A REVIEW ARTICLE ON: NEEM (AZADIRACHTA INDICA)

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ABSTRACT-

Azadirachta indica, commonly known as neem, has attracted worldwide prominence in recent years, owing to its wide range of medicinal properties. Neem has been extensively used in Ayurveda, Unani and Homoeopathic medicine and has become a cynosure of modern medicine.Neem is an attractive broad-leaved, evergreen tree that can grow up to 30m tall and 2.5m in girth. Its trunk usually straight is 30-80 cm in diameter. Its spreading branches form a rounded crown of deep-green leaves and honey-scented flowers as much as 20m across. Azadirachtin is widely used as a basis for production of biopesticides; nevertheless, other properties have been recognized for this substance, among which the anticancer and antimalarial activity stand out. The methods available for azadirachtin extraction are diverse, including solid-liquid extraction and extraction with solvents at high or low temperatures. Alcohol based solvents are associated with higher extraction yields and are therefore preferred for the isolation of azadirachtin from plant parts. Clean-up of the extracts is generally required for further purification. The highest azadirachtin levels have been obtained from Neem seeds but concentration values present a large variation between batches. Therefore, in addition to extraction procedures, it is essential to establish routine methods for azadirachtin identification and quantification. Chromatography-based techniques are preferably selected for detection and quantification of azadirachtin in plant matrices. Overall, this process will guarantee a future

reproducible, safe and effective use of the extracts in formulations for commercial applications.

KEYWORDS- Introduction, Taxonomical classification, Morphology, Sources, Macroscopical character, chemical constituents, MOA , Pharmacological implementation.

INTRODUCTION-

The neem tree Azadirachta indica A. belongs to family Meliaceae, is a tropical evergreen related to mahogany. Native to east India and Burma, it grows in much of Southeast Asia and West Africa; a few trees have recently been planted in the Caribbean and several Central American countries, including México. The people of India have long revered the neem tree; for centuries, millions have cleaned their teeth with neem twigs, smeared skin disorders with neem-leaf juice, taken neem tea as a tonic, and placed neem leaves in their beds, books, grain bins, cupboards, and closets to keep away troublesome bugs. Trees will reach up to 30 m tall with limbs reaching half as wide. The shiny dark green pinnately compound leaves are up to 30 cm long. Each leaf has 10–12 serrated leaflets that are 7 cm long by 2.5 cm wide. It will grow where rainfall is as little, and thrives in areas that experience extreme heat of up to 48°C. Even some of the most cautious researchers are saying that neem deserves to be called a “wonder plant.” The neem tree, was introduced to Baja California Sur, México, in 1989 by a group of private producers dedicated to organic horticulture in San José del Cabo. The first trees were brought from the Philippines [1,2], and in 1992, this species was introduced to Yaqui Valley, Sonora, México [3]. Since 1994, trees have been planted in small areas along roadsides, as a windbreak. Neem populations planted in Southern, Sonora, México, have phenotypic and quality differences, fruits are heterogeneous in size and form, and oil content and quality is variable. The objective of this study was to characterize 216 trees in a collection at the Instituto Tecnológico Agropecuario, in Southern Sonora Mexico.

TAXONOMICAL CLASSIFICATION

Kingdome:-Plantae,

Order:-Rutales,
Suborder:-Rutinae,

Family:-Meliaceae.
Genus :-Azadirachta,

Species:-Indica [3]

Figure- Neem leaves

MORPHOLOGY-

Neem is a medium-sized tree, reaching 15 to 30 m in height, with a large rounded crown up to 10-20 m in diameter. It is mainly evergreen but sometimes shed its leaves during the dry season. Neem has a deep taproot and is a mycorrhizal-dependent species. The bark is grey, becomes fissured and flakes in old trees. A sticky foetid sap exudates from old trees in humid climates. The branches are numerous and spreading. The leaves are alternate, petiolated, clustered at the end of the branches, unequally pinnate, glabrous and dark glossy green at

maturity, 20-40 cm in length and bearing 10-20 leaflets. The leaflets are 5-10 cm long x 1.2-4 cm broad, sickle-shaped and slightly denticulate. The flowers are numerous, fragrant, white and borne in large clusters (up to 30 cm long). Neem fruits are 1-2 cm long drupes, smooth and green with white milky juice when unripe, turning to yellow to brown when mature. They have a thin epicarp, a mucilagenous fleshy mesocarp and a hard endocarp. They contain a variable number of ovoid (1-2 cm) oil seeds. [5, 6]

SOURCES-

Biological Source:

Neem consists of the fresh or dried leaves and seed oil of Azadirachta indica J. Juss (Melia Indica or M. azadirachta Linn.).

