Review Article

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THERAPEUTIC ROLE OF NEEM (AZADIRACHTA INDICA) LEAVES PHYTOCONSTITUENTS IN ORAL LICHEN PLANUS: A MINI REVIEW

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ABSTRACT

Nature has in its store a host of constituents which have enormous beneficial effects on health. One such nature's drug is *Azadirachta indica*, commonly called as Neem tree. Considered as a cynosure of medicine, Neem has been used in different pathies. In dentistry too it has been used in periodontal diseases and as root canal irrigating material. Of all the various parts of Neem tree, Neem leaves possess various constituents whose properties could be beneficial for chronic ulcerations in oral cavity like oral lichen planus. Oral lichen planus is a chronic inflammatory pre-malignant condition in which patient experiences severe burning pain. Steroids are the standard therapy provided but at the cost of their side effects. Therefore an alternative, safe and natural medicine like Neem should be considered. This paper provides a literature review explaining the role of various phytoconstituents in Neem leaves that could have a beneficial role in oral lichen planus.

Keywords: *Azadirachta indica*, anti-inflammatory, antioxidant, Neem tree, oral lichen planus, phytoconstituents.

INTRODUCTION

Modern medicine has evidenced considerable revolution in the treatment of many diseases. But still there are certain areas in medicine, where due to unknown reasons the standard care is not responsive in bringing out the desired results. At such times one needs to go back to the basics of nature. Herbal therapy is one of the forms of natural therapy which has been used since ages. They have the potential to not only cure the disease but also have an overall healing effect on the entire body and mind. *Azadirachta indica,* commonly called as Neem has been used since ancient times because of its "Sarvaroga Nivarini" potential.[1] Each and every part of this tree exhibits considerable medicinal properties. Neem leaves specially are the 'store house' of organic compounds containing 0.13% essential oil.[1] They contain many active substances having variable pharmacological actions and hence are not only used as ethnomedicine but also as Ayurvedic, Unani and Homeopathic medicines. The constituents of leaves have following properties: immunomodulatory, anti-inflammatory, anti-hyperglycemic, anti-ulcerogenic, anti-malarial, antifungal, antibacterial, antiviral, antioxidant, anti-mutagenic and anticarcinogenic.[2] Neem tree leaves have been used in treating leprosy, eye problem, epistaxis, intestinal worms, anorexia, biliousness and skin ulcers.[3] In psoriasis it has reduced itching, pain, scaling and redness of patchy lesions.[4] Thus further explorations of the medicinal properties should be continued so as to provide safe alternative to other diseases.

Oral lichen planus is a chronic inflammatory condition affecting oral mucosa. The oral lesions can be white (reticular, plaque or papular lesions) or red (atrophic or erosive lesions) or mixed lesions. Most of the patients have periods of exacerbations and remissions. The periods of exacerbation correlate with presence of oral lesions and sever unbearable burning pain. Therefore, timely treatment and follow-up for this condition is essential as there is sufficient evidence to label it as a potentially malignant disease. The standard treatment for oral lichen planus is corticosteroids but the side effects associated with it like mucosal atrophy, secondary candidal infection and burning pain prevents it's excess and chronic use. Therefore, a safe alternative is desirable. Neem leaves constituents, because of the variety of pharmacological actions as mentioned earlier could be considered as a medicinal therapy for oral lichen planus. This literature review discusses those pharmacological mechanisms of action of Neem leaves constituents that could be considered as beneficial in treating oral lichen planus.

The relevant data was collected from online databases like Pubmed, Cochrane, Google scholar, Ebscohost, related journals and books. Duration constraint was avoided to yield maximum relevant data. All types of studies including *in vitro* and *in vivo* studies involving humans and animals were considered.

