



Review Article

PHYTOCHEMISTRY AND PHARMACOLOGICAL POTENTIAL OF ACALYPHA HISPIDA BURM.F.: A COMPREHENSIVE REVIEW

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ABSTRACT

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Acalypha hispida Burm.f. (family Euphorbiaceae), commonly known as the chenille plant, red-hot cattail or cat's-tail plant, is an ornamental tropical shrub that has attracted increasing scientific interest because of its ethnomedicinal applications and diverse phytochemical composition. Traditionally, different parts of the plant have been used for gastrointestinal, respiratory, inflammatory, infectious and dermatological disorders. Leaves, flowers, roots and bark have been employed in traditional systems of medicine as laxatives, diuretics, expectorants and remedies for conditions such as asthma, dysentery, skin infections and ulcers. Phytochemical investigations have identified phenolic compounds, flavonoids, tannins, hydrolysable ellagitannins, glycosides, saponins, steroids, alkaloids and other secondary metabolites. Particularly important constituents include geraniin, corilagin, gallic acid, ellagic acid and characteristic ellagitannins such as acalphydins M1, M2 and D1. Experimental investigations have demonstrated antioxidant, anti-inflammatory, antibacterial, antifungal, cytotoxic, trypanocidal and antidiabetic activities. Leaf extracts exhibit substantial free-radical-scavenging and metal-chelating activities, while ethanol and aqueous extracts have demonstrated anti-inflammatory effects in experimental models. Recent studies have further demonstrated α -amylase and α -glucosidase inhibitory activities and hypoglycemic effects. A 2024 investigation extended these findings by demonstrating antidiabetic activity of both conventional extract and a nanoextract, with effects associated with pancreatic β -cell preservation, insulin enhancement, glycogen restoration and modulation of histone H3 lysine-9 acetylation. Acute toxicity investigations indicate a relatively high margin of safety for ethanolic leaf extract in rats, although histological alterations warrant further investigation. Despite promising preclinical evidence, significant gaps remain regarding standardized extracts, pharmacokinetics, molecular targets, chronic toxicity, drug interactions and clinical efficacy. This review critically summarizes the botanical characteristics, ethnomedicinal applications, phytochemistry, pharmacological activities, toxicological profile and future therapeutic prospects of *A. hispida*.

Keywords: *Acalypha hispida*; Euphorbiaceae; chenille plant; phytochemistry; ellagitannins; antioxidant; anti-inflammatory; antidiabetic; antimicrobial; cytotoxicity; nanoextract; medicinal plant.

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1. INTRODUCTION

Medicinal plants remain an important source of structurally diverse bioactive compounds and continue to contribute to the discovery of pharmacologically useful molecules. Plant-derived polyphenols, flavonoids, tannins, alkaloids and terpenoids have attracted particular attention because of their antioxidant, anti-inflammatory, antimicrobial, metabolic and cytoprotective properties. Within the Euphorbiaceae family, the genus *Acalypha* represents one of the important groups of medicinally investigated plants. The genus contains several hundred

species, many of which are traditionally used in Africa, Asia and other tropical regions (Seebaluck et al., 2015).

Acalypha hispida Burm.f. is one of the best-known ornamental members of the genus. Although widely cultivated for its characteristic pendulous red inflorescences, the plant has a long history of traditional medicinal use. Ethnobotanical records describe applications involving the leaves, flowers, bark and roots for gastrointestinal, respiratory, dermatological and inflammatory conditions. Kew's Plants of the World Online database records traditional applications including laxative,

diuretic and expectorant uses and applications for asthma, leprosy, kidney ailments, dysentery, wounds and ulcers.

Interest in *A. hispida* has increased because experimental investigations have provided pharmacological support for several traditional applications. Studies have reported antioxidant, anti-inflammatory, antibacterial, antifungal, cytotoxic, antitrypanosomal and hypoglycemic effects. The pharmacological activities appear to be associated predominantly with its polyphenolic and tannin-rich phytochemical profile (Amakura et al., 1999; Adesina et al., 2000; Siraj et al., 2016).

