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Medicinal Plants Used in Sulawesi: A Review of Phenolic Diversity, Phytochemical Evidence, and Anti-Inflammatory Potential

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ABSTRACT

Sulawesi possesses substantial medicinal plant diversity and traditional knowledge, but ethnobotanical, phytochemical, and pharmacological evidence remains dispersed across different studies. This review aimed to integrate information on medicinal plants used in Sulawesi, Indonesia, with emphasis on phenolic diversity, phytochemical evidence, and anti-inflammatory potential. A structured literature review was conducted using publications retrieved from Scopus, ScienceDirect, PubMed, Google Scholar, SpringerLink, and Wiley Online Library. The evidence was synthesized into three datasets covering medicinal plant diversity, phenolic compounds and analytical methods, and anti-inflammatory activity. A total of 132 medicinal plant species were identified across six provinces of Sulawesi. Phytochemical evidence was available for 20 species, revealing diverse phenolic classes and various analytical approaches for their characterization. Among these species, nine showed documented anti-inflammatory activity supported by varying levels of in vitro, in vivo, and/or in silico evidence, with clinical evidence additionally available for *Psidium guajava* and *Curcuma longa*. The integrated findings demonstrate substantial phenolic diversity and promising anti-inflammatory potential among medicinal plants used in Sulawesi. However, a direct relationship between specific phenolic constituents and anti-inflammatory effects remains insufficiently established, highlighting the need for further compound-specific phytochemical and pharmacological investigations.

Keywords: Medicinal Plants, Sulawesi, Phenolic, Phytochemical, Anti-inflammatory

ABSTRAK

Sulawesi memiliki keragaman tumbuhan obat dan pengetahuan pengobatan tradisional yang besar, tetapi bukti etnobotani, fitokimia, dan farmakologi masih tersebar dalam berbagai penelitian. Review ini bertujuan mengintegrasikan informasi mengenai tumbuhan obat yang digunakan di Sulawesi, Indonesia, dengan fokus pada keragaman senyawa fenolik, bukti fitokimia, dan potensi antiinflamasi. Kajian literatur dilakukan terhadap publikasi yang diperoleh dari Scopus, ScienceDirect, PubMed, Google Scholar, SpringerLink, dan Wiley Online Library. Bukti yang diperoleh disintesis ke dalam tiga dataset yang mencakup keragaman tumbuhan obat, senyawa fenolik dan metode analisis, serta aktivitas antiinflamasi. Sebanyak 132 spesies tumbuhan obat teridentifikasi dari enam provinsi di Sulawesi. Bukti fitokimia tersedia untuk 20 spesies yang menunjukkan keragaman kelas senyawa fenolik dan berbagai pendekatan analisis untuk karakterisasinya. Dari spesies tersebut, sembilan menunjukkan aktivitas antiinflamasi yang didukung oleh berbagai tingkat bukti in vitro, in vivo, dan/atau in silico, sedangkan bukti klinis tersedia untuk *Psidium guajava* dan *Curcuma longa*. Hasil integrasi menunjukkan keragaman senyawa fenolik dan potensi antiinflamasi yang menjanjikan pada tumbuhan obat yang digunakan di Sulawesi. Namun, hubungan langsung antara senyawa fenolik tertentu dan aktivitas antiinflamasi masih belum dapat ditetapkan secara konsisten, sehingga diperlukan penelitian fitokimia dan farmakologi lebih lanjut yang berfokus pada senyawa spesifik.

Kata Kunci: Tumbuhan Obat, Sulawesi, Fenolik, Fitokimia, Antiinflamasi

1. Introduction

Natural products continue to play a pivotal role in modern drug discovery despite remarkable advances in synthetic chemistry. Plant-derived natural products provide structurally diverse bioactive compounds that have contributed substantially to the development of modern pharmaceuticals and remain an invaluable source of new therapeutic agents [1], [2]. Among the diverse classes of plant secondary metabolites, phenolic compounds have attracted increasing scientific attention because of their broad pharmacological activities, particularly their antioxidant and anti-inflammatory properties[3]. The continuous advancement of phytochemical analytical technologies has further accelerated the discovery and characterization of phenolic-rich medicinal plants, strengthening their potential application in pharmaceutical research and natural product-based drug development [2].

Indonesia is one of the world's megabiodiversity countries and possesses abundant medicinal plant resources that have been traditionally utilized for healthcare by numerous ethnic communities. Sulawesi represents one of the important regions contributing to this biodiversity and preserves extensive indigenous knowledge regarding medicinal plant utilization. During the last decade, ethnobotanical studies conducted in South Sulawesi, Central Sulawesi, Southeast Sulawesi, West Sulawesi, and North Sulawesi have documented numerous medicinal plant species used for treating infectious diseases, inflammatory disorders, gastrointestinal diseases, metabolic diseases, and various other health conditions [4], [5], [6], [7], [8], [9]. Although these studies have significantly enriched ethnobotanical documentation, they primarily focus on traditional medicinal uses, while phytochemical characterization and pharmacological evidence remain dispersed across different publications.

