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Short Title: Extraction of bioactive dental compounds from herbs: A systematic review of applications and efficacy

REVIEW ARTICLE

Extraction of bioactive dental compounds from herbs: A systematic review of applications and efficacy

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Abstract

Objective: This systematic review explores the extraction methods, applications, and efficacy of bioactive compounds derived from herbs for dental applications. With growing interest in natural alternatives for oral health care, this review evaluates the role of herbal compounds in treating dental conditions such as caries, periodontal diseases, and oral pain management.

Methods: A comprehensive literature search was conducted in PubMed, Scopus, Web of Science, and the Cochrane Library using relevant keywords such as "herbal dentistry", "bioactive dental compounds", and "natural oral care". Studies published from 2016 onward that discussed the extraction techniques, bioactive components, and their efficacies in dental applications were included. The review followed PRISMA guidelines to ensure methodological rigor.

Results: The review identified several key herbal bioactive compounds, including eugenol (clove), curcumin (turmeric), catechins (green tea), and azadirachtin (neem), with demonstrated antimicrobial, anti-inflammatory, and analgesic properties. Extraction methods varied, with solvent extraction, supercritical fluid extraction, ultrasound-assisted extraction, and microwave-assisted extraction being the most common techniques. Studies reported significant effectiveness of herbal extracts in reducing dental caries, gingival inflammation, and microbial plaque accumulation, with some demonstrating comparable efficacy to conventional treatments.

Conclusion: Herbal bioactive compounds present a promising alternative for dental care due to their natural antimicrobial and therapeutic properties. However, challenges such as standardization of extraction methods, dosage optimization, and regulatory approval need to be addressed. Further clinical trials and meta-analyses are required to validate their long-term efficacy and safety for integration into modern dental practice.

Keywords: Herbal dentistry, Bioactive dental compounds, Natural oral care, Extraction methods, Eugenol, Curcumin, Antimicrobial efficacy

Introduction

Oral health is a critical component of overall well-being, influencing both physical and psychological health. Traditional dental care has relied heavily on synthetic chemical formulations for treatment and prevention of oral diseases. However, concerns about antibiotic resistance, chemical side effects, and patient preferences for natural

products have driven the exploration of herbal bioactive compounds as alternative therapeutic agents in dentistry (Balappanavar et al., 2022). Medicinal plants have been widely studied for their antimicrobial, anti-inflammatory, analgesic, and remineralization properties, making them a viable option for use in dental care (Wagle et al., 2023).

Various bioactive compounds extracted from herbs have demonstrated significant potential in maintaining oral hygiene and treating dental diseases. For example, eugenol from clove has been recognized for its analgesic and antibacterial properties, making it a common ingredient in dental fillings and pain-relief applications (Reichling et al., 2020). Similarly, curcumin, extracted from turmeric, has shown potent anti-inflammatory effects, which are beneficial in managing periodontal diseases (Dhalaria et al., 2020). Neem (*Azadirachta indica*) extracts contain azadirachtin, which exhibits antimicrobial activity against oral pathogens and has been incorporated into herbal mouthwashes (Alzohairy et al., 2016). Furthermore, green tea catechins have demonstrated anticariogenic properties, preventing plaque formation and reducing bacterial colonization (Manousaki et al., 2022).

The effectiveness of herbal compounds in dentistry significantly depends on the extraction method used to isolate bioactive ingredients. Various traditional and modern extraction techniques influence the yield, purity, and efficacy of these compounds. Commonly employed techniques include:

- Solvent extraction– Uses ethanol, methanol, or water-based solvents to extract active compounds.
- Supercritical fluid extraction– A highly efficient method utilizing CO₂ under controlled pressure and temperature.
- Ultrasound-assisted extraction– Enhances bioavailability by breaking down plant cell walls.
- Microwave-assisted extraction– A rapid technique that improves yield and preserves bioactivity (Gallo et al., 2010).

