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A COMPREHENSIVE REVIEW ON *ACALYPHA INDICA*: TRADITIONAL USES AND PHARMACOLOGICAL PROPERTIES

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ABSTRACT: *Acalypha indica*, an herbaceous plant indigenous to tropical areas, has been extensively utilized in traditional medicine for the treatment of various health issues. This review presents a thorough overview of its medicinal attributes, phytochemical composition, and pharmacological effects, emphasizing its promise in drug development. Extracts from this plant have shown notable anti-inflammatory, antimicrobial, antioxidant, and anticancer activities, positioning it as a viable candidate for innovative therapeutic solutions. Historically, *Acalypha indica* has been employed in traditional practices for healing wounds, addressing respiratory ailments, and managing gastrointestinal disorders. Phytochemical investigations have revealed significant bioactive compounds, such as flavonoids, alkaloids, tannins, and anthraquinones, which play a role in its pharmacological properties. Preclinical research has assessed its effectiveness against bacterial and fungal infections, diseases related to oxidative stress, and cancer, yielding promising outcomes. However, obstacles such as the need for extract standardization, concerns regarding toxicity, and a scarcity of clinical studies impede its advancement. Future investigations should aim to clarify its mechanisms of action, refine dosage formulations, and conduct clinical trials to confirm its efficacy and safety. By overcoming these challenges, *Acalypha indica* has the potential to become a significant asset in contemporary medicine, providing a natural alternative for disease management and drug development. This review highlights the need for further scientific inquiry and pharmaceutical exploration.

INTRODUCTION: Primitive societies perceived natural products as valuable assets and harnessed them to combat human diseases. The role of plant-based products in human development is crucial, as they meet essential needs and foster health.

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Medicinal plants are known for their therapeutic benefits and form the cornerstone of various medical practices, such as Ayurvedic and Homeopathic medicine.

Approximately one-quarter of all medications are derived from plant sources [1, 2]. These natural products are associated with fewer adverse effects, reduced costs, and a growing demand for their therapeutic effectiveness. Historically, plants have been integral to human life, providing food and essential items, including paper, construction

materials, finely ground spices, and serving various purposes in the prevention and treatment of a wide range of ailments [3, 4]. The medicinal plants sector on a global scale is witnessing significant expansion, with an estimated valuation of approximately USD 165.66 billion in 2022 (Grand View Research, 2023). This growth is attributed to the heightened demand for natural and organic products, the prevalence of chronic diseases, and an increasing acceptance of traditional medicinal practices (Transparency Market Research, 2023). Projections indicate that by 2030, the industry could achieve a remarkable valuation of USD 347.50 billion, accompanied by a compound annual growth rate (CAGR) of 11.16% (Fortune Business Insights, 2023) [5]. Plant-based remedies are crucial for the advancement of humanity, functioning as a key element alongside basic necessities like food, water, and shelter. The health of individuals, which is a vital requirement, largely depends on natural resources [6, 7]. The secondary metabolism of plants is exceptionally complex, establishing them as a primary source of medicinal compounds since the dawn of humanity, while also maintaining a substantial economic significance [8].

The use of medicinal plants is a common practice across various cultures, aimed at sustaining physical, mental, and spiritual health in multiple contexts. These plants include those that have one or more components that yield compounds with clinically validated therapeutic properties, which can be applied directly or utilized as precursors in the synthesis of pharmaceuticals. Additionally, there are other plants that, despite lacking formal validation, are believed to possess therapeutic potential [9]. The plant *Acalypha indica* L. is a well-known traditional plant belonging to the family Euphorbiaceae also known as 'Indian copper leaf' or 'Indian mercury' [10, 11]. *Acalypha indica* is recognized as a weed species that possesses significant medicinal properties beneficial for human health. This plant is commonly found in regions such as India, Sri Lanka, Thailand, and Pakistan [12]. *Acalypha indica* has a long history of traditional use in the treatment of various ailments, including infertility, as an antivenom, for wound healing, as an antioxidant, to reduce inflammation, for its diuretic properties, and in combating bacterial infections and cancer. It is rich in phytoconstituents such as polyphenols, flavonoids, alkaloids, saponins, terpenoids, and tannins, which are typically present in different parts of the plant, including the roots, leaves, and shoots [13, 14]. Extensive research has been carried out to investigate the medicinal attributes of *Acalypha indica*. The purpose of this review is to consolidate the benefits, applications, and scientific findings associated with this plant, underscoring its relevance in herbal medicine.

Taxonomic Classification [15]:

Kingdom: Plantae

Class: Magnoliopsida

Order: Euphorbiales

Family: Euphorbiaceae

Genus: Acalypha

Species: *Acalypha indica* Linn.

Vernacular Names: *Acalypha indica* is identified by several local names internationally, as shown in **Table 1**. In nations such as India, Malaysia, Indonesia, and Thailand, the plant is known by different names that are influenced by regional accents, ethnic diversity, and cultural practices. European countries like Britain, Spain, France, and Germany also have their own specific names for *Acalypha indica*. Nonetheless, its prevalence in consumption is greater in Asia and Africa than in Europe [16].

TABLE 1: VERNACULAR NAMES OF THE PLANT

Local name	Country
Kuppaimeni	India
Alcalifa	Brazil
Tie Xian	China
Muktajhuri	Bangladesh
Kuppameniya	Sri Lanka
Muktabarshijhar	Nepal
KucingGalak, Lis-lis, ChekaEmas	Malaysia
Tamyae Tuaphuu, Tamyae Maeo, Haan Maeo	Thailand
Ricinela	Spain
IndischesBrennkraut	German
Ricinelle Des Indes, Oreille De Chatte, Herba Chatte	France
Ntlambissana	Mozambique
English Indian Acalypha, Indian Nettle, Three-Seeded Mercury	Britain
Baro, Berbere	Ethiopia
Tai Tuw Owjng Aasn, Tai TuwOwnjng Xanh	Vietnam
Maraotong, Bugos, Taptapingar	Philippines
Horrisa	Djibouti

Geographical Sources: *Acalypha indica* is a medicinal plant that is extensively recognized and distributed, particularly among older generations in diverse regions, notably in Asia and Africa. It flourishes in the northeastern, western, and southern regions of Africa, including Ethiopia and Somalia.

