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# **Role of Phytomedicine in Periodontics**

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#### **INTRODUCTION**

The World Health Organization (WHO) estimates that oral disorders impact around 3.5 billion people worldwide and are a major concern. Tooth decay, periodontitis, dentition loss, oral and lip malignancies, and dry mouth are the most prevalent oral health issues <sup>[1].</sup> Caries and severe periodontal infections are significant causes of tooth loss in adults, even with the natural aging process <sup>[2]</sup>. The frequency of periodontitis rises to 70–85% in people aged 60–65.<sup>[3]</sup> One of the most important issues pertaining to tooth health is periodontal disease. Only a small percentage of individuals worldwide are thought to have completely healthy teeth, and the WHO estimates that up to 3.5 billion people may be afflicted by oral disorders.

Since the beginning of time, people have been plagued by periodontal and gingival diseases, which are the most prevalent oral illnesses. According to paleopathology studies, bone loss is a sign of severe periodontal disease that afflicted early people from a variety of cultural backgrounds. Bacterial plaque and its metabolites are the main causative agent of periodontal disorders. It is also commonly known that dental plaque and poor oral hygiene are linked to the severity of periodontal disease.<sup>[4]</sup>

Currently, there has been a significant increase in the use of alternative and herbal medicines for treating various ailments. The rise of new and re-emerging infectious oral diseases has become a major concern today. Research into the emergence of multiple drug resistance in various oral pathogens has gained considerable attention worldwide, highlighting the need for new antimicrobial substances from alternative sources, particularly phytomedicine. As a result, there is a growing interest in developing phytomedicine for periodontal therapy.<sup>[5]</sup>

The term "phytotherapy" originates from Latin, where "phyto" means "plant," and "therapy" refers to "healing and curing." In essence, phytotherapy involves the use of herbal medicine for treatment purposes. This field studies the application of natural extracts as medications or substances that promote health. Plant nutrients with specific biological activity that enhance human well-being are known as phytonutrients. More specifically, phytotherapy emphasizes plant-based natural bioactive compounds that offer a variety of benefits for oral health.<sup>[6]</sup>

Herbal products are often preferred over pharmaceutical ones due to their wide-ranging biological effects, increased safety margins, and lower costs. Furthermore, the long-term use of conventional medications has contributed to antibiotic resistance and is associated with several adverse effects, including hypersensitivity, immune suppression, and allergic reactions.

#### HISTORY OF PHYTOMEDICINE

Since ancient times, many herbal plants have been used to treat and prevent certain diseases as they possess curative properties. Plant-origin drugs are usually extracted from barks, seeds, fruits, stems, roots, and other medicinal plants<sup>[7]</sup> Since 200 B.C, phytotherapy or phytomedicine has been a part of medical

traditions for treating certain diseases. The World Health Organization conducted a survey recently which estimated that almost 70–80% of the population in the developing world has resorted to traditional practices for treatment of various ailments. China and India, the two most populous countries in the world, have practiced traditional medicine for the management of oral diseases, including periodontal disease, for well over 2000 years.

The first known written record of using medicinal plants for healing was discovered on a clay board from the Sumerian civilization in Nagpur, India. It contains 12 techniques for making drugs using more than 250 different plants, including several alkaloids like poppy, mandrake, and henbane. The Vedas, which is an Indian holy book, also recommends therapy using herbs.<sup>[8]</sup>

In India, Ayurveda, a holistic medical system that developed around 5000 years ago, has been using medicinal herbs to cure patients' ailments since 800 A.C. To live in harmony with nature is what the term "Ayurveda" means. It combines the Sanskrit terms Veda (the science of knowledge) and Ayur (life). According to the traditional science of Ayurveda, three biological humors known as doshas—vata, pitta, and kapha—can heal oral and other conditions. In India Ayurveda, Siddha, and Unani are traditional medicinal practices. Susruta Samhita and Charaka Samhita, two ancient Indian ayurvedic texts, have also made contributions in this area. <sup>[9]</sup>

The first two ancient Indian medicines are the Sushruta Samhitra and the Charikasamhitra. <sup>[9]</sup>Ayurveda branches of Shalyatantra and Shalakyatantra has 65 variations of oral disease in seven anatomic regions, 15 on alveolar border, 8 on lips, 8 in connection with teeth, 5 on tongue,9 on palate,17 on oropharynx and 3 in generalized form. <sup>[10]</sup> Bleeding gums, toothaches, and swelling in the oral cavity are also addressed in Ayurvedic treatment. <sup>[11]</sup> Amla, haritaki, azadirachia indica, lavanga oil, and nimbu, or lemon solution, are herbs that reduce pain and combat infections.