More recently, research has progressed from conventional crude extracts toward characterization of specific mechanisms and nanoformulations. In particular, a 2024 study reported antidiabetic effects of an *A. hispida* leaf extract and nanoextract and investigated modulation of histone H3 lysine-9 acetylation as a possible molecular mechanism (Alfarisi et al., 2024).

Therefore, *A. hispida* represents an interesting candidate for further pharmacological and pharmaceutical investigation. The present review integrates available information concerning its taxonomy, morphology, distribution, traditional uses, phytochemistry, pharmacological properties, toxicological profile and future therapeutic applications.

2. BOTANICAL CLASSIFICATION

Taxonomic rank Classification

Kingdom	Plantae
Clade	Angiosperms
Order	Malpighiales
Family	Euphorbiaceae
Genus	<i>Acalypha</i>
Species	<i>Acalypha hispida</i> Burm.f.

The accepted scientific name is *Acalypha hispida*Burm.f. The species belongs to Euphorbiaceae and is closely related taxonomically to several other medicinally investigated *Acalypha* species. Accurate botanical identification is particularly important because pharmacological literature concerning the genus sometimes combines data from different *Acalypha* species. Recent taxonomic evaluation of medicinal *Acalypha* literature has emphasized that species-level misidentification can compromise interpretation of ethnopharmacological and pharmacological evidence.

3. COMMON NAMES

Acalypha hispida is known by several common names, including:

- Chenille plant
- Chenille flower
- Red-hot cattail
- Cat's-tail
- Hot-cat-tail
- Philippines-medusa
- Copperleaf-type names in some regions

The common name "chenille plant" refers to the long, pendulous, densely clustered inflorescences that resemble chenille fabric.

4. BOTANICAL DESCRIPTION

Acalypha hispida is a perennial tropical shrub characterized by attractive, elongated, pendulous inflorescences. The plant is generally cultivated as an ornamental shrub in tropical and subtropical climates. The flowers are particularly distinctive because of their dense, elongated, tail-like appearance.

The species is native to tropical regions associated with New Guinea, the Malay Archipelago and neighboring islands of the East Indies and is now widely cultivated in tropical and subtropical regions.

Leaves are generally simple, green and ovate to broadly ovate, with serrated margins. The plant is dioecious, with male and female flowers occurring on separate plants. Female inflorescences are particularly conspicuous because of their long, pendulous and densely flowered structure.

5. GEOGRAPHICAL DISTRIBUTION AND HABITAT

Acalypha hispida is primarily associated with tropical and humid environments. It is native to regions of the western Pacific and Southeast Asian floristic zones and is extensively cultivated elsewhere as an ornamental plant.

It grows successfully in warm climates with adequate moisture and is commonly maintained in gardens, parks and domestic landscapes. Its ability to tolerate tropical environmental conditions has contributed to its wide horticultural distribution.

6. ETHNOMEDICINAL AND TRADITIONAL USES

Traditional medicinal applications constitute an important basis for investigating the pharmacological properties of *A. hispida*. Different plant parts have been used for different therapeutic purposes.

The leaves have traditionally been described as **laxative and diuretic** and have been used for respiratory and dermatological conditions. Traditional applications include treatment of leprosy, gonorrhea, infectious diarrhea and pulmonary disorders. Leaf and flower preparations have also been used as expectorants in asthma.

Kew's botanical database records traditional use of bark, flowers and roots for asthma and respiratory complaints, root decoctions for dysentery, leaf poultices for leprosy and leaf/flower decoctions for wounds, ulcers, laxative and diuretic applications.

Table 1. Traditional uses of *Acalypha hispida*

Plant part	Traditional application
Leaves	Laxative
Leaves	Diuretic
Leaves	Leprosy
Leaves	Gonorrhea
Leaves	Skin disorders
Leaves	Wounds and ulcers

Plant part	Traditional application
Flowers	Respiratory complaints
Flowers	Asthma
Roots	Dysentery
Bark	Respiratory disorders
Root/flower decoction	Cough and hemoptysis
Leaf preparations	Infectious and inflammatory conditions

These traditional uses should be interpreted as ethnomedicinal evidence rather than proof of clinical efficacy. Nevertheless, they provide useful hypotheses for pharmacological investigation.