Active Neem compounds

The active Neem compounds are chemically diverse and complex. They belong to two groups; (i) isoprenoids which include diterpenoids, triterpenoids, vilasinin type of compounds, limonoids and its derivatives and C-secomeliacins, (ii) non isoprenoids which includes proteins, polysaccharides, sulphurous

compounds, poly phenolics, flavonoids and their glycosides, dihydrochalone, coumarin, tannins and aliphatic compounds.[5] Table 1 enlists the important constituents of Neem leaves extract and their actions.

Before reviewing the pharmacological actions of Neem leaves constituents, etiopathogenesis of oral lichen planus is discussed in brief. This will give an insight into the probable areas where Neem leaves constituents might exert their action to be effective in oral lichen planus.

Table 1: Neem (*Azadirachta indica*) leaves constituents and their action

Constituents	Action	References
Nimbidine	Anti-inflammatory	10
β-sitosterol	Anti-inflammatory, antioxidant	9
Quercetin	Anti-inflammatory, antioxidant, anticancer	8,31,32,33
Azadirachtin	Anti-inflammatory, anticancer	29,30
Nimbosterol	Antioxidant	13,14,15
B-carotene		
Ascorbic acid		
Terpenoids		
Limonoids		
Vitamin C		
Cyclic trisulphide	Antifungal	23
Cyclic tetrasulphide		
Nimbolide	Anticancer	29,30
28-deoxonimbolide		
Kaemferol	Antioxidant, anticancer	31

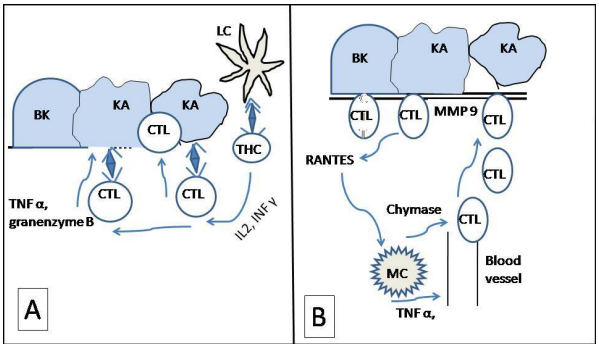

Figure 1: Schematic representation of etiopathogenesis of oral lichen planus

1A: Cytotoxic T lymphocytes undergoing basal keratinocytes apoptosis. **1B**: Vicious cycle of mast cell degranulation

BK = basal keratinocytes, KA = keratinocyte apoptosis, LC = langerhan cell, THC = T helper cell, CTL = cytotoxic T lymphocyte, IL2 = interleukin 2, INFγ = interferon gama, TNF α = tumor necrosis factor, RANTES = Regulated on activation, normal T cell expressed and secreted, MC = mast cell, MMP9 = matrix metalloproteinase 9.

