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Review article

Phytochemical diversity, therapeutic potential, and ecological roles of the *Cecropia* genus

Latifah Al Shammari

Department of Pharmaceutical Chemistry, College of Pharmacy, University of Hafr Al Batin, P.O. Box 1803, Hafr Al Batin, 31991, Saudi Arabia

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ABSTRACT

The genus *Cecropia*, a pivotal component of Neotropical flora, is renowned for its integration of traditional medicinal uses with significant ecological functions. This review aims to highlight the phytochemical diversity and pharmacological activities of the *Cecropia* genus, with a particular focus on well-documented species such as *C. angustifolia*, *C. glaziovii*, and *C. pachystachya*. Through a comprehensive review of the literature and current studies, this review identifies critical phytochemicals, including flavonoids, phenolic acids, and terpenoids, and correlates these compounds with biological activities such as anti-inflammatory, antimicrobial, and antioxidant effects. Notably, the review delves into the pharmacological potential of less than ten out of the sixty-six accepted *Cecropia* species, revealing a significant research opportunity within the genus. The findings advocate for intensified drug discovery initiatives involving advanced phytochemical analyses, bioactivity assessments, and the integration of conservation strategies. These efforts are crucial for the sustainable utilization of new therapeutic agents for *Cecropia* species. Additionally, this review discusses the ecological roles of *Cecropia*, particularly its contributions to forest regeneration and its symbiotic relationships with ants and proposes future research directions aimed at bridging current knowledge gaps and enhancing conservation measures for this valuable genus.

1. Introduction, background and ethnobotanical significance of the *Cecropia* genus

Within the rich biodiversity of the Neotropical region, the genus *Cecropia* stands as a pivotal subject of investigation, intertwining ecological significance with traditional medicinal use and emerging scientific interest [1,2]. This widespread occurrence has facilitated the incorporation of *Cecropia* species into the ethnomedical practices of various indigenous and local communities across these regions [3,4]. *Cecropia* is a genus of more than 60 species known for its distinctive presence from southern Mexico through Central America, extending into South America as far south as northern Argentina and Uruguay [2]. The *Cecropia* genus is predominantly distributed across the Neotropical regions of the Americas, with its range extending from southern Mexico to northern Argentina. *Cecropia* species are found throughout Central America, including Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, and Panama. In South America, they are widespread in Colombia, Venezuela, Guyana, Suriname, Ecuador, Peru, Brazil, Bolivia, and Paraguay. The genus is also present in the Caribbean, notably in countries like Puerto Rico, the Dominican Republic and Tobago (Fig. 1). These species primarily thrive in lowland tropical rainforests but can also be found in montane forests up to elevations of 2000 m. Due to their fast-growing and colonizing nature, *Cecropia* species are commonly found in disturbed environments, such as forest edges, clearings, and along riverbanks. Their ecological role as pioneer species in forest regeneration is well-documented, and they form mutualistic

E-mail address: lamalshammari@uhb.edu.sa.

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relationships with ants, particularly in regions with high biodiversity like the Amazon Basin and the Andean foothills [5].

Historically, *Cecropia* species have been used in traditional medicine for centuries against the backdrop of their traditional use across Latin American cultures, where these plants have been revered for their healing properties [6]. These practices leverage different parts of the plant, including leaves, bark, and roots, to treat respiratory disorders, such as asthma and bronchitis, hypertension, diabetes, kidney disorders, cardiovascular complications, and inflammatory conditions [6–10]. The versatility of *Cecropia* in traditional medicine reflects deep ethnobotanical knowledge that underscores the potential pharmacological benefits of plants.

Among the myriad of species, *C. angustifolia* [1,11], *C. obtusifolia* [12], *C. peltate* [13], *C. pachystachya* [8,14], and *C. glaziovii* [15] stand out for their distinctive roles in traditional medicine, serving as natural remedies for a spectrum of ailments, from hypertension and diabetes to inflammatory disorders [12–15]. These species have been particularly studied for their pharmacological activities because they are rich in phytochemical constituents known for their antioxidant, anti-inflammatory, and antimicrobial properties. *Cecropia* species also play pivotal roles in their ecosystems as keystone pioneer species, facilitating forest regeneration and providing habitat and nourishment for a diverse array of fauna [16]. The symbiotic relationships between *Cecropia* trees and various species of ants, for example, highlight the ecological importance of these trees in maintaining the delicate balance of tropical ecosystems [17]. Such interactions underscore the genus's ecological value, weaving it into the fabric of tropical biodiversity and conservation efforts.

Pharmacological studies have begun to unravel the bioactive compounds present in *Cecropia* species, revealing a complex phytochemical profile that includes flavonoids, terpenoids, and other secondary metabolites [13,14,18–20]. These findings have corroborated some of the traditional uses, thereby establishing a scientific foundation for further exploration.

Although notable advancements have been made, there remains a significant gap in the understanding of the pharmacological properties, mechanisms of action, and therapeutic potential of Cecropia species compared to their ethnobotanical applications. While key bioactive compounds have been identified in certain species, a comprehensive phytochemical investigation across the genus, as well as a detailed understanding of the pharmacological mechanisms underlying the observed biological effects of Cecropia extracts and compounds, is still lacking. Therefore, there is a need for systematic studies to elucidate the full spectrum of bioactive compounds present in various species, which could uncover new therapeutic agents. Thus, our aim of this review is to provide a thorough investigation of the genus *Cecropia,* exploring its ethnobotanical significance, phytochemical diversity, and pharmacological activities. This review will comprehensively illuminate the multifaceted aspects of *Cecropia* species, providing a valuable resource for researchers interested in complementary medicine and drug discovery from nature, particularly from *Cecropia* species.

