INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH AND INNOVATIVE STUDIES
ISSN: 2820-7157
www.ijsrisjournal.com

December 2025 Volume 4 Number 6 168-182

Received Date: October 20, 2025 Accepted Date: November 11, 2025 Published Date: December 01, 2025

Evaluation of Antioxidant, Anti-inflammatory and Antimicrobial Activities of the Leaf Extracts of Luffa cylindrical: A Comprehensive Review

Salma Nassir Alquraish [1], Mona Yousef Albutyan [1], Hadeer Habib Alshwaikhat [2], Basma Ahmed Alowiasheer [2], Haya Salem Alfuzia [2], Abbas Ali Al Saeed [2], Ibtisam Sultan Nasser Almohsen [2], Fatimah Ibrahim Ali Alrashdi [3], Mohammed Abdullah Abuhomed [4], Salma Hamoud Al-Qahtani [5], Rehab Abdulmohsen Alali [6], Abdullah Jubran Khbrani [7], Zainab Ahmed Al-Hassan [8], Laila Hassan Bukhader [9]

1. Abdulaziz bin Sulaiman Al-Afaliq Center for Early Detection of Tumors
2. Prince Saud bin jalawi Hospital
3. King Khaled hospital in Alkharj
4. Primary Care Laboratory in Al-Jafar
5. King Faisal General Hospital
6. Primary health care Alahsaa -MOH
7. Imam Abdulrahman Bin Faisal Hospital
8. Maternity And Children Hospital
9. Salhiya PHC

Abstract

Luffa cylindrica (L.) Roem, commonly known as sponge gourd or loofah, is a Cucurbitaceous plant widely distributed across tropical and subtropical regions of Asia and Africa. Traditionally employed in various ethnomedicinal systems for treating inflammation, pain, microbial infections, and metabolic disorders, the species has garnered significant scientific attention over the past decade. This comprehensive review synthesizes current knowledge on the phytochemical composition and pharmacological activities of *L. cylindrica* leaf extracts, with particular emphasis on antioxidant, anti-inflammatory, and antimicrobial properties. Accumulating evidence demonstrates that leaf extracts contain diverse bioactive secondary metabolites, including flavonoids (myricetin, apigenin-7-glucuronide, luteolin-7-O-β-D-glucuronide methyl ester), phenolic compounds (ferulic acid, p-coumaric acid, gallic acid, caffeic acid, chlorogenic acid), triterpenoids (oleanolic acid, echinocystic acid, lucyosides A-M), saponins, carotenoids (β-carotene), and steroids, with quantitative composition varying according to geographical origin, extraction solvent, and plant part utilized. Antioxidant activity has been consistently documented through DPPH, chelating effect, hydroxyl radical, and superoxide anion scavenging assays, with IC50 values ranging from 54.41 to 90 µg/mL depending on extract type and provenance. Anti-inflammatory effects are mediated through multiple mechanisms, including inhibition of nitric oxide and

prostaglandin E2 production, suppression of pro-inflammatory cytokines (IL-6), downregulation of iNOS and COX-2 expression, and modulation of AKT-GSK3β-CREB, NF-κB, and AP-1 signaling pathways. Antimicrobial studies reveal selective activity against Gram-positive bacteria (*Bacillus subtilis*, *Staphylococcus aureus*) and certain Gram-negative organisms (*Escherichia coli*, *Salmonella typhi*), with minimum inhibitory concentration values ranging from 12.5 to 100 mg/mL, while antifungal effects appear negligible. Recent investigations have also identified novel applications in neuroinflammation, cognitive impairment, oral carcinoma, hepatocellular carcinoma, and breast cancer through apoptosis modulation and cancer stem cell targeting. Emerging toxicological data indicate moderate toxicity at high doses (4000 mg/kg), necessitating dosage consideration. This review identifies significant research gaps, including limited standardized clinical trials, insufficient mechanistic elucidation of individual phytochemicals, incomplete structure-activity relationships, and the need for comprehensive bioavailability studies, while proposing directions for future translational research.

Keywords: *Luffa cylindrica*, leaf extracts, antioxidants, anti-inflammatory agents, antimicrobial activity, phytochemicals, flavonoids, myricetin, ferulic acid, oleanolic acid, neuroinflammation

1. Introduction

The genus *Luffa*, belonging to the family Cucurbitaceae, comprises several species of annual climbing vines that have been integral to traditional medicine systems across Asia and Africa for centuries. Among these, *Luffa cylindrica* (L.) Roem (syn. *Luffa aegyptiaca*), commonly designated as sponge gourd, vegetable sponge, or loofah, represents one of the most economically and medicinally significant species [1,2]. The plant is characterized by its rapid growth, adaptability to diverse climatic conditions, and production of fibrous fruits that have been utilized both as culinary vegetables and as biodegradable cleaning implements [3].

Ethnopharmacological records document the traditional employment of *L. cylindrica* leaves for a remarkable spectrum of therapeutic indications. Historical and contemporary ethnobotanical surveys indicate that leaf preparations have been administered for pain management, rheumatoid arthritis, backache, fever, syphilis, dysentery, and various neoplastic conditions [4,5]. In Togo, leaf formulations are used orally for edema and malaria treatment; in South Africa, Uganda, and Rwanda, leaf decoctions are employed for stomach pain, aiding childbirth, and wound healing respectively; while in the Central African Republic, pulverized leaves are administered rectally for enterobiasis therapy [6]. Additionally, traditional practitioners have prescribed the leaves as antihyperlipidemic agents, particularly for atherosclerosis therapy, as anthelmintics, carminatives, emmenagogues, galactagogues, and topical antiseptics [7,8]. This diverse therapeutic repertoire suggests the presence of multiple bioactive constituents with pleiotropic pharmacological effects.

The past two decades have witnessed a substantial expansion in scientific investigations aimed at validating these traditional applications through modern pharmacological methodologies. Concurrently, the global scientific community has demonstrated increasing interest in plant-derived natural products as alternatives or adjuncts to conventional pharmacotherapy, driven by concerns regarding antimicrobial resistance, adverse effects of synthetic anti-inflammatory agents, and the desire for cost-effective, accessible therapeutic options [9].

This comprehensive review critically evaluates and synthesizes the available scientific literature concerning the antioxidant, anti-inflammatory, and antimicrobial activities of *L. cylindrica* leaf extracts. Specific objectives include: (1) characterizing the phytochemical profiles of various leaf extract preparations; (2) comparing and contrasting quantitative findings across different bioactivity assays; (3) elucidating the putative mechanisms of action underlying observed pharmacological effects; (4) identifying geographical, environmental, and methodological factors influencing bioactivity; (5) evaluating emerging evidence for anticancer, neuroprotective, and other therapeutic applications; (6) assessing current toxicological data and safety considerations; and (7) delineating knowledge gaps to inform future research trajectories.

2. Phytochemical composition of *luffa cylindrica* leaves

2.1 Qualitative Phytochemical Screening

Systematic phytochemical investigations conducted across multiple independent laboratories have consistently demonstrated that *L. cylindrica* leaves harbor a diverse array of secondary metabolites. Qualitative screening employing standard colorimetric assays has revealed the presence of flavonoids, tannins, alkaloids, phenolic compounds, cardiac glycosides, saponins, triterpenoids, steroids, carbohydrates, proteins, and starch [10,11]. The relative abundance of these phytochemical classes exhibits considerable variation depending upon extraction methodology, plant part utilized, and geographical origin of the plant material.

Onyegbule and colleagues conducted comprehensive phytochemical evaluation of leaf extracts prepared with four different solvents—methanol, ethyl acetate, absolute ethanol, and dichloromethane [12]. Their findings indicated moderate quantities of all tested phytochemical classes across all extracts, with methanolic and ethanolic extracts demonstrating superior extraction efficiency for polar compounds including flavonoids and phenolic glycosides. This observation aligns with established principles of phytochemistry wherein hydroalcoholic solvents exhibit optimal extraction capacity for intermediate to high polarity bioactive molecules.

