



SCIENTIFIC VALIDATION OF HERBS USED IN SIDDHA MEDICINE FOR DENTAL CARE: AN INTEGRATIVE SYSTEMATIC REVIEW

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ABSTRACT

Oral health inequities persist globally due to limited access to conventional dental care, high costs, and antibiotic resistance. Siddha medicine offers a rich repository of herbal formulations for dental applications, yet scientific validation remains fragmented. This systematic review evaluates the scientific evidence for nine Siddha medicinal plants used in dental care, correlating traditional uses with modern pharmacological findings to support evidence-based clinical integration. Following PRISMA guidelines, we systematically reviewed literature from PubMed, Scopus, Web of Science, and Google Scholar (2004-2024) for nine selected plants from reputed siddha text where the plants were described in traditional basis: *Anacyclus pyrethrum*, *Syzygium aromaticum*, *Azadirachta indica*, *Curcuma longa*, *Terminalia chebula*, *Acacia catechu*, *Ficus benghalensis*, *Solanum surattense*, and *Mentha arvensis*. Data on phytochemistry, antimicrobial, anti-inflammatory, analgesic, anesthetic, and antioxidant activities were extracted and categorized using WHO evidence classification. Six plants achieved clinical readiness (Levels Ia-IIa). *Curcuma longa* demonstrated Level Ia evidence with meta-analyses confirming efficacy in periodontitis and oral mucositis. *Syzygium aromaticum*, *Azadirachta indica*, *Terminalia chebula*, and *Acacia catechu* showed Level Ib evidence from randomized trials. *T. chebula* exhibited superior anticaries activity (MIC 10 µg/ml against *S. mutans*), while *A. pyrethrum* demonstrated exceptional analgesic effects (94% pain inhibition). *A. indica* provided unique antiviral activity and broad antimicrobial spectrum. Scientific validation supports integrating six Siddha herbs into evidence-based dental practice. It is concluded that their therapeutic profiles offer accessible, cost-effective solutions for global oral health challenges, particularly anticaries, analgesic, and anti-inflammatory applications. Which will enhance the integrative dentistry in future medicine 2.0.

KEYWORDS: Antimicrobial activity, Dental caries, Herbal dental care, Integrative dentistry, Phytochemicals.

1. INTRODUCTION

Oral health remains an integral component of overall health and well-being, yet access to dental care continues to be a significant challenge globally. The World Health Organization has recognized oral health as a fundamental right that should be integrated into primary healthcare services, emphasizing the need for affordable, accessible, and culturally appropriate dental care solutions. However, conventional dental treatment approaches often face limitations including high costs, limited accessibility in rural areas, antibiotic resistance, and adverse effects of synthetic drugs (Lakshmi et al., 2015).

Siddha medicine offers a rich repository of herbal formulations specifically designed for dental care and emphasizes holistic healing through natural substances and lifestyle modifications. The Siddha pharmacopoeia contains extensive documentation of medicinal plants used for treating various oral pathologies including dental caries, tooth sensitivity, periodontal diseases, oral inflammation, and infections (Lakshmi et al., 2015).

Traditional Siddha dental care practices include various formulations such as tooth powders (*Podi*) for cleaning and strengthening teeth, mouth rinses and gargles utilizing decoctions and infusions for antimicrobial action, medicated oils (*Thailam*) for oil pulling and gum

massage, herbal pastes (*Kalimbu*) applied directly to affected areas for localized treatment, and chewing sticks from specific medicinal plants with inherent cleansing properties. These preparations traditionally utilize specific plant parts roots, bark, leaves, flowers, fruits, and latex each selected for their unique phytochemical properties and therapeutic actions (Fahim Fuard *et al.*, 2025).

1.1. Current Challenges in Oral Healthcare

Despite advances in dental science, significant populations worldwide lack permanent access to dental services, with barriers existing at multiple levels individual psychological factors, community structures, and systemic policy limitations. In developing countries, these challenges are particularly acute. Services are predominantly oriented toward emergency pain relief rather than prevention. Oral healthcare is largely confined to private clinics and urban hospitals. Rural areas have extremely limited access to qualified dental professionals. High treatment costs exclude economically disadvantaged populations. Conventional dental education remains disconnected from primary healthcare systems, with insufficient emphasis on preventive strategies and community-based care (Lakshmi *et al.*, 2015).

Integration of oral health into primary healthcare remains inadequate in most national health policies, with services not following the common risk factor approach and lacking cost-sharing mechanisms. This disconnect perpetuates health inequities and prevents comprehensive oral healthcare delivery (Kumar *et al.*, 2015).

1.2. Bridging Siddha Knowledge and Modern Science

While Siddha medicine has been practiced for centuries with documented clinical success, scientific validation of these traditional remedies through modern research methodologies is essential for their integration into evidence-based dental practice. Contemporary pharmacological research has begun investigating the phytochemical constituents of Siddha medicinal plants, elucidating their mechanisms of action at molecular levels, and validating their therapeutic efficacy through controlled clinical trials (Han & Parker, 2017).

However, a significant gap exists between traditional knowledge documentation and systematic scientific validation. Many Siddha herbs used for dental care have limited modern research despite extensive traditional use. This systematic review aims to bridge this gap by comprehensively analyzing scientific literature on Siddha

medicinal plants for dental applications, correlating traditional uses with validated pharmacological actions, identifying phytochemical constituents responsible for therapeutic effects, evaluating safety profiles through toxicological studies, and providing evidence-based recommendations for clinical integration (Jawhari *et al.*, 2020; Mittal *et al.*, 2014).

Modern dental products toothpastes, mouthwashes, tooth powders, and medicated pads can be significantly enhanced by incorporating validated Siddha herbal ingredients. Such integration would create herbal toothpastes combining fluoride with antimicrobial herbs for dual protection, herbal mouthwashes providing natural antiseptics without alcohol-related side effects, medicated tooth powders offering traditional cleaning agents with scientifically proven efficacy, herbal dental pads for localized treatment of periodontal conditions, and medicated mouth oils for oil pulling with enhanced antimicrobial properties. These integrative formulations can optimize treatment outcomes by synergistically combining the benefits of modern dental science with time-tested traditional remedies, making oral healthcare more effective, accessible, and culturally appropriate (Srivastava & Singh, 2023; Usmani *et al.*, 2016).

However, despite the long-standing traditional use of Siddha medicinal plants in oral health, scientific evidence validating their phytochemical mechanisms, clinical efficacy, safety, and optimal formulation remains fragmented, highlighting the need for a systematic review to consolidate and evaluate available data (Braga *et al.*, 2021). This review therefore aims to address these gaps by correlating traditional Siddha practices with modern pharmacological findings, identifying key dental herbs and their active constituents, assessing safety and therapeutic potential, and proposing evidence-based strategies for clinical application and product development.

2. METHODOLOGY

2.1. Study Design

This is a systematic literature review and integrative analysis following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The study combines traditional Siddha literature review for ethnobotanical documentation with analysis of modern scientific research. The PRISMA framework will be applied to ensure transparent and complete reporting of the systematic review process.

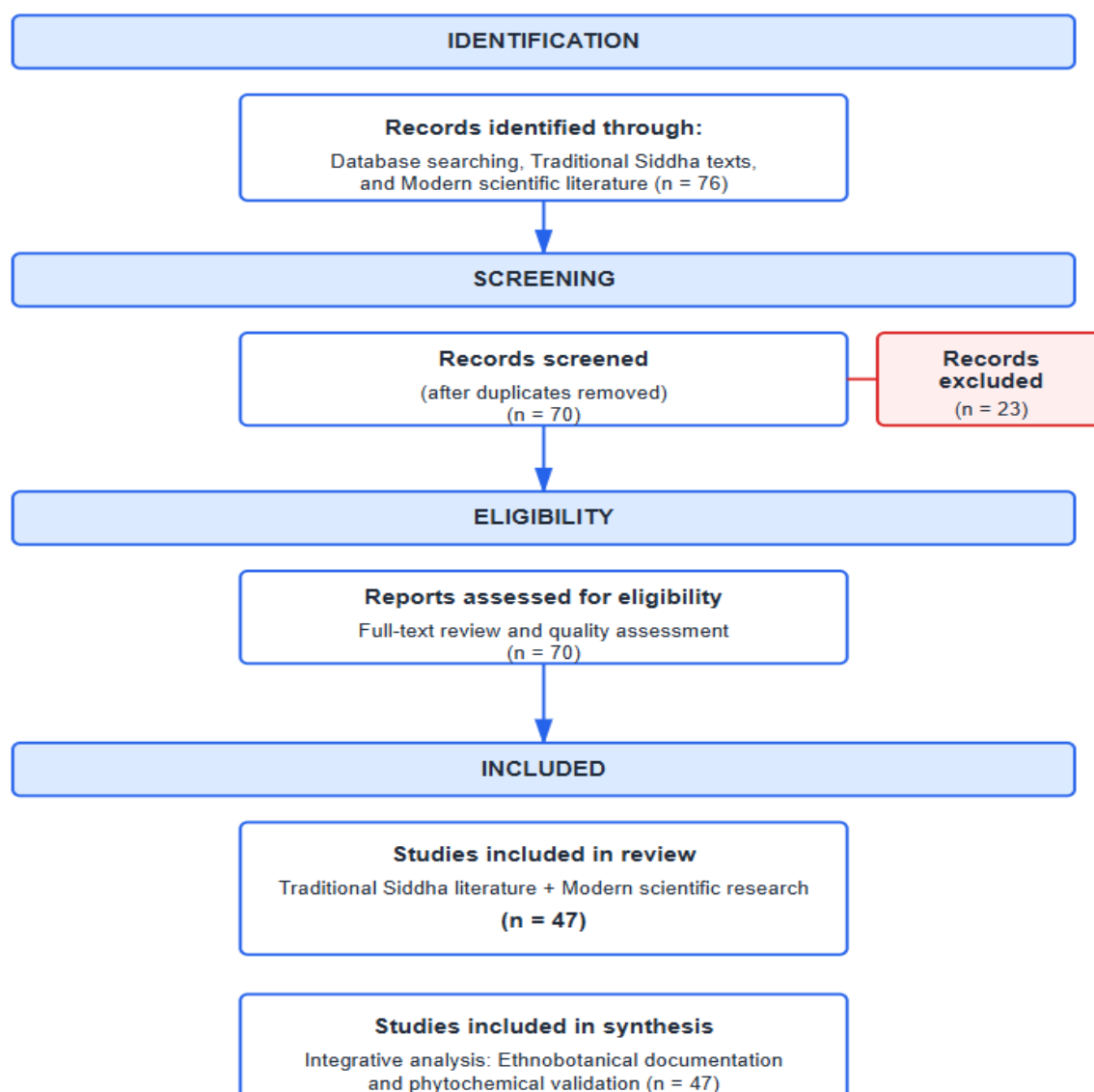


Figure 01: PRISMA 2020 Flow Diagram.

