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Review

Essential Oils from Neotropical Piper Species and Their Biological Activities

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Abstract: The Piper genus is the most representative of the Piperaceae reaching around 2000 species distributed in the pantropical region. In the Neotropics, its species are represented by herbs, shrubs, and lianas, which are used in traditional medicine to prepare teas and infusions. Its essential oils (EOs) present high yield and are chemically constituted by complex mixtures or the predominance of main volatile constituents. The chemical composition of Piper EOs displays interspecific or intraspecific variations, according to the site of collection or seasonality. The main volatile compounds identified in Piper EOs are monoterpenes hydrocarbons, oxygenated monoterpenoids, sesquiterpene hydrocarbons, oxygenated sesquiterpenoids and large amounts of phenylpropanoids. In this review, we are reporting the biological potential of Piper EOs from the Neotropical region. There are many reports of Piper EOs as antimicrobial agents (fungi and bacteria), antiprotozoal (Leishmania spp., Plasmodium spp., and Trypanosoma spp.), acetylcholinesterase inhibitor, antinociceptive, anti-inflammatory and cytotoxic activity against different tumor cells lines (breast, leukemia, melanoma, gastric, among others). These studies can contribute to the rational and economic exploration of Piper species, once they have been identified as potent natural and alternative sources to treat human diseases.

Keywords: piperaceae; neotropics; antimicrobial; cytotoxic; anticholinesterase; anti-inflammatory; analgesic

1. Introduction

The genus Piper L. has approximately 2000 species distributed in the pantropical region, in the Neotropics occurring from northern Mexico to Chile and Argentina. The Andean slopes, Central American lowlands and Central Amazonia have been considered as centers of high species richness for the genus [1,2]. Piper belongs to Piperaceae, classified in the order Piperales, Magnoliids clade included in angiosperm basal group [3]. Phylogenetic studies have confirmed the monophyly of the group with eight subgenera recognized in the Neotropics: Enckea, Macrostachys, Ottonia, Peltobryon, Piper, Pothomorphe, Radula and Schilleria [4].

Plants of the genus Piper are easy recognized in the field by their nodose shoots, inflorescences spikes, and the typical “spicy” or aromatic smell [4]. They can be herbs, shrubs and less often lianas of annual or perennial habits; aromatics; glabrous or with varied indumentum, frequently gland-dotted, with nodose stems. Leaves are mostly alternate, sometimes opposite, simple, sessile or petiolate, with variable size, shape and venation. Inflorescences are terminal, leaf opposed or axillary, commonly
spike solitary, umbellate or paniculate, erect, pendent or recurved, variable in size. Flowers are very small and numerous, generally monoic, perianthless, variable in shape; stamens usually 2–6, arising near the base of the ovary with filaments free and generally short, anthers with 1, 2, or 4 thecae, laterally or apically dehiscent, deciduous after pollination; gynoecium with superior ovary, with 1, 3, or 5 fused carpels, 1-locular. Fruit is a small berry or drupe, variously shaped, with a thin pericarp and sometimes hardened endocarp; seed small, solitary [5].

Since prehistoric times Piper spp. have been used by man, manly as spices, in mystical and cultural activities and in folk medicine to treat many diseases. For example, a decoction of the leaves of P. cavalcantei is considered by native Amazon people as excellent antipyretic and analgesic [6]; P. marginatum, which is used by indigenous communities in Central America, the Antilles, and South America for gastrointestinal problems [7]; and P. umbellatum that is traditionally used as an anti-inflammatory in Brazil, to treat wounds in Cuba, and to treat fever in Peru [8]. In the literature, there have been many studies about Asian Piper species, but a large proportion of the information has been generated from Latin American species, pointing to an enormous diversity of chemical compounds associated with its diversity of biological activities [9,10]. In tropical countries, many species of Piper are used by traditional societies by their anti-inflammatory and analgesic properties, and have large potential for the pharmaceutical industry [11].

Piper species produce a number of metabolic classes with diverse biological activities [10]. The essential oils extracted from different organs of many specimens is constituted mainly of monoterpenic hydrocarbons (e.g., α-pinene, myrcene, limonene, α-terpinene, p-cymene), oxygenated monoterpenoids (e.g., 1,8-cineole, linalool, terpinen-4-ol, borneol, camphor), sesquiterpene hydrocarbons (e.g., β-caryophyllene, α-humulene, germacrene D, bicyclogermacrene, α-cubebene), oxygenated sesquiterpenoids (e.g., spathulenol, (E)-nerolidol, caryophyllene oxide, α-cadinol, epi-α-bisabolol) and phenylpropanoids (e.g., safrole, dillapiole, myristicin, elemicin, (Z)-asarone, eugenol) (see Appendixes A and B) [12,13]. The literature reports that some tropical species of Piper have presented high yields of essential oils [14]. The yield of essential oil and its major volatile components in Piper spp. may vary according to geographical region and environmental factors, being conditioned mainly to its different chemotypes [14–16]. P. xylosteoides leaves presented a yield of 1.8% with the main compound being myrcene (31%), which is largely used in the food and cosmetic industry [17]. P. divaricatum had yielded around 46.0%, eugenol, a compound that has been used as an anesthetic for the sedation of fish, in addition to being widely used as a local anesthetic during endodontic and restorative treatments by dentists [18,19]. Essential oils of high yield, along with the presence of volatile compounds of economic value, are valued by the international market due to their wide importance to the pharmacological, cosmetics, and cleaning products industries, among other applications [14]. Piper has been a model genus for ecological and evolutionary studies, and Piper species are considered important due their association with frugivorous bats [4]. A suite of insect herbivores feeds on the leaves of Piper; the ripening fruits are attacked by a variety of seed predators, and ripe fruits provide food for frugivorous bats and birds, and other animals surely use Piper fruits as food at least occasionally [11].

Taxonomic difficulties in the genus Piper are related to the great variability and minute nature of their flowers [20]. Due to the pronounced pharmacological value and worldwide demand of Piper species, it is imperative to make efforts to the secure botanical identification, to conserve the germplasm, and to allow genetic improvement [21]. The use of biochemical and genetic markers as well as chemical studies of specimens have been shown to be effective methods [22–24]. In this review, we report the biological activities and the chemical compositions of Piper species native to the Neotropics.

2. Volatile Profiles

The essential oil compositions (major components) of Neotropical Piper species are summarized in Appendix A. For Piper species where several different essential oils were collected, there seems to be wide variation in the compositions. Thus, for example, P. aduncum leaf oils can be rich in monoterpenoids such as 1,8-cineole [25], sesquiterpenoids such as (E)-nerolidol [26], or dominated
by phenylpropanoids like dillapiole [27–30] or asaricin [31]. At least nine different chemotypes of *P. aduncum* have been characterized [32]. Likewise, *P. amalago* has shown wide variation in essential oil composition with monoterpenoid-rich [31,33] and sesquiterpenoid-rich [34,35] chemotypes. Dihydroagarofurans have dominated several leaf oils of *P. ceruum* [31,36,37] while other samples have shown monoterpenes and sesquiterpene hydrocarbons as major components [35,38,39]. *Piper divaricatum* has shown a eugenol/methyleugenol chemotype [40–43] as well as a safrole chemotype [44]. Phenylpropanoids have characterized the leaf essential oils of many samples of *P. marginatum* from Brazil [41,45], but even these show wide variation in the phenylpropanoid concentrations. Chemical structures for the major *Piper* essential oil components are shown in Appendix B.

Geographical location and habitat likely affects the chemical compositions. For example, the leaf essential oil compositions of *P. hispidum* from Cuba [46] was rich in eudesmols, while a sample from Panama was dominated by dillapiole [47], and a sample from Colombia had (E)-nerolidol as the major component [48]. *Piper umbellatum* essential oils from Monteverde, Costa Rica [49], and from São Paulo, Brazil [31], were rich in sesquiterpene hydrocarbons, while the essential oil from the Escambray Mountains of Cuba was rich in camphor and safrole [50]. The wide variations in essential oil compositions certainly impact the biological activities of the *Piper* oils (see Appendix A) and likely affects the traditional medicinal uses of the plants in their native habitats.

3. **Biological Activities**

3.1. **Antibacterial and Antifungal Activity**

The need to combat microbial resistance to present day antibiotics has boosted efforts for bioprospecting to identify new antibacterial and antifungal agents [51]. The potential of *Piper* essential oils against pathogenic Gram-positive bacteria, such as *Staphylococcus aureus*, *Bacillus cereus*, *Bacillus subtilis* and *Streptococcus pyogenes*, as well as Gram-negative microorganisms, which include *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, has been reported in several published investigations. Essential oils (EOs) from leaves of *P. abutilodes*, *P. aduncum*, *P. marginatum*, and *P. molicomum* were tested against *Escherichia coli* (EPEC 0031-2) and had minimal inhibitory concentrations (MICs) ranging from 500 µg/mL to 1000 µg/mL [52]. *P. regnellii* oils from leaves had MIC of 300 µg/mL against the serotype EPEC 0031-2. Antimicrobial assays were performed by microdilution method, but EO compositions were not reported [52]. EOs from leaves of *P. aduncum* var. *ossanum* (Bauta, Artemisa Province, Cuba) were mainly composed of piperitone (20.1%), viridiflorol (13.0%) and camphor (13.9%) and had high activity against *Staphylococcus aureus* with an IC$_{50}$ value of 39.5 µg/mL [53].

The antimicrobial activity was evaluated against *Bacillus cereus* and *S. aureus* using broth dilution assay for different *Piper* species collected in Monteverde (Costa Rica) [34]. The oils from leaves of *Piper* sp. aff. *aereum*, *P. bredemeyeri*, *P. oblanceolatum* displayed a MIC value of 78 µg/mL against *Bacillus cereus*, while *P. fimbriulatum* was more active (MIC, 39 µg/mL). In addition, *Piper* sp. aff. *aereum* showed activity against *S. aureus* (MIC, 78 µg/mL). The main compounds in these oils were mostly sesquiterpenoids and monoterpenoids: *Piper* sp. aff. *aereum* oil was composed of guaiol (41.2%), α-cadinol (9.2%) and δ-cadinene (7.3%). *P. bredemeyeri* showed β-elemene (34.0%), β-caryophyllene (24.2%) and germacrene D (21.7%) as major compounds. *P. fimbriulatum* showed germacrene D (32.9%), α-pinene (10.2%) and δ-elemene (9.4%), while *P. oblanceolatum* was rich in linalool (11.3%), δ-amorphene (9.0%) and germacrene D (8.9%) [34].

*Piper caldense* oils from different tissues displayed as major components α-cadinol (19.0%), α-murolol (9.0%), and thujopsan-2β-ol (7.4%) (leaves); terpinen-4-ol (18.5%), α-terpineol (15.3%), and α-cadinol-2β-ol (9.8%) (stems); and pentadecane (35.7%), valencene (10.5%), and selina-3,7(11)-diene (5.4%) (roots). The samples were tested against *E. coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *S. aureus* and *B. subtilis* using agar diffusion assay and showed moderate to weak bacterial activity with MIC value of 325 or 750 µg/mL in comparison to gentamicin (5.0 µg/mL) [54]. *P. ceruum*...
and P. regnellii EOs from leaves inhibited growth of S. aureus and Candida albicans when evaluated by agar diffusion assay. The main compounds in P. cernuum oil were bicyclogermacrene (21.9%), β-caryophyllene (20.7%) and α-pinene, while P. regnellii essential oil was dominated by myrcene (52.6%), linalool (15.9%) and β-caryophyllene (8.5%) [38].

The chemical composition by CG-MS and antimicrobial activity using agar dilution technique of P. cernuum oils were evaluated seasonally [37]. The main compounds identified were trans-dihydroagarofuran (30 to 36.7%), 4-epi-cis-dihydroagarofuran (11.2 to 13.4%), and γ-eudesmol (7.64 to 11.6%). The EOs showed significant activity against S. aureus (MIC 780 µg/mL, and for spring MIC, 1560 µg/mL), B. subtilis (MIC 780 µg/mL) and Streptococcus pyogenes (MIC 48–390 µg/mL) [37]. P. dossyryrifolium EO from leaves, composed of cis-eudesma-6,11-diene (21.1%), β-caryophyllene (16.8%), and γ-murolene (10.6%), was tested using agar diffusion assay and it showed significant potential against clinical fungal strains of C. albicans, C. parapsilosis, C. tropicalis in comparison to nystatin [55]. P. malacophyllum oil, composed mainly of camphor (32.8%), camphene (20.8%), and (E)-nerolidol (9.1%), displayed a weak activity against S. aureus, P. aeruginosa, Acinetobacter baumannii (MIC 3700 µg/mL), B. cereus, and E. coli (MIC 1850 µg/mL) using the broth microdilution method [56]. Furthermore, P. ilheusense oil from leaves was made up of β-caryophyllene (11.8%), patchouli alcohol (11.1%), and gleenol (7.5%), and was active against the fungi C. albicans, C. parapsilosis and C. krusei, and it partially combated B. subtilis and S. aureus [57]. P. tuberculatum EO from seeds was mostly composed of β-elemene, β-caryophyllene and β-farnesene, among others; microdilution assays indicated that this oil inhibited growth of S. aureus and B. subtilis. However, neither the EO composition nor MIC values were reported [58].

Several Piper oils have been reported to be effective to combat fungal species of Cryptococcus. P. aduncum oil from leaves was composed of linalool (31.8%), bicyclogermacrene (11.3%), and (E)-nerolidol (10.3%), and showed activity against Cryptococcus neoformans (MIC 62.5 µg/mL) [35]. Similarity, P. gaudichaudianum oil, rich in α-humulene (23.4%), β-caryophyllene (15.6%), and viridiflorene (8.1%), showed significant antifungal activity against C. krusei (MIC 31.25 µg/mL). EO from leaves of P. solmsianum was mostly composed of (E)-isoelemecin (53.5%), spathulenol (5.2%), and epi-α-muurolool (4.6%), and had significant activity against C. neoformans (MIC 62.5 µg/mL). These analyses were performed by means of broth dilution assays [35].

The activity of Piper EOs has been evaluated by direct bioautography on TLC plates against Cladosporium cladosporioides and C. sphaerospermum [59–62]. Cladosporium spp. are strong airborne contaminants that cause allergies and other serious diseases of the respiratory tract [63,64]. The oils from fruits of P. aduncum and P. tuberculatum had a higher activity in comparison to miconazole and nystatin against Cladosporium cladosporioides and C. sphaerospermum, respectively. Both oils displayed a detection limit (DL) of 10 µg [59]. Oils of P. aleurenum, P. anonfolium, P. hispidum and P. divaricatum, collected from the Brazilian Amazon, showed a higher activity with DL values between 0.1 and 5.0 µg [61]. These oils were mainly composed of terpenoids as β-elemene (16.3%), bicyclogermacrene (9.2%), and δ-elemene (8.2%) (P. aleurenum); selin-11-en-4α-ol (20.0%), β-selinene (12.7%), and α-selinene (11.9%) (P. anonfolium); and δ-3-carene (9.1%), β-caryophyllene (10.5%), and α-humulene (9.5%) (P. hispidum). P. divaricatum oil, on the other hand, was dominated by phenylpropanoids methyleugenol (63.8%) and eugenol (23.6%) [40,61]. Essential oils of P. cernuum (fruits), P. solmsianum (leaves), and P. crassinervium (leaves) displayed moderated and weak activity against these pathogens. Germacrene D (14.0%) and spathulenol (9.8%) were the main components of P. cernuum and crassinervium oils, while P. solmsianum was dominated by (E)-isoelemecin (53.9%) [60].

Piper aduncum oil, chemotype dillapiiole (85.9%), and isolated dillapiiole exhibited antifungal activity against pathogenic skin microorganisms [30]. The samples were assayed by the microdilution method and displayed MIC values of 500 µg/mL for the strains of Trichophyton mentagrophytes (ATCC 9533 and clinical isolate), T. rubrum, and Epidermophyt on floccosum. For clinical isolates of Microsporum canis, M. gypseum, and Aspergillus fumigatus (ATCC 40152 and clinical isolate), the MIC values were 250, 250 and 3.9 µg/mL, respectively. Minimum fungicidal concentration (MFC) values displayed a range of 15.6 to 1500 µg/mL for all samples. The EO and its dillapiiole-rich fraction
demonstrated significant antifungal activity against dermatophytes, filamentous fungi, and potent antifungal activity against non-dermatophyte filamentous fungi [30]. In addition, *P. aduncum* oils from the aerial parts of chemotype dillapiole (45.9%), (E)-β-ocimene (19.0%), and piperitone (8.4%), also inhibited *Trichophyton* species at 500 µg/mL [65]. *P. cernuum* oil, rich in trans-dihydroagarofuran (30.0–36.7%), 4-epi-cis-dihydroagarofuran (11.2–13.4%), and γ- eudesmol (8.3–13.3%), was active against *Microsporum gypseum* (MIC, 48–390 µg/mL), *T. mentagrophytes* (MIC, 48–195 µg/mL), *T. rubrum* (MIC, 48–195 µg/mL), *E. flocosum* (MIC 48–195 µg/mL) and opportunist yeast *Candida albicans* (MIC 48 µg/mL) [37]. *P. malacophyllum* oil was composed of camphor (32.8%), camphene (20.8%), and (E)-nerolidol (9.1%), and it showed moderate activity compared to ketoconazole against *T. mentagrophytes* and *C. neoformans*, the causal agent of meningocencephalitis in immunocompromized patients [56].