A recent investigation by Bharathidasan et al. employing aqueous extraction methodology identified phenols, tannins, terpenoids, and steroids in *L. cylindrica* peel extracts, with confirmatory testing utilizing ferric chloride for phenolics (blue-green coloration) and Salkowski's test for terpenoids (reddish-brown interface) [13]. While this study focused primarily on peel tissue, the phytochemical similarity between peel and leaf matrices suggests comparable secondary metabolite profiles, a hypothesis supported by comparative phytochemical analyses.

Alim and associates conducted an integrated phytochemical and elemental assessment of *L. cylindrica* leaves, confirming the presence of cardiac glycosides, terpenoids, saponin glycosides, tannins, flavonoids, carbohydrates, and cardenolides across various solvent extracts [14]. Their elemental analysis further revealed the presence of essential and trace minerals including calcium (941.7 mg/kg), magnesium (234.6 mg/kg), potassium (928.4 mg/kg), sodium (858.1 mg/kg), iron, zinc, and copper, which are vital for various biological and metabolic processes and may contribute synergistically to the therapeutic effects of leaf preparations.

2.2 Quantitative Phytochemical Analysis and Influencing Factors

Quantitative determinations have revealed substantial variability in phytochemical content contingent upon multiple factors. Sirisa-Ard and colleagues conducted a comparative analysis of conventional dried leaf extracts versus ash-dried leaf preparations, documenting significant differences in quantitative phytochemical determination of cardiac glycosides, alkaloids, phenolics, flavonoids, and triterpenoids [15]. The ash-dried preparation demonstrated incomplete combustion with consequent preservation of certain thermostable compounds, while conventional drying better preserved heat-labile constituents. This finding carries important methodological implications for traditional preparation methods and standardized extract manufacturing.

Geographical and climatological factors exert profound influences on secondary metabolite accumulation. Ben Hlel and associates performed a sophisticated comparative analysis of *L. cylindrica* leaves collected from two distinct Tunisian localities: Essouasi (semi-arid region) and Medenine (arid region) [16]. Using high-performance liquid chromatography coupled with time-of-flight mass spectrometry (HPLC/TOF-MS), the investigators identified 14 distinct phenolic compounds in specimens from the semi-arid region, compared with only 6 phenolics in those from the arid zone. Ferulic acid emerged as the predominant phenolic constituent in Essouasi specimens, attaining concentrations of 5128.5 ± 4.09 μg phenols/g dry weight. This remarkable geographical variation underscores the importance of detailed provenance documentation and suggests that semi-arid cultivation conditions may optimize phenolic accumulation, possibly as an adaptive response to moderate environmental stress.

Gas chromatography-mass spectrometry (GC-MS) analysis further identified the presence of omega-3 fatty acids in specimens from the semi-arid region, while these beneficial polyunsaturated fatty acids were below detectable limits in arid-region specimens [16]. This observation extends the nutraceutical potential of *L. cylindrica* leaves beyond conventional phenolic antioxidants to encompass essential fatty acids with established cardiovascular and anti-inflammatory benefits.

2.3 Major Bioactive Constituents and Their Characterization

Recent pharmacological investigations have achieved significant progress in identifying specific bioactive molecules responsible for the observed therapeutic effects. A comprehensive review by Akinwumi and colleagues catalogued an extensive array of phytochemicals isolated from various parts of *L. cylindrica* [17]. Flavonoids identified include apigenin-7-glucuronide, luteolin-7-O-β-D-glucuronide methyl ester, -O-feruloyl-β-D-glucose, kaempferol derivatives, kaempferide, diosmin, neodiosmin, eriodictyol-7-glucoside, quercetin, myricetin, rutin, catechin, luteolin, hyperoside, kaempferitrin, quercetrin, and tiliroside. Phenolic acids documented include p-coumaric acid, gallic acid, caffeic acid, and chlorogenic acid. Triterpenoids and saponins include oleanolic acid, echinocystic acid, and lucyosides A-M. Additional constituents comprise tannins (catechin), ribosome-inactivating proteins (α-luffin), carotenoids (9-cis neoxanthin, all-trans-lutein, all-trans-β-

carotene), chlorophylls (chlorophyll a and b, pheophytin), cucurbitacin B, and gypsogenin.

Park and colleagues employed high-performance liquid chromatography (HPLC) to characterize the major components of *L. cylindrica* leaf extract and identified myricetin as a principal bioactive flavonoid [18]. This flavonol compound, characterized by a 3,5,7,3',4',5'-hexahydroxyflavone structure, independently demonstrated anti-inflammatory activity in lipopolysaccharide (LPS)-stimulated BV2 microglial cells, confirming its role as a pharmacologically active constituent.

Myricetin's identification carries substantial significance, as this flavonoid has been previously documented to possess multiple biological activities including antioxidant, anti-inflammatory, anticancer, antidiabetic, neuroprotective, immunomodulatory, antimicrobial, antiviral, hepatoprotective, anti-obesity, and cardiovascular protective effects [19,20].

Beta-carotene has been identified as another bioactive constituent with potential therapeutic relevance. Bharathidasan and colleagues, referencing prior phytochemical characterization by Raut et al., selected this carotenoid for molecular docking studies based on its documented presence in *L. cylindrica* extracts and established antihyperlipidemic activity [21]. Molecular modeling revealed strong binding affinity between beta-carotene and BAX protein (-6.8 kcal/mol), with moderate binding to BCL2 (-5.8 kcal/mol), suggesting potential apoptosis-inducing activity in malignant cells.

Earlier investigations by Kao and associates provided complementary phytochemical data, demonstrating that phenolic compounds and flavonoids are abundant in aqueous peel extracts, whereas ethyl acetate extracts contain predominantly oleanolic acid (a pentacyclic triterpenoid), carotenoids, and chlorophylls [22]. This differential solubility profile enables selective extraction of specific phytochemical classes for targeted therapeutic applications.

Han and colleagues isolated lucyoside B, a triterpenoid saponin from *L. cylindrica*, and demonstrated its ability to inhibit the production of inflammatory mediators via both nuclear factor-κB (NF-κB) and activator protein-1 (AP-1) pathways in activated macrophages [23]. This finding identifies another specific bioactive constituent contributing to the anti-inflammatory properties of the plant.

3. Antioxidant activity

3.1 Assessment Methodologies and Quantitative Findings

The antioxidant capacity of *L. cylindrica* leaf extracts has been evaluated through multiple complementary in vitro assay systems, each measuring distinct aspects of free radical scavenging and oxidative stress mitigation. The 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical scavenging assay represents the most frequently employed methodology, providing a standardized, reproducible measure of hydrogen-donating capacity.

Onyegbule and colleagues reported concentration-dependent DPPH radical scavenging activity across three extract types, with percentage inhibition ranging from 41.46–58.68% for methanolic extract, 27.59–65.18% for ethyl acetate extract, and 37.58–66.29% for ethanolic extract across the concentration spectrum of 12.5–200 μg/mL [12]. The calculated IC50 values—the concentration required to achieve 50% radical scavenging—were 70 μg/mL for methanolic extract, 90 μg/mL for ethyl acetate extract, and 70 μg/mL for ethanolic extract. These values, while higher than the 20 μg/mL IC50 determined for ascorbic acid positive control, nonetheless demonstrate meaningful antioxidant capacity at pharmacologically achievable concentrations.

Ben Hlel and associates expanded the antioxidant assessment battery to encompass multiple mechanistic dimensions, including DPPH scavenging, metal chelating effect, hydroxyl radical scavenging, and superoxide anion scavenging activities [16]. Extracts derived from semi-arid region specimens (LE) demonstrated superior antioxidant performance across all assays, with DPPH IC50 of 54.41 ± 1.12 μg/mL and chelating effect IC50 of 12.12 ± 0.07 μg/mL. These values represent the most potent antioxidant parameters reported to date for *L. cylindrica* leaf extracts and correlate with the quantitatively superior phenolic content of these specimens.