Additionally, it is commonly found in moist, temperate, and tropical areas across Asia, Europe, and both North and South America. The plant typically appears as a weed in residential gardens, shrublands, along roadways, and in various natural environments [16].

Pharmacognostical Study:

Macroscopic Study: Based on the observations, *Acalypha indica*, which was collected from the Hubli-Dharwad region, is characterized as an erect annual herb, reaching heights of 30 to 60 cm. The leaves exhibit a dark green coloration on the upper surface and a lighter green on the lower surface, featuring a smooth texture and serrate-crenate edges. They are either ovate or rhombic-ovate in shape, measuring between 3 to 6 cm in length and 3 to 4 cm in width, with slender petioles that are frequently longer than the leaf blades.

The plant emits a distinctive and acceptable fragrance. The male flowers are small and grouped at the apex, while the female flowers are accompanied by broad, leafy bracts that increase in size. The capsules are typically one-seeded and hidden within the bracts, with the seeds being pale brown, ovoid, pointed, and smooth [17].

Microscopical Study: The transverse section of the *Acalypha indica* leaf displays a single-layered upper and lower epidermis characterized by a robust cuticle. The mesophyll is composed of a compact, single-layered palisade parenchyma and a multi-layered spongy parenchyma featuring intercellular spaces. Beneath the vascular bundle, one can observe thick-walled collenchymatous cells.

The vascular bundle is arranged with xylem positioned adjacent to the upper epidermis, phloem adjacent to the lower epidermis, and xylem parenchyma interspersed among the xylem cells. Additionally, multicellular trichomes are present on the lower epidermis.

The stem exhibits a circular transverse section, featuring a single-layered epidermis, alternating cork cells, and well-developed xylem fibers. Notably, the root does not contain a pith [17].

Quantitative Microscopy: Quantitative microscopy conducted on the leaf of *Acalypha indica* has unveiled distinct characteristics essential for the identification and characterization of the leaf crude drug. These characteristics include the stomatal index, vein islet number, and vein termination number.

The study determined that the stomatal index for the upper surface ranged from 15 to 16, whereas for the lower surface, it ranged from 17 to 18. Additionally, the vein islet number was identified as 2 to 3, and the vein termination number was recorded as 16 to 17, all of which serve as unique identifiers [17].

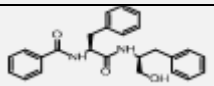
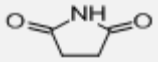
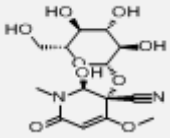
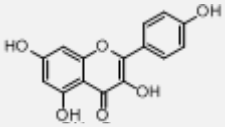
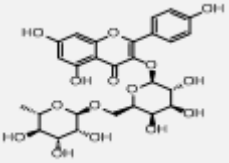
Powder Microscopy: Analysis of the dried powder from *Acalypha indica* demonstrated the presence of large lignified fibers with walls that were moderately thickened. The epidermal cells contained paracytic stomata. Calcium oxalate crystals were identified as being square in shape.

A significant number of xylem vessels were observed, which were bordered, thickened, and frequently associated with other xylem elements. Furthermore, trichomes were abundant, and the medullary rays were found to be parenchymatous and multiseriate [17].

Phytochemistry: Phytochemical studies were conducted on the extracts and fractions of *Acalypha indica* through qualitative chemical tests to identify a range of phytoconstituents. The findings confirmed the existence of Alkaloids, Steroids, Flavonoids, Glycosides, Tannins and Carbohydrates. Furthermore, the identified chemical constituents include Aurantiamide, Succinimide, Acalyphin, Kaempferol, Biorobin, Acalyphamide, and Nicotiflorin. The structures of these compounds are detailed in **Table 2**.

These constituents play a significant role in the plant's wide-ranging medicinal properties, which encompass antioxidant, antimicrobial, anti-inflammatory, and antidiabetic effects [17, 18].

TABLE 2: CHEMICAL COMPOSITION OF *ACALYPHA INDICA*

Phytoconstituent	Structure
Aurantiamide	
Succinimide	
Acalyphin	
Kaempferol	
Biorobin	
Acalyphamide	

Extraction Techniques: The extraction of *Acalypha indica* was carried out using various methods. A summary of these reported methods can be found in **Table 3**.

TABLE 3: EXTRACTION SUMMARY

Sl. no.	Extraction method	Solvent system	Ref.
1	Hot percolation method	Petroleum ether, Chloroform and methanol	19
2	Soxhlet method	Hexane, chloroform, Acetone and methanol	20
3	Maceration	Petroleum ether, Chloroform and methanol	22

Biological Activities: The therapeutic effects of *Acalypha indica* are represented in **Fig. 1**.

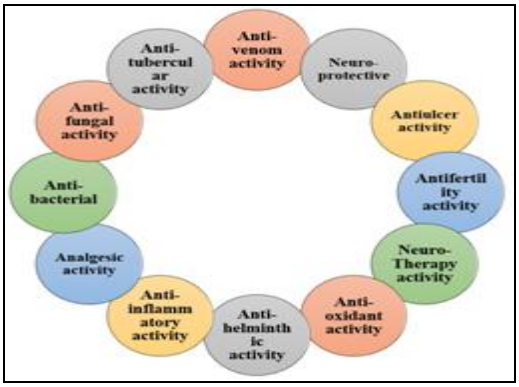


FIG. 1: THERAPEUTIC PROPERTIES OF *ACALYPHA INDICA*

In-vitro:

Anti-microbial Activity: *Ishak FD et al*., investigated the antimicrobial efficacy of *Acalypha indica* extracts through disc diffusion and minimum inhibitory concentration (MIC) methodologies. The extracts from methanol leaves and stem bark, along with the chloroform stem bark extract, revealed significant activity against *Staphylococcus aureus* and *Candida albicans*. Among these, the methanol stem bark extract exhibited the highest level of inhibition against *S. aureus*, while the methanol leaf extract demonstrated robust antifungal activity. The MIC findings indicated that methanol extracts were more potent than chloroform extracts against *C. albicans*, whereas extracts from petroleum ether showed no antimicrobial effects. These findings suggest that *Acalypha indica* has notable antimicrobial properties, particularly against Gram-positive bacteria and fungi, indicating its potential for pharmaceutical applications [22].

