



Review

Phytochemical Diversity and Multispectral Pharmacological Activities of *Azadirachta indica* A.Juss. (Meliaceae): An Evidence-Based Review of Bioactive Constituents, Therapeutic Mechanisms, and Emerging Applications

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Abstract

Azadirachta indica A.Juss. (Meliaceae), commonly designated as neem, is one of the most extensively investigated medicinal trees in tropical and subtropical phytomedicine. Its remarkable pharmacological versatility stems from an exceptionally diverse phytochemical arsenal distributed across all anatomical parts, including leaves, bark, seeds, flowers, and roots. The principal bioactive constituents belong to two broad chemical categories: isoprenoid compounds most notably the tetra-nortri-terpenoid azadirachtin, nimbin, nimbidin, and salannin and non-isoprenoid compounds encompassing flavonoids, tannins, alkaloids, saponins, coumarins, and phenolic glycosides. Collectively, these constituents confer upon the plant a broad spectrum of pharmacological properties that have been substantiated by contemporary experimental investigations, including antimicrobial, antioxidant, immunomodulatory, neuroprotective, and antidiabetic activities. Beyond its therapeutic relevance, *A. indica* has gained increasing attention in applied research for its roles in green nanotechnology, sustainable agriculture as a biopesticide, and environmental remediation via its bio-flocculant properties. The present review consolidates current evidence on the phytochemical composition and biological activities of *A. indica*, critically evaluates the mechanistic basis of its pharmacological actions, and identifies priority areas for future translational research and product standardisation.

Citation: Kapil, A. *et al.* (2026). Phytochemical Diversity and Multispectral Pharmacological Activities of *Azadirachta indica* A.Juss. (Meliaceae): An Evidence-Based Review of Bioactive Constituents, Therapeutic Mechanisms, and Emerging Applications. *AgroEnvironmental Sustainability*, xx(xx), 1–8. <https://doi.org/10.59983/s202601xx202>

Statement of Sustainability: The medicinal and ecological applications of *Azadirachta indica* support several targets of the United Nations Sustainable Development Goals. Its bioactive compounds promote plant-based therapeutics aligned with SDG 3: Good Health and Well-being. Use of neem-derived biopesticides contributes to environmentally sustainable agriculture under SDG 2: Zero Hunger and SDG 12: Responsible Consumption and Production. Moreover, its applications in green nanotechnology and environmental remediation advance ecological sustainability and biodiversity conservation, supporting global efforts toward resilient ecosystems and sustainable resource management.

1. Introduction

Azadirachta indica A.Juss., a member of the family Meliaceae, has occupied a central position in traditional medicinal systems of the Indian subcontinent for several millennia. Known colloquially as neem, the tree is referred to in Sanskrit literature as ‘Sarva Roga Nivarini’ (the curer of all ailments), a designation that reflects its extensive and varied ethnomedicinal applications in Ayurveda, Unani, Homeopathy, and Naturopathy (Reddy & Palagani, 2022). Contemporary pharmacological research has provided increasing experimental corroboration for many of these traditional uses, positioning neem among the most scientifically validated medicinal plants globally (Singh *et al.*, 2019).

The renewed scientific interest in plant-derived bioactive compounds has been driven, in part, by escalating concerns regarding antimicrobial resistance and the adverse effects associated with synthetic pharmaceuticals. Phytotherapeutic agents generally offer



ARTICLE HISTORY

Received: 21 January 2026

Revised: 19 February 2026

Accepted: 7 March 2026

Published: 18 March 2026

KEYWORDS

Azadirachta indica
azadirachtin
antimicrobial activity
antioxidant activity
biopesticide
phytochemistry
neem

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superior safety profiles and are frequently more accessible to populations in low- and middle-income countries, where approximately 80% of the population continues to rely on herbal medicine as the primary source of healthcare (Osman et al., 2025). Against this backdrop, *A. indica* represents a paradigmatic example of a medicinal plant whose phytochemical complexity has been translated into a diverse array of biological activities applicable across medicine, agriculture, and environmental science.

A. indica has been demonstrated to exert activity against both Gram-positive organisms, including *Staphylococcus aureus*, and Gram-negative pathogens such as *Salmonella dublin* and *Escherichia coli*, with inhibitory potency increasing proportionally with extract concentration (Osman et al., 2025). Additionally, the plant has been identified as a functional bio-flocculant in wastewater treatment owing to the positive surface charge of its extractable polymers, which facilitates the aggregation and removal of suspended pollutants (Zakaria et al., 2025). The purpose of the present review is to provide a comprehensive, evidence-based account of the phytochemical constituents and primary biological activities of *A. indica*, with particular attention to the mechanistic underpinnings of its pharmacological properties and its emerging translational applications.

