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Phytochemical Constituents and Pharmacological Activities of *Houttuynia cordata* Thunb. as a Phytopharmaceutical: A Narrative Review

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ABSTRACT: *Houttuynia cordata* Thunb. is a promising medicinal plant recognized for its rich diversity of secondary metabolites, particularly flavonoids and essential oils, that are differentially distributed across its plant organs. This narrative review aimed to critically synthesizes the reported pharmacological activities, specific phytochemical constituents of each organ, molecular mechanisms of isolated bioactive compounds, and contributions of the metabolites produced by associated endophytic microorganisms. Relevant literature was identified through electronic databases including PubMed, Scopus, ScienceDirect, and Google Scholar using the keywords "*Houttuynia cordata*", "phytochemical", "pharmacological activity", and "secondary metabolites", from 2015-to 2025. A broad body of literature published was examined to map the diversity of bioactive compounds, experimental models, and mechanisms of action. The findings reveal that the leaves of *H. cordata* are rich in flavonoids such as quercetin and rutin, which act as potent antioxidants and immunoprotective agents. The stems and rhizomes are dominated by monoterpenes and volatile ketones exhibiting marked antimicrobial and anti-inflammatory properties. Preclinical evidence consistently demonstrates antitumor activity via apoptosis induction, multitarget antiviral effects, antidiabetic, and antihyperlipidemic activities as well as anti-inflammatory actions mediated through the inhibition of TNF-α and PGE_2 pathways. Antibacterial and anticancer properties are also notably attributable to the secondary metabolites produced by the endophytic microbiota associated with this plant. The phytochemical diversity of *H. cordata* and its symbiotic endophytes offer promising prospects for the discovery of novel bioactive compounds from Indonesian biological resources. Collectively, *H. cordata* holds substantial potential as antioxidant, antimicrobial, antivirus, anticancer, antidiabetic, antihyperlipidemic, anti-inflammatory, immunomodulatory, and antiasthma, warranting further investigation as an innovative phytopharmaceutical candidate.

Keywords: *Houttuynia cordata*; Secondary Metabolites; Pharmacology; Phytopharmaceutical; Endophyte.

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INTRODUCTION

The World Health Organization (WHO) reports that medicinal plants remain a primary source of health care for a large proportion of the population in developing countries, with traditional medicine still widely relied upon for basic treatment needs. The WHO estimates that around 80% of the people in regions such as Africa, Asia, and Latin America use traditional medicine to meet at least part of their primary health care demands. In many high-income countries, traditional medicine and phytotherapy are more commonly categorized as complementary or alternative medicine, and their use has shown a steady increase over recent decades in parallel with conventional medical services (Newman & Cragg, 2016).

A wide range of medicinal plants has been systematically investigated, with their active constituents isolated and subsequently developed into pharmaceutical raw materials that have progressed through preclinical and clinical evaluations. One plant with notable potential to be developed as a medicinal raw material is *Houttuynia cordata* Thunb., commonly known as chameleon plant, lizard's tail, fish mint, fish leaf, rainbow plant, heart leaf, or fish wort. *H. cordata* is a member of the Saururaceae family and is traditionally used both as a medicinal plant and as a vegetable in several East Asian countries, including China, Japan, Korea, and Vietnam. In contrast, in Indonesia this species remains underutilized and is rarely cultivated largely due to limited public and scientific awareness regarding its potential health benefits, processing methods, and values as a medicinal and functional food resource (Tamhid *et al*., 2025). *H. cordata* has been reported to possess multiple pharmacological activities, including antibacterial, antidiabetic (Li *et al*., 2017) (Sekita *et al*., 2016; Wang *et al*., 2018), antiviral (Cheng *et al*., 2019; Chiow *et al*., 2016), anti-inflammatory (Shin *et al*., 2010; Woranam *et al*., 2020), and anti-cancer (Inthi *et al*., 2023). These activities are associated with a broad spectrum of phytochemical constituents, such as essential oils, alkaloids, flavonoids, fatty acids, sterols, amino acids, and various microelements (Das *et al*., 2022; Ling *et al*., 2020).

Previous reviews on *H. cordata*, including the comprehensive work by Wei *et al.* (2024), have primarily summarized traditional uses, plant-derived phytochemicals, pharmacological activities, and safety profiles based on literature published up to mid-2023. However, these reviews are limited to metabolites produced by the plant itself and do not address secondary metabolites reported from endophytic fungi associated with *H. cordata*. In recent years, increasing evidence has shown that endophytic fungi inhabiting *H. cordata* are capable of producing structurally diverse and biologically active compounds, representing an additional and largely unexplored chemical reservoir. The present review extends beyond previous syntheses by integrating recent post-2023 literature and systematically compiling reported metabolites from *H. cordata*-associated endophytic fungi, thereby expanding the current understanding of its bioactive potential.

Research on the therapeutic potential of *H. cordata* has expanded from the plant itself to its associated endophytic microorganisms. Emerging evidence shows that the endophytic fungi isolated from *H. cordata* are capable of producing important secondary metabolites that display notable antibacterial and anticancer activities (Tamhid *et al*., 2025). This reinforces that the potential of *H. cordata* as a source of medicinal raw materials extends beyond the host plant itself to encompass its associated microbiome.

The potential of *H. cordata* as a source of medicinal raw materials and as strategic support for phytopharmacy in Indonesia necessitates a robust and systematic scientific foundation, which constitutes the principal objective of this review. The existing studies, while abundant, remain fragmented and largely descriptive. Current evidence has not been sufficiently integrated across pharmacological outcomes, organ-specific chemistry, molecular mechanisms, and contributions from endophytic metabolites, limiting its translational relevance for phytopharmaceutical development. This review therefore provides a critical synthesis to consolidate existing knowledge into a coherent framework supporting future development.This study aims to provide a critical synthesis of the reported pharmacological activities, organ-specific chemical constituents, molecular mechanisms of action of isolated compounds, and the role of endophytic metabolites to generate targeted guidance for the future development of this species as a medicinal raw material.

METHODS

This article adopts a narrative literature review approach to synthesize data on the phytochemical profile and pharmacological activities of *Houttuynia cordata* Thunb. Relevant literatures were retrieved using Harzing's Publish or Perish software connected to electronic databases including PubMed, Scopus, ScienceDirect, and Google Scholar using the keywords “Houttuynia cordata”, “phytochemical”, “pharmacological activity”, and “secondary metabolites”, which were combined with the Boolean operators AND and OR. The search was primarily restricted to publications from 2015 to 2025, with the addition of earlier studies when deemed conceptually important to the scope of the review.

