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REVIEW ARTICLE

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***Azadirachta indica* (Neem) Oil: Multi-Target Applications in Mosquito Repellency, Agricultural Pest Management, and Public Health**

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ABSTRACT

Neem (Azadirachta indica) is native to the Indian subcontinent, including Pakistan, Bangladesh, Sri Lanka, and Myanmar. In Sanskrit, 'Neemba' has been used in Ayurvedic medicine and is traditionally used since 5000 years. The neem tree in Bangladesh and in Indian family's a common compound in a residential building. Most Asian sub-continent countries have been using the powerful herb in lotions, medicines, insecticides, hair care products, pest control, to treat dry skin and wrinkles, stimulate collagen production, reduce scars, heal wounds, treat acne, minimize warts and moles, and in religious ceremonies. The neem tree has 100+ biologically active compounds and the ability to treat a whole range of health issues. Turned out from the seeds of the neem tree, neem oil is nature's gift to mortality. Neem oil is hot to a tremendous number of active ingredients, which offer powerful healing properties for many medical malady, unbelievably bitter in taste, with a pungent, garlicky, sulfur-like smell, and varies in color from greenish brown to yellowish brown to shades of red. Neem oil contains some of the top ingredients, including vitamin E, nimbidin & nimbin compounds, linoleic acid, carotenoids, oleic acid, vitamin C, calcium triglycerides, fatty acids, quercetin, and the main compound azadirachtin, which is one of nature's most powerful insect repellents. Neem oil has potent antipyretic, antifungal, antibacterial, antioxidant and anti-inflammatory activity.

Key words: *Neem oil, Azadirachtin, Mosquito repellent, Biopesticides.*

INTRODUCTION

A. indica is mostly represented by trees and shrubs; the family consists of 51 genera and 550 species, many of prized for their wood, edible fruits, and ornamental qualities (Wiert, 2006). *A.*

indica is a medium-sized evergreen tree with a 30m maximum height, the bark is thick, dark gray to red in color, and a gummy colorless sap, the leaves are around 20-40 cm long, pinnate, alternate, and glabrous blond green hue. 1 cm in diameter flowers of the tree, pale yellow, white, and sweet-smelling, they are pentamerous, unisexual or bisexual on the same plant, ovate, imbricate, thin, and puberulous from inside of calyx of the flowers, spreading, imbricate, spatulate and ciliate from inside (Chatterjee et al., 2023). Fruits are small around 1-2 cm, greenish to yellow in color and an ellipsoidal seeded drupe; the tree has a thin exocarp, pulpy mesocarp, and cartilaginous endocarp. Oval, spherical, unwinged structure with thin testa of seeds, the tree has a got taproot system with widespread lateral roots; it may form suckers if roots encounter some damage (Hearne 1975; Csurhes, 2008; Hashmat et al., 2012).

Taxonomical Classification

The neem plant is taxonomically classified as (Girish and Shankara, 2008; Anon, 2011).

Kingdom: Plantae

Division: Tracheophyta

Class: Magnoliopsida

Order: Sapindles

Family: Meliaceae

Subfamily: Melioideae

Tribe: Melieae

Genus: *Azadirachta*

Species: *india*

Azadirachta indica is synonymous with *Melia azadirachta* L. and *Antelaea azadirachta* (L.) Adelb (Anon, 2011).

Regional names

A. indica has many local names, depending on the languages used in a country. The sobriquets given in the language of Bangladesh and other countries are shown in Table 1.1.

Methods of extraction of oil

Neem essential oil is collected from the seed, it has known for its high insecticidal and medicinal standard (Lokanadhan et al., 2012), the leaves, fruit, flowers are accessory sources of neem essential oil (Narsing Rao et al., 2014). Around 20% of seeds are being harvested due to scattered neem trees according to the survey. Roughly 8300 tonnes of neem oil annually produces by India, in general, neem oil produced recorded from seeds varies from 25% to 45% (Anyia et al., 2012; Ismadji et al., 2012). More recently, mechanical processing, solvent extraction, supercritical fluid extractions are among the many methods to extract neem seed oil (Liau et al., 2008). Cold crushing can be employed to procure oil from the neem seed kernel via physical crushing and in mechanical technique. Nearly 82% of neem oil can be covered by the instrumental extraction method, although mechanical crushing is a regularly used method. Besides, oil produced by instrumental crushing is mix up, containing a considerable amount of

water and metal content, therefore it has least agora charge (Adeeko and Ajibola, 1990; Lalea and Abdulrahman, 1999).

Table 1.1: Regional Names of *A. indica*. (Parotta, J. A. (2001).

