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### Abstract

The characteristics of the neem tree are briefly reviewed together with an overview of the role of neem in Ayurvedic medicine. Although dentistry *per se* is not a well-recognized specialty within Ayurvedic medicine, many of its precepts, including chewing sticks and oil pulling have been advocated as an approach to ensuring dental and oral health. The literature and anecdotal comments indicate that neem extracts possess anti-bacterial properties which should protect against dental caries and periodontal disease but there is limited published data to support these opinions.

What pertinent literature is available, however, does indicate that neem oil and neem chips, as well as neem twig chewing, exert anti-caries and anti-plaque benefits.

Keywords: Neem; Dentistry; Ayurvedic Medicine

# Introduction

The neem tree (*Azadirachta indica*), also referred to by other names, table 1, is a fast-growing evergreen tree that is resistant to drought and high temperatures.

Arishta tree	
Bead tree	
Holy tree	
Indian lilac	
Persian lilac	
Pride of china	

Table 1: Common names for the neem tree.

It is a member of the *Meliaceae* (mahogany) family and native to semi-tropical and tropical climates, and is indigenous to India, Pakistan, Bangladesh and Myanmar but also has been introduced to many other areas in the tropics [1,2]. In developed countries, neem oil formulations are widely used as a biopesticide for horticulturists and for organic farming [3]. Apparently, neem oil repels a wide variety of pests that infest plants without being harmful to mammals, birds and earthworms or to beneficial insects such as butterflies, honeybees and ladybugs - if it does not impact their habitats or food sources [4,5]. Neem oil is also used as a household pesticide as both a repellent and larvicide for ants, bedbugs, cockroaches, termites and mosquitoes.

#### Neem in systemic medicine

Before the inception and regular use of modern allopathic medicine, various infectious and chronic conditions were treated, often successfully, by traditional medicine. In fact, despite the advantages and benefits of modern medicine, there continues to be a strong reliance on traditional medicine to treat diseases because it avoids some of the detrimental side-effects of many pharmacological agents.

One type of traditional medicine is Ayurveda, a holistic ethnic medical care system that evolved some 3000 - 5000 year ago in India and which has been practiced throughout the Indian subcontinent since prebiblical times. This body of traditional medicinal knowledge for the prevention and treatment of diseases has been passed by word of mouth from generation to generation but it also is described in ancient classical and other literature, notably that of the Vedic period in India a.

Interestingly, Ayurvedic medicine is now practiced in other parts of the world as a form of complementary medicine and neem oil, extracted from the leaves and berries of the neem tree, constitute one aspect of this ancient medical approach to health.

Traditionally, all parts of the neem tree, namely the leaves, blossoms, seeds, roots and bark, have been utilized in traditional (folk) medicine for millennia to treat various systemic and oral conditions [1,6-10]. These purported therapeutic effects are summarized in table 2 although the most recognized product of the neem tree is *neem oil*, also known as margosa oil, a vegetable oil pressed from the leaves and seeds of the neem tree.

Part of Tree	Pharmacological activity
Bark	Analgesic
	Antibacterial
	Anti-inflammatory
	Antipyretic
	Antiseptic
	Anti-ulcer
	Immunomodulatory
Leaves	Antibacterial
	Anticarcinogenic
	Antifungal
	Antiulcer
	Antiviral
	Anxiolytic
	CNS depressant
	Hepatoprotective
	Hypoglycemia
	Immunomodulatory
Seeds	Antibacterial
	Antifertility
	Antifungal
	Antimalarial
	Antioxidant

Table 2: Claimed systemic pharmacological activities of neem tree parts [1,3-6].

The Vedic period or age (ca. 1500 - 500 BCE) is that period in the late Bronze Age and early Iron Age of the history of India when the Vedic literature, including the most ancient Hindu scriptures known as the Vedas (ca. 1300 - 900 BCE) were composed in the northern Indian subcontinent.

These therapeutic properties are usually ascribed to the triterpenoids azadirachtin and nimbin in neem [1,11,12]. Both compounds have recognized bioactivity against a wide variety of pathological conditions and anti-oxidant activity but whereas azadirachtin exhibits anti-bacterial properties [13-15], the anti-bacterial efficacy of nimbin is less well established [16].