2.2. Selection of Medicinal Plants

Nine medicinal plants, which were selected based on documented use in classical Siddha texts specifically for dental applications (Murugesu mudhaliyar, 1998). Selected plants include *Anacyclus pyrethrum*, *Syzygium aromaticum*, *Azadirachta indica*, *Curcuma longa*, *Terminalia chebula*, *Acacia catechu*, *Ficus benghalensis*, *Solanum surattense*, and *Mentha arvensis*. The above plants stated in the recent past research findings for dental care (Lakshmi et al., 2015; Batiha et al., 2020).

2.3. Literature Search Strategy

Databases searched included PubMed/MEDLINE, Scopus, Web of Science, Google Scholar, Science Direct and Cochrane Library. The time frame focused primarily on 2004-2024 for modern scientific research, with classical Siddha texts documentation. Landmark earlier written books were not excluded if it is inevitable.

2.4. Inclusion and Exclusion Criteria

Publications were included if they investigated plants specifically mentioned in Siddha literature for dental applications, reported original research on phytochemical analysis, pharmacological studies, or clinical trials, examined activities relevant to dental care including antimicrobial, anti-inflammatory, analgesic, antioxidant, local anesthetic, or sialagogue properties, provided clear methodology and reproducible results, were published in peer-reviewed journals, were available in English.

Study types included in vitro antimicrobial studies against oral pathogens, in vivo animal studies on relevant pharmacological activities, clinical trials on dental or oral health outcomes, phytochemical analysis and compound isolation studies, toxicological and safety studies, and traditional use surveys and ethnobotanical documentation.

Publications were excluded if they focused on non-dental applications only, were duplicate publications or

redundant data, lacked clear methodology or had significant methodological flaws, were opinion pieces, editorials, or non-peer-reviewed articles without original data, examined plants not documented in Siddha dental care traditions, or were inaccessible despite exhaustive search efforts (Prashar et al., 2006).

2.5. Data Extraction and Analysis Framework

For each selected plant, data were systematically extracted on botanical characterization including Data extraction included scientific name with taxonomic authority, family, English/Tamil/regional common names, known synonyms, and traditionally used plant parts, along with Siddha text references describing dental uses, formulations (powder, decoction, paste, oil), dosage, administration, and contraindications. Phytochemical information captured major compound classes, specific bioactive constituents, extraction methods, and quantification reports (Jawhari et al., 2021; Nahak & Sahu, 2011). Pharmacological evidence was recorded for antimicrobial, anti-inflammatory, analgesic, anesthetic, antioxidant, sialagogue, and wound-healing activities with details on study models, potency values, and mechanisms. Safety evaluation included toxicity parameters such as LD50, chronic exposure effects, organ toxicity, genotoxicity, dosage limits, adverse reactions, and herb-drug interaction reports (Braga et al., 2021; Prashar et al., 2006).

2.6. Data Synthesis and Categorization

Plants were categorized based on cumulative evidence using the World Health Organization (2000) guidelines for levels of evidence in traditional medicine research. The classification system includes: Level Ia: Evidence obtained from meta-analysis of randomized controlled trials, Level Ib: Evidence obtained from at least one randomized controlled trial, Level IIa: Evidence obtained from at least one well-designed controlled study without randomization, Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study, Level III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies, Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities. Plants achieving Level Ib or higher were considered to have strong scientific support with readiness for clinical integration. Plants at Level IIa-IIb demonstrated moderate evidence requiring further clinical validation. Plants at Level III-IV had traditional use with limited modern scientific data, representing priority candidates for rigorous investigation (World Health Organization, 2000).

3. OBSERVATION AND DISCUSSION

3.1. Plant Analysis 1: *Anacyclus pyrethrum* (Akkarakaram)

3.1.1. Botanical Profile and Traditional Applications

Anacyclus pyrethrum (L.) Link, belonging to the family Asteraceae, is known in Tamil Siddha medicine as

Akkarakaram or *Akkirakaram*. This herbaceous plant has been extensively documented in traditional medical systems including Siddha, Ayurveda, and Unani for its remarkable therapeutic properties in oral health management. The plant is characterized by its use of roots as the primary medicinal part, though recent phytochemical investigations have also explored the therapeutic potential of aerial parts including flowers, leaves, and seeds. Common names across different languages include *Akkalkadha*, Pyrethrum Root, Spanish Pellitory, and Pellitory, reflecting its widespread recognition in traditional medicine systems (Fahim Fuard et al., 2025).

Historical Siddha texts document extensive use of *A. pyrethrum* root for various oral and dental conditions. The herb has been traditionally employed to address toothache, gingivitis, dental caries-associated pain, and periodontitis. Traditional preparation methods include decoctions used alone or in combination with other medicinal plants, powdered root preparations for topical application, and various formulations targeting specific oral conditions. Classical Siddha literature recommends 0.5-1 g of root powder for anti-inflammatory and analgesic applications, with variations in dosage forms based on the specific condition being treated and the method of preparation employed (Fahim Fuard et al., 2025).

3.1.2. Phytochemical Composition

Comprehensive phytochemical analysis of *A. pyrethrum* has revealed a diverse array of bioactive compounds responsible for its therapeutic effects. The most therapeutically significant class includes pellitorine and various N-isobutyl derivatives including N-isobutyl-2,4-octadiene-6-monoynamide, N-isobutyl-2,4-undecadiene-8,10-diynamide, N-isobutyl-2,4-heptadiene-6-monoynamide, and N-isobutyl-dodeca-2,4,8,10-tetraenamide. These compounds exhibit potent anti-inflammatory, antimicrobial, antioxidant, and immunomodulatory activities (Jawhari et al., 2021).

Multiple fatty acids contribute to the antimicrobial and anti-inflammatory properties, including decanoic acid functioning as an antibacterial and anti-inflammatory agent, dodecanoic acid providing bactericidal, anti-inflammatory, antifungal, and antiviral properties, tetradecanoic acid offering antibacterial with anti-virulence properties, and hexadecanoic acid demonstrating antibacterial and anti-inflammatory activities (Fahim Fuard et al., 2025).

Analysis by Cherrat et al. (2017) revealed significant variations in phytochemical content across different plant parts. Hydro-methanol crude extracts showed total polyphenol content ranging from 7.83 to 21.84 mg gallic acid equivalent per gram of extract, with flowers and leaves containing higher concentrations compared to roots. Flavonoid content demonstrated a similar pattern, with flowers showing the highest concentration at 3.04

mg quercetin equivalent per gram of dried plant material, followed by leaves at 2.93 mg and roots at 0.96 mg. This distribution pattern reveals an important characteristic: while roots contain the highest concentration of alkylamides responsible for analgesic and local anesthetic effects, aerial parts are richer in polyphenols and flavonoids that contribute primarily to antioxidant activity (Cherrat et al., 2017).

3.1.3. Pharmacological Activities

3.1.3.1. Antimicrobial Activity

A. pyrethrum exhibits broad antimicrobial activity with notable selectivity. Methanolic aerial extracts showed strong inhibition against *Listeria monocytogenes* (100%), *Bacillus cereus* (69%), and *Staphylococcus aureus* (66%) (Fahim Fuard et al., 2025). Root extracts demonstrated potent action on *S. aureus* with MIC values of 0.39–0.78 mg/mL and inhibition zones up to 15 mm, though MBC reached 800 mg/mL (Jawhari et al., 2021; Jalayer Naderi et al., 2012). Against oral streptococci, activity was mild with *S. sanguis* (MBC 800 mg/mL) but completely absent against *Streptococcus mutans*, limiting anti-caries potential (Jalayer Naderi et al., 2012; Fahim Fuard et al., 2025). Activity against Gram-negative organisms varied by part and solvent—capitula inhibited *Pseudomonas aeruginosa* (15.65 mm zone), methanolic extracts acted on *E. coli* (MIC/MBC 800 mg/mL) and *Klebsiella pneumoniae* (15.3 mm zone) (Jawhari et al., 2021; Jalayer Naderi et al., 2012). Strong antifungal action was recorded against *Candida albicans* (81% inhibition), indicating value in oral candidiasis (Fahim Fuard et al., 2025). Thus, *A. pyrethrum* is promising for staphylococcal wounds and fungal infections but requires combination with anti-*S. mutans* herbs for caries management.

3.1.3.2. Anti-inflammatory Activity

Exceptional anti-inflammatory effects were demonstrated in carrageenan-induced edema, with root extracts (300 mg/kg) inhibiting inflammation up to 96%, while seeds, leaves, and capitula produced 60–98% inhibition (Jawhari et al., 2020). Alkylamides (notably pellitorine), levulinic acid, propanedioic acid, cinnamic acid, and γ -sitosterol contribute to COX-pathway and mediator suppression (serotonin, prostaglandins, histamine) (Jawhari et al., 2020; Jawhari et al., 2021; Fahim Fuard et al., 2025). The high inhibition rate supports its use for gingivitis, acute periodontal inflammation, and post-surgical swelling management.