Geographical source-

It is found in India, Pakistan, Sri Lanka, Malaya, Indonesia, Japan, Tropical region of Australia and Africa. In India, it is found in Uttar Pradesh, Maharashtra, Tamil Nadu, Rajasthan, and M.P.

MACROSCOPICAL CHARACTERISTICS-

1. Leaves:

i. They are imparipinnate, alternate, exstipulate, 3-6 cm long on long slender petioles; leaflets 7-17; alternate or opposite, very shortly stalked, 1-1.5 cm long.

ii. Apex: ovate-lanceolate, attenuate

iii. Base: Unequal

iv. Colour: Smooth and dark green.

v. Odour: typical.

vi. Taste: Bitter.

2. Fruits:

i. Shape: Ovoid, bluntly pointed, smooth drupe.

ii. Colour: Green (Young and unripe); Yellow to brown (Mature and ripe).

iii. Very scanty pulp and hard bony endocarp.
iv. Solitary with a thick Testa and embryo with foliaceous cotyledons in the axis of scanty endocarp.

3. Seed Oil:

i. Colour: Yellow to brown.

ii. Taste: Bitter.

iii. Odour: Garlic.

CHEMICAL CONSTITUENTS-

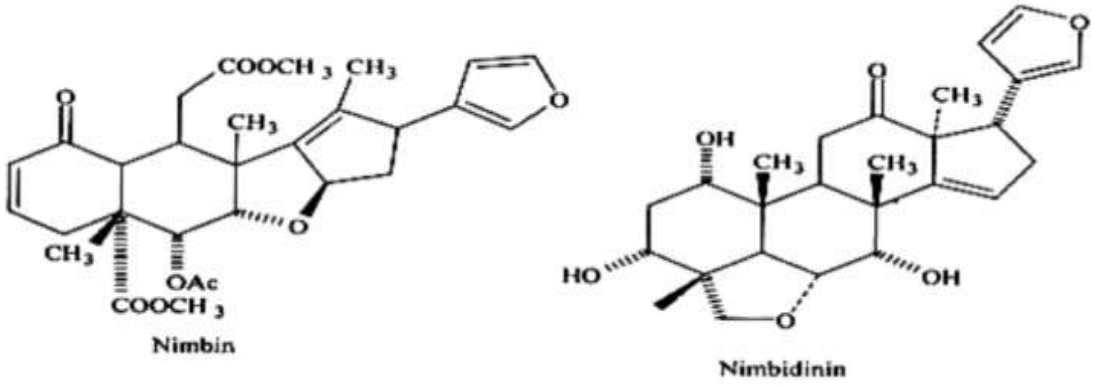
1. Leaves:

i. Nimbin, 6- desacetylnimbinene.

ii. Nimbinene, Nimbandiol, nimbolide.

iii. Quercetin, β-sitosterol.

iv. Ascorbic acid, n-hexacosanol, nonacosane and amino acid.



Nimbin & Nimbidinin

2. Fruits:

i. Gedunin.

ii. 7-deacetoxy-7α- hydroxygedunin.

iii. Azadiredione, azadirone, nimbiol.

iv. 17-epiazadiradione.

3. Seeds:

i. Tetranortriterpenoids; 1, 2-diepoxyazadiradiradione.

ii. 7-acetylneotrichilenone, 7-desacetyl-7-benzoylgedunin

iii. Azadirachtin.

