

Phytochemical and pharmacological aspects of the genus *Chamaecrista*: a systematic review

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ABSTRACT

The genus *Chamaecrista*, belonging to the family Fabaceae, is mainly distributed in the American continent and is of great interest because of its extensive use in traditional medicine. This article presents a systematic review of the pharmacological and chemical properties of the *Chamaecrista*. Articles published between 2004 and 2023 were grouped through searches in the following databases: PubMed, SciELO, Scopus, Science Direct, Web of Science, and Google Scholar. Articles were included based on the selection and classification of titles and abstracts if they indicated the country of origin of the studies, plant species studied, compounds identified, and associated pharmacological activities. The results showed that most of the studies conducted in Brazil represented 35% of the published works. Moreover, *Chamaecrista nictitans* and *Chamaecrista duckeana* have been the most studied for their pharmacological potential, especially for their antioxidant activity. In addition, flavonoids were the leading group described, obtained from different extracts of various parts of the plant, with leaves being the most utilized. Despite promising advances in understanding the chemical composition and pharmacological properties of the genus *Chamaecrista*, this review highlights that no preclinical *in vivo* and clinical studies have been reported. This study underscores the importance of continuing research to identify and isolate new bioactive molecules from this genus, aiming to elucidate their pharmacological functions and potential therapeutic applications.

INTRODUCTION

Medicinal plants are the primary source of bioactive substances with therapeutic potential. Therefore, numerous plant species have been the subject of multiple scientific investigations to elucidate their chemical, pharmacological, and toxicological composition [1,2]. Approximately 54% of the drugs used for cancer treatment and about 64% of medications for hypertension are derived from natural products. However, only 10% of the plant species in the world have been adequately

studied [3,4]. In this context, knowledge provided by the ethnopharmacology of particular species fosters research in various areas, such as phytochemistry and pharmacology, to elucidate chemical compounds with pharmacological properties [5,6].

The genus *Chamaecrista* (Fabaceae) comprises approximately 330 plant species, with over 70% native to the American continent [7]. The occurrence of these plants in South America is particularly significant in Argentina, Bolivia, Colombia, Paraguay, and Brazil. Brazil exhibits greater species diversity, with approximately 250 cataloged species, mainly in the southeastern region [8,9]. *Chamaecrista* comprises trees, shrubs, perennial herbs, and woody climbers (lianas). Bipinnate, pinnate, and bifoliolate leaves distinguish them. Their flowers are yellow and zygomorphic, with simple axillary or terminal racemes featuring up to five petals, one

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of which is banner-shaped and is covered at the base by the others. The fruits are dry and dehiscent along both sutures, and the seeds have an elongated funicular structure, sometimes with an aril [10–13].

The species found in *Chamaecrista* has been the subject of research because of its relevance in traditional medicine. The leaves of *Chamaecrista nigricans* are used to treat rheumatic pain, gastrointestinal issues, and fever [14]. The roots, seeds, and leaves of *Chamaecrista absus* are utilized as cathartics, and the leaves are also indicated for nasal diseases and cough [14]. The leaves of *Chamaecrista nictitans* are known to relieve leg swelling during pregnancy, whereas the roots are used for treating stomach colic and diarrhea [14], mainly as tea. Other species, such as *Chamaecrista flexuosa*, whose roots are used to treat renal inflammation [15], along with *Chamaecrista duckeana* and *Chamaecrista diphylla*, are noted for their applications as laxatives, anti-inflammatory agents, analgesics, and in the treatment of cutaneous parasitic diseases, hypercholesterolemia, and hypertension [15–17]. In addition to its use in traditional medicine, the genus *Chamaecrista* holds significant value in agriculture, as it is utilized for nitrogen fixation in degraded and nutrient-poor soils, helping to restore them for cultivation [18].

Native plants from the Americas are valuable resources for chemical and pharmacological research focused on the development of novel therapeutics to meet current clinical challenges across diverse diseases. This systematic review provides a comprehensive synthesis of current

knowledge regarding the pharmacological potential of natural products derived from *Chamaecrista* species. The compilation of available data on the chemical composition and associated pharmacological activities of the genus *Chamaecrista* aims to (i) gather the procedures used to identify chemical compounds and (ii) document the pharmacological activities to establish a guide for future research.

MATERIALS AND METHODS

Study design

This systematic review followed the PRISMA criteria (preferred reporting items for systematic reviews and meta-analyses) [19]. The review aimed to answer the following question: *What are the pharmacological activities and phytochemical compositions of the genus Chamaecrista plant species reported in the literature?* Based on this, the questions involved in population, intervention, comparison, and outcomes were established as follows: Population: Plant species of the genus *Chamaecrista*; Intervention: Phytochemical composition and pharmacological activity; Comparison: Plant species of the genus without studies on their phytochemical composition and pharmacological activity; Outcomes: Information on the phytochemical composition and pharmacological activity of plant species of the genus *Chamaecrista*.

The literature search began in October 2022, using the following combinations of keywords: *Chamaecrista* AND phytochemical composition OR pharmacological, and their respective terms in Spanish and Portuguese. The databases

Table 1. Scientific names and synonym(s) of reported *Chamaecrista* species (according to GBIF and WFO The Plant List).

Species	Synonym (GBIF)	Synonyms (WHO Plant List)
<i>Chamaecrista absus</i>	<i>Cassia absus</i> L.	<i>Cassia absus</i> L.
	<i>Grimaldia absus</i> (L.) Britton & Rose	<i>Grimaldia absus</i> (L.) Britton & Rose
	<i>Senna absus</i> (L.) Roxb.	<i>Senna absus</i> (L.) Roxb.
	<i>Senna quadrifolia</i> Burm.	<i>Senna quadrifolia</i> Burm.
	<i>Cassia foliolis</i> L.	<i>Cassia foliolis</i> L.
	<i>Grimaldia absus</i> (L.) Link	<i>Grimaldia absus</i> (L.) Link
<i>Chamaecrista cytisoides</i>	<i>Cassia exigua</i> Roxb.	<i>Cassia absus</i> Sesse & Moc.
	<i>Cassia cytisoides</i> DC. ex Collad.	<i>Cassia cytisoides</i>
	<i>Cassia desvauxii</i> Collad.	<i>Cassia desvauxii</i> Collad.
<i>Chamaecrista desvauxii</i>	<i>Chamaecrista tetraphylla</i> Britton & Rose ex Britton & Killip	<i>Chamaecrista tetraphylla</i> (Desv.) Britton & Rose ex Britton & Killip
	<i>Cassia tetraphylla</i> Desv.	<i>Cassia tetraphylla</i> Desv.
	<i>Cassia diphylla</i> L.	<i>Cassia diphylla</i>
<i>Chamaecrista diphylla</i> (L.)	<i>Ononis conjugata</i> Lamb.	<i>Ononis conjugata</i>
	<i>Ononis conjugata</i> Lamb. ex G.Don	<i>Chamaecrista cultrifolia</i>
	<i>Ononis conjugata</i> Sessé & Moc.	
<i>Chamaecrista duckeana</i>	<i>Cassia duckeana</i> P. Bezerra & A. Fern.	<i>Cassia duckeana</i>
<i>Chamaecrista hildebrandtii</i> (Vatke)	<i>Cassia hildebrandtii</i> Vatke	<i>Cassia hildebrandtii</i>
	<i>Cassia hildebrandtii</i> var. <i>crispata</i> Serrato	<i>Cassia hildebrandtii</i> var. <i>Crispata</i>
	<i>Cassia grantii</i> var. <i>pilosula</i> J. Léonard	

Species	Synonym (GBIF)	Synonyms (WHO Plant List)
<i>Chamaecrista mimosoides</i>	<i>Cassia amoena</i> Buch.-Ham.	<i>Cassia amoena</i>
	<i>Cassia angustissima</i> Lam.	<i>Cassia angustissima</i>
	<i>Cassia auricoma</i> var. <i>glabra</i> Ghesq.	<i>Cassia auricoma</i> var. <i>glabra</i>
	<i>Cassia capensis</i> var. <i>humifusa</i> Ghesq.	<i>Cassia capensis</i> var. <i>humifusa</i>
	<i>Cassia chamaecrista</i> f. <i>auricoma</i> Kuntze	<i>Cassia chamaecrista</i> f. <i>auricoma</i>
	<i>Cassia filipendula</i> Bojer	<i>Cassia filipendula</i>
	<i>Cassia geminata</i> Vahl	<i>Cassia geminata</i>
	<i>Cassia gracillima</i> Welw.	<i>Cassia gracillima</i>
	<i>Cassia guineensis</i> G.Don	<i>Cassia guineensis</i>
	<i>Cassia hecatophylla</i> DC.	<i>Cassia hecatophylla</i>
	<i>Cassia hecatophylla</i> DC. ex Callad.	<i>Chamaecrista hecatophylla</i>
	<i>Cassia leschenaultii</i> Wall.	<i>Cassia leschenaultii</i>
	<i>Cassia microphylla</i> Willd.	<i>Cassia microphylla</i>
	<i>Cassia microphylla</i> var. <i>guineensis</i> DC.	<i>Cassia microphylla</i> var. <i>guineensis</i>
	<i>Cassia microphylla</i> var. <i>senegalensis</i> DC.	<i>Cassia microphylla</i> var. <i>senegalensis</i>
	<i>Cassia mimosoides</i> L.	<i>Cassia mimosoides</i>
	<i>Cassia mimosoides</i> var. <i>glabriuscula</i> Ghesq.	<i>Cassia mimosoides</i> var. <i>glabriuscula</i>
	<i>Cassia myriophylla</i> Wall.	<i>Cassia microphylla</i>
	<i>Cassia roxburghiana</i> Graham	<i>Cassia roxburghiana</i>
	<i>Cassia sensitiva</i> Roxb.	<i>Cassia sensitiva</i>
	<i>Cassia mimosoides</i> var. <i>gracillima</i> (Welw.) Ghesq.	<i>Cassia thunbergiana</i>
	<i>Cassia nictitans</i> Siekmann	<i>Cassia procumbens</i>
	<i>Cassia procumbens</i> Siekmann	<i>Nictitella mimosoides</i>
	<i>Cassia geminata</i> Vahl ex DC	<i>Senna sensitiva</i>
	<i>Cassia mimosoides</i> Cordem.	<i>Senna tenella</i>
	<i>Cassia nictitans</i> L.	<i>Cassia nictitans</i>
	<i>Cassia nictitans</i> L.	<i>Cassia nictitans</i>
<i>Chamaecrista nictitans</i>	<i>Cassia nictitans</i> var. <i>conmixta</i> (Pollard & Maxon) Millsp.	<i>Cassia nictitans</i> var. <i>conmixta</i>
	<i>Chamaecrista millspaughii</i> Pollard	<i>Chamaecrista multipinnata</i>
	<i>Chamaecrista multipinnata</i> Pennell	<i>Chamaecrista nictitans</i> subsp. <i>nictitans</i>
	<i>Chamaecrista nictitans</i> var. <i>conmixta</i> Pollard & Maxon	
	<i>Chamaecrista nictitans</i> var. <i>nictitans</i> (L.) Moench	
<i>Chamaecrista nigricans</i>	<i>Cassia harneyi</i> Specht	<i>Cassia harneyi</i>
	<i>Cassia micrantha</i> Guill. & Perr.	<i>Cassia micrantha</i>
	<i>Cassia nigricans</i> Vahl	<i>Cassia nigricans</i>
	<i>Chamaecrista harneyi</i> (Specht) Govaerts	<i>Chamaecrista harneyi</i>
	<i>Cassia prostrata</i> J. Koenig	<i>Cassia prostrata</i>
<i>Chamaecrista pumila</i>	<i>Cassia pumila</i> Lam.	<i>Cassia pumila</i>
	<i>Senna prostrata</i> Roxb.	<i>Senna prostrata</i>
	<i>Cassia prostrata</i> J. Koenig ex Roxb.	
<i>Chamaecrista repens</i>	<i>Cassia repens</i> Vogel	<i>Cassia repens</i>
<i>Chamaecrista vestita</i>	No synonym	No synonym

consulted were PubMed, SciELO, Scopus, Science Direct, Web of Science, and Google Scholar for articles published between 2004 and 2023. In addition, two databases were consulted for identifying synonyms of the scientific names of the species: the Plant List from World Flora Online (WFO), accessible at <https://wfoplantlist.org/plant-list/>, and GBIF.org (Global Biodiversity Information Facility), available at <https://www.gbif.org/species/search>.

