

## Applications of neem in periodontal therapy: A narrative review

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**Abstract:** Periodontal disease is a major public health concern in the world eventually resulting in tooth loss. Successful periodontal therapy includes the use of antimicrobial agents in conjunction with mechanical debridement. However, the side effects of synthetic microbials has now shifted the focus of current research on natural plant derived agents. *Azadirachta Indica* (Neem) has been an indispensable part of traditional medicine since ancient times. This literature review is an overview of the potential applications of neem in periodontal therapy.

**Keywords:** Periodontal disease, *Azadirachta Indica*, Neem.

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### I. Introduction

Periodontitis is a polymicrobial disease involving interactions of the plaque biofilm with the host inflammatory response resulting in alterations in bone and connective tissue metabolism<sup>1</sup>. Plaque-induced gingivitis is an inflammation of the gingiva that results from an interaction between microbes and the inflammatory cells of the host. The removal of bacterial plaque results in resolution of gingival inflammation within a few days and prevents its progression to periodontitis.<sup>2</sup> Over time, periodontal treatment methodologies have been influenced by the inclination of the times. Current management of periodontal diseases includes reduction of the microbial load and modifying the environment of the niches<sup>3</sup> This may be achieved by scaling and root planing alone or in conjunction with local or systemic antibiotics.<sup>4</sup>

However, increased incidence of disease and opportunistic infections and increased antibiotic resistance led to the development of alternative treatment methodologies for periodontal diseases.<sup>5</sup> Herbs have various bioactive components which possess enormous medicinal value with least side effects.<sup>6</sup> Herbal drugs and their therapeutic use in periodontal diseases has been known and used successfully since ancient times. One such medicinal tree is *azadirachta indica* (neem).

Neem, a native tree of India, has been declared the "Tree of the 21<sup>st</sup> century" by the United Nations. It is also known as "Divine Tree," "Life-giving tree," "Nature's Drugstore," "Village Pharmacy," and "Panacea for all diseases."<sup>3</sup> The benefits of neem have been enlisted in various ancient scriptures like 'Charak-Samhita' and 'Susruta Samhita'. The therapeutic effects of neem such as its role as an antioxidant, antimicrobial, antidiabetic, anticancer, neuroprotective, anti-inflammatory and immunomodulatory effect have been extensively researched<sup>7</sup> Some of these properties of neem have been explored for their application in periodontal therapy as well.

This narrative review gives a brief overview of the general properties of neem and an insight into its potential application in periodontal therapy.

### PLANT DESCRIPTION<sup>8</sup>

Neem is a perennial plant found in tropical and semi-tropical regions of India, Pakistan, and Bangladesh. Neem has been an essential herb in traditional medicine therapies since prehistoric times. It is known in India and its neighbouring countries for more than 2000 years. It continues to be a cheap and effective drug for various health ailments in Indian folk medicine and thereby popularly termed as "village dispensary". Thus, it is commercially exploitable.

### TAXONOMICAL CLASSIFICATION<sup>7</sup>

Kingdom: Plantae, Order: Rutales, Suborder: Rutinae, Family: Meliaceae, Subfamily: Melioideae, Tribe: Melieae, Genus: *Azadirachta*, Species: *Indica*

## **PARTS OF THE TREE USED<sup>8</sup>**

Every part of the tree has significant medicinal value. Neem leaves have antimicrobial activity, anticarcinogenic activity, antiulcer effect, hypoglycaemic activity, hepatoprotective activity, central nervous system depressant and anxiolytic effect. The bark is used for its anti-inflammatory, antibacterial, analgesic, antiseptic, antiulcer and immunomodulatory properties. Lastly, the seeds exhibit antimicrobial and antioxidant activity.



VARIOUS FORMS OF NEEM THAT CAN BE USED IN PERIODONTAL THERAPY

## **COMPOSITION<sup>8</sup>**

More than 135 compounds have been isolated from neem. The main active ingredients are named nimbin, nimbinin, and nimbidin. All parts of the plant yield  $\beta$  sitosterol. Neem consists of genin, sodium nimbinate, salannin, nimbin, azadirachtin, nimbiol, quercetin and nimbidin. Neem leaves contain fiber, carbohydrates and at least 10 amino acid proteins, calcium, carotenoids, fluoride.

## **MECHANISM OF ACTION OF ACTIVE COMPOUNDS**

Periodontal disease results from host interactions with large number of anaerobic periodontal pathogens leading to tissue destruction. Oxidative stress is an important cause of cell damage associated with the initiation and progression of periodontitis. Prolonged exposure of the connective tissue to these insults results in the subsequent loss of periodontal and alveolar bone support, eventually resulting in tooth loss<sup>1</sup>. Thus, periodontal therapy should address both, the microbial load as well as the subsequent oxidative stress to prevent tissue damage.