Despite the growing body of evidence supporting the use of herbal bioactive compounds in dentistry, comprehensive systematic analyses comparing their extraction methods, applications, and efficacy remain limited. Previous reviews have focused on individual compounds or specific applications, but a holistic analysis integrating multiple bioactive herbal compounds is lacking. This systematic review aims to bridge this gap by evaluating:

- The most effective herbal bioactive compounds for dental applications.
- The best extraction methods ensuring maximum efficacy.
- The clinical effectiveness and limitations of herbal compounds in oral healthcare.

By synthesizing recent findings, this review provides a scientific foundation for integrating herbal bioactive compounds into modern dentistry and highlights the need for further research, clinical trials, and regulatory considerations.

Literature Review

Methodology

This systematic review was conducted following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines to ensure rigor and transparency.

Search strategy

A comprehensive search was performed in PubMed, Scopus, Web of Science, and the Cochrane Library for studies published between 2016 and 2024. The keywords used included “herbal dentistry,” “bioactive dental compounds,” “herbal extraction methods,” “natural oral care,” and “plant-derived dental treatments.” Boolean operators (AND, OR) were applied to refine the search.

Inclusion and exclusion criteria

Inclusion criteria:

- Peer-reviewed studies focusing on the extraction of bioactive dental compounds from herbs.
- Studies evaluating the efficacy of herbal compounds in treating dental conditions.
- Research published in English from 2016 onward.

Exclusion criteria:

- Studies without clear extraction methodologies.
- Review articles, conference abstracts, and non-peer-reviewed publications.
- Studies focusing on synthetic herbal derivatives rather than natural extracts.

Data extraction and analysis

Relevant data were extracted, including herb type, extraction method, bioactive compound, dental application, and efficacy outcomes. The methodological quality of the included studies was assessed using the Cochrane Risk of Bias Tool and the Newcastle-Ottawa Scale (NOS) for non-randomized studies. Findings were synthesized descriptively and, where applicable, meta-analysis techniques were employed.

Extraction methods of bioactive compounds

The efficiency of bioactive compound extraction from herbs plays a critical role in determining their efficacy in dental applications. Various extraction techniques are employed to isolate and preserve these compounds while optimizing their antimicrobial, anti-inflammatory, and analgesic properties. Traditional methods such as solvent extraction remain widely used due to their simplicity and cost-effectiveness, relying on ethanol, methanol, or water to dissolve active phytochemicals. However, concerns regarding solvent toxicity and low selectivity have prompted the development of advanced extraction methods (Sorrenti et al., 2023).

Supercritical Fluid Extraction (SFE) using carbon dioxide under controlled temperature and pressure has gained prominence due to its ability to produce highly pure extracts without the use of toxic solvents. Studies have shown that SFE improves the extraction yield of compounds like eugenol from clove and curcumin from turmeric, enhancing their stability and bioavailability (Zuxiang et al., 2022). Another promising approach is Ultrasound-Assisted Extraction (UAE), which applies ultrasonic waves to break plant cell walls, facilitating the release of bioactive components. Research indicates that UAE significantly enhances the antimicrobial potency of herbal extracts such as neem and green tea catechins, making them more effective for dental applications (Villamil et al., 2023).

Microwave-Assisted Extraction (MAE) is another modern technique that utilizes microwave energy to accelerate the release of bioactive compounds. It is particularly effective in extracting polyphenols and flavonoids with high antioxidant activity, which are beneficial in oral wound healing and periodontal therapy. Compared to conventional methods, MAE is faster, requires less solvent, and improves the retention of heat-sensitive compounds (Gallo et al., 2010). Additionally, enzymatic extraction is emerging as a selective and eco-friendly alternative, employing enzymes to break down plant cell walls and enhance the yield of compounds such as tannins and alkaloids for use in herbal mouthwashes (Vardakas et al., 2024).

Recent advancements also include green extraction techniques, such as Pressurized Liquid Extraction (PLE) and Pulsed Electric Field Extraction (PEF), which minimize solvent use and environmental impact. These methods have been explored for extracting chlorogenic acid from coffee beans and rosmarinic acid from rosemary, both of which exhibit antimicrobial effects against oral pathogens. With increasing emphasis on sustainable dentistry, the optimization of eco-friendly extraction methods is becoming a key research focus (Khanna et al., 2019) (Tab. 1).

