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A REVIEW ON NIMBIDIN

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Abstract: Neem is the most useful traditional medicine as a source of many therapeutic agents in the Indian culture and grows well in the tropical and semi-tropical countries. In indigenous system of medicine, every part of neem tree is used, viz. bark, leaves, fruits, seeds and extracts. Its extracts have antiviral, antibacterial, antifungal, anthelmintic, antiallergic, anti-dermatic and anti-inflammatory properties. Neem is also termed as "free tree of India", "wonder tree", "Nature's drug store", Village dispensary", "Divine tree", "heal all" and "Panacea of all Diseases". In modern era, special emphasis should be on control of diseases of human as well as animals using non-toxic herbal products. There is lot of scope for the better utilization of this wonder plant

Index Terms - Azadirachtaindica, Meliaceae, Nimbidin,Neem, Herbal products, Traditional medicine

I. INTRODUCTION

In recent years, efforts have been directed to control infectious diseases by use of herbal medicine which have fewer side effects and are ecologically safe. Neem (Azadirachta indica) is well known for its medicinal properties. Azadirachta indica is a tree in the mahogany family Maliaceae. Neem is the most useful traditional medicine as a source of many therapeutic agents in the Indian culture and grows well in the tropical and semi-tropical countries. It has been shown that neem leaves extract acts as a growth promoter [1] , improve performance and hematological parameters [2] and immune response [3,4] in broilers. In indigenous system of medicine, every part of neem tree is used, viz. bark, leaves, fruits, seeds and extracts. Its extracts have antiviral, antibacterial, antifungal, anthelmintic, antiallergic, anti-dermatic and anti-inflammatory properties [5]. Neem oil extracted from its seeds is used in medicines, pest control and cosmetics etc. and its leaves are used in the treatment of chicken pox. Neem also have anticoccidial effect in broilers and is used as pesticide [6,7] . According to the Hindus, it is believed that the goddess of the chicken pox, Sithala lives in the neem tree. Neem tea is taken to reduce headache and fever. Its flowers are used to cure intestinal problems. Neem bark act as an analgesic and can cure high fever as of malaria. Even the skin diseases can be cured from the neem leaves. India believes a lot that the neem can cure all diseases [8]. Herbs like tulsi (Oscimum sanctum), neem (Azadirachta indica), punarnava (Boerhavia diffusa); amrita (Tinospora cordifolia) and harida (Currucuma longa) act as natural anti-microbial agents and can be used in combination for treatment of anthrax in animals [9]. Centre for Traditional Medicine and Research (CTMR), Chennai, India revealed the medicinal uses of different parts viz., fruits, seeds, leaves, roots, bark etc., of neem trees. Neem leaves like most tropical tree leaves contain bioactive compounds [10,11]which may affect nutrient utilization. These bioactive compounds may also alter the hematological and serum biochemical parameters of animals. Unfortunately, the high fibre content in neem leaf meal causes serious intake and digestibility problems in poultry diets [12]. Therefore, the use of neem leaf extracts could overcome this barrier towards tapping the good nutritional characteristics of neem leaf meal. The neem leaves extract contain nimbin, nimbinene, 6-desacetylnimbiene, nimbandiol, nimbolide and quercetin (Mitra et al., 2000) [13] . An aqueous extract (10 percent) of tender leaves is reported to possess anti-viral properties against, fowl pox, infectious bursal disease and New Castle disease virus

(NDV) and significantly enhances the antibodies production against the infectious bursal disease and New Castle disease virus

ACTIVE COMPOUNDS OF NEEM

Active compounds of neem Azadirachta indica (neem) contains a number of various types of ingredients having therapeutics properties. The most important constituent is azadirachtin and others are nimbolinin, nimbin, nimbidin, nimbidol, sodium nimbinate, gedunin, salannin, and quercetin. Leaves contain ingredients such as nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7- benzoylazadiradione, 7-desacetyl7-benzoylgedunin, 17-hydroxyazadiradione, and nimbiol [14,15]. Quercetin and ßsitosterol, polyphenolic flavonoids, were purified from neem fresh leaves and were known to have antibacterial and antifungal properties [16] and seeds hold valuable constituents including gedunin and azadirachtin

BIOLOGICAL ACTIVITY OF NEEM

Its fruits are green drupes which turns green golden yellow on ripening in the months of June-august.Taxonomic position of Azadirachta indica(Neem)is classified in table1.