Somchit MN et al., examined the antimicrobial efficacy of water, ethanol, and chloroform extracts derived from *Acalypha indica*. Utilizing the disc diffusion method, they tested these extracts against four distinct bacterial and fungal strains. The study revealed that the antibacterial activity was significantly higher ($p < 0.05$) in the water and ethanol extracts, particularly effective against Gram-positive bacteria. Conversely, the chloroform extract demonstrated the most substantial antifungal activity ($p < 0.05$). These findings were compared with standard antibiotics, including penicillin, enrofloxacin, ampicillin, and chloramphenicol, as well as antifungal medications such as ketoconazole, itraconazole, and fluconazole. The outcomes support the traditional medicinal use of *Acalypha indica* for addressing various bacterial and fungal infections [23].

Anti-fungal Activity: *Menon S et al*., evaluated the antifungal activity of silver nanoparticles against common food pathogens, including *Aspergillus niger, Aspergillus flavus,* and *Aspergillus fumigatus. Among these, Aspergillus fumigatus* exhibited the highest percentage inhibition of 133%. The maximum inhibition was observed at a concentration of 75 µl of silver nanoparticles. These results highlight the potent antifungal properties of silver nanoparticles, suggesting their

potential application in controlling fungal contamination in food products [24].

Anti-bacterial Activity: *Govindarajan M et al*., investigated the antibacterial efficacy of *Acalypha indica* leaf extracts utilizing diffusion and dilution methodologies. The extracts derived from hexane, chloroform, ethyl acetate, and methanol revealed significant inhibitory effects against Gram-positive bacteria, including *Staphylococcus aureus, Staphylococcus epidermidis, Bacillus cereus,* and *Streptococcus faecalis,* as well as *Pseudomonas aeruginosa*. However, other Gram-negative bacteria remained unaffected. Notably, the methanol and ethyl acetate extract at a concentration of 5 mg/disc demonstrated the most substantial antibacterial activity. The minimum inhibitory and microbicidal concentration assessments indicated that all four extracts exhibited the highest levels of activity against the bacterial strains evaluated, thereby highlighting the antibacterial capabilities of *Acalypha indica* [25].

Krishnaraj C et al. explored the biosynthesis of silver nanoparticles and evaluated their antibacterial properties against waterborne bacterial pathogens. The synthesis of the nanoparticles was achieved rapidly using the leaf extract of *Acalypha indica*, with observable formation within 30 minutes. The confirmation of biosynthesis and characterization was accomplished through techniques such as UV–vis spectroscopy, scanning electron microscopy (SEM), X-ray diffraction (XRD), and energy dispersive spectroscopy (EDS). High-resolution transmission electron microscopy (HRTEM) analysis revealed that the particle sizes ranged from 20 to 30 nm. The resulting nanoparticles demonstrated significant antibacterial activity against *Escherichia coli* and *Vibrio cholerae,* with a minimal inhibitory concentration (MIC) of 10 µg/ml. Further analysis indicated that these nanoparticles modified membrane permeability and respiration in the affected bacterial cells, emphasizing their antibacterial effectiveness [26].

Vijayarekha P et al., assessed the antibacterial efficacy of *Acalypha indica* using the disc diffusion technique. The study investigated the antibacterial properties of extracts derived from petroleum ether, chloroform, acetone, methanol, and ethanol against four bacterial species: *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Escherichia coli*. The results demonstrated that the petroleum ether extract had the most significant antibacterial effect, surpassing those of the ethanol, acetone, and methanol extracts. Additionally, a preliminary phytochemical screening revealed the presence of considerable amounts of alkaloids, saponins, phenols, flavonoids, and tannins in the plant extracts [27].

Batubara I et al., executed antibacterial and biofilm degradation assays through the microdilution technique using a 96-well plate. The n-hexane extract from *Acalypha indica* leaves exhibited the highest level of antibacterial activity, with a minimum inhibitory concentration and minimum bactericidal concentration recorded at 500 µg/mL, in addition to significant biofilm degradation performance. The F3 fraction, obtained from the n-hexane extract through column chromatography, displayed notable biofilm degradation potential, indicated by an IC_{50} value of 56.82 µg/mL. Alkaloids were recognized as significant factors influencing both the antibacterial and biofilm degradation activities in the active fraction [28].

Shanmugapriya R et al., assessed the antibacterial efficacy of different components of *Acalypha indica* against selected bacterial strains at concentrations of 10, 20, 30, and 40 mg. The results indicated that both parts of the plant possessed antibacterial properties, exhibiting varying inhibition zones in comparison to the negative control (methanol), which recorded an inhibition zone of 6 mm. The root was found to have the highest antibacterial activity, particularly effective against *Escherichia coli* and *Salmonella typhi*, with a peak inhibition zone of 14 mm at the 40 mg concentration. The leaves displayed moderate antibacterial effects, particularly against *Staphylococcus aureus* and *Bacillus cereus* [29].

Anticancer Activity: *Kavitha S et al*., assessed the *in-vitro* cytotoxicity (anticancer) activity by cultivating *Agrobacterium tumefaciens* on yeast extract media for 48 hours at 28°C. The russet potatoes were disinfected by immersion in a 10% Clorox solution for 20 minutes, after which they were inoculated with a suspension of *A. tumefaciens* standardized to 1 × 10^9 CFU.

Cisplatin and *Acalypha indica* extracts were prepared in DMSO. The test solution consisted of 1 ml of the drug and 0.25 ml of water, while the control comprised 1.25 ml of water and 1 ml of the bacterial suspension. After staining, the potato dishes were evaluated, and tumor counts were documented. The results demonstrated that *Acalypha indica* extracts significantly reduced tumor formation relative to the control [30].

Anti-oxidant Activity: *Menon S et al*., investigated the antioxidant efficacy of silver nanoparticles (AgNPs) utilizing the DPPH assay. The findings revealed that AgNPs displayed a greater antioxidant potential than the standard ascorbic acid.

The IC_{50} value for AgNPs was found to be 5 mg/ml, in contrast to ascorbic acid, which presented a slightly higher IC50 range of 6–7 mg/ml. This evidence suggests that AgNPs possess notable free radical scavenging activity, indicating their potential for use in antioxidant applications [24].