2. Botanical Description

2.1. Taxonomic Classification

A. indica is classified within the order Sapindales, family Meliaceae, and is the sole species within the genus *Azadirachta* to achieve widespread botanical and pharmacological documentation. The species was formally described by Antoine Laurent de Jussieu and its taxonomic status has remained largely stable in contemporary classification systems. From a cladistic perspective, the Meliaceae are distinguished by their production of limonoid terpenoids, of which azadirachtin in neem represents the most structurally complex and biologically significant example (Reddy & Palagani, 2022).

Table 1. Taxonomic classification of *A. indica*.

Taxonomic Rank	Classification
Kingdom	Plantae
Division	Magnoliophyta
Class	Magnoliopsida
Order	Sapindales
Family	Meliaceae
Genus	<i>Azadirachta</i> A.Juss.
Species	<i>Azadirachta indica</i> A.Juss.
Common Names	Neem (English); Nimtree; Margosa; Sarva Roga Nivarini (Sanskrit)

2.2. Morphological Characteristics

A. indica is a medium-to-large tropical evergreen tree attaining heights of 12–20 m under typical conditions and occasionally reaching 30 m in particularly favourable environments (Azad et al., 2023). Its broad, spreading crown and dense canopy of dark-green foliage render it highly valued as a shade tree throughout its natural and introduced range. The leaves are pinnately compound, comprising 8–19 lanceolate leaflets with serrated margins, arranged alternately along the rachis (Bahri et al., 2025). The bark is characteristically thick, rough, and deeply fissured with a greyish-brown to reddish-brown colouration; it possesses a distinctly bitter taste attributable to its high concentration of triterpenoid constituents (Azis & Shofia, 2026).

The inflorescences are axillary panicles bearing small, white, bisexual flowers with a distinctive sweet fragrance, which appear predominantly during the spring season and are essential to the plant's reproductive cycle (Nagendiran & Parimala, 2025). The fruit is a smooth, olive-like drupe measuring approximately 1–2 cm in length; it is green when immature and transitions to yellow upon ripening, each containing a single seed that serves as the primary commercial source of neem oil (Ajibade et al., 2026).

2.3. Geographical Distribution

A. indica is indigenous to the Indian subcontinent, where it grows naturally across diverse climatic zones ranging from semi-arid to sub-humid. It demonstrates exceptional adaptability, tolerating poor and degraded soils, extended drought, and high ambient temperatures, which has facilitated its naturalization in the broader tropical belt. Within South Asia, the species is widely distributed in Bangladesh, Nepal, Pakistan, and Sri Lanka (Reddy & Palagani, 2022). Beyond its native range, neem has been intentionally introduced into sub-Saharan Africa, Southeast Asia, Central America, and parts of the Caribbean and the Pacific, where it is cultivated for its shade, medicinal, and agricultural utility. The species' drought resilience and ecological versatility make it one of the most cosmopolitan tropical medicinal trees.

3. Phytochemical Constituents



Table 2. Morphological characteristics and medicinal significance of plant parts of *A. indica*.

Plant Part	Morphological Description	Primary Medicinal Applications
Leaves	Pinnately compound; 8–19 lanceolate leaflets with serrated margins; dark green	Antimicrobial, antifungal, anti-inflammatory; treatment of skin diseases and febrile conditions
Bark	Thick, rough, fissured; greyish-brown to reddish-brown; intensely bitter taste	Antipyretic, antimalarial, anti-inflammatory; bark decoctions used in traditional fever management
Seeds	Enclosed in a single-seeded drupe; primary source of neem oil via cold-press extraction	Pesticidal, antifungal; source of azadirachtin and other limonoid insecticides
Flowers	Small, white, bisexual; arranged in axillary panicles; strongly fragrant	Traditional use in digestive disorders; anti-inflammatory activity reported
Roots	Lateral root system; bark similarly bitter to stem bark	Anthelmintic and antimicrobial applications in folk medicine
Oil (seed-derived)	Yellowish-brown fixed oil with characteristic odour; rich in fatty acids and limonoids	Pharmaceutical formulations, topical antimicrobials, cosmetics, agricultural pesticides