2. Taxonomic classification of the genus *Cecropia*

The genus *Cecropia*, a focal point of ecological, pharmacological, and conservation research within the Neotropical flora, exhibits a rich taxonomical hierarchy that underscores its botanical significance. Derived from the comprehensive database of the Plants of the

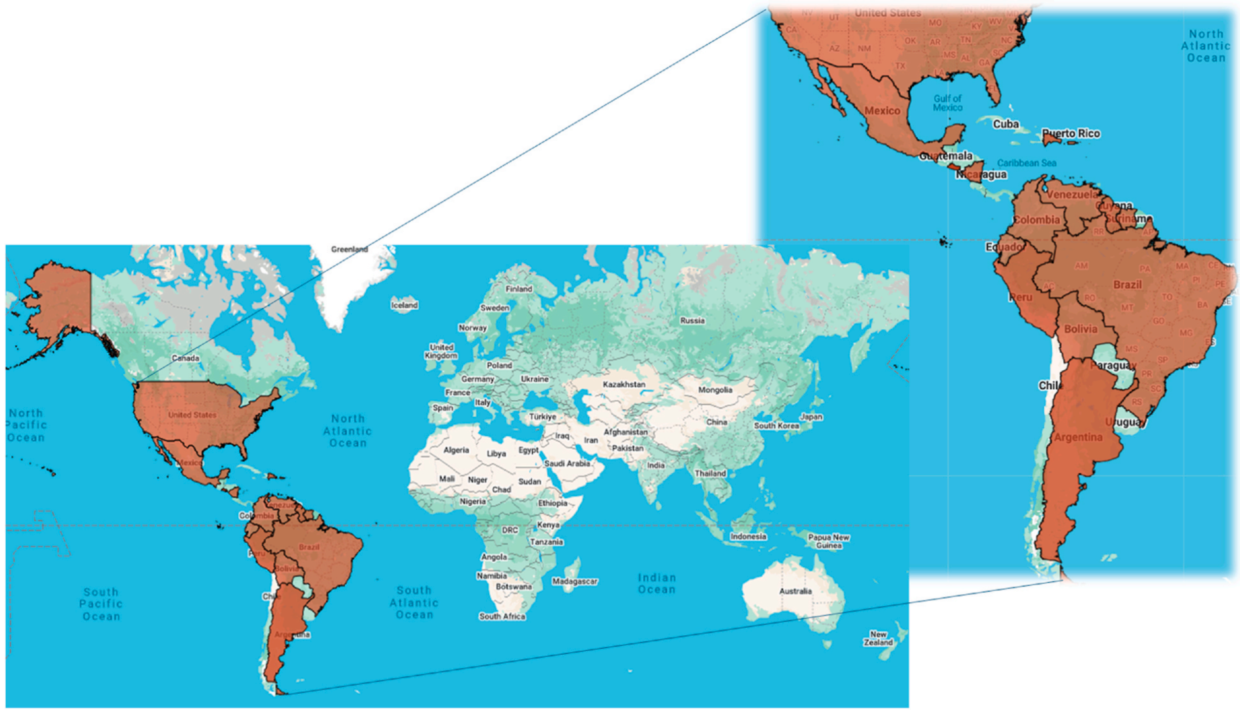

Fig. 1. Geographic Distribution of the *Cecropia* Genus Across the Americas: This map highlights key countries such as Guatemala, Nicaragua, Venezuela, Colombia, Ecuador, Peru, Brazil, and Argentina, where *Cecropia* species are commonly found.

World Online (POWO) by Kew Science (https://powo.science.kew.org/accessed on March 01, 2024), the taxonomical classification of *Cecropia* describes its placement within the broader context of plant biodiversity (Fig. 2).

3. Phytochemical diversity and biological activities of selected *Cecropia* species

According to the world flora online (WFO) plant list website (https://wfoplantlist.org, accessed on March 05, 2024), the *Cecropia* genus has two synonyms, *Coilotapalus* and *Ambaiba,* and includes 66 accepted species with a total of 164 synonyms. Moreover, there are 7 unplaced plant species still under taxonomic classification to ensure their relation to the genus *Cecropia* (Table 2). The genus *Cecropia*, with its 66 accepted species, contains intricate phytochemical constituents ranging from flavonoids and terpenes to saponins and alkaloids (Table 2), underscoring a complex phytochemical landscape poised for pharmacological exploration.

Despite the rich phytochemical diversity found within *Cecropia* spp., scientific research has been disproportionately concentrated on a select few species. This has left a vast potential for pharmacological discovery untapped within the genus. The species that have garnered the most attention in the literature to date are *C. angustifolis*, *C. hispidissima,* C. *glaziovii and C. pachystachya.* The current review endeavors to illuminate the phytochemical and pharmacological properties of these predominantly studied species within the *Cecropia* genus (Fig. 2). Therefore, this study aims to lay a foundation for a more systematic and comprehensive examination of the lesser-studied species, potentially unlocking novel bioactive compounds with significant therapeutic properties. The insights derived could thus be pivotal in advancing the domains of pharmacognosy and biodiversity, contributing to the conservation of these species and the enrichment of medical research.

3.1. *Phytochemistry of the Cecropia genus*

The *Cecropia* genus is known for its diverse range of phytochemicals, which contribute significantly to its medicinal properties and traditional uses (Table 2, Fig. 3). The genus is rich in terpenoids, phenolics, flavonoids, and saponins, each playing a vital role in the biological activities observed across various *Cecropia* species.