Recent phytochemical investigations have considerably enhanced the scientific validation of medicinal plants through the application of analytical techniques such as high-performance liquid chromatography (HPLC), liquid chromatography–mass spectrometry (LC-MS), gas chromatography–mass spectrometry (GC-MS), ultra-performance liquid chromatography (UPLC), and nuclear magnetic resonance (NMR). These analytical approaches have enabled accurate identification and characterization of phenolic compounds, facilitating the correlation between phytochemical composition and biological activities [10]. Furthermore, accumulating evidence indicates that phenolic compounds regulate inflammatory responses through multiple molecular pathways, supporting their potential application as natural anti-inflammatory agents for preventing and managing chronic inflammatory diseases [11]. However, existing reviews have generally addressed medicinal plants from either ethnobotanical, phytochemical, or pharmacological perspectives, with limited integration of these three levels of evidence within a regional context.

In contrast, this review integrates three complementary levels of evidence—ethnobotanical documentation, phenolic-focused phytochemical evidence, and anti-inflammatory pharmacological evidence—to provide a structured chemical perspective on medicinal plants used in Sulawesi. The review not only summarizes the diversity of medicinal plants documented across the region but also examines the reported phenolic classes, representative phenolic compounds, and analytical approaches used for their characterization. The available anti-inflammatory evidence is then considered alongside the phytochemical findings to identify medicinal plants with relatively strong supporting evidence and to highlight gaps requiring further compound-specific investigation. This integrated framework distinguishes the present review from previous studies that have primarily emphasized ethnobotanical documentation or the phytochemistry and pharmacology of individual plant species.

Therefore, this review aims to comprehensively summarize medicinal plants used in Sulawesi, Indonesia, by integrating ethnobotanical information with phytochemical and pharmacological evidence. Specifically, it compiles the diversity of medicinal plants reported across Sulawesi, summarizes phenolic diversity and representative constituents together with the analytical methods used for their characterization, and critically evaluates the available anti-inflammatory evidence of selected medicinal plants. This integrated approach provides a regional evidence framework for prioritizing promising medicinal plants and identifying research gaps for future phytochemical and pharmacological investigations.

2. Methods

This study was conducted as a structured literature review to compile and critically evaluate medicinal plants used in Sulawesi, Indonesia, with emphasis on phenolic diversity, phytochemical evidence, and anti-inflammatory potential. The literature search and collection were conducted from May to July 2026. Relevant

publications were retrieved from Scopus, ScienceDirect, PubMed, Google Scholar, SpringerLink, and Wiley Online Library using combinations of keywords including *Sulawesi medicinal plants*, *ethnobotany*, *phenolic compounds*, *phytochemical analysis*, and *anti-inflammatory activity*. For the ethnobotanical dataset, studies were included when they documented medicinal plant use by communities in Sulawesi. For the phytochemical dataset, studies were included when they provided information on phenolic compounds or phenolic classes and their characterization. For the pharmacological dataset, studies were included when they explicitly reported anti-inflammatory activity of the selected medicinal plants. The ethnobotanical evidence was restricted to medicinal plant use documented in Sulawesi, whereas phytochemical and pharmacological evidence was considered at the species level regardless of study location, provided that the species matched the medicinal plant inventory. Recent publications were prioritized when multiple publications provided overlapping evidence, whereas earlier studies were retained when they provided unique, original, or foundational evidence not adequately represented by newer studies.

The selected studies were reviewed in three sequential stages. Plant species reported across the eligible ethnobotanical studies were compiled into Data Set A. Scientific names were standardized, and species reported in more than one study or province were treated as a single species. After consolidating these duplicate records, a total of 132 unique medicinal plant species was obtained. Second, all species identified in Data Set A were searched for available phytochemical evidence. Species for which published phytochemical evidence, particularly information on phenolic compounds or phenolic classes and their characterization, was identified were included in Data Set B. Of the 132 species searched, 20 species met these criteria and were therefore included in Data Set B. No additional selection criteria based on geographical origin, abundance of use, or reported biological activity were applied. Accordingly, phytochemical and pharmacological findings were not interpreted as evidence obtained specifically from plant materials collected in Sulawesi unless the original study explicitly reported a Sulawesi collection site. Third, all species included in Data Set B were searched for available anti-inflammatory evidence. Species for which at least one published study explicitly reported anti-inflammatory activity were included in Data Set C. Of the 20 species searched, nine met this criterion and were included in the synthesis (Table 3).

Studies were excluded from the corresponding dataset when they did not meet the dataset-specific inclusion criteria, did not clearly identify the medicinal plant, or did not provide the evidence required for the corresponding dataset.

3. Results and Discussion

3.1. Diversity of Medicinal Plants Used in Sulawesi

A comprehensive literature review identified 132 medicinal plant species traditionally used by local communities across six provinces in Sulawesi, namely Central Sulawesi, Southeast Sulawesi, South Sulawesi, West Sulawesi, North Sulawesi, and Gorontalo [4], [5], [6], [7], [8], [9]. The geographical distribution of the reviewed studies is illustrated in Figure 1, while the complete inventory of medicinal plant species is presented in Table 1.

Figure 1 illustrates the geographical distribution of the reviewed ethnobotanical studies and the documented medicinal plant diversity across Sulawesi. Among the reviewed provinces, Central Sulawesi recorded the highest number of documented medicinal plant records (61), followed by Southeast Sulawesi (42), South Sulawesi (23), West Sulawesi (17), North Sulawesi (3), and Gorontalo (2) [4], [5], [6], [7], [8], [9]. The sum of these provincial records exceeds the total of 132 unique medicinal plant species because several species were reported from more than one province. Therefore, the provincial values represent documented species records within each province, whereas the total of 132 represents the number of unique species identified across the reviewed studies. The observed variation is likely influenced by differences in the number of ethnobotanical surveys, study coverage, and the extent of documentation conducted in each province.