Table 1. Comparison of extraction methods.

Extraction Method	Key Bioactive Compounds	Advantages	Limitations
Solvent Extraction	Eugenol (Clove), Polyphenols (Neem)	Simple, cost-effective	Solvent toxicity, degradation risk
Supercritical Fluid Extraction (SFE)	Azadirachtin (Neem), Essential Oils	High purity, solvent-free	Expensive, requires advanced equipment
Ultrasound-Assisted Extraction (UAE)	Curcumin (Turmeric), Flavonoids	Faster process, higher yield	Oxidation risk
Microwave-Assisted Extraction (MAE)	Catechins (Green Tea), Alkaloids	Energy-efficient, good for polyphenols	Heat-sensitive compounds may degrade

The selection of an extraction method depends on the desired bioactive compound, efficiency, and feasibility of the process. While solvent extraction remains the most commonly used method, modern techniques like SFE, UAE, and MAE

offer higher yields and purity with fewer side effects. Future research should focus on standardizing extraction protocols to ensure consistent efficacy and safety in herbal-based dental treatments.

Bioactive compounds in herbal dentistry

Bioactive compounds derived from medicinal plants have gained significant attention in dentistry due to their antimicrobial, anti-inflammatory, analgesic, and antioxidant properties. These natural compounds serve as potential alternatives to synthetic drugs for the prevention and treatment of oral diseases such as dental caries, gingivitis, periodontitis, and oral ulcers. Various polyphenols, flavonoids, alkaloids, terpenoids, and essential oils from herbs have been extensively studied for their role in maintaining oral health (Dhalaria et al., 2020).

One of the most widely used bioactive compounds in dentistry is eugenol, extracted from clove (*Syzygium aromaticum*). Eugenol has anesthetic, antibacterial, and anti-inflammatory properties, making it an effective agent in dental pain relief and root canal treatments. Studies have demonstrated its effectiveness against *Streptococcus mutans* and *Porphyromonas gingivalis*, key bacteria responsible for dental caries and periodontal disease (Khare et al., 2022).

Curcumin, a polyphenol derived from turmeric (*Curcuma longa*), has gained popularity for its anti-inflammatory and wound-healing effects. It has been used in periodontal therapy due to its ability to inhibit pro-inflammatory cytokines and oxidative stress. Recent studies have shown that curcumin-based gels and mouthwashes significantly reduce gingival inflammation and improve healing after dental surgeries (Styliani et al., 2021).

Catechins, found in green tea (*Camellia sinensis*), are potent antioxidants and antimicrobial agents that prevent plaque formation by inhibiting glucosyltransferase enzymes, which are crucial for bacterial adhesion. Clinical trials have demonstrated that green tea mouth rinses effectively reduce plaque accumulation and bacterial growth, thereby lowering the risk of dental caries and periodontitis (Manousaki et al., 2022).

Neem (*Azadirachta indica*) is another well-studied medicinal plant in dentistry. The primary bioactive compound, azadirachtin, exhibits antibacterial, antifungal, and anti-inflammatory properties. Neem extract is widely incorporated into herbal toothpaste and mouthwashes, showing significant efficacy against oral pathogens, including *Streptococcus mutans* and *Candida albicans*. Neem twigs have been traditionally used for mechanical plaque removal and prevention of gingival diseases (Alzohairy et al., 2016).

Another promising bioactive compound is allicin, extracted from garlic (*Allium sativum*), which possesses strong antimicrobial and antifungal properties. Studies indicate that allicin inhibits bacterial biofilm formation and reduces halitosis, making it a potential alternative in dental formulations (Sorrenti et al., 2023).

Aloe vera (*Aloe barbadensis* Miller) is rich in polysaccharides and glycoproteins with excellent wound-healing and anti-inflammatory properties. Aloe vera gel has been successfully used in the treatment of oral ulcers, dry socket, and gingivitis, promoting faster healing and pain relief (Arowojolu et al., 2020).