Terpenoids are one of the most significant classes of bioactive compounds in *Cecropia* species, particularly in species like *C. pachystachya*, *C. palmata*, and *C. hololeuca* [20–25]. Compounds such as ursolic acid and oleanolic acid, which are prevalent in these species, are well-documented for their anti-inflammatory, antioxidant, and hypoglycemic properties [26,27]. Ursolic acid, in particular, has been highlighted in numerous studies for its ability to reduce inflammation, support wound healing, and modulate metabolic pathways, making it a potential candidate for treating conditions such as diabetes and cardiovascular diseases [28,29]. Similarly, oleanolic acid has been linked to anti-inflammatory and antidiabetic effects, further validating the traditional use of these plants in treating chronic inflammatory and metabolic disorders [29,30].

Phenolic compounds, such as chlorogenic acid, caffeoylquinic acid, and rutin, are abundant in species like *C. glaziovii* and *C. hololeuca* [20,22,31–35]. These compounds are powerful antioxidants, protecting cells from oxidative stress, which is a key factor in the development of chronic diseases such as cancer, cardiovascular disease, and neurodegenerative disorders [36–39]. Chlorogenic acid, in particular, has garnered attention for its role in improving cardiovascular health and managing blood glucose levels, making it especially relevant in the context of diabetes treatment [40,41]. The phenolic-rich profile of *Cecropia* species supports their traditional use in preventing and managing diseases linked to oxidative stress and inflammation.

Saponins are another important group of bioactive compounds found in species such as *C. hispidissima* and *C. glaziovii* [31–35,42,43]. Triterpenoid saponins, including niga-ichigoside F2 and buergericic acid, have been studied for their hepatoprotective and antimicrobial properties [44–46]. These saponins have been shown to lower cholesterol levels [47], enhance immune function [48], and protect against microbial infections [49], aligning with the traditional use of *Cecropia* species in treating inflammatory and infectious diseases.

Flavonoids, including quercetin, luteolin, and vitexin, are widely distributed across the genus, particularly in *C. peltate* [50],

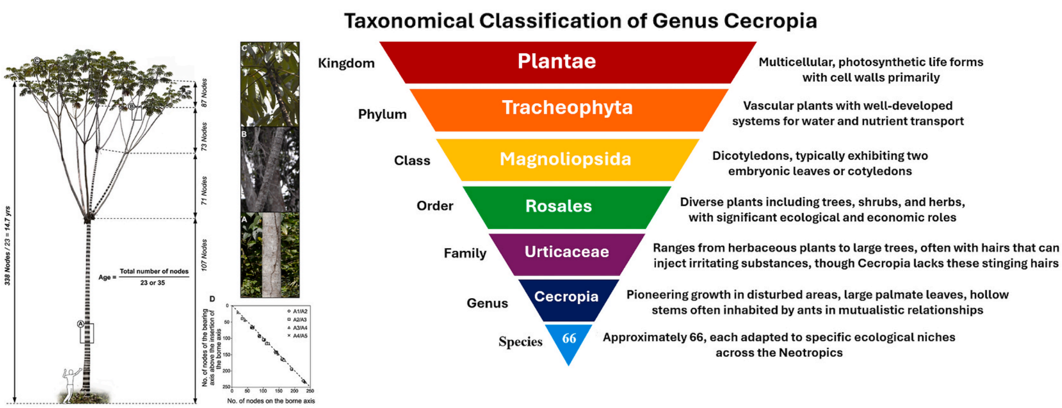

Fig. 2. Taxonomical Classification of *Cecropia* according to the Plant of the World Online database.

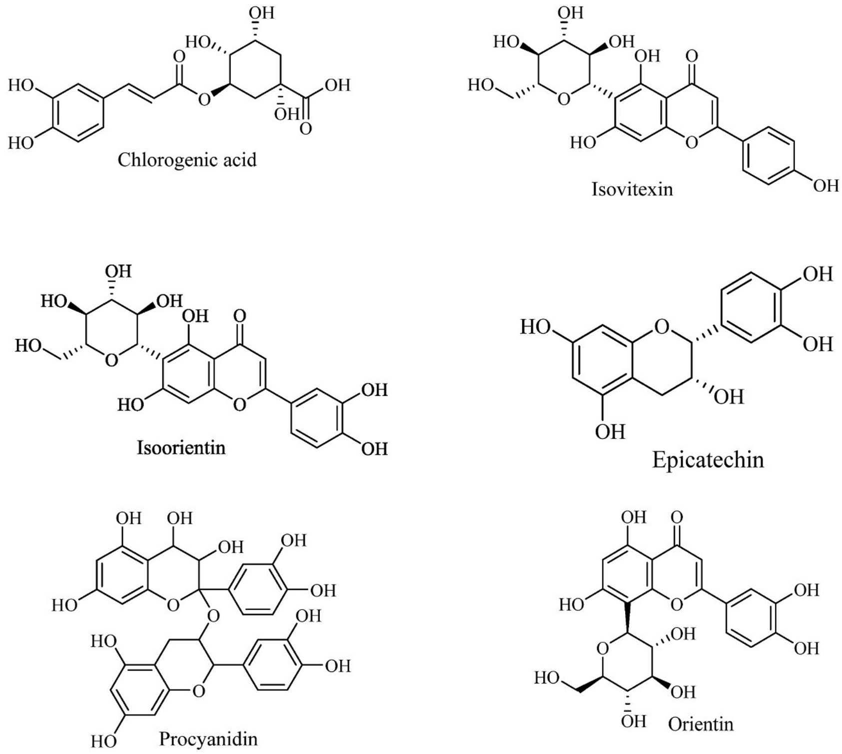

Fig. 3. Chemical structures of main phytochemicals reported for plants of the genus *Cecropia.*

C. hololeuca [20,22], and *C. glaziovii* [31–35]. These compounds are known for their antioxidant [51], anti-inflammatory [52], and neuroprotective properties [53]. Quercetin and luteolin, for example, have been extensively studied for their ability to neutralize free radicals and reduce oxidative stress, which is associated with aging and chronic disease development [54–56]. The presence of these flavonoids in *Cecropia* species reinforces their use in traditional medicine for treating inflammatory conditions and enhancing overall health.