Bharathidasan and colleagues evaluated aqueous peel extract across a broader concentration range (20–320 μg/mL), documenting progressive, dose-dependent increases in DPPH scavenging activity culminating in 69.34% inhibition at the maximum tested concentration [13]. While this investigation employed peel rather than leaf tissue, the fundamental phytochemical similarities between these plant parts support the generalizability of antioxidant findings.

Tripathi and colleagues evaluated the in vitro antioxidant activity of *L. cylindrica* leaf extract and demonstrated significant free radical scavenging capacity, correlating with

total phenolic and flavonoid content [24]. Du and colleagues previously identified antioxidant constituents in the fruits of *L. cylindrica*, including several phenolic compounds with pronounced radical scavenging activity [25].

3.2 Structure-Activity Relationships and Mechanistic Considerations

The observed antioxidant activity is predominantly attributable to the phenolic and flavonoid constituents identified in phytochemical profiling [26]. These compounds possess molecular architectures ideally suited for radical scavenging: aromatic rings bearing hydroxyl substituents that can donate hydrogen atoms or electrons to stabilize free radical species, with concomitant formation of resonance-stabilized phenoxyl radicals.

Flavonoids, including the recently identified myricetin, exhibit particularly efficient antioxidant activity attributable to several structural features: (1) the catechol moiety in the B-ring provides superior electron donation capacity; (2) the 2,3-double bond conjugated with the 4-oxo function enables electron delocalization across the molecule; and (3) the 3- and 5-hydroxyl groups facilitate metal chelation, thereby preventing transition metal-catalyzed hydroxyl radical formation via Fenton chemistry [27].

The metal chelation capacity documented by Ben Hlel and colleagues—achieving IC50 values as low as 12.12 µg/mL—carries particular physiological relevance [16]. Transition metals, particularly iron and copper, catalyze the conversion of relatively innocuous superoxide and hydrogen peroxide into the highly destructive hydroxyl radical. By sequestering these metal ions, *L. cylindrica* extracts may interrupt this pathogenic cascade at an early stage, preventing oxidative damage to lipids, proteins, and nucleic acids.

Sirisa-Ard and colleagues hypothesized that the observed antioxidant properties correlate with flavonoid content, further noting that the presence of metal ions in both conventional and ash-dried extracts may contribute to wound healing effects through mechanisms distinct from direct radical scavenging [15]. This observation invites investigation into potential interactions between phytochemical antioxidants and endogenous metal ions in tissue repair processes.

Sharma and colleagues previously demonstrated the free radical scavenging activity of methanolic extract of *L. cylindrica* leaves, establishing a correlation between total phenolic content and antioxidant capacity [28]. Yadav and colleagues further characterized the phenolic profile and antioxidant activity of thermally processed sponge gourd using high-performance thin layer chromatography (HPTLC), demonstrating that processing conditions significantly influence the retention of bioactive phenolic compounds [29].

3.3 Comparative Antioxidant Efficacy and Contextual Factors

Considerable inter-study variability in reported antioxidant parameters necessitates careful contextual interpretation. Extract concentration units (µg/mL vs. mg/mL), reference standards (ascorbic acid, butylated hydroxytoluene, Trolox), and expression of results (percentage inhibition, IC50, ascorbic acid equivalents) differ substantially across investigations, complicating direct quantitative comparison.

Geographical origin emerges as a critical determinant of antioxidant potency. The superior performance of Tunisian semi-arid region specimens relative to arid-region counterparts [16] suggests that moderate environmental stress—insufficient water availability without reaching the threshold for severe growth impairment—upregulates secondary metabolite biosynthesis as an adaptive response. This phenomenon, well-documented in medicinal plant biology, carries practical implications for cultivation site selection and standardization of raw material.

Extraction solvent polarity significantly influences both phytochemical yield and resultant antioxidant activity. Methanol and ethanol, possessing intermediate polarity indices, optimally extract both phenolic acids and flavonoid glycosides, while aqueous extraction favors highly polar compounds including tannins and certain phenolic acids [12]. Ethyl acetate, with lower polarity, preferentially extracts aglycone flavonoids, terpenoids, and less polar phenolics, yielding distinct antioxidant profiles [30].

Bulbul and colleagues conducted a comparative study of in vitro antioxidant, antibacterial, and cytotoxic activity of *L. cylindrica* and *Luffa acutangula*, demonstrating that both species possess significant antioxidant capacity with variations attributable to differences in phytochemical composition [31].

4. Anti-inflammatory activity

4.1 In Vitro Evidence and Cellular Mechanisms

The anti-inflammatory properties of *L. cylindrica* leaf extracts have been rigorously evaluated through multiple in vitro experimental models, with accumulating evidence delineating specific molecular targets and signaling pathways modulated by extract constituents.

Kao and colleagues conducted foundational investigations utilizing LPS-stimulated RAW 264.7 murine macrophage cells, a well-established model for evaluating inflammatory responses [22]. Both ethanol and ethyl acetate extracts derived from peel and pulp tissues significantly decreased nitric oxide (NO) production in activated macrophages. Nitric oxide, synthesized by inducible nitric oxide synthase (iNOS), serves as a key inflammatory mediator with pleiotropic effects including vasodilation, cytotoxicity, and immunomodulation. Ethanol extracts additionally mitigated prostaglandin E2 (PGE2) secretion, implicating modulation of the cyclooxygenase-2 (COX-2) pathway. Notably, all tested extracts significantly inhibited interleukin-6 (IL-6) production, while failing to suppress interleukin-1β (IL-1β) or tumor necrosis factor-α (TNF-α) generation, suggesting selective rather than global suppression of the inflammatory cytokine cascade.

Mechanistic exploration revealed that ethyl acetate peel extract reduced iNOS expression, consistent with diminished NO production. However, a paradoxical enhancement of COX-2 expression was observed, contrasting with the anticipated suppression based on reduced PGE2 secretion. This dissociation between COX-2 protein expression and enzymatic activity suggests potential post-translational regulatory mechanisms or direct inhibition of COX-2 catalytic activity by extract constituents. Both ethyl acetate extracts attenuated phosphorylation of IκBα, the inhibitory protein sequestering NF-κB in the cytoplasm, indicating interference with the canonical NF-κB activation pathway. Pulp extract additionally suppressed ERK phosphorylation, while no extract inhibited JNK phosphorylation, demonstrating pathway-selective modulation of mitogen-activated protein kinase (MAPK) signaling.

Park and colleagues substantially advanced mechanistic understanding through investigation of *L. cylindrica* extract effects on BV2 microglial cells, a model system for neuroinflammation [18]. Their findings confirmed concentration-dependent NO reduction and extended mechanistic analysis to identify involvement of the AKT-GSK3β-CREB signaling axis. Extract treatment significantly reduced phosphorylation of AKT and its downstream substrate GSK3β, with consequent modulation of CREB (cAMP response element-binding protein) transcriptional activity. This signaling cascade, previously unrecognized as a target of *L. cylindrica* constituents, mediates inflammatory gene expression in central nervous system immune cells and represents a promising therapeutic target for neuroinflammatory conditions including Alzheimer's disease and other dementias.

Han and colleagues demonstrated that lucyoside B, a triterpenoid saponin isolated from *L. cylindrica*, inhibits the production of inflammatory mediators via both NF-κB and AP-1 pathways in activated macrophages [23]. This dual pathway inhibition suggests that multiple constituents contribute to the overall anti-inflammatory activity of the plant through complementary mechanisms.

Abirami and colleagues evaluated the wound healing and anti-inflammatory activity of the whole plant of *L. cylindrica* in rats, providing in vivo evidence supporting traditional uses [32]. Their findings demonstrated significant anti-inflammatory effects in carrageenan-induced paw edema models, corroborating the in vitro mechanistic studies.

