Biological Properties of Essential Oils from the *Piper* Species of Brazil: A Review

Renata Takeara, Regiane Gonçalves, Vanessa Farias dos Santos Ayres and Anderson Cavalcante Guimarães

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Abstract

Piperaceae, a Latin name derived from Greek, which in turn originates from the Arabic word *babary*—black pepper, is considered one of the largest families of basal dicots, found in tropical and subtropical regions of both hemispheres. The species that belong to this family have a primarily pantropical distribution, predominantly herbaceous members, occurring in tropical Africa, tropical Asia, Central America and the Amazon region. The Piperaceae family includes five genera: *Piper*, *Peperomia*, *Manekia*, *Zippelia* and *Verhuellia*. Brazil has about 500 species distributed in the *Piper*, *Peperomia* and *Manekia* genera. The *Piper* genus, the largest of the Piperaceae family, has about 4000 species. Within the *Piper* genus, about 260–450 species can be found in Brazil. *Piper* species have diverse biological activities and are used in pharmacopeia throughout the world. They are also used in folk medicine for treatment of many diseases in several countries including Brazil, China, India, Jamaica and Mexico. Pharmacological studies of *Piper* species point toward the vast potential of these plants to treat various diseases. Many of these species are biologically active and have shown antitumor, antimicrobial, antioxidant, insecticidal, anti-inflammatory, antinociceptive, enzyme inhibitor, antiparasitic, antiplatelet, piscicide, allelopathic, antiophidic, anxiolytic, antidepressant, antidiabetic, hepatoprotective, amebicidal and diuretic possibilities.

Keywords: Piperaceae, *Piper*, essential oils, biological activities, chemical constituents

1. Introduction

Nature, in general, has produced most of the known organic substances. Among the various kingdoms of nature, the plant kingdom has contributed most significantly to the supply of
secondary metabolites. For example, essential oils derived from plants have great value due to their applications as medicines, cosmetics, food and agrochemicals [1, 2].

Essential oils constitute a complex mixture of low molecular weight substances (usually less than 500 Da) obtained by hydrodistillation or by extraction with organic solvents [2, 3]. A single plant may contain between 20 and 100 secondary metabolites belonging to different chemical classes. Terpenoids, phenylpropanoids and aromatic compounds are metabolites present in essential oils [2]. Among the terpenoids, monoterpenes and sesquiterpenes make up the largest group of substances in essential oils [2, 4].

About 3000 essential oils are produced using less than 2000 plant species, among which 300 are important from a commercial point of view. Essential oil production is 40,000–60,000 tons/year with a market value estimated at $700 million, indicating an increase in production and essential oil consumption worldwide [2].

In Brazil, the production of essential oils began at the end of the second decade of the twentieth century based on the extraction of native species to meet the demands of the foreign market. Interest in essential oils is based not only on the possibility of obtaining aromatic compounds (pleasant odor) and the application of products such as perfumes, fragrances and cosmetics, but also on possessing therapeutic properties such as insecticides, fungicides, bactericides or a precursor compound of molecules with high added value [5].

2. Piperaceae family

Piperaceae is a Latin name derived from Greek, which in turn originates from the Arabic babary, which means black pepper. It is considered one of the largest families of basal dicots, present in tropical and subtropical regions of both hemispheres [5]. In this family, there are species with a primarily pantropical distribution, having mostly herbaceous representatives (vines, shrubs and even some trees) [5, 6].

This family includes five genera: Piper, Peperomia, Manekia, Zippelia and Verhuellia [7]. They are present in tropical Africa, tropical Asia, Central America and the Amazon region [6]. Brazil is represented by about 500 species distributed in the Piper, Peperomia and Manekia genera [8]. The family is very important as a source of substances with pharmacological activities [9]. Many chemical compounds such as amides, phenylpropanoids, chromone, lignans and neolignans have been found [10].

3. Piper genus

Piper is the largest genus of the Piperaceae family [7, 11]. The species of this genus have diverse biological activities and are used in pharmacopeia throughout the world. They are also used in folk medicine for treatment of many diseases in several countries including Brazil, China, India, Jamaica and Mexico [9–11].
In Brazil, *Piper* species are distributed throughout the national territory. Among the aromatic flora of the Amazon region, there are more than a dozen species that provide essential oils that are used by the population for therapeutic purposes [12]. The decoction of *Piper callosum* leaves is used to treat diseases of the gastrointestinal tract [5, 13, 14]. Moreover, the tea of the decoction of *Piper hispidum* leaves is useful for the treatment of malaria. *Piper marginatum* is used as a tonic, carminative, stimulant, diuretic and sudorific agent against stomach, liver and gallbladder pain, toothaches, and snake and insect bites [5, 15, 16]. *Piper cavalcantei* Yuncker is called “electric sky” or “electric oil”. The decoction of its leaves is considered an excellent antipyretic and analgesic, especially for headaches. The infusion of the leaves is used as an antidiarrheal, to prevent dehydration and to combat menstrual cramps. Oil, extracted by soaking and heating, is used topically for earaches and other external pain [17].