7. PHYTOCHEMICAL PROFILE

Phytochemical investigations demonstrate that *A. hispida* contains a chemically diverse collection of secondary metabolites.

Reported classes include:

- Phenolic compounds
- Flavonoids
- Hydrolysable tannins
- Ellagitannins
- Glycosides
- Saponins
- Steroids
- Alkaloids
- Hydroxyanthraquinones
- Terpenoids
- Anthocyanins
- Essential-oil constituents

Phytochemical screening of *A. hispida* leaves has demonstrated phenolics, tannins, flavonoids, cardiac glycosides and alkaloids, while other investigations have identified saponins, steroids and glycosides (Malomo et al., 2009; Manikanta et al., 2014).

The chemical composition varies substantially according to plant part, geographical origin, extraction solvent and analytical methodology. Consequently, direct comparison between studies is difficult unless extracts are standardized.

8. MAJOR BIOACTIVE CONSTITUENTS

8.1 Ellagitannins

One of the most characteristic phytochemical features of *A. hispida* is the presence of hydrolysable tannins and ellagitannins.

Amakura et al. (1999) isolated two new monomeric hydrolysable tannins, **acalyphidin M1** and **acalyphidin M2**, together with a dimeric tannin designated **acalyphidin D1**. Fourteen additional known polyphenols were also identified from the leaves.

These findings are important because ellagitannins are recognized for their strong antioxidant and protein-

interacting properties and may contribute substantially to the biological effects of *A. hispida*.

8.2 Geraniin

Geraniin is another important hydrolysable tannin reported from *A. hispida*. Activity-directed fractionation of *A. hispida* leaves resulted in identification of **geraniin, corilagin and gallic acid** as antimicrobial constituents (Adesina et al., 2000).

Geraniin has attracted extensive interest because of antioxidant, antimicrobial, anti-inflammatory and metabolic effects reported in various experimental systems.

8.3 Gallic Acid

Gallic acid has been identified among the antimicrobial constituents of *A. hispida* leaves (Adesina et al., 2000).

Its known radical-scavenging and antimicrobial properties provide a plausible contribution to the antioxidant and antimicrobial effects of the plant extract.

8.4 Corilagin

Corilagin, another hydrolysable tannin, has been identified from *A. hispida* and implicated in its antimicrobial activity (Adesina et al., 2000).

8.5 Ellagic Acid

Siraj et al. (2016) demonstrated that both aqueous and ethanolic leaf extracts contained substantial quantities of phenolic compounds, with HPLC analysis indicating a high content of **ellagic acid**. The authors proposed that ellagic acid and other phenolics could contribute to the antioxidant and anti-inflammatory activities of the extracts.

8.6 Anthocyanins

Anthocyanin constituents have also been reported in *A. hispida*, including cyanidin derivatives. These pigments may contribute to the antioxidant characteristics of the plant.

9. ESSENTIAL OIL COMPOSITION

The flowers of *A. hispida* contain volatile constituents that have been investigated by gas chromatography and GC-MS.

Onocha et al. (2011) identified **44 compounds representing 99.98% of the essential oil composition**. The constituents included alcohols, esters, ketones, terpenes and hydrocarbons. Important constituents included 15,16-epoxylabda-13(16),14-dien-8 α -ol, 8,14-cedranoxide, curcumen, 1-hexadecene and ethyl vanillin.

The essential oil demonstrated comparatively weak DPPH radical-scavenging activity, suggesting that the antioxidant activity of *A. hispida* may depend more strongly on its polar phenolic and tannin fractions than on its volatile oil.