TABLE

S.NO	COMPOUND NAME	SOURCE	BIOLOGICAL ACTIVATY	REFERENCE
1	Nimbidin	Seed oil	Anti-inflammatory Anti-arthritic Anti-pyretic Hypoglycaemic Anti-gastric ulcer Spermicidal Antifungal Antibacterial Diuretics	17 18 19 20 21,22 23 24 24 25
2	Sodium nimbidate		Anti-inflammatory	17,18
3	Azadirachtin	Seed oil	Anti-malarial	26
4	Nimbin	Seed oil	Spermicidal	27
5	Nimbolide	Seed oil	Anti-malarial Anti-bacterial	28 29,30
6	Gedunin	Seed oil	Anti-malarial Antifungal	31 32
7	Mahmoodin	Seed oil	Antibacterial	33
8	Gallic acid,(-)epicatechin and catechin	Bark	Anti-inflammatory immunomodulatory	34
9	Margolone,margolonone and isomargolonone	Bark	Anti-bacterial	35
10	Cyclic trisulphide and cyclic tetra sulphide	Bark	Anti-fungal	36
11	Polysaccharides	Bark	Anti-inflammatory	37
12	Polysaccharides G1A,G1B	Bark	Antitumor	38
13	Polysaccharides G2A,G3A	Bark	Anti-inflammatory	39
14	NB-2 Peptidoglucan	Bark	Immunomodulatory	40,41

Medicinal Uses of Neem

PART	MEDICINAL USE
Leaf	Leprosy, eye problem, epistaxis, intestinal worms, anorexia, biliousness, skin ulcer.
Bark	Analgesic, alternative and curative of fever
Flower	Bile suppression, elimination of intestinal worms and phlegm
Fruit	Relieves piles, intestinal worms, urinary disorder, epistaxis, phlegm, eye problem, diabetes, wounds and leprosy
Twig	Relieves cough, asthma, piles, phantom tumour, intestinal worms, spermatorrhoea, obstinate urinary disorder, diabetes.
Gum	Effective against skin diseases like ringworms, scabies, wounds and ulcers
Seed pulp	Leprosy and intestinal worms.
Oil	Leprosy and intestinal worms.
Root, bark, leaf, flower and fruit together	Blood morbidity, biliary afflictions, itching, skin ulcer, burning sensation and leprosy.


There has been astronomical increase in the costs of fertilizers, pesticides, animal feeds and drugs in the developing countries, with an increasing indebtedness and acute poverty. This situation exerts enormous pressure to explore local resources handy to combat these deficits and improve quality of life of the people. One of such available resources with great potentials in the 21st century is the neem tree .The objectives of these reviews were to: elucidate the premises of neem for exploitation and utilization; identify formulations of biologically active principles, limitations against wide spread use and possible inherent dangers of neem product.....

BENEFITS OF NEEM

ANTIOXIDANT ACTIVITY

Free radical or receptive oxygen species are one of the fundamental offenders in the genesis of different illnesses. Notwithstanding, neutralization of free radical activity is one of the imperative strides in the maladies counteractive action. Antioxidants stabilize/deactivate free radicals, regularly before they assault focuses in biological cells [42] and furthermore assume job in the activation of anti oxidative protein that assumes job in the control of harm brought about by free radicals/receptive oxygen species. Therapeutic plants have been accounted for to have antioxidant activity [43]. Plants natural products, seeds, oil, leaves, bark, and roots demonstrate an essential job in illnesses aversion because of the rich source of antioxidant. Leaf and bark concentrates of A. indica have been considered for their antioxidant activity and aftereffects of the examination plainly shown that leaf and bark extracts/fractions of neem developed in the lower regions have significant antioxidant properties [44]. Another critical examination was performed dependent on leaves, fruits, flowers, and stem bark extracts from the Siamese neem tree to evaluate the antioxidant activity and results recommend that extricates from leaf, blossom, and stem bark have strong antioxidant potential [45]

ANTI CANCEROUS ACTIVITY

Malignant growth is multi-factorial malady and significant medical issue around the world. The modification of molecular/genetic pathways assumes job in the improvement and movement of malignant growth. The treatment module dependent on allopathic is compelling on one side yet in addition indicates adverse effect on the typical cell. Prior investigations detailed that plants and their constituents show inhibitory consequences for the development of malignant cells via modulation of cell expansion, apoptosis, tumour suppressor gene and different other molecular pathways [46]. Neem contains flavanoids and differentother ingredients that play an essential job in restraint of malignant growth advancement. Extensive number of epidemiological examinations suggests that high flavonoid admission might be related with a diminished danger of malignancy[47].