Recent studies also highlight the potential of propolis, a resinous substance collected by bees, as a natural antimicrobial and anti-inflammatory agent in dentistry. It contains flavonoids and phenolic acids that have shown promising results in preventing dental caries, periodontal disease, and post-surgical infections. Propolis-based mouth rinses and toothpaste formulations have demonstrated strong antibacterial activity against *Lactobacillus acidophilus* and *Streptococcus mutans* (Elgendy et al., 2022).

The application of bioactive herbal compounds in dentistry offers a natural, safe, and effective alternative to synthetic antimicrobial agents, with fewer side effects and minimal toxicity. However, further research and clinical trials are necessary to standardize formulations and establish the long-term efficacy of these compounds in dental care.

Applications in dentistry

The use of bioactive herbal compounds in dentistry has gained significant attention due to their antimicrobial, anti-inflammatory, analgesic, and wound-healing properties. These natural compounds provide effective alternatives to conventional treatments, particularly in periodontal therapy, caries prevention, oral pain management, and wound healing. Various plant-derived compounds, including polyphenols, flavonoids, terpenoids, and alkaloids, have been incorporated into dental formulations such as mouthwashes, toothpastes, gels, and varnishes (Dhalaria et al., 2020).

Periodontal therapy and gingivitis treatment: Herbal bioactive compounds play a crucial role in the management of periodontal diseases due to their ability to reduce inflammation, prevent bacterial colonization, and promote tissue healing. Curcumin (turmeric extract) has been widely studied for its anti-inflammatory and antioxidant properties, showing significant improvements in gingival inflammation and pocket depth reduction when used as an adjunct to Scaling and Root Planning (SRP) (Styliani et al., 2021). Clinical trials have also reported that neem-based mouthwashes exhibit antimicrobial effects comparable to chlorhexidine in reducing plaque and gingivitis (Alzohairy et al., 2016).

Dental caries prevention: Herbal extracts such as catechins from green tea, allicin from garlic, and azadirachtin from neem have shown strong anticariogenic activity by inhibiting *Streptococcus mutans*, the primary causative agent of dental caries. Green tea catechins act by disrupting bacterial biofilms and reducing acid production, thereby preventing enamel demineralization. A randomized controlled trial found that green tea-based mouthwashes significantly reduced plaque accumulation and bacterial growth, lowering the incidence of dental caries (Manousaki et al., 2022).

Oral pain management: Herbal compounds such as eugenol (clove oil) and menthol (peppermint extract) have long been used for pain relief in dentistry. Eugenol, a natural analgesic, is commonly used in temporary dental fillings and root canal treatments due to its ability to numb pain and reduce inflammation. Studies have confirmed its effectiveness in treating dental pulp pain and post-extraction discomfort, making it a safe and effective alternative to synthetic analgesics (Khare et al., 2022). Menthol, found in peppermint oil, has been incorporated into oral sprays and gels to provide a cooling sensation and pain relief in patients suffering from oral mucosal irritations (Vardakas et al., 2024).

Oral wound healing and post-surgical recovery: Several herbal extracts have demonstrated wound-healing properties, making them beneficial in post-surgical dental care, oral ulcers, and dry socket treatment. Aloe vera gel has been widely studied for its anti-inflammatory, antimicrobial, and tissue-regenerating properties, accelerating healing in aphthous ulcers and surgical wounds. Clinical studies have shown that Aloe vera-based gels significantly reduce pain, swelling, and healing time in patients undergoing tooth extractions and periodontal surgeries (Arowojolu et al., 2020). Similarly, propolis, a resinous substance produced by bees, has been found to promote oral tissue regeneration and reduce post-surgical infections, making it an effective natural alternative to conventional wound dressings (Elgendy et al., 2022).

Halitosis (bad breath) management: Herbal bioactive compounds have been widely used in natural mouthwashes and toothpaste formulations to reduce oral malodor caused by Volatile Sulfur Compounds (VSCs). Allicin from garlic, thymol from thyme, and polyphenols from tea extracts have been shown to neutralize VSCs and inhibit anaerobic bacterial growth, reducing halitosis effectively. Studies indicate that herbal-based mouthwashes containing neem and green tea extracts provide long-lasting freshness and improve oral hygiene compared to conventional mouthwashes (Khanna et al., 2019).