3.1.3.3. Analgesic Activity

Hydroalcoholic root extract (300 mg/kg) achieved 94.10% inhibition in acetic acid-induced pain—highest among plant parts (Jawhari et al., 2020). In the formalin test, extracts produced 88–94% inhibition across both neurogenic and inflammatory phases, and up to 91–94% in formaldehyde pain models, confirming dual central and peripheral action (Jawhari et al., 2020; Fahim Fuard et al., 2025). Pellitorine-type alkylamides and morphinan-6-one derivatives act via μ -opioid and ion-

channel modulation (Jawhari et al., 2021). This dual-mechanism effect validates use for toothache and supports development of fast-acting dental analgesic pads and gels.

3.1.3.4. Local Anesthetic Activity

A 2% ethanol root extract demonstrated significant anesthesia in guinea pigs and was clinically comparable to 2% lidocaine in humans (Usmani et al., 2016; Fahim Fuard et al., 2025). Pellitorine mediates sodium channel blockade similar to synthetic anesthetics. This supports formulation potential for natural pre-injection gels, injectable alternatives for allergic patients, and post-extraction medicated pads.

3.1.3.5. Antioxidant Activity

Hydro-methanol flower extracts exhibited highest antioxidant capacity with polyphenols 21.84 mg GAE/g and flavonoids 3.04 mg QE/g, while leaves showed 7.83–21.84 mg GAE/g and roots lower at 0.96 mg QE/g (Cherrat et al., 2017). Ethanollic root extracts also showed strong in vivo antioxidant activity (Usmani et al., 2016). Polyphenols correlated directly with antioxidant strength, supporting use in oxidative-stress-related periodontal disease and oral cancer prevention (Cherrat et al., 2017; Usmani et al., 2016).

3.1.3.6. Sialagogue Action

Root pellitorine induces rapid salivation via TRPV1/TRPA1-mediated sensory stimulation, beneficial for xerostomia, medication-related dry mouth, Sjögren's syndrome, and post-radiotherapy cases. Clinical formulation potential includes slow-release lozenges and chewable salivary stimulants (Usmani et al., 2016; Fahim Fuard et al., 2025).

3.1.4. Safety and Toxicological Profile

Safety assessment is paramount for any substance intended for human therapeutic use. *A. pyrethrum* benefits from both centuries of traditional use and modern toxicological evaluation. Jawhari et al. (2020) conducted acute toxicity studies using hydroalcoholic extracts in mice and rats. No mortality or serious adverse effects were observed at therapeutic doses. Importantly, doses up to 300 mg/kg, representing multiple-fold above typical therapeutic doses, were well-tolerated, providing a substantial safety margin. Usmani et al. (2016) reported that 2% alcoholic extract used in human subjects in a clinical study produced no serious adverse effects, demonstrating clinical safety at therapeutically effective concentrations. Centuries of documented use in Siddha, Ayurveda, and Unani medical systems without reports of major adverse effects provides additional confidence in safety (Fahim Fuard et al., 2025; Jawhari et al., 2020; Usmani et al., 2016).

The most commonly reported side effects are minor and generally represent expected pharmacological effects rather than toxicity. Burning or tingling sensation, an expected effect of pellitorine and related alkylamides, is

usually well-tolerated and indicates pharmacological activity. Local irritation may occur with concentrated preparations. Excessive salivation, while representing the desired sialagogue effect, may be uncomfortable for some individuals at higher doses (Fahim Fuard et al., 2025; Usmani et al., 2016).

3.1.5. Evidence Categorization and Clinical Readiness

A. pyrethrum is categorized as Level IIa (evidence from well-designed controlled studies without randomization) based on human clinical data available for local anesthetic activity representing controlled comparison to lidocaine (Usmani et al., 2016), multiple high-quality in vivo animal studies with consistent findings across pain and inflammation models (Jawhari et al., 2020), exceptional potency in primary indications including 94% analgesic, 96% anti-inflammatory effects, clear phytochemical characterization with identified bioactive compounds and mechanistic understanding at molecular level, traditional use validation confirming primary indications align with scientific evidence, and acceptable safety profile with only minor adverse effects documented. However, limitations include selective antimicrobial spectrum requiring combination with anti-*S. mutans* herbs for comprehensive caries prevention, no anti-*S. mutans* activity meaning it cannot serve as sole agent for caries prevention applications, and need for randomized controlled trials for advancement to Level Ib evidence. (Jawhari et al., 2020; Usmani et al., 2016; Fahim Fuard et al., 2025).

3.2. Plant Analysis 2: *Syzygium aromaticum* (Lavangam/Clove)

3.2.1. Botanical Profile and Traditional Applications

Syzygium aromaticum L. (Merr. & L.M.Perry), synonymously known as *Eugenia caryophyllata* or *Eugenia aromatica*, belongs to the family Myrtaceae. This aromatic evergreen tree is known in Tamil Siddha medicine as *Lavangam* or *Kirambu*, and has been among the most valued medicinal spices in world trade for over two millennia. The commercially valuable part of the clove tree is the unopened flower bud, harvested and dried to form the characteristic nail-shaped clove spice. While flower buds are the primary medicinal part, leaves also contain bioactive compounds and are utilized in some traditional preparations (Batiha et al., 2020).

Clove has been extensively documented in Siddha medicine for oral and dental health applications. Classical texts record its use for toothache relief as the primary and most prominent traditional indication, dental cavity pain through direct application to cavities, gum inflammation and infections utilizing its antiseptic properties, oral infections capitalizing on broad antimicrobial action, bad breath through aromatic and antimicrobial effects, and as a general oral antiseptic in various medicinal formulations. Traditional dosing varies by application method, including direct application of 1-2 whole cloves held against painful tooth until relief is achieved, topical application of a few drops of clove oil

applied directly to affected site, internal use in culinary amounts for systemic benefits, and mouth rinse using decoction 2-3 times daily for oral hygiene and infection control (Batiha et al., 2020; Mittal et al., 2014).

3.2.2. Phytochemical Composition

Clove has been subject to extensive phytochemical characterization, revealing a relatively simple but highly effective chemical profile dominated by eugenol, which constitutes the primary bioactive compound and serves as an excellent marker for standardization. The phytochemical profile comprises phenylpropanoids including eugenol (primary constituent), eugenyl acetate, and isoeugenol; sesquiterpenes notably β -caryophyllene and α -humulene; minor amounts of monoterpenes; flavonoids including quercetin and kaempferol derivatives; both condensed and hydrolysable tannins; phenolic acids such as gallic acid and ellagic acid; and complex essential oil mixtures dominated by eugenol (Batiha et al., 2020; Mittal et al., 2014).

Eugenol (4-allyl-2-methoxyphenol) represents the dominant and most therapeutically significant component, constituting 60-90% of clove essential oil, with typical concentrations around 78%. This remarkable concentration makes eugenol the primary bioactive agent responsible for most of clove's therapeutic effects including analgesic, anesthetic, antimicrobial, and anti-inflammatory activities. The high and consistent eugenol content facilitates standardization and quality control of clove preparations (Batiha et al., 2020; Srivastava & Singh, 2023).

3.2.3. Pharmacological Activities

3.2.3.1. Antimicrobial Activity

Clove oil and eugenol exhibit broad-spectrum antimicrobial activity, particularly strong against *Streptococcus mutans* and *Lactobacillus*—key organisms in dental caries—giving clove a significant advantage over *A. pyrethrum*, which lacks anti-*S. mutans* activity (Batiha et al., 2020). Eugenol achieves complete inhibition of 31 strains of *Helicobacter pylori* at 2 μ g/mL, surpassing amoxicillin with no resistance development, and shows activity against Gram-positive and Gram-negative organisms including *E. coli* O157:H7 (Batiha et al., 2020). Strong antifungal properties are noted against *Candida*, *Aspergillus*, and dermatophytes, with eugenol identified as the primary active component causing spore and micelle lysis (Mittal et al., 2014). Eugenol also enhances antibiotic penetration and synergistically improves the efficacy of vancomycin and β -lactams, supporting combined herbal-pharmaceutical use (Srivastava & Singh, 2023).

3.2.3.2. Analgesic & Anesthetic Activity

Eugenol is widely used clinically for dental pain relief, supported by extensive long-term clinical practice (Mittal et al., 2014; Srivastava & Singh, 2023). Mechanistically, it reduces pain via COX enzyme inhibition, sensory receptor suppression, sodium-

channel-mediated nerve blockade, and central pain modulation (Mittal et al., 2014; Srivastava & Singh, 2023). Clove oil also provides mild local anesthesia, demonstrated even in aquatic anesthesia studies at 60–100 ppm, producing reversible anesthetic effects (Mittal et al., 2014).

3.2.3.3. Anti-inflammatory Activity

Clove oil and eugenol exert strong multi-pathway anti-inflammatory effects. In human fibroblasts, 0.011% clove oil significantly reduced VCAM-1, IP-10, I-TAC, MIG, collagen I/III, M-CSF, and TIMP-2, while downregulating genes linked to inflammation, tissue remodeling, stress response, and metabolism (Han & Parker, 2017). Eugenol inhibits COX-2, NF- κ B, and reduces TNF- α , IL-1 β , IL-6, alongside chemokine suppression and potent antioxidant-linked inflammatory reduction (Han & Parker, 2017; Srivastava & Singh, 2023; Mittal et al., 2014).

3.2.3.4. Antioxidant Activity

Clove oil displays exceptional antioxidant capacity, inhibiting lipid peroxidation by 97.3% at 15 μ g/mL, comparable to or exceeding synthetic antioxidants (Mittal et al., 2014). Eugenol scavenges free radicals through phenolic hydrogen donation, chelates metal ions (Fe²⁺/Cu⁺), and disrupts lipid peroxidation chains. Synergy from β -caryophyllene, flavonoids, and tannins enhances total antioxidant power (Mittal et al., 2014; Srivastava & Singh, 2023).

3.2.3.5. Synergy with Antibiotics

A key therapeutic advantage is eugenol's ability to increase antibiotic permeability and produce synergistic bactericidal effects, enabling lower antibiotic doses without loss of efficacy, supporting its role in resistance-management strategies (Srivastava & Singh, 2023).