### 3.2. Antiprotozoal Activity

Parasitic protozoal diseases are the major economic and public health problems in the world causing high rates of human morbidity and mortality in developing countries [32]. The prevalence of these diseases is higher in the tropics, where a significant number of deaths are attributed to leishmaniasis, malaria, and trypanosomiasis [66]. *Piper* species have been reported as good sources of antiparasitic compounds [67].

Studies carried out with the essential oils of *Piper* species showed that *P. aduncum* leaf EO, containing (E)-nerolidol (25.2%) and linalool (13.42%), had an inhibitory effect after 24 h on the growth of *Leishmania braziliensis* promastigotes (IC50, 77.9 µg/mL) and (E)-nerolidol presented a similar inhibitory effect (IC50, 74.3 µg/mL) [67,68]. *P. aduncum* leaf EO from two localities in Cuba (Bauta and Ceiba) were active against *L. amazonensis* (IC50, 19.3 and >64 µg/mL, respectively), in both EOs, the major components were piperitone, viridiflorol, and camphor [53]. *P. angustifolium* leaf EO, dominated by spathulenol (23.8%) and carophyllene oxide (13.1%), was effective against intra-cellular amastigotes of *L. infantum*, the etiological agent of visceral leishmaniasis (IC50, 1.4 µg/mL) [69]. *P. aduncum* and *P. diospyrifolium* leaf EOs displayed high activity against of axenic amastigote forms of *L. amazonensis* (IC50, 76.1 µg/mL and 36.2 µg/mL, respectively) and were more selective for the parasite than for the mammalian macrophages [70]. The main constituents of *P. aduncum* EO were bicyclogermacrene (20.9%), (E)-β-ocimene (13.9%), and (Z)-β-ocimene (7.0%), while *P. diospyrifolium* oil was rich in selin-11-en-4α-ol (17.7%), β-caryophyllene (7.4%), and γ-gurjunene (6.9%).

The EO from fresh leaves and inflorescences of *P. clausenianum* showed high activity against a strain of *L. amazonensis*, the leaf EO, rich in (E)-nerolidol (81.4%), had greater inhibition on the growth of *L. amazonensis* than the inflorescences EO, which was rich in linalool (50.2%) (IC50 30.4 µg/mL and 1328 µg/mL, respectively) [71]. *P. demeraranum* and *P. duckei* oils inhibited the growth of promastigote forms of two species of *Leishmania* (IC50, 15.2 and 22.7 µg/mL, respectively) with greater activity against *L. guyanensis* than *L. amazonensis* [72]. The main constituents of *P. demeraranum* oil were β-elemene (33.1%), limonene (19.3%), and bicyclogermacrene (8.8%), and *P. duckei* β-caryophyllene (27.1%), γ-eudesmol (17.9%), and germacrene D (14.7%).

The *P. aduncum* EOs, chemotype piperitone (19.0–23.7%), camphor (9.4–17.1%) and viridiflorol (13.0–14.5%), obtained from the aerial parts, showed an inhibitory effect on the growth of Plasmodium falciparum with IC50 value ranging from 1.3 to 2.8 µg/mL [32,53]. The essential oils from *P. clausenianum* inflorescences and *P. lucacatum* leaves, and the pure isolated (E)-nerolidol obtained from inflorescences of *P. clausenianum*, showed a 70% decrease in the growth of chloroquine-resistant (W2) *P. falciparum*, when tested at a concentration of 25 mg/mL [73]. The *P. clausenianum* EO was dominated by linalool (56.5%) followed by (E)-nerolidol (23.7%) and α-humulene (2.4%), and *P. lucacatum* was rich in α-pinene (30.0%), α-zingiberene (30.4%) and β-sesquiphellandrene (11.1%).

The anti-trypanosomal activities have been reported for different chemotypes of *P. aduncum* EOs. The effect of *P. aduncum* EO rich in (E)-nerolidol (25.2%), linalool (13.4%) and spathulenol (15.3%), was analyzed against different developmental forms of Trypanosoma cruzi. The oil was active after 24 h against cell-derived (IC50, 2.8 µg/mL), metacyclic trypomastigotes (IC50 12.1 µg/mL), and...
intracellular amastigotes (IC\(_{50}\), 9.0 µg/mL) [68]. The chemotype piperitone (23.7%), camphor (17.1%), and viridiflorol (14.5%) also exhibited activity against \( T. cruzi \) (IC\(_{50}\) 2.0 µg/mL) [32]. In addition, \( P. aduncum \) leaf EOs from two localities in Cuba were active against \( T. brucei \) and \( T. cruzi \) with IC\(_{50}\) value of approximately 8.0 µg/mL [53]. The major components were piperitone (20.1–19.0%), viridiflorol (13–18.8%) and camphor (13.9–9.4%) in the specimens.

In addition to inhibition of the parasites themselves, inhibition of key protozoal protein targets by essential oils has been investigated [74]. \( P. bredemeyeri \) leaf essential oil inhibited cruzain, the cysteine protease from Trypanosoma cruzi, with IC\(_{50}\) of 0.96 µg/mL [34]. \( P. bredemeyeri \) EO was composed largely of the sesquiterpene hydrocarbons \( \beta \)-elemene (34.0%), \( \beta \)-caryophyllene (24.2%), germacrene D (21.7%), and germacrene A (13.2%). \( \beta \)-Caryophyllene and germacrene D have both shown cruzain inhibitory activity with IC\(_{50}\) values of 32.5 and 22.1 µg/mL, respectively, and a 1:1 binary mixture of these two compounds showed synergistic inhibitory activity (IC\(_{50}\) = 9.91 µg/mL) [75].

3.3. Anticholinesterase Potential

Acetylcholinesterase (AChE) is an enzyme involved in the termination of impulse transmission by quick hydrolysis of the neurotransmitter acetylcholine (ACh). The AChE potential of drugs is inhibition of this enzyme from breaking down ACh, increasing the level and duration of the neurotransmitter activity [76]. For this reason, studies aiming to discover compounds with anticholinesterase potential are relevant. However, there have been few investigations with this focus in Neotropical regions. The EOs from aerial parts of \( Piper \) species from the Brazilian Amazon displayed a high activity when evaluated by bioautographic method. All samples had a detection limit (DL) value of 0.01 ng, about one hundred times more effective than the standard physostigmine (DL = 1.0 ng). \( P. hispidum \) and \( P. anonifolium \) oils were mainly composed of sesquiterpenoids, such as selin-11-en-4\( \alpha \)-ol, \( \beta \)-selinene, \( \alpha \)-selinene, \( \beta \)-caryophyllene, and \( \alpha \)-humulene [61]. In contrast, EOs from the aerial parts of \( P. callosum \) and \( P. marginatum \) were mainly composed of phenylpropanoids, such as safrole and 3,4-methylenedioxypropiophenone (propiopiperone) [62]. Although there are limited data on AChE activity of \( Piper \) essential oils from the Neotropics, a significant amount of research has been performed on Old World \( Piper \) essential oils [77–81].

3.4. Anti-Inflammatory and Antinociceptive Effects

Although a considerable number of analgesic and anti-inflammatory drugs are available for the treatment of pain and inflammation, there is a continuous search for new compounds, due to the fact that some current drugs lead to adverse reactions and have low efficacy [82]. Plants used in folk medicine, including essential oils, have been shown to be promising new sources of anti-inflammatory and antinociceptive drugs [83–87].

\( P. glabratum \) leaf EO indicated \( \beta \)-pinene (13.0%), longiborneol (12.0%), and \( \alpha \)-pinene (9.7%) as the main compounds. Anti-inflammatory activity was detected by inhibition of leukocyte migration (100, 300, 700 mg/kg) and the protein extravasation into the pleural exudates (700 mg/kg) with no clinical signs of toxicity [88]. \( P. vicosanum \) EO minimized edema formation and inhibited leukocyte migration using the carrageenan-induced edema and pleurisy models at doses of 100 and 300 mg/kg [89]. The oil displayed a pronounced anti-inflammatory potential, with no acute toxicity or genotoxicity; its main compounds were \( \gamma \)-elemene (14.2%), \( \alpha \)-alaskene (13.4%) and limonene (9.1%).

The \( P. aleyreanum \) EO was tested for antinociceptive activity on two phases of pain model, early neurogenic and the second inflammatory, by formalin-induced pain through the administration of 20 mL of 2.5% formalin solution by intraplantar injection in mice [90]. The effect was significantly more pronounced on the second phase. The ID\(_{50}\) values for each phase were 281.2 and 70.5 mg/kg and the inhibitions observed were 75% and 99% at a dose of 1000 mg/kg, for the first and second phases, respectively. The main compounds of \( P. aleyreanum \) oil were caryophyllene oxide (11.5%), \( \beta \)-pinene (9.0%), and spathulenol (6.7%) [90]. \( P. mollicomum \) and \( P. rivinoides \) EOs were evaluated for their antinociceptive activity using the acetic acid-induced writhing in mice [91]. At a dose of 1 mg/kg,
the samples inhibited 50.2% and 20.9% of the writhing in mice, respectively. The main constituents of *P. mollicomum* were (E)-β-ocimene (14.0%), germacrene B (13.3%), and (Z)-β-ocimene (12.1%), and for *P. rivinoides* were α-pinene (32.9%), β-pinene (24.7%), and β-caryophyllene (7.6%). Oral administration of both oils did not induce any apparent acute toxicity [91].

3.5. Cytotoxic Activity

EOs with anticancer potential can act by two ways: chemoprevention and cancer suppression. Hence, EOs causing apoptosis in tumor cells are valuable resources in cancer suppression [92–94]. Essential oils from *Piper* species have been reported to possess antineoplastic properties against different cancer cell lines such as human colorectal carcinoma, breast tumor, melanoma, gastric tumor, leukemia, among others. The EO of *P. aequale*, rich in δ-elemene (19.0%), β-pinene (15.6%) and α-pinene (12.6%), showed significant cytotoxic activity against human colorectal carcinoma (HCT-116, IC$_{50}$ 8.69 µg/mL) and human gastric tumor (ACP 03, IC$_{50}$ 1.54 µg/mL) cell lines [95]. After 72 h of treatment, the oil has induced apoptosis in the gastric tumor cells in all tested concentrations (0.75–3.0 µg/mL). The EOs of *P. biasperatum, P. glabrescens, P. imperiale, P. oblanceolatum* and *Piper* sp. aff. *aereum* showed greater than 90% mortality against human breast adenocarcinoma cells (MCF-7) at a concentration of 100 µg/mL [34]. The main compounds identified in these samples were β-elemene (46.6%), limonene (56.6%), β-caryophyllene (25.5%) and linalool (11.3%), respectively.

*Piper aleyreanum* oil, rich in β-elemene (16.3%), bicyclogermacrene (9.2%) and δ-elemene (8.2%), showed strong cytotoxic activity (IC$_{50}$ 7.4 µg/mL) against human melanoma (SKMEL 19) [61]. The oil from leaves and branches of *P. cernuum* displayed a broad cytotoxicity spectrum (IC$_{50}$ < 30 µg/mL) including murine melanoma (B16F10-Nex2), human melanoma (A2058), human glioblastoma (U87-MG), human cervical tumor (HeLa), and human myloid leukemia (HL-60) cells [39,96]. These oils showed large amounts of β-elemene (30.0%), bicyclogermacrene (19.9%) and β-caryophyllene (16.3%) in leaves and camphene (46.4%), α-terpinene (11.6%) and carvacrol (11.6%) in the branches.

*Piper hispidum* oil, rich in α-pinene (15.3%) and β-pinene (14.8%), induced the death of cancer cell lines such as human cervical (HeLa), human lung (A-549), human breast (MCF-7) with average IC$_{50}$ values of 36 µg/mL [97]. The EO from *P. regnellii* leaves displayed an expressive cytotoxic activity against human cervical cells carcinoma (HeLa) with IC$_{50}$ value of 13 µg/mL [98]. In addition, the activity was determined to be due to its main compounds germacrene D (51.4%), β-caryophyllene (9.5%) and α-chamigrene (11.3%), which demonstrated IC$_{50}$ values of 11.0, 7.0 and 32.0 µg/mL, respectively.

4. Composition-Bioactivity Correlation

A multivariate statistical analysis was carried out in order to discern any relationship between chemical profiles and biological activities for *Piper* essential oils (described in Appendix A). The total percentage of compound classes (monoterpene hydrocarbons (MH), oxygenated monoterpenoids (OM), sesquiterpene hydrocarbons (SH), oxygenated sesquiterpenoids (OS) and phenylpropanoids (PP) to each oil was extracted from original citation (Table A1). These data were used as variables (see Appendix C). The values were normalized and submitted to Principal Component Analysis (PCA) using the Minitab software (free 390 version, Minitab Inc., State College, PA, USA).

The antimicrobial activity (fungicidal and bactericidal) displayed a correlation to all compound classes identified in *Piper* species. However, the cytotoxic activity is related to higher amounts of sesquiterpene hydrocarbons (0–94.9%), monoterpene hydrocarbons (0–83.7%). The antiprotozoal activity is related to *Piper* oils with low concentrations of monoterpene hydrocarbons (<29.9%) and high concentrations of oxygenated monoterpenoids (0–50.3%), sesquiterpene hydrocarbons (3.3–76.0%) and oxygenated sesquiterpenoids (0–86.2%). For this activity, only the *P. auritum* oil, which was rich in phenylpropanoids (88.5%), showed activity against *Leishmania* spp. *Piper* oils described as rich in phenylpropanoids and sesquiterpenes hydrocarbons displayed high insecticidal and acaricidal activities. In addition, the amounts of phenylpropanoids and sesquiterpenoids (hydrocarbons and oxygenated) are related to acetylcholinesterase inhibition. The anti-inflammatory effects were mostly
observed in *Piper* oils rich in sesquiterpene hydrocarbons (16.2–62.6%) while antinociceptive effects cover oils that showed monoterpenic hydrocarbons (16.6–65.0%) as main compounds. The essential oil composition and biological activity correlations are summarized in Figure A5 and Table 1.

### Table 1. Relationship between biological activity and compound classes presents in the *Piper* oils obtained by PCA analysis.

| Activity            | MH  | OM  | SH  | OS  | PP  |
|---------------------|-----|-----|-----|-----|-----|
| Antimicrobial       | 0–70.2 | 0–51.4 | 0–99.8 | 0–86.2 | 0–98.0 |
| Cytotoxic           | 0–83.7 | 0–23.2 | 0–94.9 | 0–29.5 | 0–6.7 |
| Antiprotozoal       | 0–29.9 | 0–50.3 | 33.3–76.0 | 0–86.2 | 0–88.5 |
| Insecticidal        | 0–44.3 | 0–12.6 | 0–66.0 | 0–45.4 | 0–98.8 |
| Enzymatic           | 6.9–18.5 | 1–4.2 | 4.9–52.2 | 2.1–17.5 | 0–80.8 |
| Anti-inflammatory   | 16.4–25.8 | 0–16.4 | 16.2–62.6 | 20.8–28.3 | 0–0.2 |
| Antinociceptive     | 16.6–65.9 | 0.8–16.4 | 16.2–33.2 | 4.8–28.3 | 0–0.6 |

### 5. Conclusions

The *Piper* genus has shown great biodiversity in the Neotropics, and essential oils from *Piper* species have likewise demonstrated abundant chemical diversity. The chemical diversity of *Piper* essential oils has led to a myriad of traditional medicinal uses as well as numerous biological activities. The promise of *Piper* essential oils to treat human diseases, infections, and suffering has already been realized, and the future exploration of this genus shows much promise. The expectation that *Piper*’s essential oils can be used to treat diseases, infections and human suffering is already a reality, and the future economical exploration of some species of this genus seems to us as very promising.

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**Conflicts of Interest:** The authors declare no conflict of interest.