4.2 In Vivo Evidence and Translational Relevance

The translational relevance of in vitro anti-inflammatory findings has been supported by emerging in vivo evidence. Park and colleagues administered oral *L. cylindrica* extract (50 or 300 mg/kg) to male ICR mice for seven days concomitant with intraperitoneal LPS challenge (0.5 mg/kg) [18]. Extract administration significantly ameliorated LPS-induced cognitive impairment as assessed by passive avoidance and Y-maze behavioral tests. Neurobiochemical analysis of hippocampal tissue revealed decreased inflammatory marker expression, corroborating the anti-inflammatory effects observed in cellular systems and extending them to the intact organism.

This investigation represents a significant translational advancement, demonstrating that orally administered extract achieves sufficient bioavailability to exert pharmacological effects within the central nervous system. The blood-brain barrier penetration of myricetin, identified as a major active constituent, has been previously documented, providing a plausible mechanistic basis for the observed neuroprotective effects.

Ha and colleagues demonstrated that *L. cylindrica* suppresses the development of *Dermatophagoides farinae*-induced atopic dermatitis-like skin lesions in Nc/Nga mice, providing

in vivo evidence for anti-inflammatory effects in a model of chronic allergic inflammation [33]. This study extends the therapeutic potential of *L. cylindrica* to dermatological inflammatory conditions.

Onyegbule and colleagues evaluated anti-inflammatory activity using the egg albumin denaturation inhibition assay, an in vitro model predictive of membrane-stabilizing and anti-inflammatory properties [12]. Methanol, ethyl acetate, and ethanol extracts demonstrated concentration-dependent inhibition of protein denaturation across the 12.5–200 mg/kg equivalent concentration range, with activity comparable to the diclofenac positive control. While this assay provides limited mechanistic specificity, it offers high-throughput screening capability and correlates reasonably with in vivo anti-inflammatory activity.

Bharathidasan and colleagues similarly employed protein denaturation inhibition methodology, documenting 85.23% inhibition at 800 μg/mL extract concentration [13]. This value represents the highest reported anti-inflammatory activity for *L. cylindrica* preparations, though direct comparison is complicated by differing concentration ranges and extract types across studies.

4.3 Specific Bioactive Constituents and Molecular Targets

The identification of specific phytochemicals responsible for anti-inflammatory activity has progressed substantially. Myricetin, isolated and characterized by Park and colleagues, independently demonstrated anti-inflammatory effects in microglial cells [18]. This flavonol has been previously documented to inhibit multiple pro-inflammatory pathways including NF-κB activation, MAPK phosphorylation, and NLRP3 inflammasome assembly, consistent with its identification as a major bioactive constituent of *L. cylindrica* leaves [19,20].

Oleanolic acid, identified by Kao and associates in ethyl acetate peel extracts, represents another established anti-inflammatory triterpenoid [22]. This pentacyclic compound has demonstrated efficacy in diverse inflammatory models through mechanisms including inhibition of phospholipase A2, suppression of iNOS and COX-2 expression, and antagonism of complement activation.

Ferulic acid, the predominant phenolic compound identified in Tunisian semi-arid region specimens [16], possesses well-characterized anti-inflammatory properties including radical scavenging, inhibition of pro-inflammatory cytokine production, and modulation of NF-κB transcriptional activity. The exceptionally high concentration documented (5128.5 μg/g) suggests that ferulic acid may contribute substantially to the anti-inflammatory effects of extracts derived from appropriately sourced plant material.

Lucyoside B, characterized by Han and colleagues, inhibits inflammatory mediator production through dual NF-κB and AP-1 pathway modulation [23]. This triterpenoid saponin represents a distinct structural class of anti-inflammatory constituents in *L. cylindrica* and contributes to the pleiotropic pharmacological profile of the plant.

Beta-carotene, evaluated through molecular docking studies by Bharathidasan and colleagues [13], demonstrated favorable binding characteristics with apoptosis-regulatory proteins. While this investigation focused primarily on anticancer applications, the established anti-inflammatory properties of carotenoids suggest potential dual therapeutic benefits.

Umehara and colleagues investigated the effects of phenolic constituents of *L. cylindrica* on UVB-damaged mouse skin, demonstrating protective effects against photo-inflammation and photo-aging [34]. This study provides evidence for the dermatological anti-inflammatory applications of *L. cylindrica* phenolics.

5. Antimicrobial activity

5.1 Antibacterial Spectrum and Potency

The antimicrobial properties of *L. cylindrica* leaf extracts have been investigated against diverse bacterial pathogens, with results demonstrating selective activity varying according to extract type, bacterial species, and methodological parameters.

Onyegbule and colleagues conducted comprehensive antibacterial evaluation against both Gram-positive and Gram-negative organisms [12]. Methanol, ethyl acetate, and ethanol extracts exhibited good antimicrobial activity against *Bacillus subtilis* (Gram-positive), *Staphylococcus aureus* (Gram-positive), *Escherichia coli* (Gram-negative), and *Salmonella typh* (Gram-negative). Among tested bacteria, *B. subtilis* demonstrated the highest sensitivity, with minimum inhibitory concentration (MIC) values of 25, 100, and 100 mg/mL for methanol, ethyl acetate, and ethanol extracts respectively. Against *S. aureus*, MIC values were 12.5 mg/mL (methanol), 12.5 mg/mL (ethyl acetate), and 100 mg/mL (ethanol). Against *S. typhi*, MIC values were 12.5, 50, and 100 mg/mL for methanol, ethyl acetate, and ethanol extracts respectively.

The investigators noted no reasonable activity against fungal test isolates, suggesting that *L. cylindrica* leaf extracts possess

selective antibacterial rather than broad-spectrum antifungal properties [12]. This selectivity may reflect fundamental differences in target site accessibility between bacterial and fungal cells or the absence of constituents with specific antifungal mechanisms.

Sirisa-Ard and colleagues extended these findings through comparative evaluation of conventional dried leaf extracts versus ash-dried preparations [15]. Both extract types demonstrated both bacteriostatic and bactericidal effects, indicating that the antibacterial principles retain activity even under the extreme thermal conditions of ash preparation. This observation carries significant ethnopharmacological relevance, as traditional preparation methods often involve heating, decoction, or combustion.

Akinwumi and colleagues, in their comprehensive review, noted that petroleum ether extract obtained from *L. cylindrica* leaves demonstrated antibacterial activity, while the ethyl acetate extract of the whole plant exhibited antifungal activity against certain dermatophytes [17]. This suggests that solvent selection and plant part utilized critically influence antimicrobial spectrum.

5.2 Factors Influencing Antibacterial Activity

Extraction solvent significantly influences antibacterial potency, with methanol and ethyl acetate extracts generally demonstrating superior activity compared to ethanol or aqueous preparations [12]. This pattern correlates with the differential solubility of phenolic compounds and flavonoids, suggesting that these phytochemical classes contribute substantially to observed antibacterial effects.

Notably divergent findings were reported in an earlier investigation evaluating cytotoxic and antibacterial activities of *L. cylindrica* leaf, stem, and seed fractions [35]. While ether fractions demonstrated potent cytotoxic activity against L1210 leukemia cells (ED50 3.5 µg/mL for leaf extract), antibacterial activity against *Streptococcus mutans* OMZ176 was characterized as insignificant across all tested fractions and plant parts. This apparent discrepancy with subsequently published studies may reflect species-specific bacterial susceptibility patterns, as *S. mutans*—an oral pathogen adapted to carbohydrate-rich environments—may possess distinct resistance mechanisms compared to enteric or cutaneous pathogens. Additionally, methodological differences including fractionation procedures, bacterial culture conditions, and susceptibility testing protocols may contribute to divergent outcomes.

Geographical origin and associated phytochemical profiles may also influence antibacterial efficacy. Specimens from semi-arid regions with enhanced phenolic accumulation [16] would be predicted to demonstrate superior antibacterial activity, though direct comparative antibacterial studies incorporating geographical provenance as an experimental variable remain to be conducted.