#### Neem and neem oil in dentistry

Dentistry was not a well-recognized specialty within Ayurvedic medicine although it was included in its Shalakya Tantra. This branch of Ayurveda specifically addresses the diagnosis, treatment and prevention of all the diseases occurring above the neck such as those affecting the eyes, nose, ear, mouth and head [17,18]. In particular, because of its anti-bacterial properties, neem bark is used as an active ingredient in a number of toothpastes and toothpowders as an effective but natural approach to treating gingival problems and maintaining oral health [10,17,19-21]. Further, in keeping with the principles of ancient Ayurveda literature, all kinds of chewing sticks but notably neem twigs are still used in rural areas of India as an oral deodorant, toothache reliever and for cleaning of the teeth [12,17,22,23]. Oil pulling using olive oil or neem oil also appears to be beneficial to dental health [17,18,24]. Nevertheless, despite the literature suggesting that neem has multiple potential uses in dentistry, its actual application is limited in routine dental practice [25].

## Anti-cariogenic properties

Despite numerous references to the anti-bacterial properties of neem, there is very limited scientific evidence available or valid clinical trials indicating anti-caries efficacy. There have been *in vitro* studies, however, that examined the effect of neem extracts on the four microorganisms most related to dental caries, namely *Streptococcus mutans, S. salivavius, S. mitis*, and *S. sanguis*. In one study, chewing twigs of the neem tree (and of the mango tree) were sun-dried, ground into a coarse powder, and weighed into 5, 10 and 50 g aliquots before being dispersed in 100 ml of deionized distilled water [22]. After soaking for 48 h at 4°C, the water was filtered, and the filtrate inoculated onto blood agar plates containing the test microorganisms and incubated at 37°C for 48 h. It was found that Neem extract produced the maximum zone of inhibition on *Streptococcus mutans* at 50% concentration and even at 5% concentration, neem extract showed some inhibition of growth for all four microorganisms. It was concluded that the use of neem chewing sticks could be effective against cariogenic bacteria.

Another and rather later study [23] following the same protocol confirmed that at the greatest concentration, neem extract showed the maximum zone of inhibition on *Streptococcus mutans* whereas at lower concentrations, neem exhibited some inhibition of growth for all four species of microorganism.

These two studies confirmed the findings of a much earlier study [26] which also showed aqueous extracts of neem at 50% concentration to be effective against *Streptococcus mutans* The findings of all three studies projected that neem twig/stick chewing will provide maximum benefits against cariogenic bacteria and, consequently, the use of chewing sticks of neem can be recommended. In other words, the ancient practice of chewing neem twigs does appear to have a preventive effect against dental caries [12,17,19,22,23], and in rural or under-served areas would be beneficial to dental health.

#### **Periodontal issues**

Microbial plaque is recognized as the primary initiating etiology for periodontal tissue inflammation and subsequent periodontal disease. Over the years, a variety of chemical agents have been evaluated with respect to their antimicrobial effects in the oral cavity, but

these agents have associated side effects that obviate their regular long-term use. Accordingly, there has been a trend in recent years to evaluate the efficacy of natural products with fewer side-effects.

There have been several studies reported over the past several years that have investigated the effectiveness of *Azadirachta indica* (neem) against plaque formation. An early double-blind, randomized, controlled clinical study compared the short-term efficacy and safety of an *Azadirachta indica* mouthrinse on gingival inflammation and microbial plaque to that of the standard 0.12% chlorhexidine gluconate treatment [27]. Fifty-four subjects were enrolled and randomly assigned into two groups, both groups being provided with a 7-day therapy of the *A. indica*-based mouth rinse or 0.12% chlorhexidine, respectively. Plaque index, gingival index and gingival bleeding index were determined at baseline and after 1 and 4 weeks. Further, the count of cariogenic bacteria (*Streptococcus mutans*) in the saliva was assessed before and after treatment. All clinical index scores were reduced in both groups at 7 and 30 days after treatment and no statistically significant difference was found between groups in clinical and microbiological parameters. It was concluded that an *A. indica* mouth rinse is highly effective and is an alternative therapy for treating periodontal disease. A later *in vitro* study using plaque samples evaluated the antimicrobial activity of neem oil and confirmed its antiplaque activity [28].

