodontic infections. With obtundent and soothing effects, it has also been used in a variety of endodontic medicaments and dressings [5].

1. Endodontics

a. Irrigants: The anatomy of the root canals is intricate with fins, webs and anastomoses and effective disinfection of this complex system is the mainstay of any endodontic treatment. In order to clear the root canal space of the bacteria, biofilms, inflammatory exudates, necrotic tissues and other debris, the root canal is instrumented with hand and rotary files while being continuously irrigated. Sodium hypochlorite (NaOCl) is the most conventional and commonly employed irrigants because of its broad antimicrobial spectrum and its effective tissue- dissolving ability. However, multiple mishaps associated with improper management of NaOCl has been well-documented in the dental literature. It has shown to cause necrosis, haemolysis and cutaneous ulcerations by oxidation of the protein and lipid membranes. Staining of clothes, ocular injuries caused due to accidental splashing, tissue necrosis on inadvertent injection beyond apical foramen, tissue emphysema, and allergic reactions are potential issues that could arise when using NaOCl to irrigate root canals [13]. These problems have sparked a rising trend of people looking for biocompatible and herbal endodontic treatment alternatives.

Extracts from the therapeutic plants green tea, white tea tree, turmeric, chamomile, mustard tree, neem tree, Indian mulberry tree have been studied as potential endodontic irrigants. In addition, propolis which is a natural resinous substance derived from honey bees (*Apis mellifera*) demonstrates a variety of biological actions such as antimicrobial, anti-inflammatory, antioxidant and has also been researched as a root canal irrigant. Al-Qathami H and Almadi E determined that propolis possesses antibacterial activity which is equivalent to NaOCl after comparing the antimicrobial efficacy of propolis, NaOCl, and saline as intracanal irrigants [14].

In a research where chamomile hydroalcoholic extract and tea tree oil were compared to 2.5% NaOCl for their cleaning effectiveness as an endodontic disinfectant and irrigant it was observed that chamomile extract was significantly more efficient than tea tree oil and distilled water [15].

Basma A et al., conducted a study in 2014 to assess the antibacterial efficacy of ginger and garlic as irrigants. In his study, he concluded that garlic extract exhibited antibacterial efficacy against *E.faecalis* and also inhibited the formation of *Streptococcus epidermidis* biofilms [16].

In India, a common medicinal tree known as *Azadirachta indica* (Neem) is revered. It is known as the rural dispensary of India and

is known by the Sanskrit name “arishtha,” which means healer of sickness [17]. Using the agar diffusion method, Hegde V and Kesaria DP evaluated the antibacterial effectiveness of 2% NaOCl, propolis, neem leaf extract, turmeric, and licorice against *E.faecalis* and *C. albicans* and observed that neem leaf extract exhibited the greatest zone of inhibition against the two endodontic pathogens [18].

b. Intracanal medicaments: Intracanal medicaments have routinely been employed in root canal therapy as interappointment antimicrobial medicine to eliminate residual microorganisms, suppress bacterial recolonisation and prevent reinfection with the goal of achieving several effects with a single application, various chemicals are frequently combined to create a “cocktail” like preparation of the intracanal medicament [19]. However, numerous in-vitro investigations have demonstrated that the routinely used intracanal medications’ phenol and aldehyde derivatives are extremely toxic to mammalian cells and that their antibacterial activity is insufficient to counteract this toxicity [20,21]. Therefore, endodontic treatment is increasingly incorporating natural therapies, with *Arctium lappa*, triphala, and propolis being evaluated as intracanal medications [5].

Aloe vera (*Aloe barbadensis*) is a succulent plant which retains and store water in the stems and leaves. It comprises of 75 possible active components: vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids, and amino acids. Aloin and aloe-emodin are the principal constituents eliciting a wide range of therapeutic action of this plant. Due to the inclusion of anthrax quinine, which prevents the growth of *S.pyogenes* and *E.faecalis*, it is effective against both of these bacteria. In an in-vitro study carried out by Kurian B et al., it was discovered that aloe vera’s Minimum Inhibitory Concentration (MIC) was superior to calcium hydroxide in the removal of *E.faecalis* and that its antibacterial activity was demonstrated to escalate with time [22].