ANTI INFLAMMATORY ACTIVITY OF NEEM

Plants or their isolated derivatives are in the practice to treat/act as anti-inflammatory agents. An examination result has affirmed that concentrate of A. indica leaves at a dose of 200mg/kg, p. o., demonstrated hugeanti-inflammatory activity in cotton pellet granuloma test in rodents [48]. Other examination results uncovered that neem leaf extricates demonstrated significant anti-inflammatory impact, yet it is less effective than that of dexamethasone [50] and examine results propose that nimbidin stifles the elements of macrophages and neutrophils pertinent to inflammation [49]. Prior finding demonstrated immune modulator and anti-inflammatory impact of bark and leave concentrates and antipyretic and anti-inflammatory exercises of oil seeds[51,52]. Experimentation was made to assess the pain-relieving action of neem seed oil on albino rats and aftereffects of the examination demonstrated that neem seed oil indicated huge pain relieving impact in the portion of 1 and 2 mL/kg and oil has dose-dependent pain relieving action [53]. Another examination was made to explore the anti-inflammatory impact of neem seed oil (NSO) on albino rats utilizing carrageen an-incited rear paw edema and results uncovered that NSO indicated expanded hindrance of paw edema with the dynamic increment in dose from 0.25mL to 2 mL/kg body weight. At the portion of 2 mL/kg body weight, NSO demonstrated most extreme (53.14%) hindrance of edema at fourth hour of carrageen an injection [54].

HEPTOPROTECTIVE EFFECT

Therapeutic plants and their ingredients play a significant activity as hepatoprotective with no antagonistic ensnarement's. An examination was performed to inquire about the hepatoprotective employment of azadirachtin-An in carbon tetrachloride (CCl4) impelled hepatotoxicity in rodents and histology and ultrastructure results certified that pretreatment with azadirachtin-A dose dependently diminished hepatocellular corruption [55]. Other than after-effects of the examination exhibit that pretreatment with azadirachtin-An at the higher dose levels bearably restores the rat liver to normal [55].

WOUND HEALING EFFECT

Different plants/their constituents accept a basic occupation in the damage recovering effect. An examination was made to evaluate the damage patching activity of the concentrates of leaves of A. indica and T. cordifoliausing extraction and cut injury models in Sprague Dawley rodents and results revealed that concentrate of the two plants basically propelled the damage mending activity in both extraction and entry point damage models [56]. In addition, in section point wound, rigidity of the recuperating tissue of the two plants treated group was seen to be significantly higher when appeared differently in relation tothe control groups [56].Distinctive results showed that leave concentrates of Azadirachta indica advance damage retouching activity through expanded provocative reaction neovascularization [57]. An examination was grasped to evaluate the 70% alcoholic neem root bark remove (NRE) in diabetes and results showed that neem root bark extricate gave measurably noteworthy results in 800mg/kg portion [58]. Another examination was performed to take a look at the pharmacological hypoglycemic action of Azadirachta indica in diabetic rodents and results exhibited that in a glucose versatility test with neem extricate 250mg/kg indicated glucose levels were fundamentally less when contrasted and the control group and Azadirachta indica basically decline glucose levels at fifteenth day in diabetic rodents [59].

ANTI BACTERIAL ACTIVITY

An examination was performed to survey antimicrobial sufficiency of home grown choices as endodontic irrigants and differentiated and the standard irrigant sodium hypochlorite and result confirmed that leaf concentrates and grape seed extricates demonstrated zones of restriction prescribing that they had antimicrobial properties [60]. Moreover, leaf extract showed fundamentally more remarkable zones of inhibition than 3% sodium hypochlorite [61]. The antibacterial development of guava and neem isolates against 21 strains of food borne pathogens was evaluated and delayed consequence of the examination recommended that guava and neem extracts have compounds containing antibacterial properties that can possibly be significant to control food borne pathogens and deterioration life forms [62].