A more detailed *in vitro* study [29] also compared the antimicrobial efficacy of chlorhexidine mouthwash, lemongrass (*Cymbopogon*) oil and neem (*Azadirachta indica*) oil against oral microflora, notably *Streptococcus mutans, Lactobacillus* and *Candida albicans*. The neem (and lemongrass) oils were suspended in saline solution at 1:1, 1:2 and 1:4 dilutions and swabbed onto test plates containing the test micro-organisms. Interestingly, the mean zones of inhibition were greatest for lemongrass oil against all three micro-organisms as compared to neem oil and chlorhexidine mouthwash with the maximum zone of inhibited growth being against *C. albicans* at 1:1 dilution. In contrast, for both neem oil and chlorhexidine mouthwash, the greatest inhibition was against *S. mutans*. The authors concluded that herbal (essential) oils were more effective in controlling the oral microflora that the standard chlorhexidine mouthwash.

Similar findings were reported in another *in vitro* study performed to compare of the antimicrobial effectiveness of neem (and clove) extract against *Streptococcus mutans* and *Candida albicans* to that of chlorhexidine [30]. The reported data indicated that neem had the highest antibacterial activity of the tested agents, followed by chlorhexidine and cloves whereas antifungal activity was highest for chlorhexidine followed by neem and clove. It was concluded that both plant extracts possess antimicrobial activity against common microbes present in the oral cavity with, clearly, neem being more effective than clove extract.

Comparable findings were reported in a randomized, double-blinded, crossover clinical trial with 40 participants aged 18 to 35 years [31]. A total of 20 participants were each randomly allocated into groups I and II. In the 1<sup>st</sup> phase, group I was provided with 0.2% chlorhexidine gluconate mouthwash and group II with 2% neem mouthwash. After gingival index (GI) scores were recorded at baseline and after 1-week, the participants then switched over to the other mouthwash for a 2<sup>nd</sup> week and GI scores were recorded again. It was found that there was a slight reduction of plaque level and a reduction in the gingival index (GI) scores with both mouthwashes, but no statistically significant difference was seen between them. It was concluded that neem mouthwash can be used as an alternative to chlorhexidine mouthwash based on the reduced scores in both the groups. The authors concluded that neem mouthwash had a better impact to chlorhexidine in prevention as well as pervasiveness of oral diseases as it is cost-effective and easily available.

Finally, a clinical study was performed that involved 20 otherwise healthy patients with bilateral periodontal probing depths of 5 - 6 mm [32]. After scaling and root planning (SRP), 10% nonabsorbable neem chips were placed in the pocket in one side of the arch., the other side received only SRP. This protocol was based on the assumption that there would be greater efficacy of neem extract in the oral cavity when delivered locally in the form of a chip. The clinical study was designed to evaluate the effectiveness of neem chip when inserted into the periodontal pocket as an adjunct to SRP. Clinical parameters were recorded on the baseline, 7<sup>th</sup> day, and the 21<sup>st</sup> day. Plaque samples were obtained for a microbiological study on the baseline and 21<sup>st</sup> day. Clinical parameters showed statistically improvement on the neem chip sites and the presence of *Porphyromonas gingivalis* strains was significantly reduced on the neem chip sites. It was

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concluded that a 10% neem oil local delivery system should provide beneficial effects against *P. gingivalis* although it was indicated that further research was needed to evaluate the efficacy of neem oil on other periodontal pathogens.

Several years ago, a study compared the antibacterial efficiency of neem leaf extracts, grape seed extracts and sodium hypochlorite against the Gram-positive *Enterococcus Faecalis* bacterium [33]. *E. Faecalis* is the predominant micro-organism recovered from root canals of teeth where previous endodontic treatment has failed. Effective endodontic treatment necessitates thorough debridement and complete elimination of micro-organisms, with adjunct intracanal irrigants routinely being used to enhance the antimicrobial effects of root canal cleaning and shaping. The standard irrigant for this purpose is 3% sodium hypochlorite solution but its antibacterial efficacy is constantly challenged by the increase in antibiotic-resistant bacterial strains. This situation has led to efforts to find alternative, simple and effective means of sanitization of root canal systems. The *in vitro* study cited here compared the antimicrobial efficacy of herbal alternatives as endodontic irrigants to the standard irrigant sodium hypochlorite against *E. faecalis* cultures.