**Abbreviations**

- ACh: Acetylcholine
- AChE: Acetylcholine esterase
- DL: Detection limit
- DPPH: 2,2-Diphenyl-1-picrylhydrazyl (radical)
- EO: Essential oil
- FIOCRUZ: Fundação Oswaldo Cruz (Oswaldo Cruz Foundation)
- GC-MS: Gas chromatography-mass spectrometry
- HD: Hydrodistillation
- IC\textsubscript{50}: Median inhibitory concentration
- ID\textsubscript{50}: Median inhibitory dose
- LC\textsubscript{50}: Median lethal concentration
- MFC: Minimum fungicidal concentration
- MH: Monoterpenic hydrocarbons
- MIC: Minimum inhibitory concentration
- MWHD: Microwave-assisted hydrodistillation
- OM: Oxygenated monoterpenoids
- OS: Oxygenated sesquiterpenoids
- PCA: Principal component analysis
- PP: Phenylpropanoids
- RI: Retention index
- SD: Steam distillation
- SH: Sesquiterpene hydrocarbons
- spp.: Species (plural)
- TLC: Thin-layer chromatography
### Table A1. Neotropical *Piper* essential oil compositions and biological activities.

| *Piper* Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|-----------------|-----------------|---------------|-------------------------|------------------|------|
| *P. abutiloides* Kunth | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD) | — | Antibacterial (Escherichia coli, MIC 700 µg/mL) | [52] |
| *P. acutifolium* Ruiz & Pav. | La Florida, Cajamarca, Peru | Leaf (HD) | (E)-β-Ocimene (8.1%), α-copaene (6.1%), β-caryophyllene (7.9%), allo-aromadendrene (6.0%), α-cadinene (6.7%), β-cadinene (6.8%), dillapiole (5.9%) | — | [99] |
| *P. aduncum* L. | Serra do Navio, Amapá state, Brazil | Aerial parts (HD) | Limonene (5.2%), γ-terpinene (7.1%), terpinen-4-ol (11.0%), pipertone (15.1%), dillapiole (31.5%) | — | [15] |
| *P. aduncum* L. | Melgaço, Pará state, Brazil | Aerial parts (HD) | γ-Terpine (6.5%), terpinen-4-ol (7.3%), pipertone (13.9%), dillapiole (50.8%) | — | [15] |
| *P. aduncum* L. | Belem, Pará state, Brazil | Aerial parts (HD) | Dillapiole (82.2%) | — | [15] |
| *P. aduncum* L. | Belem, Pará state, Brazil | Aerial parts (HD) | Dillapiole (86.9%) | — | [15] |
| *P. aduncum* L. | Manaus, Amazonas state, Brazil | Aerial parts (HD) | Dillapiole (91.1%) | — | [15] |
| *P. aduncum* L. | Manaus-Caracaraí, Amazonas, Brazil | Aerial parts (HD) | Dillapiole (97.3%) | — | [15] |
| *P. aduncum* L. | Cruzeiro do Sul, Acre state, Brazil | Aerial parts (HD) | Dillapiole (88.1%) | — | [15] |
| *P. aduncum* L. | Pinar del Río, Cuba | Leaf (HD) | Dillapiole (82.2%) | — | [27] |
| *P. aduncum* L. | Valle del Saja, Cochabamba, Bolivia | Leaf (HD) | α-Pinene (9.0%), β-pinene (7.1%), limonene (5.0%), 1,8-cineole (40.5%), asaricin (12.9%) | — | [100] |
| *P. aduncum* L. | Altos de Campana National Park, Panama | Leaf (HD) | α-Pinene (8.8%), linalool (8.6%), β-caryophyllene (17.4%), aromadendrene (13.4%) | — | [100] |
| *P. aduncum* L. | Reserva da Ripasa, Itatí, São Paulo state, Brazil | Leaf (HD) | (E)-β-Ocimene (5.0%), linalool (31.7%), β-caryophyllene (9.1%), α-humulene (5.5%), bicyclogermacrene (11.2%), (E)-nerolidol (10.4%) | Antifungal, TLC bioautography (Cladosporium sphaeareum) | [59] |
| *P. aduncum* L. | Reserva da Ripasa, Itatí, São Paulo state, Brazil | Floral (HD) | α-Terpine (6.8%), (Z)-β-ocimene (5.6%), (E)-β-ocimene (11.1%), γ-terpinene (12.0%), linalool (41.2%), (E)-nerolidol (6.1%) | — | [59] |
| *P. aduncum* L. | Reserva da Ripasa, Itatí, São Paulo state, Brazil | Stem (HD) | α-Pinene (7.2%), β-pinene (14.2%), limonene (8.7%), (Z)-β-ocimene (5.5%), (E)-β-Ocimene (13.3%), linalool (11.8%), β-caryophyllene (7.4%), α-humulene (6.3%), (E)-nerolidol (10.6%) | Antifungal, TLC bioautography (Cladosporium cladosporioides, Cladosporium sphaeareum) | [59] |
| *P. aduncum* L. | Brejo da Madre de Deus, Matas Serranas, Pernambuco state, Brazil | Leaf (HD) | (E)-Nerolidol (80.6–82.5%), longipinanol (2.4–5.6%) | — | [26] |
| *P. aduncum* L. | Serra Negra, Matas Serranas, Pernambuco state, Brazil | Leaf (HD) | (E)-Nerolidol (79.2–81.2%), longipinanol (11.1–13.6%) | — | [26] |
Table A1. Cont.

| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|---------------|-----------------|---------------|-------------------------|------------------|-----|
| *P. aduncum* L. | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD) | α-Pinene (8.0-8.9%), β-pinene (6.6-7.0%), 1,8-cineole (42.0-42.5%), (E)-β-ocimene (8.4%), bicyclogermacrene (3.8-4.0%), asaricin (9.2-10.5%) | Antibacterial (Escherichia coli, MIC 500 µg/mL) | [52] |
| *P. aduncum* L. | Bulo Bulo, Bolivia | Leaf (SD) | α-Pinene (8.0-8.9%), β-pinene (6.6-7.0%), 1,8-cineole (42.0-42.5%), (E)-β-ocimene (8.4%), bicyclogermacrene (3.8-4.0%), asaricin (9.2-10.5%) | | | |
| *P. aduncum* L. | Wasakentsa reserve, Ecuador | Aerial parts (HD) | (E)-β-Ocimene (10.4%), piperitone (8.5%), dillapiole (45.9%) | Antifungal activity against dermatophytes (Trichophyton mentagrophytes, MIC 500 µg/mL, IC₅₀ 92.7 µg/mL; Trichophyton tonsurans, MIC 500 µg/mL, IC₅₀ 108.7 µg/mL; Nantzzia cajetani, IC₅₀ 195 µg/mL) | [65] |
| *P. aduncum* L. | Ducke Reserve, Manaus, Amazonas state, Brazil | Leaf (HD) | Dillapiole (94.8%) | Acaricidal (Rhipicephalus (Boophilus) microplus, LC₅₀ 9.3 mg/mL) | [28] |
| *P. aduncum* L. | Santo Antonio do Taú, Pará state, Brazil | Aerial parts (HD) | Dillapiole (86.9%) | Larvicidal and insecticidal activity against mosquitoes (Anopheles marajoara, LC₅₀ 50.9 µg/mL, 417 µg/mL, respectively; Aedes aegypti, LC₅₀ 54.5 µg/mL, 401 µg/mL, respectively) | [16] |
| *P. aduncum* L. | Azaraquara, São Paulo state, Brazil | Leaf (HD) | (E)-β-Ocimene (5.0%), linalool (31.8%), β-caryophyllene (9.3%), α-humulene (5.5%), bicyclogermacrene (11.3%), (E)-nerolidol (10.3%) | Antifungal, broth dilution assay (Cryptococcus neoformans, MIC 62.5 µg/mL) | [35] |
| *P. aduncum* L. | Brazyândia, Distrito Federal, Brazil | Leaf (HD) | β-Phellandrene (6.8%), y-terpinene (8.3%), terpinen-4-ol (13.0%), piperitone (22.7%), asaricin (5.6%) | | | |
| *P. aduncum* L. | Parque do Guaíra, Distrito Federal, Brazil | Leaf (HD) | β-Phellandrene (6.6%), y-terpinene (8.2%), terpinen-4-ol (16.8%), piperitone (24.9%) | | | |
| *P. aduncum* L. | Corrego Bananal, Distrito Federal, Brazil | Leaf (HD) | (E)-β-Ocimene (11.6%), terpinen-4-ol (6.7%), piperitone (11.0%), asaricin (5.8%) | | | |
| *P. aduncum* L. | Fazenda Água Limpa, Distrito Federal, Brazil | Leaf (HD) | Piperitone (16.3%), dillapiole (49.5%) | | | |
| *P. aduncum* L. | Mata de Dois Irmãos, Recife, Pernambuco, Brazil | Leaf (HD) | Dillapiole (79.0%) | | | |
| *P. aduncum* L. | Belém, Pará state, Brazil | Aerial parts (HD) | Dillapiole (64.4%) | Insecticidal (Solenopsis saevissima, IC₅₀ 135 µg/mL) | [41] |
| *P. aduncum* L. | Bocaiuva, Minas Gerais state, Brazil | Leaf (HD) | α-Pinene (14.2%), β-pinene (9.0%), 1,8-cineole (37.2%) | | | |
| *P. aduncum* L. | Montes Claros, Minas Gerais state, Brazil | Leaf (HD) | (E)-β-Ocimene (13.4%), valencene (6.9%), (E)-nerolidol (9.5%) | | | |
| *P. aduncum* L. | Topes de Collantes Nature Reserve, Escambray Mountains, Cuba | Leaf (HD) | Camphene (10.9%), 1,8-cineole (8.7%), camphor (17.1%), piperitone (34.0%), viridiflorol (7.4%) | Antioxidant (DPPH radical scavenging assay, IC₅₀ 30.1 µg/mL) | [50] |
| *P. aduncum* L. | Gallery Forest, Angico River, Minas Gerais state, Brazil | Leaf (HD) | 1,8-Cineole (55.8%), α-terpinene (5.9%) | Egg hatch inhibition (Haemonchus contortus, IC₅₀ 2.6 mg/mL) | [102] |
| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO Ref. |
|---------------|-----------------|---------------|-------------------------|----------------------|
| **P. aduncum** | **P. aduncum** | **P. aduncum** | **P. aduncum** | **P. aduncum** |
| L. | Santo Antonio de Tausá, Pará state, Brazil | Aerial parts (HD) | Dillapiole (85.9%) | Antifungal activity against dermatophytes (Trichophyton mentagrophytes, MIC 500 µg/mL; Epidermophyton floccosum, MIC 500 µg/mL; Microsporum canis, MIC 250 µg/mL; Microsporum gypseum, MIC 250 µg/mL; Aspergillus fumigatus, MIC 3.9 µg/mL) [30] |
| L. | Cultivated, Federal University of Lavras, Brazil | Leaf (HD) | Linalool (9.3–13.4%), β-caryophyllene (5.1–6.7%), α-humulene (8.5–10.6%), β-pinene (14.3–16.7%), spathulenol (0.3–6.6%), α-cadin-4-en-7-ol (7.5–12.2%) | — [103] |
| L. | Cultivated, Federal University of Lavras, Brazil | Root (HD) | α-Selinene (14.1–16.5%), geranyl 2-methylbutyrate (8.9–13.6%), bulnesol (4.6–6.1%), elemicin (4.6–5.9%), dillapiole (13.0–18.4%), apiole (16.3–28.5%) | — [103] |
| L. | Monte Alegre do Sul, São Paulo state, Brazil | Leaf (HD) | α-Pinene (6.4%), safrole (13.3%), valencene (9.7%), spathulenol (10.6%), asaricin (14.9%) | — [31] |
| L. | Votuporanga, São Paulo state, Brazil | Leaf (HD) | Saffrole (10.8%), asaricin (80.1%) | — [31] |
| L. | Votuporanga, São Paulo state, Brazil | Leaf (HD) | Saffrole (10.5%), asaricin (73.4%) | — [31] |
| L. | Belém, Pará state, Brazil | Aerial parts (HD) | Dillapiole (73.0%) | — [62] |
| L. | Cerro Azul, Paraná state, Brazil | Leaf (HD) | (Z)-β-Ocimene (7.0%), (E)-β-ocimene (13.9%), safrole (6.2%), bicyclogermacrene (20.9%), γ-cadinene (5.5%), spathulenol (5.3%) | Antileishmanial (L. amazonensis promastigotes, IC₅₀ 25.9 µg/mL; L. amazonensis axenic amastigotes, IC₅₀ 36.2 µg/mL) [70] |
| L. | Universidade Federal de Lavras, Matto Grosso state, Brazil | Leaf (HD) | Linalool (13.4%), (E)-nerolidol (25.2%), spathulenol (6.3%) | Antitrypanosomal (T. cruzi trypomastigotes, IC₅₀ 2.8 µg/mL; linalool is the active agent, IC₅₀ 0.31 µg/mL) Antileishmanial (L. braziliensis promastigotes, IC₅₀ 77.9 µg/mL; (E)-nerolidol is the active agent, IC₅₀ 74.3 µg/mL) [67,68] |
| L. | Institute of Pharmacy and Food, Havana, Cuba | Aerial parts (HD) | Camphene (5.9%), camphor (17.1%) piperitonne (23.7%), viridiflorol (14.5%) | Antiprotozoal (Plasmodium falciparum, IC₅₀ 1.5 µg/mL; Trypanosoma brucei, IC₅₀ 2.0 µg/mL; Trypanosoma cruzi, IC₅₀ 2.1 µg/mL; Leishmania amazonensis, IC₅₀ 28.4 µg/mL; Leishmania donovani, IC₅₀ 0.7 µg/mL; Leishmania infantum, IC₅₀ 8.1 µg/mL) [32] |
| **P. aduncum subsp. ossanum** | Pinar del Rio, Cuba | Leaf (HD) | Camphene (6.1%), camphor (8.3%), piperitone (12.9%), β-caryophyllene (6.7%), germacrene D (8.2%), 1-epi-cubenol (6.6%) | — [104] |
| **P. aduncum subsp. ossanum** | Artemisa Province, Cuba | Leaf (HD) | Camphene (5.4–7.4%), camphor (9.4–13.9%), piperitone (19.0–20.1%), viridiflorol (13.0–18.8%) | Antiprotozoal (Plasmodium falciparum, IC₅₀ 1.5 µg/mL; Trypanosoma brucei, IC₅₀ 8.1 µg/mL; Trypanosoma cruzi, IC₅₀ 8.0 µg/mL; Leishmania amazonensis, IC₅₀ 19.3 µg/mL; Leishmania infantum, IC₅₀ 32.5 µg/mL; antibacterial (Staphylococcus aureus, IC₅₀ 39.5 µg/mL) [53] |
| **P. aequale** | Monteverde, Costa Rica | Leaf (HD) | α-Pinene (39.3%), sabineone (18.4%), limonene (6.7%) | Antibacterial (Bacillus cereus, MIC 156 µg/mL) [34] |
| **P. aequale** | Carajás National Forest, Paraíba, Brazil | Aerial parts (HD) | α-Pinene (12.6%), β-pinene (15.6%), δ-elemene (19.0%), bicyclogermacrene (5.5%), cubebol (7.2%), β-atlantol (5.9%) | Cytotoxic (HCT-116 human colorectal carcinoma, IC₅₀ 86.9 µg/mL; A549 human gastric adenocarcinoma, IC₅₀ 1.54 µg/mL; essential oil induced apoptosis in A549 cells) [95] |
| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|--------------|----------------|---------------|-------------------------|------------------|-----|
| *P. aleyreanum* C. DC. | Porto Velho, Rondônia state, Brazil | Leaf (HD) | α-Pinene (7.0%), β-pinene (14.4%), α-phellandrene (6.6%), β-caryophyllene (15.9-23.3%), germacrone D (28.9-29.4%), germacrone A (6.5-9.7%) | Antinociceptive, anti-inflammatory (mouse model) | [60] |
| *P. aleyreanum* C. DC. | Porto Velho, Rondônia state, Brazil | Aerial parts (HD) | δ-Elemene (8.2%), β-elemene (16.3%), β-caryophyllene (6.2%), germacrone D (6.9%), bicyclogermacrene (9.2%), spathulenol (5.2%) | Antifungal, TLC bioautography (*Cladosporium cladosporioides*, *Cladosporium sphaerospermum*), cytotoxic (SKMel19 human melanoma, IC50 7.4 µg/mL) | [61] |
| *P. amalago* L. | Fazenda Sucupira, Embra, Brasil, Brazil | Leaf (HD) | α-Pinene (30.5%), camphene (8.9%), limonene (6.8%), borneol (5.7%) | — | [33] |
| *P. amalago* L. | Monteverde, Costa Rica | Leaf (HD) | α-Phellandrene (1.7-8.1%), β-elemene (11.5-24.6%), β-caryophyllene (15.9-23.3%), germacrone D (28.9-29.4%), germacrone A (6.5-9.7%) | — | [34] |
| *P. amalago* L. | Morro Reuter, Rio Grande do Sul state, Brazil | Aerial parts (HD) | α-Pinene (5.2%), limonene (20.5%), δ-elemene (6.8%), zingiberene (11.2%) | — | [106] |
| *P. amalago* L. | Universidade de São Paulo, Brazil | Leaf (HD) | γ-Muurolene (7.3%), germacrone D (9.9%), bicyclogermacrene (27.9%), spathulenol (19.2%), α-cadinol (7.6%) | — | [35] |
| *P. amalago* L. | Dourados, Mato Grosso do Sul, Brazil | Leaf (HD) | p-Cymene (9.4%), methyl geranate (7.8%), α-amorphene (25.7%), cubenol (6.4%) | — | [107] |
| *P. amalago* L. | Dourados, Mato Grosso do Sul, Brazil | Stem (HD) | Longifolene (6.6%), α-amorphene (23.3%), α-muurolol (9.3%) | — | [107] |
| *P. amalago* L. | Dourados, Mato Grosso do Sul, Brazil | Root (HD) | α-Amorphene (14.4%) | — | [107] |
| *P. amalago* L. | Dourados, Mato Grosso do Sul, Brazil | Floral (HD) | p-Cymene (9.3%), limonene (10.5%), silbipiperol-6-ene (13.5%), allo-aromadendrene (18.5%), α-muurolol (5.5%) | — | [107] |
| *P. amalago* L. | Campinas, São Paulo state, Brazil | Leaf (HD) | α-Pinene (14.8%), β-phellandrene (39.3%), germacrone D (11.7%) | — | [31] |
| *P. amalago* L. | Campinas, São Paulo state, Brazil | Leaf (HD) | α-Pinene (6.7%), sabinen (6.7%), β-phellandrene (15.9%), bicyclogermacrene (20.8%), spathulenol (9.1%) | — | [31] |
| *P. amalago* L. | Campinas, São Paulo state, Brazil | Leaf (HD) | α-Pinene (11.7%), β-phellandrene (33.1%), bicyclogermacrene (15.0%) | — | [31] |
| *P. amalago* L. | Adamantina, São Paulo state, Brazil | Leaf (HD) | Sabinene (8.2%), myrcene (6.8%), β-phellandrene (12.3%), bicyclogermacrene (19.4%), γ-muurolene (3.9%), spathulenol (5.6%) | — | [31] |
| Piper Species          | Collection Site                                | Essential Oil Major Components (>5%) | Bioactivity of EO                                                                 | Ref.   |
|-----------------------|------------------------------------------------|--------------------------------------|-----------------------------------------------------------------------------------|--------|
| *P. amalago* var. medium (Jacq.) Yunck. | Fênix, Paraná state, Brazil | Floral (HD) * β-Phellandrene (7.3–8.2%), bicyclogermacrene (3.0–9.1%), δ-cadinene (2.3–6.6%), (E)-nerolidol (14.2–19.9%), germacrene D-4-ol (10.3–12.7%), α-cadinol (4.9–6.1%), α-cadinol (8.2–11.1%) | — | [108] |
| *P. amplum* Kunth | Pariquera-Açu, São Paulo state, Brazil | Leaf (HD) α-Pinene (18.1%), (E)-β-caryophyllene (10.5%), limonene (9.6%), β-caryophyllene (8.8%), germacrene D (5.5%) | Antibacterial, broth dilution assay (*Pseudomonas aeruginosa*, MIC 30 μg/mL; *Escherichia coli*, MIC 100 μg/mL); antifungal, broth dilution assay (*Trichophyton mentagrophytes*, MIC 15 μg/mL) | [31] |
| *P. angustifolium* Lam. | Cuzco, Peru | Aerial parts (HD) Camphene (22.4%), camphor (25.3%), isoborneol (12.8%) | Antibacterial, broth dilution assay (*Pseudomonas aeruginosa*, MIC 30 μg/mL; *Escherichia coli*, MIC 100 μg/mL); antifungal, broth dilution assay (*Trichophyton mentagrophytes*, MIC 15 μg/mL) | [109] |
| *P. angustifolium* Lam. | Alobral Subregion of the Pantanal of Mato Grosso do Sul, Brazil | Leaf (HD) α-Pinene (5.9%), (E)-nerolidol (5.8%), spathulenol (23.8%), caryophyllene oxide (13.1%) | Antileishmanial (*L. infantum* amastigotes, IC₅₀ 1.43 μg/mL) | [69] |
| *P. anonifolium* Kunth | Bujaru, Pará state, Brazil | Aerial parts (HD) α-Pinene (53.1%), β-pinene (22.9%) | — | [110] |
| *P. anonifolium* Kunth | Ananindeua, Pará state, Brazil | Aerial parts (HD) α-Pinene (7.3%), limonene (5.9%), isohocatane (19.1%), germacrene D (9.6%), α-sesdasmol (33.5%) | — | [110] |
| *P. anonifolium* Kunth | Carajás National Forest, Parauapebas, Pará state, Brazil | Aerial parts (HD) α-Pinene (8.8%), β-selinene (12.7%), α-selinene (11.9%), selin-11-en-4 α-ol (20.0%) | Antifungal, TLC bioautography (*Cladosporium cladosporioides*, *Cladosporium sphaerospermum*); enzyme inhibitory, TLC bioautography (acetylcholinesterase) | [61] |
| *P. arboreum* Aubl. | Chepo, Panama | Leaf (HD) β-Pinene (6.6%), α-copaene (7.4%), germacrene D (5.5%), δ-cadinene (25.8%), (E)-nerolidol (5.2%) | — | [111] |
| *P. arboreum* Aubl. | Fazenda Sucupira, Embrapa, Brasília, Brazil | Leaf (HD) Bicyclogermacrene (12.1%), spathulenol (8.4%), caryophyllene oxide (10.2%) | — | [33] |
| *P. arboreum* Aubl. | Universidade Estadual Paulista, Araraquara, São Paulo state, Brazil | Leaf (HD) β-Caryophyllene (25.1%), germacrene D (9.6%), bicyclogermacrene (49.5%) | — | [59] |
| *P. arboreum* Aubl. | Universidade Estadual Paulista, Araraquara, São Paulo state, Brazil | Floral (HD) * Limonene (6.3%), linalool (10.4%), β- elemene (5.3%), β-caryophyllene (6.6%), germacrene D (49.3%), germacrene A (8.5%) | — | [59] |
| *P. arboreum* Aubl. | Universidade Estadual Paulista, Araraquara, São Paulo state, Brazil | Stem (HD) δ-3-Carene (18.7%), α-copaene (9.0%), β-caryophyllene (26.5%), bicyclogermacrene (21.1%) | — | [59] |
| *P. arboreum* Aubl. | Antonina, Paraná state, Brazil | Leaf (HD) α-Copaene (5.6%), β-caryophyllene (12.6%), trans-cadin-16(14)-8-diene (9.6%), spathulenol (7.9%), caryophyllene oxide (9.5%), 1,4-p-cubenol (10.4%), α-cadinol (5.4%) | Antileishmanial (*L. amazonensis* promastigotes, IC₅₀ 15.2 μg/mL; *L. amazonensis* axenic amastigotes, IC₅₀ > 200 μg/mL) | [70] |
| *P. arboreum* var. latifolium (C. DC.) Yunck. | Rondônia state, Brazil | Leaf (SD) Octanal (5.5%), germacrene D (72.9%), γ-elemene (6.8%) | — | [112] |
Table A1. Cont.