3.1. Classification of Bioactive Compounds

The phytochemical architecture of *A. indica* is exceptionally rich, encompassing several hundred identified compounds distributed across all anatomical parts of the plant (Chauhan et al., 2022). These constituents are conventionally categorised into two major chemical classes: isoprenoid (terpenoid) compounds and non-isoprenoid compounds. The former include a diverse array of limonoids most notably the tetranortriterpenoids as well as steroids and diterpenes. The non-isoprenoid fraction comprises flavonoids, tannins, alkaloids, saponins, coumarins, phenolic acids, and their respective glycosides (Bahri et al., 2025; Ajibade et al., 2026; Azis & Shofia, 2026). The relative abundance and composition of these constituents vary considerably according to plant part, geographic origin, seasonality, and extraction methodology employed.

Among the major phytochemical classes: alkaloids confer antibacterial and antiprotozoal activities through mechanisms involving nucleic acid intercalation and membrane disruption; flavonoids function as potent radical scavengers and anti-inflammatory agents via inhibition of cyclooxygenase and lipoxygenase pathways; tannins exert astringent and antimicrobial effects through protein precipitation and membrane perturbation; saponins demonstrate immunomodulatory and surface-active properties; terpenoids the dominant class in neem contribute the principal insecticidal, antifeedant, and anti-inflammatory activities; and glycosides provide additional synergistic biological activity across multiple pharmacological targets (Bahri et al., 2025; Ajibade et al., 2026).

Table 3. Principal phytochemical constituents of *A. indica*: chemical class, distribution, and reported biological activity.

Compound / Class	Chemical Class	Primary Plant Part	Key Biological Activity	Selected Reference
Azadirachtin	Tetranortriterpenoid (Limonoid)	Seeds, leaves	Insecticidal, antifeedant, insect growth regulator; minimal toxicity to non-target organisms	Bahri et al. (2025); Nagendiran & Parimala (2025)
Nimbin	Triterpenoid (Limonoid)	Seeds, bark	Anti-inflammatory, antifungal, antipyretic	Bahri et al. (2025)
Nimbidin	Triterpenoid (Limonoid)	Seeds, bark	Antibacterial, anti-inflammatory, antiulcer	Bahri et al. (2025)
Salannin	Tetranortriterpenoid (Limonoid)	Seeds, leaves	Insect antifeedant; repellent activity against multiple pest species	Nagendiran & Parimala (2025)
Gedunin	Triterpenoid (Limonoid)	Seeds, bark	Antibacterial, antimalarial, antifungal	Nagendiran & Parimala (2025)
Quercetin	Flavonoid	Leaves, flowers	Antioxidant, anti-inflammatory, antiviral	Azis & Shofia (2026)
Rutin	Flavonoid glycoside	Leaves	Antioxidant, vascular protective, anti-inflammatory	Azis & Shofia (2026)
Catechins / Tannins	Polyphenol	Bark, leaves	Antimicrobial, astringent, antioxidant	Bahri et al. (2025)
Saponins	Triterpenoid glycoside	Leaves, seeds	Immunomodulatory, haemolytic, antimicrobial	Ajibade et al. (2026)
Alkaloids	Nitrogen-containing heterocycles	Leaves, bark	Antibacterial, antiprotozoal, analgesic	Bahri et al. (2025); Ajibade et al. (2026)
Terpenoids (general)	Isoprene-derived terpenes	All parts	Insecticidal, antimicrobial, anti-inflammatory	Ajibade et al. (2026)
Phenolic acids	Hydroxycinnamic / Hydroxybenzoic derivatives	Leaves, bark	Antioxidant, antimicrobial, anti-inflammatory	Azis & Shofia (2026)



3.2. Phytochemical Screening Studies

Systematic phytochemical screening of *A. indica* across multiple solvent systems and plant parts has consistently confirmed the presence of the compound classes enumerated above. Bahri et al. (2025) conducted methanol extraction of neem leaves and identified alkaloids, flavonoids, and tannins as major constituents via standard qualitative screening assays. Ajibade et al. (2026) characterised mixed distillates of neem alongside other medicinal plants, reporting the presence of terpenoids and glycosides as predominant classes. Azis and Shofia (2026) utilised ethanol-based extraction of neem leaf material and identified phenolics and flavonoids as the principal antioxidant-contributing fractions, corroborating findings reported by Nagendiran and Parimala (2025) using ethanolic flower extracts. These studies collectively affirm that solvent polarity substantially governs the extractable phytochemical profile, with polar solvents (methanol, ethanol, water) preferentially extracting flavonoids and phenolics, while less polar solvents enrich terpenoid and limonoid fractions.