3.2.4. Safety and Toxicological Profile

While clove oil and eugenol demonstrate remarkable therapeutic properties, safety considerations require careful attention, particularly regarding concentration-dependent cytotoxicity. Prashar et al. (2006) conducted crucial safety research revealing concentration-dependent cytotoxicity to human skin cells. Clove oil at concentrations as low as 0.03% (v/v) equivalent to 300 parts per million was highly cytotoxic, with up to 73% of this cytotoxic effect attributable to eugenol specifically. Pure eugenol, which constitutes 78% of clove oil, was highly cytotoxic to skin cells at concentrations as low as 0.06% (600 ppm) (Prashar et al., 2006).

The apparent contradiction between demonstrated cytotoxicity and centuries of safe clinical use can be explained by several factors: short contact time in dental applications (minutes rather than hours or days), limited surface area of application (specific tooth or small gingival area rather than widespread application), dilution by saliva (natural buffering and dilution effect), and targeted application to specific sites rather than

whole oral cavity (Prashar et al., 2006; Batiha et al., 2020).

3.2.5. Evidence Categorization and Clinical Readiness

S. aromaticum is categorized as Level Ib (evidence from randomized controlled trials) based on current use in professional dental practice worldwide representing ultimate clinical validation, FDA-approved zinc oxide-eugenol cement with regulatory approval based on clinical evidence, every traditional use strongly validated by convergent scientific evidence from multiple controlled studies, exceptional antimicrobial spectrum including critical anti-*S. mutans* activity, multi-mechanism action across all relevant dental applications, genome-level mechanistic understanding, quantified high potency in all pharmacological activities, and acceptable safety when properly formulated despite cytotoxicity concerns requiring careful concentration control in all formulations. The limitation of cytotoxicity at 0.03–0.06% requires careful concentration control but is manageable through proper formulation (Batiha et al., 2020; Mittal et al., 2014; Han & Parker, 2017; Srivastava & Singh, 2023; Prashar et al., 2006).

3.3. Plant Analysis 3: *Azadirachta indica* (Neem/Vembu)

3.3.1. Botanical Profile and Traditional Applications

Azadirachta indica A. Juss, commonly known as Neem, belongs to the family Meliaceae and represents one of the most extensively studied and widely utilized medicinal plants in traditional medicine systems worldwide. In Tamil Siddha medicine, it is known as *Vembu* or *Veppilai*, and has been revered for centuries as a "village pharmacy" due to its diverse therapeutic applications. Neem is a fast-growing evergreen tree native to the Indian subcontinent, now cultivated throughout tropical and subtropical regions globally (Lakshmi et al., 2015; Alzohairy, 2016).

Traditional applications including treatment of mouth ulcers, dental caries prevention and management, toothache pain relief, and gum disease treatment. Neem bark possesses potent antibacterial and deodorant properties, extensively used in commercial toothpastes and tooth powders. Neem twigs function as traditional tooth-cleaning sticks used for centuries across India, serving as oral deodorants, toothache relievers, mechanical plaque removal tools, and natural toothbrushes. Neem seeds and oil are used in specialized dental formulations for their antimicrobial and anti-inflammatory properties (Lakshmi et al., 2015).

3.3.2. Phytochemical Composition

The most characteristic and therapeutically significant class includes limonoids (triterpenoids) such as azadirachtin (the primary biomarker compound), nimbolide, nimbin, nimbinin, nimbidol, gedunin, and salannin. These limonoids are responsible for neem's bitter taste and many of its biological activities. An extensive array of phenolic compounds includes

quercetin, catechin, epicatechin, gallic acid, ellagic acid, and chlorogenic acid. The total phenolic content varies significantly by plant part and extraction method, with neem oil showing the highest content at 132 µg/ml (Alzohairy, 2016; Nahak & Sahu, 2011).

Multiple flavonoid glycosides and aglycones contribute significantly to antioxidant and anti-inflammatory activities. Unique sulfonoquinovosyldiacylglyceride (SQDG) and related compounds demonstrate potent antiviral activities. Neem seed oil contains oleic acid, palmitic acid, stearic acid, and linoleic acid contributing to antimicrobial and anti-inflammatory effects. Various proteins including antimicrobial peptides, complex carbohydrates with immunomodulatory properties, and complex essential oil mixtures with antimicrobial components complete the phytochemical profile (Alzohairy, 2016; Wylie & Merrell, 2022).

3.3.3. Pharmacological Activities Relevant to Dental Care

3.3.3.1. Antimicrobial Activity

Neem exhibits broad-spectrum antimicrobial and antibiofilm activity, making it one of the most versatile dental antimicrobials. MIC values of neem extract against major oral pathogens including *Enterococcus faecalis*, *Streptococcus mutans*, and *Candida albicans* range 1.88–7.5%, confirming relevance for caries and endodontic infections (Wylie & Merrell, 2022). Strong antibiofilm activity is demonstrated against *Staphylococcus aureus* (MBIC 100 µg/ml; MBEC 300 µg/ml), indicating efficacy in plaque control (Wylie & Merrell, 2022). Neem also inhibits resistant pathogens including MRSA, vancomycin-resistant *E. faecalis*, and biofilm-forming *Pseudomonas aeruginosa* (Wylie & Merrell, 2022). Antiviral effects extend to HIV, HSV-1 (EC₅₀ 9.1 µg/ml), HSV-2 (EC₅₀ 8.5 µg/ml), dengue, influenza, and SARS-CoV-2, supporting use for oral herpes lesions (Wylie & Merrell, 2022). Antifungal activity covers *Candida* spp., *Aspergillus*, and dermatophytes via membrane disruption, DNA/RNA interference, and immune activation, reducing resistance risk (Wylie & Merrell, 2022; Alzohairy, 2016).

3.3.3.2. Anti-inflammatory Activity

Neem significantly reduces inflammation relevant to periodontitis. In carrageenan-induced edema, neem leaf extract (125–500 mg/kg) inhibited swelling dose-dependently, with 63.01% inhibition at 500 mg/kg, nearing aspirin's 72.05% (Kumar et al., 2015). Neem modulates COX, LOX, and NF-κB, reducing PGE₁, serotonin-mediated inflammation, and pro-inflammatory cytokines—highly relevant in gingival tissue inflammation and bone resorption (Kumar et al., 2015; Alzohairy, 2016).

3.3.3.3. Analgesic Activity

Neem leaf extract shows strong analgesic effects. In tail-flick study, 250 mg/kg and 500 mg/kg NLE produced 70% analgesic response, exceeding morphine's 50%

(Kumar et al., 2015). Analgesia works via µ-opioid receptor interaction and prostaglandin inhibition, addressing inflammatory and nociceptive dental pain (Kumar et al., 2015).

Local Anesthetic Activity

Neem seed powder demonstrated anesthetic action in aquaculture models. At 5–10 g/L, fish achieved stage-3 anesthesia within 8.83–16.85 min, dose-dependent, with no mortality observed, indicating safety and potential for topical dental anesthetic exploration (Hassan et al., 2024).

3.3.3.4. Antioxidant Activity

Neem possesses strong antioxidant capacity exceeding clove, thyme, and rosemary. Neem seed oil showed 66.34±0.06% scavenging activity with 132 µg/ml phenolic content, while ethanolic flower extract showed 64.17±0.02% radical scavenging (Nahak & Sahu, 2011). Phytochemicals including azadirachtin, nimbolide, quercetin, catechins, gallic and ellagic acids act through free-radical scavenging, metal chelation, and lipid peroxidation inhibition (Nahak & Sahu, 2011; Alzohairy, 2016).

3.3.3.5. Anticancer Activity

Neem modulates cancer pathways with relevance to oral cancer prevention. It upregulates p53 & pTEN, induces caspase-mediated apoptosis, inhibits VEGF-driven angiogenesis, suppresses c-Myc, and blocks NF-κB signaling (Alzohairy, 2016). Useful for high-risk oral cancer groups.

3.3.3.6. Sialogogue (Saliva-Stimulating) Activity

Chewing neem leaves increases salivary pH after sugar exposure. In humans, significant pH elevation was maintained at 5, 30, and 60 min, enhancing remineralization and reducing caries risk (Murthy et al., 2020). Mechanisms include buffering proteins, salivary stimulation, and reduction of acidogenic bacteria, supporting development of neem-based chewing gums, lozenges, post-meal rinses (Murthy et al., 2020).

3.3.4. Safety and Toxicological Profile

Neem's safety profile is complex, with generally favorable safety for traditional oral and topical uses but documented toxicity concerns at higher doses or with certain administration routes. Comprehensive toxicological evaluation by Braga et al. (2021) provides critical safety data. In aquatic animals, neem extracts generally showed low acute toxicity, while neem pesticides and derivatives were moderately to highly toxic. Studies revealed toxic effects on aquatic organisms including *Daphnia magna* and *Oreochromis mossambicus*, with genotoxic effects observed in some studies. However, aquatic toxicity data has limited direct relevance to controlled human dental use at therapeutic concentrations (Braga et al., 2021).

Favorable safety indicators include centuries of traditional oral use without major documented adverse effects, low oral toxicity in animal studies, topical application (predominant dental use) minimizing systemic exposure, and small quantities used in dental products. The antimicrobial MIC values (1.88-7.5%) and MBIC (100 µg/ml) are well below toxic concentrations for topical oral use, providing substantial safety margins for dental applications (Wylie & Merrell, 2022).

3.3.5. Evidence Categorization and Clinical Readiness

A. indica is categorized as Level Ib (evidence from randomized controlled trials) based on human clinical trials demonstrating salivary pH elevation with statistically significant effects at multiple time points (Murthy et al., 2020), the most comprehensive antimicrobial spectrum documented (bacteria, viruses, fungi, parasites) with well-characterized MIC/MBC values, unique antibiofilm capability (MBIC/MBEC characterized), critical anti-*S. mutans* activity matching clove, exceptional antioxidant potency exceeding clove, thyme, and rosemary, antiviral properties not documented in other reviewed plants, drug-resistant bacteria coverage (MRSA, VRE), multiple validated mechanisms, centuries of traditional validation, commercial products available, and comprehensive coverage of all traditional dental claims. The limitation is pregnancy contraindication due to documented reproductive effects requiring appropriate screening and labeling (Lakshmi et al., 2015; Wylie & Merrell, 2022; Kumar et al., 2015; Alzohairy, 2016; Nahak & Sahu, 2011; Braga et al., 2021).