Shanmugapriya R et al., investigated the radical scavenging activity of *Acalypha indica* utilizing the DPPH assay across different concentrations. The results revealed that both the leaves and roots of *Acalypha indica* displayed moderate antioxidant activity relative to the standard antioxidant, L-ascorbic acid. The antioxidant activity was noted to follow this order: root (53.27%) > leaves (31.14%). The maximum activity was noted at a concentration of 200 µg, with further concentration increases showing minimal influence on antioxidant capacity [29].

Kavitha S et al., assessed the total antioxidant capacity of *Acalypha indica* extracts, specifically those derived from ethanol (EtOH) and water. This evaluation involved the formation of a phosphomolybdenum complex, which was analyzed spectrophotometrically at 695 nm. The antioxidant capacities were determined to be 442 nmol/g for the EtOH extract and 338 nmol/g for the water extract. The researchers tested various concentrations of these extracts, ranging from 100 to 500 µg/ml, for their antioxidant activity using an *in-vitro* antilipid peroxidation model. At the highest concentration of 500 µg/ml, the EtOH extract exhibited a maximum inhibition of 78.6%, while the water extract showed 70.2% inhibition [30].

Anti-malarial Activity: *Govindarajan M et al.*, evaluated the larvicidal, ovicidal, and oviposition attractancy effects of *Acalypha indica* leaf extracts, which were prepared using benzene, chloroform, ethyl acetate, and methanol. The results indicated that larval mortality occurred within 24 hours, with LC_{50} values of 19.25, 27.76, 23.26, and 15.03 ppm for the respective solvents. Ovicidal activity was assessed 120 hours after treatment, revealing a reduction in hatchability that was inversely related to the concentration of the extracts. The highest oviposition attractancy rates at 100 ppm were recorded at 90.09%, 94.20%, 85.43%, and 95.75% for benzene, chloroform, ethyl acetate, and methanol, respectively. Conversely, the lowest rates at 25 ppm were 47.17%, 61.94%, 49.28%, and 68.12%. The findings suggest that *Acalypha indica* leaf extracts exhibit considerable efficacy as larvicidal and ovicidal agents, as well as strong oviposition attractants against the malaria vector *A. stephensi* [31].

Breast Cancer: *Chekuri S et al*., aimed to evaluate the cytotoxic potential of the hexane leaf crude extract of *Acalypha indica* Linn. on MCF-7 cell lines, employing the MTT (3-(4,5-Dimethylthiazol-2)-2,5-Diphenyltetrazolium Bromide) assay method, with Cisplatin utilized as a positive control. The hexane crude extract was tested at different concentrations (10 µg/mL, 25 µg/mL, 50 µg/mL, and 100 µg/mL). The results indicated that the 50 µg/mL concentration produced the most significant inhibitory effect, as evidenced by the IC_{50} value. This study sought to systematically explore the anti-cancer properties of *Acalypha indica* extracts and to isolate and characterize the active principles responsible for the observed activity [32].

Krishnaraj C et al., assessed the cytotoxic effects of silver and gold nanoparticles utilizing an MTT-reduction assay with slight modifications. They examined a range of concentrations of $AgNO_3$, $HAuCl_4$, silver nanoparticles, gold nanoparticles, and *Acalypha indica* leaf extract (1–100 mg/mL) on MDA-MB-231 cells to evaluate cell viability and toxicity. The findings revealed that $HAuCl_4$, $AgNO_3$, and the plant extract, which acted as a positive control, exhibited minimal toxicity across all concentrations, with $AgNO_3$-treated cells maintaining over 60% viability at 100 mg/mL.

Gold nanoparticles were found to be slightly more cytotoxic than silver nanoparticles at concentrations of 1, 10, and 50 mg/mL. However, at the concentration of 100 mg/mL, both silver and gold nanoparticles showed a significant increase in cytotoxicity, leading to a decrease in cell viability to around 40%, indicating a dose-dependent toxicity pattern. The study concluded that biologically synthesized silver and gold nanoparticles displayed concentration-dependent cytotoxic effects, with gold nanoparticles showing slightly higher toxicity at lower concentrations compared to silver nanoparticles [33].

Anthelmintic Activity: *Chengaiah B et al.,* aimed to investigate the anthelmintic potential of the crude alcoholic extract from the roots of *Acalypha indica*, employing *Pheretima posthuma* as the test organism. The study examined three concentrations (10, 25, and 50 mg/mL) of the alcoholic extract and its various fractions through a bioassay that measured the time to paralysis (P) and time to death (D) of the test worms. Albendazole at a concentration of 10 mg/mL served as the standard reference, while distilled water acted as the control. Results indicated that the crude alcoholic extract significantly caused paralysis and death in the worms, particularly at the 50 mg/mL concentration, when compared to Albendazole. *Acalypha indica* was found to exhibit the highest anthelmintic activity, thereby confirming the anthelmintic potential of its roots. It is recommended that further studies be conducted to isolate the active principles responsible for this activity [34].

Anti-inflammatory Activity: *Muzammil MS et al.,* focused on evaluating the anti-inflammatory properties of the methanolic extract from *Acalypha indica* leaves through the human red blood cell (HRBC) membrane stabilization method. The extract showed a considerable inhibition of hemolysis triggered by a hypotonic solution, with effects that were dependent on the dosage. Diclofenac sodium was utilized as the control drug at concentrations of 125, 250, 500, and 1000 mg/mL. The results indicate that *Acalypha indica* may have noteworthy anti-inflammatory effects [35].

Anti-arthritic Activity: *Jayaprakasam R et al.,* focused on assessing the anti-arthritic effects of a methanolic extract of *Acalypha indica* through three separate *in-vitro* models. The extract was formulated at concentrations between 10 and 200 µg/mL using DMSO, with diclofenac acting as the positive control. Each assay protein denaturation inhibition, proteinase inhibitory action, and anti-hyaluronidase activity was performed in triplicate. Results demonstrated a dose-dependent increase in percentage inhibition across all models. The inhibitory concentration (IC_{50}) was identified as 52 µg/mL for the protein denaturation assay, 37 µg/mL for the proteinase inhibitory test, and 18 µg/mL for the anti-hyaluronidase assay.