The *Piper* species found in the Northeast of Brazil also have many uses in folk medicine, such as *Piper corcovadensis* used for toothaches [11]. The species found in the Atlantic rainforest are also used. For example, *Piper regnellii* (L.) Miq. is used as an anesthetic and anti-inflammatory agent. *Piper cernuum* Vell. is used as an analgesic (mainly for stomach aches) against liver and kidney diseases. Chewing the leaves of *Piper gaudichaudianum* Kunth. fights toothaches, while *Piper cf. lhostzkyanum* Kunth. is used to combat pain in the stomach, liver and kidney [17].

The decoction of *Piper umbellatum* leaves is used by those in the working class especially in the treatment of diseases in the digestive, urinary and respiratory tracts, and treatment of stomatitis, vaginitis and liver disorder [18, 19]. *Piper aduncum*, popularly known as pimenta-de-macaco and aperta-ruão, has been used in the treatment of gynecological diseases and intestinal disorders [14]. *Piper* sp, known as Jaborandi, is used to treat toothaches [19]. *Peperomia pellucida* H.B.K., popularly known as folha-de-vidro, is used against gastrointestinal ailments and high blood pressure and acts as a mild diuretic. The juice of the plant can be used to treat ocular diseases in general [20].

Many *Piper* species are biologically active and have shown antitumor [21], antimicrobial [22], antioxidant, insecticide, larvicide [5], anti-inflammatory, antinociceptive, enzyme inhibitor, trypanocidal, antiplatelet, piscicidal, allelopathic, anti-malaria, antileishmaniasis, anisilithiocto/antidepressant, antituberculosis, antidiabetic, nematocide, herbicide, hepatoprotective, anti-*Helicobacter pylori* [23], amebicide [24] and diuretic [25] potential.

Piperaceae’s contribution to scientific and technological knowledge is considered very significant. Chemistry studies of *Piper* species have led to the identification of a variety of new chemical compounds belonging to different classes, including alkaloids [26], amides [27], chromenes [28], derivatives of benzoic acids [29], lignans, neolignans, propenyl phenols, terpenes, steroids, chalcones, dihydrochalcones, flavones, flavanones, kavalactones, piperolides, ceramides, fatty acids [5, 10] and flavonoids [23, 26].

4. Chemical composition of essential oils of the *Piper* species from Brazil

From a chemical point of view, essential oils are complex mixtures of volatile substances that are lipophilic and usually odoriferous and liquid. They are endowed with aromas that are
almost always pleasant and colorless when recently extracted [29]. They can contain from 20 to 60 or more different compounds at various concentrations [30].

The composition of essential oils is constantly being transformed, according to seasonal variation and circadian rhythms. It may also be determined by genotype, environmental factors, and plant cultivation and collection procedures. It can vary according to geographical origin, drying, harvest time, type of fertilizer, but the main components responsible for the aroma seem to remain constant [31].

The *Piper* essential oils are characterized by the presence of monoterpenes, sesquiterpenes and phenylpropanoids with significant biological effects [10]. Essential oils of many *Piper* species in Brazil have been studied for their chemical composition (Table 1). We highlight the following species:

An analysis of the essential oil from the leaves and stem of a *P. marginatum* specimen collected in the city of Itacoatiara in the state of Amazonas showed the presence of the following: safrole (0.51 and 0.10%); 3,4-(methylenedioxy) propiophenone (8.01 and 8.92%); 2-methoxy-4,5-(methylenedioxy) propiophenone (1.10 and 1.35%); β-caryophyllene (4.01 and 5.57%); elemicin (1.32 and 1.53%); α-terpinene (0.73 and 0.45%); (E)-ocimene (2.31 and 0.68%); α-terpinolene (1.11 and 0.85%); myristicin (0.23 and 9.23%); α-pinene (0.84 and 0.68%); α-copaene (2.47 and 1.71%); γ-elemene (3.75% and trace) and α-humulene (1.34 and 0.59%) [47].

In Ref. [34], 35 constituents were identified in the essential oil from the leaves and stem of *Piper aleyreanum* collected in Porto Velho in the state of Rondônia and reported as the major components: Caryophyllene oxide (11.5%), β-pinene (9%), spathulenol (6.7%), camphene (5.2%), β-elemene (4.7%), myrtenal (4.2%), verbenone (3.3%) and pinocarvone (3.1%).

In Ref. [48] mainly non-oxygenated sesquiterpenes were identified in the chemical composition of the essential oil of seven *Piper* species of the Brazilian Atlantic Forest, with *E*-caryophyllene and germacrene D being the most frequent. However, the non-oxygenated monoterpenes (Z)-β-ocimene, α-pinene and β-pinene were also present.

From the literature about the phytochemical study of the essential oil of *Piper tuberculatum* extracted from the fruit and fine stems from a specimen collected in Rondônia, the predominance of sesquiterpenes was demonstrated, with caryophyllene oxide (32.1 and 26.6%) and (E)-caryophyllene (17.7 and 12.3%) as the major compounds [48].

According to Ref. [49], the essential oil from the leaves of *P. aduncum* collected in the city of Bocaiuva, in the state of Minas Gerais, has as major constituents the compounds 1,8-cineole (55.8%), α-terpineol (5.9%), (E)-ocimene (4.8%), (E)-pinene (4.7%) and α-pinene (4.5%). The composition analysis of the essential oil from the leaves of *Piper hispidinervum* and *P. callosum* collected in the Amazon showed that both species have safrole (98.12 and 64%) as the major constituent [12].