There are currently very few studies that focus on the essential oil content of Cecropia species [57]. However, recent research has confirmed the presence of essential oils in the leaves of *C. pachystachya*, identifying these oils as potential candidates for anti-inflammatory activity. The study highlights that specific terpenoids and phenolic compounds in the essential oil exhibit significant anti-inflammatory properties, making this species a promising subject for further exploration in the field of natural anti-inflammatory agent [58]. Essential oils contribute to the notable therapeutic effects of many plant species as anti-inflammatory [59], antioxidant [60], antimicrobial [61], and antitumor properties [62]. The chemical composition of these essential oils is highly dependent on several factors, including the plant part utilized (e.g., leaves, bark, or roots), geographical location, environmental conditions, and the time of harvest [63]. These variations influence both the efficacy and potency of the essential oils, underlining the importance of proper extraction and analysis for pharmacological applications [64].

Overall, the phytochemical diversity of the *Cecropia* genus contributes to its wide range of medicinal applications. The presence of terpenoids, phenolics, flavonoids, and saponins in these plants underlines their potential in treating diseases related to oxidative stress, inflammation, and metabolic disorders. The traditional uses of *Cecropia* species, such as treating diabetes, cardiovascular diseases, and respiratory issues, are supported by modern phytochemical research, which highlights the therapeutic value of these bioactive compounds. Continued research into the lesser-known *Cecropia* species and their phytochemistry could uncover additional therapeutic applications and validate the traditional medicinal knowledge associated with this genus.

3.2. Traditional uses of Cecropia species

Cecropia species have been utilized for centuries in traditional medicine throughout Central and South America, particularly among indigenous populations and rural communities. Table 2 highlights the medicinal uses of *Cecropia* species, drawn from ethnobotanical research and various scientific sources. The *Cecropia* genus plays a vital role in traditional healthcare across the Neotropics, with species such as *C. peltata* commonly prepared as infusions to address cardiovascular, metabolic, and respiratory ailments due to their reputed anti-inflammatory and wound-healing capabilities [13,65]. In Colombia, *C. peltata* is also employed as a sedative and anti-microbial agent [66], while in French Guiana, it is traditionally used to treat kidney infections, heart conditions, nervous system disorders, and albuminuria, and to support kidney function [6,67].

Similarly, C. pachystachya has been used in folk medicine to manage renal diseases, as well as for its diuretic, anti-inflammatory, antihypertensive, and antidiabetic properties [8]. Other species, such as C. glaziovii and C. pachystachya, are recognized for their diuretic and sedative effects, which are beneficial in managing conditions such as edema and insomnia [68,69]. These medicinal activities are attributed to the presence of bioactive compounds like flavonoids and terpenoids, which have been identified in these species.

The use of C. obtusifolia in managing diabetes and cardiovascular diseases is well-documented, particularly in regions such as Mexico, Guatemala, and the Amazon Basin [4,70,71]. This species is traditionally recognized for its hypoglycemic properties, supported by pharmacological studies that demonstrate its efficacy in regulating blood glucose levels [18].

In addition to their systemic medicinal applications, various Cecropia species are renowned for their wound-healing properties. For instance, C. peltata, C. glaziovii, and C. pachystachya are frequently used in the Amazon region to treat cuts and other injuries, likely due to their potent antioxidant and anti-inflammatory effects [13,14,72–76]. The antimicrobial activity of these species further supports their use in traditional wound care [77,78].

Many Cecropia species rely on their potent antioxidant, anti-inflammatory, and antimicrobial properties for their traditional uses (Table 1), which is consistent with studies that highlight their ability to combat oxidative stress and microbial infections. These therapeutic benefits are primarily linked to the presence of secondary metabolites, including tannins and phenolic acids, which contribute to their pharmacological activity.

3.3. Phytochemistry and biological activity of Cecropia glaziovii

The extensive catalogue of compounds from *C. glaziovii*, including chlorogenic acid, various C-glycosyl flavonoids, and proanthocyanidins, highlights a species with considerable potential in the treatment of metabolic disorders [80–82]. Chlorogenic acid and C-glycosyl flavonoids, in particular, have been recognized for their role in modulating glucose and lipid metabolism, suggesting that *C. glaziovii* is a valuable source of antidiabetic and antiobesity agents [83–85]. A recent study confirmed and linked the anti-inflammatory and antioxidant effects of *C. glaziovii* through *in vivo* and *in vitro* assays to the presence of chlorogenic acid and the C-glycosyl flavonoid (iso-orientin and isovitexin), which were identified as major compounds through HPLC-based quantitative analysis [31].