Criteria and study selection

Specific inclusion criteria included: (i) type of contribution: only original articles; (ii) language: English, Portuguese, and Spanish; (iii) keywords: present in the title and/or abstract; and (iv) methods used: studies that included methods of extraction, identification of chemical groups, isolation of secondary metabolites, and the evaluation of pharmacological activity of extracts and/or fractions through *in vitro* and, *in vivo* assays of any *Chamaecrista* species. The exclusion criteria were as follows: (i) articles on plant species belonging to the genus *Chamaecrista* that mentioned agronomic and/or botanical characteristics; (ii) articles that did not analyze the chemical profile or pharmacological activity of this genus; and (iii) other review articles, meta-analyses, abstracts, conference proceedings, editorials/correspondence, and reports.

The articles were manually examined using the following steps: (i) determining eligibility by considering the title, (ii) reading the abstract based on the criteria, and (iii) conducting a complete reading of the manuscript to exclude those not meeting the inclusion criteria. Subsequently, a consensus was reached among the researchers to resolve any discrepancies in the final selection of manuscripts. We evaluated the evidence concerning possible pharmacological effects and classified each plant extract as follows: (1) presenting potential pharmacological effects when compared to its controls; (2) inconclusive—when studies do not clearly show the data; or (3) evidence does not support plant extract having potential pharmacological effects (Table 2).

Data extraction

Initially, the records were evaluated by two reviewers, Domitila Villalba Fariña and Melissa Escobar Avalos (D.V.F. and M.E.A.), with one reviewer (D.V.F.) responsible for the search and selection process, while the second reviewer (M.E.A.) conducted an independent assessment. The data from the literature search were extracted and organized into templates, including year of publication, country where the study was conducted, plant species, part of the plant used, extraction method, isolated chemical compounds, and evaluation of pharmacological activity. For the latter, extracts and/or fractions, concentrations, methods employed (encompassing both *in vitro* and *in vivo* experimental models), and results are included. Using a free interactive map generator, a location map was created based on the absolute frequency of articles published in the genus (www.mapinseconds.com). Microsoft Excel® (version 365) was used to generate graphs. Chemical molecules were designed using ACD/ChemSketch FREEWARE 2020 1.2.

Table 2. Assessment of the pharmacological activity of the genus *Chamaecrista*.

Plant species	Part used/extract/solvent	Results	Possible pharmacological effects ^a	References
<i>Chamaecrista absus</i>	Seeds/oil/petroleum ether	Antibacterial ID: <i>Listeria ivanovii</i> (RBL 30) 10–12 mm, <i>Listeria innocua</i> (RBL 29) 8–10 mm, <i>Escherichia coli</i> (ATCC 25922) 9–10 mm, <i>Staphylococcus aureus</i> (ATCC 6539) 8 mm, <i>Bacillus subtilis</i> (168) 9–12 mm and <i>Bacillus cereus</i> (ATCC 11778) 10 mm. No activity against: <i>Pseudomonas aeruginosa</i> (ATCC 15442) and <i>Enterococcus hirae</i> (ATCC 10541)	1	[46]
		ID: <i>B. subtilis</i> (UFPEDA 86) 14 mm, <i>E. coli</i> (UFPEDA 224) 11 mm, <i>Micrococcus luteus</i> (UFPEDA 100) 21 mm. No activity against: <i>Klebsiella pneumoniae</i> (UFPEDA 396) and <i>S. aureus</i> (UFPEDA 02)	1	[33]
		No antibacterial or antibiofilm activity against <i>Staphylococcus epidermidis</i> (ATCC 35984)	3	[33]
<i>Chamaecrista cytisoides</i>	Leaves/extract/water:Ethanol	At 4 mg/ml of fruit extract, 12.6% biofilm formation of <i>S. epidermidis</i> (ATCC 35984)	1	[33]
<i>Chamaecrista desvauxii</i>	Leaves, fruits/extract/water	ID at 100 mg/ml: <i>E. coli</i> (MTCC 1610) 24 mm, <i>P. aeruginosa</i> (MTCC 741) 19.5 mm and <i>K. pneumoniae</i> (MTCC618) 18.5 mm	1	[66]
<i>Chamaecrista nigricans</i>	Leaves/extract/water	Anticholinesterase IC ₅₀ : 0.35 ± 0.02 mg/ml IC ₅₀ : 0.03 ± 0.08 mg/ml	1	[16]
<i>Chamaecrista mimosoides</i>	Roots/extract/water		1	[16]
	Roots/extract/dichloromethane:methanol		1	[16]

Continued

Plant species	Part used/extract/solvent	Results	Possible pharmacological effects ^a	References
Antifungal				
<i>Chamaecrista desvauxii</i>	Leaves, fruits/extract/ethanol (leaves), water (fruits)	ID: <i>Candida albicans</i> (UFPEDA 1007) 15 mm (leaf extract) and 19 mm (fruit extract)	1	[33]
	Leaves/extract/methanol	Fungistatic activity against <i>Trichophyton rubrum</i> (TRU31), fungistatic and fungicidal activity against <i>Epidermophyton floccosum</i> (EPF32) and <i>Trichophyton mentagrophytes</i> (TME22)	1	[34]
<i>Chamaecrista nictitans</i>	Leaves/extract/methanol	Fungistatic and fungicidal activity against <i>T. rubrum</i> (TRU31) and <i>E. floccosum</i> (EPF32), fungicidal activity against <i>T. mentagrophytes</i> (TME22)	1	[34]
<i>Chamaecrista rotundifolia</i>	Leaves/extract/methanol	No activity against <i>T. rubrum</i> (TRU31), <i>E. floccosum</i> (EPF32) and <i>T. mentagrophytes</i> (TME22)	3	[34]
<i>Chamaecrista vestita</i>	Leaves/extract/methanol	Fungicidal activity against <i>T. rubrum</i> (TRU31) and <i>E. floccosum</i> (EPF32)	1	[34]
Antioxidant				
<i>Chamaecrista absus</i>	Seeds/oil/petroleum ether	IC ₅₀ : 16.78 ± 0.06 µg/ml	1	[46]
	Leaves/extract/water	EC50: 5.42 mg/ml	1	[25]
	Leaves/extract/ethanol	EC50: 0.35 mg/ml	1	[25]
	Leaves/extract/ethanol	4.29 ± 0.20 mmol TE/g	1	[25]
<i>Chamaecrista diphylla</i>	Leaves/fraction/ethyl acetate	9.44 ± 0.09 mmol TE/g	1	[25]
	Leaves/fraction/ethyl acetate	EC50: 0.11 mg/ml	1	[72]
	Leaves/fraction/ethanol: Water	EC50: 3.86 mg/ml	1	[72]
	Leaves/fraction/hexane	EC50: 2.62 mg/ml	1	[72]
	Leaves/fraction/methanol	6.59 ± 0.27 mmol TE/g	1	[25]
<i>Chamaecrista duckeana</i>	Leaves, stems, fruits/extract/methanol	IC ₅₀ : 165.71 ± 6.94 µg/ml (stem extract), 261.08 ± 2.53 µg/ml (fruit extract) and 283.48 ± 4.19 µg/ml (leaf extract)	1	[31]
<i>Chamaecrista hildebrandtii</i> (Vatke)	Leaves/extract/methanol	IC ₅₀ : 8.7 mg/ml	1	[32]
<i>Chamaecrista mimosoides</i>	Roots/extract/water	IC ₅₀ not determined, maximum inhibition less than 50% at maximum concentration evaluated	3	[16]
	Roots/extract/dichloromethane: methanol	IC ₅₀ : 0.72 ± 0.03 mg/ml and 0.3 ± 0.05 mg/ml	1	[16]
	Aerial parts/extract/dichloromethane: methanol	ED50: 112.1 µg/µmol	1	[35]
<i>Chamaecrista nictitans</i>	Aerial parts/oligomeric fraction/bioassay-guided	ED50: 78.6 µg/µmol	1	[35]
	Aerial parts/polymetric fraction/bioassay-guided	ED50: 115.6 µg/µmol	1	[35]
<i>Chamaecrista repens</i>	Aerial parts/extract/methanol	IC ₅₀ : 2 mg/ml and %AA: 68.3	1	[73]

Continued

Plant species	Part used/extract/solvent	Results	Possible pharmacological effects ^a	References
<i>Chamaecrista nictitans</i>	Aerial parts/extract/dichloromethane/methanol	Antiviral CPE100%: 168.75 and 675 µg/ml against herpes simplex virus (ATCC-VR-733)	1	[35]
	Aerial parts/fraction/water	No inhibition against herpes simplex virus (ATCC-VR-733)	3	[35]
	Aerial parts/fraction/dichloromethane	CPE100%: 51.56 µg/ml against herpes simplex virus (ATCC-VR-733)	1	[35]
	Aerial parts/fraction/methanol: Water	CPE50%: 41.41 and 82.81 µg/ml against herpes simplex virus (ATCC-VR-733)	1	[35]
	Aerial parts/fraction/n-butanol	CPE100%: 76.36 µg/ml against herpes simplex virus (ATCC-VR-733)	1	[35]
<i>Chamaecrista duckeana</i>	Aerial parts/oligomeric fraction/bioassay-guided	CPE: 68.7 µg/ml against herpes simplex virus (ATCC-VR-733)	1	[35]
	Cytotoxicity Extracts showed growth inhibition of human tumor cell line HL60 (leukemia) by 86.62%–89.32%. GI% < 58.17 for SNB19 (central nervous system), HCT116 (human colon), and PC3 (prostate) for all three extracts.			
	Leaves, stems, fruits/extract/methanol.	IC ₅₀ : 133.4 µmol/ml (fruit extract), 137.3 µmol/ml (stem extract), and >200 µmol/ml (leaf extract) against HL60 (leukemia) IC ₅₀ : 106.8 µmol/ml (stem extract) and >200 µmol/ml (fruit and leaf extracts) against RAJI (leukemia)	1	[31]
<i>Chamaecrista mimosoides</i>	Leaves/extract/methanol	Antitrypanosomal Complete cessation of motility of <i>Trypanosoma brucei brucei</i> at 45 minutes (1 mg/ml), 30 minutes (2 mg/ml), and 25 minutes (4 mg/ml)	1	[77]
<i>Chamaecrista mimosoides</i>	Whole plant/fraction/ethyl acetate	Acute toxicity LD50: 3,808 mg/kg in mice via intraperitoneal route	1	[81]
	Whole plant/fraction/chloroform	LD50: 3,808 mg/kg in mice via intraperitoneal route	1	[81]
	Whole plant/fraction/n-butanol	LD50: >5,000 mg/kg in mice via intraperitoneal route	1	[81]
<i>Chamaecrista repens</i>	Whole plant/extract/methanol	LC50 269.3 µg/ml in <i>Artemia salina</i>	1	[73]

AA = antioxidant activity; CPE = inhibition of cytopathic effect; EC50 = half maximal effective concentration; ED50 = half maximal effective dose; GI% = growth inhibition; ID = inhibition diameter; IC₅₀ = half maximal inhibitory concentration; LD50 = median lethal dose; LC50 = median lethal concentration; TE = trolox equivalents.