ANTI VIRAL ACTIVITY

Results exhibited that neem bark (NBE) remove basically blocked HSV-1 entry into cells at obsessions stretching out from 50 to 100 g/mL [63]. Furthermore, blocking development of NBE was seen when the concentrate was preincubated with the disease anyway not with the objective cells proposing a quick enemy of HSV1 property of the neem bark [64]. Leaves concentrate of neem (Azadirachta indica A. Juss.) (NCL-11) has shown virucidal development against coxsackievirus contamination B-4 as proposed by methods for disease inactivation and yield decline look at other than interfering at an early event of its replication cycle [65].

ANTI FUNGAL ACTIVITY

Investigation was made to assess the adequacy of different concentrates of neem leaf on seed borne parasites Aspergillus and Rhizopus and results affirmed that development of both the contagious species was fundamentally repressed and controlled with both alcoholic and water extract. Moreover, alcoholic concentrate of neem leaf was best.

DENTISTRY

An investigation was made to survey the adequacy of neem dependent on mouth flush with respect to its anti gingivitis impact and concentrate affirmed that A. indica mouth flush is similarly viable in diminishing periodontal records as chlorhexidine [66]. Another investigation was completed to assess the antimicrobial properties of natural concentrates of neem against three bacterial strains causing dental caries and results demonstrated that oil ether and chloroform remove indicated solid antimicrobial action against S. mutans.

IMMUNO STIMULATORY COMPOUND:

Immuno invigorating properties of neem is most critical advantage. It helps both the lymphocytic and cell-intervened frameworks, including "Killer T" cells which can obliterate organisms, infections and malignancy cells by infusing poisonous synthetic compounds into the intruders.

SEXUALLY TRANSMITTED DISEASES:

Neem demonstrates extraordinary potential to control explicitly transmitted maladies. Neem gave 75% security from the HIV infection

ULCERS:

Utilizing Neem bark diminishes 77% gastric corrosive emission just as gastric discharge volume 63% and pepsin movement 50%, because of its anti-inflammatory ingredients, gastric harm is decreased.

ARTHRITIS:

Neem has a long history of relieving inflamed joints. Neem helps in diminishing aggravation as well as smother the agony. It is likewise valuable in Rheumatism.

HEART DISEASE:

Significant reasons for a heart attack incorporate blood clumps, elevated cholesterol, arrhythmic heart activity and hypertension. Its leaf removes have diminished coagulating, brought down circulatory strain and awful cholesterol, impeded fast or strangely high heartbeat and repressed sporadic heart rhythms.

LUNGS:

neem underpins clear breathing and a sound respiratory framework**.**

SKIN MOISTURE AND SOFTNESS:

Neem's skin benefits work both inside and externally. As an outer application, Neem oil or cleanser mitigates and grease up the skin.

HAIR

For those with overabundance pitta and warmth caught in the scalp and hair follicles, neem is tremendous for cooling the scalp and supporting the development of shiny, smooth hair.

INSECT REPELLENT:

Early research demonstrates that applying concentrate of neem root or leaf to the skin repulses blak flies. Likewise, applying neem oil cream to the skin appears to secure against certain kinds of mosquitos.

MALARIA:

Jungle fever (Malaria)is very basic in India and all through the tropics. Neem leaf extricates forestalls typical advancement of the jungle fever (Malaria) infection. Despite the fact that Neem might be successful against skin inflammation and other relentless conditions. Psoriasis is effectively treated with Neem oil.

VIRAL DISEASES:

In India, Neem is likewise used to treat viral infections, for example, smallpox, chicken-pox. Neem has antibacterial qualities also.

AIDS:

The absolute best news is that Neem may help in the scan for anticipation or a remedy for AIDS. AIDS may perhaps be treated by ingesting Neem leaf separates or the entire leaf or by drinking a Neem tea.