10. ANTIOXIDANT ACTIVITY

Oxidative stress is associated with lipid peroxidation, DNA damage, protein oxidation, inflammation and the development of several chronic disorders. The antioxidant

potential of *A. hispida* has been investigated using several in vitro models.

Onocha et al. (2011) evaluated the essential oil of *A. hispida* flowers and found relatively weak DPPH radical-scavenging activity compared with BHA.

In contrast, Onocha et al. (2010/2011) reported strong antioxidant effects from several fractions obtained from the non-polar extract of *A. hispida* leaves and twigs. Several fractions demonstrated high DPPH and hydrogen-peroxide scavenging activities.

Siraj et al. (2016) provided stronger evidence for the antioxidant activity of polar leaf extracts. Both aqueous and ethanolic extracts demonstrated DPPH scavenging, iron-chelating activity, nitric-oxide scavenging and concentration-dependent reducing power. The DPPH IC₅₀ values were approximately 14 and 17 µg/mL for ethanol and aqueous extracts, respectively.

The antioxidant effect appears to correlate with the presence of phenolics, flavonoids and hydrolysable tannins.

Possible antioxidant mechanisms

The antioxidant activity of *A. hispida* may involve:

1. Direct scavenging of free radicals.
2. Chelation of transition metals.
3. Inhibition of oxidative chain reactions.
4. Reduction of reactive oxygen species.
5. Modulation of nitric oxide-related oxidative processes.
6. Protection against lipid peroxidation.
7. Enhancement of endogenous antioxidant defenses.

11. ANTI-INFLAMMATORY ACTIVITY

Inflammation represents an important pathological component of many chronic diseases. Siraj et al. (2016) evaluated the anti-inflammatory effects of aqueous and ethanolic leaf extracts using carrageenan- and histamine-induced paw edema models in rats.

Both extracts demonstrated significant inhibition of paw edema at doses of **200 and 400 mg/kg**. The antioxidant and anti-inflammatory effects were associated with a high content of phenolic and flavonoid constituents, particularly ellagic acid.

The observed activity suggests that *A. hispida* polyphenols may interfere with inflammatory mediator generation and oxidative stress. However, detailed studies involving COX-1/COX-2, lipoxygenase, NF-κB, MAPK and cytokine signaling are still required.

12. ANTIMICROBIAL ACTIVITY

Antimicrobial activity is one of the most frequently reported biological properties of *A. hispida*.

Adesina et al. (2000) performed activity-directed fractionation of *A. hispida* leaves and identified **gallic acid, corilagin and geraniin** as antimicrobial constituents.

Bokshi et al. (2012) reported antibacterial activity of ethanolic leaf extract against several bacterial species. Significant activity was reported against *Salmonella typhi*, with moderate effects against organisms including *Escherichia coli*, *Streptococcus saprophyticus* and *Streptococcus agalactiae*.

A later investigation of medicinal plants traditionally used for oral and skin infections also found antibacterial activity of *A. hispida*. Against the tested organisms, the extract demonstrated inhibition zones of approximately 21 mm against *Klebsiella pneumoniae*, 11 mm against *Staphylococcus aureus* and 17 mm against *E. coli*, while MIC values were in the 256–512 µg/mL range.

Potential antimicrobial mechanisms

The antimicrobial activity may be related to:

- Tannin-mediated protein precipitation
- Cell-wall disruption
- Membrane damage
- Enzyme inhibition
- Metal chelation
- Oxidative stress induction in microbial cells
- Interference with microbial adhesion

The identification of geraniin, corilagin and gallic acid provides a useful basis for future mechanism-oriented research.

13. ANTIFUNGAL ACTIVITY

Traditional use of *A. hispida* for skin disorders and infections has encouraged investigation of antifungal activity. Available studies summarized in the literature report antifungal activity of leaf extracts.

However, compared with antioxidant and antidiabetic research, the antifungal evidence remains relatively limited. Future studies should determine minimum inhibitory concentrations, minimum fungicidal concentrations, effects on fungal biofilms and the specific constituents responsible for activity.