^a(1) Presenting potential pharmacological effects, (2) inconclusive, or (3) the evidence does not support the extract having potential pharmacological effects.

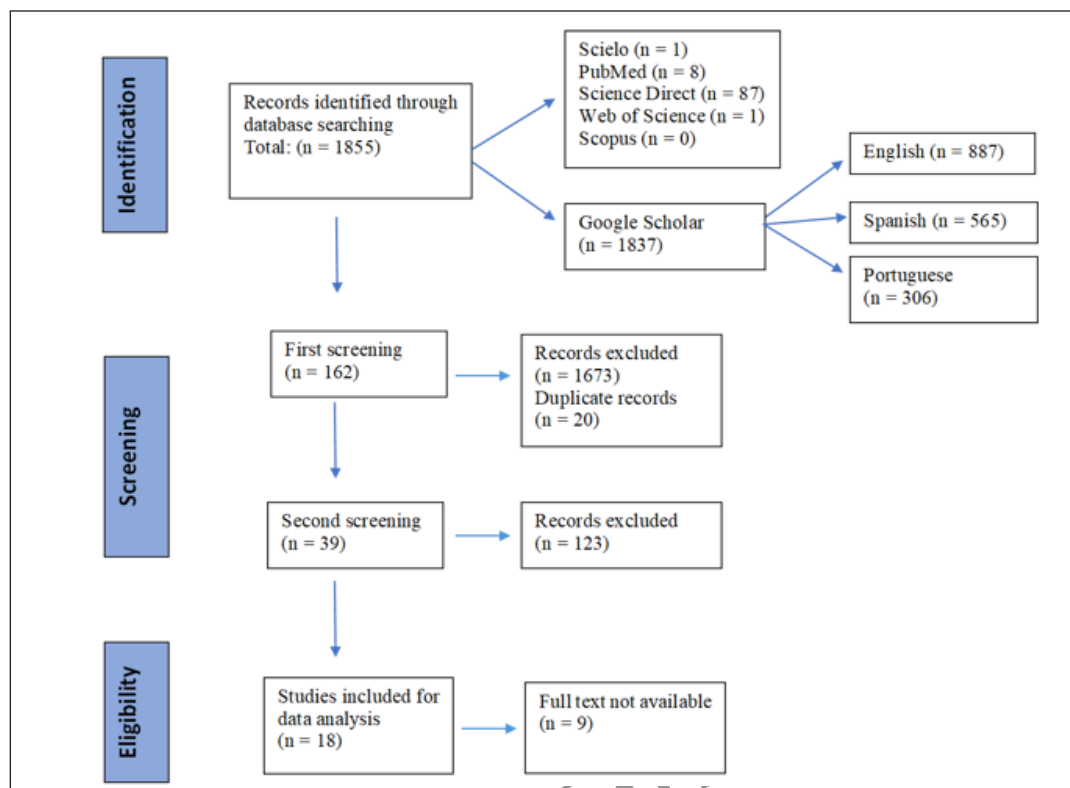


Figure 1. PRISMA flow diagram for article selection.

RESULTS AND DISCUSSION

During the literature search, 1,855 articles were obtained. Google Scholar was the database with the most articles ($n = 1,837$) and the only one that provided information in all three selected languages (English, Spanish, and Portuguese). In contrast, the other databases only presented articles in English.

In the first stage, 1,673 articles were excluded because they did not meet the initial criteria. In addition, 20 duplicates reported in more than one database were removed. Subsequently, 123 articles were excluded based on the reading of the abstracts, leaving 39 articles, of which nine were excluded due to inaccessibility. Eighteen articles were considered for full reading at the end of the selection process. This process of identifying and selecting the articles is presented in Figure 1.

In Figure 2, the geographical map shows the countries where studies on the chemical-pharmacological analysis of the genus *Chamaecrista* have been reported. Brazil had the highest number of recorded articles ($n = 7$), followed by Costa Rica ($n = 3$), India ($n = 3$), Nigeria ($n = 2$), Kenya ($n = 1$), South Africa ($n = 1$), and Tunisia ($n = 1$). The geographical variability and number of published articles can be attributed to the notable and greater diversity of species that prevail in warm regions, such as Brazil.

The first record of scientific publications on the genus *Chamaecrista* dates back to 2004, with no articles found before this period. The first peak of publications occurred in 2014, followed by a steady period between 2019 and 2021 ($n = 2$) (Fig. 3A). This indicates that, despite time, the exploration of

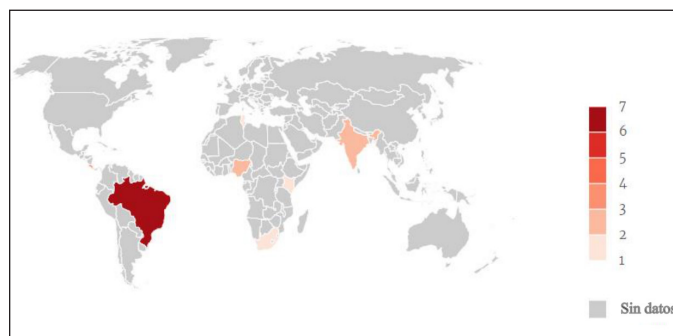


Figure 2. Geographic distribution of research on the chemical composition and pharmacological activity of the genus *Chamaecrista*.

the chemical composition and pharmacological properties of this genus is limited.

Regarding chemical and pharmacological investigations, *C. mimosoides* and *C. nictitans* had the highest reports. However, for *C. cytisoides*, *C. pumila*, and *C. repens*, only studies on their pharmacological properties are available, with no data on their chemical composition (Fig. 3B).

Considering the correlation between chemical composition and pharmacological activity, highlighting the importance and necessity of combining both evaluations underscores the utility and significance of this genus as a potential source of therapeutic agents. In addition, given the multiple botanical nomenclatures for the same species within the genus *Chamaecrista* observed in the selected articles,

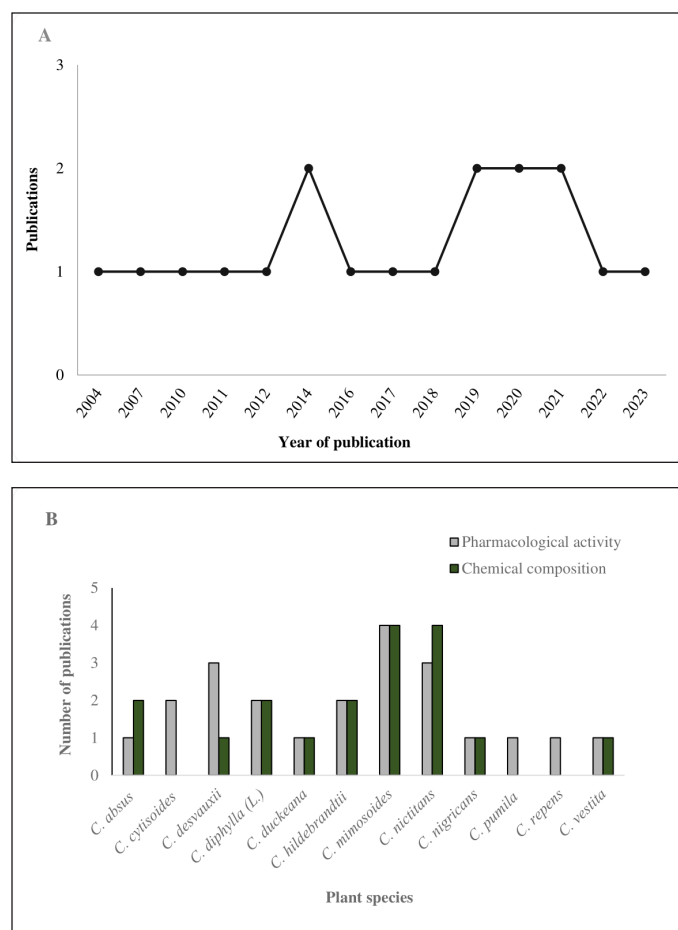


Figure 3. Number of articles selected for the systematic review: A) based on the year of publication, and B) according to the study of pharmacological activity and/or chemical composition.

data compiled from databases for synonym identification are presented in Table 1.

Phytochemical aspects

The leaves were the most commonly used for obtaining extracts, accounting for 48%, followed by the aerial parts (including branches, leaves, and stems) at 28%. The remaining percentages were distributed among the fruits (12%), roots (8%), and seeds (4%), although in smaller proportions. Phytochemical analysis revealed the presence of 159 compounds distributed across different species and tissues of *Chamaecrista*, with phenolic compounds (78%), fatty acids, and aliphatic esters (8%) as the main groups of identified secondary metabolites, followed by sterols, anthraquinones, and other compounds (Fig. 4).

Phenolic compounds

Phenolic compounds are widely distributed in the plant kingdom and have garnered significant scientific interest in recent years because of their antioxidant capacity, which neutralizes free radicals in the body [20,21]. This phenomenon has significant health implications, as it is associated with a reduced risk of heart disease, cancer, and other disorders linked to

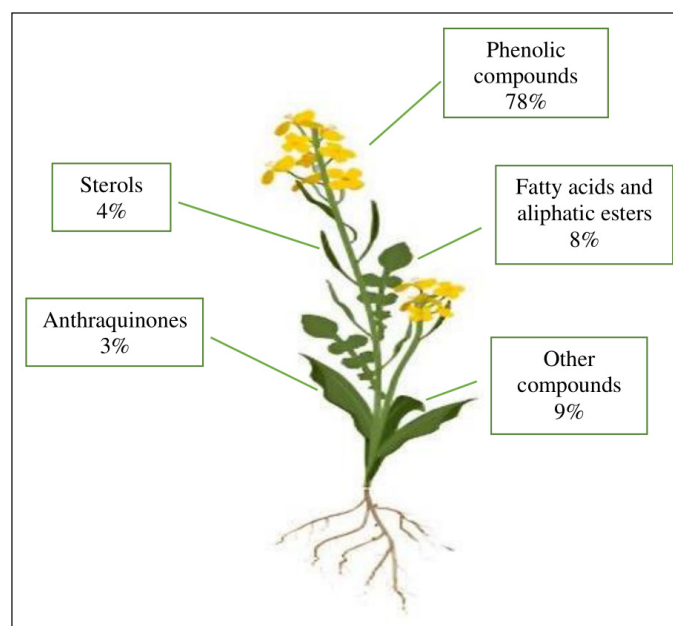


Figure 4. Groups of identified secondary metabolites from the genus *Chamaecrista*.

oxidative stress [22,23]. In addition to their antioxidant activity, phenolic compounds exhibit various beneficial properties, including anti-inflammatory, anti-cancer, antimicrobial, and antiviral activities [22,23].

Among the identified phenolic compounds, notable groups included flavones, phenolic acids, flavonols, flavanones, flavanonol derivatives, coumarins, and isocoumarins.

Quirós-Guerrero *et al.* [24] reported the highest number of identified phenolic compounds in *Chamaecrista*, using liquid chromatography with electrospray ionization quadrupole time-of-flight mass spectrometry (LC-ESI-QTOF-MS) in negative ionization mode from a methanolic extract of aerial parts. They identified a total of 44 metabolites in the species *C. nictitans*, of which 70% were reported for the first time for this species, as shown in Figure 5 as compounds 6, 7, 10, 12, 14, 16, 17, 18, 21, 22, 25, 27-32, 41, 44-46, 48-50, 54, 55, 65, 67-69.