Several studies have reported the antihypertensive properties of *C. glaviozii* and linked them to its chemical constituents. In 2007, Lima-Landman et al. reported the antihypertensive activity of standardized aqueous and butanolic extracts of *C. glaziovii* due to interference with calcium handling mechanisms in smooth muscle cells and neurons [86], following an earlier study confirming that the antihypertensive activity of *C. glaviozii* is not linked to angiotensin converting enzyme (ACE) [87]. The *C. glaviozii* extract was standardized based on its catechin, flavonoid, and procyanidin contents [86–88]. Subsequent investigations not only corroborated the findings of previous studies but also refined our understanding of the molecular mechanism of flavonoids and procyanidins present in *C. glaviozii*, including isoorientin, isovitexin, epicatechin, and procyanidin [82]. This study explored the pharmacological mechanisms underlying the hypotensive and vasodilatory effects of these compounds through *in vivo* assays. The observed cardiovascular benefits are mediated through a multifaceted mechanism involving the blockade of L-type calcium channels, modulation of muscarinic pathways across M1 to M5 metabotropic receptors, and potentiation of the nitric oxide signalling pathway [82]. These findings provide a deeper understanding of the biochemical interactions responsible for the medicinal efficacy of *C. glaziovii*, aligning closely with its traditional use in managing blood pressure and enhancing vascular health. Additionally, the high flavonoid, catechin and procyanidin contents in *C. glaviozii* were attributed to other pharmacological activities, including anti-inflammatory [31], antidepressant [88], anti-gastric ulcer [89], anti-herpes [90], and wound healing effects [75].

3.4. Phytochemistry and biological activity of Cecropia angustifolia

Among different *Cercopia* species, *C. angustifolia,* distinguished by its pentacyclic triterpenes [91], has the ability to produce compounds with potential anti-inflammatory and anticancer properties given the recognized biological activities of triterpenes [92–94]. These compounds, which are related to the flavonoid class, are known for their strong antioxidant properties and vascular-protective effects through diverse mechanisms, which can either directly neutralize reactive oxygen species (ROS) or indirectly influence the expression of genes that enhance the cell's innate antioxidant defenses [51,95,96]. Although *C. angustifolia* has

Table 1
Traditional uses of the most reported *Cercopia* species in literature.

Species	Parts Used	Ref.
Cecropia peltata	Treatment of cardiovascular, metabolic, respiratory conditions; Sedative; Antimicrobial; Kidney infections; Wound healing	[13,65]
Cecropia pachystachya	Anti-inflammatory; Diuretic; Antihypertensive; Antidiabetic; Wound healing	[8]
Cecropia glaziovii	Diuretic; Sedative; Anti-inflammatory; Wound healing; Sedative tea; Treatment of arthritis, rheumatism, inflammation, cardiovascular diseases; Cough, asthma, bronchitis, fever, hepatic and kidney diseases, diuretic effects	[68,69]
Cecropia obtusifolia	Management of diabetes and cardiovascular conditions; Hypoglycemic effects	[4,70,71]
Cecropia insignis	diuretic, for the treatment of hypertension, asthma, bronchitis and inflammation.	[42]
Cecropia hololeuca	diuretic, antihypertensive, sedative, anti-inflammatory, expectorant antiasthmatic, cough suppressant, anti-thermal, and anticancer agent	[6,79]

Table 2
The scientific name of all 66 accepted *Cecropia* species according to WFO Plant List Website with phytochemical scompounds identified according to literature data.