14. CYTOTOXIC ACTIVITY

Cytotoxic activity has been reported for several *A. hispida* preparations.

Bokshi et al. (2012) evaluated ethanolic leaf extract using the *Artemia salina* brine shrimp lethality assay and reported an LC₅₀ of approximately **19.95 µg/mL**, indicating substantial cytotoxicity in this preliminary model.

Onocha et al. also evaluated fractions of *A. hispida* leaves and twigs and observed varying levels of cytotoxicity. Some fractions showed LC₅₀ values above 1000 µg/mL, indicating relatively low toxicity in that assay.

The essential oil from flowers has also demonstrated cytotoxic activity in the brine shrimp model.

These findings should **not** be interpreted as evidence of anticancer efficacy. Brine shrimp lethality is a preliminary cytotoxicity screen and does not establish selective tumor-cell toxicity. Further studies using cancer cell lines, normal cells, mechanistic assays, apoptosis markers and in vivo tumor models are necessary.

15. TRYPANOCIDAL ACTIVITY

One of the earliest pharmacological investigations of *A. hispida* demonstrated trypanocidal activity.

Okanla et al. (1990) investigated an aqueous extract of *A. hispida* leaves against *Trypanosoma brucei* infection in laboratory animals. The study provides experimental support for the traditional medicinal relevance of the species and indicates possible antiparasitic activity. The trypanocidal potential is particularly noteworthy because it expands the pharmacological profile of *A. hispida* beyond antioxidant and antimicrobial effects.

16. ANTIDIABETIC AND HYPOGLYCEMIC ACTIVITY

Antidiabetic activity is currently one of the most promising research areas for *A. hispida*. Alfarisi et al. (2020) investigated leaf extracts prepared using different extraction conditions and evaluated antioxidant, α -amylase and α -glucosidase inhibitory activities as well as hypoglycemic effects. The study demonstrated that *A. hispida* leaf extracts possessed polyphenols, antioxidant activity and inhibitory activity against carbohydrate-digesting enzymes, together with hypoglycemic effects in vivo.

Possible mechanisms

The antidiabetic effects may involve:

- α -amylase inhibition
- α -glucosidase inhibition
- Reduction of postprandial glucose absorption
- Antioxidant protection of pancreatic β -cells
- Improvement of insulin secretion
- Preservation of pancreatic architecture
- Improvement of hepatic glycogen storage
- Regulation of lipid metabolism

The presence of flavonoids, phenolic acids and tannins provides a plausible phytochemical basis for these effects.

17. NANOEXTRACT AND EPIGENETIC ANTIDIABETIC EFFECTS

A particularly important recent development was reported by Alfarisi et al. (2024), who investigated both conventional *A. hispida* leaf extract and a nanoextract in streptozotocin-induced diabetic rats.

The study used:

- Conventional extract: 300 mg/kg
- Nanoextract: 30 and 60 mg/kg
- Treatment period: 28 days

The nanoextract was approximately **733 nm** in size. Both conventional extract and nanoextract demonstrated antidiabetic effects, while the 60 mg/kg nanoextract produced the strongest overall response. Reported effects included:

- Reduced blood glucose
- Increased pancreatic β -cell number
- Increased β -cell density
- Increased insulin levels
- Increased hepatic glycogen
- Improved lipid metabolism
- Reduced H3K9 acetylation in pancreatic islets and liver

This finding is significant because it suggests that *A. hispida* may influence not only conventional metabolic pathways but also **epigenetic regulation**.

Proposed mechanism

A simplified mechanistic hypothesis can be represented as:

***A. hispida* polyphenols → antioxidant/metabolic modulation → preservation of β -cells → improved insulin secretion → improved glucose utilization**
with a potentially additional pathway:

***A. hispida* bioactives → modulation of histone acetylation → altered gene expression → β -cell and metabolic regulation → improved glycemic control**

This mechanism requires independent confirmation using molecular biology, transcriptomics and epigenomic studies.