3.4. Plant Analysis 4: *Curcuma longa* (Turmeric/Manjal)

3.4.1. Botanical Profile and Traditional Applications

Curcuma longa Linn., belonging to the family Zingiberaceae, is commonly known as turmeric or "Indian Saffron." This herbaceous perennial plant has been extensively utilized in traditional medicine systems for its remarkable therapeutic properties, particularly in oral health management. The rhizome serves as the primary medicinal part, from which curcumin (diferuloylmethane) is extracted as the main active compound. The plant's widespread recognition across traditional medicine systems has established it as one of the most studied natural therapeutic agents (Umapathy et al., 2022; Inchingolo et al., 2024).

Historical texts document extensive use of *C. longa* for various oral and dental conditions. Traditional preparation methods include mouth rinses prepared by boiling 5 grams of turmeric powder with two cloves and two dried guava leaves in 200 grams of water to quickly reduce inflammation. Roasted, ground turmeric can be directly massaged on painful teeth to relieve pain and swelling. Classical formulations recommend a paste made with 1 teaspoon turmeric, 1/2 teaspoon salt, and 1/2 teaspoon mustard oil, applied twice daily, for treating

gingivitis and periodontitis (Umapathy et al., 2022; Nagpal & Sood, 2013).

3.4.2. Phytochemical Composition

The most therapeutically significant class includes curcuminoids, which comprise bisdemethoxycurcumin (existing in both keto and enol forms), demethoxycurcumin (existing in both keto and enol forms), and curcumin (existing in both keto and enol forms). These curcuminoids represent the major bioactive compounds in the extract, with the enol forms exhibiting higher ion intensities compared to the keto forms. Additional phenolic compounds identified include coumaric acid and calebic acid, both contributing to the overall therapeutic profile (Wu et al., 2024).

Tannin content showed an inverse pattern, with aqueous extracts containing higher concentrations (up to 28.33%) compared to ethanolic extracts. The Khulna chora variety ethanolic extract contained the highest tannin content among ethanolic preparations at 20.31%. This distribution pattern reveals that solvent selection significantly impacts the phytochemical profile of turmeric extracts, with ethanolic extraction favoring polyphenols and flavonoids while aqueous extraction enhances tannin recovery (Tanvir et al., 2017).

3.4.3. Pharmacological Activities

3.4.3.1. Antimicrobial Activity

C. longa exhibits broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative organisms as well as fungal pathogens. The antimicrobial effects demonstrate concentration-dependent patterns across multiple extraction methods (Wu et al., 2024; Gul & Bakht, 2013).

Antifungal activity was demonstrated against *Candida albicans*, with methanol, chloroform, and n-hexane extracts showing effectiveness while aqueous extracts exhibited weaker antimicrobial effects. This solvent-dependent activity pattern suggests that the lipophilic curcuminoids extracted more effectively by organic solvents contribute significantly to antimicrobial action (Gul & Bakht, 2013).

3.4.3.2. Anti-inflammatory Activity

Exceptional anti-inflammatory effects have been demonstrated through multiple mechanistic pathways. Curcumin regulates key inflammatory signaling pathways including nuclear factor kappa B (NF-κB), mitogen-activated protein kinase (MAPK), and Janus kinase/signal transducers and activators of transcription (JAK/STAT). The compound inhibits production of inflammatory mediators including interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF-α) (Peng et al., 2021).

In periodontal diseases specifically, curcumin gel or nanoparticles used as adjuncts to scaling and root planning have demonstrated improvements in clinical

parameters including plaque index, gingival index, and pocket depth. The paste formulation with salt and mustard oil provides relief from gingivitis and periodontitis through combined anti-inflammatory and antimicrobial mechanisms (Nagpal & Sood, 2013; Inchingolo et al., 2024).

3.4.3.3. Analgesic Activity

Significant analgesic activity has been demonstrated in animal models using standardized pain assessment methods. Ethanolic extracts of turmeric at doses of 100, 200, and 400 mg/kg body weight showed significant ($p < 0.05$) increases in mean basal reaction time compared to control groups in the Eddy's hot plate test using Wistar rats (Jogdand & Bhattacharjee, 2017).

3.4.3.4. Antioxidant Activity

Comprehensive antioxidant evaluation reveals potent free radical scavenging capacity through multiple mechanisms. Turmeric ethanolic extract demonstrated free radical scavenging capacities against ABTS^{•+} (2,2'-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radical cation), DPPH[•] (2,2-diphenyl-1-picrylhydrazyl radical), and HO[•] (hydroxyl radical), indicating broad-spectrum antioxidant activity (Wu et al., 2024).

Comparative analysis of extraction methods revealed that ethanolic extracts showed significantly higher DPPH radical-scavenging activity and ferric reducing antioxidant power (FRAP) values compared to aqueous extracts. The Khulna mura variety ethanolic extract demonstrated the lowest IC₅₀ value for DPPH at 1.08 µg/mL, indicating highly potent radical scavenging activity. The Khulna chora variety showed the highest FRAP value at 4204.46 ± 74.48 µM Fe(II) per 100g, demonstrating exceptional reducing power (Tanvir et al., 2017).

3.4.3.5. Clinical Applications in Oral Health

Beyond periodontal applications, curcumin-based formulations have demonstrated effectiveness in managing oral mucositis and oral potentially malignant disorders. Curcumin oral gels and mouthwashes reduce the severity of radiation-induced oral mucositis in head and neck cancer patients, providing symptomatic relief and promoting healing (Inchingolo et al., 2024).

For oral potentially malignant disorders, curcumin either alone or in combination with other natural compounds has shown promise in managing conditions including oral submucous fibrosis and oral lichen planus. The multi-mechanistic action involving anti-inflammatory, antioxidant, and immunomodulatory effects contributes to therapeutic efficacy in these conditions (Inchingolo et al., 2024).

3.4.4. Safety and Toxicological Profile

Safety assessment of curcumin benefits from extensive traditional use and modern toxicological evaluation. The compound has demonstrated an excellent safety profile

across multiple studies. The safe dosage of curcumin has been reported to be up to 12 g/day for 3 months without serious adverse effects, providing a substantial therapeutic window (Inchingolo et al., 2024).

3.4.5. Evidence Categorization and Clinical Readiness

C. longa is categorized as Level Ia (evidence from meta-analysis of randomized controlled trials) based on extensive human clinical trials demonstrating efficacy in multiple oral health applications with systematic reviews and meta-analyses available (Inchingolo et al., 2024), comprehensive mechanistic understanding at molecular level including NF-κB, MAPK, and JAK/STAT pathway modulation, validation across all traditional indications with modern scientific evidence, exceptional safety profile with documented tolerance up to 12 g/day for 3 months, multiple successful formulations already developed and clinically tested (mouthwash, gel, irrigant), superior performance to chlorhexidine in some applications, and broad-spectrum activity encompassing antimicrobial, anti-inflammatory, analgesic, and antioxidant effects (Umapathy et al., 2022; Nagpal & Sood, 2013; Peng et al., 2021; Wu et al., 2024). Limitations include yellow staining potential requiring formulation considerations to minimize cosmetic concerns, relatively lower antimicrobial potency compared to clove or neem requiring higher concentrations or combination approaches, and poor bioavailability of curcumin requiring formulation enhancements such as nanoparticles or complexation with cyclodextrins (Inchingolo et al., 2024; Gul & Bakht, 2013).

3.5. Plant Analysis 5: *Terminalia chebula* (Myrobalan/Kadukkai)

3.5.1. Botanical Profile and Traditional Applications

Terminalia chebula Retz., belonging to the family Combretaceae, is commonly known as 'myrobalan' or 'chebulic myrobalan.' In Tamil Siddha medicine, it is known as *Kadukkai*. This deciduous tree has been extensively utilized in traditional medicine systems, particularly in India and Iran, for its remarkable therapeutic properties across multiple health conditions including dental diseases. The fruit serves as the primary medicinal part, though leaves have also been investigated for therapeutic applications. The plant holds significant importance in Ayurvedic medicine where it is considered one of the most valuable medicinal plants (Lee & Hwang, 2021; Promila & Madan, 2018).

Historical texts document extensive use of *T. chebula* fruit for various oral and dental conditions. The plant has been traditionally employed to address throat pain, oral infections, and dental diseases. Traditional preparation methods include decoctions, powdered fruit preparations for topical application, and various formulations targeting specific oral conditions (Lee & Hwang, 2021).

3.5.2. Phytochemical Composition

Phenolic compounds constitute a major category of bioactive constituents. Total phenolic content has been measured at 118.5 mg gallic acid equivalent (GAE) per gram in standardized hydroalcoholic extracts. Phenolic carboxylic compounds contribute to the overall therapeutic profile through antioxidant and antimicrobial mechanisms. The significant phenolic content correlates directly with observed antioxidant activities (Bag et al., 2013; Saha & Verma, 2016).

Flavonoids represent another important class of compounds present in *T. chebula* fruits and leaves. These compounds contribute to antioxidant, anti-inflammatory, and antimicrobial activities through multiple mechanisms including free radical scavenging and enzyme modulation (Promila & Madan, 2018; Saha & Verma, 2016).

3.5.3. Pharmacological Activities

3.5.3.1. Antimicrobial Activity

T. chebula exhibits broad-spectrum antimicrobial activity with notable potency against both Gram-positive and Gram-negative organisms. The ethanol extract of *T. chebula* demonstrated exceptional activity against *Streptococcus mutans*, the primary etiological agent of dental caries, with MIC of 10 µg/ml and MBC of 20 µg/ml. This low concentration requirement indicates highly potent anticaries potential, positioning *T. chebula* as a promising natural agent for caries prevention and management (Lee & Hwang, 2021).