In comparison, diclofenac yielded lower IC_{50} values of 40 µg/mL and 13 µg/mL in the respective assays. The methanolic extract of *Acalypha indica* exhibited notable anti-arthritic activity, supporting its traditional use in treating arthritis. The authors recommended that further *in-vivo* studies be conducted to validate these findings and to explore the mechanisms by which this plant may offer protection against autoimmune diseases [19].

Vasoconstrictor Activity: *Machineni KM et al.,* focused on evaluating the vasoconstrictor activity of extracts from the aerial parts of *Acalypha indica*, specifically petroleum ether, chloroform, ethyl acetate, and ethanolic extracts. This assessment was performed *ex-vivo* using frog blood vessels. Among the extracts analyzed, only the petroleum ether extract and the standard vasoconstrictor, adrenaline, showed significant vasoconstrictor effects, as indicated by a decrease in the liquid drop from the frog vessel due to constriction. The findings revealed that 8.56 mg of the petroleum ether extract was necessary to achieve vasoconstriction, while only 0.3 mg of adrenaline was sufficient for the same outcome. The researchers attributed the vasoconstrictor effects of the petroleum ether extract to the presence of various phytochemical groups, including alkaloids, tannins, phenolics, and saponins. Furthermore, they suggested that *Acalypha indica* may hold therapeutic potential for treating primary disorders such as headaches and migraines, as well as serving as a diuretic. Thus, the raw aerial parts of *Acalypha indica* may be viable candidates for therapeutic applications in vasoconstriction [36].

Alpha-amylase Inhibitory Activity: *Nandhakumar M et al.,* assessed the α-amylase

inhibitory activity of different extracts (hexane, chloroform, and ethanol) from *Acalypha indica* using the porcine pancreatic amylase (PPA) inhibitory assay. The results indicated that the hexane extract did not inhibit α-amylase activity, while the chloroform and ethanol extracts demonstrated significant inhibition, with values of 75.32% and 84.51% for dose-dependent inhibition, respectively. These outcomes suggest that *Acalypha indica* may have potential applications in diabetes management by inhibiting the digestion of carbohydrates [37].

Alpha-glucosidase Inhibitory Activity: *Hakim RW et al.,* aimed to investigate the antihyperglycemic properties of *Acalypha indica* through *in-vitro* assessments of alpha-glucosidase inhibition. This enzyme is crucial for carbohydrate digestion and is associated with postprandial increases in blood glucose levels. The findings revealed that Ai extract exhibited alpha-glucosidase inhibition with an IC_{50} value of 19.429 mg/ml, which is less potent compared to the standard inhibitor acarbose, which has an IC_{50} of 1.515 mg/ml. The inhibitory effect was attributed to flavonoids and phenolic compounds, particularly hesperetin, acaindinin, and glucogalin, which formed robust hydrogen bonds with the enzyme's active sites. These results suggest that Ai may play a role in regulating glucose absorption, indicating its potential as a natural antidiabetic agent [38].

In-vivo:

Neutralization Potential of Russell's Viper: *Shirwaikar A et al.,* focused on evaluating the venom-neutralizing potential of the ethanol leaf extract of *Acalypha indica* (Euphorbiaceae) against Viper russellirusselli venom. The extract was administered in doses of 250, 500, and 750 mg/kg. Results indicated that the intraperitoneal administration of 500 and 750 mg/kg significantly mitigated venom-induced lethality, hemorrhage, necrosis, and mast cell degranulation in a dose-dependent manner in rats. Moreover, the extract reduced cardiotoxic and neurotoxic effects in isolated frog tissues. It also significantly reduced lipid peroxidation caused by the venom in red blood cells and preserved GSH and catalase levels in rat kidney tissues. These observations confirm the strong venom-neutralizing potential of the ethanol leaf extract of *Acalypha indica* [21].

Anti-hyperlipidemic Activity: *Rajasekaran S et al.,* aimed to investigate the hypolipidemic effects of *Acalypha indica* Linn. leaf extracts on hyperlipidemia induced by an atherogenic diet. The study involved administering aqueous and ethanolic extracts of the leaves at a dose of 400 mg/kg/day orally for 10 days. The findings revealed that these extracts significantly ($p<0.001$) prevented the elevation of serum levels of total cholesterol, triglycerides, LDL-C, VLDL-C, and the atherogenic index, while also significantly ($p<0.01$) increasing HDL-C levels [39].

Anti-fertility Activity: *Hiremath SP et al.,* investigated four sequential solvent extracts from the whole plant *Acalypha indica* L. (Euphorbiaceae) for their antifertility effects post-coitus in female albino rats. The findings revealed that the petroleum ether and ethanol extracts produced the most significant anti-implantation effects. Remarkably, the antifertility activity was reversible after the treatment was discontinued. Both extracts, when given at a dosage of 600 mg/kg body weight, demonstrated estrogenic activity, which was validated through histological analysis of the uterine tissue [40].

Wound Healing Activity: *Ganeshkumar M et al*., focused on the biochemical and molecular foundations of *Acalypha indica*'s therapeutic effects on dermal wounds in rats. A topical application of the extract (40 mg/kg) was administered daily to full-thickness excision wounds. The analysis of wound tissue included assessments of biochemical, biophysical, and histopathological changes, both with and without the extract. Serum TNF-α levels were measured at various intervals using ELISA, while RT-PCR was employed to evaluate the expression of TGF-β1, Col 1a (I), and Col 3a (I). Linear incision wounds were also created to measure tensile strength. Control rats displayed inadequate wound healing, marked by reduced inflammatory cell infiltration, minimal granulation tissue, collagen deficiency, and lower biomechanical strength. In contrast, *Acalypha indica* treatment led to a reduction in oxidative stress, decreased lipid peroxidation, and an increase in ascorbic acid levels. This treatment promoted cellular proliferation, raised TNF-α levels in the early stages of healing, upregulated TGF-β1, and enhanced collagen synthesis.

Rats receiving the treatment demonstrated accelerated wound contraction, improved epithelialization, higher shrinkage temperature, and enhanced tensile strength, thereby confirming the extract's notable wound-healing efficacy [41].