It was found that both neem leaf and grape seed extracts, and hypochlorite, showed zones of inhibition in agar diffusion tests, indicating anti-microbial properties but with the former showing significantly greater zones of inhibition than 3% sodium hypochlorite. The anti-microbial properties of grape seed extracts were less effective than those of neem leaf extracts. Overall, the data indicate that neem leaf extract has a significant antimicrobial effect against *E. faecalis* and has potential as an intracanal medication.

## Conclusions

In vitro data indicate that neem (*Azadirachta indica*) is an effective antimicrobial against the cariogenic *Streptococcus mutans* but its effectiveness against other bacteria is less certain. Both *in vitro* and *in vivo* studies indicate that neem oil and locally placed neem chips are effective anti-bacterials and possibly exceed the efficacy of chlorhexidine gluconate in treating periodontal problems. However, it would appear that whereas *in vitro* data suggest that neem may be a more effective anti-bacterial (and anti-fungal) than chlorhexidine, clinical trials do not complete support this contention.

The potential use of neem leaf extracts as an endodontic irrigant was also an interesting finding, particularly as it was shown *in vitro* to be more effective than the standard hypochlorite treatment.

The research findings discussed here support the putative inclusion of neem in dentifrices and oral rinses to control both dental caries and periodontal problems while eliminating some of the problems associated with allopathic oral care products. The use of natural preventive and treatment aids may obviate such problems as an unpleasant taste, a propensity towards tooth staining as well as having a lower cost. Nevertheless, it is clear that more clinical trials should be undertaken to support the applications of neem in routine dental care suggested here.

## Bibliography

- 1. Neem: A tree for solving global problems. "Report of an Ad Hoc Panel of the Board of Science and Technology for International Development, National Research Council". National Academies Press, Washington, DC (1992).
- Hao F., et al. "Neem components as potential agents for cancer prevention and treatment". Biochimica et Biophysica Acta 1846.1 (2014): 247-257.
- 3. Bhandari S., *et al.* "Use of neem (Azadirachta indica A. Juss) as a biopesticide in agriculture: A review". *Journal of Agriculture and Applied Biology* 1.2 (2020): 100-117.
- 4. Isman MB. "Botanical insecticides, deterrents, and repellents in modern agriculture and an increasingly regulated world". *Annual Review of Entomology* 51 (2006): 45-66.