NO.	Scientific name of plant species	Phytochemical constituents	Ref.
1.	*Cecropia albicans* Trécul.	–	
2.	*Cecropia andina* Cuatrec.	–	
3.	*Cecropia angulate* I.W.Bailey	–	
4.	*Cecropia angustifolia* Trécul	pentacyclic triterpenes	[91]
5.	*Cecropia annulate* C.C.Berg & P. Franco	–	
6.	*Cecropia bullata* C.C.Berg & P. Franco	–	
7.	*Cecropia candida* Snethl.	–	
8.	*Cecropia chlorostachya* C.C.Berg & P.Franco	–	
9.	*Cecropia concolor* Willd.	–	
10.	*Cecropia david-smithii* C.C.Berg	–	
11.	*Cecropia dealbata* B.S.Williams	–	
12.	*Cecropia distachya* Huber	quercetin-3β-D-glucoside, rutin and luteolin.	[19]
13.	*Cecropia elongate* Rusby	–	
14.	*Cecropia engleriana* Snethl.	–	
15.	*Cecropia ficifolia* Warb. ex Snethl.	–	
16.	*Cecropia gabrielis* Cuatrec.	–	
17.	*Cecropia garciae* Standl.	–	
18.	*Cecropia glaziovii* Snethl.	chlorogenic acid, proanthocyanidin, orientin, isoorientin, vitexin, isovitexin, isoquercitrin, catechin, epicatechin, and isoquercitrin, procyanidin B2, Procyanidin C1	[31–35]
19.	*Cecropia goudotiana* Trécul	–	
20.	*Cecropia granvilleana* C.C.Berg	–	
21.	*Cecropia herthae* Diels	–	
22.	*Cecropia heterochroma* C.C.Berg & P.Franco	–	
23.	*Cecropia hispidissima* Cuatrec.	triterpenoid saponin-O-hexosides, chlorogenic acid, favonol-O-glycosides, niga-ichigoside F2, buergericic acid 28-O-glucoside, quercetin- O-glycosides, Isoorientin, Luteolin-*O*-malonyl-*C*-hexoside.	[42,43]
24.	*Cecropia hololeuca* Miq.	Quinic acid, Galloyl-rhamnoside, 5-O-Caffeoylquinic acid, chlorogenic acid, 3-O-Caffeoylquinic acid, Sinapic acid hexoside, 5-O-Feruloylquinic acid, Geniposide, (−)-Epicatechin, Procyanidin, Procyanidin A2 – rhamnoside, Isoorientina-2″-O-rhamnoside, Vitexin, Vitexin-2″-O-xyloside, Vitexin-2″-O-glycoside, Isovitexin-2″-O-xyloside, Quercetin-3-O-hexoside, Isovitexina, Rutin, Vitexin-2″-O-rhamnoside, Scoparin, Scoparin-2″-O-rhamnoside, Luteolin-7-O-hexoside, Isorhamnetin-3-O-hexoside, Isorhamnetin-3-O-rutinoside, Luteolin-7-O-hexoside, gallic acid, catechin, caffeic acid.	[20,22]
25.	*Cecropia idroboi* Cuatrec.	–	
26.	*Cecropia insignis* Liebm.	–	
27.	*Cecropia integra* Merr.	–	
28.	*Cecropia kavanayensis* Cuatrec.	–	
29.	*Cecropia latiloba* Miq.	–	
30.	*Cecropia litoralis* Snethl.	–	
31.	*Cecropia longipes* Pittier	–	
32.	*Cecropia marginalis* Cuatrec.	–	
33.	*Cecropia maxima* Snethl.	–	
34.	*Cecropia megastachya* Cuatrec.	–	
35.	*Cecropia membranacea*Trécul	–	
36.	*Cecropia metensis* Cuatrec.	–	
37.	*Cecropia montana* Warb.	–	
38.	*Cecropia multisecta* P.Franco	–	
39.	*Cecropia mutisiana* Mildbr.	–	
40.	*Cecropia obtuse* Trécul	Catechin, gallic acid	[50]
41.	*Cecropia obtusifolia* Bertol.	Isoorientin, chlorogenic acid	[18]
42.	*Cecropia pachystachya* Trécul	Quinic acid, Galloyl-rhamnoside, chlorogenic acid, 3-O-Caffeoylquinic acid, Sinapic acid hexoside 1, Sinapic acid hexoside 2, Geniposide isomer 1, Procyanidin B2, (−)-Epicatechin, Procyanidin dimer, Procyanidin A2, (+)-Catechin, Procyanidin trimer C1, Galloyl-procyanidin trimer, chlorogenic acid, isoorientin, orientin, isovitexin, vitexin, rutin, pomolic acid, b-sitosterol, tormentic acid.	[21–24]
43.	*Cecropia palmata* Willd.	Escoparone, ursolic acid, pomolic acid, α-amyrin, β-amyrin and derivatives of stigmasterol	[25]
44.	*Cecropia pastasana* Diels	–	
45.	*Cecropia peltate* L.	ferulic acid, gallic acid, catechin, quercitrin, resveratrol	[50]
46.	*Cecropia pittieri* B.L.Rob.		
47.	*Cecropia plicata* Cuatrec.	–	
48.	*Cecropia polystachya* Trécul	–	
49.	*Cecropia purpurascens* C.C.Berg	–	
50.	*Cecropia putumayonis* Cuatrec.	–	
51.	*Cecropia radlkoferana* Aladar.	–	
52.	*Cecropia reticulata* Cuatrec.	–	
53.	*Cecropia sararensis* Cuatrec.	–	

(*continued on next page*)

Table 2 (*continued*)

NO.	Scientific name of plant species	Phytochemical constituents	Ref.
54.	*Cecropia saxatilis* Snethl.	–	
55.	*Cecropia schreberiana* Miq.	Pomolic acid, α-amyrin, Tormentic acid, Vitexin, Orientin, isoorientin, Catechin, epicatechin, procyanidin B2, arjunolic acid, cinchonain Ia, cinchonain Ib, procyanidins B2	[110]
56.	*Cecropia sciadophylla* Mart.	–	
57.	*Cecropia silvae* C.C.Berg	–	
58.	*Cecropia strigose* Trécul	–	
59.	*Cecropia subintegra* Cuatrec.	–	
60.	*Cecropia tacuna* C.C.Berg& P. Franco	–	
61.	*Cecropia telealba* Cuatrec.	–	
62.	*Cecropia telenitid* Cuatrec.	–	
63.	*Cecropia ulei* Snethl.	–	
64.	*Cecropia utcubambana* Cuatrec.	–	
65.	*Cecropia velutinella* Diels	–	
66.	*Cecropia virgusa* Cuatrec.	–	

been the subject of numerous phytochemical studies, there remains a notable scarcity of research concerning its biological activities. This gap in the literature signals fertile ground for future research endeavors. A thorough investigation into the biological effects and potential therapeutic applications of *C. angustifolia*'s chemical constituents is essential to fully elucidate the pharmacological potential of this species and could significantly contribute to the development of new medicinal agents.

3.5. *Phytochemistry and biological activity of Cecropia pachystachya*

C. pachystachya, widely recognized as "ambay" in Argentina, is traditionally employed in South American herbal medicine to alleviate symptoms of cough and asthma [97]. The phytochemical properties of *C. pachystachya* are similar to those of related species such as *C. glaziovii*, particularly because of the presence of flavonoids such as orientin and isoorientin, as well as the presence of chlorogenic acid as a major compound [22]. Considering the shared spectrum of phytochemicals, it is plausible that *C. pachystachya* could display biological activities that are comparable to those observed in its related species. An *in vivo* study revealed that the hypoglycemic and antioxidant activity of *C. pachystachya* was attributed to chlorogenic acid and the C-glycosylated flavones orientin and isoorientin [98].