Aboh and colleagues conducted phytochemical screening and antifungal activity evaluation of leaves extracts of *L. cylindrica*, reporting moderate antifungal effects against certain fungal strains [36]. This finding contrasts with Onyegbule and colleagues' report of negligible antifungal activity [12], suggesting that antifungal efficacy may be strain-specific and influenced by extraction methodology.

5.3 Putative Mechanisms of Antibacterial Action

The antibacterial mechanisms of *L. cylindrica* extracts have not been definitively established through targeted mechanistic investigation, but reasonable inferences can be drawn from phytochemical composition and established antibacterial mechanisms of identified constituents.

Flavonoids, abundantly present in active extracts, exert antibacterial effects through multiple complementary mechanisms: (1) disruption of bacterial cell membrane integrity with consequent leakage of cytoplasmic contents; (2) inhibition of nucleic acid synthesis through topoisomerase interference; (3) suppression of energy metabolism and ATP synthesis; (4) attenuation of virulence factor expression; and (5) synergism with conventional antibiotics through efflux pump inhibition [37].

Phenolic acids, including the abundant ferulic acid documented in semi-arid region specimens [16], exhibit antibacterial activity through membrane disruption and intracellular acidification with consequent enzyme inhibition. Triterpenoids, such as oleanolic acid identified in ethyl acetate extracts [22], demonstrate activity against Gram-positive organisms through membrane-active mechanisms.

The observed differential susceptibility between Gram-positive and Gram-negative bacteria likely reflects the barrier function of the Gram-negative outer membrane, which restricts access of hydrophobic compounds to the cytoplasmic membrane and peptidoglycan layer. *B. subtilis* and *S. aureus*, both Gram-positive organisms lacking this additional permeability barrier, demonstrate greater susceptibility consistent with this mechanistic framework.

6. Emerging therapeutic applications

6.1 Anticancer Activity

Recent investigations have substantially expanded the therapeutic landscape for *L. cylindrica* leaf extracts beyond traditional indications to encompass anticancer applications. Abdel-Salam and colleagues conducted a series of investigations examining the cytotoxic effects of aqueous ethanol extract of *L. cylindrica* leaves against various cancer types [38-40].

In breast cancer research, Abdel-Salam and colleagues demonstrated that *L. cylindrica* leaf extract affects the expression of caspase-8, caspase-3, and the proliferation marker Ki67 in intrinsic molecular subtypes of breast cancer in vitro [38]. The extract exhibited selective cytotoxicity against breast cancer cells while sparing normal cells, suggesting a favorable therapeutic index. Further investigation revealed that the extract effectively targets cancer stem cells characterized by the CD44+/24- phenotype in breast cancer patients with various molecular subtypes [39]. This finding carries particular significance, as cancer stem cells are implicated in tumor initiation, metastasis, therapeutic resistance, and disease recurrence.

In hepatocellular carcinoma, Abdel-Salam and colleagues demonstrated the cytotoxicity of *L. cylindrica* leaf extract against circulating cancer stem cells [40]. The ability to target this particularly aggressive and therapy-resistant cell population suggests potential application in preventing metastasis and recurrence in liver cancer patients.

Ben Hlel and colleagues evaluated the anticancer activity of *L. cylindrica* leaf extracts against HeLa cervical cancer cell lines using xCELLigence real-time cell analyzer and lactate dehydrogenase cytotoxicity assay [16]. The antiproliferative capacity was time- and dose-dependent, with extracts from semi-arid region specimens (LE) presenting the lowest HeLa cell index (CI = 0.035 ± 0.018 at 250 μg/mL) and the best cytotoxic capacity (56.49 ± 0.8%). These findings correlate with the superior phenolic content of LE specimens and suggest that ferulic acid and other phenolic compounds contribute to the observed anticancer effects.

Bharathidasan and colleagues investigated the antioxidant and anti-inflammatory activity of *L. cylindrica* extract in the context of oral carcinoma [13]. Molecular docking studies revealed strong binding affinity of beta-carotene, a bioactive compound present in the extract, with BAX (-6.8 kcal/mol) and moderate binding with BCL2 (-5.8 kcal/mol), suggesting potential apoptosis-inducing activity in oral squamous cell carcinoma cells. The extract demonstrated potent antioxidant (69.34% DPPH inhibition at 320 μg/mL) and anti-inflammatory (85.23% protein denaturation inhibition at 800 μg/mL) activities, supporting its potential as a therapeutic adjunct in oral cancer management.

6.2 Neuroprotective and Cognitive Enhancement Effects

The investigation by Park and colleagues represents a significant advancement in understanding the neuroprotective potential of *L. cylindrica* leaf extract [18]. Using an LPS-induced mild cognitive impairment model, the study demonstrated that oral extract administration ameliorated cognitive deficits as assessed by passive avoidance and Y-maze behavioral tests. The identification of myricetin as a major active constituent, combined with mechanistic evidence of AKT-GSK3β-CREB pathway modulation, provides a molecular basis for the observed cognitive-enhancing effects.

This research opens new therapeutic avenues for *L. cylindrica* extracts in neuroinflammatory and neurodegenerative conditions, including Alzheimer's disease, Parkinson's disease, and age-associated cognitive decline. The demonstrated blood-brain barrier penetration of myricetin supports the translational potential of these findings.

6.3 Hepatoprotective Activity

Sharma and colleagues evaluated the hepatoprotective activity of *L. cylindrica* leaf extract in paracetamol-intoxicated rats [41]. The methanolic extract demonstrated significant protection against paracetamol-induced hepatotoxicity, as evidenced by reduced serum levels of hepatic enzymes (SGOT, SGPT, ALP) and bilirubin, along with improved antioxidant status. Histopathological examination confirmed reduced hepatocellular necrosis in extract-treated animals. These findings validate traditional uses of *L. cylindrica* for liver disorders and suggest potential applications in managing drug-induced hepatotoxicity.

6.4 Wound Healing Activity

Abirami and colleagues evaluated the wound healing and anti-inflammatory activity of the whole plant of *L. cylindrica* in rats [32]. The extract demonstrated significant wound contraction and reduced epithelialization time in excision wound models, along with increased breaking strength in incision wound models. These effects were attributed to the presence of flavonoids, triterpenoids, and other bioactive constituents that promote collagen synthesis, angiogenesis, and fibroblast proliferation. The wound healing activity provides scientific validation for traditional topical applications of *L. cylindrica* leaves.

6.5 Anthelmintic Activity

Tripathi and colleagues evaluated the in vitro antioxidant and anthelmintic activity of *L. cylindrica* leaf extract [24]. The extract demonstrated dose-dependent anthelmintic activity against *Pheretima posthuma*, with parameters including time of paralysis and time of death comparable to the standard drug piperazine citrate. This activity may be attributable to tannins and other phenolic compounds that interfere with energy metabolism in helminths.

7. Toxicological considerations and safety profile

Despite the widespread traditional use of *L. cylindrica* leaves, systematic toxicological evaluation has been limited until recently. Alim and colleagues conducted an integrated phytochemical and elemental assessment specifically addressing the therapeutic potential and toxicity threshold of *L. cylindrica* leaves [14].

Acute toxicity evaluation demonstrated moderate toxicity at a high dose (4000 mg/kg), suggesting that while the extract may be relatively safe at lower concentrations, caution is warranted at higher doses. The study recommended careful consideration of dosage and treatment duration to ensure safety and avoid adverse effects. Elemental analysis revealed the presence of essential minerals within acceptable limits, with no detection of toxic heavy metals at hazardous concentrations.

Nirmal and colleagues investigated nonpolar compounds from *L. cylindrica* and contributed to the phytochemical characterization that informs safety assessment [42]. Odioko and colleagues evaluated the acute toxicity of *L. cylindrica* fruit extract on African catfish (*Clarias gariepinus*) juveniles, providing ecotoxicological data relevant to environmental safety considerations [43].

The 2019 investigations by Abdel-Salam and colleagues on cytotoxic effects against cancer stem cells [39,40] included assessments of selective toxicity, demonstrating preferential cytotoxicity against malignant cells with relative sparing of normal cells. This selectivity profile is encouraging from a therapeutic safety perspective.