The inclusion criteria comprised original research articles and review papers that discussed the phytochemical constituents, biological activities, or mechanisms of action of H. cordata, were available in full text, and were published in either English or Indonesian. Articles that were not relevant to the topic, available only as abstracts, categorized as editorials, or lacking clear information on H. cordata were excluded. Study selection was conducted through title and abstract screening, followed by full-text assessment of eligible articles.

A total of 303 records was initially identified; after removing 64 duplicates, 239 unique articles underwent title/abstract screening, yielding 159 for full-text assessment. Of these, 107 were excluded (76 irrelevant, 31 no full-text), leaving 52 studies that met inclusion criteria (original research/review articles on phytochemicals, biological activities, or mechanisms of H. cordata, full-text available in English/Indonesian, 2015-2025 with select earlier conceptually important studies) for narrative synthesis. The selection process followed the PRISMA flow diagram (**Figure 1**)

Extracted data included plant parts used, major bioactive compounds, experimental models, and activity parameters, which were subsequently synthesized narratively into the following thematic domains: morphology, organ-specific phytochemical profiles, and major pharmacological activities.

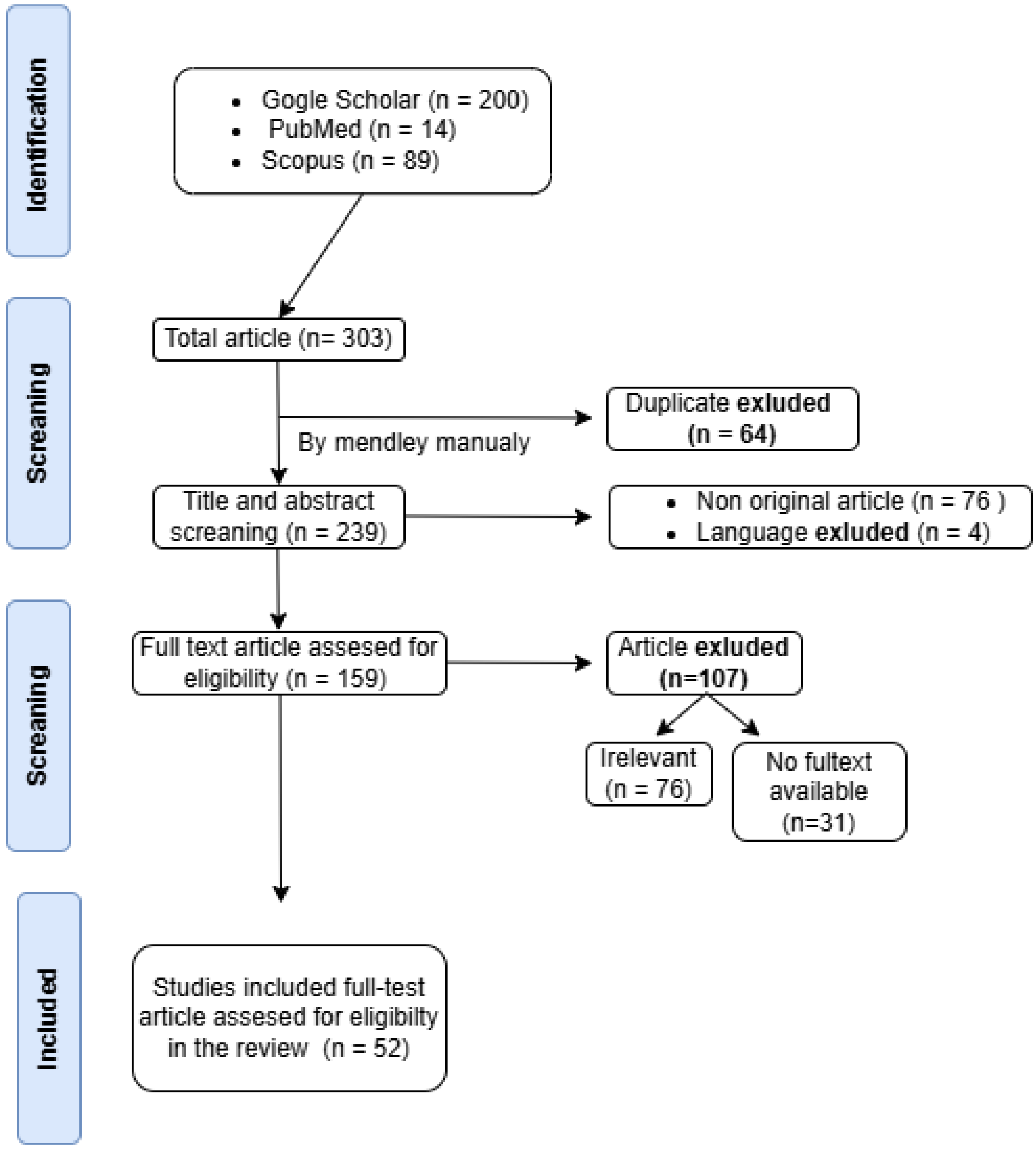

Figure 1. PRISMA flow diagram of study selection (n=303 identified, n=52 included).

RESULT AND DISCUSSION

Related Research

The trend in scientific publications related to *H. cordata* over the past decade is illustrated in Figure 1. The data demonstrate a steady increase in the number of publications from 2015 to 2025, with an average of approximately 35 articles per year, which reflect the growing global interest in the biological potential of this species.

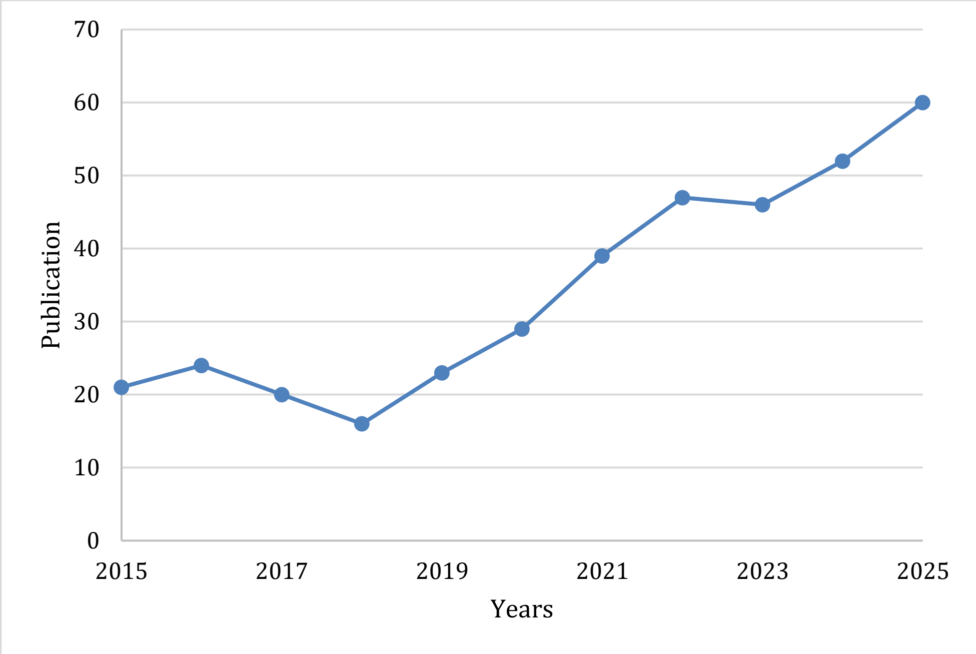

Figure 2. Research trends related to *H. cordata* according to PubMed 2015 – 2025