The study of the essential oil of three *Piper* species collected in different areas of the Federal District revealed the predominance of sesquiterpenes in all species. In the essential oil of *Piper arboreum*, the only monoterpenes identified were δ-3-carene (0.9%) and linalool (1.1%). The constituents present in the highest concentrations were bicyclogermacrene (12.1%), 10-epi-γ-eudesmol (11.6%), spathulenol (8.4%), caryophyllene oxide (10.1%)
| Species            | Part of plant used | Main chemical compounds                                      | Biological properties                                                                 | References |
|--------------------|--------------------|----------------------------------------------------------------|--------------------------------------------------------------------------------------|------------|
| *Piper angustifolium* | Leaves             | Spathulenol; caryophyllene oxide                              | Anti-leishmania (*Leishmania infantum*)                                               | [32]       |
| *P. anonifolium*    | Aerial parts       | α-pinene; β-selinene; α-selinene; selin-11-en-4-α-ol          | Cytotoxic; antifungal; antioxidant; anticholinesterase                                  | [33]       |
| *P. aleyreanum*     | Leaves, stems,    | Caryophyllene oxide; spathulenol; β-pinene; camphene; δ-elemene; β-elemene; β-caryophyllene; germacrene D; bicyclogermacrene | Antinociceptive; anti-inflammatory; gastric antiulcer; cytotoxic; antifungal; antioxidant; anticholinesterase | [33, 34] |
|                     | aerial parts       |                                                                |                                                                                      |            |
| *P. aduncum*        | Fruits, leaves    | β-pinene; E-caryophyllene; β-cubebeene; β-elemene; α-copaene; α-farnesene; 1,8-cineole; α-terpineol; dillapiole | Larvicidal (*A. aegypti L.*); osmotic and morphologic fragility of erythrocytes; antihelmintic (*Haemonchus contortus*); Antiacarid (*Rhipicephalus (Boophilus) microplus*) | [35–38]   |
| *P. callosum*       | Leaves             |                                                                | Antifungal (*C. perniciosa, P. palmivora and P. capsici*)                             | [39]       |
| *P. cernuum*        | Branches           | Camphene                                                      | Antitumoral                                                                          | [21]       |
| *P. corcovadensis*  | Leaves             | 1-butyl-3, 4-methylenedioxybenzene; terpinolene; trans-caryophyllene; α-pinene | Larvicidal (*A. aegypti L.*)                                                         | [11]       |
| *P. dioxyphyllophium* | Leaves            | (E)-eudesma-6,11-diene; (E)-caryophyllene; γ-murolene; limonene; germacrene; (E)-β-ocimene | Antifungal                                                                           | [40]       |
| *P. enckea*         | Leaves             |                                                                | Antifungal (*C. perniciosa, P. palmivora and P. capsici*)                             | [39]       |
| *P. gaudichaudianum* | Leaves            | E-caryophyllene; α-humulene; bicyclogermacrene; E-nerolidol; viridiflorol; aromadendrene; β-selinene | Cytotoxic (*Saccharomyces cerevisiae*); larvicidal (*A. aegypti L.*)               | [41]       |
| *P. hispidum*       | Aerial parts       | δ-3-carene; limonene; α-copaene; β-caryophyllene; α-humulene; β-selinene; caryophyllene oxide | Cytotoxic; antifungal; antioxidant; anticholinesterase                                  | [33]       |
| *P. hispidinervum*  | Leaves             | Safrol, α-terpinolene                                         | Antifungal (*B. sorokiniana, F. oxysporum and C. gloeosporioides*); insecticidal (*S. frugiperda*); amoebicidal (*A. polyphaga*) | [24, 42, 43]|
| *P. hostmanianum*   | Leaves             | Asaricin; myristicin                                         | Larvicidal (*A. aegypti L.*)                                                          | [44]       |
| *P. humaytanum*     | Leaves             | β-selinene; caryophyllene oxide                               | Larvicidal (*A. aegypti L.*)                                                          | [44]       |
| *P. malacophyllum*  | Leaves             | α-pinene; camphene; camphor; E-nerolidol                     | Antimicrobial; antifungal                                                             | [45]       |
| *P. marginatum*     | Leaves             | Isoelemicin; Apiol; δ-guaiene                                | Antifungal (*C. perniciosa, P. palmivora and P. capsici*); larvicidal (*A. aegypti L.*) | [35, 39]   |
| *P. nigrum*         | Seeds              | Limonene; E caryophyllene; caryophyllene oxide               | Larvicidal (*A. aegypti L.*)                                                          | [35]       |
| *P. permucronatum*  | Leaves             | Dillapiole; myristicin                                       | Larvicidal (*A. aegypti L.*)                                                          | [45]       |
| *P. vicosanum*      | Leaves             | α-Alaskene; Y-elemene; limonene                              | Anti-inflammatory                                                                     | [46]       |

Table 1. *Piper* species of Brazil with biological properties.
and \( \gamma \)-eudesmol (6.7%). The constituents with the greatest quantities in the oil obtained from the leaves of *Piper dilatatum* were \((Z)\)-\(\beta\)-ocimene (19.6%), \(\beta\)-caryophyllene (11.3%), sesquiterpene (8.8%), bicyclogermacrene (8.8%), spathulenol (6.5%) and caryophyllene oxide (5.3%). The analysis of the essential oil of *P. hispidum* leaves revealed the presence of \(\beta\)-pinene (19.7%), \(\alpha\)-pinene (9.0%), \(\delta\)-3-carene (7.4%), \(\alpha\)-cadinol (6.9%) and spathulenol (6.2%) as major compounds [50].