However, comprehensive toxicological evaluation following international guidelines (OECD) remains incomplete. Specific gaps include: (1) chronic toxicity studies with extended duration; (2) genotoxicity assessment through Ame's test, micronucleus assay, and chromosome aberration tests; (3) reproductive and developmental toxicity screening; (4) carcinogenicity bioassays; and (5) clinical safety monitoring in human subjects. These gaps must be addressed to support regulatory approval for therapeutic applications.

8. Discussion and future perspectives

8.1 Integration of Findings and Mechanistic Synthesis

The accumulated evidence reviewed herein establishes *L. cylindrica* leaf extracts as promising sources of bioactive phytochemicals with documented antioxidant, anti-inflammatory, antibacterial, anticancer, neuroprotective, hepatoprotective, and wound healing activities. These pharmacological properties are neither random nor independent but rather represent interconnected manifestations of underlying phytochemical composition.

The antioxidant activity, mediated predominantly by phenolic compounds and flavonoids, contributes mechanistically to anti-inflammatory effects through multiple pathways: (1) direct scavenging of reactive oxygen and nitrogen species that serve as inflammatory signaling molecules; (2) prevention of oxidative activation of pro-inflammatory transcription factors including NF-κB and AP-1; (3) preservation of cellular redox homeostasis and antioxidant enzyme function; and (4) mitigation of oxidative damage to biomolecules that would otherwise perpetuate inflammatory cascades.

Similarly, the anti-inflammatory activity contributes to antimicrobial efficacy through attenuation of pathogen-induced inflammatory pathology without necessarily exerting direct microbicidal effects. This immunomodulatory mechanism, wherein the host inflammatory response is calibrated to eliminate pathogens while minimizing tissue damage, represents an underexplored dimension of *L. cylindrica* pharmacology.

The identification of myricetin as a major bioactive constituent with both antioxidant and anti-inflammatory activities provides a phytochemical bridge linking these pharmacological domains [18]. This multifunctional flavonoid exemplifies the concept of "polypharmacology" wherein a single molecule modulates multiple therapeutic targets, offering potential advantages over highly selective agents in complex disease states characterized by concurrent oxidative stress and inflammation.

The emerging anticancer applications, particularly the targeting of cancer stem cells by Abdel-Salam and colleagues [39,40] and the apoptosis modulation demonstrated by Bharathidasan and colleagues [13], suggest that *L. cylindrica* constituents may modulate fundamental cellular processes including proliferation, differentiation, and programmed cell death. The molecular docking studies with beta-carotene provide preliminary evidence for direct interactions with

apoptosis-regulatory proteins, though confirmatory biochemical studies are required.

8.2 Research Gaps and Methodological Limitations

Despite substantial progress in characterizing the pharmacological properties of *L. cylindrica* leaf extracts, significant knowledge gaps and methodological limitations persist and should be addressed in future investigations.

Standardization deficits: Current literature reveals substantial heterogeneity in extract preparation methodologies, phytochemical characterization approaches, and bioassay protocols. The absence of standardized reference extracts, authenticated marker compounds, and validated analytical methods precludes meaningful quantitative comparison across studies and impedes regulatory advancement toward clinical applications. Marker-based standardization using myricetin, ferulic acid, oleanolic acid, or lucyoside B as reference compounds should be prioritized.

Limited in vivo data: While recent investigations have incorporated animal models [18,32,33,41], the majority of published studies remain confined to in vitro systems. Comprehensive pharmacokinetic profiling—including absorption, distribution, metabolism, and excretion parameters—remains conspicuously absent. Dose-response relationships, bioavailability determinations, identification of circulating metabolites, and tissue distribution studies represent critical translational prerequisites.

Incomplete mechanistic elucidation: Although signaling pathways including AKT-GSK3β-CREB [18], NF-κB [22,23], and AP-1 [23] have been implicated, the precise molecular targets of individual phytochemical constituents remain incompletely characterized. The majority of mechanistic studies have employed complex extracts rather than isolated compounds, making attribution of specific effects to particular constituents challenging. Advanced approaches including chemical proteomics, cellular thermal shift assays (CETSA), surface plasmon resonance, and CRISPR-based genetic screening could accelerate target identification and mechanism-of-action validation.

Limited structure-activity relationship studies: While numerous bioactive constituents have been identified, systematic structure-activity relationship investigations examining how specific structural features influence pharmacological activity have not been conducted. Such studies would inform rational design of semi-synthetic derivatives with enhanced potency, selectivity, and pharmacokinetic properties.

Toxicological insufficiency: Systematic toxicological evaluation following international regulatory guidelines has not been comprehensively conducted. While traditional use suggests favorable safety profiles and recent studies provide preliminary acute toxicity data [14], regulatory approval for therapeutic applications requires rigorous toxicological characterization including chronic toxicity, genotoxicity, reproductive toxicity, and carcinogenicity studies.

Clinical translation gap: Published investigations remain exclusively preclinical, with no registered clinical trials evaluating *L. cylindrica* leaf extracts in human subjects. The evidentiary gap between promising preclinical findings and documented clinical efficacy must be addressed through appropriately designed phase I/II clinical studies evaluating safety, tolerability, pharmacokinetics, and preliminary efficacy in relevant patient populations.

Quality control and adulteration risks: The absence of pharmacopoeial monographs and validated analytical methods for *L. cylindrica* leaf extracts creates risks of adulteration, substitution, and inconsistent product quality. Development of chromatographic fingerprinting methods, DNA barcoding techniques, and validated quantitative assays for marker compounds is urgently needed.

8.3 Future Research Directions

Based on the identified knowledge gaps and emerging research trends, several priority directions for future investigation are proposed.

Metabolomics-guided phytochemical profiling: Contemporary analytical platforms, including ultra-high-performance liquid chromatography coupled with high-resolution mass spectrometry (UHPLC-HRMS/MS) and nuclear magnetic resonance spectroscopy (NMR), enable comprehensive metabolomic characterization of complex plant extracts. Application of these methodologies to *L. cylindrica* leaves would facilitate identification of minor constituents that may contribute to observed pharmacological effects through additive or synergistic interactions. Metabolomics approaches can also be employed to correlate phytochemical profiles with bioactivity, identifying previously unrecognized bioactive constituents.

Bioavailability enhancement strategies: The therapeutic potential of myricetin and other bioactive flavonoids is constrained by limited oral bioavailability attributable to poor aqueous solubility, extensive phase II metabolism (glucuronidation, sulfation), and active efflux transport (P-glycoprotein, MRPs). Nanotechnological formulations—

including polymeric nanoparticles, liposomes, phytosomes, solid lipid nanoparticles, and nanoemulsions—warrant investigation as delivery systems to enhance systemic exposure and therapeutic efficacy. Prodrug strategies to mask metabolically susceptible functional groups also merit exploration.

Combination therapy investigations: The demonstrated antibacterial activity of *L. cylindrica* extracts against clinically relevant pathogens invites investigation of potential synergism with conventional antibiotics. Such combinations may enable dose reduction of toxic antimicrobial agents, resensitization of resistant organisms, and expansion of therapeutic spectrum. Checkerboard assays and time-kill curve studies should be employed to characterize synergistic, additive, or antagonistic interactions.

Expanded therapeutic applications: The recent identification of neuroprotective effects in cognitive impairment models [18], apoptosis-modulating activity in oral carcinoma cells [13], cancer stem cell targeting in breast and hepatocellular carcinoma [38-40], hepatoprotective effects [41], and wound healing activity [32] suggests broader therapeutic applications beyond traditional indications. Systematic evaluation of anticancer (with emphasis on apoptosis induction, cell cycle arrest, metastasis inhibition, and angiogenesis modulation), neuroprotective (with emphasis on microglial modulation, amyloid-β clearance, and tau phosphorylation), metabolic (with emphasis on glucose homeostasis and lipid metabolism), and immunomodulatory (with emphasis on macrophage polarization and T-cell regulation) activities represents a fertile area for future investigation.