Anti-asthmatic Effect: *Ninave PB et al*., investigated the anti-asthmatic properties of ethanolic extracts derived from the leaves of *Acalypha indica* (EAIL) through various experimental animal models. The evaluation of the extract involved several screening techniques, such as assessing acetylcholine- and histamine-induced contractions in goat tracheal chains, clonidine-induced catalepsy, and milk-induced leucocytosis and eosinophilia in mice. Additionally, the study examined clonidine-induced mast cell degranulation in rats, passive paw anaphylaxis in rats, histamine-induced bronchoconstriction in guinea pigs, and histopathological changes induced by ovalbumin (OVA) in mice. The results indicated that EAIL significantly inhibited contractions induced by acetylcholine and histamine in the goat tracheal chain, suggesting its anticholinergic and antihistaminic properties. Furthermore, it reduced clonidine-induced immobility in mice, indicating potential H_1 receptor antagonism. In models of milk-induced leucocytosis and eosinophilia, EAIL notably decreased the counts of leucocytes and eosinophils, underscoring its adaptogenic and anti-allergic effects. The extract also demonstrated the ability to stabilize mast cells by inhibiting clonidine-induced degranulation and reduced paw edema in passive paw anaphylaxis, confirming its antianaphylactic properties. Moreover, EAIL provided protection against histamine-induced bronchoconstriction in guinea pigs, highlighting its bronchodilator capabilities. Histopathological assessments further indicated that the lung tissue architecture remained largely intact, reinforcing its protective role against asthma-related changes [42].

Analgesic Activity: *Rahman MA et al*., examined the analgesic efficacy of the methanol extract derived from *Acalypha indica* in Swiss albino mice, employing the acetic acid-induced writhing reflex method. The extract exhibited a significant reduction in writhing reflexes, achieving pain relief of 51.1% and 57.2% at dosages of 200 mg/kg and 400 mg/kg, respectively, within 10 minutes post-acetic acid administration. However, the analgesic effect was found to be less effective compared to aminopyrine, which demonstrated superior pain relief at a dose of 50 mg/kg. These findings indicate that *Acalypha indica* possesses noteworthy analgesic properties, though it is less potent than aminopyrine [43].

Anti-inflammatory Activity: Rahman MA *et al.* focused on the anti-inflammatory effects of the methanol extract of *Acalypha indica*, employing the carrageenan-induced paw edema technique in rats. The study assessed the extract's influence on paw edema by measuring the percentage inhibition of paw volume in comparison to a control group. The findings revealed a significant ($p<0.001$) dose-dependent inhibition of paw edema, with both doses showing marked effects until the fourth hour. The peak inhibition occurred at the third hour, with reductions of 21.5% and 30.6% observed at doses of 125 mg/kg and 250 mg/kg, respectively. Although the extract's effect was inferior to that of phenylbutazone (100 mg/kg), its duration of action was comparable to that of the standard drug up to the fourth hour. These observations suggest that *Acalypha indica* has moderate anti-inflammatory properties [43].

Hepatoprotective Activity: *Kumar SS et al.*, assessed the hepatoprotective effects of the methanol extract (ME) and its methanolic fraction (MFME) against liver damage induced by thioacetamide in albino rats. They evaluated serum levels of glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALKP), total bilirubin (TBL), total cholesterol (CHL), total protein (TPTN), and albumin (ALB), in conjunction with histopathological examinations of liver sections. The administration of thioacetamide (100 mg/kg i.p.) led to a significant rise in GOT, GPT, ALKP, TBL, and CHL levels, while TPTN and ALB levels were reduced, indicating necrosis of parenchymal cells. Treatment with ME (300 mg/kg) and MFME (250 mg/kg) effectively restored these parameters to levels comparable to those observed in the silymarin-treated group. The hepatoprotective activity of the methanol extract from *Acalypha indica* is likely attributed to its flavonoid content [44].

Anti-hyperglycemic Activity: *Priya CL et al*., conducted a study to investigate the antihyper-

glycemic effects of *Acalypha indica* extract (AIS) in both normal and diabetic Albino-Wistar rats induced by streptozotocin (STZ). The research primarily aimed to evaluate the efficacy of AIS in managing postprandial hyperglycemia following carbohydrate intake. The rats received AIS at doses ranging from 300 to 600 mg/kg of body weight, resulting in a notable reduction in blood glucose levels.

Specifically, AIS led to a decrease of 69.10% in blood glucose levels in maltose-loaded diabetic rats and 80.35% in sucrose-loaded diabetic rats when compared to the diabetic control group. The findings suggest that AIS effectively mitigates postprandial hyperglycemia through the inhibition of the α-glucosidase enzyme, indicating its potential as a nutraceutical option for the management of type 2 diabetes [45].

Anti-ulcer Activity: *Kalimuthu S et al.,* focused on evaluating the anti-ulcer activity of the methanolic extract of *Acalypha indica* (MEAI) utilizing pylorus ligation and swim stress-induced ulcer models in Wistar rats. The findings revealed that MEAI led to a significant reduction in gastric volume secretion, acidity, and ulceration across both models, with results achieving statistical significance at $p < 0.001$. This evidence suggests that *Acalypha indica* has considerable anti-ulcer potential and may be an important addition to the medicinal plant kingdom [46].

Anti-uretic: *Sathya M et al.,* investigated the biopotency of the ethanolic extract of *Acalypha indica* on marker enzymes in urolithiasis-induced male Wistar albino rats. Calcium oxalate urolithiasis was induced by administering 0.75% ethylene glycol in drinking water for 30 days. A significant decrease in marker enzymes, including Aspartate Transaminase (AST), Alanine Transaminase (ALT), Acid Phosphatase (ACP), and Alkaline Phosphatase (ALP), was observed in the liver and kidney, while their levels increased in the serum and urine of rats. Therapeutic treatment with the plant extract (200 mg/kg body weight per day, orally) significantly restored these enzyme levels to near normalcy in the curative group. These findings suggest that *Acalypha indica* may play a crucial role in preventing disorders associated with kidney stone formation [47].

Clinical Characteristics of *Acalypha indica* Poisoning: *Pradoo et al.,* analyzed cases of poisoning resulting from the consumption of *Acalypha indica*, a plant widely recognized in herbal medicine. The research involved eight patients, predominantly male, with a median age of 61.5 years. The plant was ingested in the form of either fresh juice or a boiled decoction. The most commonly reported symptoms included dark urine, jaundice, fever, and hemolysis.