| Piper Species      | Collection Site                        | Essential Oil                  | Major Components (>5%) | Bioactivity of EO                           | Ref. |
|--------------------|----------------------------------------|--------------------------------|-------------------------|---------------------------------------------|------|
| *P. artanthe* C. DC. | San Migues, Santander, Colombia        | Aerial parts (HD)              | δ-Elemene (11.7%), β-caryophyllene (10.2%), α-crip, cubebol (9.6%), cubebol (6.3%), myristicin (6.4%), apoiole (14.5%) | —    | [113] |
| *P. augustum* Rudge | Reserva Biológica Alberto Manuel Brenes, Costa Rica | Leaf (HD)                     | α-Pine (10.5%), α-phellandrene (14.7%), limonene (13.0%), β-phellandrene (5.6%), linalool (10.3%), β-caryophyllene (13.5%) | —    | [114] |
| *P. augustum* Rudge | Valle de Anton, Cerro Caracoral, Coce, Panama | Leaf (HD)                     | α-Pine (6.0%), α-elemene (12.3%), cembrene (11.7%), cembratrienol 1 (25.4%), cembratrienol 2 (8.6%) | —    | [47]  |
| *P. auritum* Kunth | Boca de Uruclío, Colon Province, Panama | Leaf (HD)                     | Safrole (70%)           | —    | [115] |
| *P. auritum* Kunth | Guía de Melena, Cuba                   | Leaf (HD)                     | Safrole (64.5%)         | —    | [116] |
| *P. auritum* Kunth | Monteverde, Costa Rica                 | Floral (HD)                   | Safrole (93.2%)         | —    | [49]  |
| *P. auritum* Kunth | Universidad de La Habana, Cuba         | Aerial parts (HD)              | Safrole (68.6%)         | —    | [117] |
| *P. auritum* Kunth | Cali, Valle del Cauca, Colombia        | Aerial parts (MWHD)            | Safrole (91.3%)         | —    | [118] |
| *P. auritum* Kunth | Topes de Collantes Nature Reserve, Escambray Mountains, Cuba | Leaf (HD)                     | Camphene (5.5%), safrole (71.8%) | —    | [50]  |
| *P. brachypodon* (Benth.) C. DC. | Amazonas region, Peru | Aerial parts (HD)              | Crocatone (10.9%), (E)-isocubebol (14.1%), apoiole (8.0%), 2′-methoxy-4′,5′-methylenedioxy-propiophenone (29.5%) | —    | [119] |
| *P. brachypodon* var. hirsuticaule Yunck. | Samurindo, Chocó, Colombia | Aerial parts (MWHD)            | β-Elemene (6.4%), β-caryophyllene (9.8%), α-quinine (5.9%), germacre D (16.7%), bicyclogermacrene (6.2%) | —    | [120] |
| *P. barbatum* Kunth | Amazonas region, Peru | Aerial parts (HD)              | β-Caryophyllene (20.2%), 9-epi-β-caryophyllene (5.5%), germacre D (5.9%), bicyclogermacrene (8.1%), spathulenol (5.7%), caryophyllene oxide (10.8%) | —    | [118] |
| *P. bogotense* C. DC. | Ipiales, Narino, Colombia              | Aerial parts (MWHD)            | α-Pine (8.7%), α-phellandrene (13.7%), limonene (5.3%), trans-sabinene hydrate (14.2%) | —    | [118,120,121] |
| *P. brachypodon* (Benth.) C. DC. | Quibdó, Chocó, Colombia | Aerial parts (MWHD)            | β-Caryophyllene (20.2%), 9-epi-β-caryophyllene (5.5%), germacre D (5.9%), bicyclogermacrene (8.1%), spathulenol (5.7%), caryophyllene oxide (10.8%) | —    | [120] |
| *P. brachypodon* (Benth.) C. DC. | Tutunendo, Chocó, Colombia             | Aerial parts (MWHD)            | β-Caryophyllene (20.2%), 9-epi-β-caryophyllene (5.5%), germacre D (5.9%), bicyclogermacrene (8.1%), spathulenol (5.7%), caryophyllene oxide (10.8%) | —    | [118] |
| *P. brachypodon* var. hirsuticaule Yunck. | Samurindo, Chocó, Colombia | Aerial parts (MWHD)            | β-Elemene (6.4%), β-caryophyllene (9.8%), α-quinine (5.9%), germacre D (16.7%), bicyclogermacrene (6.2%) | —    | [118] |
Table A1. Cont.

| Piper Species          | Collection Site                  | Essential Oil | Major Components (>5%)                                                                 | Bioactivity of EO                                                                 | Ref. |
|------------------------|----------------------------------|---------------|----------------------------------------------------------------------------------------|------------------------------------------------------------------------------------|------|
| **P. bredemeyeri Jacq.** | Monteverde, Costa Rica           | Leaf (HD)     | β-Elemene (34.0%), β-caryophyllene (24.2%), germacrene D (11.4%), germacrene A (11.4%) | Antibacterial, broth dilution assay (Bacillus subtilis, MIC 78 µg/mL), enzyme inhibitory (cruzain, IC₅₀ 0.96 µg/mL) | [34] |
|                        | Pueblo Bello, Cesar, Colombia    | Aerial parts  | α-Pinene (20.3%), β-pinene (32.3%), β-caryophyllene (6.3%)                            | Anti-fungal, broth dilution assay (Trichophyton rubrum, MIC 157 µg/mL, Trichophyton mentagrophytes, MIC 125 µg/mL), cytotoxic (Vero cells, IC₅₀ 15.2 µg/mL) | [121]|
| **P. caldense C. DC.**  | Recife, Pernambuco state, Brazil | Leaf (HD)     | β-Cadinene (5.6%), thujopsan-2β-ol (7.4%), α-muurolol (9.0%), α-cadinol (19.0%)          | Antibacterial, agar diffusion assay (Bacillus subtilis, Staphylococcus aureus, Klebsiella pneumoniae) | [54] |
|                        | Recife, Pernambuco state, Brazil | Root (HD)     | Valencene (10.5%), pentadecane (35.7%), selina-3,7(11)-diene (3.4%)                    | Antibacterial, agar diffusion assay (Bacillus subtilis, Pseudomonas aeruginosa)      | [54] |
| **P. callosum Ruiz & Pav.** | Marituba, Pará state, Brazil   | Aerial parts  | Safrole (68.2%), methyl eugenol (8.0%)                                                  | Insecticidal (Solenopsis saevissima, IC₅₀ > 500 µg/mL)                               | [41] |
|                        | Barcarena, Pará state, Brazil   | Leaf (HD)     | α-Pinene (6.3%), caryophyllene oxide (21.3%)                                            | —                                                                                  | [122]|
| **P. cernuum Vell.**    | Porto Velho, Rondônia state, Brazil | Leaf (HD)     | α-Pinene (8.0%), β-pinene (19.0%), spathulenol (23.7%), caryophyllene oxide (7.8%)       | —                                                                                  | [122]|
|                        | Cajamarca region, Peru          | Leaf (HD)     | α-Terpineol (12.1%), p-cymene (10.9%), 1,8-cineole (13.0%), safrole (14.9%), bicyclod germacrene (6.7%), spathulenol (9.5%) | —                                                                                  | [123]|
| **P. carpunya Ruiz & Pav.** | Cajamarca region, Peru       | Floral (HD)   | α-Pinene (6.2%), α-terpineol (9.8%), p-cymene (7.7%), 1,8-cineole (30.2%), safrole (32.0%) | —                                                                                  | [123]|
|                        | Universidade de São Paulo, Brazil | Leaf (HD)     | α-Pinene (7.2%), β-pinene (6.2%), β-caryophyllene (20.7%), germacrene D (6.7%), bicyclod germacrene (21.9%) | Antimicrobial, agar diffusion assay (Staphylococcus aureus, Candida albicans)         | [38] |
|                        | São Francisco de Assis Natural Reserve, Blumenau, Santa Catarina state, Brazil | Aerial parts | trans-Dihydroagarofuran (31.0%), elemol (12.0%), 10-epi-γ-eudesmol (13.0%)               | —                                                                                  | [124]|
| **P. carniconnectivum C. DC.** | Porto Velho, Rondônia state, Brazil | Leaf (HD)     | α-Pinene (8.0%), β-pinene (19.0%), spathulenol (23.7%), caryophyllene oxide (7.8%)       | —                                                                                  | [122]|
|                        | Cajamarca region, Peru          | Leaf (HD)     | α-Terpineol (12.1%), p-cymene (10.9%), 1,8-cineole (13.0%), safrole (14.9%), bicyclod germacrene (6.7%), spathulenol (9.5%) | —                                                                                  | [123]|
| **P. carpunya Ruiz & Pav.** | Cajamarca region, Peru       | Floral (HD)   | α-Pinene (6.2%), α-terpineol (9.8%), p-cymene (7.7%), 1,8-cineole (30.2%), safrole (32.0%) | —                                                                                  | [123]|
|                        | Universidade de São Paulo, Brazil | Leaf (HD)     | α-Pinene (7.2%), β-pinene (6.2%), β-caryophyllene (20.7%), germacrene D (6.7%), bicyclod germacrene (21.9%) | Antimicrobial, agar diffusion assay (Staphylococcus aureus, Candida albicans)         | [38] |
|                        | Universidade de São Paulo, Brazil | Leaf (HD)     | β-Elemene (7.2%), β-caryophyllene (22.2%), germacrene D (9.3%), bicyclod germacrene (21.1%), (2)-α-bisabolene (5.7%), spathulenol (27.2%) | —                                                                                  | [35,60]|
| **P. carpunya Ruiz & Pav.** | Universidade de São Paulo, Brazil | Floral (HD)   | α-Copaene (6.5%), β-caryophyllene (9.8%), germacrene D (14.3%), bicyclod germacrene (6.5%), spathulenol (9.7%) | Antifungal, TLC bioautography (Cladosporium cladosporioides, C. sphaerospermum)      | [60] |
|                        | Reserva da Matinha, Ilhéus, Bahia state, Brazil | Leaf (HD)     | β-Elemene (11.6%), β-caryophyllene (8.3%), cis-β-guaiene (8.2%), γ-muurolene (7.6%), α-p-cubebol (13.1%), spathulenol (9.6%), caryophyllene oxide (7.7%), valeranone (9.1%) | —                                                                                  | [125]|