Sustainable production and biotechnological approaches: The pronounced geographical variation in phytochemical content and bioactivity [16] necessitates development of strategies ensuring consistent, high-quality raw material production. Controlled environment cultivation with optimized irrigation, nutrient management, and light conditions; elicitor treatment (methyl jasmonate, salicylic acid, chitosan) to upregulate secondary metabolite biosynthesis; and in vitro propagation systems (callus culture, cell suspension culture, hairy root culture) merit investigation as approaches to optimize bioactive constituent accumulation independent of environmental stochasticity.

Network pharmacology and systems biology approaches: Given the multi-component, multi-target nature of plant extracts, network pharmacology approaches integrating phytochemical profiling, target prediction, protein-protein interaction networks, and pathway enrichment analysis can provide holistic understanding of the pharmacological mechanisms of *L. cylindrica* extracts. Such approaches may reveal unexpected relationships between traditional uses and modern therapeutic applications.

Ethnopharmacological directed discovery: Systematic documentation and bioassay-guided investigation of traditional preparation methods and specific therapeutic indications can yield clinically relevant leads. The demonstration that ash-dried preparations retain antibacterial activity [15] validates traditional processing methods and suggests that other traditional preparations warrant similar scientific investigation.

9. Conclusion

The collective scientific evidence substantiates the traditional medicinal applications of *Luffa cylindrica* leaves and reveals previously unrecognized pharmacological activities with therapeutic potential. Leaf extracts demonstrate concentration-dependent antioxidant activity across multiple assay systems, with efficacy correlating with phenolic and flavonoid content. Anti-inflammatory effects are mediated through modulation of NO, PGE2, and IL-6 production via interference with AKT-GSK3β-CREB, NF-κB, and AP-1 signaling pathways, with downregulation of iNOS and COX-2 expression. Antibacterial activity is selectively effective against Gram-positive organisms (*B. subtilis*, *S. aureus*) and certain Gram-negative pathogens (*E. coli*, *S. typhi*), while antifungal effects appear limited and strain-dependent.

Geographical origin, extraction methodology, and plant part selection critically influence phytochemical profiles and resultant bioactivity, with semi-arid cultivation conditions and intermediate-polarity solvent systems generally yielding superior pharmacological performance. Myricetin, ferulic acid, oleanolic acid, lucyoside B, and beta-carotene have been identified as bioactive constituents contributing to the observed therapeutic effects.

Emerging evidence for anticancer activity—particularly against breast cancer, hepatocellular carcinoma, cervical cancer, and oral carcinoma—with selective targeting of cancer stem cells represents a significant expansion of the therapeutic landscape for *L. cylindrica* extracts. Similarly, neuroprotective effects in cognitive impairment models, hepatoprotective activity, and wound healing properties provide scientific validation for additional traditional uses and suggest novel clinical applications.

While substantial progress has been achieved in phytochemical and pharmacological characterization,

translation of these preclinical findings into clinical applications requires addressing persistent gaps in standardization, mechanistic elucidation, toxicological profiling, bioavailability assessment, and clinical validation. The emerging evidence of neuroprotective and anticancer activities, coupled with the established antioxidant, anti-inflammatory, and antimicrobial properties, positions *L. cylindrica* leaf extracts as promising candidates for continued pharmaceutical development and potential integration into evidence-based complementary medicine. Systematic, methodologically rigorous investigation guided by contemporary pharmacological paradigms and regulatory requirements will be essential to realize the full therapeutic potential of this versatile medicinal plant.

References

[1] Partap S, Kumar A, Sharma NK, Jha KK. *Luffa cylindrica*: An important medicinal plant. J Nat Prod Plant Resour. 2012;2(1):127-134.

[2] Lim TK. *Luffa cylindrica*. In: Edible Medicinal and Non-Medicinal Plants. Dordrecht: Springer; 2012. p. 240-257. DOI: 10.1007/978-94-007-1764-0_46

[3] Mazali IO, Alves OL. Morphosynthesis: High fidelity inorganic replica of the fibrous network of loofa sponge (*Luffa cylindrica*). An Acad Bras Cienc. 2005;77(1):25-31. DOI: 10.1590/S0001-37652005000100003

[4] Achigan-Dako EG, N'Danikou S, Vodouhê RS. *Luffa cylindrica* (L.) M.Roem. In: Brink M, Achigan-Dako EG, editors. PROTA (Plant Resources of Tropical Africa/Ressources Végétales de l'Afrique Tropicale). Wageningen, Netherlands: PROTA; 2011. Available from: http://www.prota4u.org/search.asp

[5] Duke JA. CRC Handbook of Medicinal Herbs. 2nd ed. Boca Raton: CRC Press; 2002. p. 30-35. DOI: 10.1201/9781420040463

[6] Akinwumi KA, Eleyowo OO, Oladipo OO. A review on the ethnobotanical uses, phytochemistry and pharmacological effect of *Luffa cylindrinca*. In: El-Shemy HA, editor. Natural Drugs from Plants. London: IntechOpen; 2021. DOI: 10.5772/intechopen.98405

[7] Sutharshana V. Protective role of *Luffa cylindrica*. J Pharm Sci Res. 2013;5(9):184-186.

[8] Stephens JM. Ground Luffa. J Hortic Sci. 2003; 3:19-21.

[9] Middleton E Jr, Kandaswami C, Theoharides TC. The effects of plant flavonoids on mammalian cells: Implications for inflammation, heart disease, and cancer. Pharmacol Rev. 2000;52(4):673-751.

[10] Muthumani P, Meera R, Subin Mary Jeenamathew, Devi P, Kameswari B, Eswara Priya B. Phytochemical screening, anti-inflammatory, bronchodilator and antimicrobial activities of the seeds of *Luffa cylindrica*. Res J Pharm Biol Chem Sci. 2010;1(4):11-22.

[11] Gandhamalla P, Shiva GB, Pravalika R, Ramya DM, Boggula N. Plant preliminary phytochemical analysis and thrombolytic screening of *Luffa cylindrica* Linn. fruits: An in-vivo study. IJIPSR. 2018;6(1):61-74.

[12] Onyegbule FA, Okoye C, Ikeh C, Umeokoli BO, Emezie AU. Evaluation of phytochemicals, antimicrobial, anti-inflammatory and antioxidant activities of extracts of *Luffa cylindrica* leaves. Planta Med. 2014;80: LP17. DOI: 10.1055/s-0034-1395077

[13] Bharathidasan P, Ranganathan P, Singh R, Barman P, Randhawa S, Chauhan M. Phytochemical screening, antioxidant, and anti-inflammatory activity of *Luffa cylindrica* extract in oral carcinoma: An in vitro and in silico analysis. J Contemp Dent Pract. 2025;26(4):356-361. DOI: 10.5005/jp-journals-10024-3856

[14] Alim MCH, Ifeoma MR, Ikechukwu OR, William Chukwuka O, Uchendu N. The therapeutic potential and toxicity threshold of *Luffa cylindrica* (L) Reom leaves: An integrated phytochemical and elemental assessment. Afr J Biol Sci. 2025;7(8):373-400. DOI: 10.48047/AFJBS.7.8.2025.373-400

[15] Sirisa-Ard P, Pholsonklam K, Xuyen DT, Hang DTD, Chinh VD, et al. Chemical composition, antibacterial and antioxidant activities of extracts from dry leaves and ash-dry leaves of *Luffa cylindrica* (L.) Roem cultivated in Vietnam. Asian J Res Med Pharm Sci. 2023;12(4):38-51. DOI: 10.9734/AJRIMPS/2023/v12i4231

[16] Ben Hlel T, Belhadj F, Gül F, Altun M, Şahin Yağlıoğlu A, Smaali I, et al. The molecular characterization and biological assessment of the leaves extracts of loofah reveal their nutraceutical potential. Recent Pat Food Nutr Agric. 2021;12(1):63-72. DOI: 10.2174/2212798412666210108113338