Additionally, another *in vivo* study highlighted the cardiotonic properties of *C. pachystachya* extract, showing its ability to induce hypotension via central blockade of sympathetic innervation to blood vessels and to trigger tachycardia through central cholinergic inhibition of the heart [97]. Importantly, such pharmacological effects were achieved at dosages surpassing traditional ethno-therapeutic application, particularly at levels exceeding approximately 340 mg of dried leaves/kg [97]. This finding underscores the importance of dose considerations in the therapeutic use of *C. pachystachya* to optimize its cardiotonic benefits while avoiding potential adverse reactions.

Interestingly, another study highlighted the mechanism responsible for the positive inotropic effect observed with *C. patchystachya*. This effect is counteracted by pretreatment with potassium media, which activates the sodium-potassium pump (Na^+/K^+-ATPase), indicating the potential ability of *C. patchystachya* extract to inhibit this pump [99]. In addition to its cardiac activity, this *Cecropia* genus is known for its anti-inflammatory, antinociceptive and cytotoxic activities [100,101]. A related study demonstrated the anti-inflammatory activity of pomolic acid (terpenoid) isolated from *C. patchystachya* through the inhibition of interleukin-1β and the viability of human polymorphonuclear (PMN) cells via apoptosis [21]. Other terpenoids identified in *C. patchystachya,* namely, b-sitosterol and tormentic acid, have been shown to have antimalarial effects *in vivo* [24].

Brango-Vanegas et al. also revealed the antibacterial effect of *C. patchystachya* via a disturping quorum sensing (QS) process due to the presence of C-glycosyl flavonoids, isoorientin, orientin, isovitexin, vitexin, and rutin [23]. Flavonoids demonstrate anti-quorum sensing (QS) properties by modulating the transcription of QS-controlled genes and reducing virulence factor production, highlighting their potential as nontraditional anti-infectives that neither kill nor inhibit bacterial growth directly [102]. Moreover, an extract of *C. pachystachya* containing glucoside flavonoids such as orientin inhibits Leishmania (*Amazonensis promastigote*) proliferation and arginase activity without exerting cytotoxic effects on splenocytes, as revealed through LC–ESI-MS and *in vitro* analyses [103, 104].

C. pachystachya has shown potential in modulating central activity related to aging and memory through its neuroprotective and antioxidant effects [101,105,106]. In studies involving animal models of mania induced by ketamine, pretreatment with *C. pachystachya* effectively mitigated manic behavior and oxidative stress [105]. This effect is attributed to the plant's ability to modulate oxidative damage in critical brain regions such as the prefrontal cortex and hippocampus, thereby preventing behavioural and biochemical alterations associated with manic episodes [105]. Additionally, it exhibits promising properties as an antidepressant and potential agent for aging-related cognitive decline [106]. Its neuroprotective effects, demonstrated in preclinical models, suggest that it could mitigate the oxidative stress often implicated in aging and neurodegenerative disorders [106,107]. Specifically, its ability to modulate neurotransmitter systems and reduce oxidative damage in the brain supports its use in improving cognitive functions and mood disorders [104]. These findings suggest that *C. pachystachya* could be considered for developing preventive strategies for various aging and related neuropsychiatric conditions, where oxidative stress plays a significant role in disease progression.

Biologically evaluated *C. pachystachya* have been extensively studied, revealing its potential as a promising ingredient for anti-ageing and skin whitening cosmetic products. This is primarily attributed to its high flavonoid content, which includes potent antioxidants such as quinic acid, chlorogenic acid isomers, and various flavonoids such as orientin and vitexin. These compounds have been demonstrated to exhibit significant tyrosinase inhibition, a key mechanism in skin whitening, as well as high antioxidant activities, which are crucial for anti-aging effects by mitigating oxidative stress in skin cells [108,109].

3.6. Phytochemistry and biological activity of Cecropia hispidissima

C. hispidissima contains a diverse array of triterpenoid saponin-O-hexosides and flavonol-O-glycosides, compounds known for their antimicrobial and cardioprotective activities. This suggests that *C. hispidissima* could be particularly useful in developing treatments for infectious diseases and conditions associated with oxidative stress and inflammation. The richness of *C. hololeuca* in caffeoylquinic acids and procyanidins, among others, underscores its potential in neuroprotective and cognitive-enhancing therapeutics. These compounds, known for their antioxidant and neuroprotective properties, could contribute to mitigating the progression and symptoms of neurodegenerative diseases.

Moreover, the species-specific variation in phytochemical profiles across *Cecropia* underscores the importance of conserving biodiversity not only for ecological balance but also as a reservoir for medicinal discovery. The identification of bioactive compounds in these species provides a molecular basis for their traditional uses and suggests a wealth of untapped therapeutic potential. In light of these findings, it is imperative to advocate for integrated conservation strategies that protect these species and their habitats. This not only ensures the preservation of ecological services but also secures a living library of phytochemicals for future drug discovery and development.

Furthermore, the varying phytochemical compositions across *Cecropia* species highlight the necessity of adopting a nuanced approach to studying these plants. Future research should not only aim to expand the phytochemical and bioactivity databases but also explore the synergistic effects of these compounds in complex extracts, which could offer therapeutic benefits beyond the scope of single isolated constituents.