The expansion of multidisciplinary approaches in natural product research, particularly in pharmacology, biotechnology, and herbal drug development, becomes a key driver of this upward trend. *H. cordata* exhibits a wide range of biological activities, including anti-inflammatory, antiviral, antibacterial, antioxidant, antidiabetic, antihyperlipidemic, antiasthma, and anticancer effects, which have stimulated extensive research aiming to elucidate the mechanisms of action and explore the therapeutic applications.

Morphology of *H. cordata*

H. cordata is an herbaceous perennial plant that typically grows 20-80 cm in height, bearing simple, ovate-cordate leaves (Figure 3A). The rhizomes are white and covered with fine hairs (Figure 3B). The inflorescences consist of brownish-yellow spikes with yellowish-white flowers borne on terminal stalks of 2–3 cm long, subtended by 4–6 conspicuous white basal bracts (Figure 3C).

When crushed, *H. cordata* emits a characteristic fishy odour and has a slightly bitter taste. This species grows optimally in moist to wet soils on shaded hillsides, riverbanks, roadsides, and field ridges at elevations of approximately 300-2600 m. *H. cordata* propagates predominantly by vegetative means through the formation and separation of underground stems and by parthenogenesis rather than sexual reproduction (Luo *et al.*, 2022). The morphology of the leaves, radix, and flowers of *H. cordata* is illustrated in **Figure 3.**

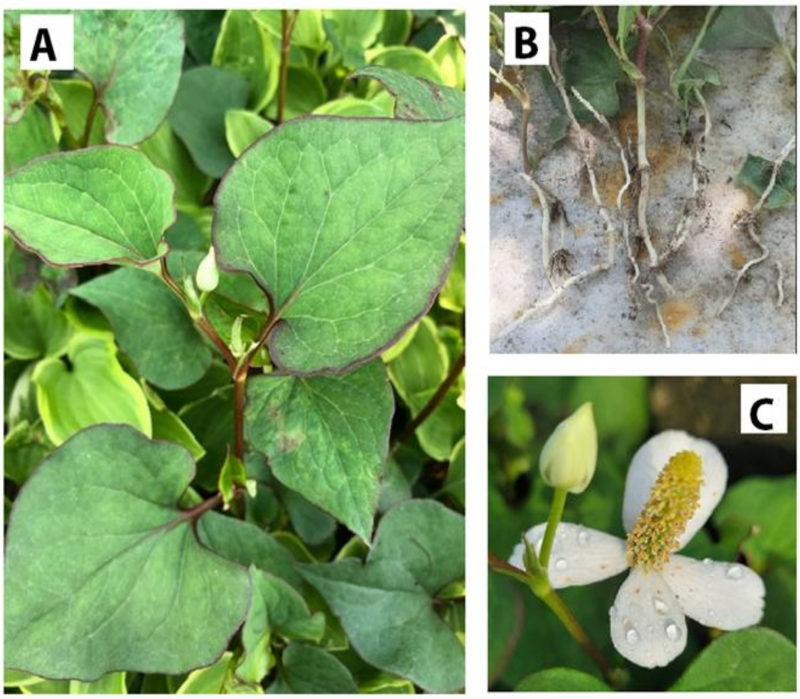

Figure 3. Morphology of Houttuynia *cordata,* Thunb. (A) leaves, (B) stems and radix, and (C) flowers

Main Bioactive Components and Phytochemical Profile of *H. cordata*

H. cordata is recognized as a medicinal plant with a highly complex secondary metabolite profile, comprising terpenoids, flavonoids, aldehydes, and polyphenolic compounds. This phytochemical diversity reflects the plant's physiological adaptation to environmental stress and underpins its broad spectrum of biological activities, including antioxidant, antimicrobial, and anti-inflammatory effects. Differences in chemical composition among the leaves, stems, and radix have been systematically characterized using the Gas Chromatography-Mass Spectrometry (GC-MS) and Headspace Solid-Phase Microextraction-based (HS-SPME-based) volatile analyses, which demonstrate organ-specific distributions of the key metabolites (Lin *et al*., 2022)(Qi *et al*., 2022). The bioactive phytochemical profile of *H. cordata* is summarized in Table 1, describing the constituents identified in different plant parts. In general, monoterpene volatiles are distributed throughout all organs (leaves, stems, radix), whereas flavonoid compounds are predominantly localized in the leaves.

Table 1. Phytochemical profile of *H. cordata*

Plant parts	**Compound**	**Class of Compounds**	**Reference**
Leaves	(Z)-3-Hexenal	Aliphatic aldehydes (volatile)	(Lin *et al*., 2022)
Leaves	(Z)-β-Ocimene & (4E,6E)-Allo-Ocimene	Monoterpenes	(Lin *et al*., 2022)
Leaves	Flavonoids (Quercetin, Rutin, Isoquercitrin)	Flavonoid	(Lin *et al*., 2022)