The analysis of the essential oil of *Piper* species of the Amazon revealed the presence of the sesquiterpenes \(\alpha\)-copaene, \((E)\)-caryophyllene and spathulenol in all species analyzed. The major compounds identified in *Piper anapense* oil were \((E)\)-caryophyllene (25.0%), \(\beta\)-selinene (15.0%) and caryophyllene oxide (17.0%). The oil of *Piper duckei* had a predominance of \((E)\)-caryophyllene (23.5%), caryophyllene oxide (18.4%), \(\beta\)-eudesmol (9.4%) and \(\alpha\)-eudesmol (9.1%). The major volatile compounds found in *Piper bartlingianum* were \(\alpha\)-cadinol (11.2%), \(\beta\)-elemene (10.5%), \(\alpha\)-muurolol (9.4%) and \((E)\)-nerolidol [51].

Analyses of the essential oils from the leaves, stems and flowers of *P. regnellii* collected in Dourados in the state of Mato Grosso do Sul revealed the presence of myrcene and anethole, with the major constituent in the stem being dillapiole. In the leaves, the main compounds were myrcene (21.9%), anethole \((E)\) (16.0%) and bicyclogermacrene (9.4%). In the stem, they were anethole \((E)\) (13.4%), dillapiole (30.4%) and myrcene (14.9%). For the flowers, they were anethole \((E)\) (28.2%), myrcene (23.0%) and bicyclogermacrene (9.6%) [52].

5. Biological activities of essential oils of the *Piper* species from Brazil

Due to their complex chemical composition, essential oils show a range of pharmacological actions, making them potential sources for the development of new drugs [53].

The antimicrobial activity of essential oils, both *in vitro* and *in vivo*, has justified research on traditional medicine focused on the characterization of their antimicrobial activity [54]. The search for more effective antimicrobial agents has become a challenge for the medical field and has gained increasing importance. According to studies by Ref. [45], the essential oil of *Piper malacophyllum* collected in Florianopolis in the state of Santa Catarina showed significant antimicrobial activity, especially antifungal activity shown to be moderate against the *Cryptococcus neoformans* yeast and the *Trichophyton mentagrophytes* filamentous fungus, both of clinical interest. This activity is attributed to the synergism of the chemical constituents present in the essential oil.

Work done with essential oils obtained from medicinal plants has shown activity on plant pathogen control that could replace the use of pesticides, which, in the long term, cause negative impacts on society and the environment due to pollution from their chemical waste [55]. The essential oils of *P. callosum*, *P. marginatum* and *Piper enckea* collected in the state of Pará showed inhibitory activity against several pathogens, including *Crinipellis perniciosa*, *Phytophthora palmivora* and *Phytophthora capsici*. *P. callosum* caused 100% mycelial inhibition of *P. capsici* at a concentration of 0.75 \(\mu\)L/mL, the best fungitoxic action on the three pathogens tested [39]. The essential oil of *P. hispidinervum* inhibited growth of the *Bipolaris sorokiniana*, *Fusarium oxysporum* and *Colletotrichum gloeosporioides* pathogens,
attributing the fungicidal effect observed in the essential oil to the presence of safrole (89%), its major component [42].

Ref. [43] evaluated the insecticidal activity of the essential oil of *P. hispidinervum*, collected in Lavras in the state of Minas Gerais, on *Spodoptera frugiperda* (Fall armyworm), attributing the effect to safrole (82%), the major component of the essential oil being analyzed. The essential oil of *Piper betle* showed insecticidal activity by inhibiting the development of *Spodoptera litura* pupae without causing damage to the *Eudrilus eugeniae* organism [56].

Ref. [33] reported anticholinesterase activity for the essential oils of *Piper anonifolium* and *P. hispidum* collected in Bahia, while the oil of *P. aleyreanum* showed high cytotoxic activity against melanoma. The oils of the three species of *Piper* analyzed showed strong antifungal activity against *Cladosporium sphaerospermum* and *Cladosporium cladosporioides*.

Essential oils from the fruits of *P. aduncum*, leaves of *P. marginatum* and seeds of *Piper nigrum*, collected in Paraíba, were tested against dengue mosquito larvae and were shown to be active. The *P. marginatum* species had the greatest larvicidal effect [35]. The essential oil of *P. corcovadensis* revealed a potent larvicidal activity against the oviposition of *Aedes aegypti* [11].

In a study conducted by Girola et al. [21], the monoterpane camphene isolated from essential oil of *P. cernuum*, collected in Cubatão in the state of São Paulo, induced apoptosis in melanoma cells, and showed antitumor activity in vivo, thus showing itself to be a promising compound in cancer therapy.