**Table A1**: Table A1. Cont.
| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|--------------|----------------|--------------|------------------------|------------------|-----|
| *P. cernuum* Vell. | Parque Ecológico do Perequê, Cubatão, São Paulo state, Brazil | Leaf (HD) | β-Elemene (30.0%), β-caryophyllene (16.3%), germacrene D (12.7%), bicyclogermacrene (19.9%) | Cytotoxic (B16F10-Neu2 murine melanoma, IC₅₀ 30 µg/mL), A2058 human melanoma, IC₅₀ 24 µg/mL; U87-MG human glioblastoma, IC₅₀ 19.1 µg/mL; HeLa human cervical tumor, IC₅₀ 23 µg/mL; HL-60 human myeloid leukemia, IC₅₀ 16 µg/mL | [20] |
| *P. cernuum* Vell. | Parque Ecológico do Perequê, Cubatão, São Paulo state, Brazil | Branches (HD) | Camphene (46.4%), p-cymene (5.8%), linalool (8.7%), α-terpineol (11.6%), carvacrol (11.6%)<sup>a</sup> | Cytotoxic (B16F10-Neu2 murine melanoma, IC₅₀ 39.0 µg/mL; A2058 human melanoma, IC₅₀ 24.6 µg/mL; U87-MG human glioblastoma, IC₅₀ 19.0 µg/mL; HeLa human cervical tumor, IC₅₀ 23.6 µg/mL), HL-60 human myeloid leukemia, IC₅₀ 15.5 µg/mL | [86] |
| *P. cernuum* Vell. | Ubatuba, São Paulo state, Brazil | Leaf (HD) | α-Pinene (10.0%), camphene (6.3%), trans-dihydroagarofuran (28.7%), 10-epi-α-eudesmol (13.5%), 4-epi-α-cis-dihydroagarofuran (10.8%) | — | [31] |
| *P. cernuum* Vell. | Paripueira-Açu, São Paulo state, Brazil | Leaf (HD) | α-Pinene (11.8%), camphene (8.7%), trans-dihydroagarofuran (33.8%), 10-epi-α-eudesmol (12.2%) | — | [31] |
| *P. cernuum* Vell. | Antonina, Paraná state, Brazil | Leaf (HD) | α-Pinene (11.4%), β-pinene (7.9%), β-elemene (10.1%), β-caryophyllene (6.9%), spathulenol (11.5%), caryophyllene oxide (5.1%), α-muurocol (6.2%), α-muurocol (5.8%) | Antileishmanial (L. amazonensis promastigotes, IC₅₀ 27.1 µg/mL; L. amazonensis axenic amastigotes, IC₅₀ > 200 µg/mL), anti-Mycobacterium tuberculosis (MIC 125 µg/mL) | [70] |
| *P. cernuum* Vell. | Blumenau, Santa Catarina state, Brazil | Leaf (HD) | α-Pinene (2.6–5.4%), β-caryophyllene (5.9–8.7%), 4-epi-α-cis-dihydroagarofuran (11.2–13.4%), trans-dihydroagarofuran (30.0–36.7%), elemol (5.9–9.2%), γ-eudesmol (8.3–13.3%) | Antibacterial, agar dilution assay (Bacillus subtilis, MIC 48 µg/mL; Staphylococcus aureus, MIC 780 µg/mL; Streptococcus pyogenes, MIC 780 µg/mL); antifungal, agar dilution assay (Microsporum canis, Microsporum gypseum, Trichophyton mentagrophytes, Trichophyton rubrum, Epidermophyton floccosum, Cryptococcus neoformans, MIC 48 µg/mL) | [37] |
| *P. cernuum* Vell. var. *cernuum* | Tijucu Forest, Rio de Janeiro state, Brazil | Leaf (HD) | α-Pinene (10.2%), camphene (5.3%), β-pinene (7.4%), cis-dihydroagarofuran (32.3%), elemol (6.7%) | — | [36] |
| *P. clausenianum* (Miq.) C. DC. | São Manoel, Castelo, Espírito Santo, Brazil | Leaf (HD) | Linalool (2.1–5.2%), (E)-nerolidol (81.4–83.3%) | Antileishmanial (promastigotes of L. amazonensis, IC₅₀ 30.24 µg/mL), Anticandidal (C. albicans, MIC 0.2–1.26%) | [71,126] |
| *P. clausenianum* (Miq.) C. DC. | São Manoel, Castelo, Espírito Santo, Brazil | Floral (HD) | Linalool (50.2–54.5%), (E)-nerolidol (22.7–24.3%) | Antileishmanial (promastigotes of L. amazonensis, IC₅₀ 1328 µg/mL), Anticandidal (C. albicans, MIC 0.04–0.1%), Antiparasitic (Plasmodium falciaparum W2, IC₅₀ 7.9 µg/mL) | [71,126] |
| *P. corcoronum* (Miq.) C. DC. | Jardim Botânico do Recife, Pernambuco, Brazil | Leaf (HD) | α-Pinene (5.9%), terpinolene (17.4%), 4-buty-1,2-methylenedioxybenzene (30.6%), β-caryophyllene (6.3%) | Mosquito larvicidal activity (Aedes aegypti; LC₅₀ 30.5 µg/mL) | [127] |
| *P. corrugatum* (Kuntze) | Valle de Anton, Cerro Caracoral, Coche, Panama | Leaf (HD) | α-Pinene (12.2%), β-pinene (26.6%), limonene (8.2%), p-cymene (8.6%), 1,8-cineole (5.9%), (E)-nerolidol (12.8%), caryophyllene oxide (8.5%) | — | [47] |
Table A1. Cont.

| Piper Species | Collection Site                  | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref.  |
|---------------|----------------------------------|---------------|-------------------------|-------------------|-------|
| *P. crassinervium* Kunth | Universidade de São Paulo, Brazil | Leaf (HD)     | β-Caryophyllene (8.1%), germacrene D (14.0%), bicyclogermacrene (9.2%), α-pinene (5.0%), (E)-nerolidol (8.2%), spathulenol (9.8%), guaiol (5.8%), β-eudesmol (10.1%) | Antifungal, TLC bioautography (Cladosporium cladosporioides, Cladosporium sphaerospermum) | [35,60] |
| *P. crassinervium* Kunth | Mococa, São Paulo state, Brazil  | Leaf (HD)     | α-Pinene (11.5%), β-pinene (11.6%), β-caryophyllene (7.3%), germacrene D (9.2%), bicyclogermacrene (5.1%), guaiol (5.5%) | — | [31] |
| *P. curtispicum* C. DC. | Altos de Campana, Panama        | Leaf (HD)     | α-Pinene (19.4%), limonene (8.1%), β-caryophyllene (13.9%) | — | [47] |
| *P. cyrtopodon* C. DC. | Marituba, Pará state, Brazil    | Aerial parts (HD) | α-Cubebene (8.1%), β-caryophyllene (19.2%), germacrene D (10.0%), bicyclogermacrene (6.6%), spathulenol (8.4%) | — | [128] |
| *P. cyrtopodon* C. DC. | Santarém, Pará state, Brazil    | Aerial parts (HD) | β-Cymene (6.3%), germacrene D (17.9%), bicyclogermacrene (23.3%), (E)-nerolidol (6.6%), spathulenol (9.4%) | — | [128] |
| *P. cyrtopodon* C. DC. | Ananindeua, Pará state, Brazil  | Aerial parts (HD) | α-Pinene (7.5%), β-pinene (6.0%), β-caryophyllene (34.6%), germacrene D (13.6%), bicyclogermacrene (21.4%), spathulenol (8.4%) | — | [128] |
| *P. cyrtopodon* C. DC. | Manaus, Amazonas state, Brazil  | Aerial parts (HD) | Germacrene D (7.5%), bicyclogermacrene (8.3%), α-cadinol (9.5%), α,β-bisabolol (26.3%) | — | [128] |
| *P. dactylostigmum* Yunck. | Itacoatiara, Amazonas State, Brazil | Aerial parts (HD) | β-Caryophyllene (8.9%), γ-muurolene (5.9%), α-pinene (9.3%), α-selinene (8.0%), caryophyllene oxide (6.0%), γ-muurolol (7.5%), α-cadinol (21.7%) | — | [129] |
| *P. darwinense* C. DC. | Parque Nacional Chaves, Panama | Leaf (HD) | Limonene (6.3%), (E)-β-farnesene (63.7%) | — | [47] |
| *P. demeraranum* (Miq.) C. DC. | Belém, Pará state, Brazil | Aerial parts (HD) | α-Pinene (7.3%), α-sabinene (12.9%), β-pinene (7.7%), limonene (20.2%) | — | [130] |
| *P. demeraranum* (Miq.) C. DC. | Ananindeua, Pará state, Brazil | Aerial parts (HD) | α-Pinene (6.1–12.3%), α-sabinene (17.0–22.7%), β-pinene (8.2–14.4%), limonene (30.6–40.3%) | — | [130] |
| *P. demeraranum* (Miq.) C. DC. | Adolpho Ducke Reserve, Manaus, Amazonas state, Brazil | Leaf (HD) | β-Pinene (6.7%), limonene (19.3%), β-elemene (33.1%), β-caryophyllene (6.0%), germacrene D (5.2%), α-selinene (5.0%), bicyclogermacrene (8.8%) | Antileishmanial (L. amazonensis promastigotes, IC₅₀ 86.0 µg/mL; L. amazonensis amastigotes, IC₅₀ 22.7 µg/mL) | [72] |
| *P. dilatatum* Rich. | Fazenda Sucupira, Embrapa, Brasilia, Brazil | Leaf (HD) | (E)-β-Ocimene (19.7%), β-caryophyllene (11.4%), germacrene D (8.9%), bicyclogermacrene (8.8%), spathulenol (6.5%), caryophyllene oxide (5.3%) | — | [33] |
| *P. dilatatum* Rich. | Alto Alegre, Roraima state, Brazil | Aerial parts (HD) | β-Caryophyllene (11.7%), germacrene D (6.7%), α-selinene (6.1%), β-cadinene (5.4%), caryophyllene oxide (6.1%), α-cadinol (12.2%) | — | [131] |
Table A1. Cont.

| Piper Species | Collection Site                | Essential Oil | Major Components (>5%)                                                                 | Bioactivity of EO                                      | Ref. |
|---------------|--------------------------------|---------------|----------------------------------------------------------------------------------------|------------------------------------------------------|------|
| *P. dilatatum* Rich. | Alto Alegre, Roraima state, Brazil Aerial parts (HD) | β-Caryophyllene (15.5%), germacrene D (10.2%), α-selinene (6.9%), δ-cadinene (8.5%), α-cadinol (7.0%) | — [131] | |
| *P. dilatatum* Rich. | Benfica, Pará state, Brazil Aerial parts (HD) | Germacrene D (12.6%), bicyclogermacrene (7.4%), (E)-nerolidol (10.2%), spathulenol (11.8%), hinesol (6.4%), α-cadinol (5.8%) | — [131] | |
| *P. dilatatum* Rich. | Belterra, Pará state, Brazil Aerial parts (HD) | α-Pinene (9.7%), β-pinene (14.8%), (Z)-β-ocimene (10.0%), β-caryophyllene (7.4%), bicyclogermacrene (22.6%), spathulenol (15.0%) | — [131] | |
| *P. dilatatum* Rich. | Marituba, Pará state, Brazil Aerial parts (HD) | p-Cymene (11.7%), β-selinene (6.4%), curzerene (13.8%), (E)-nerolidol (5.7%), α-eudesmol (8.0%), atractylene (5.1%) | — [131] | |
| *P. dilatatum* Rich. | Marituba, Pará state, Brazil Aerial parts (HD) | Germacrene D (30.2%), bicyclogermacrene (9.4%), spathulenol (40.6%), hinesol (6.4%), α-cadinol (5.8%) | — [131] | |
| *P. dilatatum* Rich. | Serra dos Carajás, Pará state, Brazil Aerial parts (HD) | (Z)-β-Farnesene (7.0%), germacrene D (24.5%), bicyclogermacrene (6.7%), β-bisabolene (39.3%) | — [131] | |
| *P. dilatatum* Rich. | Angico, Tocantins state, Brazil Aerial parts (HD) | Germacrene D (8.5%), bicyclogermacrene (34.7%), spathulenol (35.2%) | — [131] | |
| *P. dilatatum* Rich. | Xambioá, Tocantins state, Brazil Aerial parts (HD) | Germacrene D (15.2%), curzerene (28.7%), β-bisabolene (5.5%), (Z)-α-bisabolene (23.2%) | — [131] | |
| *P. dilatatum* Rich. | Carolina, Maranhão state, Brazil Aerial parts (HD) | Limonene (19.4%), germacrene D (43.0%), bicyclogermacrene (13.2%) | — [131] | |
| *P. diospyrifolium* Kunth | Universidade de São Paulo, Brazil Leaf (HD) | (E)-Nerolidol (18.2%), spathulenol (25.4%), β-caryophyllene oxide (7.7%), globulol (6.6%), humulene epoxide II (6.9%) | — [35,60] | |
| *P. diospyrifolium* Kunth | Universidade de São Paulo, Brazil Floral (HD) | α-Copaene (47.7%), β-caryophyllene (12.3%), α-humulene (5.7%) | — [60] | |
| *P. diospyrifolium* Kunth | Maringá, Paraná state, Brazil Leaf (HD) | Limonene (8.5%), (E)-β-ocimene (5.8%), β-caryophyllene (16.8%), γ-muurolene (10.6%), cis-eudesma-6,11-diene (21.1%), germacrene B (6.2%) | Antifungal, agar diffusion assay (Candida albicans, Candida parapsilosis, Candida tropicalis) [55] | |
| *P. diospyrifolium* Kunth | Antonina, Paraná state, Brazil Leaf (HD) | α-Pinene (6.7%), limonene (6.7%), α-copaene (5.4%), β-caryophyllene (7.4%), γ-gurjene (6.9%), germacrene B (6.7%), selin-11-ene-4-α-ol (17.7%) | Antileishmanial (L. amazonensis promastigotes, IC₅₀ 13.5 µg/mL; L. amazonensis axenic amastigotes, IC₅₀ 76.1 µg/mL; anti-Mycobacterium tuberculosis, MIC 125 µg/mL) [70] | |
| *P. divorciatum* G. Mey. | Guaramiranga Mountain, Ceará state, Brazil Leaf (HD) | α-Pinene (9.0–18.8%), β-pinene (19.9–23.3%), 1,8-cineole (8.9–9.6%), linalool (23.4–23.7%), germacrene D (6.3–6.5%) | — [132] | |
| Piper Species          | Collection Site                                | Essential Oil       | Major Components (>5%)                                                                 | Bioactivity of EO                                                                 | Ref.     |
|-----------------------|------------------------------------------------|---------------------|----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|----------|
| *P. friedrichthali* C. DC. | Pacayas, Cartago, Costa Rica                   | Floral (HD) a       | α-Pinene (13.4%), β-phellandrene (5.2%), trans-p-menth-2-en-1-ol (7.3%), cis-p-menth-2-en-1-ol (5.1%) | —                                                                                | [133]    |
| *P. friedrichthali* C. DC. | Fortuna, Quebrada Honda, Chiriquí, Panama       | Leaf (HD)           | Germacrene D (9.6%), α-selinene (12.0%), β-selinene (7.9%), selin-11-en-4α-ol (12.8%) | —                                                                                | [133]    |
| *P. gaudichaudianum* Kunth | Sapiranga, Rio Grande do Sul state, Brazil      | Leaf (HD)           | β-Pinene (5.8%), β-caryophyllene (17.4%), α-humulene (37.5%), allo-aromadendrene (7.7%) | —                                                                                | [134]    |
| *P. gaudichaudianum* Kunth | Universidade de São Paulo, Brazil Aerial parts (HD) | β-Caryophyllene (12.1%), α-humulene (13.3%), β-selinene (15.7%), α-selinene (16.6%) | —                                                                                | [135]    |
| *P. gaudichaudianum* Kunth | Universidade de São Paulo, Brazil Aerial parts (HD) | β-Caryophyllene (19.3%), α-humulene (29.2%), α-selinene (8.9%) | —                                                                                | [135]    |
| *P. gaudichaudianum* Kunth | State of Rondônia, Brazil Leaf (HD)             | Terpinolene (5.4%), safrole (85.1%) | —                                                                                | Amebicidal (Acanthamoeba polyphaga trophozoites, LC_{50} 66 µg/mL) | [139]    |
| *P. glabratum* Kunth | Reserva da Matinha, Ilhéus, Bahia state, Brazil | Leaf (HD)           | α-Pinene (12.2%), β-pinene (7.0%), β-caryophyllene (8.5%), trans-β-guaiene (6.9%), (E)-nerolidol (17.5%), carvophyllene oxide (8.5%) | —                                                                                | [31]     |
| *P. glabratum* Kunth | Antonina, Paraná state, Brazil Leaf (HD)        | δ-3-Carene (5.9%), γ-elemene (5.4%), β-cadinene (45.3%) | —                                                                                | Antileishmanial (L. amazonensis promastigotes, IC_{50} 93.5 µg/mL) | [70]     |
| *P. glabrum* (Michx.) C. DC. | Monteverde, Costa Rica Leaf (HD)                | α-Pinene (26.0%), limonene (56.6%) | —                                                                                | Cytotoxic (MCF-7 human breast adenocarcinoma)                                   | [34]     |
| *P. grande* Valh | Parque Nacional Camino de Cruces, Panama         | Leaf (HD)           | α-Pinene (3.6%), β-pinene (14.5%), γ-terpinene (8.0%), p-cymene (43.9%) | —                                                                                | [47]     |
| *P. heterophyllum* Ruiz & Pav. | Estancia, Bolivia                              | Leaf (SD)           | α-Pinene (9.3%), β-pinene (6.2%), 1,8-cineole (39.0%), (E)-β-ocimene (6.3%), asaricin (8.8%) | —                                                                                | [101]    |
| *P. hispidinervum* C. DC. | Porto Alegre, Rio Grande do Sul state, Brazil Leaf (HD) | Terpinolene (5.4%), safrole (85.1%) | —                                                                                | Amebicidal (Acanthamoeba polyphaga trophozoites, LC_{50} 66 µg/mL) | [139]    |
| *P. hispidum* Sw. | Rondônia state, Brazil Leaf (SD)                | α-Pinene (5.2%), camphene (15.6%), β-phellandrene (9.7%), β-caryophyllene (5.4%), α-guaiene (11.5%), γ-cadinene (23.1%), γ-elemene (10.9%) | —                                                                                | —        | [112]    |
| Piper Species                  | Collection Site                        | Essential Oil | Major Components (>5%)                                                                 | Bioactivity of EO                                                                 | Ref. |
|-------------------------------|----------------------------------------|---------------|----------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|------|
| *P. hispidum* Sw.             | Pinar del Río, Cuba                    | Leaf (HD)     | Curzerene (12.9%), elemol (7.6%), γ-eudesmol (9.3%), β-eudesmol (17.5%), α-eudesmol (8.1%), 14-Hydroxy-α-muurolene (8.0%) | —                                                                               | [46] |
| *P. hispidum* Sw.             | Fazenda Sucupira, Embrapa, Brasilia, Brazil | Leaf (HD)     | α-Pinene (9.0%), β-pinene (19.7%), δ-3-carene (7.4%), spathulenol (6.2%), α-cadinol (6.9%) | —                                                                               | [35] |
| *P. hispidum* Sw.             | Pacurita, Chocó, Colombia               | Leaf (HD)     | β-Elemene (5.1%), β-caryophyllene (5.1%), (E)-nerolidol (23.6%), carvophyllene oxide (9.4%) | —                                                                               | [48] |
| *P. hispidum* Sw.             | Fênix, Paraná state, Brazil            | Floral (HD) * | α-Pinene (7.1–13.9%), β-pinene (7.5–13.3%), α-copaene (28.7–36.2%)                      | Antibacterial (*Bacillus subtilis*, MIC 12.5 µg/mL; *Bacillus cereus*, MIC 12.5 µg/mL; *Staphylococcus aureus*, MIC 12.5 µg/mL; *Staphylococcus epidermidis*, MIC 12.5 µg/mL; *Enterococcus faecalis*, MIC 15.0 µg/mL), antifungal (*Candida albicans*, MIC 200 µg/mL), cytotoxic (*HeLa* human cervical carcinoma, IC₅₀ 36.6 µg/mL; *A.549* human lung carcinoma, IC₅₀ 37.5 µg/mL; *MCF-7* human breast adenocarcinoma, IC₅₀ 34.2 µg/mL) | [108]|
| *P. hispidum* Sw.             | Reserva da Matinha, Ilhéus, Bahia state, Brazil | Leaf (HD)     | α-Pinene (6.6%), β-pinene (12.0%), khusimene (12.1%), γ-cadinene (15.2%), δ-cadinene (6.3%), ledol (8.8%) | —                                                                               | [125]|
| *P. hispidum* Sw.             | Carajás National Forest, Parauapebas, Pará state, Brazil | Aerial parts (HD) | δ-3-Carene (9.1%), limonene (6.9%), α-copaene (7.3%), β-caryophyllene (10.3%), α-humulene (9.9%), β-selinene (5.1%), carvophyllene oxide (5.9%) | Antifungal, TLC bioautography (*Cladosporium cladosporioides*, *Cladosporium sphaerospermum*); enzyme inhibitory, TLC bioautography (acyetylcholinesterase) | [61] |
| *P. hispidum* Sw.             | Atrato, Chocó, Colombia                 | Aerial parts (MWHD) | β-Elemene (5.1%), β-caryophyllene (5.1%), (E)-nerolidol (23.6%), carvophyllene oxide (5.9%) | Antifungal, broth dilution assay (*Fusarium oxysporum*, MIC 500 µg/mL; *Trichophyton rubrum*, MIC 99 µg/mL; *Trichophyton mentagrophytes*, MIC 125 µg/mL), cytotoxic (Vero cells, IC₅₀ 51.7 µg/mL) | [121]|
| *P. hispidum* Sw.             | Altos de Campana, Panama               | Leaf (HD)     | Piperitone (10.0%), dillapiole (57.4%)                                                  | Mosquito larvicidal (*Aedes aegypti*, LC₅₀ 250 µg/mL)                             | [47] |
| *P. hostmannianum* (Miq.) C. DC. | State of Rondônia, Brazil              | Leaf (HD)     | Piperitone (5.6%), germacrene D (6.8%), asaricin (27.4%), myristin (20.3%), dillapiole (7.7%) | Mosquito larvicidal (*Aedes aegypti*, LC₅₀ 54 µg/mL)                             | [136]|
| *P. humaytanum* Yunck         | State of Rondônia, Brazil              | Leaf (HD)     | β-Selinene (15.8%), sesquicinole (5.0%), spathulenol (6.3%), carvophyllene oxide (16.6%), β-oplapophene (6.0%) | Mosquito larvicidal (*Aedes aegypti*, LC₅₀ 156 µg/mL)                             | [136]|
| *P. ilheusense* Yunck         | Ilhéus, Bahia, Brazil                  | Leaf (HD)     | β-Caryophyllene (11.8%), γ-cadinene (6.9%), germacrene B (7.2%), gleenol (7.9%), patchouli alcohol (11.1%) | Antimicrobial, agar diffusion assay (*Bacillus subtilis*, *Staphylococcus aureus*, *Candida albicans*, *Candida crusei*, *Candida parapsilosis*) | [57] |
### Table A1. Cont.