Thus, the possible therapeutic actions of Neem that may find their application in periodontal therapy are as follows<sup>7</sup>

1. Antimicrobial activity - inhibition of microbial growth/ cell wall breakdown.
2. Prevention of adhesion of plaque by inhibition of glucosyl transferase.
3. Free radical scavenging properties due to presence of antioxidants like azadirachtin and nimbolide
4. Regulation of cell signalling pathways.eg.various growth factors
5. Anti-inflammatory action via regulation of proinflammatory enzyme activities including cyclooxygenase (COX), and lipoxygenase (LOX) enzyme.

## **ROLE OF NEEM IN MANAGEMENT OF PERIODONTAL DISEASE**

The ancient practise of using neem in various forms for prevention of periodontal disease is verified in modern clinical studies.

### **USE OF NEEM CHEWING STICKS FOR BRUSHING**

Traditionally, slender neem twigs (called Datun) are first chewed as a toothbrush and then split as a tongue cleaner.<sup>9</sup> Two clinical studies conducted to compare and evaluate the plaque removal assessment of neem stick and toothbrush concluded that the use of neem chewing stick could be as effective as the toothbrush.<sup>9,10</sup> The active components of neem plant like gallotannins reduce the adhesion of bacteria to the tooth surface.<sup>9,10</sup> Some of this activity of neem sticks may be attributed to the mechanical plaque removal caused by the fibrous sticks.

### **USE OF NEEM IN A DENTIFRICE**

In a clinical study, neem-based toothpaste showed significant improvement in gingival health in patients with confirmed gingivitis.<sup>11</sup> An *In vitro* study used formulations in the form of both tooth powder and toothpaste from tender neem twigs. They concluded that powdered form of neem twigs were more effective compared to paste form on microbes.<sup>12</sup>

### **USE OF NEEM AS A CONSTITUENT OF MOUTHWASH**

Various studies were conducted to assess the efficacy of neem mouth rinse in reduction of gingival, bleeding, and plaque indices.<sup>13,14</sup> An *In vitro* study was conducted to evaluate the cytotoxic effects of chlorhexidine and neem extract on human fibroblasts. The authors concluded that neem did not adversely affect the fibroblasts even up to 50% concentration in comparison to chlorhexidine.<sup>15</sup>

However, a systematic review carried out by Dhingra et al. (2015) concluded that the evidence concerning the clinical use of neem mouthrinse is inconclusive and needs further reinforcement with high-quality randomized controlled trials.<sup>16</sup>

### **USE OF NEEM IN LOCAL DRUG DELIVERY**

Vennila K. et al conducted a study to evaluate the efficacy of 10% whole (neem) chip as an adjunct to scaling and root planning in 20 chronic periodontitis patients. They concluded that 10% neem oil local delivery system improved the clinical parameters and also reduced P.gingivalis population.<sup>3</sup>

A similar study was conducted by Mehta et al. comparing neem with tetracycline as local drug delivery system. The authors concluded that neem extracts exhibited good antibacterial property, and was found to be marginally better though not statistically significant than commercially available tetracycline<sup>17</sup>

### **NEEM OIL PULLING**

Sanadi et al. (2020)<sup>18</sup> conducted a study to evaluate the effect of neem oil pulling on plaque induced gingivitis and compare its efficacy with coconut oil pulling. They concluded that neem oil is more effective than coconut oil when used for oil pulling in reducing plaque induced gingivitis.

Commercially available oral care products like Colgate Active salt and neem toothpaste, Himalaya complete care toothpaste and Himalaya neem and pomegranate toothpaste have neem as their basic ingredient. However, isolated neem preparations have to be formulated.

### **TOXICITY OF NEEM**

Although various clinical trials have shown promising therapeutic benefits of the neem plant, there is evidence of neem associated toxicity. Neem oil is known to produce refractory seizures, metabolic acidosis, renal failure, encephalopathy, auditory and visual disturbances, and ataxia<sup>19</sup>

## **II. Conclusion**

The neem plant promises to offer a plethora of therapeutic benefits in periodontal therapy. Moreover, it is easily available, cost effective and has a long era of use with almost no side effects. However, greater number of well controlled double blinded clinical trials with large sample sizes are required so as to validate these benefits. Also, research for effective delivery of these neem extracts into deep pockets using micro spheres, nanoparticles and nano-emulsion techniques would further expand the spectrum of their therapeutic benefits. Focussed research on standardization and quality of neem products must be carried out in the future so as to avail the hidden medicinal treasure of the neem plant.