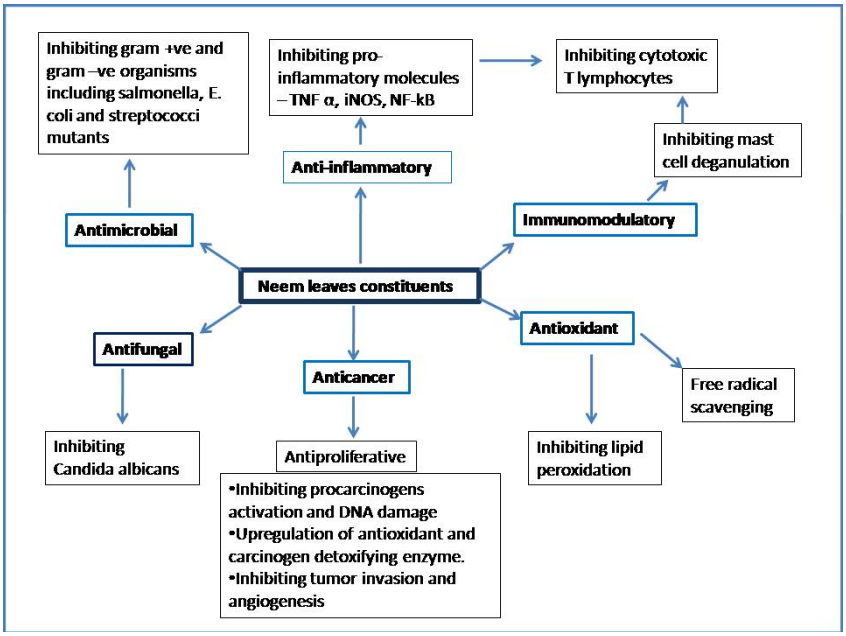

Figure 2: Mechanisms of actions of Neem leaves constituents: anti-inflammatory, immunomodulatory and antioxidant, anticancer, antifungal and antimicrobial actions

Etiopathogenesis of Oral lichen planus

Even though the etiopathogenesis of oral lichen planus is controversial, a large group of evidence suggests oral lichen planus to be an antigen (Ag) specific cell-mediated immune response. The basal keratinocytes of the oral mucosa are the ones to be targeted by the Ag of unknown origin. This leads to the activation of cytotoxic T cells and a cascade of inflammatory reaction follows. The langerhan cells present Ag and activate T helper cells which in turn activate T cytotoxic cells by Interleukin 2 (IL 2) and Interferon gamma (IF ɤ). The cytotoxic cells bind to the basal keratinocytes via FAS ligand and produces granzyme B and tumor necrosis factor α (TNFα) which contributes to the apoptosis of basal keratinocytes.[6] (Figure 1A)

Normally the basal keratinocytes secrete collagen IV and laminin V. These contribute in maintaining the normal epithelial basement membrane integrity which in turn sends a survival signal to keratinocytes. But as in oral lichen planus the basal cells undergo apoptosis, the epithelial basement membrane integrity is not maintained leading to basement membrane disruption and entry of cytotoxic T cells into the epithelium, all of which leads to further apoptosis of epithelial cells.[6] (Figure 1A)

Mast cells release TNF α and chymase which has dual action. Firstly, it stimulates extravasation of T lymphocytes from blood vessels which releases matrix metalloproteinase 9 (MMP 9) disrupting the basement membrane. Secondly the extravasated T lymphocytes release RANTES (Regulated on activation, normal T cell expressed and secreted) which further degranulate the mast cells, thus setting in a vicious cycle.[6] (Figure 1B)

Among the markers of oxidative stress, malonaldehyde and nitric oxide are the ones reported to have increased in oral lichen planus patients, thus indicating the increased levels of lipid peroxidation in these patients.[7]

Pharmacological actions of Neem leave constituents (Figure 2)

Oral lichen planus being an inflammatory, T cell mediated autoimmune and a potentially malignant lesion, the following actions of Neem leaves constituents could be considered to be beneficial for it.

Anti-inflammatory, antioxidant and immunomodulatory action

The most active constituents of Neem leaves to exhibit anti-inflammatory, antioxidant and immunomodulatory effects are nimbin, nimbidine, isomeldenin, β-sitosterol, quercetin and azadirachtin.[8-10] These effects are mainly due to-

1. The inhibition of pro-inflammatory molecules, such as tumor necrosis factor (TNF-α), inducible nitric oxide synthase (iNOS) and nuclear factor kappa B (NF –κB).
2. Reducing the oxidative stress.
3. Preventing mast cell degranulation.

TNF, a pro-inflammatory Th1 cytokine, is known to regulate the immune cells controlling apoptosis, cellular proliferation, inflammation etc. Its dysregulation or overproduction has been reported in variety of human diseases including oral lichen planus and cancer. In oral lichen planus it plays a key role in apoptosis of basal keratinocytes.[6] Studies have shown that Quercetin,[8] β-sitosterol[9] and nimbidine[10] from the Neem leaves extract (NLE) has inhibitory effect on pro inflammatory molecules like TNFα, iNOS and NF –κB. Schumacher M *et al* in their study showed the mechanism of Neem extract's anti-inflammatory potential via the inhibition of TNF-α-activated nuclear factor- κB (NF- κB) signaling pathway.[11]