Plant parts	Compound	Class of Compounds	Reference
Leaves	β-Myrcene	Monoterpene hydrocarbons	(Dai *et al*., 2015)
Leaves	2-Undecanone	Aliphatic ketone	(Dai *et al*., 2015)
Leaves	(Z)-β-Ocimene	Monoterpenes, hydrocarbons	(Dai *et al*., 2015)
Leaves	Camphene, Limonene, β-Pinene	Monoterpene hydrocarbons	(Dai *et al*., 2015)
Leaves	Aliphatic Ketones (minor)	Aliphatic Ketones (minor)	(Dai *et al*., 2015)
Leaves	Quercitrin, Chlorogenic acid, Ferulic acid, Methyl linoleate, Gallic acid	Flavonoid, Phenolic acid, Fatty acid	(Xie *et al*., 2025)
Leaves	Caryophyllene	Monoterpenoid	(Hung et al., 2023)
Leaves	Quercetin, p-coumaroyl vitisin A, cinnamoyl-CoA, epicatechin-3-gallat	Flavonoid, Phenylpropanoid, Alkaloid, Sterol	(Boonchaisri et al., 2024)
Leaves and Stems	β-ocimene	Monoterpenes (volatiles)	(Lin *et al*., 2022)
Leaves and stems	Afzelin	Flavonoid	(Lee *et al*., 2015)
Leaves and stems	Hyperoside, Quercitrin	Flavonoid	(Lee *et al*., 2015)
Stem	Camphene, Geranyl acetate, Nerolidol, α-pinene, β-pinene, β-myrcene, limonene	Monoterpenes, Monoterpene esters, Sesquiterpenes, Monoterpene hydrocarbons	(Lin *et al*., 2022)
Stem	Camphene, β-myrcene, α-pinene, β-pinene	Monoterpene hydrocarbons	(Qi *et al*., 2022)
Sterm	Limonene, sabinene, p-cymene, γ-terpinene	Monoterpene hydrocarbons	(Qi *et al*., 2022)
Stem	Linalool, borneol, terpinen-4-ol, α-terpineol	Monoterpene oxygen	(Qi *et al*., 2022)
Stem	Geranyl acetate	Monoterpene esters	(Qi *et al*., 2022)
Stem	2-undecanone, 2-tridecanone	Aliphatic ketone	(Qi *et al*., 2022)
Stem	Camphene, β-myrcene, α-pinene, β-pinene	Monoterpene hydrocarbons	(Qi *et al*., 2022)
Stem	Limonene, sabinene, p-cymene, γ-terpinene	Monoterpene hydrocarbons	(Qi *et al*., 2022)
Stem	Aldehyde	Aldehyde	(Verma *et al*., 2017)
Stem	β-pinene	Monoterpenes (volatiles)	Hung et.al 2023
Rhizome	α-pinene, sabinene, β-pinene, β-myrcene, limonene	Monoterpene hydrocarbons	(Lin *et al*., 2022)
Rhizome	Bornyl acetate, decanoyl acetaldehyde	Terpenoid esters, aldehydes	(Lin *et al*., 2022)

Plant parts	Compound	Class of Compounds	Reference
Rhizome and stems	Bornyl acetate	Sesquiterpene esters/terpenoid esters	(Lin *et al.*, 2022)
Radix	2-Undecanone (methyl nonyl ketone)	Aliphatic ketone	(Lin *et al.*, 2022)
Radix	2-Tridecanone	Aliphatic ketone	(Lin *et al.*, 2022)
Radix	α-Pinene	Monoterpenes	(Lin *et al.*, 2022)
Radix	β-Pinene	Monoterpenes	(Lin *et al.*, 2022)
Radix	Limonene	Monoterpenes	(Lin *et al.*, 2022)
Radix	Bornyl acetate/bornyl isoval	Terpenoid esters	(Lin *et al.*, 2022)
Radix	Flavonoids (minor)	Flavonoid	(Wu *et al.*, 2021)
Radix	Alkaloids (houttuynine, aristolic acid)	Alkaloid	(Wu *et al.*, 2021)
Radix	Decanal	Aldehyde	(Yang *et al.*, 2016)
Radix	Decanoyl acetaldehyde	Volatile aldehyde	(Yang *et al.*, 2016)
Herba	Acteoside, Verbascoside, Kanzonol V, Progeldanamycin, Rhodoxanthin	Flavonoid, Sesquiterpene, Phenylpropanoid	(Bharathi et al., 2022)

Leaf Parts

H. cordata leaves are recognized as the plant part richest in structurally diverse secondary metabolites, particularly flavonoids and volatile constituents. Multiple studies have demonstrated that the leaves contain high concentrations of flavonoids such as quercetin, rutin, isoquercitrin, hyperoside, and afzelin, which function as potent antioxidants capable of neutralizing free radicals and supporting immune-protective mechanisms (Wei *et al.*, 2024; Wu *et al.*, 2021). The leaves also contain abundant volatile monoterpenes, including (Z)-3-hexenal, (Z)-β-ocimene, and camphene, which contribute a fresh, herbaceous aroma and function as signalling molecules in plant defence responses (Dai *et al.*, 2015)(Lin *et al.*, 2022).

Polyphenols and tannins present in leaf extracts further enhance the antioxidant capacity of *H. cordata*, making the leaves effective as anti-inflammatory and cytoprotective agents in various experimental models (Wei *et al.*, 2024). The occurrence of phenolic acids such as gallic acid and chlorogenic acid further broadens the pharmacological spectrum of the leaves, contributing to antibacterial, antiviral, and anti-inflammatory activities (Wu *et al.*, 2021). The phytochemical profile of *H. cordata* leaves is collectively characterized by an abundance of bioactive components and a comprehensive range of secondary metabolite classes, including flavonoids, polyphenols, monoterpenes, and phenolic acids (Dai *et al.*, 2015)(Lin *et al.*, 2022)(Wei *et al.*, 2024)(Wu *et al.*, 2021).

Stem Section

The stem of *H. cordata* is characterized by a chemical profile dominated by monoterpenes and terpenoid esters as revealed by GC-MS analyses. Major constituents such as camphene and β-myrcene are volatile monoterpenes that contribute to the characteristic aroma and function as defensive compounds against microbial attack (Lin *et al*., 2022)(Qi *et al*., 2022).

In addition, bornyl acetate and geranyl acetate, classified as terpenoid esters, impart balsamic aromatic notes and are reported to exhibit anti-inflammatory and antimicrobial activities. The sesquiterpene nerolidol shows cytoprotective properties and enhances cell membrane permeability, suggesting its potential as a penetration enhancer in topical drug delivery systems. The aldehydes present in the stem further contribute medium-chain volatile components that support essential oil stability and reinforce antibacterial effects. These features collectively indicate that the stem of *H. cordata* represents a major source of volatile constituents with both aromatic and pharmacologically relevant functions (Verma *et al*., 2017).