The essential oil of *Piper vicosanum* collected in the city of Dourados, in the state of Mato Grosso do Sul, demonstrated anti-inflammatory activity in rodents and did not cause acute toxicity or mutagenicity [46]. The essential oil of *P. aleyreanum* extracted from a specimen from Porto Velho in the state of Rondônia, showed antinociceptive action, as well as anti-inflammatory and gastroprotective properties with great potential for the development of phytomedicines [34].

The literature reports a wide range of essential oils from the *Piper* genus with different biological properties. The essential oil of *P. hispidinervum* collected in Porto Alegre, in the state of Rio Grande do Sul, showed amebicide action against the trophozoites of *Acanthamoeba polyphaga*, preventing its encysting. This suggests that this essential oil has the potential to develop new drugs to treat keratitis. It also demonstrated little toxic effect against Vero cells (renal cells of the African green monkey) and is not toxic at concentrations less than 0.25 mg/mL [24]. The essential oil of *Piper diospyrifolium* collected in Maringá, in the state of Parana, showed antifungal activity against *Candida albicans*, *Candida parapsilosis* and *Candida tropicalis* isolated from catheter urine, blood culture and orotracheal tube samples donated by the University Hospital of Maringá, demonstrating effective activity as a possible new phytotherapy or natural fungicide [40].

6. Conclusions and future perspectives

According to the literature, we can say that the essential oils from the *Piper* species of Brazil have many uses. In addition, they are endowed with interesting biological activities and have
a therapeutic potential. For example, they exhibit antimicrobial, anticholinesterase, antitu-
mor, anti-inflammatory activities and may be useful as natural remedies and it seems that they can be used as a suitable therapy for many pathologies. Therefore, economic importance of essential oils from the *Piper* species of Brazil is indisputable. It appears therefore imperative to preserve our natural, diverse flora and support its protection in order to keep this inexhaustible source of molecules destined for multiple targets.

**Author details**

Renata Takeara*, Regiane Gonçalves, Vanessa Farias dos Santos Ayres and Anderson Cavalcante Guimarães

*Address all correspondence to: rtakeara@yahoo.com

Federal University of Amazonas, Institute of Science and Technology, Itacoatiara, AM, Brazil

**References**

[1] Pinto AC, Silva DHS, Bolzani V, Lopes N, Epifanio RA. Produtos Naturais: Atualida-
dade, Desafios e Perspectivas. Química Nova. 2002;25:45–61. DOI: 10.1590/S0100-404220 0200080009

[2] Raut JS, Karuppayil SM. A status review on the medicinal properties of essential oils, Industrial Crops and Products. 2014;62:250–264. DOI:10.1016/j.indcrop.2014.05.055

[3] Nakatsu T, Lupo AT, Chinn JW, Kang RKL. Biological activity of essential oils and their constituents, Studies in Natural Products Chemistry. 2000;21:571–631. DOI: 10.1016/ S1572-5995(00)80014-9

[4] Carson CF, Hammer KA, Riley TV. *Melaleuca alternifolia* (Tea Tree) oil: a review of anti-
microbial and other medicinal properties, Clinical Microbiology Reviews. 2006;19:50–62. DOI: 10.1128/CMR.19.1.50-62.2006

[5] Andrade EHA, Guimarães EF, Maia JGS. Variabilidade química em óleos essenciais de espécies de *Piper* da Amazônia. FEQ/UFPA: Belém; 2009. 448p.

[6] Jaramillo MA, Manos PS. Phylogeny and patterns of floral diversity in the Genus *Piper* (Piperaceae), American Journal of Botany. 2001;88:706–716. DOI: 10.2307/2657072

[7] Samain M, Vrijdaghs A, Hesse M, Goetghheuer P, Rodriguez FJ, Stoll A, Neinhuis C, Wanke S. Verhuellia is a segregate lineage in *Piperaceae*: more evidence from flower, fruit and pollen morphology, anatomy and development, Annals of Botany. 2010;1–12. DOI: 10.1093/aob/mcq031

[8] Guimarães EF, Carvalho-Silva M. Uma nova espécie e novos nomes em *Piper* seção *Ottonia* (Piperaceae) para o Sudeste do Brasil, Hoehnea. 2009;36: 431–435. DOI: 10.1590/ S2236-89062009000300004
[9] Di Stasi LC, Oliveira GP, Carvalhaes MA, Queiroz-Junior M, Tien OS, Kakiname, SH, Reis MS. Medicinal plants popularly used in the Brazilian Tropical Atlantic Forest, Fitoterapia. 2002;73:69–91. DOI: 10.1016/S0367-326X(01)00362-8

[10] Parmar VS, Jain SC, Bisht KS, Jain R, Taneja P, Jha A, Tyagi OD, Prasad AK, Wengel J, Olsen CE, Boll PM. Phytochemistry of the Genus Piper, Phytochemistry. 1997;46:591–673. DOI: 10.1016/S0031-9422(97)00328-2

[11] Silva MFR, Bezerra-Silva PC, Lira CS, Albuquerque BNL, Neto ACA, Pontual EV, Maciel JR, Paiva PMG, Navarro DMAP. Composition and biological activities of the essential oil of Piper corcovadensis (Miq.) C. DC (Piperaceae), Experimental Parasitology. 2016;165:64–70. DOI: 10.1016/j.exppara.2016.03.017

[12] Maia JGS, Silva ML, Luz AIR, Zhogbi MGB, Ramos LS. Espécies de Piper da Amazônia Rica em Safrol, Química Nova. 1987;10:200–2004.