NF-κB is a central transcription factor that plays an important role in the expression of inflammatory genes such as TNF α and IL 6. It is activated by these inflammatory regulators and influenced by oxidative stress.[11]

The effect of excessive oxidative stress on NF-κB can be as follows:

i. It affects the NF-κB genomic integrity as well as lead to mutagenesis.
ii. It affects the signaling complexes which activate several signaling pathways such as NF-κB pathways.
iii. And finally enhance inflammation by increasing the expression of pro-inflammatory cytokines, chemokines and adhesion molecules.[11,12]

Similarly, oxidative stress can affect T cell receptor (TCR) signaling. TCR signaling is very important to maintain the integrity of T cells and successive phosphorylation cascade. Increased oxidative stress can dysregulate TCR signaling, causing T cell hyper activation, leading to an autoimmune disease.[11,12]

Studies on oral lichen planus have clearly directed the role of increased oxidative stress and impaired defense mechanism towards its pathophysiology.[7] Neem leaves extract (NLE) acts on different levels of the NF-kB pathways down regulating it and hence suppressing the inflammation.[11]

NLE contain poly phenolic flavonoids like Quercetin, β-sitosterol, nimbosterol, β- carotene and ascorbic acid, terpenoids, limonoids and vitamin C which have free radical scavenging effect preventing lipid peroxidation.[13-15] *In vitro* and *in vivo* animal studies have shown NLE to enhance the activities of glutathione dependent antioxidants, superoxide dismutase and catalyse and reduce the incidence of bone marrow micronuclei and chromosomal aberrations.[16,17] In a study, aqueous leaf extract showed 50% scavenging activity at 26.5 µg/ml and total antioxidant activity of extracts was found to be 0.959 nM of standard trolox.[18] In an *in vitro* study evaluating the combined effects of Neem extract, bacteria, red blood cells and lysozyme, it was shown that Neem polyphenols could bind to the surfaces of both microbes (dead or alive, serving as carriers) and mammalian cells and this adhesion was enhanced by RBC and salivary cationic lysozymes.[19] Thus Neem leaves polyphenols can provide long lasting antioxidant activity in the oral mucosa because of the abundant lysozyme present there and RBCs which are usually present near the inflamed areas; a clinical setting similar to atrophic, erosive or ulcerative types of oral lichen planus.

Prevention of mast cell degranulation by NLE have been reported,[20] preventing the progression of the vicious cycle of release of T lymphocytes from the blood capillaries, apoptosis of basal keratinocytes, release of RANTES and further mast cell degranulation.[6] Thus the inhibitory effect on T cells by Neem leaves constituents are mainly attributable due to the inhibition of pro-inflammatory cytokines, antioxidant action and inhibition of mast cell degranulation.

Antifungal action

Studies have shown that 17.4 to 16.4% of the oral lichen planus lesions are super infected by *Candida albicans* which might further add to the oral discomfort ultimately contributing to the

development and progression of oral lichen planus[21] or might be responsible for its malignant transformation.[22] The antifungal property of NLE exhibited by its compounds, cyclic trisulphide and cyclic tetrasulphide could be beneficial against the fungal infection. The minimum inhibitory concentration (MIC) of NLE to *C. albicans* has been reported to be 3.75%.[23] Pavithra JM *et al*. in an *in vitro* study have shown that aqueous and ethanolic Neem extracts inhibit the adherence of *C. albicans* to human buccal epithelial cells thus providing a base for anti-adherent therapy.[24]