| Piper Species                  | Collection Site                              | Essential Oil   | Major Components (>5%)                                                                 | Bioactivity of EO                                                                                     | Ref.      |
|-------------------------------|----------------------------------------------|-----------------|----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------|-----------|
| *P. imperiale* (Miq.) C. DC.  | Monteverde, Costa Rica                       | Leaf (HD)       | β-Elemene (5.2%), β-caryophyllene (25.5%), α-guaiene (7.6%), germacrene D (5.5%),      | Antibacterial (*Bacillus cereus*, MIC 156 µg/mL), cytoxic (*MCF-7 human breast adenocarcinoma*)       | [34]      |
|                               |                                              |                 | bicyclogermacrene (19.7%), germacrene A (8.5%), α-bulnesene (10.8%), dillapiole (6.7%) |                                                                                                       |           |
| *P. jacquemontianum* Kunth    | Lachúa, Alta Verapaz, Guatemala              | Leaf (HD)       | Linalool (89.4%), (E)-nerolidol (8.0%)                                                 |                                                                                                       |           |
| *P. jacquemontianum* Kunth    | Parque Nacional Soberania, Panama            | Leaf (HD)       | α-Pinene (9.6%), β-pinene (10.1%), α-phellandrene (13.8%), limonene (12.2%), p-cymene |                                                                                                       | [116]     |
|                               |                                              |                 | (7.4%), linalool (14.5%)                                                               |                                                                                                       |           |
| *P. klotzschianum* (Kunth) C. DC. | Vila do Rio, Gimuna Forest, Aracruz, Espírito Santo, Brazil | Leaf (HD)   | 4-Butyl-1,2-methylenedioxybenzene (81.0%), γ-asarone (9.1%)                             | Mosquito larvicidal activity (*Aedes aegypti*, LC$_{50}$ 10.0 µg/mL)                               | [141]     |
|                               |                                              |                 |                                                                                       |                                                                                                       |           |
| *P. klotzschianum* (Kunth) C. DC. | Vila do Rio, Gimuna Forest, Aracruz, Espírito Santo, Brazil | Root (HD)   | 4-Butyl-1,2-methylenedioxybenzene (96.2%)                                               |                                                                                                       |           |
|                               |                                              |                 |                                                                                       |                                                                                                       |           |
| *P. klotzschianum* (Kunth) C. DC. | Vila do Rio, Gimuna Forest, Aracruz, Espírito Santo, Brazil | Seed (HD)   | α-Phellandrene (17.0%), α-cymene (47.4%), limonene (17.8%), 4-Butyl-1,2-methylenedioxybenzene (36.9%), α-tansygermacrene (8.8%) | Mosquito larvicidal activity (*Aedes aegypti*, LC$_{50}$ 13.3 µg/mL)                               | [141]     |
|                               |                                              |                 |                                                                                        |                                                                                                       |           |
| *P. klotzschianum* (Kunth) C. DC. | Vila do Rio, Gimuna Forest, Aracruz, Espírito Santo, Brazil | Stem (HD)    | 4-Butyl-1,2-methylenedioxybenzene (84.8%), γ-asarone (5.4%)                             |                                                                                                       |           |
| *P. kraughii* Yunck.         | Carajás National Forest, Parauapebas, Pará state, Brazil | Aerial parts (HD) | β-Elemene (1.7-8.2%), myristicen (26.7-40.6%), 4-terpinenol (2.0-5.7%), apiole (25.3-34.1%) |                                                                                                       |           |
| *P. lanceifolium* Kunth      | San Isidro del Tejar, Costa Rica             | Leaf (HD)       | β-Caryophyllene (20.6%), germacrene D (12.5%), elemicin (24.4%), apiole (11.7%)        |                                                                                                       |           |
| *P. lanceifolium* Kunth      | San Isidro del Tejar, Costa Rica             | Floral (HD) 4   | α-Pinene (13.7%), β-pinene (15.8%), γ-terpinene (6.9%), β-caryophyllene (5.1%), elemicin (16.4%), apiole (9.8%) |                                                                                                       |           |
| *P. lanceifolium* Kunth      | Monteverde, Costa Rica                       | Leaf (HD)       | Dillapiole (74.6%)                                                                     |                                                                                                       | [34]      |
| *P. lanceifolium* Kunth      | Bagadó, Chocó, Colombia                      | Aerial parts (MWHD) | β-Pinene (5.4%), β-caryophyllene (11.6%), germacrene D (10.7%), β-selinene (7.8%), δ-cadinene (6.1%), carophyllene oxide (5.9%) |                                                                                                       | [118]     |
|                               |                                              |                 | Antiprotozoal (*Trypanosoma cruzi* epimastigotes, IC$_{50}$ 7.48 µg/mL), *Leishmania infantum* promastigotes, IC$_{50}$ 37.8 µg/mL; cytoxic (*Vero cells*, IC$_{50}$ 46.0 µg/mL, *THP-1 human monocytic leukemia*, IC$_{50}$ 53.7 µg/mL) |                                                                                                       |           |
| *P. leptorum* Kunth          | Monte Alegre do Sul, São Paulo state, Brazil | Leaf (HD)       | Seychellene (34.7%), carophyllene oxide (12.5%)                                       |                                                                                                       | [31]      |
| *P. longispicum* C. DC.       | Altos de Campana, Panama                     | Leaf (HD)       | β-Caryophyllene (45.2%), carophyllene oxide (5.5%)                                     | Mosquito larvicidal (*Aedes aegypti*, LC$_{100}$ 250 µg/mL)                                         | [47]      |
| *P. lucidum* var. granulosum Yunck. | Rio de Janeiro state, Brazil               | Leaf (HD)       | α-Pinene (30.0%), β-caryophyllene (8.0%), α-zingiberene (30.4%), β-sesquiphellandrene (11.1%) |                                                                                                       | [73]      |
| *P. madeirensis* Yunck.      | Reserva da Matinha, Ilhéus, Bahia state, Brazil | Leaf (HD)       | β-Caryophyllene (11.2%), germacrene D-4-ol (11.1%), 1,10-di-epi-cubenol (7.0%), α-vulvalol (7.1%), epio-α-vulvalol (5.4%) |                                                                                                       | [125]     |
| Piper Species                      | Collection Site                  | Essential Oil        | Major Components (>5%)                                                                 | Bioactivity of EO                                                                 | Ref. |
|-----------------------------------|----------------------------------|----------------------|----------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------|
| *P. malacophyllum* (C. Presl) C. DC. | Florianópolis, Santa Catarina, Brazil | Leaf (HD)            | α-Pinene (5.0%), camphene (30.8%), camphor (32.8%)                                      | Antibacterial (Staphylococcus aureus, MIC 3700 µg/mL, Bacillus cereus, MIC 1800 µg/mL, Acinetobacter baumannii, MIC 3700 µg/mL, Escherichia coli, MIC 1800 µg/mL; Pseudomonas aeruginosa, MIC 3700 µg/mL; antifungal (Epidermophyton floccosum, MIC 1000 µg/mL; Microsporum gypseum, MIC 1000 µg/mL; Trichophyton mentagrophytes, MIC 500 µg/mL; Trichophyton rubrum, MIC 1000 µg/mL; Candida albicans, MIC 1000 µg/mL; Cryptococcus neoformans, MIC 500 µg/mL; antiparasitic (Trypanosoma cruzi epimastigotes, K_{50} 312 µg/mL) | [56] |
| *P. manausense* Yunck.            | Ananindeua, Pará state, Brazil   | Aerial parts (HD)    | α-Pinene (5.2–6.6%), β-pinene (4.7–6.5%), β-caryophyllene (7.7–8.5%), germacrene D (3.5–6.1%), bicyclogermacrene (32.0–34.0%), δ-cadinene (5.8–7.0%), globulol (6.8–9.4%) | —                                                                                   | [144]|
| *P. manausense* Yunck.            | Acareí, Pará state, Brazil       | Aerial parts (HD)    | α-Pinene (9.1%), β-pinene (9.2%), β-caryophyllene (5.9%), bicyclogermacrene (41.0%), δ-cadinene (5.8%) | —                                                                                   | [144]|
| *P. manausense* Yunck.            | Marituba, Pará state, Brazil     | Aerial parts (HD)    | β-Caryophyllene (6.0%), aromadendrene (5.0%), bicyclogermacrene (7.8%), spathulenol (15.0%), globulol (9.4%), α-muurolol (7.8%) | —                                                                                   | [144]|
| *P. marginatum* Jacq.             | Itacoatiara, Amazonas State, Brazil | Leaf (HD)           | (E)-β-Ocimene (5.2%), α-copaene (5.9%), β-caryophyllene (9.1%), γ-elemene (8.5%), propiopiperone (18.2%) | —                                                                                   | [143]|
| *P. marginatum* Jacq.             | Itacoatiara, Amazonas State, Brazil | Stem (HD)           | δ-3-Carene (6.9%), β-caryophyllene (11.6%), myristicin (19.3%), propiopiperone (18.6%)     | —                                                                                   | [143]|
| *P. marginatum* Jacq.             | Monteverde, Costa Rica           | Aerial parts (HD)    | p-Cymene (7.1%), estragole (6.6%), p-anisaldehyde (22.0%), (E)-anethole (45.9%), anisyl methyl ketone (14.2%) | —                                                                                   | [49]  |
| *P. marginatum* Jacq.             | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD)           | —                                                                                     | Antibacterial (Escherichia coli, MIC 700 µg/mL)                                   | [52]  |
| *P. marginatum* Jacq.             | Monte Alegre, Pará state, Brazil | Leaf (HD)           | (E)-β-Ocimene (5.6%), safrole (63.9%), methylcugenol (5.9%), propiopiperone (7.3%)     | —                                                                                   | [45]  |
| *P. marginatum* Jacq.             | Xambioá, Tocantins state, Brazil | Leaf (HD)           | Safrole (52.3–52.5%), myristicin (6.3–9.3%), propiopiperone (11.8–14.1%)               | —                                                                                   | [45]  |
| *P. marginatum* Jacq.             | Nazaré, Tocantins state, Brazil  | Leaf (HD)           | Safrole (41.1%), myristicin (8.2%), propiopiperone (30.4%)                             | —                                                                                   | [45]  |
| *P. marginatum* Jacq.             | Monte Alegre, Pará state, Brazil | Leaf (HD)           | (Z)-β-Ocimene (5.3%), (E)-β-ocimene (13.5%), safrole (23.9%), β-caryophyllene (6.0%), propiopiperone (33.2%) | —                                                                                   | [45]  |
| *P. marginatum* Jacq.             | Belém, Pará state, Brazil        | Leaf (HD)           | p-Mentha-1(7),8-diene (39.0%), (E)-β-ocimene (9.8%), propiopiperone (19.0%)             | —                                                                                   | [45]  |
| *P. marginatum* Jacq.             | Alter do Chão, Pará state, Brazil | Leaf (HD)           | α-Pinene (5.0%), p-mentha-1(7),8-diene (34.8%), (E)-β-ocimene (8.7%), propiopiperone (23.1%), elemicin (6.5%) | —                                                                                   | [45]  |
| Piper Species       | Collection Site       | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|--------------------|-----------------------|---------------|-------------------------|------------------|------|
| *P. marginatum* Jacq. | Belterra, Pará state, Brazil | Leaf (HD) | p-Mentha-1(7),8-diene (22.9%), (E)-β-ocimene (8.2%), propiopiperone (40.7%) | — | [45] |
| *P. marginatum* Jacq. | Melgaço, Pará state, Brazil | Leaf (HD) | (E)-β-Ocimene (8.0%), safrole (10.4%), germacrene D (8.1%), bicyclogermacrene (6.4%), myristicin (16.0%), propiopiperone (17.4%) | — | [45] |
| *P. marginatum* Jacq. | Xinguara, Pará state, Brazil | Leaf (HD) | (Z)-β-Ocimene (8.8%), (E)-β-ocimene (15.2%), germacrene D (10.4%), myristicin (5.4%), propiopiperone (14.5%), τ-muurolol (5.0%) | — | [45] |
| *P. marginatum* Jacq. | Manaus, Amazonas state, Brazil | Leaf (HD) | Safrole (6.4%), α-copaene (7.4%), β-caryophyllene (9.5%), germacrene D (5.5%), propiopiperone (25.0%) | — | [45] |
| *P. marginatum* Jacq. | Macapá, Amapá state, Brazil | Leaf (HD) | (E)-β-Ocimene (5.5%), β-caryophyllene (10.6%), myristicin (9.6%), propiopiperone (22.9%) | — | [45] |
| *P. marginatum* Jacq. | Monte Alegre, Pará state, Brazil | Leaf (HD) | (Z)-β-Ocimene (5.7%), (E)-β-ocimene (13.5%), β-caryophyllene (9.3%), propiopiperone (40.2%) | — | [45] |
| *P. marginatum* Jacq. | Viseu, Pará state, Brazil | Leaf (HD) | γ-Terpinene (14.4%), myristicin (5.0%), propiopiperone (29.6%), spathulenol (6.6%) | — | [45] |
| *P. marginatum* Jacq. | Alta Floresta, Mato Grosso state, Brazil | Leaf (HD) | γ-Terpinene (6.5%), safrole (5.7%), β-caryophyllene (13.3%), germacrene D (8.7%), propiopiperone (7.9%) | — | [45] |
| *P. marginatum* Jacq. | Manaus, Amazonas state, Brazil | Leaf (HD) | γ-Terpinene (5.2%), (E)-β-ocimene (8.7%), α-copaene (13.4%), β-caryophyllene (10.2%), germacrene D (7.6%), bicyclogermacrene (8.2%), propiopiperone (10.4%) | — | [45] |
| *P. marginatum* Jacq. | Salvaterra, Pará state, Brazil | Leaf (HD) | p-Mentha-1(7),8-diene (5.2%), (Z)-anethole (8.4%), (E)-anethole (16.5%), isoosmorhizole (37.4%), (E)-isoosmorhizole (29.1%) | — | [45] |
| *P. marginatum* Jacq. | Manaus, Amazonas state, Brazil | Leaf (HD) | (Z)-Anethole (6.0%), (E)-anethole (26.4%), isoosmorhizole (11.2%), (E)-isoosmorhizole (32.2%) | — | [45] |
| *P. marginatum* Jacq. | Obidos, Pará state, Brazil | Leaf (HD) | (E)-Anethole (13.6%), isoosmorhizole (24.5%), (E)-isoosmorhizole (46.8%) | — | [45] |
| *P. marginatum* Jacq. | Medicilândia, Pará state, Brazil | Leaf (HD) | β-Caryophyllene (6.7%), (E)-isoosmorhizole (15.8%), crocatone (21.9%), 2′-methoxy-4′,5′-methylenedioxypropiophenone (26.3%) | — | [45] |
| *P. marginatum* Jacq. | Paredão, Roraima state, Brazil | Leaf (HD) | β-Caryophyllene (13.6%), bicyclogermacrene (11.7%), (Z)-asarone (8.8%), exalatacin (7.9%), (E)-asarone (30.8%) | — | [45] |
| *P. marginatum* Jacq. | Venadillo, Tolima, Colombia | Aerial parts (HD) | α-Phellandrene (11.1%), limonene (7.5%), β-caryophyllene (11.0%), elemicin (18.0%), isoelemicin (9.2%) | — | [120] |
| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|---------------|----------------|---------------|------------------------|------------------|------|
| P. marginatum Jacq. | Universidade Federal Rural de Pernambuco, Recife, Brazil | Leaf (HD) | β-Caryophyllene (7.5%), α-acoradene (5.1%), bicyclogermacrene (9.4%), elemol (9.7%), (Z)-asarone (30.4%), patchouli alcohol (16.0%), (E)-asarone (6.4%) | Mosquito larvicidal (Aedes aegypti, LC₅₀ 23.8 µg/mL) | [146] |
| P. marginatum Jacq. | Universidade Federal Rural de Pernambuco, Recife, Brazil | Floral (HD) | α-Copaene (9.4%), β-caryophyllene (13.1%), α-acoradene (9.7%), patchouli alcohol (23.4%), (E)-asarone (21.1%) | Mosquito larvicidal (Aedes aegypti, LC₅₀ 19.9 µg/mL) | [146] |
| P. marginatum Jacq. | Universidade Federal Rural de Pernambuco, Recife, Brazil | Stem (HD) | β-Caryophyllene (6.8%), seychellene (5.8%), elemicin (6.9%), (E)-asarone (8.5%), patchouli alcohol (25.7%), (E)-asarone (32.6%) | Mosquito larvicidal (Aedes aegypti, LC₅₀ 19.9 µg/mL) | [146] |
| P. marginatum Jacq. | Belém, Pará state, Brazil | Aerial parts (HD) | p-Mentha-1(7),8-diene (59.0%), (E)-β-cineole (9.8%), propiopiperone (59.0%) | Insecticidal (Solenopsis saevissima, IC₅₀ 240 µg/mL) | [41] |
| P. marginatum Jacq. | Manaus, Amazonas state, Brazil | Aerial parts (HD) | (E)-Anethole (26.4%), isosororhizol (11.2%), (E)-isosororhizol (32.2%) | Insecticidal (Solenopsis saevissima, IC₅₀ 439 µg/mL) | [41] |
| P. marginatum Jacq. | Venadillo, Tolima, Colombia | Aerial parts (MWHD) | α-Phellandrene (11.2%), limonene (7.6%), β-caryophyllene (11.1%), elemicin (18.4%), isoelemicin (9.3%) | Antiprotozoal (Trypanosoma cruzi epimastigotes, IC₅₀ 6.2 µg/mL, Leishmania infantum promastigotes, IC₅₀ 88.7 µg/mL), cytotoxic (Vero cells, IC₅₀ 40.2 µg/mL) | [118,122] |
| P. marginatum Jacq. | Belém, Pará state, Brazil | Aerial parts (HD) | β-Caryophyllene (5.0%), propiopiperone (21.8%), elemol (5.9%) | Antifungal, TLC bioautography (Cladosporium cladosporioides, Cladosporium sphaerospermum), enzyme inhibition (acetylcholinesterase) | [62] |
| P. mikanianum (Kunth) Steud. | Sapiranga, Rio Grande do Sul state, Brazil | Leaf (HD) | α-Piene (6.5%), myrcene (5.6%), limonene (14.8%), β-caryophyllene (10.5%), bicyclogermacrene (14.3%) | — | [134] |
| P. mikanianum (Kunth) Steud. | Atalanta, Santa Catarina state, Brazil | Leaf (HD) | Safrole (82.0%) | — | [147] |
| P. mikanianum (Kunth) Steud. | Curitiba, Paraná state, Brazil | Leaf (HD) | Bicyclogermacrene (5.3%), (Z)-isoelemicin (21.5%), (E)-asarone (11.6%), β-vetivone (33.5%) | — | [148] |
| P. mikanianum (Kunth) Steud. | Picada Café, Rio Grande do Sul state, Brazil | Aerial parts (HD) | Bicyclogermacrene (6.6%), germacrene B (7.8%), α-selinol (5.1%), apothe (64.9%) | Aacaricidal (Rhipicephalus (Boophilus) microplus, LC₅₀ 2.33 µL/mL) | [106] |
| P. mikanianum (Kunth) Steud. | Atalanta, Santa Catarina state, Brazil | Leaf (HD) | α-Thujene (8.0%), safrole (72.4%) | — | [70] |
| P. malicorum Kunth | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD) | — | Antibacterial (Escherichia coli, MIC 1000 µg/mL) | [52] |
| P. malicorum Kunth | Cultivated, FIOCRUZ, Rio de Janeiro, Brazil | Leaf (HD) | (Z)-β-Ocimene (14.1%), (E)-β-ocimene (12.1%), germacrene D (10.8%), germacrene B (13.4%), myrtenic acid (7.3%), α-selinol (9.9%), (E)-nerolidol (9.6%) | Antinociceptive (mouse model, 1 mg/kg) | [91] |
| P. mikanianum (Kunth) Steud. | Antonina, Paraná state, Brazil | Leaf (HD) | β-Caryophyllene (8.6%), α-humulene (11.3%), bicyclogermacrene (7.4%), bicyclogermacrene oxide (12.1%), viridiflorol (5.8%), humulene-epoxide II (6.5%) | Antileishmanial (L. amazonensis promastigotes, IC₅₀ 17.4 µg/mL, L. amazonensis axenic amastigotes, IC₅₀ > 200 µg/mL), Anti-Mycobacterium tuberculosis (MIC 250 µg/mL) | [70] |
| **Piper Species** | **Collection Site** | **Essential Oil** | **Major Components (>5%)** | **Bioactivity of EO** | **Ref.** |
|------------------|-------------------|------------------|--------------------------|----------------------|---------|
| *P. multiplinervium* C. DC. | Parque Nacional Soberania, Panama | Leaf (HD) | α-Pinene (7.1%), β-pinene (7.9%), α-phellandrene (11.8%), limonene (11.4%), p-cymene (9.0%), linalool (16.5%), (E)-nerolidol (5.9%) | — | [47] |
| *P. nemorense* C. DC. | Monteverde, Costa Rica | Leaf (HD) | α-Phellandrene (8.8%), limonene (6.3%), α-copaene (5.7%), β-bourbonene (14.0%), β-caryophyllene (5.6%), β-copaene (15.0%), γ-elemene (6.8%), germacrene D (8.4%), bicyclogermacrene (7.5%) | — | [34] |
| *P. oblanceolatum* Trel. | Monteverde, Costa Rica | Leaf (HD) | β-Caryophyllene (27.6%), spathulenol (10.6%), caryophyllene oxide (8.3%) | | [111] |
| *P. oblum* Ruiz & Pav. | Altos de Campana National Park, Panama | Leaf (HD) | β-Caryophyllene (27.6%), spathulenol (10.6%), caryophyllene oxide (8.3%) | — | [111] |
| *P. peltatum* L. [syn. *Pothomorphe peltata* (L.) Miq.] | Pinar del Río, Cuba | Leaf (HD) | α-Copaene (5.2%), trans-calamencene (5.4%), spathulenol (9.0%), caryophyllene oxide (22.9%) | | [27] |
| *P. permutatum* Yunck. | Tijuca Forest, Rio de Janeiro state, Brazil | Leaf (HD) | β-Caryophyllene (6.8%), δ-cadinene (12.7%), α-cadinol (6.9%) | | [149] |
| *P. ovatum* Vahl | Fazenda Sucupira, Embrapa, Brasilia, Brazil | Leaf (HD) | α-Pinene (23.1%), β-pinene (14.2%), β-caryophyllene (5.3%), germacrene D (10.3%), (E)-cubebol (10.7%) | — | [33] |
| *P. regulii* (Miq.) C. DC. | Universidade de São Paulo, Brazil | Aerial parts (HD) | Myrcene (52.6%), linalool (15.9%), β-caryophyllene (8.5%) | | [38] |
| *P. pseudolindenii* C. DC. | Turrialba, Cartago, Costa Rica | Leaf (HD) | β-Pinene (6.7%), β-elemene (15.0%), β-caryophyllene (11.8%), α-humulene (7.0%), germacrene D (9.0%), germacrene B (5.4%) | — | [133] |
| *P. regnellii* (Miq.) C. DC. | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD) | β-Caryophyllene (23.4%), (E)-nerolidol (13.7%), spathulenol (11.1%), globulol (6.1%) | — | [133] |
| *P. regnellii* (Miq.) C. DC. | Cultivated (State University of Campinas, São Paulo, Brazil) | Leaf (HD) | Myrcene (52.6%), linalool (15.9%), β-caryophyllene (8.5%) | | [38] |
| *P. regnellii* (Miq.) C. DC. | Universidade de São Paulo, Brazil | Leaf (HD) | β-Pinene (13.3%), myrcene (13.5%), β-caryophyllene (7.2%), aromadendrene (8.3%), bicyclogermacrene (9.7%), (E)-nerolidol (8.4%), spathulenol (7.8%) | — | [35] |
| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|---------------|-----------------|---------------|-------------------------|------------------|-----|
| *P. regnellii* (Miq) C. DC. var. regnellii (C. DC.) Yunck | Universidade de São Paulo, Brazil | Leaf (HD) | β-caryophyllene (8.2–9.5%), germacrene D (45.6–51.4%) and α-chamigrene (8.9–11.3%) | Cytotoxic (B16F10-Nex2 murine melanoma, IC<sub>50</sub> 66 µg/mL, A2058 human melanoma, IC<sub>50</sub> 57 µg/mL, HeLa human cervical carcinoma, IC<sub>50</sub> 13 µg/mL, SHLa human cervical, IC<sub>50</sub> 71 µg/mL, HCT human colon carcinoma, IC<sub>50</sub> 61 µg/mL, SKBR3 breast cancer, IC<sub>50</sub> 79 µg/mL, U87 human glioblastoma, IC<sub>50</sub> 71 µg/mL, β-caryophyllene, germacrene D, α-chamigrene cytotoxic to HeLa cells: IC<sub>50</sub> 11, 7, 32 µg/mL, respectively) | [98] |
| *P. renitens* (Miq.) Yunck. | Mirante da Serra, Rondonia, Brazil | Aerial parts (HD) | α-pinene (12.5%), camphene (5.6%), β-pinene (12.4%), (Z)-caryophyllene (6.9%), germacrene D (13.8%), bicyclogermacrene (6.6%), guaiol (13.9%), eudesm-7(11)-en-4-ol (9.3%) | — | [150] |
| *P. reticulatum* L. | Costa Arriba, Rio Cascajal, Colón, Panama | Leaf (HD) | β-Elemene (16.1%), β-selinene (19.0%), α-selinene (15.5%), spathulenol (6.1%) | — | [47] |
| *P. rivinoides* Kunth | Cultivated, FIOCRUZ, Rio de Janeiro, Brazil | Leaf (HD) | α-Pinene (32.5%), β-pinene (20.7%), β-caryophyllene (7.6%), germacrene B (6.7%) | Antinociceptive (mouse model, 1 mg/kg) | [91] |
| *P. rivinoides* Kunth | Ubatuba, São Paulo state, Brazil | Leaf (HD) | α-Pinene (73.2%), β-pinene (5.2%) | — | [31] |
| *P. rivinoides* Kunth | Antonina, Paraná state, Brazil | Leaf (HD) | β-Caryophyllene (66.6%), α-humulene (10.0%), dehydromadadrenane (7.8%), bicyclogermacrene (11.8%), (Z)-α-bisabolene (10.9%), spathulenol (5.1%) | Antileishmanial (L. amazonensis promastigotes, IC<sub>50</sub> 10.9 µg/mL, L. amazonensis axenic amastigotes, IC<sub>50</sub> >200 µg/mL), anti-Mycobacterium tuberculosis (MIC 125 µg/mL) | [70] |
| *P. septulinerivum* (Miq.) C. DC. | Pandó, Chocó, Colombia | Aerial parts (MWHD) | β-Caryophyllene (5.0%), epi-cubebol (9.0%), δ-cadinene (10.9%), germacrene D-4-ol (5.6%), viridiflorol (7.9%) | Antiprotozoal (Trypanosoma cruzi epimastigotes, IC<sub>50</sub> 14.0 µg/mL, Leishmania infantum promastigotes, IC<sub>50</sub> 30.1 µg/mL, L. infantum amastigotes, IC<sub>50</sub> 64.8 µg/mL), cytotoxic (Vero cells, IC<sub>50</sub> 42.7 µg/mL, THP-1 human monocytic leukemia, IC<sub>50</sub> 48.8 µg/mL) | [118] |
| *P. solmsianum* C. DC. | Teresópolis, Rio de Janeiro state, Brazil | Leaf (HD) | δ-3-Carene (23.3%), asaricin (39.2%) | The essential oil and the major component asaricin cause depressant and ataxia effects in mice | [151] |
| *P. solmsianum* C. DC. | Universidade de São Paulo, Brazil | Leaf (HD) | Spathulenol (5.2%), isoaselenec (53.5%) | Antifungal, broth dilution assay (Cryptococcus neoformans, MIC 62.5 µg/mL) Antifungal, TLC bioautography (Candida tropicalis, C. glabrata, C. krusei, C. tropicalis, C. parapsilosis) | [35,60] |
| *P. solmsianum* C. DC. | Ubatuba, São Paulo state, Brazil | Leaf (HD) | α-Pinene (22.7%), myrcene (26.1%), δ-3-carene (66.9%), α-selinene (5.5%) | — | [31] |
| *P. tectoniaefolium* (Kunth) Kunth ex C. DC. | Fazenda Sucupira, Embrapa, Brasilia, Brazil | Leaf (HD) | α-Pinene (12.9%), β-pinene (8.8%), caryophyllene oxide (10.9%) | — | [33] |
| *P. trigonum* C. DC. | Altos de Campana, Panama | Leaf (HD) | α-Copaene (6.0%), β-elemene (8.4%), β-caryophyllene (71.7%), germacrene D (19.7%), δ-cadinene (7.2%), α-cadinol (5.8%) | — | [47] |
Table A1. Cont.