4. Oils:

i. Fatty acid:- Myristic acid, palmitic acid, stearic acid, oleic acid and linoleic acid.

ii. Glycerides:- Oleopalmitostearin, oleodistearin, odiolein and linoleodiolein.

iii. Bitter principle:- Nimbidin, nimbidinin, Nimbin, nimbinin and nimbidol.[7]

MECHANISM OF ACTION OF ACTIVE COMPOUNDS:-

Azadirachta indica has therapeutic implication in the desease prevention and treatment .but exact molecular mechanism in the prevention of pathogenesis is not understood entirely. It is considered that azadirachta indica shows therapeutic activity due ro rich source of antioxidant and other valueable compohnd such as azadirachtin ,salanin and quercetin, possible mechanism of action of azadirachta indica is presented as

follows:-

★ Azadirachta indica (Neem) plant parts shows anti-microbial role through inhibitory effect on microbial growth/potentiality of cell wall break down.Azadirachtin acomllex tetranortriterpenoid limonois present in seed is the key constituents responsible for the both antifeedant and toxic effect in insect.[6] Result suggest that the ethanol extract of neem leaves showed in vitro anti-bacterial activity against both staphylococcus aureus and MRSA with greatest uzones of inhibition noted at 100% concentration.[8]

★ Neem plays role as free radical scavenging properties due to rich source of antioxidant. Free radical scavenging activity and reductive potential in the following order:-

{ Nimbolide>Azadirachtin>Ascorbic acid}

★Neem also plays role as anti inflammatory via regulation of pro inflammatory enzyme activitiese inclueding & cycloxigenase(COX) Lipooxygenase(LOX) enzyme[9]

PHARMACOLOGICAL IMPLIMENTATION OF AZADIRACHTA INDICA:-

• **ANTI-OXIDENT ACTIVITY:-**Free radical or reactive oxygen speciese are one of the fundamental offenders in ghe genesis of different illness. Notwith standing, neutralization of free radical activity is one of the imperative strides in the maladies counteractive action.

Antioxidants stabilize/deactivate free radicals, regularly begore they assault focuses in biolohical cells.[9] Furthuremore assume job in the control of harm brought about free radicals by activating the anti-oxidative protein.[10] Plant product such as seed, oil, root, bark, leaves, demostrate an essential job in illness aver sion because of the rich source of anti-oxidant[11]

• **ANTI-INFLAMMATORY ACTIVITY:-**Plants and their isolated derivatives are in the practice to treat /act as Anti - inflammatory agent. A study result has confirmed that extract of Azadirachta indica leaves at a dose of 200mg/kg P.P.O., showed significant anti-inflammatory effect in ctton pellet granuloma assay in rodent.[12] An examination result praposed that the nimbidin stifles the element of macro-phages and neutrophils pertinent to inflammation[13]. It is also found that immunemodulator and

anti-inflammatory impact of bark and leaves concentra-tes and anti-pyretic and anti-inflammatory exercise of oil and seeds[14]

- **ANTI-BACTERIAL ACTIVITY:-**Acetone extract of Azadirachta indica exhibit stronger inhibition against gm(+ve)bacteria (E.choli,and p.auruginosa) with MIC values of 10mg/mland 25 mg/ml respectively. In contrast chloroform extract exhibit stronger inhibiyion against gm(-ve)bacteria (B.subyilis, B.cereus, S.pneumonae and S.aureus) with MIC value of 10mg/ml for all bacteria.The cytotoxicity was evaluated based on the LC50 values of the extract [15]

- **ANTI-DIABETIC ACTIVITY:-** The hypoglycemic activity of azadirachta indica has examined on a diabetic rates. After 24 hours of treatment Azadirachta indica 250mg/kg (single dose study)
reducedGlucose(18%),Cholestrol(15%),Triglycerides(32%), Urea(13%), Creat-inine(23%) and Lipid(15%). In a glucise tolerancetest in diabetic rats with neem extract 250 mg /kg demostrate glucose levels were significantly less compared to the controll-ed group. Azadirachta indica significantly reduce glucose level at 15th day in diabetic rat [16]