4. Biological Activities

4.1. Antimicrobial Activity

The antimicrobial properties of *A. indica* extracts have been among the most thoroughly documented pharmacological attributes of the plant (Shah et al., 2021). Experimental investigations employing extracts from leaves, bark, and seeds prepared in various solvents have demonstrated inhibitory activity against a broad panel of bacterial and fungal pathogens. Studies by Vadivel et al. (2025), Akabandi (2026), Tiranya and Munasinghe (2025), Azis and Shofia (2026), and Osman et al. (2025) collectively confirm significant antibacterial activity, particularly against *Staphylococcus aureus* and *Escherichia coli*, which serve as reference organisms for Gram-positive and Gram-negative antibacterial screening, respectively.

The mechanisms underlying the antimicrobial activity of neem extracts are multifactorial. Flavonoids and phenolic compounds are capable of forming complexes with bacterial cell wall proteins, thereby compromising structural integrity. Terpenoids, particularly limonoids such as nimbidin, have been shown to disrupt membrane permeability, leading to cellular lysis. Alkaloids may intercalate with bacterial DNA and interfere with topoisomerase function. The broad-spectrum nature of neem's antibacterial action is therefore attributable to the synergistic action of multiple phytochemical classes acting on distinct molecular targets (Osman et al., 2025; Azis & Shofia, 2026).

Table 4. Summary of antimicrobial studies on *A. indica* extracts.

Author (Year)	Plant Part / Extract	Test Organism(s)	Principal Finding	Methodology
Vadivel et al. (2025)	Homeopathic dilutions of leaf	<i>S. aureus</i> , <i>E. coli</i>	Inhibitory activity demonstrated; correlated with LC-MS identified phenolic fractions	Disc diffusion, LC-MS analysis
Akabandi (2026)	Leaf extract (solvent unspecified)	Multiple bacterial strains	Antibacterial activity confirmed; inhibition zones recorded against reference strains	Disc diffusion / Agar well diffusion
Tiranya & Munasinghe (2025)	Whole plant extract	<i>E. coli</i> , <i>S. aureus</i>	Strong antibacterial activity; bioactive compound screening conducted concurrently	MIC determination, phytochemical screening
Azis & Shofia (2026)	Ethanol leaf extract	Skin-pathogenic bacterial and fungal strains	Broad-spectrum activity against dermatological pathogens	Disc diffusion, MIC/MBC
Osman et al. (2025)	Aqueous bark extract	Multiple bacterial pathogens	Dose-dependent inhibition; activity increased proportionally with extract concentration	Agar well diffusion, spectrophotometric quantification

4.2. Antioxidant Activity

Oxidative stress arising from an imbalance between the generation of reactive oxygen species (ROS) and the capacity of endogenous antioxidant defence systems is implicated in the pathogenesis of numerous chronic diseases including cardiovascular disorders, diabetes mellitus, neurodegenerative conditions, and carcinogenesis. *A. indica* extracts have been shown to exhibit potent free-radical scavenging activity in multiple in vitro assay systems, including DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging and ferric-reducing antioxidant power (FRAP) assays (Suthar et al., 2025; Nagendiran & Parimala, 2025; Yahaya et al., 2025). The principal antioxidant-active constituents are the leaf phenolics particularly flavonoids such as quercetin and rutin which function as hydrogen donors capable of neutralising ROS through electron transfer and hydrogen atom transfer mechanisms.

Yahaya et al. (2025) reported comparative in vitro antioxidant activity of n-hexane and ethyl acetate fractions of *A. indica*, demonstrating fraction-dependent variation in radical scavenging capacity that reflects the differential distribution of active phenolic constituents. Nagendiran and Parimala (2025) similarly documented antioxidant activity in ethanolic flower extracts, expanding the range of plant parts characterised for antioxidant function. These findings collectively support the utility of neem-derived phytochemicals in the development of natural antioxidant formulations applicable in both nutraceutical and pharmaceutical contexts.