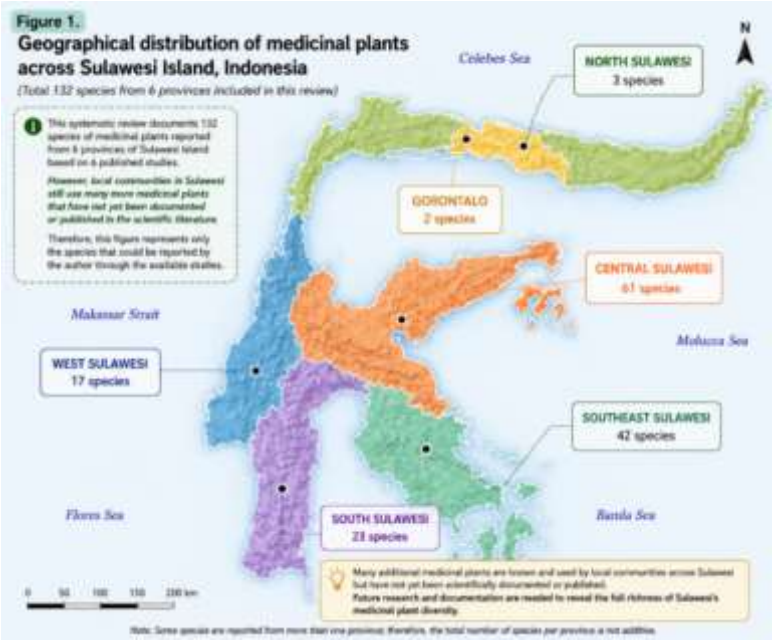


Figure 1. Geographical distribution of ethnobotanical studies and workflow for compiling medicinal plant diversity in Sulawesi

Table 1. Medicinal plants reported from ethnobotanical studies conducted in Sulawesi

No.	Scientific Name	Province / Study Area	Ref.
1-2	*Ficus septica* Burm. f.; *Gynura procumbens* (Lour.) Merr.	Southeast & West Sulawesi	[4], [5], [6], [7]
3	*Psidium guajava* L.	South, Central & West Sulawesi	[4], [5], [7]
4-12	*Curcuma longa* L.; *Morinda citrifolia* L.; *Orthosiphon aristatus* (Blume) Miq.; *Annona muricata* L.; *Cocos nucifera* L.; *Carica papaya* L.; *Physalis angulata* L.; *Ageratum conyzoides* L.; *Peperomia pellucida* (L.) Kunth;	Central & West Sulawesi	[4], [5], [6], [7], [8], [9]
13-14	*Allium cepa* L.; *Cymbopogon citratus* (DC.) Stapf	South & West Sulawesi	[4], [5], [8]
15	*Andrographis paniculata* (Burm. f.) Nees	Central & North Sulawesi	[8], [9]
16-17	*Carthamus tinctorius* L.; *Blumea balsamifera* (L.) DC.	North Sulawesi	[4]
18-19	*Averrhoa carambola* L.; *Averrhoa bilimbi* L.	Gorontalo	[4]
20-69	*Lansium domesticum* Corrêa; *Zingiber officinale* Roscoe; *Kaempferia galanga* L.; *Tinospora crispa* (L.) Hook. f. & Thomson; *Mangifera indica* L.; *Alstonia scholaris* (L.) R. Br.; *Areca catechu* L.; *Elephantopus scaber* L.; *Cheilocostus speciosus* (J. Koenig) C. D. Specht; *Aleurites moluccanus* (L.) Willd.; *Euphorbia hirta* L.; *Crotalaria spectabilis* Roth; *Senna alata* (L.) Roxb.; *Sesbania grandiflora* (L.) Pers.; *Spatholobus littoralis* Hassk.; *Macrosolen cochinchinensis* (Lour.) Tiegh.; *Lawsonia inermis* L.; *Theobroma cacao* L.; *Arcangelisia flava* (L.) Merr.; *Musa paradisiaca* L.; *Syzygium aromaticum* (L.) Merr. & L. M. Perry; *Pandanus amaryllifolius* Roxb.; *Imperata cylindrica* (L.) P. Beauv.; *Oryza sativa* L.; *Coffea canephora* Pierre ex A. Froehner; *Citrus aurantiifolia* (Christm.) Swingle; *Capsicum frutescens* L.; *Nicotiana tabacum* L.; *Solanum torvum* Sw.; *Solanum melongena* L.; *Clerodendrum japonicum* (Thunb.) Sweet; *Justicia gendarussa*	Central Sulawesi	[4], [6], [7], [8], [9]