Remarkably, seven of the eight patients were found to have methemoglobinemia, with methemoglobin levels reaching as high as 23.9%. Furthermore, four cases of acute kidney injury were documented, three of which necessitated hemodialysis. The results indicate that *Acalypha indica* may cause acute hemolysis, especially in individuals with glucose-6-phosphate dehydrogenase (G6PD) deficiency, as well as methemoglobinemia, likely attributed to the presence of quinone and anthraquinone compounds. The study highlights the necessity for additional research to confirm these toxic effects and to ensure the safe application of this herbal remedy [48].

***In-silico* Studies:**

Molecular Docking Studies: *Rajkumar P et al*., carried out molecular docking using Schrödinger software to evaluate the interactions between phytochemicals from *Acalypha indica* and various target proteins. Their study revealed that the compound 2-Methoxy-4-vinylphenol (2M4VP) exhibited a strong binding affinity with three key proteins (as detailed in **Table 4**). These strong interactions, particularly with tumor suppressor proteins, suggest that 2M4VP may have promising anticancer and anti-inflammatory potential [12].

TABLE 4: DOCKING SCORE

Targets (PDB ID)	Hydrogen Bond	Docking Score	Glide Energy (kcal/mol)
pRB (PDB ID: 4CRI)	PRO-808 & MLY-810	-5.79	-21.486
JAK2 (PDB ID: 5USY)	LEU-932 & GLU-930	-8.989	-48.093
COX-2 (PDB ID: 5IKR)	SER-530 & TYR-385	-7.518	-26.195

Molecular Dynamic Studies: *Asnawi A et al.*, performed molecular dynamics (MD) simulations to investigate the stability of phytochemicals derived from *Acalypha indica* as potential inhibitors of BRAF kinase, a crucial receptor implicated in melanocytic tumours. Utilizing GROMACS 2019.6, the research evaluated the binding stability of selected ligands, including chrysin, stigmasterol, and γ-sitosterol, over a simulation duration of 100 ns. The Root Mean Square Deviation (RMSD) analysis indicated that all ligands exhibited fluctuations within an acceptable range (<2.0 Å), thereby confirming their structural stability. Notably, stigmasterol and γ-sitosterol displayed enhanced inhibitory potential, establishing robust binding interactions with critical amino acids such as Val471, Ala481, and Phe583. Additionally, binding free energy assessments conducted *via* the MM-PBSA method revealed that stigmasterol and γ-sitosterol demonstrated stronger interactions compared to the native ligand, SM5. These results imply that both phytochemicals may represent promising lead compounds for the development of BRAF kinase inhibitors targeting melanocytic tumours [49].

Analytical Methods:

FTIR: *Ravi S et al*., analyzed the FTIR spectrum of the methanolic extract of *Acalypha indica* across a range of 500 to 4000 cm^{-1}. The extract displayed IR absorbance at various wavelengths, which indicated different patterns of chemical bond stretching. The broad peaks observed were representative of numerous chemical functional groups, while the shorter peaks indicated a lesser quantity. The IR absorbance findings highlighted the functional groups, which are compiled in **Table 5** [50].

TABLE 5: IR SPECTRA OF *ACALYPHA INDICA*

Range	Functional group
3318 cm^{-1}	O–H and N–H stretch
2930 cm^{-1}	C–H stretch (alkanes)
2108 cm^{-1}	C≡C stretch (alkynes)
1636 cm^{-1}	N–H bend (amines)
1363 cm^{-1}	C–H rock (alkanes)
1244 cm^{-1}	C–H wag (alkyl halides)
1043 cm^{-1}	C–N stretch (amines)
921 cm^{-1}	O–H bend (carboxylic acids)
828 cm^{-1}	C–H "oop" (aromatics)
768 cm^{-1}	C–Cl stretch (alkyl halides)
646 cm^{-1}	C≡C–H bend (alkynes)

UV-spectrophotometric Method: *Sneha K et al.*, developed a UV spectrophotometric technique for the quantification of gallic acid, utilizing distilled water as the solvent.

The method underwent validation for linearity, precision, robustness, and accuracy in accordance with ICH guidelines. A maximum absorbance (λmax) of 256 nm was recorded for both gallic acid and *Acalypha indica* extract, thereby confirming the method's specificity. Linearity was established within the range of 5–30 µg/mL, yielding a regression coefficient of 0.999. The method exhibited a high accuracy rate of 97.6% recovery and precision with a relative standard deviation (RSD) of less than 2%. The ruggedness and robustness of the method were confirmed, indicating minimal influence from variations in analyst or wavelength. The limits of detection and quantification were determined to be 0.045 µg/mL and 0.119 µg/mL, respectively. Consequently, this validated method has proven to be dependable for the estimation of gallic acid in leaf extracts and pharmaceutical formulations [51].

TLC Profile: *Solomon RJ et al*., performed Thin Layer Chromatography (TLC) utilizing plates coated with 0.25 mm silica gel-G, which were dried at ambient temperature (28 ± 1°C). They applied ten microlitres of extracts from the leaf, stem, and root in acetone, chloroform, hexane, and methanol separately onto the TLC plates. The analysis was conducted using a chloroform/methanol solvent system in a 10:1 (v/v) ratio. Following complete elution, the spots were visualized with iodine vapor. The findings indicated that the Rf value of Clotrimazole was 0.371. Likewise, the extracts of *Acalypha indica* in the respective solvents produced distinct spots with an Rf value of 0.371 ± 0.0009, closely resembling that of Clotrimazole [20].

HPLC: *Jayaprakasam R et al.*, optimized a high-performance liquid chromatography (HPLC) method that employed a mobile phase of methanol and water in a 99:1 (v/v) ratio, operating at a flow rate of 1 mL/min and detecting at 202 nm. The calibration curve was found to be linear across the concentration range of 20-60 µg/mL, with a slope of 3264.29, an intercept of -4675.4, and a correlation coefficient of 0.9927.

The limits of detection (LOD) and quantification (LOQ) were determined to be 5 µg/mL and 20 µg/mL, respectively. The method's precision and accuracy were confirmed by low relative standard deviation (RSD) and high recovery percentages [52].