Leaf extracts demonstrated significant antibacterial activity against enteric pathogens. Methanol and aqueous extracts showed potent bactericidal activity against *Escherichia coli*, *Salmonella* species, *Shigella* species, and *Vibrio cholerae*. The methanol and aqueous extracts proved more effective than chloroform and ethyl acetate extracts, with chloroform extract showing no significant activity. Notably, the plant extracts demonstrated efficacy against *E. coli* and *Shigella* species that sometimes exceeded standard antibiotics, suggesting potential for resistant strain management (Mostafa et al., 2011).

3.5.3.2. Anti-inflammatory Activity

Exceptional anti-inflammatory effects were demonstrated in carrageenan-induced rat paw edema model. Hydroalcoholic extract at 250 mg/kg dose achieved maximum inhibition of 69.96%, indicating potent anti-inflammatory activity comparable to non-steroidal anti-inflammatory drugs. The dose-dependent pattern of inhibition confirms a pharmacological relationship between extract concentration and anti-inflammatory effect (Bag et al., 2013).

3.5.3.3. Analgesic Activity

Significant analgesic activity has been demonstrated in human clinical trials using mechanical pain models. *T. chebula* significantly increased pain threshold force and

time compared to placebo, indicating elevation of the minimum stimulus intensity required to produce pain sensation. Pain tolerance force and time also increased significantly, representing enhanced ability to withstand painful stimuli. The increase in pain threshold was more pronounced than the increase in pain tolerance, suggesting predominant effects on sensory pain perception rather than purely on pain endurance (Pokuri et al., 2016).

The authors concluded that *T. chebula* has genuine analgesic effects and recommended further studies in patients with painful conditions including osteoarthritis and rheumatoid arthritis. For dental applications, the demonstrated analgesic activity supports development of *T. chebula*-based formulations for toothache, post-extraction pain, and periodontal pain management (Pokuri et al., 2016).

3.5.3.4. Local Anesthetic Activity

Surface anesthetic activity was evaluated using the cornea of albino rabbits as a sensitive model for local anesthetic assessment. The alcoholic extract of *T. chebula* fruit demonstrated dose-dependent increases in both onset and duration of local anesthetic activity compared to standard 2% xylocaine. Higher concentrations of the extract showed longer duration of surface anesthesia, confirming a concentration-effect relationship (Promila & Madan, 2018).

3.5.3.5. Antioxidant Activity

Comprehensive antioxidant evaluation reveals potent free radical scavenging capacity through multiple mechanisms. The polyphenolic extract demonstrated significant reducing power and total antioxidant capacity in dose-dependent patterns. DPPH radical scavenging activity showed an IC₅₀ of 14 µg/ml, indicating exceptional potency that exceeded standard ascorbic acid. Nitric oxide radical scavenging demonstrated an IC₅₀ of 30.51 µg/ml, important for managing inflammation-associated oxidative stress. Hydrogen peroxide scavenging activity showed an IC₅₀ of 265.53 µg/ml, contributing to protection against oxidative damage (Saha & Verma, 2016).

In the hydroalcoholic extract, strong antioxidant activity was demonstrated with an IC₅₀ of 42.14 mg/ml in DPPH radical scavenging assay. The standardized extract containing 118.5 mg GAE per gram of total phenolics showed direct correlation between phenolic content and antioxidant capacity. These findings support use in oxidative stress-related periodontal disease, oral mucosal disorders, and oral cancer prevention (Bag et al., 2013).

3.5.4. Safety and Toxicological Profile

Safety assessment of *T. chebula* benefits from both traditional use and comprehensive modern toxicological evaluation. Acute toxicity studies demonstrated excellent safety profile with a single oral dose of 5,000 mg/kg body weight producing no signs of toxicity in both

female and male rats. This dose represents a substantial multiple of therapeutic doses, providing a wide safety margin (Panunto et al., 2010-2011).

In human clinical trials evaluating analgesic activity, both *T. chebula* and placebo were well-tolerated with no adverse events reported. This clinical safety data in humans complements the animal toxicology studies and provides direct evidence of human tolerability (Pokuri et al., 2016).

3.5.5. Evidence Categorization and Clinical Readiness

T. chebula is categorized as Level Ib (evidence from randomized controlled trials) based on human clinical trial data for analgesic activity in healthy volunteers using placebo-controlled, double-blind, cross-over design (Pokuri et al., 2016), exceptional anti-S. mutans activity (MIC 10 µg/ml, MBC 20 µg/ml) representing the lowest concentrations among all plants reviewed, comprehensive toxicological evaluation including both acute (5,000 mg/kg) and chronic studies demonstrating excellent safety, potent anti-inflammatory activity (69.96% inhibition) with remarkable membrane stabilization (95-98%), demonstrated local anesthetic activity with dose-dependent effects, antioxidant potency exceeding ascorbic acid in certain assays, and centuries of traditional validation in Ayurvedic medicine (Lee & Hwang, 2021; Bag et al., 2013; Panunto et al., 2010-2011). Limitations include astringent taste potentially limiting patient acceptability requiring flavor masking in formulations, relatively high concentrations needed for some applications, and need for additional randomized controlled trials specifically in dental patient populations (Promila & Madan, 2018; Mostafa et al., 2011).

3.6. Plant Analysis 6: *Acacia catechu* (Karungali)

3.6.1. Botanical Profile and Traditional Applications

Acacia catechu (L.f.) Willd., belonging to the family Fabaceae, subfamily Mimosoideae, is commonly known as catechu, black cutch, or *khadira*. In Tamil Siddha medicine, it is known as *Karungali*. This deciduous tree has been extensively utilized in traditional medicine systems for its remarkable therapeutic properties, particularly in oral and dental health management. The heartwood and bark serve as the primary medicinal parts, though leaves and young pods have also been investigated for therapeutic applications. The concentrated aqueous extract known as Khair gum or cutch represents a traditional preparation form with diverse medicinal uses (Lakshmi, 2021; Kumari et al., 2022).

Historical texts document extensive use of *A. catechu* for various oral and dental conditions. The plant has been traditionally employed as an astringent, cooling, and digestive agent with specific applications for sore gums and mouth ulcers. Traditional preparation methods include topical applications for indolent ulcers, which have been commonly used in India as ointments. The concentrated aqueous extract (cutch) is beneficial in

treating cough, diarrhea, and skin conditions including ulcers, boils, and eruptions. Decoction of the bark mixed with milk is taken to cure cold and cough, while infusions have been used to treat chronic gonorrhea (Lakshmi, 2021).

3.6.2. Phytochemical Composition

Comprehensive phytochemical analysis of *A. catechu* has revealed a diverse array of bioactive compounds with significant variation across different plant parts. The most therapeutically significant class includes catechins and related flavan-3-ols. Heartwood contains exceptionally high amounts of catechin, with concentrations ranging from 3.30% to 66.9%, with one analysis reporting 3.580%. This remarkable catechin content represents the dominant bioactive constituent and contributes significantly to antioxidant, anti-inflammatory, and antimicrobial properties (Kumari et al., 2022).

Related flavan-3-ol compounds include epicatechin, a stereoisomer of catechin with potent antioxidant properties, epigallocatechin contributing to antioxidant and anti-inflammatory activities, and procyanidin, an oligomeric catechin providing enhanced biological activity through polymerization. These compounds work synergistically to produce the therapeutic effects observed in traditional and modern applications (Kumari et al., 2022; Stohs & Bagchi, 2015).

3.6.3. Pharmacological Activities

3.6.3.1. Antimicrobial Activity

A. catechu exhibits broad-spectrum antimicrobial activity against both Gram-positive and Gram-negative bacteria as well as fungal pathogens. Methanolic extract of *A. catechu* leaves demonstrated antimicrobial activity against several pathogenic and non-pathogenic microorganisms including *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhi*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Candida albicans* (Indian Journal of Microbiology, 2010).

3.6.3.2. Anti-inflammatory Activity

Exceptional anti-inflammatory effects have been demonstrated through multiple studies and mechanisms. The heartwood extract, rich in catechins, epicatechins, and flavonoids, exhibits potent anti-inflammatory activity demonstrated in both in vitro and in vivo studies. The antioxidant activity of these compounds is believed to be primarily responsible for the observed anti-inflammatory effects, as oxidative stress and inflammation are closely interconnected processes (Stohs & Bagchi, 2015).

A standardized bioflavonoid composition called UP446, containing catechin from *A. catechu* heartwood combined with baicalin from *Scutellaria baicalensis*, demonstrated significant anti-inflammatory activity in animal models. The composition exhibited effects comparable to the reference drug ibuprofen in

carrageenan-induced paw edema model. The anti-inflammatory mechanism involves inhibition of cyclooxygenase (COX) and lipoxygenase (LOX) enzymes, thereby reducing production of inflammatory mediators including prostaglandins and leukotrienes (Yimam et al., 2012).

3.6.3.3. Analgesic Activity

Significant analgesic activity has been demonstrated in multiple animal models using standardized pain assessment methods. The standardized bioflavonoid composition UP446, containing catechin from *A. catechu* heartwood, was evaluated for antinociceptive (pain-inhibiting) activity in three distinct animal models: carrageenan-induced paw edema, formalin test, and acetic acid-induced writhing test (Yimam et al., 2012).

The demonstrated analgesic activity supports traditional use for toothache, oral pain, and inflammatory pain conditions. The combination of analgesic and anti-inflammatory effects provides comprehensive pain management potential for dental applications including post-extraction pain, periodontal pain, and oral mucosal pain (Yimam et al., 2012; Stohs & Bagchi, 2015).

3.6.3.4. Antioxidant Activity

Young pods of *A. catechu* demonstrate significant antioxidant potential. Sequential extraction using solvents of decreasing polarity yielded different extracts with varying antioxidant activities. The ethyl acetate and petroleum ether extracts showed good peroxide and DPPH free radical scavenging activity, comparable to ascorbic acid, the standard antioxidant reference compound. This comparability to ascorbic acid indicates highly potent antioxidant capacity (Verma & Pandey, 2014).