No.	Scientific Name	Province / Study Area	Ref.
	Burm. f.; *Centella asiatica* (L.) Urb.; *Chromolaena odorata* (L.) R.M.King & H.Rob.; *Bidens pilosa* L.; *Mikania micrantha* Kunth; *Melastoma malabathricum* L.; *Phyllanthus niruri* L.; *Premna serratifolia* L.; *Abelmoschus moschatus* (L.) Medik.; *Curanga fel-terrae* (Lour.) Merr.; *Dendrocalamus strictus* (Roxb.) Nees; *Elmerrillia ovalis* (Miq.) Dandy; *Gliricidia sepium* (Jacq.) Kunth ex Walp.; *Glinus oppositifolius* (L.) Aug. DC.; *Piper majusculum* Blume; *Scurrula atropurpurea* (Blume) Dans.; *Synedrella nodiflora* (L.) Gaertn.; *Talinum paniculatum* (Jacq.) Gaertn.; *Apium graveolens* L.		
70-109	*Rhizophora apiculata* Blume; *Leea indica* (Burm. f.) Merr.; *Acalypha indica* L.; *Adenanthera pavonina* L.; *Cenchrus echinatus* L.; *Cinnamomum zeylanicum* Garcin ex Blume; *Citrus hystrix* DC.; *Coleus scutellarioides* (L.) Benth.; *Coriandrum sativum* L.; *Cosmos caudatus* Kunth; *Crassocephalum crepidioides* (Benth.) S.Moore; *Curcuma heyneana* Valeton & Zijp; *Curcuma zedoaria* (Christm.) Roscoe; *Cymbopogon nardus* (L.) Rendle; *Cyperus rotundus* L.; *Eleusine indica* (L.) Gaertn.; *Eleutherine palmifolia* (L.) Merr.; *Euphorbia heterophylla* L.; *Euphorbia tirucalli* L.; *Graptophyllum pictum* (L.) Griff.; *Gynura pseudochina* (L.) DC.; *Hedyotis corymbosa* L.; *Kalanchoe pinnata* (Lam.) Pers.; *Kleinhovia hospita* L.; *Lantana camara* L.; *Melaleuca leucadendra* L.; *Moringa oleifera* Lam.; *Musa acuminata* Colla; *Myristica fragrans* Houtt.; *Nigella sativa* L.; *Olea europaea* L.; *Passiflora foetida* L.; *Pedilanthus tithymaloides* (L.) Poit.; *Phaleria macrocarpa* (Scheff.) Boerl.; *Piper crocatum* Ruiz & Pav.; *Piper retrofractum* Vahl; *Plantago major* L.; *Clausena excavata* Burm. f.; *Polygala paniculata* L.; *Punica granatum* L.	Southeast Sulawesi	[4], [9]
110-129	*Acorus calamus* L.; *Piper betle* L.; *Allium schoenoprasum* L.; *Eryngium foetidum* L.; *Colocasia esculenta* (L.) Schott; *Artemisia vulgaris* L.; *Pseudoelephantopus spicatus* (Juss. ex Aubl.) C.F.Baker; *Vernonia amygdalina* Delile; *Diplazium esculentum* (Retz.) Sw.; *Anredera cordifolia* (Ten.) Steenis; *Blechnum capense* (L.) Schltdl.; *Symphytum officinale* L.; *Drynaria cordata* (L.) Willd. ex Roem. & Schult.; *Commelina benghalensis* L.; *Ipomoea batatas* (L.) Lam.; *Sechium edule* (Jacq.) Sw.; *Pteridium aquilinum* (L.) Kuhn; *Sauropus androgynus* (L.) Merr.; *Piper umbellatum* L.; *Saccharum spontaneum* L.	South Sulawesi	[4], [8]
130-132	*Momordica charantia* L.; *Celosia cristata* L.; *Persea americana* Mill.	West Sulawesi	[5]

The inventory presented in Table 1 demonstrates that medicinal plants are traditionally used to manage a wide range of health conditions, including inflammatory, infectious, gastrointestinal, metabolic, respiratory, and skin disorders [4], [5], [6], [7], [8], [9]. Several species, including *Curcuma longa*, *Psidium guajava*, *Ficus septica*, *Gynura procumbens*, *Orthosiphon aristatus*, and *Morinda citrifolia*, were reported in more than one province, indicating their repeated utilization by different ethnic communities across Sulawesi. This repeated occurrence may reflect their wider distribution, accessibility, and incorporation into traditional healthcare practices among different communities, and may indicate wider ethnomedicinal importance. However, repeated documentation across provinces should not be interpreted as direct evidence of greater therapeutic efficacy, as the frequency of reporting may also be influenced by differences in ethnobotanical study coverage.

Although the available ethnobotanical studies provide valuable information on medicinal plant diversity and traditional uses, most publications remain descriptive and rarely include phytochemical characterization or biological validation. Consequently, further evaluation based on phytochemical evidence is required to establish the relationship between traditional medicinal use and the bioactive constituents responsible for the reported therapeutic properties. The phytochemical evidence of selected medicinal plants is discussed in the

following section.

3.2 Phenolic Diversity and Phytochemical Evidence

Phytochemical evidence was identified for 20 medicinal plant species from the ethnobotanical inventory, as summarized in Table 2. The reported phytochemical profiles varied in the phenolic categories or compound groups identified, the plant parts investigated, and the analytical methods employed. The available evidence ranged from broad phenolic class-level descriptions to more specific subclass and compound-level characterization.

Phenolic compounds comprise a structurally diverse group of secondary metabolites that can be classified into several major groups according to their chemical skeleton and substitution patterns. Phenolic acids generally contain a carboxylic acid group together with a phenolic structure and are commonly divided into hydroxybenzoic and hydroxycinnamic acids. Flavonoids are characterized by a C6–C3–C6 carbon skeleton and include subclasses such as flavones, flavonols, flavanones, and their glycosides. Tannins comprise polymeric or oligomeric polyphenolic compounds and are commonly classified into hydrolyzable and condensed tannins. Other groups reported in the reviewed species include phenylpropanoids, diarylheptanoids, caffeoylquinic acid derivatives, phenylethanoid glycosides, and gingerol-related phenolics. The representative compounds listed in Table 2 illustrate this structural diversity across the reviewed medicinal plants [12].