Phenolic compounds have been identified in the ethanolic extract and ethyl acetate fraction of *C. diphylla* leaves using ultra-high-resolution liquid chromatography coupled with high-resolution mass spectrometry and tandem mass spectrometry [25]. Among these, sinapic acid (38) was identified, which shows antibacterial, antihyperglycemic, hepatoprotective, anti-inflammatory, and potentially anticancer properties [26]. Resveratrol (70) is known for its antioxidant and anti-inflammatory effects and ability to protect the cardiovascular system. It has been the subject of numerous studies [27-29]. These findings underscore the richness of phenolic compounds present in *C. nictitans*. However, the identification of these compounds has been reported in only two species. It is crucial to emphasize the importance of your continued research on other species of the genus *Chamaecrista*, as it is integral to advancing our understanding of these beneficial compounds.

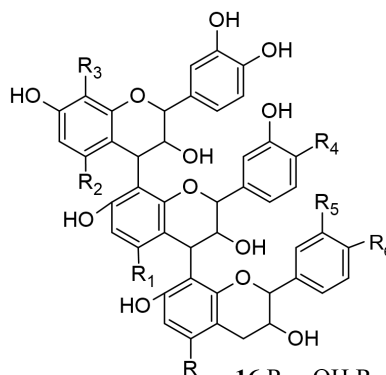
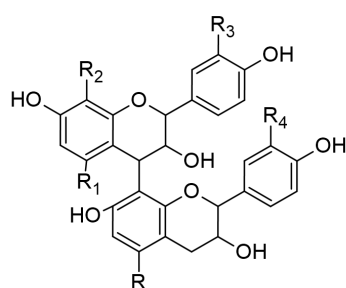
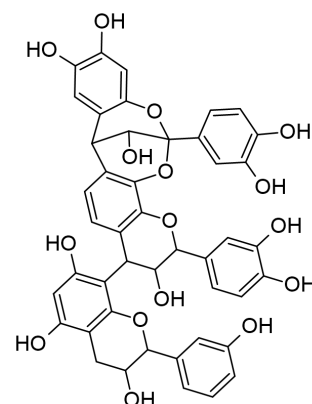
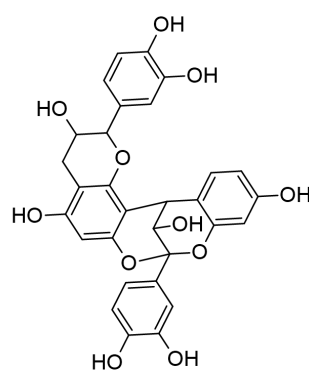
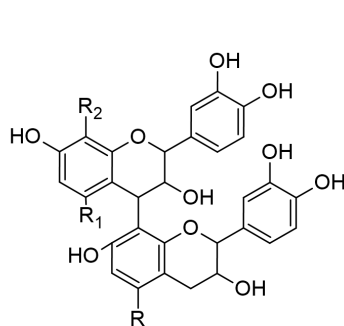
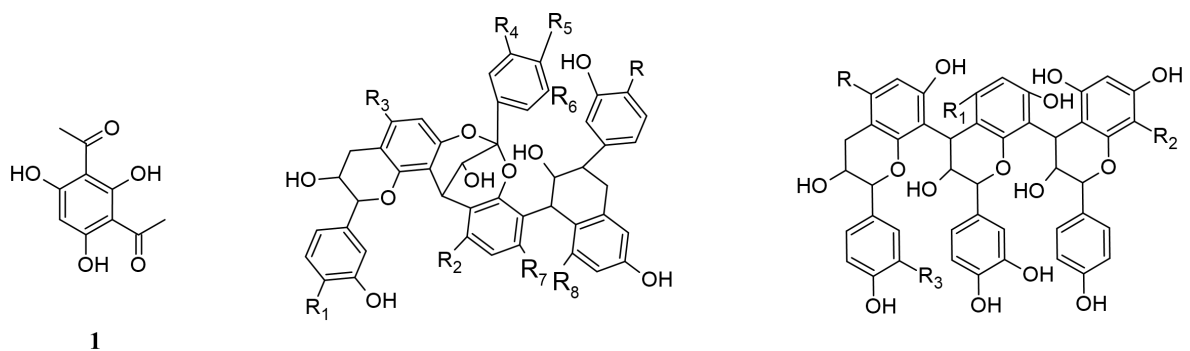


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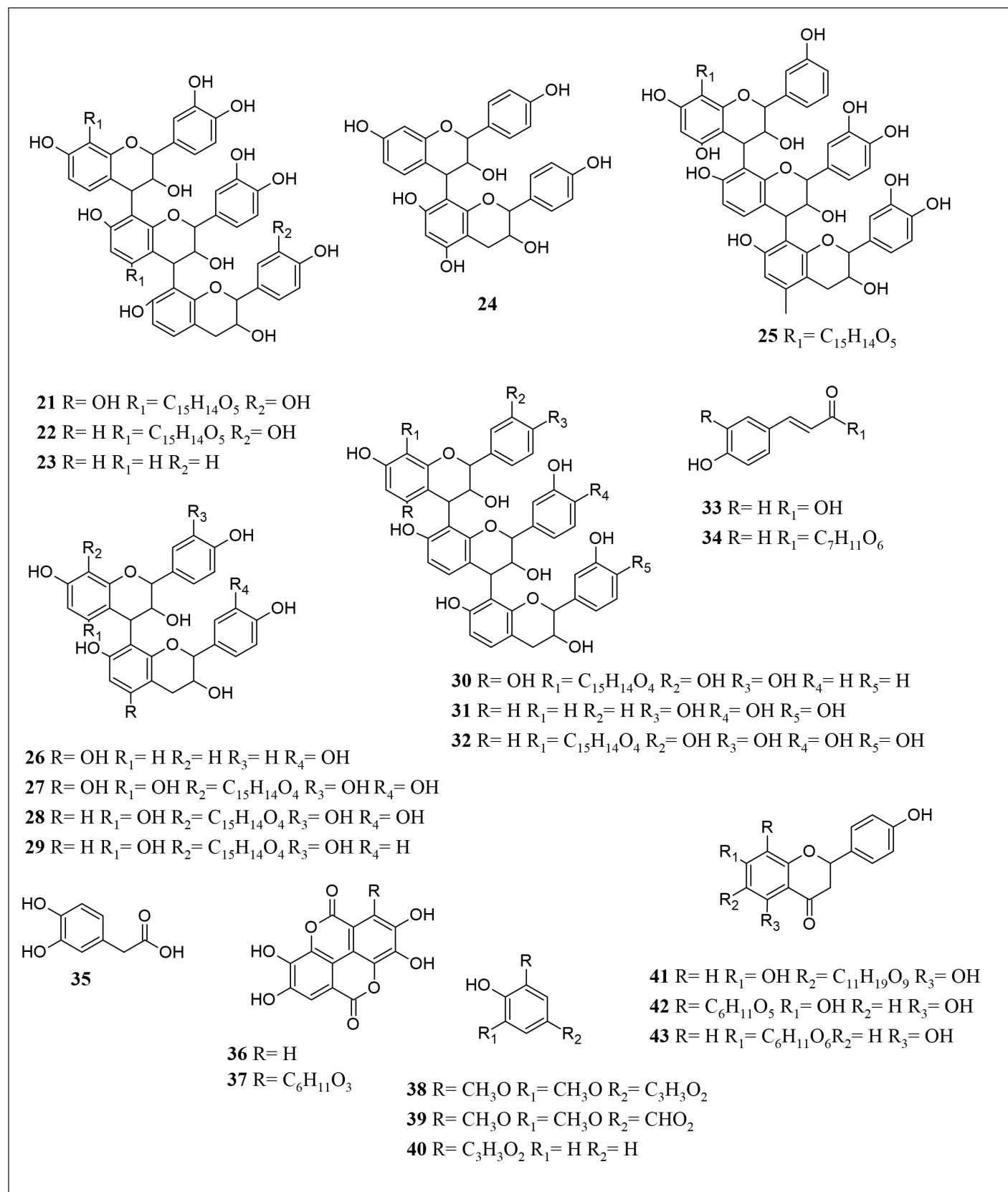
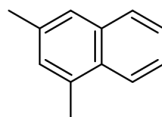
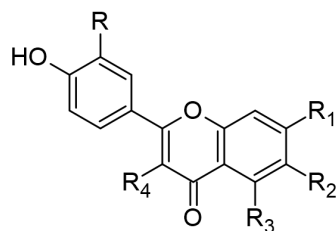
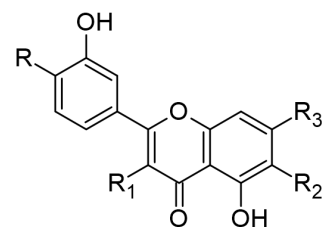


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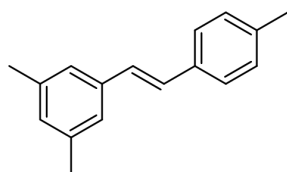


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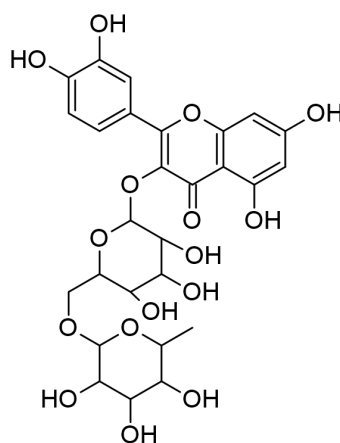


- 44 R= H R₁= OH R₂= H R₃= OH R₄= C₁₂H₂₁O₁₀
 45 R= H R₁= OH R₂= H R₃= OH R₄= C₁₂H₂₁O₁₀
 46 R= H R₁= OH R₂= H R₃= OH R₄= C₁₃H₂₀O₁₁
 47 R= H R₁= C₁₂H₂₁O₁₀ R₂= H R₃= C₆H₁₁O₆ R₄= OH
 48 R= H R₁= OH R₂= H R₃= OH R₄= C₁₄H₂₃O₁₁
 49 R= H R₁= OH R₂= C₁₂H₁₉O₈ R₃= OH R₄= H
 50 R= H R₁= OH R₂= C₁₂H₁₉O₈ R₃= OH R₄= H
 51 R= H R₁= OH R₂= C₁₂H₁₉O₈ R₃= OH R₄= H
 52 R= OH R₁= OH R₂= C₁₂H₁₉O₈ R₃= OH R₄= H
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 54 R= OH R₁= OH R₂= C₁₁H₂₁O₉ R₃= OH R₄= H
 55 R= OH R₁= OH R₂= C₁₁H₂₁O₉ R₃= OH R₄= H
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 57 R= C₆H₁₁O₆ R₁= C₆H₁₁O₆ R₂= H R₃= OH R₄= H
 58 R= OH R₁= C₆H₁₁O₆ R₂= H R₃= OH R₄= H

- 60 R= OH R₁= OH R₂= H R₃= OH
 61 R= OH R₁= C₆H₁₁O₅ R₂= H R₃= OH
 62 R= OH R₁= C₆H₁₁O₆ R₂= H R₃= OH
 63 R= C₆H₁₁O₆ R₁= OH R₂= H R₃= C₂H₃O₂
 64 R= OH R₁= C₁₂H₂₁O₁₀ R₂= H R₃= OH
 65 R= OH R₁= C₁₆H₂₉O₁₃ R₂= H R₃= OH
 66 R= OH R₁= C₅H₉O₅ R₂= H R₃= OH
 67 R= OH R₁= C₈H₁₃O₇ R₂= H R₃= CH₃O
 68 R= OH R₁= C₁₂H₂₁O₁₀ R₂= H R₃= CH₃O
 69 R= OH R₁= C₈H₁₃O₇ R₂= CH₃O R₃= H



70



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Figure 5. Continued.