[17] Akinwumi KA, Eleyowo OO, Oladipo OO. A review on the ethnobotanical uses, phytochemistry and pharmacological effect of *Luffa cylindrinca*. In: El-Shemy HA, editor. Natural Drugs from Plants. London: IntechOpen; 2022. DOI: 10.5772/intechopen.98405

[18] Park J, Kim Y, Lee JE, Kim YT. Effects of *Luffa cylindrica* (L.) Roem extract on microglial activation-mediated mild cognitive impairment via regulation of CREB signaling pathway. J Microbiol Biotechnol. 2025;35: e2506049. DOI: 10.4014/jmb.2506.06049

[19] Semwal DK, Semwal RB, Combrinck S, Viljoen A. Myricetin: A dietary molecule with diverse biological activities. Nutrients. 2016;8(2):90. DOI: 10.3390/nu8020090

[20] Song X, Tan L, Wang M, Ren C, Guo C, Yang B, et al. Myricetin: A review of the most recent research. Biomed Pharmacother. 2021; 134:111017. DOI: 10.1016/j.biopha.2020.111017

[21] Raut NA, Gaikwad NJ. Antihyperlipidemic, antioxidant and anti-inflammatory activities of β-carotene and its combination with statins in experimental animals. Int J Pharm Pharm Sci. 2018;10(7):127-132.

[22] Kao TH, Huang CW, Chen BH. Functional components in *Luffa cylindrica* and their effects on anti-inflammation of macrophage cells. Food Chem. 2012;135(2):386-395. DOI: 10.1016/j.foodchem.2012.04.128

[23] Han Y, Zhang X, Qi R, Li X, Gao Y, Zou Z, Cai R, Qi Y. Lucyoside B, a triterpenoid saponin from *Luffa cylindrica*, inhibits the production of inflammatory mediators via both nuclear factor-κB and activator protein-1 pathways in activated macrophages. J Funct Foods. 2020; 69:103941. DOI: 10.1016/j.jff.2020.103941

[24] Tripathi A, Tandon M, Chandekar A, Soni N, Upmanyu N. In vitro antioxidant and anthelmintic activity on *Luffa cylindrica* leaf extract. J Herbs Spices Med Plants. 2016;22(4):348-355. DOI: 10.1080/10496475.2016.1224211

[25] Du Q, Xu Y, Li L, Zhao Y, Jerz G, Winterhalter P. Antioxidant constituents in the fruits of *Luffa cylindrica* (L.) Roem. J Agric Food Chem. 2006;54(12):4186-4190. DOI: 10.1021/jf0604790

[26] Sofidiya MO, Odukoya OA, Familoni OB, Inya-Agha SI. Free radical scavenging activity of some Nigerian medicinal plant extracts. Pak J Biol Sci. 2006; 9:1438-1441.

[27] Bors W, Heller W, Michel C, Saran M. Flavonoids as antioxidants: Determination of radical-scavenging efficiencies. Methods Enzymol. 1990; 186:343-355. DOI: 10.1016/0076-6879(90)86128-i

[28] Sharma NK, Sangh P, Jha KK, Singh HK, Shrivastava AK. Free radical scavenging activity of methanolic extract of *Luffa cylindrica* leaves. Int J Green Pharm. 2012;6(3):231-234. DOI: 10.4103/0973-8258.104938

[29] Yadav R, Yadav BS, Yadav RB. Phenolic profile and antioxidant activity of thermally processed sponge gourd (*Luffa cylindrica*) as studied by using high performance thin layer chromatography (HPTLC). Int J Food Prop. 2016;20(9):2096-2112. DOI: 10.1080/10942912.2016.1230872

[30] Nirmal SA, Kothawade PC, Datir SB, Pal SC, Mandal SC, Pattan SR. Nonpolar compounds from *Luffa cylindrica*. Facta Univ Ser Phys Chem Technol. 2009;7(1):69-72. DOI: 10.2298/FUPCT0901069N

[31] Bulbul J, Zulfiker A, Hamid K, Khatun M, Begum Y. Comparative study of in vitro antioxidant, antibacterial and cytotoxic activity of two Bangladeshi medicinal plants—*Luffa cylindrica* L. and *Luffa acutangula*. Pharmacogn J. 2011;3(23):59-66. DOI: 10.5530/pj.2011.23.9

[32] Abirami MS, Indhumathy R, Devi GS, Kumar DS, Sudarvoli M, Nandini R. Evaluation of the wound healing and anti-inflammatory activity of whole plant of *Luffa cylindrica* (Linn) in rats. Pharmacologyonline. 2011; 3:281-285.

[33] Ha H, Lim HS, Lee MY, Shin IS, Jeon WY, Kim JH, Shin HK. *Luffa cylindrica* suppresses development of *Dermatophagoides farinae*-induced atopic dermatitis-like skin lesions in Nc/Nga mice. Pharm Biol. 2015;53(4):555-562. DOI: 10.3109/13880209.2014.932392

[34] Umehara M, Yamamoto T, Ito R, Nonaka S, Yanae K, Sai M. Effects of phenolic constituents of *Luffa cylindrica* on UVB-damaged mouse skin and on dome formation by MDCK I cells. J Funct Foods. 2018; 40:477-483. DOI: 10.1016/j.jff.2017.11.027

[35] Anonymous. Cytotoxic and antibacterial activities of *Luffa cylindrica* leaf, stem and seed extracts. Korean J Pharmacogn. 1991;22(4).

[36] Aboh MI, Oladosu P, Adeshina G, Olayinka B, Olonitola SO. Phytochemical screening and antifungal activity of leaves

extracts of *Luffa cylindrica* (Roem). Afr J Microbiol Res. 2017;11(44):1681-1687.

[37] Cushnie TPT, Lamb AJ. Antimicrobial activity of flavonoids. Int J Antimicrob Agents. 2005;26(5):343-356. DOI: 10.1016/j.ijantimicag.2005.09.002

[38] Abdel-Salam IM, Ashmawy AM, Hilal AM, Eldahshan OA, Ashour M. Chemical composition of aqueous ethanol extract of *Luffa cylindrica* leaves and its effect on representation of caspase-8, caspase-3, and the proliferation marker Ki67 in intrinsic molecular subtypes of breast cancer in vitro. Chem Biodivers. 2018;15(8): e1800045. DOI: 10.1002/cbdv.201800045

[39] Abdel-Salam IMB, Abou-Bakr AA, Ashour M. Cytotoxic effect of aqueous ethanol extract of *Luffa cylindrica* leaves on cancer stem cells CD44+/24- in breast cancer patients with various molecular sub-types using tissue samples in vitro. J Ethnopharmacol. 2019; 238:111877. DOI: 10.1016/j.jep.2019.111877

[40] Abdel-Salam IMA, Awadein NE, Ashour M. Cytotoxicity of *Luffa cylindrica* (L.) M. Roem. extract against circulating cancer stem cells in hepatocellular carcinoma. J Ethnopharmacol. 2019; 229:89-96. DOI: 10.1016/j.jep.2018.09.034

[41] Sharma NK, Priyanka KKJ, Singh HK, Shrivastava AK. Hepatoprotective activity of *Luffa cylindrica* (L.) MJ Roem. leaf extract in paracetamol intoxicated rats. Indian J Nat Prod Resour. 2014;5(2):143-148.

[42] Nirmal SA, Kothawade PC, Datir SB, Pal SC, Mandal SC, Pattan SR. Nonpolar compounds from *Luffa cylindrica*. Facta Univ Ser Phys Chem Technol. 2009;7(1):69-72. DOI: 10.2298/FUPCT0901069N

[43] Odioko E, Sikoki FD, Vincent-Akpu IF, Utibe DI. Acute toxicity of sponge plant (*Luffa cylindrica*) fruit extract on African catfish (*Clarias gariepinus*, Buchell 1822) juveniles. Int J Life Sci Res. 2016;4(1):148-159.