Table 2. Phenolic classes and analytical methods reported for selected medicinal plants used in Sulawesi

No.	Scientific Name	Plant Part Studied	Phenolic Classes / Categories Reported	Representative Phenolic Compounds Reported	Analytical Methods Used	Ref.
1	*Psidium guajava* L.	Leaves	Phenolic acids; Flavonoids	Gallic acid; Ellagic acid; Catechin; Quercetin; Guajaverin; Reynoutrin	HPLC-DAD-QTOF-MS	[13]
2	*Curcuma longa* L.	Rhizome; Tuberous root	Curcuminoids	Curcumin; Demethoxycurcumin; Bisdemethoxycurcumin	HPLC-DAD; UHPLC-ESI-MS/MS	[14]
3	*Orthosiphon aristatus* (Blume) Miq.	Leaves; Aerial parts	Flavones; Flavonol glycosides; Caffeic acid derivatives; Phenolic acids	Rosmarinic acid; 2,3-Dicaffeoyltartaric acid; Sinensetin; Eupatorin	HPLC; UPLC-TOF-MS; NMR; HRESIMS	[15], [16], [17]
4	*Phyllanthus niruri* L.	Whole plant	Tannins; Flavonoids; Polyphenols	Gallic acid; Corilagin; Ellagic acid; Quercetin; Rutin; Catechin; Epicatechin	HPLC	[18]
5	*Tinospora crispa* (L.) Hook. f. & Thomson	Not specified	Flavonoids; Phenylpropanoids	Apigenin; Naringenin; Luteolin; trans-Ferulic acid; Vanillin	LC-MS/MS	[19]
6	*Zingiber officinale* Roscoe	Rhizome	Phenolic compounds; Gingerol-related phenolics	6-Gingerol; 8-Gingerol; 10-Gingerol; 1-Dehydro-6-gingerdione; Diacetoxy-8-gingerdiol	UPLC-DAD-QTOF-MS	[20]
7	*Kaempferia galanga* L.	Rhizome	Phenolic compounds; Flavonoids; Diarylheptanoids	Vanillic acid; Ferulic acid; trans-p-Hydroxycinnamic acid; Kaempferol; Luteolin	IR; 1D/2D NMR; HR-ESI-MS; ECD	[21], [22]
8	*Centella asiatica* (L.) Urb.	Aerial parts	Caffeoylquinic acids; Dicaffeoylquinic acids; Flavonoids	Chlorogenic acid (3-CQA); 1,3-Dicaffeoylquinic acid; 1,5-Dicaffeoylquinic acid; Quercetin; Kaempferol	LC-MRM-MS; UPLC-HRMS; NMR	[23], [24]
9	*Andrographis paniculata* (Burm. f.) Nees	Leaves; Stems	Phenolic acids; Flavonoids	7-O-Methyldihydrowogonin; Dihydroskullcapflavone I; 7-O-Methylwogonin; Caffeoylquinic Acid; Feruloylquinic acid	HPLC-ESI-MS/MS	[25], [26]
10	*Peperomia pellucida* (L.) Kunth	Leaves; Stems; Roots	Flavonoids; C-glycosyl flavonoids	Luteolin-6-C-glucoside-8-C-arabinoside; Isoschaftoside	UHPLC-MS/MS	[27], [28]

No.	Scientific Name	Plant Part Studied	Phenolic Classes / Categories Reported	Representative Phenolic Compounds Reported	Analytical Methods Used	Ref.
11	*Moringa oleifera* Lam.	Leaves	Phenolic acids; Flavonoids	1-caffeoylquinic acid; 3-caffeoylquinic acid; 4-caffeoylquinic acid; Kaempferol; Quercetin	HPLC–ESI–QTOF–MS	[29], [30]
12	*Melastoma malabathricum* L.	Aerial parts	Flavonoids; Tannins	Quercitrin; Quercetin; Kaempferol; Rutin; Ellagic acid	UHPLC-Q-Orbitrap-MS/MS	[31], [32]
13	*Gynura procumbens* (Lour.) Merr.	Leaves; Stems	Phenolic acids; Flavonoids	Chlorogenic acid; p-Coumaric acid; Caffeic acid; Astragalin; Kaempferol	UHPLC-Q-Orbitrap-HRMS	[33], [34]
14	*Elephantopus scaber* L.	Aerial parts	Phenolic acids	Gallic acid; Protocatechuic acid; Chlorogenic acid; Ferulic acid	RP-HPLC	[35], [36]
15	*Senna alata* (L.) Roxb.	Leaves	Phenolic compounds; Flavonoids	Phloretin; 7,4′-Dihydroxyflavone; Isorhamnetin; Apigenin; Naringenin	HPLC-ESI-QTOF-MS	[37], [38]
16	*Lawsonia inermis* L.	Leaves	Phenolic compounds; Flavonoids; Phenolic acids	Gallic acid; Eugenol; Luteolin	RP-HPLC-DAD-ESI-MS	[39], [40]
17	*Premna serratifolia* L.	Leaves	Phenylethanoid glycosides; Flavonoids	Isoacteoside; Forsythoside A; Forsythoside B; Lavandulifolioside; Scroside E; Campneoside I; Diosmin	LC-QTOF-MS/MS	[41]
18	*Syzygium aromaticum* (L.) Merr. & L. M. Perry	Flower buds	Phenolic compounds; Phenolic acids; Flavonoids	Gallic acid; Catechin; Chlorogenic acid; Caffeic acid; Ellagic acid; Rutin; Quercitrin; Quercetin; Kaempferol; Luteolin	HPLC-DAD	[42], [43]
19	*Ficus septica* Burm. f.	Leaves	Phenolic compounds; Phenolic derivatives; Flavonoids	Pungenin; 5-Acetyl-2-hydroxyphenyl-β-D-glucopyranoside; Genistin; Kaempferitrin	GC–MS; literature reports	[44], [45]
20	*Carica papaya* L.	Leaves	Phenolic compounds; Flavonoids	Myricetin; Caffeic acid; trans-Ferulic acid; Kaempferol; Quercetin; Rutin; p-Coumaric acid; Vanillic acid; Isochlorogenic acid	UPLC-QTOF/MS; HPTLC	[46], [47]