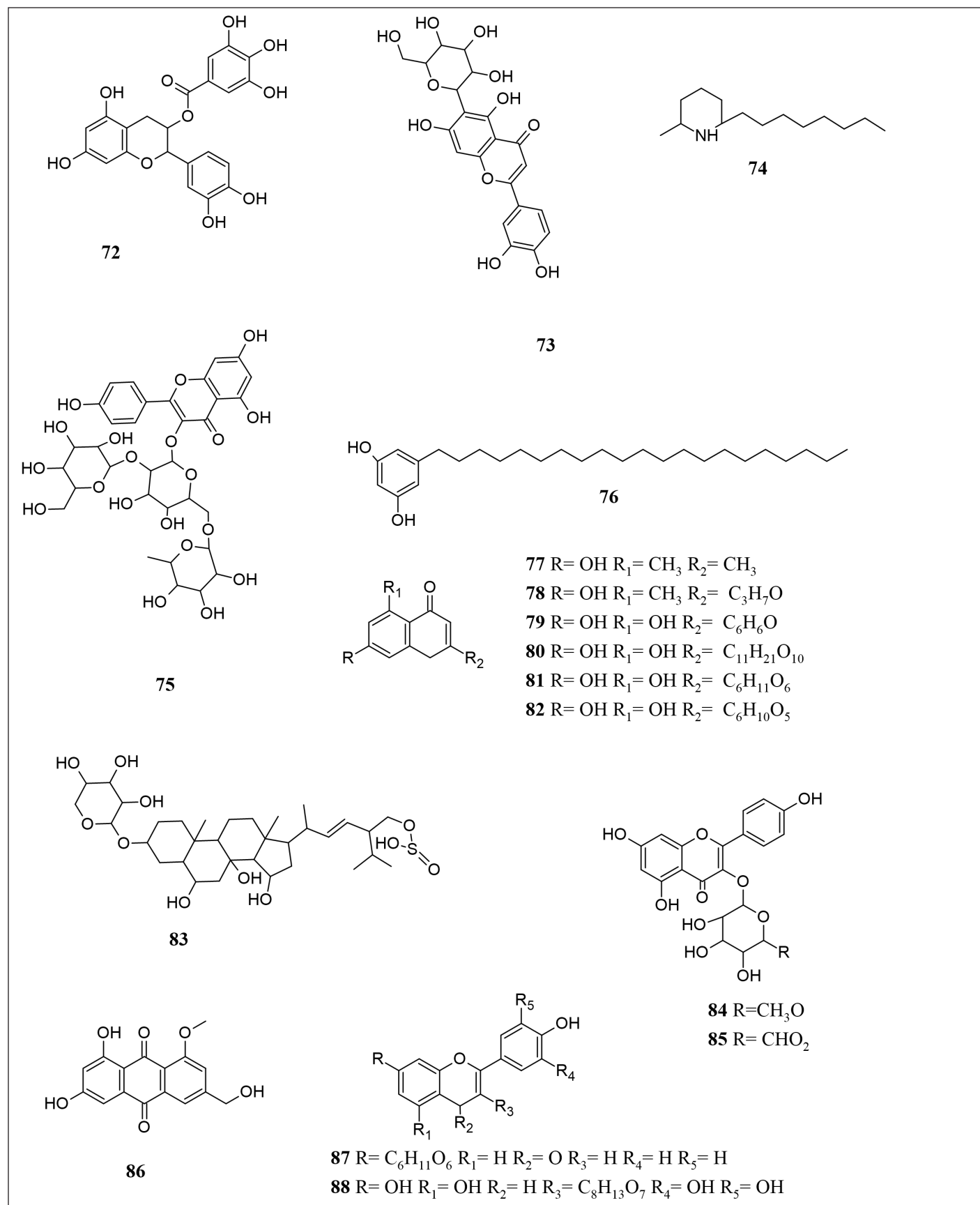


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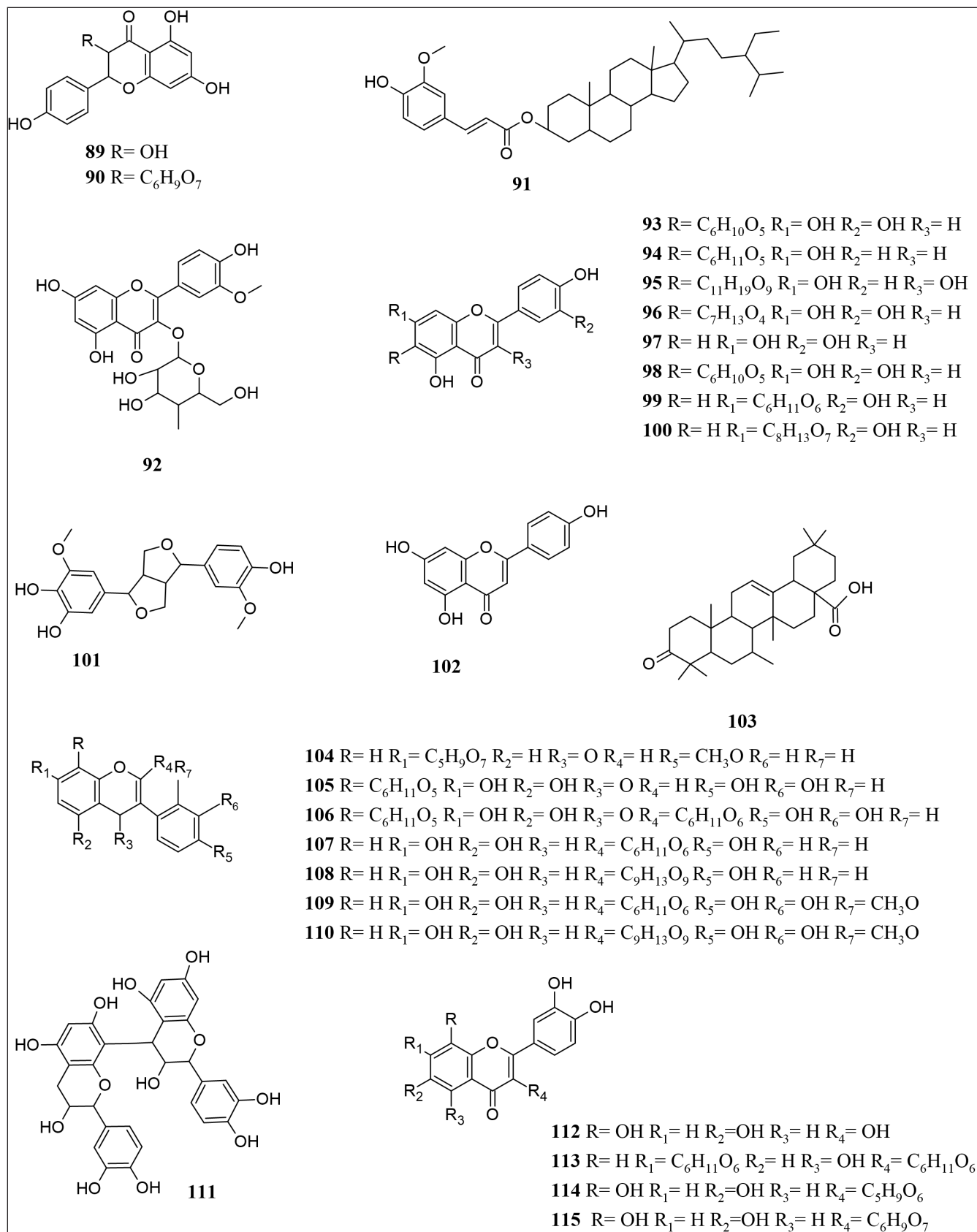


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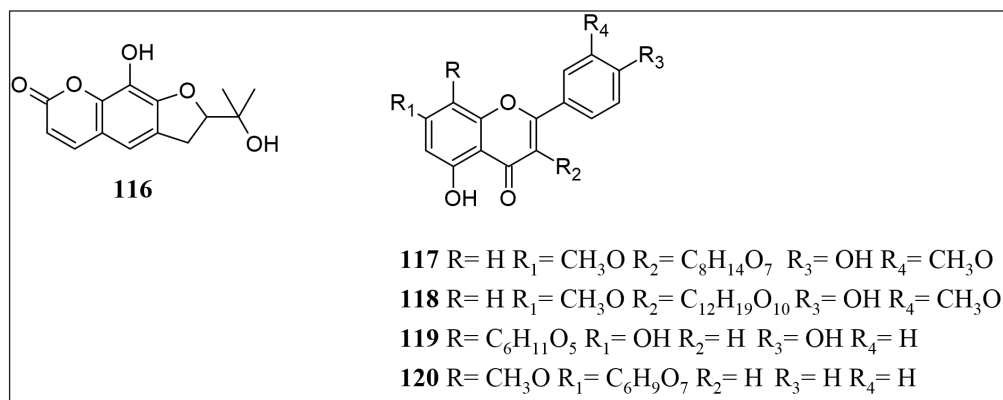


Figure 5. Phenolic compounds reported in species of *Chamaecrista*.

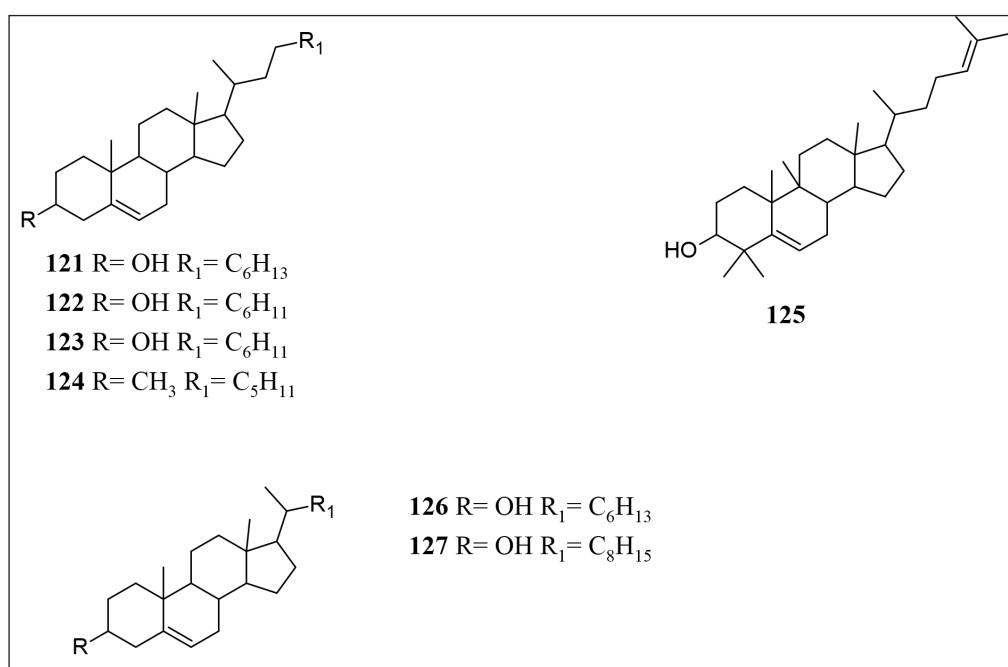


Figure 6. Sterols reported in genus *Chamaecrista*.