Radix/Rhizome Section

The radix or rhizomes of *H. cordata* display the most complex phytochemical profile among the plant organs and are particularly rich in volatile aliphatic ketones and aldehydes. The dominant constituents such as 2-undecanone (methyl nonyl ketone), 2-tridecanone, and decanoyl acetaldehyde (houttuynine) becomes the key volatile compounds that confer the characteristic pungent aroma and are associated with notable antimicrobial and anticancer activities. In addition, α-pinene, β-pinene, and limonene, belonging to the monoterpene class, are present at high levels in the underground parts and contribute to anti-inflammatory, bronchodilatory, and immunomodulatory effects, while also serving as important markers of essential oil composition. The detection of bornyl acetate in the radix indicates partial chemical similarity with the stem; however, in the underground organ, this constituent is thought to support essential oil stability and participate in metabolic defence processes. Overall, the radix or rhizome of *H. cordata* represents a highly bioactive tissue enriched in ketones, aldehydes, and monoterpenes that collectively underpin its antimicrobial, anticancer, and antioxidant potential (Lin *et al*., 2022)(Yang *et al*., 2016).

Phytochemical analyses of the leaves, stems, and radix clearly demonstrate that each organ of *H. cordata* possesses a distinct, organ-specific distribution of secondary metabolites. The diversity of both volatile and non-volatile constituents reflects the biochemical complexity of this species in adapting to environmental pressures. Among the identified compound classes, essential oils and flavonoids emerge as the principal bioactive groups responsible for the major biological and pharmacological effects of *H. cordata*. Notably, the characteristic fishy odour is primarily attributed to decanoyl acetaldehyde (also known in the context of the traditional Chinese medicinal herb Yu-Xing-Cao) (Ma *et al*., 2017) which exerts potent antibacterial activity and can be readily converted to 2-undecanone (methyl n-nonanone) at elevated temperatures, making it a useful indicator for evaluating the quality of *H. cordata* essential oil (Chen *et al*., 2014).

The steam distilled extracts of *H. cordata* yield essential oils composed mainly of monoterpenes, sesquiterpenes and their oxides, oxidized diterpenes, and phenylpropanoid derivatives, with nonyl ketone (2.10–40.36%), bornyl acetate (0.4–8.61%), and β-myrcene (2.58–18.47%) identified as the major constituents. Interestingly, notable quantitative and qualitative differences are observed between the aboveground and underground parts, whereas the contents of 2-undecanone, myrcene, ethyl decanoate, ethyl dodecanoate, 2-tridecanone, and decanal tend to be higher in aerial tissues than in subterranean ones; moreover, several constituents are uniquely detected either in the leaves or in the radix.

Regional variation has also been reported, with some studies describing differences in the antibacterial activity of *H. cordata* samples collected from different geographic locations, although current evidence remains limited and requires further systematic investigation (Lu *et al*., 2006)(Řebíčková *et al*., 2020)(Verma *et al*., 2017).

Pharmacological Activity of *H. cordata*

The presence of bioactive compounds in *H. cordata* is closely related to its biological and pharmacological activities. These properties include anticancer (Inthi *et al*., 2023), antiviral (Ghosh *et al*., 2022), anti-inflammatory (Li & Zhao, 2015), anti-asthma (Huang *et al*., 2023), antibacterial (Tamhid *et al*., 2025), antioxidant (Chen *et al*., 2023), and anti-COVID-19 (Bahadur Gurung *et al*., 2021). The following is an explanation of these various activities.

Table 2. Summary of the pharmacological activity studies of *H. cordata* plant

Plant parts used	Solvent/sample form	Research Model	Result	Reference
Herbaceous	Extract in standardized water	In Vitro (Herpes Simplex Virus Type 2/HSV-2)	Inhibiting HSV-2 infection by blocking the activation of the transcription factor NF-KB in host cells	(M. X. Chen et al., 2023)
Herbaceous	Ethanol Extract	STZ-induced diabetic rats	Lowering blood glucose, increasing insulin levels, improving lipid profiles and liver and kidney function, increasing GLUT-2 and GLUT-4 expression, decreasing caspase-3, and improving mitochondrial function	(Kumar *et al*., 2014)
Herbaceous	Ethyl Acetate Extract (*Extract in ethyl acetate*)	In vitro (Mouse Hepatitis Virus/MHV & Dengue Virus Type 2/DENV-2)	Inhibiting MHV and DENV-2 infectivity before the virus adsorption stage. Its activity is higher than single flavonoids (Quercetin, Quercitrin, Rutin)	(Chiow *et al*., 2016)
Herbaceous	Ethanol extract (*Extract in ethanol*)	Streptozotocin (STZ)-induced diabetic rats	Reducing fasting blood glucose (FBG), cholesterol (CHO), triglycerides (TG), and LDL levels, improving kidney and	(Poolsil *et al*., 2017)

Plant parts used	Solvent/sample form	Research Model	Result	Reference
			liver function (decreasing BUN, AST, ALT, ALP). Non-toxic up to 3000 mg/kg)	
Herbaceous	Standardized water extract	*In vitro*, Murine Norovirus-1/MNV-1, surrogate for human Norovirus (*In Vitro, Murine Norovirus-1/MNV-1, surrogate for human Norovirus*)	Showing strong antiviral effects (Results show strong antiviral effects)	(Cheng *et al.*, 2019b)
Herbaceous	Fermented extract in ethanol	*HFD + STZ-induced diabetic rats and 3T3-L1 adipocytes*	Lowering blood glucose and HbA1c, improving glucose tolerance, and reducing oxidative stress (MDA) and inflammatory mediators, improving pancreatic β- cell function and increasing glucose uptake in 3T3-L1	(Sakuludomkan *et al.*, 2021)
Herbaceous	Bioactive Compounds (Alkaloids, Polyphenols, Flavonoids)	*Molecular Docking* Simulation (Target: SARS-CoV-2 RdRp Enzyme)	Showing high affinity for the SARS-CoV-2 RdRp enzyme, potentially inhibiting COVID-19 virus replication	(Bahadur Gurung *et al.,* 2021)
Herbaceous	Water extract	Anaphylaxis model in mice	Inhibiting mast *cell degranulation*	(Li *et al.*, 2005)
Leaves and stems	Nano AgNPs from water extract	*In vitro* non-*cellular* in microorganisms	Increasing antimicrobial and antioxidant activity compared to the regular extract	(Moorthy *et al.*, 2023)
Fermented *Leaves*	Fermented extract	In vivo, intestinal carcinogenesis model in mice	Reducing DNA damage and genotoxicity	(Singai *et al.,* 2024)