## **BENEFITS OF PHYTOTHERAPY**

For a very longtime, Phytotherapy has been practiced all over the world, as plants and their extracts are known to possess anti-inflammatory, anti-microbial, anti-cancer and immune mediating effects. The constituents of plants are widely researched in chemistry and pharmacology and various studies have proven its efficacy.

The benefits of using phytotherapy is

(1) Typically, low side effect profiles

(2) Unique mechanism of action

(3) Low cost

(4) A high level of acceptance <sup>[6]</sup>

# MANAGEMENT OF PERIODONTAL DISEASE USING PHYTOMEDICINES

Because of their anti-inflammatory and anti-plaque qualities, herbal medications are recommended for the treatment of periodontal disease. There aren't many plants used as a preventative measure against illnesses. Antimicrobial resistance and serious adverse effects are more likely to emerge as a result of long-term usage of conventional medications. Therefore, phytoconstituents may be safe substitutes for antibiotics.<sup>[12]</sup> The availability of medicinal plants is simple in emerging nations with great agroclimatic, cultural, and ethnic biodiversity, such as India. Herbal medicine has contributed a wide range of beneficial medications to current medical science all across the world. The herbs with therapeutic effect in the treatment of periodontal disorders are discussed below.

# 1. CURCUMIN (CURCUMA LONGA)

A perennial herbaceous rhizomatous plant, turmeric is a member of the Zingiberaceae family. It thrives in temperatures ranging from 20 to 30 degrees Celsius and is native to tropical South Asia. This perennial plant produces orange, oblong tubers that are tapering or pointed at one end, measuring two to three inches in length and approximately one inch in diameter. When dried, turmeric turns into a yellow powder with a sweet and slightly pungent taste. Additionally, turmeric is beneficial in dentistry due to its antibacterial, antioxidant, and astringent properties.<sup>[13]</sup>

Turmeric contains three different types of curcuminoids: demethoxycurcumin, bisdemethoxycurcumin, and curcumin (diferuloylmethane). Regarding curcumin's antibacterial qualities, several modes of action have been documented. Both Gram-positive and Gram-negative bacteria may experience irreversible harm and cellular death as a result of curcumin's ability to suppress bacterial cell division and cause bacterial membrane permeabilization.<sup>[14]</sup> Curcumin prevents Streptococcus mutans from forming biofilms by inhibiting sortase A, an enzyme that allows bacteria to adhere to extracellular matrix proteins and the surfaces of human teeth. <sup>[15,16]</sup> Numerous studies have shown that curcumin works in concert with other antibiotics, including cefixime, tetracycline, and vancomycin, to inhibit the growth of P. aeruginosa and S. aureus by impairing their pathogenicity, quorum sensing, and biofilm formation.<sup>[17]</sup>

# 2. GUAVA (PSIDIUM GUAJAVA)

Essential oils, flavonoids, phenolic compounds, tannins, triterpenoid acids, sesquiterpene alcohols, and vitamins are among the many phytoconstituents found in guavas. These substances have potent antimicrobial anti-inflammatory, analgesic, antihyperglycemic properties. Its main component, vitamin C (ascorbic acid), has strong antioxidant qualities and is known to change fibroblast differentiation and regulate procollagen gene expression through its impact on the extracellular matrix after collagen production.<sup>[18]</sup> Vitamin C aids in the healing process in addition to bioflavonoids. Guava contains a flavonoid called quercetin, which has strong antibacterial properties against the periodontal pathogens Fusobacterium nucleatum (Fn), Porphyromonas gingivalis (Pg), Aggregatibacter actinomycetemcomitans (Aa), and Prevotella intermedia (Pi). Because the bark contains tannins, it also has antibacterial qualities.<sup>[19]</sup>