HPLTC: *Jayaprakasam R et al.,* developed a high-performance thin-layer chromatography (HPTLC) technique for the quantification of stigmasterol. This method utilized aluminium plates coated with silica gel 60F254 as the stationary phase, while the mobile phase consisted of a toluene: methanol mixture in a 9:1 v/v ratio. Following the development process, the plates were analyzed and quantified at a wavelength of 525 nm. The method demonstrated a linear response within a concentration range of 100-900 ng/spot, achieving a correlation coefficient (r) of 0.9920. The limit of detection (LOD) and limit of quantification (LOQ) were found to be 70 ng/spot and 100 ng/spot, respectively [52].

GC-MS: *Rajkumar P et al.,* involved a GC-MS analysis of *Acalypha indica* seed extracts, employing a Perkin-Elmer GC-Clarus 680 system, which featured an AOC-20i auto-sampler and an Elite 5MS fused capillary column. The research aimed to elucidate the phytochemical composition of the methanolic leaf extract, which led to the discovery of 30 bioactive compounds. These compounds were further assessed for their biological activities using the PASS online database, revealing their potential anticancer and anti-inflammatory properties. **Table 6** displays some of the significant compounds identified [12].

TABLE 6: COMPOUNDS IDENTIFIED BY GC-MS

Name of the compound	Pass online activity
Benzoic acid	Potential enzyme inhibitor
Phytol	Antioxidant and antimicrobial properties.
E-2-Hexenyl benzoate	Lipid peroxidase inhibitor.
2-Methoxy-4-vinylphenol	Exhibited strong interactions with target proteins in molecular docking studies, suggesting anticancer and anti-inflammatory potential
Beta-curcumene	Anti-inflammatory and antioxidant properties.

Miscellaneous Research Work:

Extraction and Characterization Studies: *Jeyabalaji V et al.,* focused on the characterization of cellulosic fibers extracted from the roots of *Acalypha indica* L. to assess their viability for use in green composites. The physical characterization indicated a density of 1.356 g/cm³, affirming the fibers' potential as reinforcements.

Chemical composition analysis revealed that cellulose accounted for 67.86% by weight, with amorphous components including hemicellulose (0.24%) and lignin (18.75%), in addition to wax, ash, and moisture contents of 0.86%, 2.13%, and 10.16%, respectively. X-ray diffraction (XRD) confirmed the presence of both amorphous and crystalline cellulose, with a crystallinity index of 46.62% and a crystallite size of 3.68 nm. Thermo-gravimetric analysis indicated good thermal stability at 225°C. Scanning electron microscopy and atomic force microscopy revealed fibril aggregation and surface roughness. These fibers were identified as promising candidates for sustainable composite materials [53].

Accumulation Efficiency: *Venkatachalam P et al.,* evaluated the physiological and biochemical changes occurring in the roots and shoots of *Acalypha indica* under hydroponic conditions, specifically during exposure to lead (Pb) concentrations of 100 to 500 mg L^{-1} over a span of 1 to 12 days. The findings revealed that Pb accumulation in the roots reached a maximum of 121.6 mg g^{-1}, while the shoots exhibited an accumulation of 17.5 mg g^{-1} at the highest concentration of 500 mg L^{-1}. The presence of Pb in the stem, root, and leaf tissues was substantiated by Scanning Electron Microscopy (SEM) and Energy Dispersive X-ray Spectroscopy (EDX) analyses [54].

Biodiesel Production using Waste Cooking Oil: *Cholapandian K et al.,* synthesized a calcium oxide (CaO) nanocatalyst from *Acalypha indica* aimed at producing biodiesel from waste cooking oil (WCO). The study focused on optimizing the transesterification reaction conditions, which included catalyst concentration, methanol-to-oil molar ratio, reaction temperature, and time.

Through Response Surface Methodology (RSM), the optimal conditions were established as 2.4 wt% catalyst concentration, an 11.8:1 methanol-to-oil molar ratio, a reaction temperature of 63.7°C, and a reaction duration of 70 minutes, achieving a biodiesel yield of 94.74%. The catalyst's chemical bonds, size, and morphology were analyzed using FTIR, XRD, and SEM techniques. The biodiesel produced was characterized *via* GC–MS, and its physicochemical properties were assessed. The findings indicate that utilizing a CaO nanocatalyst from *Acalypha indica* for biodiesel production from WCO is an efficient approach [55].

Biosynthesis of Yttrium Oxide Nanoparticles: *Kannan SK et al.,* focused on the antibacterial effects of Yttrium oxide (Y_2O_3) nanoparticles synthesized from *Acalypha indica* leaf extract. The study evaluated the antibacterial efficacy against *Escherichia coli, Pseudomonas aeruginosa, Serratia marcescens,* and *Staphylococcus aureus* through disc diffusion and turbidimetric methods. The findings revealed that the Y_2O_3 nanoparticles exhibited notable antibacterial activity, with inhibition zones ranging from 10 to 13 mm. The minimum inhibitory concentration (MIC) for the various bacterial strains was found to be between 8 and 14 µg/mL. The mechanism proposed for this activity involves the inactivation of enzymes, binding to proteins, and the production of hydrogen peroxide, which ultimately leads to the death of bacterial cells. These findings highlight the potential application of Y_2O_3 nanoparticles as effective antimicrobial agents in both medical and industrial fields [56].

CONCLUSION: *Acalypha indica*, a medicinal plant of significant traditional importance, has shown considerable therapeutic efficacy against a range of health issues. This review provides a thorough overview of the current literature regarding its phytochemical composition, pharmacological properties, and medicinal uses. The plant's diverse phytochemical constituents, including flavonoids, alkaloids, and terpenoids, are responsible for its anti-inflammatory, antimicrobial, antioxidant, and anticancer effects. Historically, *Acalypha indica* has been employed in the treatment of respiratory ailments, skin disorders, and gastrointestinal problems. Although the existing literature underscores its medicinal significance, additional research is essential to fully uncover its therapeutic capabilities. It is imperative to standardize its extracts, clarify the underlying molecular mechanisms, and perform comprehensive clinical trials to bridge traditional practices with contemporary medical applications. Moreover, the development of innovative formulations such as nanoparticles or phytosomes may improve its bioavailability and therapeutic effectiveness. A more profound comprehension of its pharmacological actions and clinical safety will be instrumental in positioning *Acalypha indica* as a viable option for plant-based therapies.

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