Flavonoids constitute a vast chemical group of various plant species and are classified into flavones, flavonols, flavanones, isoflavonoids, anthocyanidins, and catechins. They exhibit various pharmacological properties, including antioxidant, diuretic, antispasmodic, antiulcer, and anti-inflammatory [30]. In the studies analyzed, 35% of the chemical groups identified in *Chamaecrista* species corresponded to flavonoids. For instance, a study on *C. duckeana* identified 17 flavonoids in methanolic extracts from the stems, roots, fruits, and leaves using UPLC-ESI-HRMS [31]. Most (47%) of these flavonoids were found in the stem extracts (compounds **80**, **82**, **84**, **87**, **90**, **92**, **104**, and **113**, Table S1), detailed in Figure 5. In comparison, the remaining 47% were distributed among the leaves (compounds **100**, **114**, and **118**, Table S1) and fruit extracts (compounds **84**, **85**, **111**, **115**, and **117**, Table S1). Another species, *C. hildebrandtii*, presented 13 compounds, including flavonoids and phenolic derivatives (**72**, **74**, **76**, **83**,

88, **91**, **96**, **98**, **101**, **103**, **107–110**, Table S1) identified via LC-QTOF-MS in methanolic leaf extracts [32].

Certain compounds have also been identified in several *Chamaecrista* species. For example, vitexin (**119**), reported in extracts from *C. rotundifolia*, *C. desvauxii*, and *C. diphylla*, exhibits antimicrobial, anti-inflammatory, and antioxidant effects and is particularly relevant in cosmetology for potential anti-aging benefits [33,34]. In addition, two flavonoids, apigenin, and luteolin, are present in both *C. diphylla* and *C. nictitans* extracts [25,35]. Apigenin (**79**) has antioxidant, anti-inflammatory, and anti-cancer effects, particularly by inhibiting the proliferation of cancer cells in the ovaries, prostate, and colon [36–38]. Luteolin (**97**) demonstrates various effects, including antioxidant, anti-inflammatory, anti-cardiovascular, anti-cancer, and anti-neurodegenerative properties [38–40]. Isovitexin (**94**) has been identified in several species, such as *C. desvauxii*, *C. diphylla*, *C. nictitans*, and *C. rotundifolia*, displays

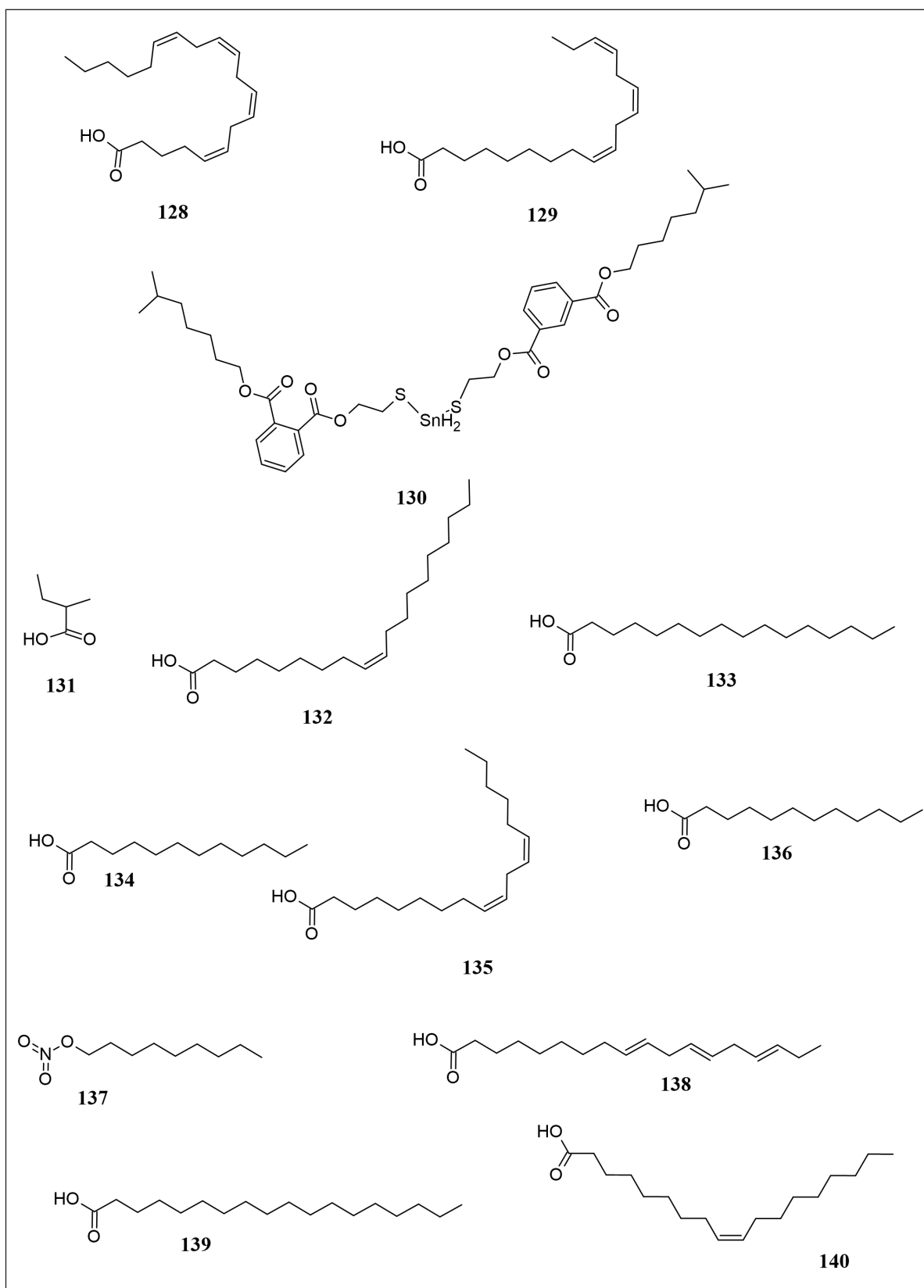


Figure 7. Fatty acids and aliphatic esters reported in genus *Chamaecrista*.

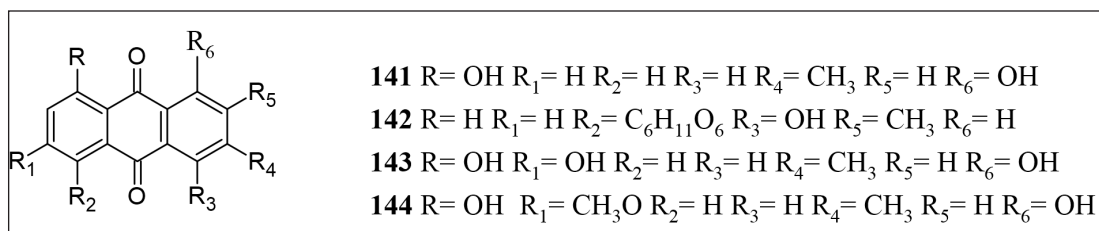


Figure 8. Anthraquinones reported in genus *Chamaecrista*.

anti-inflammatory and antioxidant effects, and is particularly beneficial in skincare and anti-aging treatments. Among the flavonoids identified in extracts of *C. desvauxii*, *C. nictitans*, and *C. rotundifolia*, quercetin (**112**) has been widely studied for its antioxidant, anti-inflammatory, and potential anticancer properties [41–43].

Chemical analysis of the *Chamaecrista* genus has revealed a richness of flavonoids, suggesting its potential application in various fields such as food, cosmetics, and pharmaceutical development. Despite promising research, information remains limited to this genus, and this review represents an initial step toward studying other species within the genus based on reported findings.

Sterols

Sterols are a group of lipids that play crucial roles in the structure of cell membranes and the regulation of various biological processes. They can originate from multiple sources, including animals, plants, and fungi. Those derived from plants are known as phytosterols, which are significant in cholesterol absorption and hormone synthesis. In addition, phytosterols have been observed to exhibit anti-inflammatory, antitumor, and antimicrobial effects, highlighting their broad therapeutic potential in various health areas [44,45].

They were primarily identified in the seed oil of *C. absus*, representing 5% of the total chemical groups identified in this genus (Table S1), as shown in Figure 6. Notably, three major phytosterols were present: campesterol (**124**), stigmasterol (**127**), and β -sitosterol (**121**), with β -sitosterol being the most abundant. The analysis was performed using gas chromatography with flame ionization detection (GC-FID) [46].

β -sitosterol is utilized as a nutritional supplement and is recognized for its therapeutic potential, including antioxidant, analgesic, antimicrobial, antidiabetic, and hepatoprotective effects, underscoring its multiple health benefits [47,48].

Fatty acids and aliphatic esters

Fatty acids are essential for human and animal diets and play crucial roles in various physiological functions, such as energy production and cell membrane formation. They are classified as saturated, unsaturated, and polyunsaturated, and balanced consumption promotes optimal cardiovascular health [49]. On the other hand, aliphatic esters are compounds of significant industrial and commercial importance, used as solvents and lubricants in food products, cosmetics, and fragrances. Their versatile properties make them highly valuable in the industry.

Two species, *C. absus* and *C. nigrigans*, have reported the presence of two fatty acids: n-hexadecanoic acid (compound **133**, Table S1) and octadecanoic acid (compound **139**, Table S1). In addition, three essential fatty acids were identified in *C. absus*: α -linolenic acid (Ω 3), linoleic acid (Ω 6), and oleic acid (Ω 9), as shown in Figure 7 [46,50].

Alpha-linolenic acid is known for its beneficial properties in preventing and treating cardiovascular and neurodegenerative diseases [51]. It also shows potential anti-inflammatory effects, with preliminary trials reporting its supplementation in patients with SARS-CoV-2 infection to combat inflammation [52]. Moreover, it has been included in the feed of both ruminant and non-ruminant animals, along with linoleic and oleic acids, resulting in improved meat quality in rabbits and poultry, increased egg mass in birds, and enhanced milk quality [53].

Furthermore, the percentage of α -linolenic acid reported in the oil was similar to that found in soybean oil (7%) and slightly lower than that in canola oil (9%), suggesting that it could be a viable alternative [54]. For these reasons, further research on *Chamaecrista* species is of interest.

Anthraquinones

Anthraquinones are a group of compounds that are widely distributed in nature and found in the roots, leaves, and flowers. These compounds are classified as quinones, benzoquinones, and naphthoquinones. They are known for their pharmacological properties, including anti-inflammatory, antitumor, antimicrobial, and laxative effects [55,56].

Anthraquinones have been reported in three species: *C. duckeana*, *C. nigrigans*, and *C. diphylla*, as determined by Ultra-High-Performance liquid chromatography (UPLC-ESI-HRMS), Electron Ionization Mass Spectrometry-m/z, Infrared spectroscopy, and ¹³C and ¹H nuclear magnetic resonance spectroscopy techniques, detailed in Figure 8, respectively (Table S1) [25,31,50].

Emodin (compound **143**, Table S1) has been detected in the leaves of *C. diphylla* and *C. nigrigans*. Its pharmacological properties include anti-inflammatory, antitumor, antimicrobial, antidiabetic, and neuroprotective properties, which help prevent diseases such as Alzheimer's and Parkinson's [57,58].

Other chemical compounds

Finally, it is worth mentioning that compounds within the following groups have been reported: triterpene alcohols, xanthone derivatives, triterpene derivatives, and sesquiterpenes, which are compiled in Table S1.