Country	Regional language
Bangladesh	Nim, nimgachh.
India	Danujhada, limbado, limbra, limdo, Balnimb, neem, nim, nimb, nind, vempu, veppam, Bemu, bevinamara, bivu, kaybevu.
Myanmar	Bowtamaka, thinboro, tamarkha, tamar, tamaka, tamabin.
Nepal	Neem.
Thailand	Sadao, kadao, sadao India, khwinin, saliam, cha-tang.
Malaysia	Sadu, baypay, mambu, veppam
Saudi Arabia	Nim, neem
Vietnam	Saafudaau, sàu-dàu.
Indonesia	Mind, intaran, membha, imba, mempheuh, mimba.
England, Canada, America	Persian lilac, neem tree, bastard tree, Indian lilac, bead tree, margosa tree, cornucopia, Indian cedar.
France	Margousier, margosier, neem, nim, azadirac de l'Inde.

As per to an instruction conveyed by Nitiéma-Yefanova et al. (2012), the oil outturn by cold crushing has a sure effect on provoked kernel compression, abate particle size, and abatement cage loading. Finally, that the oil generation ((40.3% $\pm$ 0.0) from ground kernels can be gained by cold crushing at 25°C, 33.7 MPa $\pm$ 2.9 pressure. Whatever, cold crushing method is easier and least expensive to acquire high-quality oil for commercial scale production (Ismadji et al., 2012). The solvent extraction process is usually choice for gaining neem oil and it embellish anexalted output and obvious oil contrasted with mechanical extraction method. Neem oil percentage corresponded to 92.3%-99.1%, in the Soxhlet extraction method, with the azadirachtin content (4658.4 $\pm$ 92.5 ppm) tripled more than that obtained from the cold-pressed extraction procedure. Besides, the conventional solvent extraction method has a relatively low operational cost and is economical compared with the other modern methods of extraction, such as supercritical fluid extraction (Liau et al., 2008; Adewoye and Ogunleye, 2012; Ismadji et al., 2012). Hexane is generally used solvent in the extraction of seed oil, adding neem seeds, due to its compatible functional properties, nonpolar nature, that simplify the high solubility of hydrocarbons, glycerides, and lipids at mild temperature, moreover, hexane is inexpensive and nonreactive oil (Ayoola et al., 2014). The n-hexane and ethanol solvents as a medium of neem oil extraction according to Liauw et al. (2008) compared. At a low extraction temperature (50°C), neem oil produced were 41.11% and 44.29% with ethanol and n-hexane.

Petroleum ether (42.60%) exhibited higher efficiency than ethanol (39.17%) for neem oil extraction, at the same temperature (Satyanandam et al., 2011). It was expected which ethanol is a good choice for hexane, as there is a probability to enhance oil extractability using ethanol at high temperatures (Liauw et al., 2008; Ayoola et al., 2014).

Later, it was anticipated that ethanol may be a good substitute for hexane, as there is a possibility to enhance oil extractability using ethanol at high temperatures (Liauw et al., 2008; Ayoola et al., 2014). Ethanol-hexane mixtures utilized for oil extraction by the Soxhlet extraction method in ratios of 60/40, 50/50 and 40/60 (v/v) furnished oil yields of 44%, 43%, and 41.2%, respectively. At 55°C for 6 hours, the ethanol-hexane mixtures given a better output than 100% hexane (40.25%) (Ayoola et al., 2014). Extracted neem oil output a least of 17.60% using only n-hexane through the Soxhlet extraction method according to Edres (2014).

