Neem in Oral Diseases - An Update

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Abstract
Herbal Medicines are a fast emerging trend in recent times, as they provide safer, effcective and economical treatment to patients**.** Azadirachta indica (neem) has been an integral part of health and oral care since times immemorial. It has shown to be an effective antimicrobial, antinflammatory and anticancer agent. In india it has been an indespensible part of oral care and is still a popular dental care agent in rural india. Incorporation of neem extract in oral health care products provides a natural solution to oro-dental problems and in maintaining oral health.

Keywords: Azadirachta indica, Antibacterial, Anti inflammatory, Anticancer**.**

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Introduction
Azadirachta indica (Neem) belongs to the mahogany family meliaceae and is a species of genus Azadirachta. Neem has two species: A. Indica, A. Juss and M. Azedarac which are known as Indian neem (margosa tree) or Indian lilac and Persian lila respectively [1]. Neem is a perinenial plant found in tropical and semi-tropical regions of India, Pakistan, and Bangladesh [2]. Azadirachta indica is derived from Persian "Azad" meaning free and "dirakat" meaning tree, indica means of Indian origin hence it signifies"free tree of india". Neem has been indespensible herb in ayurveda, unani and other traditional medicine therapies since prehistoric times. Neem continues to be a cheap and effective drug for various health ailments in indian folk medicine and thereby popularly termed as "village dispensary"[3]. Siddiqui was first to identify medicinal properties of neem in 1942. He isolated Nimbin and nimbinin along with a bitter component nimbidin from neem. He stated that nimbidin has antiarthritic, antiulcer and anti-inflammatory properties whereas former two had antipyretic and anti inflammatory properties[4]. Various parts of neem plant have shown medicinal properties such as anti-inflammatory, antipyretic, analgesic, antimicrobial, anti-tumourogenic, antioxidant, antiulcer and immunostimulant activity [5].

Part of tree	Pharmacological activity
Leaf	Antifungal activity, Antibacterial activity, Antiviral activity, Anti-carcinogenic activity, Antiulcer effect, Hypoglycaemic activity, Hepatoprotective activity, central nervous system depressant, anxiolytic.
bark	anti-inflammatory, antibacterial, analgesic, antiseptic, Antiulcer and immunomodulatory
Seed	Antimalarial activity, Antifungal activity, Antibacterial activity, Antioxidant activity, Antifertility effect

Therapeutic Effect of Neem in Oral Diseases
Anti-bacterial action- Azadirachtin and nimbinin are principal constituents of neem extract responsible for its antibacterial properties[6]. Neem leaf extract has shown significant reduction in plaque index and bacterial count especially S.mutans and lactobacilli species[7]. Elavarasu et al also demonstrated in their study definite anti plaque activity of neem oil[8]. Hedge & Kesaria compared antimicrobial efficacy of neem, propolis, turmeric, liquorice and sodium hypochlorite as root canal irrigants against E. Faecalis and C. Albicans in their study. They showed excellent efficacy of neem extract in inhibition of most resistant species E. fecalis and candida in root canal disinfection[9]. Adyanthaya et al studied antimicrobial effect of methanol extract of neem twig. They found efficacy of neem extract in reducing cariogenic as well as periodontal disease causing bacteria and suggested incorporation of methanol extract of neem twig into oral care products [10].

Antifungal Properties- Neem oil and leaves have demonstrated antifungal properties and have been effective in reduction of candida induced denture Stomatitis [11]. Mahmoud et al. conducted a study to evaluate the effect of aqueous, ethanolic and ethyl acetate extracts from neem leaves on growth of various fungi (Aspergillus flavus, Aspergillus fumigatus, Aspergillus niger, Aspergillus terreus, Candida albicans and Microsporum gypseum*)* in vitro. They found that alchol based neem extract have excellent inhibitory effect on fungi and can be used as an antifungal agent [12]**.**

Anti-cariogenic Effect- Neem bark and twigs have been used as natural toothbrush since ages. Neem bark extract has shown significant anti cariogeneic properties on various cariogenic bacteria inhabiting oral flora. Bhuiyan et al showed anti cariogeneic effect of acetone extract of neem on S.sorbinus [13]. Almas Khalid in his study showed inhibition of Strept mutans and Strept faecalis at 50% concentration of neem bark extract [14]**.** Neem extract has demonstrated inhibition of Streptococcus mutans, Streptococcus salivarius, Streptococcus mitis, and Streptococcus sanguis at various concentrations, antibacterial properties were seen at even 5% of concentration [15]. N. C. J. Packia Lekshmi et al evaluated the antibacterial activity of neem extracts againt oral pathogenic bacteria using disc diffusion method. She found significant reduction in Streptococcus salivarious and Fusobacterium nucleatum. she concluded that chloroform extracts of neem has a strong antimicrobial activity and suggest that it can be useful in the treatment of dental caries [16].

Antinflammatory Role- Neem extract have shown efficacy in reducing acute as well as chronic inflammation [17]. Bothello et al. suggested in their study that neem based mouth rinses can be used in gingival and periodontal diseases as neem extract showed significant reduction in plaque and gingival inflammation [18]. Chatterjee et al. suggested in their study that neem extract based mouth rinses are efficient in controlling plaque induced gingivitis and had fewer long term usage side effects than cholorhexidiene based mouthwashes [19].

Antioxidant properties- Neem extract prevents oxidative and hydroxyl ion induced mucosal damage thereby exerting an antiulcer effect [20]**.** Pandey et al studied phytochemicals in neem for antioxidant properties. They found presence of β-sitosterol, lupeol, rutin, ellagic acid, ferulic acid and quercetin and the extract showed significant free radical scavenging activity there by implicating its incorporation in various orofacial and skin ailments [21].

Anticancer action- Neem exerts anticancer effect on malignant cells by inhibition of cell proliferation, induction of cell death, suppression of cancer angiogenesis, restoration of cellular reduction/oxidation (redox) balance and enhancement of the host immune responses against tumor cells. Though mechanism pathway for the above activity is unclear but the suppression of NF-κB signaling pathway has been involved. Neem extracts not only exerts anticancer activity but also sensitizes cancer cells to immunotherapy and radiotherapy thereby enhancing the efficacy of other chemo and radio therapeutic agents [22]. Subapriya et al studied chemopreventive effects of ethanolic neem leaf extract in the initiation and post-initiation phases of hamster buccal pouch (HBP) carcinogenesis. She demonstrated that ethanolic neem leaf extract inhibits carcinogenesis by protecting against oxidative stress [23]**.** Hence neem extract can be employed as an effective anticancer agent or as an adjunct to chemo-radiotherapy of oral and head and neck carcinomas.

Conclusion

Neem is an omnipotent tree and nature's gift to mankind for prevention and treatment of various health ailments. In past years extensive research on therapeutic benefits of neem in oral and dental problems had proved its efficacy as an excellent and cheap antimicrobial, antinflammatory and anticancer agent. It's time that neem extracts are incorporated in present day oral and dental care products as well as in treatment of various oral premalignant and malignant lesions.

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