• **ANTI-DENTAL CARIES:-**A Neem extract dental gel significantly reduce plaque and bacteria (streptococus mutants) and Lactobacilli species were tested) over the control group that used commercially available mouthwash containing the germicidal Chlorhex-idin gluconate(0.2%w/v)[17]

• **ANTI-ULCER ACTIVITY:-**It is reported that the gastro-protective property of dried bark rxtract of azadirachta indica in the merceptomethylimidazole ,indomethacine, LU, HST induce ulcer .It act mainly by inhibiting acid secretion and blocking the oxidative damage of gastric mucousa.Inhibition of acid secretion is done by inhibiting the activity of proton pump and inhibition of oxidative damage of mucousa are done by blocking of lipid peroxidase and scavenging of endogenous. Hydroxyl radical(OH)[18]

• **ANTI-TUMOUR AND ANTI-VIRAL ACTIVITIES:-**Researchers in India,Europe and Japan found that polysachharides and limonoids found in neem bark, leaves ,seed and oil reduced the tumour and cancers showed effectiveness against lymphocytic lukemia.mitotic inhibition activity by Neem leaf extract was observed .several reports have also highlighted the pronounced anti viral efficacy of aq.extract of neem oil[NIM-76]have also been report to supress HIVand Polio viruses.[19]

• **HEPATO PROTECTIVE ACTIVITY:-**Extract of neem leaf helps to protect fhe liver from damage which in turn helps to cleanse the blood ,Neem leaf minimise the factor thatinduce chemically damage of hepatic cell by stabilizing serum marker enzyme and boosting levels of anti oxidant ,like those found in vitamin C and E and carotenoid ,which neutralize the free radical and protect from damage.

• **ANTI -STRESS :-** Low doses of Neem leaf extract produced sedative effect .the effecf disappear at higher doses aprox 400or 800mg/kg of body weight. It also reduced the anxiety and stress.

• **ANTI -VITILIGO:-** Vitiligo is belived to be an auto immune disorder thar cause patches of skin yo loss its colour .the doses of four grams of neem leaves three times a day ,ideally taken before each meal.Neem oil is applied on over the affected areas aid in thereversal of discolouration.[20]

• **SKIN DISORDER:-** Neem are used in to treat the many skin disorder, inclueding Scabies and lice in a paste cimbination with curcuma longa (Turmeric), Neem (A.indica) was used to treat scabies in 814 people 97% of them cured within 3-15 days of application.[21]

CONCLUSION-

Neem (Azadirachta indica) has much importance. Usefulness of neem has already mentioned in several literature. Ayurveda has mentioned its use in many disease conditions. Now public awareness for herbal products are increasing highly so it has been found demand of neem products are increasing day by day. Neem is a plant who's every parts holds multiple usage. Researcher has reported many medicinal benefits of neem. Neem is known for its anti diabetic, anti-inflammatory, anti cancer effect. Neem is used in many hindu rituals. This review work represents several usage of neem which will provide a great knowledge to people and let them know about the wonder of neem.

5. REFERENCES-

1. Leos, M.J. and R.P. Salazar S. 2002. The insecticide neem tree Azadirachta indica A. Juss in México. Universidad Autonóma de Nuevo León. Agronomy Faculty. Tech. Brochure 3. Marín, N.L. México.

2. Osuna, L.E. 2000. Plant production and plantation establishment of

neem tree Azadirachta indica A. Juss. INIFAP-CIRNO-CETS. Technical Brochure 5. Todos Santos Experimental Field. La Paz, B.C.S. México.

3. Moreno, M.I. 1996. The neem tree Azadirachta indica A. Juss in the Southern Sonora, México. Tech. Rpt. Yaqui Valley Experimental Field-INIFAP. Ciudad Obregón, Sonora, México.

4. Ogbuewu IP,Odoemenam VU,Obikaonu HO,Opara MN,Emenalom OO,UchegbuMC,MC,et al .the growing importance of neem (Azadirachta indicaA.juss.)in agriculture,Industry,medicine and environment:a review.Res.J Med plants,vol.5 ,pp 230-45(2011).