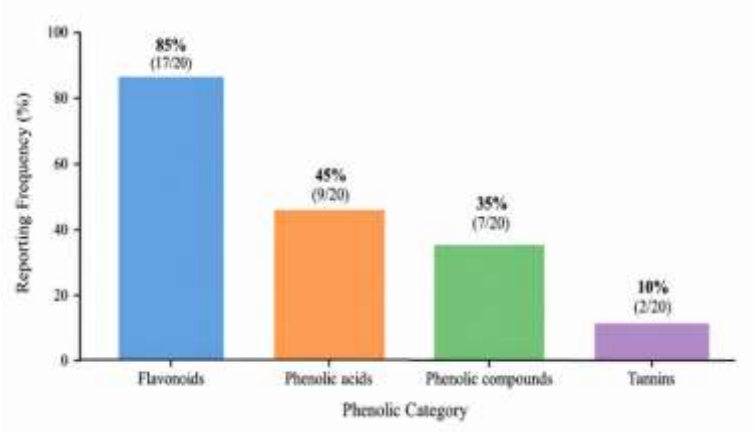


Figure 2. Reporting frequency of phenolic categories

In terms of reporting frequency, flavonoids were the most frequently reported major phenolic category, occurring in 17 of the 20 species (85%), followed by phenolic acids in 9 species (45%), phenolic compounds in 7 species (35%), and tannins in 2 species (10%) (Figure 2). For the quantitative summary presented in Figure

2, reported phenolic descriptors were grouped under their corresponding broader phenolic categories using a hierarchical chemical classification. Thus, flavones, flavonol glycosides, and C-glycosyl flavonoids were counted under the broader flavonoid category, while caffeoylquinic acids and dicaffeoylquinic acids were counted under phenolic acids. Each major category was counted once per species, and because individual species could be associated with multiple categories, the frequencies are not mutually exclusive and represent reporting frequency rather than relative abundance or concentration.

Note: Frequencies were calculated by grouping reported phenolic descriptors under broader phenolic categories using a hierarchical chemical classification. Flavones, flavonol glycosides, and C-glycosyl flavonoids were counted under the flavonoid category, while caffeoylquinic acids and dicaffeoylquinic acids were counted under phenolic acids. Other specific phenolic groups were retained as separate descriptors unless the broader category was explicitly reported in Table 2. Each major category was counted once per species. Because species could be associated with multiple categories, frequencies are not mutually exclusive and represent reporting frequency rather than relative abundance or concentration.

At the more specific descriptor level, several subclasses or compound groups were reported in only one species, including curcuminoids, flavones, flavonol glycosides, caffeic acid derivatives, phenylpropanoids, diarylheptanoids, caffeoylquinic acids, dicaffeoylquinic acids, C-glycosyl flavonoids, phenylethanoid glycosides, gingerol-related phenolics, and phenolic derivatives. Although some descriptors were grouped under broader parent categories for the quantitative analysis, their separate reporting in Table 2 highlights the structural specificity of the phytochemical evidence available for individual species.

Based on the number and variety of phenolic categories or descriptors reported in Table 2, *Orthosiphon aristatus* showed one of the broadest reported profiles, with four distinct descriptors, including flavones, flavonol glycosides, caffeic acid derivatives, and phenolic acids. *Phyllanthus niruri*, *Kaempferia galanga*, and *Centella asiatica* each showed three reported phenolic descriptors or categories, whereas several other species were characterized by one or two major descriptors. This comparison reflects the breadth and specificity of the reported phytochemical characterization rather than the absolute chemical richness or abundance of phenolic compounds in the plants.

The analytical methods also varied among the reviewed plants and provided different types and levels of phytochemical information. HPLC and related chromatographic techniques are useful for separating, detecting, and, when validated against standards, quantifying phenolic constituents. LC-MS and high-resolution MS provide chromatographic separation combined with accurate mass and fragmentation information, making them particularly useful for profiling and tentative annotation of phenolic metabolites in complex extracts. NMR provides complementary structural information and is especially valuable for elucidating molecular structures when sufficient amounts of purified compounds are available. GC-MS can provide useful profiles of volatile, semi-volatile, or derivatized constituents, although its applicability to polar and thermally labile phenolics is more limited without appropriate derivatization. For example, *Centella asiatica* was investigated using LC-MRM-MS, whereas *Kaempferia galanga* was characterized using NMR, HR-ESI-MS, and IR. *Carica papaya* leaves were characterized using UPLC-QTOF/MS together with HPTLC. These techniques should therefore be regarded as complementary rather than interchangeable approaches to phytochemical characterization[48].