- Mishra AK., et al. "Use of neem oil as a mosquito repellent in tribal villages of Mandla district, Madhya Pradesh". Indian Journal of Malariology 32.3 (1995): 99-103.
- 6. Puri HS. "Neem: The Divine Tree". Azadirachta indica. Harwood Academic Publications, Amsterdam (1999).
- 7. Shareef M and Akhtar MS. "Neem (Azadirachtaindica) and its potential for safeguarding health, prevention and treatment of diseases". *Matrix Science Medica* 2.1 (2018): 4-8.
- 8. Noorul Aneesa N and Saveetha G. "Beneficial effects of neem oil-An updated review". *Journal of Pharmaceutical Sciences and Research* 8.8 (2016): 756-758.
- 9. Giri RP., et al. "Neem the wonder herb: A short review". International Journal of Trend in Scientific Research and Development 3.3 (2019): 962-967.
- Chaurasia A. "Neem in oral diseases an update". Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology 2.1 (2016): 1-3.
- Kraus W. "Biologically active ingredients: Section 2.1". IN: The Neem Tree: Azadirachta indica A. Juss. and other meliaceous plants. (Edition: H. Schmutterer) VCH Verlagsgesellschaft mbH, Weinheim (1995): 35-74.
- 12. Lakshmi T., et al. "Azadirachta indica: A herbal panacea in dentistry An update". Pharmacognosy Reviews 9.17 (2015): 41-44.
- 13. Morgan ED. "Azadirachtin, a scientific gold mine". Bioorganic and Medicinal Chemistry 17.12 (2009): 4096-4105.
- 14. Fernandes SR., *et al.* "Chemistry, bioactivities, extraction and analysis of azadirachtin: State-of-the-art". *Fitoterapia* 134 (2019): 141-150.
- 15. Ghimeray AK., *et al.* "Antioxidant activity and quantitative estimation of azadirachtin and nimbin in Azadirachta Indica A. Juss grown in foothills of Nepal". *African Journal of Biotechnology* 8 (2009): 3084-3091.
- 16. Usman A., *et al.* "Anti-Bacterial, Anti-Oxidant and Cytotoxic Activities of Nimbin Isolated from African Azadirachta Indica Seed Oil". *Advanced Journal of Chemistry, Section B* 2.2 (2020): 81-90.
- 17. Bhardwaj VK. "Ayurveda and holistic approach in oro-dental care: An overview". *SRM Journal of Research in Dental Sciences* 6 (2015): 181-186.
- 18. Bhowmik D., *et al.* "Herbal remedies of Azadirachta indica and its medicinal application". *Journal of Chemical and Pharmaceutical Research* 2.1 (2010): 62-72.
- 19. Ravishankar TL., et al. "Neem (Azadirachta indica): An Elixir in Dentistry". Chronicles of Dental Research 7.1 (2018): 7-17.
- 20. Hassan SA., et al. "Neem in dentistry a review". Indian Journal of Integrative Medicine 2.1 (2020): 10-12.
- 21. Chaurasia A. "Neem in oral diseases An update". *Journal of Oral Medicine, Oral Surgery, Oral Pathology and Oral Radiology* 2.1 (2016): 1-3.
- Prashant GM., *et al.* "The effect of mango and neem extract on four organisms causing dental caries: Streptococcus mutans, Streptococcus salivavius, Streptococcus mitis, and Streptococcus sanguis: An in vitro study". *Indian Journal of Dental Research* 18.4 (2007): 148-151.

- Chava VR., et al. "The efficacy of neem extract on four microorganisms responsible for causing dental caries viz Streptococcus mutans, Streptococcus salivarius, Streptococcus mitis, and Streptococcus sanguis: An in vitro study". The Journal of Contemporary Dental Practice 13.6 (2012): 769-772.
- 24. Carlson RE and Von Fraunhofer JA. "Olive oil, oil pulling and dental health". EC Dental Science 21.3 (2022).
- 25. Kaushik A., et al. "Ethnomedicine: Applications of neem (Azadirachta indica) in dentistry". Dental Hypotheses 3.3 (2012): 112-114.
- 26. Khalid A. "Antimicrobial effects of extracts of Azadirachta indica (Neem) and Salvadora persica (Arak) chewing sticks". *Indian Journal of Dental Research* 10 (1999): 23-26.
- 27. Botelho MA., *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". *Journal Of Medicinal Plants Research* 2.11 (2008): 341-346.
- 28. Elavarasu S., *et al.* "Evaluation of anti-plaque microbial activity of Azadirachta indica (neem oil) in vitro: A pilot study". *Journal of Pharmacy and Bioallied Sciences* 4.2 (2012): S394-S396.
- Subhashree M., et al. "Comparison of antimicrobial efficacy of chlorhexidine mouthwash, lemongrass (cymbopogon) oil and neem (Azadirachta indica) oil against oral microflora: An in vitro study". *Indian Journal of Public Health Research and Development* 10.10 (2019): 369-374.
- Bansal V., et al. "Assessment of antimicrobial effectiveness of neem and clove extract against Streptococcus mutans and Candida albicans: an in vitro study". Nigerian Journal of Medicine 60.6 (2019): 285-289.
- 31. Jalaluddin M., *et al.* "Comparative evaluation of neem mouthwash on plaque and gingivitis: a double-blind crossover study". *The Journal of Contemporary Dental Practice* 18.7 (2017): 567-571.
- 32. Vennila K., *et al.* "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 Journal of Dental Research* 27.1 (2016): 15-21.
- 33. Ghonmode WN., *et al.* "Comparison of the antibacterial efficiency of neem leaf extracts, grape seed extracts and 3% sodium hypochlorite against E. feacalis – An in vitro study". *Journal of International Oral Health* 5.6 (2013): 61-66.

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