Anticancer action

Neem leaves possess potent anti-carcinogenic properties which could be beneficial in preventing malignant conversion of oral lichen planus. With a malignant transformation rate of 1-2%, oral lichen planus lesions have the potential to exhibit field cancerization.[25] The risk factor could be repeated exacerbations, atrophic or erosive ulcerative areas and refractory cases all of which indicate a state of persistent chronic inflammation leading to a cytokine based microenvironment and increased oxidative stress.[26] Expression of apoptosis and cell cycle-regulating proteins such as p53 protein, p21 protein, p16 protein, bcl-2, and bax could also be altered in the transformation process.[27] These changes in the epithelial cells might be responsible for the conversion to malignancy. Limonin 17 β-D-glucopyranoside a limonoid found in Neem leaves has shown to inhibit 7, 12 dimethylbenz [a] anthracene (DMBA) induced oral carcinogenesis in the Hamster buccal pouch (HBP) which reiterate many of the features observed in human oral squamous cell carcinomas.[28] Nimbolide, 28-deoxonimbolide and azadirachtin have also been identified as cytotoxic constituents of Neem leaves.[29,30] In concentration dependent manner they are effective in prevention of activation of pro carcinogens, oxidative DNA damage and up regulation of antioxidant. Also, they have inhibitory effects on carcinogen detoxifying enzymes, tumor invasion and angiogenesis. [30]

Neem leaves flavonoids quercetin and kaempferol have inhibitory role of cancer development due to their radical scavenging properties.[31] They retard carcinogenesis and inhibit growth of tumor cells at initiation and promotional phases. The suggested anti proliferative effects of quercetin have been documented in experimental animals and humans as follows: inhibition of cytochrome P-450-dependent mono oxygenase system and down regulation of the expression of mutant p53 protein and p21-ras oncogene, thus regulating the cell cycle.[32,33]

Antibacterial action

In oral lichen planus patients, strict oral hygiene maintenance is a very crucial factor. Gingival lesions might prevent the patients from performing routine hygiene procedure which might aggravate the condition. In such cases antibacterial properties of Neem leaves could be beneficial. In a study to evaluate the effect of Neem-containing mouthwash on plaque and gingivitis it was shown that the Neem leaves extract mouthwash was effective in reducing the periodontal and gingival index scores.[34] This could be probably due to the inhibitory effects of Neem on the growth of both gram positive and gram negative organisms including *Salmonella, Escherichia coli* and *Streptococcus* mutants.[35]

Toxicity

NLE is well tolerated with toxicity not reported up to 1000 mg/kg by oral route in mice, whereas intravenous administration at dose greater than 40 mg/kg body weight produced toxic manifestation in guinea pigs.[5]

Thus, considering the above discussed mechanisms of actions, Neem leaves could be considered as a medicinal therapy in oral lichen planus. Being cost effective and widely available it can have the potential to treat various chronic inflammatory conditions.

CONCLUSION

Neem, a multifaceted herb has proved its medicinal potential in many diseases. Because of its various useful constituents, Neem leaves possess an array of pharmacological actions which could be considered beneficial in oral lichen planus. Research in this perspective would definitely help to further explore the benefits of Neem in health and disease.

This literature review is a part of a randomized control trial which is being carried out in the institute and it is a non-funded project.

Limitations

Case reports, case series or clinical trials could not be obtained for review and comparison as studies of Neem in oral lichen planus have not been conducted earlier. For the same reason a standard systematic review could not be performed.

Recommendations

To confirm the therapeutic role of Neem in oral lichen planus, either in topical or systematic form, clinical trials should be carried out. This will give an insight about the efficacy of Neem leaves extract in reducing the signs and symptoms of oral lichen planus.