[13] Ritter RM, Monteiro MVB, Monteiro FOB, Rodrigues ST, Soares ML, Silva JCR, Palha, MDC, Biondi GF, Rahal SC, Tourinho MM. Ethnoveterinary knowledge and practices at Colares island, Pará state, eastern Amazon, Brazil, Journal of Ethnopharmacology. 2012;144:346–352. DOI: 10.1016/j.jep.2012.09.018

[14] Van Den Berg ME. Plantas medicinais na Amazônia — contribuição ao seu conhecimento sistemático, 2nd ed. Museu Paraense Emílio Goeldi: Belém; 1993. 207p.

[15] Brú J, Guzman JD. Folk medicine, phytochemistry and pharmacological application of Piper marginatum, Revista Brasileira de Farmacognosia. DOI: 10.1016/j.bjp.2016.03.014

[16] D'angelo LCA, Chavier HS, Torres LMB, Lapa AJ, Souccar C. Pharmacology of Piper marginatum Jacq. a folk medicinal plant used as an analgesic, anti-inflammatory and hemostatic, Phytomedicine. 1997;4:33–40. DOI: 10.1016/S0944-7113(97)80025-6

[17] Di Stasi LC, Hiruma-Lima CA. Plantas medicinais na Amazônia e na Mata Atlântica, 2nd ed. Editora UNESP: São Paulo; 2002. 604p.

[18] Roesch CMFB. Piper umbellatum L.: a comparative cross-cultural analysis of its medicinal uses and an ethnopharmacological evaluation, Journal of Ethnopharmacology. 2010;131:522–537. DOI: 10.1016/j.jep.2010.07.045 2010

[19] Brandão MGL, Pignal M, Romanuic S, Grael CFF, Fagg CW. Useful Brazilian plants listed in the field books of the French naturalist Auguste de Saint-Hilaire (1779–1853), Journal of Ethnopharmacology. 2012;143:488–500. DOI: 10.1016/j.jep.2012.06.052 2012

[20] Almeida MZ. Plantas medicinais, 3rd ed. EDUFBA: Salvador; 2011. 221p.

[21] Girola N, Figueiredo CR, Farias CF, Azevedo RA, Fereira AK, Texira SF, Capello TM, Martins EGA, Matsuo AL, Travessos LR, Lago JHG. Camphene isolated from essential oil of P. cernuum (Piperaceae) induces intrinsic apoptosis in melanoma cells and displays antitumor activity in vivo, Biochemical and Biophysical Research Communications. 2015;467:928–934. DOI: 10.1016/j.bbrc.2015.10.041
[22] Kitamura ROS, Romoff P, Young MCM, Kato MJ, Lago JHG. Chromenes from Peperomia serpens (Sw.) Loudon (Piperaceae), Phytochemistry. 2006;67:2398–2402. DOI: 10.1016/j.phytochem.2006.08.007

[23] Nascimento JC, Paula VF, David JM, David JP. Occurrence, biological activities and $^{13}$C NMR data of amides from Piper (Piperaceae), Quimica Nova. 2012;35:2288–2311. DOI: 10.1590/S0100-40422012001100037

[24] Sauter IP, Rossa GE, Lucas AM, Cibulski SP, Roehe PM, Silva LAA, Rott MB, Vargas RMF, Cassel E, Poser GL. Chemical composition and amoebicidal activity of Piper hispidinervum (Piperaceae) essential oil, Industrial Crops and Products. 2012;40:292–295. DOI: 10.1016/j.indcrop.2012.03.025

[25] Novaes AS, Mota JS, Barison A, Veber CL, Negrão FJ, Kassuya CAL, Barros ME. Diuretic and antilithiasic activities of ethanolic extract from Piper amalago (Piperaceae), Phytomedicine. 2014;21:523–528. DOI: 10.1016/j.phymed.2013.10.014

[26] Facundo AV, Bálico LJ, Lima DKS, Santos ARS, Morais SM, Silva GVJ, Militão JLT. Non-substituted B-ring flavonoids and an indole alkaloid from Piper aleyreanum (Piperaceae), Biochemical Systematics and Ecology. 2012;45:206–208. DOI: 10.1016/j.bse.2012.07.010

[27] Kaou AM, Mahiou-Leddet V, Canlet C, Debraver L, Hutter S, Azas N, Ollivier E. New amide alkaloid from the aerial part of Piper capense L.f. (Piperaceae), Fitoterapia. 2010;81:632–635. DOI: 10.1016/j.fitote.2010.03.006

[28] Parra JE, Delgado WA, Cuca LE. Cumanensic acid, a new chromene isolated from Piper cf. cumanense Kunth. (Piperaceae), Phytochemistry Letters. 2011;4:280–282. DOI: 10.1016/j.phytol.2011.04.015

[29] Parra JE, Patiño OJ, Pietro J, Delgado WA, Cuca LE. A new benzoic acid derivative isolated from Piper cf. cumanense Kunth (Piperaceae), Phytochemistry Letters. 2013;6:590–592. DOI: 10.1016/j.phytol.2013.07.014

[30] Simões CMO, Schenkel EP, Gosman G, Mello JCP, Mentz LA, Petrovick PR. Farmacognosia: da Planta ao medicamento, 6th ed. UFRGS: Porto Alegre; 2007. 1102p.