NEEM IN AYURVEDA

Neem is very unpleasant in taste, which gives it a ground-breaking cooling vitality (virya). This cooling principle, joined with its ability to help healthy blood, balances pitta—especially when there is heat in rakta dhatu (the blood). Excess pitta can show in various ways; one unmistakable area is the skin. Neem glues and oils have customarily been connected to the skin as a methods for mitigating and greasing up it, quieting aggravated and warmed sensations, keeping up agreeable body temperature, and supporting healthy skin and nails. Neem's light and dry characteristics enable it to counter kapha also. Neem supports healthy assimilation and arouses meda dhatu agni (the metabolic/stomach related rule inside fat tissue), empowering appropriate digestion, and supporting glucose levels that are now in the typical range. Usually taken inside to encourage

a condition of parity in the liver, pancreas, and stomach related tract. Neem's bitterness likewise improves taste, which is at the foundation of sound digestion. Neem has a comparable adjusting impact on pitta and kapha in prana vaha srotas (the respiratory sections). On a more extensive scale, neem bolsters normal purifying of the directs in the body just as the revival of solid tissues. Because neem is vata irritating without anyone else, it is joined with different herbs relying upon the ideal impact.

CONCLUSION

Popularity of natural products or their derivatives role in diseases cure and prevention is increasing worldwide due to less side effect properties. Neem and its ingredients have therapeutics implication and have been traditionally used worldwide especially in Indian Subcontinent since ancient time. Clinical based studies confirmed that neem plays pivotal role in prevention of various diseases. The role of active ingredients as chemo preventive effect has been noticed in various tumour via modulation of numerous cell signalling pathways. The detailed study should be made based on animal to know the exact mechanism of action in the diseases management.

References

1) Landy N, Ghalamkari G, Toghiani M, Yazdi FF. Humoral immune responses of broiler chickens fed with antibiotic and neem fruit powder (Azadirachta indica) as feed additive supplemented diet. IPCBEE. 2011; 3:153- 155.
2) Nayaka HBS, Umakantha B, Ruban SW, Murthy HNN, Narayanaswamy HD. Performance and hematological parameters of broilers fed neem, turmeric, vitamin E and their combinations. Emir J Food Agric. 2013; 25:483- 488
3) Nayaka HBS, Umakantha B, Ruban SW, Murthy HNN, Narayanaswamy HD. Effect of neem, turmeric, vitamin E and their combinations on immune response in broilers. Global Vet. 2012; 9:486-489.