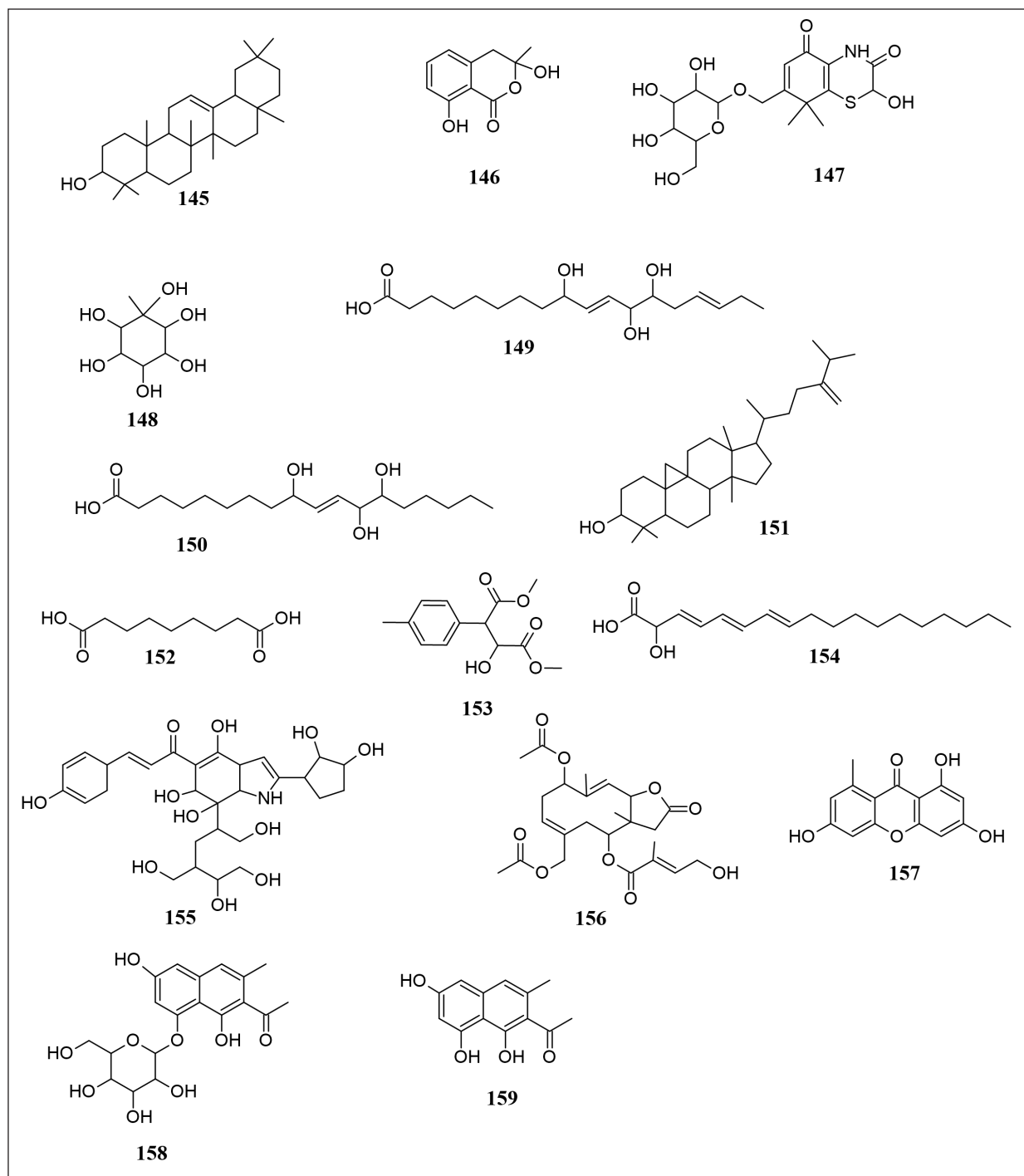


Figure 9. Other chemical compounds reported in different species of *Chamaecrista*.

Compounds **146**, **149**, **150**, **152–154**, and **157–159** were found in the leaves of *C. diphylla*, and compounds **147**, **155**, and **156** were found in the fruits of *C. ducleana*. The latter was also identified in the stem using UPLC-ESI-HRMS [25,31].

In contrast, compounds **145** and **151** have been reported in the seeds of *C. absus* using GC-FID and in the leaves of *C. nigricans* (compound **148**) using Gas Chromatography-Mass Spectrometry [46,50].

Among the compounds identified in the genus is β -amyrin, compound **145** (Fig. 9) reported in *C. absus*, which decreases blood glucose levels in mice and increases insulin levels [59].

Another compound reported was eupalinolide A (**156**) in the stems and fruits of *C. ducleana*. This compound has been studied for its potential anti-inflammatory and antitumor effects [60].

Azelaic acid was identified in the leaf extracts of *C. diphylla*. It has anti-inflammatory, antioxidant, and antibacterial properties and acne-inhibiting effects and is used to develop cosmetic products [61].

In conclusion, it is essential to highlight the significance of studies on chemical groups reported for the genus *Chamaecrista*. This genus has gained relevance since a previous review noted some species, emphasizing the importance of *Chamaecrista* [62]. Even so, it is necessary to continue with future research because 40% of the identified compounds do not report studies on their pharmacological properties, and other chemical groups, such as alkaloids, which have been reported in species belonging to the same subfamily Caesalpinoideae, have not been studied in *Chamaecrista*. These may represent promising research fields, expanding the knowledge of the pharmacological properties that they may present and their potential applications in health.

In conclusion, advancing the identification and isolation of chemical compounds in *Chamaecrista* species is essential, especially considering that only one of the studies reviewed has undertaken a comprehensive chemical analysis [24]. The remaining works are largely limited to preliminary identification efforts.

Nevertheless, the field offers significant opportunities for future research. Notably, around 40% of the compounds identified so far have not been investigated for their pharmacological activities. Furthermore, chemical groups such as alkaloids, well-documented in other species within the Caesalpinoideae subfamily, have yet to be explored in *Chamaecrista*. Addressing these gaps could unlock valuable pharmacological insights and open new pathways for applications in health and medicine. We encourage further multidisciplinary collaborations to fully realize the potential of *Chamaecrista* species in drug discovery and development [63,64].

Pharmacological activity of the genus *Chamaecrista*

The preclinical pharmacological properties reported in the selected scientific literature of the extracts and their fractions of various species of this genus have been compiled, with a total of seven properties, where antimicrobial and antioxidant activities stand out, with 36% each.

Chamaecrista spp. are traditionally used in folk medicine and exhibit various pharmacological properties. Based on the studies included in this review, the most frequently reported activities were antimicrobial and antioxidant (each accounting for 36% of the studies), followed by cytotoxic and antiviral activities (8% each), and antitrypanosomal, anticholinesterase, and acute toxicity effects (4% each) (Table 2).

Antimicrobial activity

The increasing resistance to conventional antimicrobial agents, mainly owing to their overuse in medicine and agriculture, poses a significant public health challenge, contributing to high morbidity and mortality rates worldwide. This issue also leads to increased healthcare costs and frequent therapeutic failures. Moreover, antimicrobial therapies

themselves can cause severe adverse effects, and the use of specific agents is restricted owing to their toxicity [65].

Oil extracted from *C. absus* seeds exhibited antibacterial activity against a range of gram-positive bacteria, including *Staphylococcus aureus*, *Listeria ivanovii*, *Listeria innocua*, *Bacillus subtilis*, and *Bacillus cereus*, as well as the gram-negative bacteria *Escherichia coli*. The most vigorous activity was observed against *L. ivanovii* and *B. subtilis*, with an inhibition zone reaching up to 12 mm, possibly owing to sterols and triterpenoid alcohols in the seed oil [46]. The aqueous extract of *C. nigricans* leaves, when combined with iron oxide nanoparticles, demonstrated enhanced antibacterial efficacy, producing inhibition of 24 mm against *E. coli*, 19.5 mm *Pseudomonas aeruginosa* and 18.5 mm *Klebsiella pneumoniae* at a concentration of 100 µg/ml [66]. Similarly, the leaf extract of *C. cytisoides* displayed notable antibacterial activity, particularly against *Micrococcus luteus* (21 mm), and inhibited the growth of *B. subtilis* and *E. coli*. The comparatively lower activity of many extracts against gram-negative bacteria may be explained by their outer membrane, which acts as an additional barrier to antimicrobial agents [34]. At a concentration of 4 mg/ml, the fruit extract of *C. desvauxii* inhibited *Staphylococcus epidermidis* biofilm formation (12.6%). *Staphylococcus epidermidis* is closely associated with nosocomial infections, and inhibiting virulence factors such as biofilm formation presents an innovative therapeutic approach [33].

Regarding antifungal activity, extracts of *C. desvauxii* showed inhibition against *Candida albicans*, with fruit extract being the most effective (19 mm) [34]. These results suggest that different plant parts may exhibit distinct antimicrobial profiles, likely owing to variations in their chemical composition. The methanolic leaf extracts of *C. desvauxii*, *C. nictitans*, and *Chamaecrista vestita* demonstrated both fungistatic and fungicidal activity against dermatophytes such as *Trichophyton rubrum*, *Epidermophyton floccosum*, and *Trichophyton mentagrophytes* at 500 mg/ml, indicating strong anti-dermatophyte potential [34].

The antimicrobial efficacy of *Chamaecrista* extracts appears to be influenced by the presence and degree of hydroxylation of the phenolic compounds. Nevertheless, there is a notable gap in studies on antifungal activity within this genus, highlighting the need for further research. Natural products from *Chamaecrista* offer considerable promise owing to their chemical diversity, particularly phenolics with known antifungal properties. Future studies should focus on the isolation and characterization of bioactive compounds, elucidating their mechanisms of action, evaluation using *in vivo* models, structure-activity relationship studies, and exploration of chemical modifications. Investigating the potential synergistic effects between plant extracts or conventional antimicrobial agents may also reveal new approaches to overcoming microbial resistance.

Anticholinesterase activity

Alzheimer's disease (AD) is the most common neurodegenerative disorder and the primary cause of dementia worldwide. Current treatments are primarily symptomatic, with acetylcholinesterase (AChE) inhibitors being the most widely

prescribed. These agents inhibit AChE, thereby increasing acetylcholine levels in the brain and enhancing cognitive function through prolonged neurotransmitter availability [67]. However, many of the existing inhibitors have limitations such as adverse side effects, poor bioavailability, and insufficient modulation of acetylcholine levels to achieve a complete therapeutic effect. This has driven ongoing research into the discovery of new AChE inhibitors, particularly those derived from natural sources that may offer better efficacy and safety profiles.

In this regard, Adewusi *et al.* [16] reported that root extracts of *C. mimosoides* exhibited significant AChE inhibitory activity. Notably, the organic extract demonstrated the lowest IC₅₀ value (0.03 mg/ml), in contrast to the aqueous extract (0.35 mg/ml), indicating stronger inhibition of the enzyme [16]. The increased activity observed in the organic extract may be due to the greater efficiency of the organic solvents in extracting bioactive compounds with anticholinesterase potential.

Flavonoids, which are abundant in various *Chamaecrista* species, are natural compounds known for their anticholinesterase properties. Their occurrence in this genus highlights the relevance of further exploration of *Chamaecrista* as a promising source of new candidates for developing alternative or complementary therapies for AD.

Antioxidant activity

Antioxidants are compounds capable of mitigating oxidative stress by regulating free radicals formation, scavenging reactive species, halting chain reactions, and preventing lipid peroxidation. Free radicals, such as reactive oxygen species and reactive nitrogen species, can damage biomolecules, contributing to the pathogenesis of chronic diseases, including cardiovascular and neurodegenerative disorders, diabetes, and cancer [68]. Given their therapeutic potential, natural antioxidants represent a promising alternative to synthetic compounds, which are often associated with undesirable side effects, making their identification and development of natural antioxidants essential for the prevention and treatment of human diseases and for promoting overall health [69]. The phenolic compounds possess structural features such as hydroxyl groups capable of donating hydrogen atoms, which are key to neutralizing free radicals by cleaving the O–H bond, thereby explaining their high antioxidant capacity [70,71].