18. ANTIDIARRHEAL POTENTIAL

Traditional use of *A. hispida* for diarrhea is supported by phytochemical and experimental investigations. Manikanta et al. (2014) investigated combined extracts of *A. hispida*, *A. nervosa* and *A. fruticosa* for antidiarrheal activity.

Because the study used a combination of three species, the observed activity cannot be attributed exclusively to *A. hispida*. Nevertheless, the findings provide a rationale for conducting dedicated antidiarrheal studies using standardized *A. hispida* extracts.

19. POSSIBLE HEPATOPROTECTIVE AND ORGAN-PROTECTIVE POTENTIAL

Direct evidence specifically establishing hepatoprotective activity of *A. hispida* remains limited compared with the evidence for antioxidant and antidiabetic activity. Nevertheless, the plant's antioxidant and anti-inflammatory properties may theoretically contribute to organ protection.

The 2024 antidiabetic study reported improved metabolic parameters and increased hepatic glycogen in diabetic animals following *A. hispida* treatment.

However, dedicated models of hepatotoxicity, nephrotoxicity and oxidative organ injury are necessary before hepatoprotective or nephroprotective claims can be established.

20. TOXICOLOGICAL PROFILE

Safety evaluation is essential before medicinal development of *A. hispida*.

Alfarisi et al. (2020) investigated acute toxicity of ethanolic *A. hispida* leaf extract in female Sprague-Dawley rats using single oral doses of 2, 4, 8 and 16 g/kg. The reported LD50 was greater than 16 g/kg body weight, and no major clinical signs of acute toxicity or significant changes in serum ALT, AST, creatinine and urea were observed during the observation period.

However, histological observations of the liver showed changes involving eosinophilic cytoplasm and basophilic

nuclei. Therefore, the finding of a high acute LD50 should not be interpreted as proof of complete safety.

Important toxicological gaps

Further studies should evaluate:

1. Subacute toxicity.
2. Chronic toxicity.
3. Reproductive toxicity.

4. Genotoxicity.
5. Developmental toxicity.
6. Immunotoxicity.
7. Hepatic and renal histopathology.
8. Drug-herb interactions.
9. Pharmacokinetic interactions.
10. Safety of concentrated or nanoformulated extracts.

21. PHARMACOLOGICAL ACTIVITIES: SUMMARY

Table 2. Pharmacological activities reported for *Acalypha hispida*

Activity	Plant part/extract	Experimental evidence	Major findings
Antioxidant	Leaves	DPPH, H2O2, NO, reducing power	Strong radical-scavenging activity
Anti-inflammatory	Leaves	Carrageenan/histamine paw edema	Significant inhibition
Antibacterial	Leaves	Disc diffusion/MIC	Activity against several bacteria
Antifungal	Leaves	In vitro assays	Reported activity
Cytotoxic	Leaves/flowers	Brine shrimp assay	Variable cytotoxicity
Trypanocidal	Leaves	Animal model	Activity against Trypanosoma
Hypoglycemic	Leaves	Animal model	Reduction in blood glucose
α -Amylase inhibition	Leaves	In vitro	Enzyme inhibition
α -Glucosidase inhibition	Leaves	In vitro	Enzyme inhibition
Antidiabetic	Leaves	STZ-rat model	Improved glycemia and insulin
Nano-antidiabetic	Nanoextract	STZ-rat model	Enhanced metabolic effects
Antidiarrheal	Combined <i>Acalypha</i> extracts	Experimental	Traditional claim supported
Antimicrobial	Leaves	Activity-guided fractionation	Geraniin, corilagin, gallic acid implicated

22. RELATIONSHIP BETWEEN PHYTOCHEMISTRY AND PHARMACOLOGICAL ACTIVITY

The biological activities of *A. hispida* can potentially be related to its phytochemical composition.

Phenolics and ellagitannins

Phenolic compounds can donate hydrogen or electrons to reactive species and may also chelate transition metals. Ellagitannins such as geraniin, corilagin and acalyphidins may therefore contribute to antioxidant activity.