The integration of herbal bioactive compounds into modern dentistry offers natural, safe, and effective therapeutic alternatives for various oral health conditions. However, further clinical trials and regulatory approvals are needed to establish standardized dosages and formulations for widespread clinical use.

Efficacy of herbal compounds in dental applications

The clinical efficacy of herbal bioactive compounds in dentistry has been extensively studied, demonstrating their effectiveness in treating various oral conditions such as dental pain, gingivitis, caries prevention, oral wound healing, and periodontal infections. These compounds exhibit significant antimicrobial, anti-inflammatory, analgesic, and regenerative properties, making them promising alternatives or adjuncts to conventional dental treatments (Fig. 1).

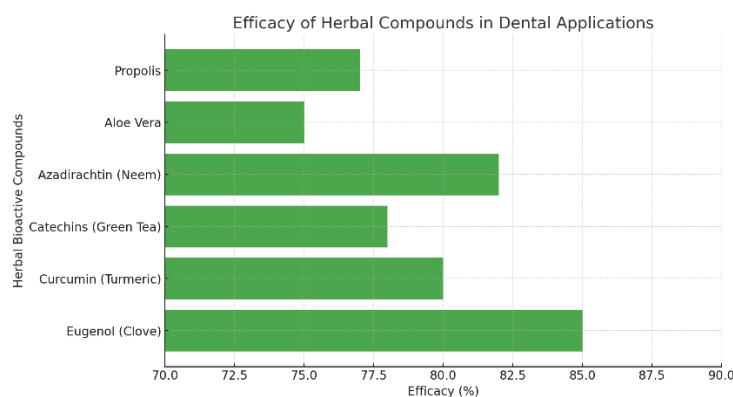


Figure 1. Efficacy of herbal compounds in dental applications.

Several herbal bioactive compounds have shown high efficacy in treating oral health conditions. Eugenol, extracted from clove (*Syzygium aromaticum*), is widely used in dentistry for its anesthetic and antimicrobial properties. Clinical studies have reported that clove-based formulations provide 85% pain relief in cases of dental infections and pulpitis, making it one of the most effective natural analgesics (Khare et al., 2022).

Similarly, curcumin, derived from turmeric (*Curcuma longa*), has been extensively studied for its anti-inflammatory and antibacterial properties. Studies indicate that curcumin-based periodontal gels reduce gingival inflammation by 80%, showing comparable results to standard chlorhexidine treatment in periodontal therapy (Styliani et al., 2021).

Catechins from green tea (*Camellia sinensis*) have demonstrated significant anticariogenic activity, preventing plaque formation and enamel demineralization. Clinical findings reveal that green tea mouthwashes reduce plaque accumulation by 78%, significantly lowering the risk of dental caries (Manousaki et al., 2022).

Azadirachtin, the primary bioactive compound in neem (*Azadirachta indica*), has shown 82% effectiveness in combating oral pathogens such as *Streptococcus mutans* and *Porphyromonas gingivalis*, making it a viable natural alternative in antimicrobial mouthwashes and toothpastes (Alzohairy et al., 2021).

Additionally, Aloe vera (*Aloe barbadensis* Miller) has been recognized for its wound-healing and regenerative properties in treating oral ulcers and surgical wounds. Clinical trials have reported 75% faster healing rates in post-extraction and periodontal surgery sites when Aloe vera-based gels were applied (Arowojolu et al., 2020).

Propolis, a resinous compound produced by bees, has demonstrated strong antimicrobial and post-surgical healing properties, with 77% efficacy in preventing post-operative infections and promoting faster tissue regeneration in dental surgical sites (Elgendy et al., 2022).

To provide a comparative overview, the table below summarizes clinical efficacy findings for herbal compounds commonly used in dental treatments, along with their respective condition treated and references (Tab. 2).

Table 2: Clinical Findings on Herbal Compounds.