Arctium lappa, also known as burdock, is a plant that was imported from Japan and domesticated in Brazil [23]. Due to its well-known therapeutic actions, it is used extensively in popular medicine across the world [5]. Sesquiterpene lactones and the sugar inulin are the active ingredients in burdock. Research by Gentil M et al., and Chikkanna M et al., have revealed its significant antimicrobial activity against endodontic pathogens which paved the way for its use as an intracanal medicament [24,25].

c. Retreatment agents: Not all root canal treatments result in optimum long-term healing and failures in the primary treatment might necessitate the need for retreatment. In order to retreat previously filled canal systems, antimicrobial irrigants and medications must be able to reach all canal system ramifications that might be harbouring organic debris and microbes. There are several removal techniques available, ranging from mechanical instrumentation, application of heat, to use of gutta percha dissolving agents and these techniques may either be used individually or in conjunction. Over the years, numerous herbal preparations have been studied for endodontic retreatment using the oil’s solvent properties, such as Blue-Gum tree oil and Orange oil [26,27]. Besides having a pleasant smell which is easily tolerated by patients, herbal alternatives such as orange oil is inexpensive and has a viscosity close to water facilitating easy administration through endodontic syringes.

Traditional solvents like halothane and chloroform were shown to be less effective than orange oil at softening gutta-percha, according to research conducted by Oyama KO et al., [28].

In comparison to eucalyptol and distilled water, xylol and orange oil were found to be more effective at removing a variety of endodontic sealers, including those made of zinc oxide and eugenol (Endofill and Intrafill), silicon-polydimethylsiloxane (RoekoSeal), and calcium hydroxide (Sealer 26) [29].

d. Pulp capping agents: Direct pulp capping involves covering exposed pulp tissue with a material which facilitates pulpal healing

and induces reparative dentine formation [30]. Various materials have been used as pulp capping agents including calcium hydroxide and different calcium silicate cements such as Mineral Trioxide Aggregate (MTA) and Biodentine [31]. The use of herbal remedies for pulp capping may also be an effective alternative [5].

Propolis was examined by Parolia A et al., along with the effects of two currently available and widely utilised pulp-capping agents, MTA and Dycal, on mechanically exposed human pulp tissues [32]. On the 15th as well as the 45th day, teeth treated with Dycal had higher pulp irritation than teeth treated with Propolis and MTA. Compared to teeth treated with Dycal, on the 45th day, more teeth with Propolis and MTA demonstrated development of dentinal bridge which was closer to the pulp capping material. As a pulp capping agent, Propolis has a similar effect on pulp corresponding to MTA and Dycal [32].

2. Dental Traumatology

Dental avulsion is amongst the most traumatic dental injuries which is characterised by complete displacement of a tooth from its socket causing damage to the pulp tissues, gingiva and the periodontium. The extra-alveolar storage medium and storage period have a significant impact on the prognosis and success of tooth replantation. The usage of storage media like saliva, milk, Hank’s Balanced Salt Solution (HBSS), and ViaSpan have been recommended and well-documented. Recent studies, however, has recommended using herbal substitutes as potential interim transport media for an avulsed tooth [33].

In an in-vitro study to determine the efficacy of Green Tea Extract (GTE) as an alternative method of storing avulsed teeth, Hwang JY et al., concluded that HBSS media and GTE had the same amount of cell viability and that GTE could be used as an appropriate alternate storage medium for avulsed teeth [34].

Coconut water is sterile and known to possess regenerative and antioxidant properties. According to Omar SL et al., coconut water is superior to milk and comparable to HBSS and saline for preserving the viability of periodontal ligament cells of an avulsed tooth [35].

3. Herb-based Dental Materials

Medicinal herbs find various applications as biomaterials. The origins of almost all contemporary dental materials can be found in these phytochemicals. The frequently used materials of herbal origin used in routine dental practice includes zinc oxide eugenol cement as a constituent of endodontic sealers, gutta percha as endodontic obturating material, agar agar and alginate as impression materials, Camphorated Monochlorophenol (CMCP) as endodontic intracanal medicament and thymol in mouthwashes [5].