Flavonoids

Flavonoids can participate in free-radical scavenging and modulation of cellular signaling pathways. Their reported presence in *A. hispida* may contribute to antioxidant and metabolic effects.

Tannins

Tannins can precipitate proteins and interfere with microbial enzymes and membranes, potentially explaining part of the antimicrobial activity.

Anthocyanins

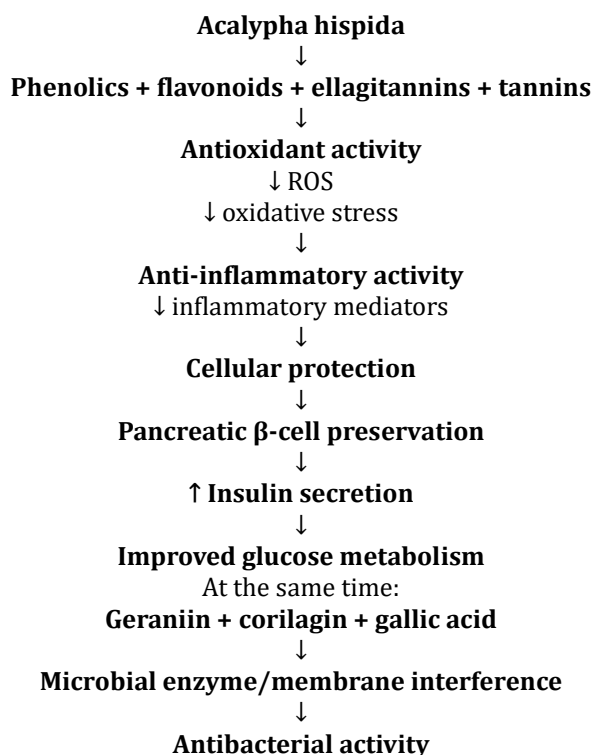
Cyanidin derivatives may contribute to antioxidant capacity.

Volatile constituents

The flower essential oil contains terpenoid, ester, alcohol and hydrocarbon constituents that may contribute to biological effects, although the essential oil appears less potent as a DPPH antioxidant than polar extracts.

23. PROPOSED PHARMACOLOGICAL MECHANISMS

Based on current evidence, the following hypothetical pharmacological network can be proposed:



The 2024 nanoextract study further suggests:

A. hispida nanoextract → H3K9 acetylation modulation → altered cellular gene regulation → β -cell/metabolic improvement.

These pathways remain partly hypothetical and should be validated experimentally.

24. PHARMACEUTICAL AND NANOTECHNOLOGY POTENTIAL

The development of nanoformulations may represent an important future direction for *A. hispida*.

Plant extracts often suffer from:

- Variable phytochemical content
- Poor aqueous solubility of some constituents
- Limited bioavailability
- Rapid metabolism
- Instability
- Batch-to-batch variability

Nanotechnology may improve:

- Solubility
- Stability
- Absorption
- Cellular uptake
- Dose efficiency
- Targeted delivery

The 2024 study demonstrated the feasibility of producing a nanosized *A. hispida* leaf extract and reported stronger antidiabetic activity at a lower nanoextract dose compared with conventional extract.

Future studies could investigate:

- Phytosomes
- Liposomes
- Polymeric nanoparticles
- Solid lipid nanoparticles
- Nanostructured lipid carriers
- Nanoemulsions
- Green-synthesized nanoparticles containing standardized *A. hispida* fractions

25. STANDARDIZATION CHALLENGES

Despite promising pharmacological findings, clinical translation is limited by the lack of standardized preparations.

Important standardization parameters should include:

- Botanical authentication
- Voucher specimen deposition
- Geographical origin
- Plant age
- Harvesting season
- Plant part
- Drying conditions
- Extraction method
- Extraction solvent
- Total phenolic content
- Total flavonoid content
- Ellagic acid content
- Geraniin content
- Corilagin content
- Chromatographic fingerprint
- Microbial limits
- Heavy-metal limits
- Pesticide residues
- Stability

HPLC/HPTLC/LC-MS fingerprinting should be incorporated into future studies.