# 3. NEEM (AZADIHATA INDICA)

Since ancient times, people in South Asia and India have utilized neem as a practical remedy to keep their gums and teeth healthy. Nimbin, nimbidin, azadirachtin, nimbolide, epicatechin, catechin, gallic acid, and margolone are examples of biochemical ingredients. The tree Azadirachta indica, popularly referred to as "neem," belongs to the Meliaceae family and is found throughout Asia and Africa. Nearly every aspect of the tree was employed in indigenous medical systems to cure a variety of human ailments, particularly those caused by germs and fungi. Neem leaves and seeds were traditionally chewed after meals, while neem twigs were used for brushing. It has been applied as an antiseptic and astringent. Antifungal, antiviral, antibacterial, antipyretic, anti-inflammatory, anticariogenic, anti-carcinogenic, antihelminthic, analgesic, and antioxidant properties are all present in neem.

Excellent antihyperglycemic and antiviral properties have been demonstrated by neem leaf extract in both in vitro and in vivo animal studies. <sup>[20]</sup> For the treatment of other oral infections and the management of periodontal disorders, it also demonstrated exceptional effectiveness in preventing the formation of plaque. <sup>[21]</sup> It possesses a wide range of antibacterial action, according to several research. <sup>[22]</sup> Neem is utilized to treat periodontitis, gingivitis, and tooth cavities, according to studies.

## 4. TULSI (OCIMUM SANCTUM) :

Ocimum sanctum linn plant commonly known as Tulsi belongs to the family Labiatae characterized by square stem and specific aroma. It is found on large scale in India, Malaysia, Australia, West Africa and some of the Arab countries. Tulsi acts as anti-bacterial especially E. coli, S. Mutans and S.aureus.<sup>[23]</sup> It also has anti-fungal, anti-viral, ant cariogenic and anti-ulcerogenic properties.

The antibacterial properties of O. sanctum leaves are primarily found in the form of essential oils. The five main components of these essential oils are eugenol, caryophyllene, germarene-A, clemene, and caryophyllene oxide. The additional physiologically active substances that are found as phytochemicals are oleanolic acid, ursolic acid, and rosmarinic acid. Because of their antibacterial qualities, these essential oils and physiologically active substances work well against both Gram-positive and Gram-negative bacteria. <sup>[24]</sup> By inducing cellular potassium release, they can harm microbial strains' cytoplasmic membranes. The periodontal pathogen A. actinomycetemcomitans in human tooth plaque may have been harmed by the same mechanisms that are effective against germs that cause systemic disease.

#### 5. POMEGRANATE (PUNICA GRANATUM)

In the Punicaceae family, this fruit is often referred to as pomegranate. The terms "pomegranate" and "granatus" refer to apples and seeds, respectively. Ellagitannins, flavonoids, punicic acid, anthocyanins, anthocyanidins, and estrogenic flavones are the most advantageous parts of pomegranates. The peel of pomegranates possesses antifungal, anti-inflammatory, and antimutagenic properties. Pomegranate juice's tannin concentration offers anti-aging, anti-oxidant, antihypertensive, and anti-atherosclerotic qualities. <sup>[25]</sup> Another important component of pomegranates is punicic acid, a potent anti-inflammatory substance that also has the ability to inhibit the formation of PG. Additionally, it can decrease NF-κB activity, which is a promising treatment method for periodontitis and will stop inflammation-induced bone resorption. <sup>[26]</sup> The ability of pomegranate extract to heal wounds is well-known. It is known to promote angiogenesis, collagen synthesis, and enhanced fibroblast migration and proliferation