[31] Bakkali F, Averbeck S, Averbeck D, Idaomar M. Biological effects of essential oils—a review, Food and Chemical Toxicology. 2008;46:446–475. DOI: 10.1016/j.fct.2007.09.106

[32] Bosquirolí LSS, Demarque DP, Rizk YS, Cunha MC, Marques MCS, Matos MFC, Kadri MCT, Carollo CA, Arruda CCP. In vitro anti-Leishmania infantum activity of essential oil from Piper angustifolium, Revista Brasileira de Farmacognosia. 2015;25:124–128. DOI: 10.1016/j.bjp.2015.03.008

[33] Silva JKR, Pinto LC, Burbano RMR, Montenegro RC, Guimarães EF, Andrade EHA, Maia JGS. Essential oils of Amazon Piper species and their cytotoxic, antifungal, antioxidant and anti-cholinesterase activities, Industrial Crops and Products. 2014;58:55–60. DOI: 10.1016/j.indcrop.2014.04.006

[34] Lima DKS, Ballico LJ, Lapa FR, Gonçalves HP, Souza LM, Iacomini M, Werner MFP, Baggio CH, Pereira IT, Silva LM, Facundo VA, Santos RS. Avaliação da antinociceptivo
antiúlcera, anti-inflamatória e gástrica atividades do óleo essencial de *Piper aleyreanum* C.DC em roedores, *Journal of Ethnopharmacology*. 2012;142:274–282. DOI: 10.1016/j.jep.2012.05.016

[35] Costa JGM, Santos PF, Brito SA, Rodrigues FFG, Coutinho HDM, Botelho MA, Lima SG. Composição Química e Toxicidade de Oleos Essenciais de Espécies de *Piper* Frente a Larvas de *Aedes aegypti* L. (*Diptera: Culicidae*), *Latin American Journal of Pharmacy*. 2010;29:463–467.

[36] Barros FJ, Costa RJO, Cesário FRAS, Rodrigues LB, Costa JGM, Coutinho HDM, Galvão HBF, Menezes IRA. Activity of essential oils of *Piper aduncum* anf and *Cinnamomum zeylanicum* by evaluating osmotic and morphologic fragility of erythrocytes. *European Journal of Integrative Medicine*. 2015. DOI: 10.1016/j.eujim.2016.02.011

[37] Oliveira GL, Vieira TM, Nunes VF, Ruas MO, Duarte ER, Moreira DL, Kaplan MAC, Martins ER. Chemical composition and efficacy in the egg-hatching inhibition of essential oil of *Piper aduncum* against *Haemonchus contortus* from sheep, *Revista Brasileira de Farmacognosia*. 2014;24:288–292. DOI: 10.1016/j.rbfp.2014.07.004

[38] Silva WC, Martins JRS, Souza HEM, Heinzen H, Cesio MV, Mato M, Albrecht F, Azevedo JL, Barros NM. Toxicity of *Piper aduncum* L. (Piperales: Piperaceae) from the Amazon forest for the cattle tick *Rhipicephalus* (Boophilus) microplus (Acari: Ixodidae), *Veterinary Parasitology*. 2009;164:267–274. DOI:10.1016/j.vetpar.2009.06.006

[39] Silva DMH, Bastos CN. Atividade antifúngica de óleos essenciais de espécies de *Piper* sobre *Crinipellis perniciosa, Phytophthora palmivora* e *Phytophthora capsici*, *FEBS Letters*. 2007;32:143–145. DOI: 10.1590/S0100-41582007000200008

[40] Vieira SCH, Paulo LF, Svidzinski TIE, Dias-Filho BP, Nakamura CV, Young MCM, Cortez DAG. Antifungal activity of *Piper diospyrifolium* kunth (Piperaceae) essential oil, *FEBS Letters*. 2011;42:1001–1006. DOI: 10.1590/S1517-83822011000300020

[41] Sperotto ARM, Moura DJ, Péres VF, Damasceno FC, Caramão EB, Henriques JAP, Saffi J. Cytotoxic mechanism of *Piper gaudichaudianum* Kunth essential oil and its major compound nerolidol, *Food and Chemical Toxicology*. 2013;57:57–68. DOI: 10.1016/j.fct.2013.03.013

[42] Zacaroni LM, Cardoso MG, Souza PE, Pimentel FA, Guimarães LGL, Salgado APSP. Potencial fungitóxico do óleo essencial de *Piper hispidinervum* (pimenta longa) sobre os fungos fitopatogênicos *Bipolaris sorokiniana, Fusarium oxysporum* e *Colletotrichum gloeosporioides*, *Acta Amazonica*. 2009;39:193–198. DOI: 10.1590/S0044-59672009000100020