5. Orwa, C.; Mutua, A.; Kindt, R.; Jamnadass, R.; Anthony, S., 2009. Agroforestree Database: a tree reference and selection guide version 4.0. World Agroforestry Centre, Kenya

6. FAO, 2015. Grassland Index. A searchable catalogue of grass and forage legumes. FAO, Rome, Italy.

7. C.Kokate, A.P.Purohit and S..B.Gokhàte "A book of Pharmacognosy", Nirali prakashan ,Maharashtra,India 2010.

8. W.C.Sarmiento,C.C.Maramba,M.L.M.Gonzales,"An in vitro study on the antibacterial effect of neem (Azadirachta indica) leaf extract on nethicillin-sensitive and methicillin resistance staphylococcus aureus ,"PIDSPjournal;vol12 ,no.1 ,pp.40-45.(2011)

9. M.A.Hossain, W.A.S.Al-toubi, A.M.weli, Q.A.Al-Riyami, J.N.Al-sahabi, "Identification and Charecterization of chemical compound in diffrent crued extracts from keaves of omani neem, journal of Taibah university for science, Vol.7,No.4,pp.181-188,(2013)

10. P.X. Nunes, S.F. Siliva, R.J. Guedesand S.Almeida, "Biological oxidation and anti-oxidant activity of natural products, "in

phytochemical as Nutraceuticals -Global Approach to their role in Nutrition and health, In tech, 2012

11 A.H. Rahmani and S.M. Aly, "Nigella sativa and its active constituents thymoquino-ne shows pivotal role in desease prevention and treatment, "Asian journal of Pha-rmaceuticals and clinical research, vol.8, no.1, pp.48-53, 2015.

12. A.K. Ghimeray, C.W. Jin B.K., Ghimire and D.H.Cho., "Antioxidant activity and quantitative estimation of azadirachta indicaA.juss grown in foothills of Nepal ,"African journal of Biotechnology, vol.8, no.13, pp.3084-3091 (2009).

13. R.R.Chattopadhyay,"possible biochemical mode of Anti-inflammatory action of Azadirachta indica A.juss.in rat ,"Ifian journal of experimental Biology,vol36.no.4 pp.418-420.(2008).

14. G. Kaur, M. Sarawar Alam and M. Athar, "Nimbidin supresses function of macroph-ges and neutrophils relevence to its Anti-inflammatory mechanism, "Physiotherapy Research ,vol.8 ,no.5, pp.419-424 (2004)

15. N.Arora, A.kaul and M.P.Bansal, "Chemo preventive action of Azadirachta indica o two stage skin carcinogenesis in murin model, " physioyherapy Research vol.25, no.3, pp.408-416 (2011)

16. Vinoth B, A.kaul and M.P.Bansal, "Chemopreventive activity of azadirachta indica on two stage skin carcinogenesis in murin model, "physiotherapy Research vol.18, no.5pp. 419-424 (2004).

17. Shravan K.D., Ramakrishna R., Santosh K.M., Kannapan N., In vivo anti-diabetic evaluation of neem leaf extract in alloxan induce rat's, journal of applued pharma-ceutical science, vol.1, no.4, pp.100-105 (2011).

18. Vanka A. Tandon S., Rao S.R.,Udupa N., Ramkumar, the effect of indegenous neem (Azadirachta indica)mouth wash on streptococcus mutants and lacyobacilli growth ,indian journal. dental research, vol.12, no.3, pp.133-144 (2001).

19. P.Dharmani, G Palit, Exploring Indian medicinal plants for antiulcer activity, Indian journal Pharmacology, vol38, issue.2, pp.95-99, April 2006.

20. Hassan Amer, Wafaa A.Helmy, Hanan A.A.Taie, InVitro anti ulcer and anti viral activities of seeds and leaves from neem (A.Indica)extract .international journal of academic research, vol.2, no.2, march 2010.

21. Debjit Bhowmik, Chiranjib, jitender yadav ,K.K.Tripathi, K.P.sampath kumar, Herbal remedies of Azadirachta indica and its medicinal application journal of chem.pharm.Res., Vol.2, no. 1, pp.62-72. (2010).