## 6. GREEN TEA (CAMELLIA SINENSIS)

Camelia sinensis, a plant in the Theaceae family, has been shown to have therapeutic benefits, mostly because of its powerful antioxidant properties. Only Camellia sinensis leaves that have experienced little oxidation during processing are used to make green tea. Various methods are used to grow and process green tea, depending on the type that is preferred. These techniques preserve the highest levels of polyphenols and antioxidants, maximizing the health benefits of green tea. Catechins, such as epicatechin, epigallocatechin gallate, and epigallocatechin, are the primary constituents of the leaf extract.<sup>[27]</sup> Green tea contains a class of antioxidants called catechins that may have anti-inflammatory properties of their own. One aspect of gingivitis is inflammation. Green tea may be able to prevent the harm that might otherwise occur by reducing inflammation. Through the inhibition of periodontal inflammation and the reduction of cytokines and TRAP-positive multinucleated osteoclasts, Camelia sinensis extract can decrease alveolar bone resorption.<sup>[28]</sup> After four weeks of daily usage, green tea gel adjunctive topical extract therapy lowers inflammation.<sup>[29]</sup>

## 7. PROPOLIS

This is made from resins that bees gather from poplar and fir trees or from clusia flowers. Flavonoids, phenolics, and aromatics are the pharmacologically active components of propolis. Because propolis contains phenethyl ester (CAPE) and caffeic acid, it has anti-inflammatory properties. Numerous biologic actions, such as antibacterial, anti-inflammatory, antioxidant, anesthetic, and cytotoxic qualities, are displayed by propolis

<sup>[30]</sup>. In order to preserve the viability of periodontal ligament cells, it can also be utilized as a storage medium for avulsed teeth <sup>[31].</sup>

Brazilian propolis, sometimes referred to as "green propolis," is a variation that has unique chemical and biological properties. Nevertheless, it has anti-inflammatory, antioxidant, antiparasitic, and anticarcinogenic properties just like other forms of propolis. Brazilian propolis, sometimes known as "green propolis," is a kind with special biological and chemical characteristics. However, like other types of propolis, it contains anti-inflammatory, antioxidant, antiparasitic, and anticarcinogenic uniflammatory, antioxidant, antiparasitic, and anticarcinogenic qualities.

# 8. TRIPHALA

An Indian herb known as triphala ("three fruits") has been discovered to have full body cleansing properties. It is frequently employed by natural healers with knowledge in Indian Ayurvedic treatment, which literally translates to "long life practice," and is well-known in ancient Indian folklore.

Phyllantus emblica (emblic myrobalan), Terminalia chebula (chebulic myrobalan), and Terminalia bellirica (beleric myrobalan) are among the fruits.Among their many additional health advantages are their beneficial antiviral and antibacterial properties <sup>[32]</sup>.Triphala's ability to suppress PMN-type matrix metalloproteinase (MMP-9) expression in patients with chronic periodontitis was assessed in a study. Its inhibitory activity was contrasted with that of doxycycline, a recognized inhibitory agent, and kamillosan, a natural medication. When the medicines were used, MMP activity was considerably reduced.

# 9. NONI (MORINDA CITRIFOLIA L.)

The South Pacific region is home to the widespread traditional plant known as noni, or Indian Mulberry. <sup>[33]</sup> Their entire plant is used to cure a wide range of illnesses. Because of its many qualities, including analgesic action, immunomodulatory, antibacterial, anticancer, and anti-tubercular effects, noni has become a potent medicinal plant in modern times. These qualities have led to its current use as a supplemental health beverage<sup>[34,35]</sup> Scopolettin, octoanoic acid, terpenoids, alkaloids, anthraquinones,  $\beta$ -sitosterol, carotene, flavone glycosides, linoleic acid, amino acids, potassium, vitamin C, vitamin A, calcium, and phosphorus are among the phytochemicals and nutrients found in noni <sup>[36.37].</sup>

Because of its antibacterial and anti-inflammatory qualities, noni is shown to be useful against gingivitis, and when ripe noni fruit extract was used as a mouthwash, gingival condition improved. <sup>[38,39]</sup> In vitro studies have also shown that noni extracts increase cell proliferation while decreasing proteolysis, matrix deposition, and mineralization.Because it promotes the differentiation of osteoblasts from bone marrow stem cells, it has osteoinductive potential and contributes in the repair of periodontal tissue <sup>[40,41]</sup>.Therefore, it can be used to bone deficiencies caused by periodontal disease as a bone regenerative material. <sup>[42]</sup>

# RECENT ADVANCES IN HERBAL THERAPY GREEN-SYNTHESIZED METAL NANOPARTICLES

Nanotechnology is a branch of science that studies objects called nanoparticles (NPs) that are smaller than a nanometer.Physicist Richard Feynman's speech at an American Physical Society meeting at Caltech on December 29, 1959, touched on the idea of nanotechnology with the phrase "there's plenty of room at the bottom." In 1974, Tokyo Science University's Norio Taniguchi provided the first definition of the term "nanotechnology."<sup>[43]</sup>

Nanomaterials' enhanced and unique physicochemical characteristics, such as their extremely small size, large surface area relative to mass, and increased reactivity, make them promising for use in antibacterial therapy.