[43] Lima RK, Cardoso MG, Moraes JC, Melo BA, Rodrigues VG, Guimarães PL. Atividade inseticida do óleo essencial de pimenta longa (*Piper hispidinervum* C. DC.) sobre lagartado-cartucho do milho *Spodoptera frugiperda* (J. E. Smith, 1797) (*Lepidoptera: Noctuidae*), *Acta Amazonica*. 2009;39:377–378. DOI: 10.1590/S0044-59672009000200016

[44] Morais SM, Facundo VA, Bertimi LM, Cavalcanti ESB, Junior JFA, Ferreira SA, Brito ES, Neto MAS. Chemical composition and larvicidal activity of essential oils from *Piper* species, *Biochemical Systematics and Ecology*. 2007;35:670–675. DOI: 10.1016/j.bse.2007.05.002
[45] Santos TG, Rebelo RA, Dalmarco EM, Guedes A, Gasper AL, Cruz AB, Schmit AP, Cruz RCB, Steindel M, Nune RK. Composição química e avaliação da atividade antimicrobiana do óleo essencial das folhas de *Piper malacophyllum* (C. PRESL.) C. DC, FEBS Laters. 2012;35:477–481. DOI: 10.1590/S0100-40422012000300007

[46] Brait DRH, Vaz MSM, Arrigo JS, Carvalho NMB, Araújo FHS, Vani JM, Mota JS, Cardoso CAL, Oliveira RJ, Negrão FJ, Cassuya, CAL, Arena AC. Toxicological analysis and anti-inflammatory effects of essential oil from *Piper vicosanum* leaves, Regulatory Toxicology and Pharmacology. 2015;73:699–705. DOI: 10.1016/j.yrtph.2015.10.028

[47] Gobbo-Neto L, Lopes PN. Plantas medicinais: fatores de influência no conteúdo de metabólitos secundários, Química Nova. 2007;30:374–381. DOI: 10.1590/S0100-4042200700200026

[48] Santos PRD, Moreira DL, Guimarães EF, Kaplan MAC. Essential oil analysis of 10 Piperaceae species from the Brazilian Atlantic forest, Phytochemistry. 2001;58:547–551. DOI: 10.1016/S0031-9422(01)00290-4

[49] Facundo VA, Pollli AR, Rodrigues RV, Militão JSLT, Stabelli RG, Cardoso CT. Constituentes químicos fixos e voláteis dos talos e frutos de *Piper tuberculatum* Jacq. e das raízes de *P. hispidum* H. B. K, Acta Amazonica. 2008;38:733–742. DOI: 10.1590/S0044-59672008000400018

[50] Potzernheim CL, Bizzo HR, Vieira FV. Nálise dos óleos essenciais de três espécies de *Piper* coletadas na região do Distrito Federal (Cerrado) e comparação com óleos de plantas procedentes da região de Paraty, RJ (Mata Atlântica) Brazilian Journal of Pharmacognosy. 2006;16:246–251. DOI: 10.1590/S0102-695X2006000200019

[51] Santos AS, Andrade EHA, Zoghbi MGB, Luz AIR, Maia JGS. Sesquiterpenes of Amazonian *Piper species*, Acta Amazonica. 1998;28:127–130. DOI: 10.1590/1809-43921998282130

[52] Santos AL, Polidoro AS, Schneider JK, Cunha ME, Saucier C, Jacques RA, Cardoso CA, Mota JS, Camarão EB. Comprehensive two-dimensional gas chromatography time-of-flight mass spectrometry (GC × GC/TOFMS) for the analysis of volatile compounds in *Piper regnellii* (Miq.) C. DC, Microchemical Journal. 2015;118:242–251. DOI: 10.1016/j.microc.2014.07.007

[53] Amaral JFD. Atividade antiinflamatória, antinociceptiva, e gastroprotetora do óleo essencial de croton sonderianus muell.arg. [dissertação]. Fortaleza: Universidade Federal do Ceará; 2004.

[54] Agarwal V, Lal P, Pruthi V. Effect of plant oils on *Candida albicans*. Jounal of Microbiology, Immunology and Infection. 2010;43:447–451. DOI: 10.1016/S1684-1182(10)60069-2

[55] Moreira MR, Ponce AG, Del-Valle CE, Roura SL. Inhibitory parameters of essential oils to reduce a foodborne pathogen, LWT—Food Science and Technology. 2005;38:565–570. DOI: 10.1016/j.lwt.2004.07.012
[56] Vasantha-Srinivasan P, Senthil-Nathan S, Thanigaivel A, Edwin E-S, Ponsankar A, Selin-Rani S, Pradeepa V, Sakthi-Bhagavathy M, Kalaivani K, Hunter WB, Duraipandiyan V, Al-Dhabi NA. Developmental response of *Spodoptera litura* Fab. to treatments of crude volatile oil from *Piper betle* L. and evaluation of toxicity to earthworm, *Eudrilus eugeniae* Kinb, Chemosphere. 2016;155:336–347. DOI: 10.1016/j.chemosphere.2016.03.139