4) Jawad Z, Younus M, Rehman MU, Maqbool A, Munir R, Muhammad K et al. Effect of neem leaves (Azadirachta indica) on immunity of commercial broilers against new castle disease and infectious bursal disease. Afr. J of Agric. Res. 2013; 8:4596-4603.
5) Raheja S. Studies on the effect of neem (Azadirachta indica) leaf extract on the pathology of experimental fowl typhoid in broiler chickens. M.V.Sc Thesis, CCSHAU, Hisar, 2004.
6) Tipu MA, Pasha TN, Zulfaqar. Comparative effect of Salinomycine sodium and neem fruit (A. indica) as feed additive anticoccidials in broilers. Int. J Poult. Sci. 2002; 1(4):91-93.
7) Esonu BO, Opara MN, Okoli IC, Obikaonu HO, Udedibie C, Iheshiulor OOM. Physiological responses of laying birds to Neem (Azadirachta indica) leaf meal based diets, body weight, organ characteristics and hematology. Online J Health Allied Sci. 2006, 2(4). http//www.ojhas.org/issue 18/2006-2-4.htm 2006.
8) Biswas K, Chattopadhyay I, Banerjee RK, Bandyopadhyay U. Biological activities and medicinal properties of neem (Azadirachta indica). Curr. Sci. 2002; 82:1336-1345.
9) Junnarkar. Anthrax in Ayurveda. http:// www. healthepic.com / ayurveda/ article.htm, 2006.
10) .Kausik B, Ishita C, Ranajit KB, Uday B. Biological activities and medicinal properties of neem (Azadirachta indica). Curr. Sci. 2002; 82(11):1336-1345.
11) .Akpan MJ, Enyenihi GE, Obasi OL, Solomon IP, Udedibie ABI. Effects of dietary neem leaf extract on the performance of laying hens. Proceedings of 33rd Annual Conference Nigerian Society Animal Production. 2008, 396-398.
12) Udedibie ABI, Opara CC. Responses of growing broilers and laying hens to the dietary inclusion of leaf meal from alchorniacordifolia. Anim. Feed Sci. Techno. 1998; 71:157-164.
13) .Mitra R, Szezypel B, Perez A, Gonzale A, Estrada. Efficiency of neem oil (A. indica A. Juss) in hens naturally infested with ectoparasites. Revista Cubana de Ciencia Avicola. 2000;
14) 24(2):125-131.
15) Hossain MA, Shah MD, Sakari M. Gas chromatography– mass spectrometry analysis of various organic extracts of Merremia borneensis from Sabah. Asian Pacific Journal of Tropical Medicine. 2011; 4(8):637-641.
16) Kokate C, Purohit AP, Gokhale SB. Pharmacognosy. Maharashtra, India: Nirali Prakashan. 2010.
17) Govindachari TR, Suresh G, Gopalakrishnan G, Banumathy B, Masilamani S. Identification of antifungal compounds from the seed oil of Azadirachta indica. Phytoparasitica. 1998; 26(2):109-116.
18) Bhargava KP, Gupta MB, Gupta GP, Mitra CR. Anti-inflammatory activity of saponins and ot-her natural products. Indian J Med Res. 1970 Jun; 58(6):724–730.
19) Pillai, N. R. and Santhakumari, G., Anti-arthritic and anti-inflammatory actions of nimbi din, Planta Medica, 1981, 43, 59–63.
20) David, S. N., Mediscope, Anti-pyretic of Neem oil and its constituents, 1969, 12, 25–27.