| Piper Species | Collection Site | Essential Oil | Major Components (>5%) | Bioactivity of EO | Ref. |
|---------------|-----------------|---------------|-------------------------|------------------|-----|
| *P. tuberculatum* Jacq. var. *tuberculatum* | Rondônia state, Brazil | Leaf (HD) | α-Pinene (8.4%), β-pinene (7.0%), limonene (6.7%), (E)-β-ocimene (9.0%), β-caryophyllene (26.3%), (E)-β-farnesene (6.1%), α-cadinol (13.7%) | — | [152] |
| *P. tuberculatum* Jacq. | Universidade Estadual Paulista, Araraquara, São Paulo state, Brazil | Leaf (HD) | α-Pinene (10.4%), β-pinene (12.5%), (E)-β-ocimene (6.6%), β-caryophyllene (40.2%), (E)-β-farnesene (8.3%), germacrene D (5.3%) | — | [59] |
| *P. tuberculatum* Jacq. | Universidade Estadual Paulista, Araraquara, São Paulo state, Brazil | Floral (HD) | α-Pinene (28.7%), β-pinene (38.2%), (E)-β-ocimene (9.8%), β-caryophyllene (14.0%) | — | [59] |
| *P. tuberculatum* Jacq. | Universidade de São Paulo, Brazil | Leaf (HD) | (E)-Nerolidol (12.7%), spathulenol (15.8%), viridiflorol (13.5%), γ-cadinol (6.3%) | — | [35] |
| *P. umbellatum* L. | Monteverde, Costa Rica | Aerial parts (HD) | β-Elemene (6.9%), β-caryophyllene (28.3%), germacrene D (16.7%), bicyclogermacrene (6.6%), (E,E)-α-farnesene (14.5%) | — | [49] |
| *P. umbellatum* L. | Araraquara, São Paulo state, Brazil | Leaf (HD) | γ-Muurolene (8.9%), germacrene D (34.2%), bicyclogermacrene (9.0%), γ-cadinene (5.9%), α-cadinine (15.0%) | — | [35,60] |
| *P. umbellatum* L. | Topos de Collantes Nature Reserve, Escambray Mountains, Cuba | Leaf (HD) | Camphor (9.6%), safrole (26.4%), β-caryophyllene (6.6%) | Antioxidant (DPPH radical scavenging assay, IC₅₀ 32.3 µg/mL) | [50] |
| *P. variabile* C. DC. | Lachua, Alta Verapaz, Guatemala | Leaf (HD) | α-Pinene (6.1%), 1,8-cineole (10.4%), limonene (45.5%) | — | [140] |
| *P. vicosanum* Yunck. | Parque Estadual do Rio Doce, Minas Gerais state, Brazil | Aerial parts (HD) | α-Pinene (7.2%), 1,8-cineole (15.0%), limonene (40.0%), terpinolene (10.1%) | — | [153] |
| *P. vicosanum* Yunck. | Universidade Federal de Minas Gerais, Belo Horizonte, Minas Gerais state, Brazil | Aerial parts (HD) | Limonene (9.1%), γ-elemene (14.2%), α-alaskene (13.4%) | Anti-inflammatory (rat paw edema, 100–300 mg/kg) | [89] |
| *P. vicosanum* Yunck. | Dourados, Mato Grosso do Sul, Brazil | Leaf (HD) | Limonene (33.2%), (E)-nerolidol (20.6%), carvone (13.4%) | — | [129] |
| *P. xylosteoides* (Kunth) Steud. | Fazenda Sucupira, Embrapa, Brasilia, Brazil | Leaf (HD) | Myrcene (31.0%), α-terpinene (11.3%), β-caryophyllene (12.4%), γ-terpinene (26.1%) | — | [17,33] |
| *P. xylosteoides* (Kunth) Steud. | São Francisco de Paula, Rio Grande do Sul state, Brazil | Aerial parts (HD) | α-Pinene (6.0%), limonene (1.5%), zingiberene (9.3%), safrole (47.8%) | Acaricidal (Rhipicephalus (Boophilus) microplus, LC₅₀ 6.15 µL/mL) | [108] |
Table A1. Cont.