4.3. Immunomodulatory Activity

The immunomodulatory properties of *A. indica* have been evaluated in both monotherapy and combination therapy experimental models. Suthar et al. (2025) demonstrated that the administration of *A. indica* extract, both alone and in combination with *Tinospora cordifolia*, produced significant enhancement of antioxidant and immunological parameters in broiler chickens, indicating synergistic augmentation of host immune responses when neem is used in conjunction with other immunomodulatory botanicals. The immunostimulatory effects of neem are partly attributed to its saponin constituents, which have been demonstrated to stimulate lymphocyte proliferation and macrophage activation, as well as to its polysaccharide fractions that may function as adjuvant-like immunopotentiators.

4.4. Neuroprotective Activity

Emerging evidence from preclinical investigations points to a neuroprotective role for *A. indica* phytochemicals in models of neurological dysfunction. Rao et al. (2025) demonstrated that neem extract administration ameliorated memory deficits and reduced anxiety-like behaviours in an animal model of depression, with the observed effects attributed to modulation of cholinergic neurotransmission. The cholinergic hypothesis of cognitive decline proposes that impairment of acetylcholinergic signalling in the hippocampus and cortex underlies deficits in learning and memory; neem extracts may therefore exert their cognitive protective effects through inhibition of acetylcholinesterase or upstream neuroprotective mechanisms involving anti-inflammatory and antioxidant pathways. These findings justify further mechanistic investigation and eventual clinical evaluation of neem-derived compounds for the management of neurodegenerative disorders.

4.5. Antidiabetic Activity

Multiple bioactive compounds present in *A. indica* have demonstrated potential in modulating glucose homeostasis and metabolic parameters relevant to diabetes mellitus. Nagendiran and Parimala (2025) conducted comparative evaluation of antidiabetic activity in ethanolic extracts of *A. indica* and *Melia dubia* flowers, reporting significant alpha-amylase and alpha-glucosidase inhibitory activity that suggests interference with post-prandial glucose absorption at the intestinal level. The antidiabetic mechanisms proposed for neem phytochemicals include: inhibition of carbohydrate-hydrolysing enzymes (alpha-amylase, alpha-glucosidase); enhancement of peripheral glucose uptake via insulin-sensitising effects; reduction of oxidative stress in pancreatic beta cells; and modulation of lipid metabolism, which is often dysregulated in type 2 diabetes. The flavonoid quercetin, present in significant concentrations in neem leaf, has been independently documented as an inhibitor of protein tyrosine phosphatase 1B, a validated antidiabetic drug target.

Table 5. Consolidated summary of pharmacological activities of *A. indica*.

Pharmacological Activity	Active Constituent(s) Implicated	Proposed Mechanism(s)	Key Reference(s)
Antimicrobial	Nimbidin, alkaloids, tannins, phenolics	Cell wall disruption, membrane permeabilisation, enzyme inhibition, DNA intercalation	Vadivel et al. (2025); Osman et al. (2025); Azis & Shofia (2026)
Antioxidant	Quercetin, rutin, flavonoids, phenolic acids	Free-radical scavenging via hydrogen atom transfer and electron transfer mechanisms; ROS neutralisation	Suthar et al. (2025); Nagendiran & Parimala, (2025); Yahaya et al. (2025)
Immunomodulatory	Saponins, polysaccharides, polyphenols	Lymphocyte proliferation stimulation; macrophage activation; cytokine modulation	Suthar et al. (2025)
Neuroprotective	Terpenoids, flavonoids, phenolics	Acetylcholinesterase inhibition; anti-inflammatory neuroprotection; antioxidant-mediated neuronal protection	Rao et al. (2025)
Antidiabetic	Quercetin, flavonoids, terpenoids	Alpha-amylase and alpha-glucosidase inhibition; insulin sensitisation; pancreatic beta-cell protection	Nagendiran & Parimala (2025)
Insecticidal / Biopesticidal	Azadirachtin, salannin, nimbin	Ecdysteroid antagonism; antifeedant activity; hormonal disruption of insect moulting cycle	Cece et al. (2026); Bahri et al. (2025)
Bio-flocculant / Water Treatment	Cationic polymers, phenolics	Charge neutralisation of suspended particulates; floc formation and sedimentation enhancement	Zakaria et al. (2025)

5. Nanotechnology Applications

5.1 Green Biosynthesis of Nanoparticles

The application of plant extracts in the environmentally sustainable synthesis of metal nanoparticles represents an active frontier of nanoscience research. *A. indica* extracts have been extensively investigated for their capacity to function as reducing and stabilising agents in the synthesis of silver and iron nanoparticles, offering a non-toxic, energy-efficient alternative to conventional



133 chemical reduction methods (Siddiqui et al., 2026). The flavonoids, terpenoids, and phenolic compounds present in neem extracts
134 are principally responsible for the reduction of ionic silver (Ag^+) and ferric iron (Fe^{3+}) to their respective zero-valent metallic
135 nanoparticle forms, while simultaneously capping the nascent nanoparticles to prevent aggregation and confer colloidal stability.