4. Action of Herbs on the Lesions of Oral Mucosa

Gingivitis, aphthous ulcers, thrush, and numerous bacterial and viral infections are examples of mucosal lesions. Herbal remedies are primarily supportive in nature as most of these infections are self-limiting. Aloe vera, rhatany, licorice and various other herbs have been proven to be effective in treating these lesions [5]. The efficiency of licorice bio adhesive hydrogel patches to reduce pain and hasten the recovery of recurrent aphthous ulcers was examined by Moghadamnia AA et al., [36]. The findings of this study indicate that licorice bio adhesive may be useful in reducing pain, as well as the inflammatory halo and necrotic centre of aphthous ulcers [36]. Mazzanti G et al., assessed the effectiveness of a hydroalcoholic extract of lemon balm leaves as an antiviral agent against type 2 Herpes Simplex Virus (HSV-2). With 0.5 mg/mL of the extract, the maximum inhibitory effect (60%) was attained. The authors advocate conducting clinical research on this medicinal plant and encourage the usage of lemon balm for the treatment of herpes simplex lesions [37].

5. Surgical Uses

Phytochemicals have demonstrated promising outcomes in promoting wound healing and as haemostatic agents. Ankaferd Blood Stopper® (ABS) is a special traditional medicinal extract which is derived from the following plants: *Thymus vulgaris*, *Glycyrrhiza glabra*, *Vitis vinifera*, *Alpinia officinarum* and *Urtica dioica* [38]. The effectiveness of topical application of ABS on haemorrhagic diathesis after dental treatments under various circumstances was evaluated by Baykul T et al., [39]. The majority of individuals who underwent dental surgery found that ABS was efficient at controlling bleeding within 10 to 20 minutes. These findings imply that ABS can be used as an effective haemostatic agent in patients with haemorrhagic diathesis after tooth extraction [39].

6. Periodontal Uses

To limit caries or biofilm formation, a range of antimicrobial agents and therapeutic medicinal herbal extracts are added to dentifrice and mouthwash formulations. Pistorius A et al., reported a significant reduction in both Sulcus Bleeding Index (SBI) and Gingival Index (GI) for a herbal mouthwash containing *S.officinalis*, *M.piperita*, menthol, *M.chamomilla*, *C. myrrha*, *Carum carvi* (Umbelliferae), *Eugenia caryophyllus* (Myrtaceae) and *E.purpurea* and came to the conclusion that individuals with any periodontal diseases could use the mouthwash daily as a supplementary therapy to minimise gingival inflammation [40].

SAFETY AND DRUG INTERACTIONS OF HERBAL MEDICINES

Although the majority of herbal products are presumably harmless under most conditions, few are identified to be harmful at increased dosage and others may have possible adverse reactions under certain circumstances [41]. The severity of side-effects varies with dosage, sensitive individuals' responses based on genetic predisposition, diet, drug interactions, and other factors [41]. Despite a wide spectrum of side-effects linked to phytomedicine in humans, allergy, dermatitis, headache, dizziness and gastrointestinal disturbances are a few of the side-effects that are specific to the phytotherapeutic medications that are most frequently used in dentistry [42].

Another concern regarding the use of herbal medicines is the possibility for adverse drug interactions when co-administered with therapeutic drugs, which have been observed more frequently recently [43,44]. Concurrent use of herbal medicines may cause changes in the pharmacokinetic and/or pharmacodynamic profiles of prescription drugs, enhancing or suppressing their effects which may potentially lead to adverse effects [45]. Warfarin, for example is an anticoagulant administered to prolong blood clot formation and this action could be potentiated by co-administration of garlic, ginkgo, ginger which have similar effects [46]. The following further elaborates well-documented reports on certain side-effects and drug interactions of medicinal herbs [Table/Fig-3] [46-55].