21) Pillai, N. R. and Santhakumari, G., Hypoglycaemic activity of Melia azadirachta Linn (Neem), Indian Journal of Medical Research, 1981, 74, 931–933.
22) Pillai, N. R. and Santhakumari, G., Effects of nimbidin on acute and chronic gastro-duodenal ulcer models in experimental animals, Planta Medica, 1984, 50, 143– 146.
23) Pillai, N. R., Seshadri, D. S. and Santhakumari, G., Indian Journal of Medical Research, 1978, 68, 169–175.
24) Sharma VN, Saxena KP., Spermicidal action of Sodium Nimbinate, Indian Journal of Medical Research, 1959, 47, 322-324.
25) Murthy, S.P. and Sirsi, m. 1958. Pharmacological studies on Melia Azadirachta indica. Indian Journal of Physiology and Pharmacology 2, 387-396.
26) Bhide, N.K., Mehta, D.J. and Lewis, R.A. 1958. Diuretic action of sodium nimbidinate. Indian journal of Medical science 12,141-145
27) Jones, I., Ley, S. V., Denholm, A. A., Lovell, H., Wood, A. and Sinden, R. E., Sexual development of malaria parasites is inhibited in vitro by the neem extract azadirachtin and its semi-synthetic analogues, FEMS Microbiol. Lett. 15 July 1994, 120(3), 267–273.
28) Sharma, V. N. and Saksena, K. P., 'sodium nimbidinate-in vitro study of its spermicidal action, Indian Journal of Medical Rearch, 13 Dec 1959, 1038-1042
29) Rojanapo, W., Suwanno, S., Somaree, R., Glinsukon, T. and Thebtaranonth, Y., Screening of Antioxidants from some Thia vegetables and herbs, J. Sci. Thailand, 1985, 11, 177–188.
30) Rochanakij, S., Thebtaranonth, Y., Yenjal, C. H. and Yuthavong, Y., Nimbolide, a constitute of Azadirachta indica inhibits plasmodium falciparum in culture, Southeast Asian J. Trop. Med. Public Health, 1985, 16, 66–72.
31) Khalid, S. A., Duddeck, H. and Gonzalez-Sierra, M., Isolation and characterization of antimalarial agent of the neem tree, Azadirachta indica, Journal of Natural Product, 1989, 52, 922–927.
32) Rao, B. S., Nazma and Rao, M.J, Antifungal activity of gedunin, Curr. Sci., 1977, 46, 714–716.
33) Deva Kumar, C. and SukhDev, in Neem (Eds Randhawa and Parmar, B. S.), 1996, 2nd edn, pp. 77–110.
34) Van der Nat, J. M., Van der Sluis, W. G., 't Hart, L. A., Van Disk, H., de Silva, K. T. D. and Labadie, R. P., Planta Med., 1991, 57, 65–68.
35) Ara, I., Siddiqui, B. S., Faizi, S. and Siddiqui, S., Strucurally novel diterpenoid constituents from the stem bark of azadirachta indica (melieceae), J. Chem. Soc., Perkin Trans., 1989, 2, 343–345.
36) Pant, N., Garg, H. S., Madhusudan an, K. P. and Bhakuni, D. S., Fitoterapia, Sulphurous compounds from Azadirachta indica leaves, 1986, 57, 302–304.
37) Kakai T., Koho, J. P., Anti-inflammatory Polysaccharides from Melia azadirachta, Chem. Abstr., 1984, 100, 91350.
38) Fujiwara, T., Takeda, T., Ogihara, Y., Shimizu, M., Nomura, T. and Tomita, Y., Studies on the structure of polysaccharides from the bark of Melia azadirachta, Chem. Pharm. Bull., 1982, 30, 4025–4030.
39) Fujiwara, T., Sugishita, E., Takeda, T., Ogihara, Y., Shimizu, M., Nomura, T. and Tomita, Y.,) Further studies on the structure of polysaccharides from bark of Melia azadirachta. Chem. Pharm.Bull. ibid, 1984, 32, 1385 –1391.
40) Vander Nat, J. M., Kierx, J. P. A. M., Van Dijk, H., De Silva, K. T. D. and Labadie, R. P., J. Ethnopharmacol., 1987, 19, 125–131.
41) Vander Nat, J. M., Hart, L. A. T., Vander Sluis, W. G., Van Dijk, H., Vander Berg, A. J. J., De Silva, K. T. D. and Labadie, R. P., ibid, 1989, 27, 15–24nimbidinate. Indian Journal of Medical Sciences 12, 141-145.
42) P. X. Nunes, S. F. Silva, R. J. Guedes, and S. Almeida, "Biological oxidations and antioxidant activity of natural products," in Phytochemicals as Nutraceuticals—Global Approaches to Their Role in Nutrition and Health, InTech, 2012.
43) A. H. Rahmani and S. M. Aly, "Nigella sativa and its active constituents thymoquinone shows pivotal role in the diseases prevention and treatment," Asian Journal of Pharmaceutical and Clinical Research, vol. 8, no. 1, pp. 48–53, 2015.
44) A. K. Ghimeray, C. W. Jin, B. K. Ghimire, and D. H. Cho, "Antioxidant activity and quantitative estimation of azadirachtin and nimbin in Azadirachta indica A. Juss grown in foothills of Nepal," African Journal of Biotechnology, vol. 8, no. 13, pp. 3084–3091, 2009.
45) P. Sithisarn, R. Supabphol, and W. Gritsanapan, "Antioxidant activity of Siamese neem tree (VP 1209)," Journal of Ethno pharmacology, vol. 99, no. 1, pp. 109– 112, 2005.
46) A. H. Rahmani, M. A. Alzohairy, M. A. Khan, and S. M. Aly, "Therapeutic implications of black seed and its constituent thymoquinone in the prevention of cancer through inactivation and activation of