3.6.4. Safety and Toxicological Profile

The human clinical study using a combination product containing *A. catechu* extract in subjects with osteoarthritis showed no adverse effects, providing direct evidence of human tolerability at therapeutic doses. This clinical safety data demonstrates that *A. catechu* extract can be safely administered to humans for therapeutic purposes when properly formulated (Stohs & Bagchi, 2015).

3.6.5. Evidence Categorization and Clinical Readiness

A. catechu is categorized as Level Ib (evidence from randomized controlled trials) based on human clinical trial data demonstrating anti-inflammatory efficacy in osteoarthritis patients without adverse effects in a standardized formulation (Stohs & Bagchi, 2015), exceptional catechin content (up to 66.9%) providing standardization marker and therapeutic potency, analgesic activity comparable to ibuprofen in multiple animal models, broad-spectrum antimicrobial activity with MBC 1,000 µg/ml against *S. aureus*, antioxidant activity comparable to ascorbic acid, COX and LOX enzyme inhibition mechanisms clearly characterized, and

synergistic effects demonstrated when combined with other natural compounds (Yimam et al., 2012; Indian Journal of Microbiology, 2010; Verma & Pandey, 2014; Kumari et al., 2022). Limitations include allergic potential in sensitive individuals requiring screening and monitoring, astringent taste requiring flavor masking in consumer products, need for randomized controlled trials specifically in dental applications, and antimicrobial potency lower than clove or neem requiring higher concentrations or combination approaches (Kumari et al., 2022).

3.7. Plant Analysis 7: *Ficus benghalensis* (Banyan Tree/Aal)

3.7.1. Botanical Profile and Traditional Applications

Ficus benghalensis Linn., belonging to the family Moraceae, is commonly known as the Banyan tree. In Tamil Siddha medicine, it is known as *Aal*. This tree is considered sacred in Indian culture and holds significant religious and cultural importance. The tree is distributed widely and has been extensively used in traditional Indian medicine systems including Ayurveda, Siddha, Unani, and Homeopathy (Sharma et al., 2023; Gopukumar & Praseetha, 2015).

Traditional dental applications include the use of latex from *F. benghalensis* to treat toothaches, pyorrhea, and other dental issues by local populations. Modern pharmaceutical research has developed various candy formulations (F1 to F9) containing different concentrations of *F. benghalensis* latex, citric acid, methyl cellulose, glycerin, β-cyclodextrin, and isomalt for toothache management. Specific dosage information for these formulations was not provided in the available literature (Sharma et al., 2023; Gopukumar & Praseetha, 2015).

3.7.2. Phytochemical Composition

Preliminary phytochemical analysis of underground root extracts revealed the presence of multiple compound classes. Carbohydrates were detected in the root extracts. Flavonoids represent an important class of bioactive compounds present in the extracts. Amino acids were identified through phytochemical screening. Steroids were detected in the root extracts. Saponins were found to be present in the phytochemical analysis. Tannins were identified as constituents of the root extracts (Aswar et al., 2008).

3.7.3. Pharmacological Activities

3.7.3.1. Antimicrobial Activity

The bacterial species tested included *Bacillus subtilis*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *E. coli*, *E. coli* mutant, and *Klebsiella pneumoniae*. The fungal species tested was *Aspergillus niger*. Among the extracts tested, the methanolic extract was found to be more effective in inhibiting the growth of microbes compared to the aqueous and chloroform extracts (Aswar et al., 2008).

3.7.4. Safety and Toxicological Profile

No specific toxicological data was provided in the available literature. The review highlights the immense medicinal potential of *F. benghalensis* and its use in traditional Indian medicine systems like Ayurveda, Siddha, Unani, and Homeopathy (Gopukumar & Praseetha, 2015).

3.7.5. Evidence Categorization and Clinical Readiness

F. benghalensis is categorized as Level IV (evidence from expert opinions and traditional experience) based on extensive traditional documentation for toothache, pyorrhea, and dental issues across multiple traditional medicine systems, modern pharmaceutical formulation development (candy formulations F1-F9) indicating commercial interest, preliminary phytochemical characterization identifying multiple bioactive compound classes, and preliminary antimicrobial activity demonstrated against bacterial and fungal pathogens (Sharma et al., 2023; Gopukumar & Praseetha, 2015; Aswar et al., 2008). Limitations include absence of specific toxicological safety data, lack of quantitative antimicrobial activity data (MIC/MBC values), no controlled clinical studies in humans for dental applications, absence of specific phytochemical quantification and bioactive compound identification, no studies on anti-inflammatory, analgesic, or antioxidant activities relevant to dental care, insufficient data on optimal extraction methods and standardization, and need for progression through Level III (descriptive studies) and Level II (quasi-experimental or controlled studies) before clinical recommendation (Aswar et al., 2008; Gopukumar & Praseetha, 2015).

3.8. Plant Analysis 8: *Solanum surattense* (Yellow-berried Nightshade/Kandankathiri)

3.8.1. Botanical Profile and Traditional Applications

Solanum surattense seeds are utilized in traditional medicine through a unique fumigation method. In Tamil Siddha medicine, it is known as *Kandankathiri*. The practice is popular among the aborigines of certain districts in Uttar Pradesh, India. The traditional method involves heating the dried seeds in mustard oil on a hot iron plate and applying the fumes to the patient's mouth. This fumigation technique represents a distinctive approach to dental treatment in traditional Indian medicine (Pandey, 2004).

Clinical trials conducted by the author showed that approximately 75% of patients with issues including dental caries, pain, and swelling were completely cured after 3-4 treatments. This success rate demonstrates significant therapeutic efficacy for various dental conditions (Pandey, 2004).

3.8.2. Evidence Categorization and Clinical Readiness

S. surattense is categorized as Level III (evidence from non-experimental descriptive studies) based on documented clinical observations in aboriginal communities with specific fumigation method showing

75% complete cure rate after 3-4 treatments, effectiveness demonstrated for dental caries, pain, and swelling covering multiple dental conditions, unique fumigation delivery method representing innovative traditional approach, and systematic documentation by clinical practitioner (Pandey, 2004). Limitations include absence of randomized controlled trial design with comparison groups and statistical rigor, lack of phytochemical characterization of seed fumes and active principles, no toxicological or safety data for fumigation exposure, absence of mechanism of action studies, limited replication beyond single author's clinical observations, and need for advancement to Level IIb (well-designed quasi-experimental study) and ultimately Level Ib (randomized controlled trial) for evidence-based clinical recommendation (Pandey, 2004).

3.9. Plant Analysis 9: *Mentha arvensis* (Peppermint/*Pudhina*)

3.9.1. Botanical Profile and Traditional Applications

Mentha arvensis, commonly known as peppermint, has been investigated for its antimicrobial activity against oral pathogens. In Tamil, it is known as *Pudhina*. Leaf extracts represent the plant material evaluated for therapeutic applications (Raghavan et al., 2018).

3.9.2. Pharmacological Activities

3.9.2.1. Antimicrobial Activity

The antimicrobial activity of *M. arvensis* leaf extracts was evaluated against oral pathogens including *Streptococcus mutans*, *Aggregatibacter actinomycetemcomitans*, and *Candida albicans*. The maximum inhibition zone was observed with *M. arvensis* extracts and 0.2% chlorhexidine against *S. mutans*, followed by *A. actinomycetemcomitans* and *C. albicans*. Statistical analysis showed a statistically significant association of *M. arvensis* extracts with p-value <0.001 (Raghavan et al., 2018).

3.9.3. Evidence Categorization and Clinical Readiness

M. arvensis is categorized as Level III (evidence from well-designed descriptive comparative study) based on documented antimicrobial activity against key oral pathogens including *S. mutans*, *A. actinomycetemcomitans*, and *C. albicans* in controlled in vitro comparison, statistical significance (p<0.001) confirming genuine antimicrobial effects beyond chance, comparison with 0.2% chlorhexidine gold standard providing clinical relevance benchmark, and activity against multiple pathogen types covering anticaries, antiperiodontal, and antifungal applications (Raghavan et al., 2018). Limitations include absence of phytochemical characterization and identification of specific antimicrobial compounds, lack of quantitative antimicrobial data (MIC/MBC values) limiting dose-response understanding, no safety or toxicological data provided, absence of in vivo animal studies or clinical trials in dental patients, no studies on anti-inflammatory, analgesic, or antioxidant activities, limited documentation to single study requiring independent

replication, and need for progression to Level IIb (quasi-experimental in vivo studies) and Level Ib (randomized controlled trials) for clinical recommendation (Raghavan et al., 2018).

4. COMPARATIVE ANALYSIS ACROSS ALL PLANTS

4.1. Antimicrobial Spectrum Comparison

The nine Siddha medicinal plants demonstrate diverse antimicrobial spectra with distinct therapeutic positioning. For anticaries activity targeting *Streptococcus mutans*, *Terminalia chebula* demonstrates the most potent activity with MIC 10 µg/ml and MBC 20 µg/ml, positioning it as the primary natural anticaries agent. *Syzygium aromaticum* shows strong anti-S. mutans activity validated through extensive clinical use. *Azadirachta indica* demonstrates critical anti-S. mutans activity with MIC 1.88-7.5% and unique antibiofilm capability. *Mentha arvensis* exhibits validated activity with statistical significance ($p < 0.001$) and comparison to chlorhexidine. *Anacyclus pyrethrum* notably lacks anti-S. mutans activity, requiring combination with other herbs for caries prevention. *Curcuma longa* shows moderate activity requiring higher concentrations (Lee & Hwang, 2021; Batiha et al., 2020; Wylie & Merrell, 2022; Raghavan et al., 2018; Jalayer Naderi et al., 2012; Gul & Bakht, 2013).