It is used in several medical specialties, including clinical diagnostics, pharmacological research, immune system augmentation, and cryogenic tissue storage. Despite their possible antibacterial qualities, the majority of methods for creating these nanoparticles are expensive and, because they include hazardous and toxic materials, may have detrimental effects on biological systems, the environment, and human health. Consequently, "green" nanoparticle synthesis technologies have emerged.

Green methods are attractive because they can reduce the toxicity of nanoparticles. Consequently, the use of plant extracts is growing in popularity. In a typical plant-mediated metal nanoparticle production process, the first step is to collect and purify the plant component of interest. The herb is then dried and ground into a powder. In order to produce plant extract, deionized distilled water is often added to the plant powder in the proper concentration. After that, this solution is boiled and filtered. The appropriate amount of metal salt solution is mixed with a certain volume of the extract. The mixture is well mixed and heated to the desired temperature for the allotted amount of time. When metal ions are converted to metal nanoparticles, the solution changes color, which can be verified by UV visible spectra.<sup>[44]</sup>

# HERBAL NANOMATERIALS FOR PERIODONTAL DISEASE

Due to its superior therapeutic qualities and lower side effects as compared to contemporary medications, herbal remedies have been utilized all over the world. For the treatment of oral illnesses, numerous herbal preparations have been created. Curcumin was proven to be useful in treating periodontal disorders and reducing the activation of inflammatory mediators by Farjana et al. (2014) and Zambrano et al. (2018). Compared to topical versions, curcumin nanocurcumin capsules have a systemic target location with greater bioavailability.

In their 2020 study, Malekzadeh M et al. examined how oral nano-curcumin affected gingival inflammation in patients with mild periodontitis and gingivitis. They found that it had a good impact on reducing gingival bleeding and inflammation. The antibacterial properties of silver nanoparticle composites including pomegranate (Punica granatum) rind extract were investigated by Yang Hui et al. in 2016. According to the results of the antibacterial experiment, Ag/Ag+/Ag3+ nanocomposites exhibited high bacteriostatic activity against both gram positive and gram-negative bacteria at concentrations of  $1.16 - 10_4 \text{ mol/L}$ . <sup>[42]</sup>

## PHYTOMEDICINE'S FUTURE IN DENTISTRY

Nanoscale phytomedicines have a promising future in boosting biological activity and can solve problems related to chemical and synthetic pharmaceuticals. As a result, the use of green pharmaceuticals in nanodrug delivery systems aids in the treatment of many illnesses and can be more widely used to the prevention of oral diseases, dentures, implants, oral cancer, and oral health care. Significant research should also be conducted on the various compounds present in herbal treatments and the subsequent production of nanoparticles from them. The effectiveness of herbal nanomedicine technologies and their potential use in dentistry require careful research. All plant nanoparticles that show anticancer promise in a variety of cancers should undergo in vivo testing. In order to support a variety of dental treatments, plant nanoparticles' antioxidant qualities should also be investigated.<sup>[43]</sup>

## CONCLUSION

Herbal medicine has been used for daily maintenance and to cure tooth conditions since ancient times. Contrary to conventional treatments, which have the drawback of poor benefit to high risk, plant materials therapy typically has a favorable safety profile with fewer side effects. It is important to know when adverse effects could lead to the discontinuation of treatment, particularly in cases of polypharmacy and chronic conditions. The effects of periodontitis include tooth loss and associated disorders, as well as other conditions

that increase the likelihood of developing them and require vigorous treatment or a more severe course. Thus, it is essential to start preventing periodontitis and managing it safely and effectively from the very beginning of development.

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