molecular pathways," Evidence-Based Complementary and Alternative Medicine, vol. 2014,Article ID 724658, 13 pages, 2014.
47) L. Le Marchand, "Cancer preventive effects of flavonoids—a review," Biomedicine and Pharmacotherapy, vol. 56, no. 6, pp. 296–301, 2002.
48) R. R. Chattopadhyay, "Possible biochemical mode of anti-inflammatory action of Azadirachta indica A. Juss. in rats," Indian Journal of Experimental Biology, vol. 36, no. 4, pp. 418– 420, 1998.
49) A. S. M. Mosaddek and M. M. U. Rashid, "A comparative study of the anti-inflammatory effect of aqueous extract of neem leaf and dexamethasone," Bangladesh Journal of Pharmacology, vol. 3, no. 1, pp. 44–47, 2008.
50) G. Kaur,M. Sarwar Alam, andM. Athar, "Nimbidin suppresses functions of macrophages and neutrophils: relevance to its anti-inflammatory mechanisms," Physiotherapy Research, vol. 18, no. 5, pp. 419–424, 2004.
51) N. Arora, A. Koul, and M. P. Bansal, "Chemo preventive activity of Azadirachta indica on two-stage skin carcinogenesis in murine model," Physiotherapy Research, vol. 25, no. 3, pp. 408– 416, 2011.
52) K. Biswas, I. Chattopadhyay, R. K. Banerjee, andU. Bandyopadhyay, "Biological activities and medicinal properties of Neem (Azadirachta indica)," Current Science, vol. 82, no. 11, pp. 1336– 1345, 2002.
53) S. Kumar, D. Agrawal, J. Patnaik, and S. Patnaik, "Analgesic effect of neem (Azadirachta indica) seed oil on albino rats," International Journal of Pharma and Bio Sciences, vol. 3, no. 2, pp. P222–P225, 2012.
54) M. R. Naik, A. Bhattacharya, R. Behera, D. Agrawal, S. Dehury, and S. Kumar, "Study of anti-inflammatory effect of neem seed oil (Azadirachta indica) on infected albino rats," Journal of Health Research and Reviews, vol. 1, no. 3, pp. 66–69, 2014.
55) N. S. Baligar, R. H. Aladakatti, M. Ahmed, and M. B. Hiremath, "Hepatoprotective activity of the neembased constituent azadirachtin-A in carbon tetrachloride intoxicated Wistar rats," Canadian Journal of Physiology and Pharmacology, vol. 92, no. 4, pp. 267– 277, 2014.
56) D. A. Of usori, B. A. Falana, A. E. Ofusori, T. A. Abayomi, S. A. Ajayi, andG. B. Ojo, "Gastro protective effect of aqueous extract of neem Azadirachta indica on induced gastric lesion in rats," International Journal of Biological and Medical Research, vol. 1, p. 219–222, 2010.
57) C. C. Barua, A. Talukdar, A. G. Barua, A. Chakraborty, R. K. Sarma, and R. S. Bora, "Evaluation of the wound healing activity of methanolic extract of Azadirachta Indica (Neem) and Tinospora cordifolia (Guduchi) in rats," Pharmacology online,vol. 1, pp. 70–77, 2010.
58) A. Osunwoke Emeka, J. Olotu Emamoke, A. Allison Theodore, and C. Onyekwere Julius, "The wound healing effects of aqueous leave extracts of azadirachta indica on wistar rats," Journal of Natural Science and Research, vol. 3, no. 6, 2013.
59) P. R. Patil, S. P. Patil, A. Mane, and S. Verma, "Antidiabetic activity of alcoholic extract of Neem (Azadirachta indica) root bark," National Journal of Physiology, Pharmacy and Pharmacology, vol. 3, no. 2, pp. 142–146, 2013.
60) S. K. Dholi, R. Raparla, S. K. Mankala, andK. Nagappan, "Invivo antidiabetic evaluation of Neem leaf extract in alloxan induced rats," Journal of Applied Pharmaceutical Science, vol. 1, no. 4, pp. 100–105, 2011.
61) W. N. Ghonmode, O. D. Balsaraf, V. H. Tambe, K. P. Saujanya, A. K. Patil, and D. D. Kakde, "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, vol. 5, no.6,pp. 61–66, 2013.
62) M. D. Mahfuzul Hoque, M. L. Bari, Y. Inatsu, V. K. Juneja, and S. Kawamoto, "Antibacterial activity of guava (Psidium guajava L.) and neem (Azadirachta indica A. Juss.) extracts against food borne pathogens and spoilage bacteria," Food borne Pathogens and Disease, vol. 4, no. 4, pp. 481–488, 2007.
63) M. B. Yerima, S. M. Jodi, K. Oyinbo, H. M. Maishanu, A. A. Farouq, and A. U. Junaidu, "Effect of neem extracts (Azadirachta indica) on bacteria isolated from adult mouth," Journal of Basic and Applied Sciences, vol. 20, pp. 64–67, 2012.
64) V. Tiwari, N. A. Darmani, B. Y. J. T. Yue, andD. Shukla, "In vitro antiviral activity of neem (Azardirachta indica L.) bark extract against herpes simplex virus type-1 infection," Physiotherapy Research, vol. 24, no. 8, pp. 1132–1140, 2010.