## **References**

- [1]. Kornman, K.S. 2008. Mapping the pathogenesis of periodontitis: A New Look. *J Periodontol*, 79:1560-8.
- [2]. Newman, Takei, Klokkevold, Carranza, *Clinical periodontology*. 10th ed. Saunders An imprint of Elsevier; 2006. p. 100– 9.
- [3]. Vennila K, Elanchezhian S, Ilavarasu S. Efficacy of 10% whole *Azadirachta indica* (neem) chip as an adjunct to scaling and root planning in chronic periodontitis: A clinical and microbiological study. *Indian J Dent Res* 2016;27:15-21.
- [4]. Slots J and Jorgensen MG. Effective, safe, practical and affordable periodontal antimicrobial therapy: Where are we going, and are we there yet? *Periodontology* 2000 2002; 28:298-312.
- [5]. AnartheR, Mani A , Kale P, Maniyar S, Anuraga S. Herbal Approaches in Periodontics *GIJSR* 2017 2(1)

- [6]. Sangeetha J. and Vijayalakshmi, K. Antimicrobial activity of rind extracts of *Punicagranatum* Linn. 2011 *The Bioscan* 6:119-24.
- [7]. Alzohairy MA. Therapeutics Role of *Azadirachta indica* (Neem) and Their Active Constituents in Diseases Prevention and Treatment. *Evidence-Based Complementary and Alternative Medicine*. 2016;1–11.
- [8]. Chaurasia A. *Neem in Oral Diseases - An Update Journal of Oral Med Oral Surg Oral Pathol and Oral Radiol*, 2016;2(1):1-3
- [9]. Ajay B, Kothari S, Saxena S, Jain M. Comparative effect of neemstick and toothbrush on plaque removal and gingival health - A clinical trial *J Adv Oral Res* 2011;2(3):51-6.
- [10]. Chandra A, Sharma VK, Kaur N, Agnihotri A, Bhardwaj P, Shukla AK *Gingival Health and Plaque Removal Assessment by Neem Stick and Toothbrush: A Comparative Study*. *Int J Med Res Prof*. 2018 Sept; 4(5):198-202.
- [11]. George J, Hegde S, Rajesh KS, Kumar A. The efficacy of a herbal-based toothpaste in the control of plaque and gingivitis: a clinico-biochemical study. *Indian J. Dent Res* 2009; 20(4):480-2.
- [12]. Jadge DR, Patil SV, Purohit RN. Formulation of toothpaste from various forms and extracts of tender twigs of neem. *J. PharmRes* 2008; 1(2): 148-152
- [13]. Chatterjee A, Saluja M, Singh N, Kandwal A. To evaluate the antigingivitis and antiplaque effect of an *Azadirachta indica* (Neem) mouthrinse on plaque induced gingivitis: A double-blind, randomized, controlled trial. *J Indian Soc Periodontol*. 2011;15:398–401
- [14]. Botelho MA, Santos RA, Martins JG, Carvalho CO, Paz MC, Azenha C, et al. Efficacy of a mouthrinse based on leaves of the neem tree (*Azadirachta indica*) in the treatment of patients with chronic gingivitis: A double-blind, randomized, controlled trial. *J Med Plant Res*. 2008;2:341–6
- [15]. Verma UP, Gupta A, Yadav RK, Tiwari R, Sharma R, Balapure AK. Cytotoxicity of chlorhexidine and neem extract on cultured human gingival fibroblasts through fluorescence-activated cell sorting analysis: An in-vitro study. *Eur J Dent* 2018;12:344-9.
- [16]. Dhingra K, Vandana KL. Effectiveness of *azadirachta indica* (neem) mouthrinse in plaque and gingivitis control: a systematic review. *Int J Dent Hygiene*. (2015)
- [17]. Mehta PW, Kudva P, Kudva HP. Comparative Evaluation Of The Efficacy Of Neem And Tetracycline When Incorporated In A Local Drug Delivery System When Used As An Adjunct To Scaling And Root Planing A Clinico-Microbiological Study. *IOSR-JDMS* 2015; 14(4) Ver. VIII. PP 47-50
- [18]. Sanadi RM, Sawarkar MS, Kadri KA, Jain P. *Neem Oil Pulling Vs Coconut Oil Pulling: A Clinico-microbiological Study*. *IJRAR* May 2020, 7(2), 928-33.
- [19]. Dhongade RK, Kavade SG, Damle RS. *Neem oil poisoning*. *Indian Pediatr*. 2008;45:56–7.

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