Methods of Analysis of Oil

Essential oils are widely used for medicinal, perfumery, cosmetic, and agricultural products, this essential oils of secondary metabolites, their chemical composition is fundamental for industrial and economic purposes, where organic chemistry plays a vital role (Ntabakirabose et al., 2024). The chromatographic methods have made important progress in the estimation of the chemical invention of essential oils such as high-performance liquid chromatography, gas chromatography, gas chromatography-mass spectrometry, and capillary electrophoresis (Forim et al., 2010; Djenontin et al., 2012). Gas chromatography is important methods for analyzing oils, for both quantitative and qualitative determination. Gas chromatography exploration needs 30–60 m columns and 30–60 min to furnish a chromatogram. The criteria for authentication usually add, accuracy, precision, recovery, linearity, specificity, limits of quantification and detection, and repeatability in HPLC methods (Forim et al., 2012). Neem oil is an essential oil, it is potently aromatic and viscus, and predominately constitutes fatty acids with hydrocarbons (Djenontin et al., 2012). Fatty acid profile of neem oil derivatives was injected into a GC equipped with a flame ionization detector with a glycol succinate column (Hossain, 2005). Both internal and external standards were used, ascertainment of single fatty acids. The neem oil profile by GC-FID involving both determination and quantification of its components. It was observed the fatty acids, oleic acid (43.5%), linoleic (18.7%), palmitic (17.8%), and stearic (17.4%) acids (Oyege et al., 2025). HP-INNO wax capillary column and helium as the carrier gas were used during analysis. Neem oil was query by both chromatographic and spectral methods, like quantitative thin-layer chromatography (TLC), GC, GC-MS, and ¹³C nuclear magnetic resonance (NMR). The fatty acids of neem oil were also investigated by highspeed countercurrent chromatography (HSCCC) (Gossé et al., 2005). Via the HSCCC mehdods resolved different fatty acids and organic compounds. Azadirachtin is a good-quality control biomarker compound in neem essential oil, possibly simplifies the demands of various equipment, time, and the cost required for extensive analyses, to check the purity of the oil and its industrial formulations. The quantity of azadirachtin is usually found out in various neem oil products by a simple, sensitive, and selective method (Ambrosino et al., 1999; Sidhu et al., 2003). Forim et al. (2010) developed a method for simultaneous quantification of two important limonoids of NSO, that is, azadirachtin and 3-tigloylazadirachtol, by using HPLC

equipped with an ultraviolet (UV)–visible detector. The chromatographic analyses were performed isocratically with a ratio of 35:65 (v/v) of acetonitrile and water as the mobile phase, and the UV wavelength was selected at 217 nm (maximum) to measure low-concentration marker compounds. In study, analysis was performed by a reverse phase Spherisorb C-18 ODS 5 µm column with an acetonitrile–water gradient system to determine the azadirachtin content in neem formulations and oil (Sundaram and Curry, 1993).

Composition of Oil

The essential chemical constituents reported from neem essential oil can be separated into individual classes, as described in the Table 1.2.

Table 1.2. Essential chemical constituents of neem oil.

Hydrocarbons	El-Hawary et al. 2013.
Fatty acids	Mongkholkhajornsilp et al., 2005; Ismadji et al., 2012; Narsing Rao et al., 2014; Momchilova et al. 2007.
Limonoids	Hallur et al., 2002; Ismadji et al., 2012; Sidhu et al., 2003; Siddiqui, S. 1942.
Azadirachtins	Ambrosino et al., 1999; Morgan, 2009; Rembold et al., 1984, 1987; Sinha et al., 1999; Sundaram and Curry, 1993; Sidhu et al., 2003; Ismadji et al., 2012
Sterols	Momchilova et al., 2007; Djenontin et al., 2012

Physical and Chemical Properties of neem oil

The results of some recent research on the physical and chemical properties of neem oil are presented in Table 1.3.

Table 1.3: Standard physicochemical properties of neem seed oil.

Properties	Value
Odor	Garlic
Specific gravity at 30°C	0.908–0.934
Viscosity at 37.8°C (mm ² /s)	49.79
Refractive index at 30°C	1.4615–1.4705
pH	5.7–6.5
Iodine value	65–80 g/g
Acid value	40 mg of KOH/g
Saponification value	175–205 mg of KOH/g

Sources: Mongkholkhajornsilp et al., 2005; Usman et al., 2013; Edres, 2014; Okonkwo et al., 2013; Djibril et al., 2015; Satyanandam et al., 2011; Liauw et al., 2008; Satyanandam et al., 2011; Khraisha, 2000; Choe and Min, 2006; Erakhrumen 2011; Adeeko and Ajibola, 1990.

Table 1.4. Properties of neem seed oil obtained by various methods are presented.

Extraction Method	AV (mg/g)	SV (mg of KOH/g)	IV (g/100 g)	PV (mg/g)	References
Cold pressing	18.24	172.88	93.11	1.42	Erakhrumen, 2011
Solvent (hexane–ethanol, 60:40)	12.90	199.99			Ayoola et al., 2014
Solvent (Soxhlet extractor, cyclohexane)	10.2	200	72.82		Djibril et al., 2015
Solvent (Soxhlet extractor, hexane)	17.40	186.4	58.20	78.40 mEq/g	Zaku et al., 2012
Solvent (hexane)	1.411 g/g	176.64 mg/g	89.35 g/g		Sodeinde and Samuel, 2014

General uses of oil

Medicine

Indians 4000 years ago, the application of neem had been identified, since the Vedic period. Neem tree is recognized in Sanskrit “Arishtha,” meaning “reliever of sickness.”Neem tree has been used in various against human malady (Aidoo et al., 2021). It has been used for control of leprosy, syphilis, eczema, chronic ulcer, and intestinal helminthiasis (Hashmat et al., 2012). Neem oil has multiple pharmacological activities that include anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, diuretic, spermicidal, antifungal, antibacterial, antigastric ulcer, antiviral, and antipsoriasis activities (Brahmachari, 2004).