Plant parts used	Solvent/sample form	Research Model	Result	Reference
Dried *Leaves*	Water extract	In vivo hypercholesterolemic *male* hamster	Reducing plasma cholesterol levels and atherosclerotic plaque	(Lin *et al.*, 2024)
Endophytes of *H. cordata*	Endophytic fungi extract in ethyl acetate	Antibacterial and *Anticancer*	*Ceratobasidium sp.* isolates having significant antibacterial and anticancer activity	(Tamhid *et al.*, 2025)
Leaves and *Stems*	Ethanol extract	STZ-induced diabetic Long-Evans rats	Significantly lowering blood glucose ($p < 0.001$), improving lipid profiles (LDL, TG, HDL), and improving liver, kidney, and heart function, containing active flavonoids such as routine, isochlorogenic acid C, and diosmin	(Rahman *et al.*, 2024)
Fresh *Leaves*	70% ethanol extract	In vitro, Human Gingival Epithelial Cells (HGECs)	Decreasing IL-1β and TNF-α expression, inhibiting oral inflammation	(Kunimatsu *et al.*, 2025)

Antimicrobial

H. cordata contains several key antimicrobial constituents, particularly decanoyl acetaldehyde (houttuynine), as well as limonene, bornyl acetate, and methyl nonyl ketone, which exhibit antibacterial activity against Gram-positive bacteria, such as Sarcina ureae and Staphylococcus aureus, and are also effective in inhibiting MRSA strains. The essential oil fraction rich in aldehydes, including caprylic aldehyde (decanal), lauryl aldehyde (dodecanal), and decanoyl acetaldehyde (3-oxo-dodecanal), shows strong activity against Gram-positive bacteria, with decanoyl acetaldehyde displaying the highest antibacterial potency but relatively low stability (Sekita *et al.*, 2016).

The ethanolic extracts of *H. cordata* obtained by maceration and formulated as topical preparations, such as clay masks or face scrubs, have demonstrated inhibitory effects on S. aureus associated with acne, and the highest tested concentration (30%) produces the largest inhibition zone in vitro, with an inhibition diameter of 1.806 cm (Rahardhian, 2024). In a periodontitis model, *H. cordata* at a concentration of 0.5 μg/mL reduces the mRNA overexpression of MMP-3, IL-8, IL-6, and ICAM-1 in HGEC cells stimulated by *Aggregatibacter actinomycetemcomitans* (Kabir *et al.*, 2015). In other pathogens, such as *S. aureus* and *P. aeruginosa*, *H. cordata* also inhibits bacterial growth and is not cytotoxic to healthy eukaryotic cells; in addition, in patients with diabetic foot ulcers, *H. cordata* treatment is more effective than methicillin and meropenem and significantly reduces serum TNF-α and IL-6, thus highlighting its potential as a new clinical alternative to antibiotics (Geng *et al*., 2025).

Adding to this antimicrobial potential, recent research shows that the endophytic microbiome associated with *H. cordata* also produces biologically active metabolites. The endophytic fungal isolates obtained from *H. cordata* exhibit significant antibacterial activity, indicating that this plant serves as a host for microorganisms that may represent a valuable reservoir for the discovery of novel antibacterial agents, which is particularly important in the context of global antibiotic resistance (Tamhid *et al*., 2025).

Antioxidants

Continuous exposure to various triggering factors can induce oxidative stress in living cells across species, including humans, animals, and plants. Oxidative stress may arise from exogenous sources such as persistent exposure to toxic pollutants and ionizing radiation, and its severity in biological systems is reflected either by increased oxidant levels or by a decline in endogenous antioxidant defences (Chen *et al*., 2023). In this context, *H. cordata* is a promising antioxidant medicinal plant with the potential to protect cells against oxidative stress-induced damage. This is demonstrated in a study using an ethyl acetate extract of *H. cordata*, where the DPPH assays show that doses of 250 and 500 μg/mL produce significant antioxidant activity, with quercitrin identified by Liquid Chromatography-Mass Spectrometry (LC-MS) as a key bioactive compound responsible for this effect (Kim *et al*., 2024).

An additional antioxidant evaluation has been performed by using *H. cordata* as a bioreducing agent for the green synthesis of silver nanoparticles (*H. cordata* E-AgNP) under optimized microwave conditions (100°C for 10 minutes). The resulting *H. cordata* E-AgNP displays a characteristic UV-Vis absorption peak at 430 nm and a nanoscale particle size of 19.7 ± 4.2 nm, with further characterization by the zeta potential, FT-IR, XRD, and XPS confirming their physicochemical properties (Moorthy *et al*., 2023). From the perspective of traditional Chinese medicine, *H. cordata* is regarded as a phytonutrient-rich herb with strong antioxidant potential, and nanoparticle formulation is shown to enhance its antioxidant capacity compared with the crude extract alone (Moorthy *et al*., 2023).

Antivirus

H. cordata is an herbal plant rich in bioactive compounds such as decanoyl acetaldehyde (houttuynine), decanal, dodecanal, methyl-n-nonyl ketone, and major flavonoids including quercetin, quercitrin, and rutin, the combined volatile and polyphenolic components of which underlie their broad pharmacological activities, particularly the antiviral effects mediated either by direct virucidal action or by modulation of host cell signalling pathways. In vitro, the ethyl acetate fraction of *H. cordata* inhibits the infectivity of Mouse Hepatitis Virus (MHV) and Dengue Virus serotype-2 (DENV-2) with IC_{50} values of 0.98 μg/mL and 7.50 μg/mL, respectively, without detectable cytotoxicity to host cells, with the strongest effect observed at the post-penetration stage, thus suggesting suppression of viral replication likely associated with flavonoids such as quercetin and rutin that can interfere with RNA virus replication enzymes (Chiow *et al*., 2016).

A hot water extract of *H. cordata* also demonstrates antiviral activity against Herpes Simplex Virus type 2 (HSV-2) by inhibiting activation of the transcription factor NF-κB, a key regulator of viral replication and virus-induced inflammatory responses; in addition, HCWE reduces viral protein expression with an IC_{50} of approximately 50 μg/mL, indicating concurrent antiviral and immunomodulatory effects (Chen *et al*., 2011). Meanwhile, the polysaccharide fraction of *H. cordata* shows significant activity against murine norovirus-1 (MNV-1) at an effective concentration of around 305.6 μg/mL, acting primarily by disrupting viral particle integrity and inhibiting early replication steps, which is consistent with a direct virucidal mechanism (Cheng *et al*., 2019a). Furthermore, flavonoids, especially quercetin, have been reported to act against multiple enveloped viruses, including SARS-CoV, HSV, and influenza viruses, through inhibition of essential replication enzymes such as 3CLpro and RNA-dependent RNA polymerase (RdRp), as well as by interfering with viral attachment to host receptors, thus highlighting the multi-target antiviral potential of flavonoids derived from *H. cordata* (Ghosh *et al*., 2022).