However, the level of phytochemical characterization was not uniform among the 20 species. Some studies provided compound- or subclass-level information using chromatographic and spectrometric techniques, whereas others relied primarily on broader phytochemical descriptions or literature-based evidence. Therefore, the entries in Table 2 should be interpreted according to the analytical evidence available for each species rather than as evidence of equivalent chemical richness or abundance.

3.3. Anti-inflammatory Evidence of Selected Medicinal Plants

Among the 20 medicinal plants with available phytochemical evidence, nine species showed documented anti-inflammatory activity and were therefore selected for further evaluation (Table 3). The available evidence comprised in vitro, in vivo, in silico, and, for *Psidium guajava* and *Curcuma longa*, clinical evidence. The studies reported different levels of mechanistic information, ranging from demonstrated anti-inflammatory activity to specific modulation of inflammation-related signaling pathways.

Clinical evidence was identified for *Psidium guajava* and *Curcuma longa* based on original randomized controlled studies. Kakuo et al. conducted a randomized, double-blind, placebo-controlled, parallel pilot study in Japanese subjects with knee pain who had no previous history of knee treatment. Participants received 1 g of *Psidium guajava* leaf extract or placebo daily for 12 weeks. At week 12, the guava extract group showed lower knee pain and stiffness scores and lower visual analogue scale (VAS) scores for knee pain than the placebo group. For *Curcuma longa*, Wang et al. conducted a randomized, double-blind, placebo-controlled trial involving 70 participants with symptomatic knee osteoarthritis and ultrasound-defined effusion-synovitis. Participants received two 500-mg capsules of *C. longa* extract or matched placebo daily for 12 weeks. The study reported improved VAS knee pain and WOMAC knee pain with *C. longa* compared with placebo, whereas no significant between-group difference was observed for MRI-defined effusion-synovitis volume. These clinical studies provide direct human evidence for symptomatic outcomes, while the differences in study design, sample size, and duration should be considered when interpreting the available clinical evidence [49], [50], [51], [52].

Table 3. Anti-inflammatory evidence of selected medicinal plants used in Sulawesi

No.	Scientific Name	Experimental Evidence	Molecular Target / Mechanism	Principal Anti-inflammatory Evidence	Ref.
1	*Psidium guajava* L.	In vitro; In vivo; Clinical	Not explicitly reported	Anti-inflammatory activity demonstrated	[49], [50], [51]
2	*Curcuma longa* L.	In vitro; In vivo; Clinical	Inflammatory signaling pathways (curcumin-mediated)	Curcumin suppresses inflammatory responses	[52], [53]
3	*Zingiber officinale* Roscoe	In vitro; In vivo	Nrf2; Akt; NF-κB; pro-inflammatory cytokines	Suppresses inflammatory signaling pathways	[54]
4	*Peperomia pellucida* (L.) Kunth	In silico; In vitro; In vivo	NOS; NF-κB; PPARγ	Modulates inflammation-related molecular targets	[27]
5	*Moringa oleifera* Lam.	In vitro; In vivo	pro-inflammatory cytokines; TIMP-1; KIM-1	Suppresses pro-inflammatory mediators	[29]
6	*Gynura procumbens* (Lour.) Merr.	In vitro; In vivo	Not explicitly reported	Experimental anti-inflammatory activity reported	[33]
7	*Lawsonia inermis* L.	In vitro; In vivo	Not explicitly reported	Anti-inflammatory activity demonstrated	[55]
8	*Ficus septica* Burm. f.	Preclinical	Not explicitly reported	Anti-inflammatory activity reported in preclinical studies	[44]
9	*Carica papaya* L.	In vitro; In vivo	Not explicitly reported	Anti-inflammatory and anti-arthritic activity	[46]

The evidence summarized in Table 3 shows that the nine selected medicinal plants have been investigated using different experimental approaches and provide varying levels of evidence for anti-inflammatory activity. *Curcuma longa* was reported to act through inflammatory signaling pathways associated with curcumin[53], while *Zingiber officinale* involved Nrf2, Akt, NF-κB, and pro-inflammatory cytokines[54]. *Peperomia pellucida* was investigated through in silico, in vitro, and in vivo approaches involving NOS, NF-κB, and PPARγ[27]. *Moringa oleifera* was reported to suppress pro-inflammatory mediators[29], whereas the studies of *Psidium guajava*, *Gynura procumbens*, *Lawsonia inermis*, *Ficus septica*, and *Carica papaya* reported anti-inflammatory activity without explicitly specifying molecular targets in the reviewed sources[33], [44], [46], [50], [55].

The different levels of mechanistic information indicate that the available anti-inflammatory evidence is not uniform across the nine species[27], [29], [33], [44], [46], [50], [53], [54], [55]. Some studies provide information on specific molecular targets or signaling pathways, whereas others primarily demonstrate anti-inflammatory effects through experimental models. Therefore, the reported activity should be interpreted

according to the type and depth of evidence available for each species rather than assuming a common mechanism across all plants.

When considered together with Data Set B, these findings provide an initial link between the diversity of phenolic constituents and the reported anti-inflammatory potential of the selected medicinal plants[11]. However, the available evidence does not consistently establish that the phenolic constituents identified in Data Set B are directly responsible for the anti-inflammatory effects reported in Data Set C. Such a relationship requires compound-specific experimental validation and should therefore be considered an important direction for future research.