Public Health

Neem oil is used for public health like as an antilouse and antimalarial agent (Al-Quraishy et al., 2015), neem oil mixed with coconut oil acts as effective mosquito repellent (Brahmachari, 2004).

Agriculture

Neem oil is widely used as a naturally occurring pesticide and insecticidal (Ahmad et al., 2015; Jhalegar et al., 2015; Rodrigues et al., 2015; Sridharan et al., 2015), neem-based agrochemical applied as a nitrification inhibiting agent.

Personal Care Products

NSO and its components are utilized in toiletries and cosmetics such as skin care (soap, eczema cream, antiseptic cream, nail care, and balm), hair care (shampoo and hair oils), oral hygiene (toothpaste), and other household products (insect repellent spray and lotion, candles, wax, and lubricants) (Hashmat et al., 2012; Shetty et al., 2016). Purified NSO is also exploited in nail polish and another cosmetics preparation (Shetty et al., 2016).

Table 1.5. Recent Research on neem essential oil for agricultural and public health pest control.

Effected Organism	Pathogen/Disease	Treatment	Effects	Reference
<i>Mangifera indica</i> L. (Taimour mango)	Powdery mildew and deformity	Neem oil (1%)	Powdery mildew disease severity index (DSI) was 18.17%, more efficient against mango malformation	Ismail, 2016
Cowpea (Brazil)	<i>Spodoptera eridania</i> (southern armyworm)	Neem oil (0.35% and 0.7%)	Reduced leaf consumption	Rodrigues et al., 2015
Humans	<i>Aedes aegypti</i> (dengue mosquito)	<i>Metarhiziumanisopliae</i> (entomopathogenic fungi) + neem oil (0.001%)	12% survival	Gomes et al., 2015
Humans	<i>Pediculus humanus capitis</i> (head louse)	Antilouse shampoo Licener® (shampoo + neem oil)	Oxygen uptake is prohibited in 3–10 min	Al-Quraishy et al., 2015
Cowpea	<i>Maruca vitrata</i>	Multinucleopolyhedrovirus (MaviMNPV) + neem oil	Induced MaviMNPV infection in <i>M. vitrata</i> populations	Sokame et al., 2015
Humans	<i>Anopheles arabiensis</i> (Ethiopian malaria mosquito)	Neem oil (20%)	More than 70% repellency (protection) in 3 h	Abiy et al., 2015

Kinnow mandarin (<i>Citrus nobilis</i> × <i>Citrus deliciosa</i>)	<i>Penicillium digitatum</i> and <i>Penicillium italicum</i>	Neem essential oil	Influenced overall acceptability of postharvest crop	Jhalegar et al., 2015
Cultivated crops	<i>Helicoverpa armigera</i> (moth)	Neem oil (1% emulsifiable concentrate [EC] azadirachtin)	Reduction in fecundity, reproductive rates, immature development	Ahmad et al., 2015
Humans	<i>Aedes albopictus</i> (Asian tiger mosquito) filariasis	Neem seed oil	Larvicidal toxicity and field oviposition deterrence	Benelli et al., 2015
Cotton	Cotton pest	<i>Beauveria bassiana</i> (entomopathogenic fungi) + neem oil	Damaged reproductive organs of pests	Togbé et al., 2015
Kale plant	<i>Brevicoryne brassicae</i> (cabbage aphid)	Neem oil (1%)	Less cabbage aphid population	Pissinatti and Ventura 2015
Okra (<i>Abelmoschus esculentus</i> L. Moench)	Bemisia tabaci (whitefly)	Mineral oil + neem oil (2%) 95%	mortality (after 48 h)	Sridharan et al., 2015
Western white pine	<i>Zootermopsis augustinus</i> (dampwood termite)	Neem oil	Rapid mortality	Fatima and Morrell, 2015
Cashew trees	Toxoptera odinae (cashew aphid)	Neem oil	Killed 72.7%–78.9% of aphid population	Ambethgar, 2015b