26. RESEARCH GAPS

Although *A. hispida* has demonstrated a wide range of experimental pharmacological activities, several important gaps remain.

26.1 Lack of clinical trials

Most evidence remains preclinical. There is insufficient clinical evidence to establish therapeutic efficacy in humans.

26.2 Limited pharmacokinetic information

The absorption, distribution, metabolism and elimination of major *A. hispida* constituents remain inadequately characterized.

26.3 Limited molecular studies

Although antioxidant and antidiabetic effects have been reported, molecular targets require further clarification.

26.4 Lack of standardized extracts

Different studies use different solvents, extraction ratios and plant parts, making comparisons difficult.

26.5 Insufficient chronic toxicity studies

Acute toxicity data are encouraging but cannot substitute for long-term safety evaluation.

26.6 Limited bioavailability studies

The pharmacokinetic behavior of ellagitannins and other polyphenols requires detailed investigation.

26.7 Limited research on nanoformulations

The 2024 nanoextract investigation represents an important advance, but additional nanocarriers and pharmacokinetic studies are required.

27. FUTURE PERSPECTIVES

Future research on *A. hispid*a should move from preliminary screening toward mechanism-based and standardized drug-discovery studies.

Priority areas include:

1. Isolation and structural characterization of new bioactive constituents.
2. HPLC/HP TLC/LC-MS standardization.
3. Metabolomic profiling.
4. Molecular docking and target validation.
5. Transcriptomic and proteomic investigations.
6. Epigenetic studies.
7. Detailed antidiabetic mechanism studies.
8. β -cell protection studies.
9. Chronic toxicity evaluation.
10. Pharmacokinetic investigations.
11. Bioavailability enhancement.
12. Development of nanoformulations.
13. Evaluation in validated animal models.
14. Drug-herb interaction studies.
15. Well-designed clinical trials.

The newly reported relationship between *A. hispid*ananoextract and H3K9 acetylation provides an especially interesting direction for future research because it connects traditional medicinal plant research with contemporary epigenetic pharmacology.

28. CONCLUSION

*Acalypha hispid*aBurm.f. is a pharmacologically promising medicinal plant belonging to the Euphorbiaceae family. Although commonly cultivated as an ornamental plant, its leaves, flowers, roots and bark have a documented history of traditional medicinal use. Phytochemical studies have demonstrated the presence of diverse secondary metabolites, particularly phenolic compounds, flavonoids, tannins and hydrolysable ellagitannins. Compounds such as geraniin, corilagin, gallic acid, ellagic acid and acaliphidins provide a plausible chemical basis for several biological effects.

Experimental studies demonstrate significant antioxidant and anti-inflammatory activities, together with antibacterial, antifungal, cytotoxic and trypanocidal effects. Of particular importance is the growing evidence for antidiabetic activity. Conventional leaf extracts demonstrate carbohydrate-digesting enzyme inhibition and hypoglycemic activity, while recent research has shown that a nanoextract can improve glucose homeostasis, pancreatic β -cell parameters, insulin levels, hepatic glycogen and lipid metabolism. The observed modulation of H3K9 acetylation introduces a potentially novel epigenetic mechanism for *A. hispid*a-mediated metabolic regulation.

Acute toxicity studies suggest a relatively broad safety margin for ethanolic leaf extract; however, histological findings and the absence of comprehensive chronic toxicity and clinical studies indicate that safety cannot yet be considered fully established.

Overall, *A. hispid*a represents a valuable candidate for further pharmacognostic, phytochemical, pharmacological and pharmaceutical research. The combination of traditional medicinal knowledge, chemically characterized polyphenols, experimentally demonstrated pharmacological activities and emerging nanoformulation approaches provides a strong foundation for future development. Nevertheless, standardized extracts, validated molecular mechanisms, pharmacokinetic characterization, long-term safety studies and controlled clinical trials are essential before therapeutic claims can be translated into evidence-based human medicine.

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