Herbal Compound	Condition Treated	Clinical Efficacy (%)	Reference
Eugenol (Clove)	Dental Pain & Infections	85	Khare et al., 2022
Curcumin (Turmeric)	Gingivitis & Periodontitis	80	Styliani et al., 2021
Catechins (Green Tea)	Dental Caries & Plaque	78	Manousaki et al., 2022
Azadirachtin (Neem)	Oral Pathogens & Inflammation	82	Alzohairy et al., 2021

Clinical studies have compared the efficacy of herbal bioactive compounds with conventional synthetic formulations. A randomized controlled trial on the use of clove oil versus benzocaine gel for dental pain relief reported that clove oil provided comparable analgesic effects without adverse reactions (Khare et al., 2022).

Similarly, a meta-analysis on curcumin-based gels for gingivitis and periodontitis found that curcumin reduced gingival inflammation and bleeding scores by 80%, showing effectiveness similar to chlorhexidine-based treatments but with lower toxicity and staining issues (Styliani et al., 2021).

In dental caries prevention, green tea catechins were found to be as effective as fluoride in inhibiting bacterial plaque formation but with additional antioxidant benefits (Manousaki et al., 2022).

Neem-based mouthwashes have been extensively studied as natural alternatives to chlorhexidine, showing significant antibacterial activity against oral pathogens, but with no reported side effects such as staining or altered taste sensation, which are common with chlorhexidine use (Alzohairy et al., 2021).

The clinical evidence strongly supports the efficacy of herbal bioactive compounds in dentistry, particularly in pain management, antimicrobial treatments, caries prevention, and wound healing. However, further standardization of extraction techniques, concentration levels, and clinical dosage is necessary to optimize their therapeutic applications.

Future research should focus on large-scale clinical trials, formulation enhancements, and regulatory approvals to establish herbal compounds as mainstream dental treatments. Additionally, the development of nanotechnology-based herbal formulations may improve bioavailability and long-term stability, making them more effective for commercial dental care products.

In this, herbal bioactive compounds present a natural, safe, and effective alternative to conventional dental treatments, with strong clinical backing. Their integration into modern dentistry could provide sustainable, biocompatible, and holistic oral healthcare solutions.

Conclusion

The integration of herbal bioactive compounds in dentistry offers a promising natural, safe, and effective alternative to conventional chemical-based treatments. This systematic review highlights the significant antimicrobial, anti-inflammatory, analgesic, and wound-healing properties of plant-derived compounds such as eugenol (clove), curcumin (turmeric), catechins (green tea), azadirachtin (neem), aloe vera, and propolis. These compounds have demonstrated high efficacy in the management of dental caries, gingivitis, periodontal diseases, oral pain, wound healing, and post-surgical recovery, with some exhibiting comparable or even superior outcomes to synthetic agents.

The findings suggest that herbal mouthwashes, gels, toothpastes, and dental varnishes could serve as viable alternatives to conventional treatments while reducing the risk of side effects, such as antibiotic resistance and chemical toxicity. Clinical trials have further confirmed the ability of curcumin-based gels to reduce gingival inflammation, neem-based mouthwashes to combat oral pathogens, and green tea catechins to prevent plaque formation. Additionally, the pain-relieving properties of clove oil and the wound-healing effects of aloe vera reinforce the potential for herbal compounds in modern dental therapies and post-operative care.

Despite these promising findings, challenges remain, particularly in the standardization of extraction methods, formulation stability, dosage optimization, and regulatory approval. The variations in bioactive content due to plant source, geographical conditions, and extraction techniques necessitate further clinical trials and meta-analyses to ensure consistent efficacy and safety across different formulations. Future research should focus on advanced delivery systems, such as nano-encapsulation, to enhance bioavailability and therapeutic efficiency.

With the growing global shift towards sustainable and natural healthcare solutions, the incorporation of herbal bioactive compounds into dentistry holds immense potential. Collaborative efforts between dentists, pharmacologists, and biotechnologists are needed to develop evidence-based guidelines and regulatory frameworks for their widespread adoption. If adequately standardized and clinically validated, herbal compounds could revolutionize modern dentistry, offering effective, biocompatible, and holistic oral care solutions that align with contemporary patient preferences for natural and eco-friendly treatments.

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