| Piper Species          | Collection Site                     | Essential Oil | Major Components (>5%)                                                                 | Bioactivity of EO                                      | Ref. |
|------------------------|-------------------------------------|---------------|----------------------------------------------------------------------------------------|--------------------------------------------------------|------|
| *P. xylosteoides* (Kunth) Steud. | Orleans, Santa Catarina state, Brazil | Leaf (HD)     | α-Pinene (7.7%), safrole (84.1%)                                                       | Antibacterial, broth dilution assay (*Bacillus cereus*, MIC 2091 µg/mL, *Staphylococcus aureus*, MIC 2091 µg/mL) | [154]|
| *P. xylosteoides* (Kunth) Steud. | São Bonifácio, Santa Catarina state, Brazil | Leaf (HD)     | α-Pinene (15.3%), safrole (75.8%)                                                       | Antibacterial, broth dilution assay (*Bacillus cereus*, MIC 2091 µg/mL, *Staphylococcus aureus*, MIC 2091 µg/mL) | [154]|
| *P. xylosteoides* (Kunth) Steud. | Ubatuba, São Paulo state, Brazil    | Leaf (HD)     | Germacrene B (10.6%), trans-β- guaiene (7.8%), (E)-nerolidol (8.2%), spathulenol (12.3%), β-copaen-4α-ol (9.4%) | —                                                      | [31] |
| *P. xylosteoides* (Kunth) Steud. | Cerro Azul, Paraná state, Brazil    | Leaf (HD)     | α-Thujene (7.9%), β-phellandrene (22.6%), δ-elemene (6.6%), β-caryophyllene (7.0%), bicyclogermacrene (7.2%), (E)-nerolidol (8.5%) | —                                                      | [70] |

a Floral = Inflorescences or infructescence “spikes”. b The essential oil had two unidentified major components (11.6% and 13.5%). c Based on retention indices (RI), this analysis is doubtful. γ-Elemene should elute before germacrene D. The compound identified as γ-elemene is probably bicyclogermacrene. γ-Cadinene should elute after germacrene D. The compound identified as γ-cadinene may be γ-muurolene. d Percentages are based on isolated yields and not by GC integration. e Only 56.6% of the essential oil composition identified.
Appendix B

Figure A1. Major monoterpenoids found in Neotropical Piper species.
Figure A2. Cont.
Figure A2. Major sesquiterpene hydrocarbons found in Neotropical Piper species.
Figure A3. Major oxygenated sesquiterpenoids found in Neotropical Piper species.

Figure A4. Major phenylpropanoids and miscellaneous compounds found in Neotropical Piper species.
### Appendix C

**Table A2.** Chemical classes and concentrations of *Piper* essential oils used for the principal component analysis.

| *Piper* Species | Classes (%) | Biological Activity | Ref. |
|-----------------|-------------|---------------------|------|
|                 | PP | MH | OM | SH | OS | Total |
| *P. aduncum*    | 0.0 | 13.7 | 40.8 | 16.8 | 24.3 | 95.6 | Antiprotozoal | [53] |
| *P. aduncum*    | 0.0 | 20.9 | 7.5 | 42.2 | 18.3 | 88.9 | Antiprotozoal | [70] |
| *P. aduncum*    | 87.8 | 0.9 | 0.0 | 6.5 | 2.4 | 97.6 | Antimicrobial | [30] |
| *P. aduncum*    | 0.0 | 14.1 | 31.8 | 26.0 | 11.6 | 83.5 | Antimicrobial | [35] |
| *P. aduncum*    | 0.9 | 9.7 | 13.4 | 19.3 | 43.9 | 87.2 | Antiprotozoal | [68] |
| *P. aduncum*    | 0.0 | 9.7 | 50.3 | 8.3 | 29.3 | 97.6 | Antiprotozoal | [32] |
| *P. aduncum*    | 0.0 | 13.7 | 31.7 | 39.8 | 11.8 | 97.0 | Antimicrobial | [59] |
| *P. aduncum*    | 0.0 | 55.1 | 11.8 | 3.7 | 11.3 | 97.6 | Antiprotozoal | [32] |
| *P. aduncum*    | 0.0 | 13.7 | 31.7 | 39.8 | 11.8 | 97.0 | Antimicrobial | [59] |
| *P. aduncum*    | 46.8 | 25.1 | 15.7 | 6.3 | 1.0 | 94.8 | Antimicrobial | [59] |
| *P. aequale*    | 0.0 | 29.2 | 0.0 | 42.9 | 20.9 | 93.0 | Antimicrobial | [34] |
| *P. aequale*    | 3.7 | 70.2 | 0.2 | 12.4 | 13.5 | 100.0 | Antimicrobial | [34] |
| *P. angustifolium* | 0.0 | 13.4 | 4.7 | 21.9 | 53.0 | 93.0 | Antiprotozoal | [69] |
| *P. anonifolium* | 0.0 | 11.7 | 0.0 | 38.6 | 38.9 | 89.2 | Antimicrobial | [61] |
| *P. aleyreanum* | 0.0 | 10.1 | 0.0 | 56.7 | 23.1 | 89.9 | Antimicrobial | [61] |
| *P. arboreum*   | 0.0 | 0.0 | 1.7 | 46.7 | 41.0 | 89.4 | Antiprotozoal | [70] |
| *P. aurotum*    | 88.5 | 3.4 | 0.7 | 3.2 | 0.6 | 96.4 | Antiprotozoal | [117] |
| *P. brendemegeri* | 0.0 | 4.5 | 0.0 | 94.9 | 0.0 | 99.4 | Cytotoxic | [34] |
| *P. caldense*   | 0.0 | 0.0 | 47.1 | 7.2 | 24.3 | 78.6 | Antimicrobial | [54] |
| *P. caldense*   | 0.0 | 0.0 | 6.5 | 17.2 | 59.7 | 83.4 | Antimicrobial | [54] |
| *P. caldense*   | 0.0 | 0.4 | 0.0 | 63.5 | 20.1 | 84.0 | Antimicrobial | [54] |
| *P. callous*    | 80.1 | 6.9 | 4.2 | 4.9 | 2.1 | 98.2 | Enzyme inhibitory | [62] |
| *P. carinum*    | 0.0 | 18.9 | 0.0 | 62.4 | 16.7 | 97.9 | Antimicrobial | [38] |
| *P. carinum*    | 0.0 | 3.1 | 0.0 | 81.5 | 15.0 | 99.4 | Antimicrobial | [38] |
| *P. corcovadensis* | 0.0 | 0.0 | 0.0 | 78.9 | 0.0 | 78.9 | Cytotoxic | [39] |
| *P. corcovadensis* | 0.0 | 52.2 | 23.2 | 0.0 | 0.0 | 75.4 | Cytotoxic | [96] |
| *P. crassinervium* | 0.0 | 20.5 | 0.0 | 31.0 | 35.0 | 86.5 | Antiprotozoal/Antimicrobial | [70] |
| *P. crassinervium* | 0.0 | 12.3 | 1.2 | 10.4 | 75.5 | 99.4 | Antimicrobial | [37] |
| *P. clausenianum* | 0.0 | 0.3 | 0.0 | 9.1 | 86.2 | 95.6 | Antiprotozoal/Antimicrobial | [71,126] |
| *P. clausenianum* | 0.0 | 1.5 | 51.4 | 7.5 | 28.3 | 88.7 | Antiprotozoal/Antimicrobial | [71,126] |
| *P. concaudatum* | 30.6 | 35.1 | 0.2 | 20.4 | 6.4 | 82.7 | Insecticidal | [127] |
| *P. crociolus*  | 0.0 | 7.8 | 0.0 | 54.8 | 37.1 | 99.7 | Antimicrobial | [60] |
| *P. demestianum* | 0.0 | 29.9 | 0.0 | 63.0 | 0.0 | 92.9 | Antiprotozoal | [72] |
| *P. diospyrifolium* | 0.0 | 19.5 | 1.3 | 68.2 | 11.2 | 100.0 | Antimicrobial | [34] |
| *P. divisum*    | 0.0 | 16.1 | 0.0 | 46.5 | 28.5 | 91.1 | Antiprotozoal | [70] |
| *P. dinicinum*  | 89.6 | 3.3 | 0.0 | 5.6 | 0.6 | 99.1 | Anticardiovascular | [40] |
| *P. dinicinum*  | 98.0 | 0.0 | 0.0 | 0.0 | 0.0 | 98.0 | Antimicrobial | [44] |
| *P. dinicinum*  | 89.1 | 7.2 | 0.1 | 1.9 | 0.2 | 98.5 | Antimicrobial | [42] |
| *P. duckei*     | 0.0 | 1.1 | 5.8 | 60.2 | 23.0 | 90.1 | Antiprotozoal | [72] |
| *P. fimbriatum* | 0.0 | 19.5 | 0.0 | 76.4 | 4.1 | 100.0 | Antimicrobial | [34] |
| *P. gaudichaudianum* | 0.0 | 2.4 | 0.0 | 44.5 | 44.0 | 90.8 | Insecticidal | [136] |
| *P. gaudichaudianum* | 0.0 | 0.1 | 0.1 | 65.4 | 28.3 | 93.8 | Cytotoxic | [139] |
| *P. gaudichaudianum* | 0.1 | 4.2 | 0.4 | 56.0 | 29.5 | 90.2 | Cytotoxic | [137] |
| *P. gaudichaudianum* | 0.0 | 0.9 | 0.0 | 72.6 | 14.4 | 87.9 | Antimicrobial | [35] |
| *P. gaudichaudianum* | 0.0 | 7.1 | 0.0 | 76.0 | 9.9 | 93.0 | Antiprotozoal | [70] |
| *P. globatum*   | 0.2 | 25.8 | 1.0 | 50.4 | 21.2 | 98.6 | Anti-inflammatory | [88] |
| *P. glabrescens* | 0.0 | 83.7 | 0.0 | 15.3 | 1.0 | 100.0 | Cytotoxic | [34] |
Table A2. Cont.

| Piper Species          | Classes (%) | Biological Activity | Ref. |
|------------------------|-------------|---------------------|------|
|                        | PP | MH | OM | SH | OS | Total |                  |
| P. hostmannianum      | 85.5 | 9.3 | 0.0 | 2.5 | 0.8 | 98.0 | Antimicrobial     |
| P. hostmannianum      | 0.0 | 18.5 | 1.0 | 52.2 | 16.6 | 88.3 | Antimicrobial/Enzyme inhibitory |
| P. hostmannianum      | 0.0 | 43.9 | 1.7 | 27.8 | 15.4 | 88.8 | Antimicrobial/Cytotoxic |
| P. hostmannianum      | 58.3 | 5.0 | 12.6 | 14.2 | 5.0 | 95.1 | Insecticidal |
| P. hostmannianum      | 57.0 | 1.0 | 5.6 | 20.1 | 10.6 | 94.3 | Insecticidal |
| P. hostmannianum      | 0.0 | 1.5 | 0.0 | 34.0 | 45.4 | 80.9 | Insecticidal |
| P. hostmannianum      | 0.0 | 0.0 | 0.0 | 46.5 | 34.1 | 80.6 | Antimicrobial |
| P. imperiale          | 6.7 | 2.7 | 0.0 | 89.4 | 1.2 | 100.0 | Antimicrobial/Cytotoxic |
| P. klotzschianum      | 98.5 | 0.0 | 0.0 | 0.6 | 0.5 | 99.6 | Insecticidal |
| P. klotzschianum      | 39.4 | 44.3 | 0.0 | 14.5 | 0.0 | 98.2 | Insecticidal |
| P. longispicum        | 1.1 | 1.4 | 0.2 | 66.0 | 11.9 | 80.6 | Insecticidal |
| P. marginatum         | 0.0 | 1.4 | 0.7 | 2.2 | 26.2 | 30.5 | Insecticidal |
| P. marginatum         | 28.4 | 0.0 | 0.0 | 44.6 | 26.2 | 99.2 | Insecticidal |
| P. marginatum         | 51.6 | 0.0 | 0.0 | 21.7 | 26.4 | 99.7 | Insecticidal |
| P. marginatum         | 42.0 | 10.3 | 1.6 | 17.6 | 17.5 | 89.0 | Antimicrobial/Enzyme inhibitory |
| P. mikanianum         | 67.9 | 0.5 | 0.0 | 23.4 | 8.6 | 100.4 | Acaricidal |
| P. mikanianum         | 0.6 | 24.2 | 9.8 | 33.2 | 25.1 | 92.9 | Antinociceptive |
| P. mikanianum         | 0.0 | 7.2 | 0.0 | 41.5 | 37.7 | 86.4 | Antiprotozoal/Antimicrobial |
| P. oblongocladatum    | 0.0 | 17.6 | 14.9 | 61.4 | 9.8 | 100.0 | Antimicrobial/Cytotoxic |
| P. obtusinerveum      | 98.5 | 0.0 | 0.0 | 0.0 | 0.0 | 99.6 | Insecticidal |
| P. regnellii          | 0.0 | 60.8 | 17.8 | 13.8 | 6.1 | 98.5 | Antimicrobial |
| P. regnellii          | 0.3 | 0.0 | 0.4 | 82.0 | 10.8 | 93.5 | Cytotoxic |
| P. rimosides          | 0.0 | 65.9 | 0.8 | 21.8 | 4.8 | 93.2 | Antinociceptive |
| P. rimosides          | 0.0 | 10.4 | 0.0 | 54.7 | 20.1 | 85.2 | Antiprotozoal |
| P. solmsianum         | 40.3 | 30.3 | 0.0 | 5.8 | 4.2 | 80.7 | Depressant/Ataxia |
| P. solmsianum         | 53.5 | 0.0 | 0.0 | 12.4 | 12.3 | 78.2 | Antimicrobial |
| P. tuberculatum       | 0.0 | 35.7 | 0.3 | 60.2 | 2.9 | 99.1 | Antimicrobial |
| P. tetracarpum        | 0.0 | 16.4 | 0.0 | 62.6 | 20.8 | 99.8 | Anti-inflammatory |
| P. tetracarpum        | 48.5 | 17.0 | 0.4 | 23.7 | 10.4 | 100.0 | Acaricidal |

Figure A5. □: Antimicrobial (fungal and bactericidal), ◆: Cytotoxic activity, ▲: Antiprotozoal (Trypanosoma spp. and Leishmania spp.), ●: Insecticidal (Aedes aegypti), ▶: Acaricidal, ♦: Anti-inflammatory; ○: Anticholinesterase, ●: Antinociceptive, ◄: Central nervous system depressant, ▲: Antimicrobial and cytotoxic, ▼: Fungicidal and Anticholinesterase.
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