The nine species selected in Data Set C should therefore be regarded as medicinal plants with documented anti-inflammatory evidence within the literature reviewed, rather than as the only anti-inflammatory plants used in Sulawesi. The remaining species identified in Data Set A may also possess biological potential, but their anti-inflammatory activity was not explicitly established in the sources included in this review. This limitation highlights the need for further integrated phytochemical and pharmacological investigations of medicinal plants from Sulawesi.

To integrate the evidence across the three datasets, Table 4 summarizes the ethnobotanical occurrence, phenolic characterization, anti-inflammatory evidence, and remaining research gaps for the nine medicinal plants included in Data Set C. The table is intended to facilitate evidence-based comparison rather than to rank the plants, because the available studies differ in design, analytical depth, and level of mechanistic or clinical validation.

Table 4. Integrated evidence and research gaps

No.	Scientific Name	Ethnobotanical Occurrence	Phenolic Evidence	Anti-inflammatory Evidence	Evidence-based Research Gap
1	*Psidium guajava* L.	South, Central, West Sulawesi [4], [5], [7]	Phenolic acids; flavonoids; representative compounds including gallic acid, ellagic acid, catechin, quercetin[13]	In vitro, in vivo, clinical; clinical study reported effects on knee pain and stiffness [49], [50], [51]	Direct linkage between specific phenolic constituents and the reported anti-inflammatory/clinical effects remains insufficiently established
2	*Curcuma longa* L.	Central, West Sulawesi [4], [5], [6], [7], [8], [9]	Curcuminoids; curcumin, demethoxycurcumin, bisdemethoxycurcumin [14]	In vitro, in vivo, clinical; curcumin-associated inflammatory signaling reported [52], [53]	Direct linkage between individual curcuminoids, molecular mechanisms, and clinical outcomes remains insufficiently established
3	*Zingiber officinale* Roscoe	Central Sulawesi [4], [6], [7], [8], [9]	Gingerol-related phenolics; 6-, 8-, and 10-gingerol [20]	In vitro and in vivo; Nrf2, Akt, NF-κB, and pro-inflammatory cytokines [54]	No clinical evidence was identified in the reviewed literature; compound-specific mechanistic validation remains limited
4	*Peperomia pellucida* (L.) Kunth	Central and West Sulawesi [4], [5], [6], [7], [8], [9]	Flavonoids and C-glycosyl flavonoids; luteolin-6-C-glucoside-8-C-arabinoside, isoschaftoside [27], [28]	In silico, in vitro, in vivo; NOS, NF-κB, PPARγ [27]	No clinical evidence was identified; translation of preclinical and in silico findings to human evidence remains unresolved
5	*Moringa oleifera* Lam.	Southeast Sulawesi [4], [9]	Phenolic acids and flavonoids; caffeoylquinic acids,	In vitro and in vivo; pro-inflammatory mediators [29]	No clinical evidence was identified; direct contribution of specific

No.	Scientific Name	Ethnobotanical Occurrence	Phenolic Evidence	Anti-inflammatory Evidence	Evidence-based Research Gap
			kaempferol, quercetin [29], [30]		phenolic constituents to the reported activity remains insufficiently established
6	*Gynura procumbens* (Lour.) Merr.	Southeast and West Sulawesi [4], [5], [6], [7]	Phenolic acids and flavonoids; chlorogenic acid, p-coumaric acid, caffeic acid, astragalin, kaempferol [33], [34]	In vitro and in vivo; molecular targets not explicitly reported [33]	Molecular targets were not explicitly reported; no clinical evidence was identified
7	*Lawsonia inermis* L.	Central Sulawesi [4], [6], [7], [8], [9]	Phenolic compounds, flavonoids, phenolic acids; gallic acid, eugenol, luteolin [39], [40]	In vitro and in vivo; molecular targets not explicitly reported [55]	Molecular targets were not explicitly reported; no clinical evidence was identified
8	*Ficus septica* Burm. f.	Southeast and West Sulawesi [4], [5], [6], [7]	Phenolic compounds, phenolic derivatives, flavonoids; pungenin, genistin, kaempferitrin [44], [45]	Preclinical; molecular targets not explicitly reported [44]	Mechanistic targets were not explicitly reported, and no clinical evidence was identified
9	*Carica papaya* L.	Central and West Sulawesi [4], [5], [6], [7], [8], [9]	Phenolic compounds and flavonoids; myricetin, caffeic acid, ferulic acid, kaempferol, quercetin [46], [47]	In vitro and in vivo; anti-inflammatory/anti-arthritic activity [46]	Molecular targets were not explicitly reported; no clinical evidence was identified

4. Conclusion

This review identified 132 medicinal plant species traditionally used across six provinces of Sulawesi, demonstrating the considerable diversity of medicinal plants documented in the region. Among these species, 20 plants had available phytochemical evidence describing diverse phenolic classes and different analytical approaches for their characterization. Further evaluation identified nine species with documented anti-inflammatory activity supported by different levels of in vitro, in vivo, and in silico evidence, while clinical evidence was identified for *Psidium guajava* and *Curcuma longa.* However, the strength of the available evidence varied among species, and a direct relationship between the reported phenolic constituents and anti-inflammatory effects could not consistently be established. These findings highlight the potential of medicinal plants from Sulawesi as sources of phenolic bioactive compounds while also indicating the need for further integrated phytochemical and pharmacological studies to clarify compound-specific mechanisms and strengthen the scientific validation of their traditional medicinal uses.

5. Conflict of Interest

The authors declare no conflict of interest.

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