REFERENCES

1. Puri HS. Plant sources. In: Neem. The divine tree. *Azadirachta indica*. 1st ed. Singapore: Harwood Academic Publishers; 1999. p. 9-21.
2. Akihisa T, Takahashi A, Kikuchi T, Takagi M, Watanabe K, Fukatsu M, Fujita Y, Banno N, Tokuda H, Yasukawa K. The melanogenesis-inhibitory, anti-inflammatory and chemo preventive effects of limonoids in n-hexane extract of *Azadirachta indica* A. Juss. (Neem) seeds. J Oleo Sci 2011; 60(2): 53-9.
3. Ganguli S. Neem: A therapeutic for all seasons. Curr Sci 2002; 82(11): 1304.
4. Tiwari R, Chakraborty S, Dhama K. Miracle of herbs in antibiotics resistant wounds and skin infections: Treasure of nature- a review/ perspective. Pharm. Sci. Monitor 2013; 4: 214-48.
5. Biswas, K. Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and medicinal properties of Neem (*Azadirachta indica*) Curr. Sci 2002; 82(11): 1336-45.
6. Roopashree MR, Gondhalekar RV, Shashikanth MC, George J, Thippeswamy SH, Shukla A. Pathogenesis of oral lichen planus – a review. J Oral Pathol Med 2010; 39(10): 729–34.
7. Ergun S, Trosala SC, Warnakulasuriya S, Ozel S, Onal AE, Ofluoglu D, Güven Y, Tanyeri H. Evaluation of oxidative stress and antioxidant profile in patients with oral lichen planus. J Oral Pathol Med 2011; 40(4): 286–93.
8. Chang YC, Tsai MH, Sheu WH, Hsieh SC, Chiang AN. The therapeutic potential and mechanisms of action of quercetin in relation to lipopolysaccharide-induced sepsis *in vitro* and *in vivo*. PLoS One 2013; 8(11): e80744.
9. Loizou S, Lekakis I, Chrousos GP, Moutsatsou P. Beta-sitosterol exhibits anti-inflammatory activity in human aortic endothelial cells. Mol Nutr Food Res 2010; 54(4): 551-8.