In vitro and in vivo studies show that *H. cordata* extract effectively inhibits Coxsackievirus A4 (CVA4) replication at the post-entry stage while simultaneously reducing pro-inflammatory cytokines such as TNF-α and IL-6, improving survival, and attenuating tissue damage in infected mice, which therefore underscore its dual antiviral and anti-inflammatory actions in RNA virus infections (Su *et al*., (2025). Overall, *H. cordata* exhibits broad antiviral activity via multifactorial mechanisms, including direct inactivation of viral particles, inhibition of replication, and modulation of host immune and inflammatory pathways, with ethyl acetate, aqueous, and polysaccharide fractions as the most active and low-toxicity components, which support its candidacy for the development of natural antiviral phytotherapeutic agent (Chen *et al*., 2011)(Cheng *et al*., 2019)(Chiow *et al*., 2016) (Ghosh *et al*., 2022)(Su *et al*., 2025).

Anticancer

Various types of cancer affecting individuals across age groups require different therapeutic strategies, and although radiotherapy and chemotherapy remain the mainstay of malignant tumour treatment, both are associated with significant adverse effects and complications. In recent years, non-conventional approaches, including traditional Chinese medicine, have been increasingly proposed as adjuncts to standard therapy because they may alleviate side effects and enhance therapeutic efficacy. In this context, extracts and derivatives of *H. cordata* show promising anti-tumour potential. The antiproliferative activity of *H. cordata* has been evaluated in multiple cancer cell lines, including HeLa, HT-29, T116, MCF-7, and Jurkat cells, by using MTT assays and flow cytometry with apoptosis induction and cell-cycle arrest being the key mechanisms, and one of the earliest reports of its efficacy against cancer is in adenocarcinoma cells (Laldinsangi, 2022).

The ethanolic extracts of *H. cordata* exhibit significant cytotoxic effects against HT-29 colon cancer cells, where treatment at 450 μg/mL induces apoptosis, decreases mitochondrial membrane potential, and increases intracellular reactive oxygen species, indicating mitochondrial-mediated cell death. *H. cordata* also shows activity against breast cancer, particularly in HER2/neu-overexpressing cells, where it dose-dependently inhibits HER2 phosphorylation in MDA-MB-453 cells with an IC_{50} of 5.52 μg/mL, without altering total HER2/neu protein expression, and blocks downstream ERK1/2 and AKT signalling, while the ethanol extracts at 100–500 μg/mL significantly enhance apoptosis in breast cancer cells (Rafiq *et al*., 2022). These findings collectively support the anti-tumour properties of *H. cordata*.

Anticancer research on *H. cordata* is not limited to plant-derived metabolites. Recent studies reveal that its associated microbiota, particularly endophytic fungi, also produce secondary metabolites with notable biological activity. The endophytic fungal isolates from *H. cordata* demonstrate significant antibacterial and anticancer effects, with *Ceratobasidium* sp. identified as a prominent anticancer candidate (Tamhid *et al*., 2025). These observations highlight the importance of exploring both the host plant and its endophytic microbiome as complementary reservoirs of novel bioactive molecules and further reinforce the evidence that *H. cordata* possesses meaningful anti-tumour activity (Inthi *et al*., 2023).

Antidiabetic

Multiple studies show that *H. cordata* has significant antidiabetic potential mediated by diverse biochemical and physiological mechanisms. In STZ-induced diabetic rats, 80% ethanolic herb extract reduces fasting blood glucose, improves lipid profiles, and ameliorates liver and kidney functions by lowering AST, ALT, and ALP activities while showing no overt toxicity at doses up to 3000 mg/kg, indicating acceptable safety for oral use in preclinical settings (Poolsil *et al*., 2017). Consistent findings from other experiments show that the ethanolic extracts at 200 and 400 mg/kg not only decrease blood glucose but also increase serum insulin and enhance the expression of key glucose transporters GLUT-2 and GLUT-4, suggesting improved insulin sensitivity and glucose uptake in peripheral tissues; in addition, reduced caspase-3 expression indicates protection of pancreatic β-cells from STZ-induced, oxidative stress-mediated apoptosis (Kumar *et al*., 2014).

The development per se has progressed beyond simple extracts to fermented *H. cordata* preparations formulated as tablets and tested in high-fat diet/STZ-induced diabetic rat models. The administration of fermented extract at 100 mg/kg lowers blood glucose, improves glucose tolerance, and decreases oxidative stress markers such as MDA, whereas the histopathology reveals restoration of pancreatic β-cell structure and function. In vitro, the ethanolic extract enhances glucose uptake and reduces lipolysis in palmitate-treated 3T3-L1 adipocytes, indicating enhanced insulin sensitivity which is an effect likely related to biotransformation-enhanced levels of flavonoids, phenolics, and β-glucans in the fermented product (Sakuludomkan *et al*., 2021).

More recent work with 500 mg/kg ethanolic extract of *H. cordata* in STZ-induced Long Evans rats confirms the strong antihyperglycemic and antidyslipidemic effects, and identifies rutin, isochlorogenic acid C, and diosmin as key constituents by using metabolomics and molecular docking, with predicted inhibitory activity against α-glucosidase and α-amylase as well as modulatory effects on insulin receptor signalling and PPAR-γ (Rahman *et al*., 2024). Besides normalizing blood glucose and lipid parameters, the extract attenuates histological damage in the pancreas, liver, kidney, and heart, indicating a multi-organ protective effect relevant to diabetic complications (Rahman *et al*., 2024).

These four studies collectively indicate that the antidiabetic activity of *H. cordata* is closely linked to its rich content of flavonoids (quercetin, rutin, kaempferol), phenolic acids (chlorogenic and rosmarinic acids), β-glucans, and alkaloids, which act as antioxidants and anti-inflammatory agents, enhance insulin sensitivity, and protect pancreatic β-cells from apoptosis. Variations in the extraction and processing methods (ethanolic, air-dried, fermented) influence the profile and potency of active constituents, with ethanolic extracts generally yielding the strongest effects and fermentation further increasing the flavonoid and β-glucan levels through biotransformation. Overall, *H. cordata* shows consistent antihyperglycemic and antidyslipidemic effects via multifactorial mechanisms including increased GLUT-4 expression, improved insulin sensitivity, inhibition of carbohydrate-digesting enzymes, and robust antioxidant and anti-inflammatory actions supporting its potential development as a safe and effective antidiabetic phytotherapeutic agent.