The seed oil of *C. absus* exhibited remarkable free radical scavenging capacity with an IC₅₀ value of 16.78 µg/ml, suggesting the presence of hydrogen-donating constituents capable of efficiently neutralizing DPPH radicals. A study by Reis *et al.* [72] evaluated the antioxidant activity of *C. diphylla* using the DPPH method, which revealed significant variations among the different extracts and fractions. The ethyl acetate fraction demonstrated the highest activity, with a CE₅₀ value of 0.11 mg/ml, surpassing the ascorbic acid standard (0.13 mg/ml). The ethanolic extract also exhibited notable activity (CE₅₀: 0.35 mg/ml) [72]. These results correlated with the high content of phenolic compounds, flavonoids, and condensed tannins in both samples.

Similarly, Gomes *et al.* [25] confirmed the antioxidant potential of *C. diphylla*, reporting that the ethyl acetate fraction

of its leaves had the highest activity (9.44 mmol ET/g) according to the oxygen radical absorbance capacity assay, followed by the methanolic and ethanolic fractions (6.59 and 4.29 mmol ET/g, respectively). The higher antioxidant activity in the fractions than in the crude extract suggests bioactive compound enrichment during the fractionation process [25].

In the case of *C. duckeana*, the methanolic extract of the stems displayed the highest antioxidant activity, with an IC₅₀ value of 165.71 µg/ml surpassing the standard synthetic antioxidant butylated hydroxytoluene, which had an IC₅₀ of 175.18 µg/ml [31]. Similarly, the methanolic extract of *C. hildebrandtii* leaves exhibited potent antioxidant activity (IC₅₀: 8.7 mg/ml), likely due to the synergistic action of various secondary metabolites [32]. The organic extract of *C. mimosoides* roots showed potent antioxidant activity against 2,2-Diphenyl-1-picrylhydrazyl (DPPH) and 2,2'-Azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) radicals, with low IC₅₀ values of 0.72 and 0.3 mg/ml, respectively [16].

In addition, the radical scavenging activity of the phenolic fractions of *C. nictitans* was analyzed. The oligomeric fraction demonstrated the highest activity (DE₅₀: 78.6 µg/µmol), while the polymeric fraction showed values similar to the crude extract (DE₅₀: 115.6 and 112.1 µg/µmol, respectively) [35]. In *C. repens*, the methanolic extract displayed 68.3% antioxidant activity in the β-carotene bleaching assay, whereas its DPPH radical scavenging capacity yielded an IC₅₀ of 2 mg/ml [73].

Chamaecrista species are promising natural antioxidant sources, primarily attributed to the presence of polyphenolic compounds, particularly flavonoids.

Antiviral activity

Viral infections cause various chronic and acute diseases in humans and animals. These infections are associated with high morbidity and mortality in humans [74]. Current antiviral drugs present several problems, such as high costs, drug resistance, safety concerns, and limitations in efficacy. Viral replication poses a unique challenge, as targeting the virus without harming the host cells is difficult. Viral variability, particularly in RNA viruses, and accumulated genetic mutations contribute to drug resistance, leading researchers to develop new antiviral options [15,35,74]. Emerging and re-emerging viruses represent a significant problem in viral pathogenesis, leading to outbreaks, epidemics, and pandemics. A current example is COVID-19, which is caused by the spread of SARS-CoV-2 and has impacted global social and economic conditions. Therefore, searching for new antiviral agents is crucial, and natural products offer valuable sources of novel chemical compounds with antiviral activity. Numerous preclinical studies have identified natural products with potential *in vitro* and *in vivo* antiviral activities, some of which have progressed to clinical trials for drug development [74,75].

However, the antiviral activity of *Chamaecrista* has not been exhaustively investigated. So far, only *C. nictitans* has been evaluated for its antiviral properties against herpes simplex virus (HSV). This virus, which is globally distributed, remains a significant public health issue, infecting 45%–98% of the world's population [74]. Uribe *et al.* [15] suggest effective antiviral action, as a dose-dependent effect was recorded as the

inhibitory effect of the extract. This activity was attributed to the polar components, initially identified in the aqueous methanolic fraction and later in the dichloromethane and butanol fractions, with inhibition of cytopathic effect (CPE) values ranging from 41.41 to 76.56 $\mu\text{g/ml}$. The crude extract also exhibited antiviral activity, with a CPE value of 168.75 $\mu\text{g/ml}$.

Mateos-Martín *et al.* [35] observed that the oligomeric fraction, at a concentration of 68.7 $\mu\text{g/ml}$, was the most effective among the analyzed fractions. They suggested that this fraction of *C. nictitans* extract exerts its action through a particularly effective combination of proanthocyanidins, which have two structural characteristics: monohydroxyphenolic structures and type A linkages. These have been associated with antiviral effects, primarily through inhibiting late transcription. *C. nictitans* exhibits antiviral properties and acts against herpes simplex virus (HSV), which can be attributed to the presence of polyphenolic compounds. Although acyclovir inhibits the secondary transcription of the virus, the extract of this species inhibits two stages of the HSV replication cycle, adsorption, and secondary transcription, exerting its action intracellularly [15,35,74].

These findings suggested that *C. nictitans* has therapeutic potential. The structural characterization and isolation of biomolecules are crucial for studying their absorption, distribution, metabolism, excretion, and toxicity properties. As a new natural source for preventing and treating viral diseases, further studies are required.

Antitrypanosomal activity

Trypanosomiasis is caused by a protozoan parasite belonging to the genus *Trypanosoma*. It is primarily responsible for chronic anthroponotic infections in West and Central Africa and can have severe consequences if not treated adequately [69]. Furthermore, it is classified as a neglected infectious disease, primarily affecting populations in developing countries that receive limited attention in the research and development of new treatments despite its significant impact on public health. Treatment options are limited, underscoring the need for further research to improve the therapeutic possibilities [76].

Only one report has documented the anti-trypanosomal properties of this genus. The crude methanolic extract of *C. mimosoides* leaves showed significant cessation of parasite motility with increased incubation time and extract concentration. Complete cessation of *Trypanosoma brucei brucei* motility was observed within 25 minutes at the highest concentration evaluated (4 mg/ml) [77]. These findings indicate that the extract of this species possesses notable *in vitro* antitrypanosomal activity, which could be attributed to its phytoconstituents, such as flavonoids, terpenes, sterols, and polyphenols. This suggests that these compounds represent a promising source for *in vivo* treatment of trypanosomiasis [77].

Cytotoxicity

Cancer poses a significant challenge to the global public health. Global demographic trends suggest an increase in cancer incidence in the coming decades, with projections indicating more than 20 million new cases annually by 2025 [78]. Chemotherapy remains a cornerstone of clinical cancer treatment. However, this

therapeutic strategy is hindered by challenges, such as tumor heterogeneity, side effects, toxicity, and acquired multidrug resistance, which limit its therapeutic efficacy. Consequently, searching for drugs with reduced toxicity and improved efficacy is a critical priority in medical research. Between 1981 and 2019, approximately 25% of all newly approved cancer drugs were derived from natural products, underscoring the immense potential of this rich resource [79].

Lima *et al.* [31] demonstrated that methanolic extracts of *C. duckeana* exhibited over 80% inhibition of cell growth in HL60 leukemia cells and less than 58.17% inhibition against SNB19 (central nervous system), HCT116 (human colon), and PC3 (prostate) cell lines. Stems showed notable cytotoxicity with IC_{50} values of 137.3 and 106.8 $\mu\text{mol/ml}$ for HL60 and RAJI cells, respectively. These findings highlight the potential of extracts from this plant species for their promising antitumor and cytotoxic activities [31]. The observed cytotoxicity may be attributed to the presence of the sesquiterpene Eupalinolide A in *C. duckeana* extracts, which has been noted in the literature for its potent cytotoxic activity [79].

However, further preclinical and clinical studies are required to confirm the anticancer effects of *C. duckeana*. Once the active compounds responsible for anticancer activity have been identified, such studies could explore the antitumor mechanisms of its constituents. These compounds could serve as promising candidates for developing new cancer treatments or for use in complementary therapies alongside conventional approaches.

Acute toxicity

Acute toxicity testing is generally the first step in assessing the toxicity of a substance. It provides crucial information on the health risks associated with short-term exposure to substances such as drugs. Moreover, these studies can identify early signs of potentially serious adverse effects, enabling the implementation of appropriate preventive measures such as dose adjustments. Such research is paramount before using the substance and lays the groundwork for future clinical toxicity studies [80].

Very few toxicity studies have been conducted in the genus *Chamaecrista*. Among them, Medugu *et al.* [81] evaluated the acute toxicity of *C. mimosoides* extract fractions in mice via the intraperitoneal route, obtaining LD50 values $>5,000$ mg/kg for the butanol fraction and 3,808 mg/kg for the chloroform and ethyl acetate fractions. These results suggest the low toxicity of the evaluated fractions, with LD50 values $\geq 1,500$ mg/kg.

David *et al.* [73] conducted an acute toxicity assessment of the methanolic extract of *C. repens*, obtaining an LC50 value of 269.3 $\mu\text{g/ml}$ in *Artemia salina*. Extracts with LC50 values above 200 mg/l in the *A. salina* lethality assay were considered low toxicity.

Continued investigation of the toxicity of natural product extracts, particularly those with pharmacological activity, is essential for developing Natural Product-Based Libraries. These studies play a critical role in comprehensively evaluating the safety profiles of bioactive compounds, thereby ensuring safe and effective drug discovery [82].

CONCLUSION AND FUTURE PERSPECTIVES

A review of the genus *Chamaecrista* underscores its therapeutic potential while revealing critical research gaps. Phytochemical studies have identified a diverse array of bioactive compounds, including flavonoids (e.g., vitexin, luteolin, and quercetin), polyphenols, terpenoids, and anthraquinones, which contribute to their antioxidant, antimicrobial, antiviral, cytotoxic, anticholinesterase, and antitrypanosomal activities. Notably, *C. nictitans* and *C. duckeana* exhibited the most robust pharmacological evidence, with flavonoids and sesquiterpenes, such as eupalinolide A, linked to their antioxidant and cytotoxic effects. However, despite these promising findings, over 40% of the identified compounds remain pharmacologically uncharacterized. Key chemical groups, such as alkaloids, well-documented in related genera, are yet to be explored in *Chamaecrista*.

A significant limitation of the current study is its heavy reliance on *in vitro* assays. For instance, while *C. nictitans* shows promising antiviral activity against HSV, and *C. duckeana* demonstrates cytotoxicity against leukemia cells (HL60); these effects lack validation *in vivo* models. Translational applications are hindered by the absence of safety and efficacy profiles in physiological contexts. Thus, future studies must prioritize *in vivo* preclinical research to elucidate the mechanisms, assess toxicity, and establish dosage parameters as a foundation for clinical trials.

This review highlights *Chamaecrista* as a chemically rich and pharmacologically versatile genus with an untapped potential. This study provides a roadmap for future research to unlock novel therapeutic alternatives by bridging traditional uses, phytochemical diversity, and observed bioactivities. Addressing these gaps could position *Chamaecrista* as a valuable resource for drug discovery and innovation in herbal medicine.

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AUTHOR CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agree to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

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The authors report no financial or any other conflicts of interest in this work.

ETHICAL APPROVALS

This study does not involve experiments on animals or human subjects.

DATA AVAILABILITY

All the data is available with the authors and shall be provided upon request.

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USE OF ARTIFICIAL INTELLIGENCE (AI)-ASSISTED TECHNOLOGY

The authors declares that they have not used artificial intelligence (AI)-tools for writing and editing of the manuscript, and no images were manipulated using AI.

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SUPPLEMENTARY MATERIAL

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