136 5.2. Biomedical Applications of Neem-Mediated Nanoparticles

137 Silver nanoparticles synthesised via neem-mediated green routes have demonstrated superior antimicrobial activity against a
138 broad spectrum of pathogenic microorganisms in comparison with unmodified plant extracts alone. The enhanced activity is at-
139 tributable to the high surface area-to-volume ratio of nanoparticles, which facilitates intimate contact with microbial cell walls and
140 membranes, promoting oxidative damage and cellular dysfunction (Siddiqui et al., 2026). Furthermore, neem-mediated nanopar-
141 ticles have been investigated for catalytic applications in environmental remediation, capitalising on their high surface reactivity
142 to accelerate the degradation of chemical pollutants. These attributes position *A. indica*-mediated nanoparticles as multifunctional
143 agents at the interface of green chemistry, nanomedicine, and environmental biotechnology.

144 6. Agricultural Applications

145 6.1. Biopesticidal Properties

146 The biopesticidal utility of *A. indica* is well established and represents one of its most commercially developed applications. Azadirachtin,
147 the principal active compound, exerts its insecticidal effects primarily through antagonism of ecdysone, the principal insect moult-
148 ing hormone, thereby disrupting larval development, ecdysis, and reproductive function. This mechanism of action, which is
149 highly specific to arthropods and does not affect vertebrate hormonal systems, confers upon azadirachtin an excellent selectivity
150 profile relative to conventional broad-spectrum synthetic insecticides (Cece et al., 2026). Additional limonoids salannin, nimbin,
151 and nimbidin contribute antifeedant and repellent activities, further reducing pest fitness and population pressure.

152 6.2. Efficacy Against Economically Important Pests

153 Cece et al. (2026) evaluated the biopesticidal activity of *A. indica* seed and leaf extracts against the fall armyworm (*Spodoptera*
154 *frugiperda*), one of the most economically damaging polyphagous pests affecting maize production globally. The investigators
155 documented significant inhibition of larval feeding behaviour and reductions in survival rates, supporting the utility of neem-
156 based formulations as integrated pest management tools in sub-Saharan African agricultural systems. The ecological safety profile
157 of neem-based pesticides, arising from their rapid photodegradation and low persistence in soil, reduces the risk of non-target
158 toxicity and environmental bioaccumulation compared with synthetic organophosphate and pyrethroid alternatives.

159 7. Environmental Applications

160 7.1. Wastewater Treatment and Bio-flocculant Properties

161 The application of *A. indica*-derived materials in water treatment is an emerging area of environmental biotechnology. The presence
162 of cationic polymers and polyphenolic compounds in neem extracts enables these materials to function as natural coagulants and
163 bio-flocculants, aggregating suspended particulate matter through charge neutralisation and bridging mechanisms. Zakaria et al.
164 (2025) demonstrated the efficacy of *A. indica* as a bio-flocculant in reducing turbidity and suspended solids in landfill leachate, a
165 particularly recalcitrant wastewater stream characterised by high pollutant load and variable composition. The performance of
166 neem-based bio-flocculants was attributed to the positive surface charge of extractable components, which effectively neutralises
167 the negative charge of colloidal particles in suspension, inducing floc formation and subsequent sedimentation.

168 The use of plant-derived coagulants in water treatment offers several sustainability advantages over inorganic chemical coagulants
169 such as aluminium sulphate: they are biodegradable, produce lower sludge volumes, do not introduce toxic metal residues into
170 treated water, and can be sourced from locally available plant biomass in low-income settings (Zakaria et al., 2025). These charac-
171 teristics position *A. indica* as a candidate for incorporation into sustainable, decentralised water treatment systems, particularly in
172 tropical regions where the plant grows abundantly.