Antihyperlipidemic

Elevated serum lipid levels, particularly total cholesterol, are a major contributor to the development of atherosclerosis and coronary artery disease (Ross, 1999). *H. cordata* has been identified as a promising antihyperlipidemic plant, with several studies demonstrating the beneficial effects on lipid metabolism. The water extracts of *H. cordata* are shown to suppress corn-oil-induced increases in plasma triglycerides in rats, decrease the elevations in plasma oleic acid, glycerol, and non-esterified fatty acids, and exhibit anti-obesity effects in high-fat-diet models (Lau *et al*., 2008)(Miyata *et al*., 2010).

Further *in vivo* work in hyperlipidaemic Wistar rats reveals that the oral administration of ethanolic leaf extract of *H. cordata* at 500 mg/kg body weight significantly reduces total cholesterol, triglycerides, and LDL-cholesterol while increasing HDL-cholesterol, thus indicating a favourable modulation of the atherogenic lipid profile (Tassa *et al*., 2023). The acute toxicity testing yields an LD_{50} above 2000 mg/kg body weight with no mortality, thus supporting a wide safety margin and reinforcing the potential of this extract as a candidate antihyperlipidemic phytotherapeutic agent (Tassa *et al* , 2023).

Anti-inflammatory and immunomodulatory

H. cordata aqueous extract has proved to stimulate mouse splenic lymphocyte proliferation in a dose-dependent manner and increase the proportions of $CD4^+$ and $CD8^+$ T cells, which are crucial for macrophage activation, cytotoxic T-cell responses against intracellular pathogens, and Th2-mediated anti-helminth and allergic responses (Lau *et al*., 2008b).

H. cordata also exhibits robust anti-inflammatory properties across several experimental models. Essential oil administration reduces inflammation in carrageenan-induced pleuritis and ear oedema in mice (Lu *et al*., 2006). The aqueous extract demonstrates anti-SARS-CoV activity in vivo by enhancing $CD4^+/CD8^+$ T-cell counts and upregulating IL-2 and IL-10 expression (Lau *et al*., 2008b). The supercritical fluid extracts suppress exudation, albumin leakage, and inflammatory cell infiltration in carrageenan-induced inflammation while decreasing TNF-α, nitric oxide (NO), and prostaglandin E_2 (PGE_2) levels, thus indicating the inhibition of TNF-α–NO and COX-2–PGE_2 pathways and reduced capillary permeability and C-reactive protein at doses of 0.54 and 1.08 mL/100 g (Shin *et al*., 2010). These data are consistent with the traditional use of *H. cordata* in East Asian medicine for inflammatory conditions such as ulcerative colitis (Shin *et al*., 2010).

Another study using *H. cordata* fermentation broth demonstrates concordant anti-inflammatory activity in both *in vitro* (LPS-stimulated RAW 264.7 macrophages) and in vivo (carrageenan-induced paw oedema) models. The methanolic and aqueous extracts reduce NO production and downregulate LPS-induced expression of PGE_2, iNOS, IL-1β, TNF-α, and IL-6 *in vitro*, while orally administered preparations attenuate paw oedema in rats to a degree comparable to diclofenac at 150 mg/kg, thus supporting the conclusion that *H. cordata* exerts meaningful anti-inflammatory effects via suppression of key inflammatory mediators (Woranam *et al*., 2020).

Anti-asthma

Asthma is a chronic inflammatory airway disease frequently associated with allergic sensitization and characterized clinically by bronchial hyperresponsiveness and reversible airflow obstruction, leading to dyspnoea, chest tightness, and wheezing that typically worsens at night or in the early morning. *H. cordata* has been reported to exert anti-asthmatic effects in several experimental models. In house-dust-mite (HDM)-induced asthma models, HDM exposure increases Ca^{2+} release and inositol 1,4,5-trisphosphate receptor (IP_3R) activity, both of which contribute to bronchoconstriction; in addition, nebulized *H. cordata* essential oil in DMSO (10 mg/mL, 10 mL) significantly attenuates these responses compared with the negative control, sodium houttuyfonate (Huang *et al*., 2023). In a separate study, *H. cordata* inhibits systemic anaphylaxis and mast-cell activation in mice challenged with degranulating agents, thereby preventing histamine release and interrupting early allergic responses (Li *et al*., 2005).

In vivo experiments in ovalbumin (OVA)-induced asthmatic mice further demonstrate that oral administration of *H. cordata* reduces airway hyperresponsiveness and inflammation. Network pharmacology and profiling approaches identify six putative bioactive constituents, including isoramanone, kaempferol, spinasterol, C09747 1-methyl-2-nonacosyl-4-quinolone, and quercetin, as the key mediators of these effects. Treatment with *H. cordata* significantly decreases neutrophil, eosinophil, and lymphocyte counts, as well as IL-1β, IL-4, IL-6, and IL-13 concentrations in bronchoalveolar lavage fluid, and downregulates mRNA and protein expression of p38 MAPK, PI3K, AKT, and VEGF in lung tissue, all of which are elevated in untreated asthmatic mice. These findings suggest that *H. cordata* exerts multi-target anti-asthmatic activity by modulating calcium signalling, mast-cell degranulation, T-helper-2 cytokines, and key inflammatory signalling pathways (Yang *et al*., 2016).

CONCLUSION

The herbal plant *Houttuynia cordata* Thunb. exhibits a strong phytopharmaceutical profile, supported by a wealth of secondary metabolites especially flavonoids and essential oils that are specifically distributed in each of its organs. Preclinical evidence consistently confirms its antitumor activity through apoptosis induction, anti-inflammatory through inhibition of the TNF-α/PGE2 pathway, antiviral, and antidiabetic properties. Interestingly, prominent anticancer and antibacterial activities also originate from plant-associated endophytic fungi, such as *Ceratobasidium sp.* isolates, opening new avenues for the discovery of bioactive agents and drugs.

However, current evidence remains largely preclinical and heterogeneous, with substantial variation in plant part selection, extraction methods, and bioassay design, which hampers direct comparison and pharmaceutical standardization. Furthermore, the pharmacological relevance of endophytic metabolites is still insufficiently integrated into mainstream phytopharmaceutical development frameworks. Future advancement of *H. cordata* as a medicinal raw material therefore requires systematic standardization of organ-specific extracts, deeper elucidation of molecular targets, safety and pharmacokinetic evaluation, and clearer positioning of endophyte-derived metabolites within regulatory and development pathways. Addressing these challenges is essential to translate the promising bioactivity of *H. cordata* into clinically and industrially viable phytopharmaceutical products.

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AUTHOR CONTRIBUTION

AST: Creating research concept, drafting article, revising final manuscript
UZH: Collecting research data, drafting article, revising final manuscript
PTA: Collecting research data, drafting article
JDA: Collecting research data, drafting article

ETHICS APPROVAL

Not applicable

CONFLICT OF INTEREST

None to declare

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