For broad-spectrum antibacterial activity, *Azadirachta indica* provides the most comprehensive coverage including MRSA, vancomycin-resistant *E. faecalis*, and *P. aeruginosa* biofilms. *Terminalia chebula* demonstrates activity exceeding standard antibiotics against *E. coli* and *Shigella* species. *Acacia catechu* shows equal effectiveness against Gram-positive and Gram-negative bacteria with 20 mm zone against *S. aureus*. *Syzygium aromaticum* exhibits broad activity including complete inhibition of 31 *H. pylori* strains at 2 µg/ml. *Anacyclus pyrethrum* shows selective activity with 100% inhibition of *L. monocytogenes* but absent activity against *S. mutans* (Wylie & Merrell, 2022; Mostafa et al., 2011; Indian Journal of Microbiology, 2010; Batiha et al., 2020; Fahim Fuard et al., 2025).

For antifungal activity, *Anacyclus pyrethrum* demonstrates the strongest activity with 81% inhibition of *Candida albicans*. *Azadirachta indica* provides comprehensive coverage against *Candida* spp., *Aspergillus*, and dermatophytes. *Syzygium aromaticum* exhibits strong activity with eugenol causing spore and micelle lysis. *Acacia catechu* and *Curcuma longa* show moderate activity requiring higher concentrations. For unique antiviral activity, *Azadirachta indica* stands alone with documented activity against HSV-1 (EC₅₀ 9.1 µg/ml), HSV-2 (EC₅₀ 8.5 µg/ml), and SARS-CoV-2, not documented in other plants reviewed (Fahim Fuard et al., 2025; Wylie & Merrell, 2022; Batiha et al., 2020; Indian Journal of Microbiology, 2010; Gul & Bakht, 2013).

4.2. Anti-inflammatory Potency Comparison

Quantitative comparison of anti-inflammatory activities reveals distinct potency hierarchies. *Anacyclus pyrethrum* demonstrates exceptional activity with 96% inhibition in carrageenan-induced edema at 300 mg/kg, representing the highest potency among plants tested. *Terminalia chebula* achieves 69.96% inhibition at 250 mg/kg with remarkable 95-98% membrane stabilization. *Azadirachta indica* shows 63.01% inhibition at 500 mg/kg approaching aspirin's 72.05%. *Curcuma longa* demonstrates multi-pathway regulation of NF-κB, MAPK, and JAK/STAT with extensive clinical validation. *Acacia catechu* exhibits effects comparable to ibuprofen through COX and LOX inhibition. *Syzygium aromaticum* reduces multiple inflammatory markers including VCAM-1, IP-10, and cytokines at 0.011% concentration (Jawhari et al., 2020; Bag et al., 2013; Kumar et al., 2015; Peng et al., 2021; Yimam et al., 2012; Han & Parker, 2017).

4.3. Analgesic Activity Comparison

Analgesic potency demonstrates interesting patterns across evaluation methods. *Anacyclus pyrethrum* shows exceptional activity with 94.10% inhibition in acetic acid-induced pain and 88-94% in formalin test, representing dual central and peripheral mechanisms. *Curcuma longa* demonstrates dose-dependent analgesia with 400 mg/kg comparable to aspirin in hot plate test. *Terminalia chebula* provides human clinical trial validation with increased pain threshold and tolerance in healthy volunteers. *Azadirachta indica* achieves 70% analgesic response at 250-500 mg/kg exceeding morphine's 50% in tail-flick study. *Acacia catechu* exhibits effects comparable to ibuprofen in multiple pain models. *Syzygium aromaticum* provides widely recognized clinical analgesic effects through COX inhibition and nerve blockade (Jawhari et al., 2020; Jogdand & Bhattacharjee, 2017; Pokuri et al., 2016; Kumar et al., 2015; Yimam et al., 2012; Mittal et al., 2014).

4.4. Local Anesthetic Activity Comparison

Local anesthetic capabilities vary significantly among plants. *Anacyclus pyrethrum* demonstrates clinical validation with 2% ethanol root extract comparable to 2% lidocaine in humans, representing the highest validation level. *Syzygium aromaticum* provides mild local anesthesia through sodium channel blockade, demonstrated even in aquatic models at 60-100 ppm. *Terminalia chebula* shows dose-dependent surface anesthesia exceeding 2% xylocaine duration in rabbit cornea model. *Azadirachta indica* demonstrates anesthetic action at 5-10 g/L with dose-dependent stage-3 anesthesia in 8.83-16.85 minutes. Other plants lack documented local anesthetic activity, representing a specific therapeutic gap (Usmani et al., 2016; Mittal et al., 2014; Jayasree et al., year not provided; Hassan et al., 2024).

4.5. Antioxidant Capacity Comparison

Antioxidant potencies reveal hierarchical rankings based on IC₅₀ values and comparative analyses. *Azadirachta indica* demonstrates exceptional capacity exceeding clove, thyme, and rosemary, with neem seed oil showing 66.34±0.06% scavenging and 132 µg/ml phenolic content. *Curcuma longa* exhibits highly potent activity with Khulna mura variety showing IC₅₀ 1.08 µg/mL DPPH and Khulna chora variety demonstrating 4204.46 µM Fe(II) FRAP. *Terminalia chebula* surpasses ascorbic acid with IC₅₀ 14 µg/ml DPPH, representing exceptional potency. *Acacia catechu* shows activity comparable to ascorbic acid in ethyl acetate and petroleum ether extracts. *Syzygium aromaticum* inhibits lipid peroxidation by 97.3% at 15 µg/mL, comparable to or exceeding synthetic antioxidants. *Anacyclus pyrethrum* demonstrates strong activity with flowers showing 21.84 mg GAE/g polyphenols (Nahak & Sahu, 2011; Tanvir et al., 2017; Saha & Verma, 2016; Verma & Pandey, 2014; Mittal et al., 2014; Cherrat et al., 2017).

4.6. Unique Therapeutic Properties

Certain plants possess unique properties not shared by others in the review. *Anacyclus pyrethrum* alone demonstrates clinically validated sialogogue action inducing rapid salivation via TRPV1/TRPA1 stimulation, beneficial for xerostomia, medication-induced dry mouth, Sjögren's syndrome, and post-radiotherapy cases. *Azadirachta indica* uniquely provides antiviral activity against HSV-1, HSV-2, and SARS-CoV-2, not documented in other reviewed plants, and demonstrates pH elevation maintaining elevated salivary pH at 5, 30, and 60 minutes post-sugar exposure. *Syzygium aromaticum* shows unique antibiotic synergy enhancing vancomycin and β-lactam penetration, enabling lower antibiotic doses. *Curcuma longa* demonstrates effectiveness in radiation-induced oral mucositis and oral potentially malignant disorders not documented for other plants. *Solanum surattense* presents a unique fumigation delivery method with 75% complete cure rate in clinical trials, representing innovative traditional approach (Usmani et al., 2016; Wylie & Merrell, 2022; Murthy et al., 2020; Srivastava & Singh, 2023; Inchingolo et al., 2024; Pandey, 2004).

4.7. Clinical Readiness Hierarchy

Based on the WHO (2000) classification system for levels of evidence in traditional medicine, plants were ranked as follows: Level Ia (Meta-analysis of RCTs - Exceptional Evidence): *Curcuma longa*: Extensive human clinical trials with systematic reviews and meta-analyses available, multiple validated formulations, and superior performance to chlorhexidine in some applications (Inchingolo et al., 2024); Level Ib (At least one RCT - Strong Evidence): *Syzygium aromaticum*: Current clinical use worldwide, FDA-approved applications, and every traditional use validated through controlled studies (Batiha et al., 2020), *Azadirachta indica*: Human clinical trials for salivary pH effects, comprehensive antimicrobial spectrum, and commercial

products available (Murthy et al., 2020; Wylie & Merrell, 2022), *Terminalia chebula*: Human analgesic trial with double-blind placebo-controlled design, exceptional anti-S. mutans activity, and comprehensive toxicology (Pokuri et al., 2016; Lee & Hwang, 2021), *Acacia catechu*: Human clinical anti-inflammatory validation in osteoarthritis patients and analgesic effects comparable to ibuprofen (Stohs & Bagchi, 2015); Level IIa (Controlled studies without randomization - Moderate Evidence): *Anacyclus pyrethrum*: Human clinical data for anesthetic activity with lidocaine comparison and exceptional anti-inflammatory/analgesic potency in animal models (Usmani et al., 2016; Jawhari et al., 2020); Level III (Descriptive comparative studies - Limited Evidence): *Mentha arvensis*: Validated antimicrobial activity against oral pathogens with statistical significance versus chlorhexidine in vitro (Raghavan et al., 2018), *Solanum surattense*: Clinical observations showing 75% cure rate but lacking controlled trial design (Pandey, 2004); Level IV (Expert opinion/traditional experience - Preliminary Evidence): *Ficus benghalensis*: Preliminary antimicrobial data and traditional documentation but lacking controlled studies (Sharma et al., 2023; Gopukumar & Praseetha, 2015); This evidence hierarchy provides clear guidance for clinical integration priorities, with Level Ia-Ib plants ready for immediate incorporation into evidence-based dental practice, Level IIa plants suitable for clinical use with appropriate monitoring and documentation, and Level III-IV plants requiring progression through higher levels of evidence before widespread clinical recommendation.

5. CONCLUSION AND SUGGESTIONS

This systematic review successfully validates six of nine medicinal plants for integration into evidence based dental practice according to WHO (2000) classification standards. *Curcuma longa* achieved remarkable potency, while *Syzygium aromaticum*, *Azadirachta indica*, *Terminalia chebula*, and *Acacia catechu* demonstrated significant therapeutic effects and remaining herbs showed marginal effects towards the dental care. These herbs exhibit integrative therapeutic profiles such as *Terminalia chebula* provides superior anticaries activity, *Anacyclus pyrethrum* offers exceptional analgesic effects, *Azadirachta indica* delivers broad-spectrum antimicrobial coverage with anti-viral potency, and *Curcuma longa* excels in anti-inflammatory applications with the strongest clinical evidence base. Herbal potentiality is evidenced by recent past scientific research findings. The convergence of traditional Siddha knowledge with modern scientific validation creates accessible, cost-effective solutions for global oral health challenges. Future research should focus on advancing plants which are in the marginal level, through controlled trials, investigating synergistic combinations, developing standardization protocols, and conducting meta-analyses to strengthen the evidence base for integrative dental formulations.

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