10. Pillai NR, Santhakumari G. Anti-arthritic and anti-inflammatory actions of nimbidin. Planta Med 1981; 43(1): 59-63.
11. Schumacher M, Cerella C, Reuter S, Dicato M, Diederich M. Anti-inflammatory, pro-apoptotic and anti-proliferative effects of a methanolic Neem (*Azadirachta indica*) leaf extract are mediated via modulation of the nuclear factor-κB pathway. Genes Nutr 2011; 6(2): 149–160.
12. Larbi A, Kempf J, Pawelec G. Oxidative stress modulation and T cell activation. Exp Gerontol 2007; 42(9): 852-8.
13. Suda D, Schwartz J, Shklar G. Inhibition of experimental oral carcinogenesis by topical beta carotene. Carcinogenesis 1986; 7(5): 711-5.
14. Ekaidem IS, Akpan HD, Usoh IF, Etim OE, Ebong PE. Effects of ethanolic extract of *Azadirachta indica* leaves on lipid peroxidation and serum lipids of diabetic Wistar rats. Acta Biologica Szegediensis 2007; 51(1): 17-20.
15. Chattopadhyay RR. Possible biochemical mode of anti-inflammatory action of *Azadirachta indica* A. Juss. in rats. Indian J. Exp. Biol 1998; 36(4): 418-20.
16. Arivazhagan S, Balasenthil S, Nagini S. Garlic and Neem leaf extracts enhance hepatic glutathione and glutathione dependent enzymes. Cell Biochem Funct 2000; 14(4): 291-3.
17. Subapriya R, Bhuvaneswari V, Ramesh V, Nagini S. Ethanolic leaf extract of Neem (*Azadirachta indica*) inhibits buccal pouches carcinogenesis in hamsters. Cell Biochem Funct 2005; 23(4): 229-38.
18. Sithisarn P, Supabphol R, Gritsanapan W. Antioxidant activity of Siamese Neem tree (VP1209). J Ethnopharmacol 2005; 99(1): 109–12.
19. Heyman L, Houri Haddad Y, Heyman SN, Ginsburg I, Gleitman Y, Feuerstein O. Combined antioxidant effects of Neem extract, bacteria, red blood cells and Lysozyme: possible relation to periodontal disease. BMC Complementary and Alternative Medicine 2017; 17(1): 399.
20. Garg GP, Nigam SK, Ogle CW. The gastric antiulcer effects of the leaves of the Neem tree. Planta Med 1993; 59(3): 215-7.
21. Zeng X, Chen QM, Nie MH, Li BQ. The attribute of *Candida albicans* isolates from patients with oral lichen planus. Zhonghua Kou Qiang Yi Xue Za Zhi 2004; 39: 149-52.
22. Krogh P, Hald B, Holmstrup P. Possible mycological etiology of oral mucosal cancer: catalytic potential of infecting *Candida albicans* and other yeasts in production of N-nitrosobenzylmethylamine. Carcinogenesis 1987; 8(10): 1543-8.
23. Nayak A, Nayak RN, Soumya GB, Bhat K, Kudalkar M. Evaluation of antibacterial and anti candidal efficacy of aqueous and alcoholic extract of Neem (*Azadirachta indica*): An *in vitro* study. IJRAP 2011; 2(1): 230-5.
24. Pavithra JA, Srinikethan G, Shubhada C, Pradeep K, Gopala M, Kulkarni R, Praveenchandra K R. Effect of five plant extracts on adhesion of *Candida albicans* onto human buccal epithelial cells: an *in-vitro* study. Egyptian pharmaceutical Journal 2014; 13(2): 137-43.
25. Mignogna MD, Fedele S, Lo Russo L, Mignogna C, De Rosa G, Porter SR. Field cancerization in oral lichen planus. Eur J Surg Oncol 2006; 33(3): 383–9.
26. Mignogna MD, Fedele S, Lo Russo L, Lo Muzio L, Bucci E. Immune activation and chronic inflammation as the cause of malignancy in oral lichen planus: is there any evidence? Oral Oncol 2004; 40(2): 120–30.
27. Ebrahimi M, Nylander K, Van der Waal I. Oral lichen planus and the p53 family: what do we know? J Oral Pathol Med 2011; 40(4): 281–5.
28. Miller EG, Gonzales-Sandeers AP, Couvillon AM, Wright JM, Hasegawa S, Lam LKT. Inhibition of hamster buccal pouch carcinogenesis by limonin 17-β-D-glucopyranoside. Nutr. Cancer 1992; 17(1): 1.
29. Kigodi PG, Blasko G, Thebtaranonth Y, Pezzuto JM, Cordell GA. Spectroscopic and biological investigation of nimbolide and 28-deoxonimbolide from *Azadirachta indica*. J Nat Prod 1989; 52(6): 1246–51.
30. Priyadarshini RV, Manikandana P, Kumar GH, Nagini S. The Neem limonoids azadirachtin and nimbolide inhibit hamster cheek pouch carcinogenesis by modulating Xenobiotic – metabolizing enzymes, DNA damage, antioxidants, invasion and angiogenesis. Free Radic RES 2009; 43(5): 492-405.
31. Le Marchand L. Cancer preventive effects of flavonoids – a review. Biomed Pharmacother 2002; 56(6): 296–301.
32. Lamson DW, Brignall MS. Antioxidants and cancer, part 3: quercetin. Altern Med Rev 2000; 5(3): 196-208.
33. Avila MA, Velasco JA, Cansado J, Notario V. Quercetin mediates the downregulation of mutant p53 in the human breast cancer cell line MDA-MB468. Cancer Res 1994; 54(9): 2424-8.
34. Jalaluddin M, Rajasekaran UB, Paul S, Dhanya RS, Sudeep CB, Adarsh VJ. Comparative Evaluation of Neem Mouthwash on Plaque and Gingivitis: A Double-blind Crossover Study. J Contemp Dent Pract 2017; 18(7): 567-71.
35. Wolinsky LE, Mania S, Nachnani S, Ling S. The inhibiting effect of aqueous *Azadirachta indica* (Neem) extract upon bacterial properties influencing *in vitro* plaque formation. J Dent Res 1996; 75(2): 816-22.

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