Authors	Place and year of study	Study	Herbs	Botanical name	Side-effects	Contraindicated drug	Drug interaction
West I and Maibach HI [47]	University of California Medical School, San Francisco, 1995	Contact urticaria syndrome from multiple cosmetic components. Contact Dermatitis	Lemon balm	<i>Melissa officinalis</i>	Contact dermatitis, Nausea and diarrhoea (West I and Maibach HI, 1995) [47]	Sedatives	Synergistic effects (Kennedy DO et al., 2002) [48]
Kennedy DO et al., [48]	Human Cognitive Neuroscience Unit, Division of Psychology University of Northumbria, Newcastle upon Tyne, UK, 2002	Modulation of mood and cognitive performance following acute administration of <i>Melissa officinalis</i> (lemon balm)					
Subiza J et al., [49]	Centro de Alergia e Inmunología Clínica, General Pardiñas, Madrid, Spain, 1990	Allergic conjunctivitis to chamomile tea	Chamomile	<i>Matricaria recutita</i>	Allergic conjunctivitis (Subiza J et al., 1990) [49]	Warfarin	Potentiate the anticoagulation effects (Segal and Pilote, 2006) [50]
Segal R and Pilote L [50]	Montreal General Hospital, 2006	Warfarin interaction with <i>Matricaria chamomilla</i>					
Smith GW et al., [51]	1993	Vasculitis associated with herbal preparation containing <i>Passiflora</i> extract	Purple Passion-flower	<i>Passiflora incarnata</i>	Emesis, narcotic effects, spasms (Smith GW et al., 1993) [51]	CNS depressants	Potentiates the depressant activity (Miller LG, 1998) [46]
Miller LG [46]	Department of Pharmacy Practice, Texas Tech University Health Sciences Center, 1998	Herbal medicinals: selected clinical considerations focusing on known or potential drug-herb interactions					
Hughes TM et al., [52]	Department of Dermatology, Royal Gwent Hospital, Newport, Gwent, UK, 2002	Occupational contact dermatitis from a garlic and herb mixture	Garlic	<i>Allium sativum</i>	Occupational contact dermatitis (Hughes TM et al.,) [52]	Warfarin	Potentiate the anticoagulation effects (Vaes LP and Chyka PA 2000) [53]
Vaes LP and Chyka PA [53]	Faculty of Pharmacy, The University of Utrecht, The Netherlands, 2000	Interactions of warfarin with garlic, ginger, ginkgo, or ginseng: nature of the evidence					
Hunter D and Frumkin A [54]	College of Medicine, University of Oklahoma Health Sciences Center, Okhaloma City, 1991	Adverse reactions to Vitamin E and aloe vera preparations after dermabrasion and chemical peel	Aloe vera	<i>Aloe barbadensis</i>	Redness, burning sensation, dermatitis in sensitive individuals (Hunter D and Frumkin A, 1991) [54]	Oral hypoglycaemic agents	Synergistic effect (Yongchaiyudha S et al., 1996) [55]
Yongchaiyudha S et al., [55]	Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, 1996	Clinical trial in new cases of diabetes mellitus					

[Table/Fig-3]: Side-effects and drug interactions of herbal medicines [46-55].

STANDARDISATION AND QUALITY CONTROL OF MEDICINAL HERBS

The stability and quality of herbal medicines are crucially dependent on the source and quality of their base materials. Apart from this, temperature, light exposure, water accessibility, nutrients, collection time and manner, drying, packing, storage, and transportation of raw ingredients can adversely influence the quality and, as a result, the clinical efficacy of herbal medicines [6]. This explains why the composition of herbal medicines is quite variable. Thus, proper standardisation and quality control of herbal preparations should be carried out that serves to optimise the batch-to-batch consistency of the botanical product. Adjusting the herbal preparation to a defined amount of the active ingredient is known as standardisation [56]. For analytical purposes where these active constituents are unknown, marker compounds should be established. Markers are chemically defined constituents, with or without therapeutic activity which are used for control purpose and serves as a powerful tool in the finished form of herbal drug preparations [57]. The concept of standardisation is increasingly gaining popularity and is a rational method to promote patients' and doctors' acceptance of therapeutic plants.

CONCLUSION(S)

Phytotherapeutic agents could represent a source of new anti-infective agents against antibiotic resistance pathogens. Although the number of clinical trials for these products is encouraging, more research on their safety and effectiveness is necessary to determine if they render medicinal value independently or in combination with existing medications, that may contribute to a reduction in the global burden of oral diseases. Studies addressing concerns especially like sufficient statistical power, blinding, standardisation of extracts or purified chemicals and quality control would be very beneficial.

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