Stone fruits	<i>Moniliniafructicola</i>	Neem oil (3.53 g/L)	50% inhibition of mycelial growth	Lalancette andMcFarland, 2015
Watermelon	<i>Aphis gossypii</i> (watermelon aphid)	Neem oil	Dose-dependent decrease in population growth rate	Souza et al., 2015
Humans	<i>Cimexlectularius</i> L. (bed bug)	Commercial neem oil	Killed 100% bed bugs	Feldlaufer and Ulrich, 2015
Humans	<i>Aedes aegypti</i> (dengue mosquito)	Leaf essential oil	Effective against first-instar larvae and pupal stage (48 h)	Nasir et al., 2015a
Humans (contaminated food)	<i>Penicillium verrucosum</i> and <i>Penicillium nordicum</i> (produce ochratoxin)	Neem essential oil (15 µl/ml)	100% and 77.52%–92.49% inhibition, respectively	Koteswara Rao et al., 2015
Coconut	<i>Aceria guerreronis</i> (coconut mite)	Neem oil (3%)	31.31% reduction in mite population	Balaji and Hariprasad, 2015
Cultivated crops	<i>Helicoverpa armigera</i> (moth/ cotton bollworm)	PONNEEM (neem + pongam oils, 1:1 ratio) (20 ppm)	Feeding deterrence and genotoxicity	Packiam et al., 2015
Humans	<i>Aedes aegypti</i> and <i>Aedes albopictus</i>	Neem essential oil (10% solution with canola oil)	Insect repellency of 246 ± 15.78 and 256 ± 14.87 min	Nasir et al., 2015b

<i>Jasminum auriculatum</i>	<i>Aceriajasmini</i> (eriophyid mite)	Neem oil (30 ml/L)	Reduced mite population	Devi et al., 2015
Tomato	Whitefly and leaf miner	Neem oil (2.5 L/ha)	Effective after 20 days of transplanting	Chavan et al., 2015
Cashew	<i>Ferrisia virgata</i> (Cockerell)	Neem oil	Effective to a limited extent after two rounds of spraying at 7-day intervals	Ambethgar, 2015a
Okra	<i>Bemisia tabaci</i> Genn. (whitefly), yellow vein mosaic	Neem oil	8.89% of disease intensity	Kumar et al., 2015
Tomato	<i>Tuta absoluta</i> Meyrick (tomato moth)	Neem seed oil	Significant effect recorded	Salem and Abdel-Moniem, 2015
<i>Phaseolus vulgaris</i> L. (dry bean plants)	<i>Bemisia tabaci</i> Genn. biotype B	Neem oil	High nymphal mortality (>81%) was achieved	de Almeida Marques et al., 2015

Recent research on the adverse effect of neem seed oil on humans and animals, as described in the Table 1.6.

Table 1.6. Adverse Effect of neem seed oil on humans and animals.

Effected Organism	Exposure	Dose	Investigated effects	References
Humans (old female)	Ingestion		Multiple organ failure, toxic encephalopathy	Shetty et al., 2016
<i>Ceraeochrysa claveri</i> (predator insect)	Intake of neem oil-contaminated prey, <i>Diatraea saccharalis</i> eggs	0.5%, 1%, and 2% neem oil	Sublethal effect: Cytotoxic effects in the adult midgut	Scudeler et al., 2016

<i>Oreochromis niloticus</i> (Nile tilapia fish)	Treated with NSO	112.5 ppm	Interfered with the antioxidant defense system; decrease in GST, CAT, and SOD	El-Badawi et al., 2015
Rats	Ingestion	2.0, 3.3, 4.6 ml/ kg of bw	Subacute toxicity: Antifertility in females	Dhaliwal et al., 1998
Mice	Ingestion	1.0–28.2 g/kg of bw	Acute toxicity	Tandan et al., 1995
Humans (child)	Oral droplets	5 ml	Toxic encephalopathy	Lai et al., 1990
Rabbits, rats	Ingestion	10–80 ml/kg of bw	Acute toxicity	Gandhi et al., 1988
Humans (child)	Ingestion	12 ml	Changes in the liver and kidneys	Sinniah et al., 1982

Note: CAT, catalase; GST, glutathione-S-transferase; SOD, superoxide dismutase.

CONCLUSION

Neem essential oil has used as a folk remedy around the world, and used in many conditions, and also used in a variety of beauty products like body lotions, hair products, cosmetics, and creams. Various scientific evaluation shown severe side effects were only calculated when neem oil was consumed directly in large quantity. Lactating and pregnant women should be ignored directly and indirectly contact. Neem essential oil applied as pesticide and entering the food chain of humans. However, neem essential oil breakdown rapidly prior to it reaches the consumer. Neem essential oil is easily contaminated with aflatoxin, aflatoxin concentration in neem essential oil-based pesticides should be properly controlled to avoid an unnecessary risk factor. As per as the solvent extraction method is more favor/preferred pleasure because it is low and least cost. SFE is of great interest for being a green, efficient, and effective method for the recovery of essential oils and active metabolites.

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