4. The ecological role of *Cecropia* species: symbiosis and dynamics

The *Cecropia* genus is renowned for its unique ecological role as a myrmecophyte, as it forms symbiotic relationships with ants [17,111–113]. *Cecropia* trees, commonly found in tropical forests of Central and South America, are characterized by rapid growth and large, hollow stems (domatica) and branches [3,111,114]. These structural features, known as internodes, form natural cavities that serve as ideal nesting sites for ant colonies [111]. The entrances to these cavities are typically small holes through which ants can easily defend against intruders and predators. In return for shelter, ants offer *Cecropia* plants protection against herbivores and competing plants by aggressively warding off intruders and clearing surrounding vegetation [5,115,116]. This mutualistic relationship is a fascinating example of coevolution, with both the plant and the ants deriving significant survival benefits. *Cecropia* plants also produce nutrient-rich food bodies, known as Müllerian bodies, which are glycogen-rich structures produced on the petioles of leaf stems [117,118]. This interdependent relationship highlights the complexity of ecological interactions in tropical forest ecosystems and underscores the evolutionary adaptations of the *Cecropia* genus to its environment. Therefore, the *Cecropia* genus plays a pivotal role not only in the medical field but also in maintaining biodiversity through nuanced plant-fungal interactions.

This symbiotic relationship highlights a sophisticated form of coevolution, where both the *Cecropia* species and their resident ants have coadapted to benefit mutually [113]. Such interactions are vital for understanding ecological dynamics and evolutionary processes in tropical rainforests. They illustrate how mutualism can drive the evolutionary trajectories of both plant and animal species in complex ecosystems.

4.1. Toxicological aspects of Cecropia species

Toxicological studies on *Cecropia* species are limited, with most data focusing on *C. obtusifolia*. Toxicological studies on *C. obtusifolia* have provided clear evidence of its safety in both *in vivo* and *in vitro* settings. A study utilizing the *Drosophila* wing somatic mutation and recombination test (SMART) tested extract concentrations ranging from 0.82 to 13.32 mg/ml and found no genotoxic effects. Furthermore, the human micronucleus assay, conducted on lymphocytes from six type 2 diabetic patients who consumed 13.5 g/day of the extract for 32–85 days, reported no significant increase in cytotoxicity or genotoxicity. These findings indicate that *C. obtusifolia* does not pose a genotoxic risk, and its use in traditional medicine, particularly for diabetes management, appears to be safe [119].

For other *Cecropia* species, available toxicological data is sparse. However, initial studies on *C. pachystachya* extracts suggest they are well-tolerated at therapeutic doses in preclinical models, with no significant adverse effects reported in short-term studies. The leaves of *C. pachystachya*, which are traditionally used for treating asthma and diabetes, were evaluated for both acute and subacute toxicity in an animal model. In vivo, Wistar rats administered a single dose of 2000 mg/kg of the crude aqueous extract of *C. pachystachya* showed a reduction in hemoglobin levels after 14 days, although no significant toxicity was observed after 28 days of treatment. While these results suggest that *C. pachystachya* has some potential cytotoxic and genotoxic effects *in vitro*, no severe toxicity was detected in animal studies under the tested conditions. Further research is needed to clarify the long-term safety of *C. pachystachya* extracts and establish safe dosage ranges for its medicinal use [120].

This highlights the need for more comprehensive toxicological assessments of *Cecropia* species beyond *C. obtusifolia* and *C. pachystachya*, especially as these species hold significant potential for therapeutic applications in traditional and modern medicine.

5. Conclusions

This review offers an extensive examination of the *Cecropia* genus, which plays a crucial role both in traditional medicine and as a key ecological component in Neotropical forests. Of the 66 recognized species of *Cecropia,* only 11 have been subjected to detailed phytochemical analysis, and even fewer, less than 10, have had their pharmacological activities thoroughly studied. The available data reveal a rich composition of terpenoids, flavonoids, and phenolic acids, with c-glycosyl flavonoids and chlorogenic acid being predominant in the species analysed. The pharmacological potential of the specifically reviewed species—*C. angustifolia*, *C. glaziovii*, and *C. pachystachya*—are primarily linked to these compounds and exhibit diverse health-promoting activities, including anti-inflammatory, antioxidant, anti-aging, cardiovascular, and antimicrobial effects.

However, this review identified a significant research gap in the comprehensive understanding of the full phytochemical landscape and bioactivity of the *Cecropia* genus. There is a critical need for more expansive phytochemical studies and bioactivity profiling to fully elucidate the therapeutic potential of these plants. To address these gaps, this review advocates for the initiation of robust drug discovery initiatives that incorporate advanced analytical techniques and detailed bioactivity studies. There is a particular emphasis on the necessity of expanding pharmacological research to include less-studied *Cecropia* species, which could yield novel and effective bioactive compounds. Moreover, there is a call for more detailed ecological studies to further elucidate the role of *Cecropia* in forest regeneration and its interactions with symbiotic ants. By enhancing the understanding of both the medicinal and ecological aspects of the *Cecropia* genus, this review aims to bridge the current scientific gaps and promote the conservation and sustainable use of this valuable genus. This approach aligns ecological preservation efforts with biomedical innovations, thereby fostering a more holistic understanding of *Cecropia*'s potential benefits.

Furthermore, the economic potential of *Cecropia* species for pharmaceutical and nutraceutical industries remains underexplored. Future research should investigate the feasibility of large-scale extraction and cultivation of *Cecropia* species to support sustainable commercial applications. This includes evaluating the environmental and economic viability of cultivating Cecropia as a renewable resource for bioactive compounds. Collaborative efforts between academia, industry, and governmental organizations are essential to accelerate the discovery of new pharmacological candidates. International partnerships focused on exploring the therapeutic and ecological value of *Cecropia* species could foster innovative approaches to drug development while ensuring biodiversity conservation.

Data availability statement

The dataset used in this study can be obtained by interested parties upon request.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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