173 8. Future Research Perspectives

174 Despite the considerable body of evidence accumulated to date, several critical knowledge gaps remain that must be addressed
175 to realise the full translational potential of *A. indica*. At the phytochemical level, systematic isolation, structural elucidation, and
176 quantitative profiling of minor constituent classes particularly the non-limonoid alkaloids and phenylpropanoids are needed across
177 a broader range of geographic accessions and seasonal time points. Advances in high-resolution mass spectrometry and nuclear
178 magnetic resonance-based metabolomics offer powerful tools for comprehensive phytochemical characterisation that should be
179 applied systematically to this species.

180 In the pharmacological domain, the majority of available evidence derives from in vitro assay systems and limited animal model



181 studies; rigorous randomised controlled clinical trials evaluating the efficacy and safety of standardised neem formulations in
182 human subjects are conspicuously absent for most claimed indications. Mechanistic studies employing molecular docking, target
183 identification, and pharmacokinetic profiling are required to validate proposed mechanisms of action and to identify the most
184 promising lead compounds for drug development pipelines (Suthar et al., 2025; Rao et al., 2025).

185 In the domain of agricultural applications, field-scale evaluation of neem-based biopesticide formulations under diverse agrocli-
186 matic conditions, and their integration into evidence-based integrated pest management protocols, represents a priority research
187 area (Cece et al., 2026). Standardisation of neem-based products, encompassing phytochemical authentication, quality control,
188 and stability testing, is prerequisite for regulatory approval and commercialisation of herbal formulations in both domestic and
189 international markets. The application of nanotechnology to enhance the bioavailability and targeted delivery of neem-derived
190 phytochemicals likewise represents a productive intersection of multiple research frontiers (Siddiqui et al., 2026).

191 9. Conclusion

192 *A. indica* is a botanically and pharmacologically exceptional species whose extensive phytochemical diversity underpins a corre-
193 spondingly broad spectrum of experimentally validated biological activities. The present review has synthesised evidence demon-
194 strating that neem extracts, derived from multiple anatomical parts of the plant, exhibit antimicrobial, antioxidant, immunomod-
195 ulatory, neuroprotective, and antidiabetic activities attributable to a complex and synergistic ensemble of limonoid terpenoids,
196 flavonoids, tannins, alkaloids, saponins, and phenolic acids. Beyond therapeutic applications, *A. indica* has demonstrated substan-
197 tial utility in green nanotechnology, as a source of sustainable biopesticides in integrated crop protection, and as a bio-flocculant
198 in environmentally responsible water treatment processes.

199 The convergence of traditional ethnomedicinal knowledge with contemporary experimental investigation positions *A. indica* as a
200 priority candidate for translational pharmacognosy. Future research should prioritise: rigorous clinical evaluation of standardised
201 neem formulations; advanced mechanistic studies elucidating the molecular basis of pharmacological activity; comprehensive
202 phytochemical profiling using modern analytical platforms; and systematic quality standardisation of neem-derived products
203 for regulatory acceptance. Interdisciplinary collaboration spanning phytochemistry, pharmacology, toxicology, agronomy, and
204 environmental science will be essential to translate the accumulated basic science evidence into tangible therapeutic, agricultural,
205 and environmental innovations.

206 Author Contributions

207 Archit Kapil: Conceptualization; Data curation; Investigation; Methodology; Resources; Software; Validation; Visualization; Writ-
208 ing – original draft; Writing – review and editing; Anshul: Data curation; Methodology; Software; Visualization; Writing – original
209 draft; Vansh Gupta: Data curation; Methodology; Visualization; Writing – original draft; Sandeep Kumar Barwal: Supervision;
210 Writing – original draft; Writing – review and editing; Harsh Singh: Writing – original draft; Writing – review and editing.

211 Funding

212 This research received no external funding.

213 Acknowledgements

214 The authors acknowledge the School of Botany, Maa Shakumbhari University, Saharanpur, for institutional support throughout
215 the preparation of this manuscript.

216 Declarations

217 **Conflicts of interest:** The authors report no conflict of interest in relation to the publication of this manuscript.

218 **Ethics approval:** As this study did not involve human or animal subjects, ethical approval was not required.

219 **Consent for publication:** All authors have reviewed and approved the manuscript and consent to its publication in *Society for*
220 *Agri-environmental Sustainability*.

221 **Data availability:** The data supporting the conclusions of this study can be obtained from the corresponding author upon reason-
222 able request.

223 **Supplementary material:** No supplementary material is associated with this manuscript.

224 **Additional information:** No additional information is provided for this study.

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