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Review

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Introduction

The Acanthaceae family, order Scrophulariales, superorder Lamiiflorae (sensu Dahlgren), comprises almost 250 genera with 2500 species. Its species are widespread in tropical regions of the world (Wasshausen & Wood, 2004) and are poorly represented in temperate regions (Mabberley, 1997). *Justicia* is the largest genus of Acanthaceae, with approximately 600 species that are found in pantropical and tropical regions (Durkee, 1986).

The species of *Justicia* are described as erect or scandent perennial herbs or subshrubs. Leaves present cystoliths and are petiolate with a leaf margin that is usually entire. Inflorescences are in spikes or panicles cimas, and the species rarely has solitary, terminal, or axillary flowers. The bracts and bracteoles are usually conspicuous and imbricate. The species of *Justicia* can be easily recognized by their bilabial corolla, with a posterior lip that is generally two-lobed, an anterior lip that is three-lobed, two stamens, a capsule with four seeds, and a basal sterile portion (Graham, 1990; Braz et al, 2002).

Table 1 shows the vegetal species of the genus *Justicia* with previous chemical and/or biological studies, indicating their botanical synonymy, popular name, and geographical distribution. Few species of *Justicia* have been studied (36 species of approximately

Chemical constituents and biological activities of species of *Justicia* - a review

Geone M. Corrêa,*,1,2 Antônio F. de C. Alcântara¹

¹Departamento de Química, ICEx, Universidade Federal de Minas Gerais, Brazil, ²Instituto de Ciências Exatas e Tecnologia, Universidade Federal do Amazonas, Brazil.

Abstract: The Acanthaceae family is an important source of therapeutic drugs, and the ethnopharmacological knowledge of this family requires urgent documentation as several of its species are near extinction. *Justicia* is the largest genus of Acanthaceae, with approximately 600 species. The present work provides a review addressing the chemistry and pharmacology of the genus *Justicia*. In addition, the biological activities of compounds isolated from the genus are also covered. The chemical and pharmacological information in the present work may inspire new biomedical applications for the species of *Justicia*, considering atom economy, the synthesis of environmentally benign products without producing toxic by-products, the use of renewable sources of raw materials, and the search for processes with maximal efficiency of energy.

600 cataloged species), with fifteen species found in the Americas, thirteen species in Asia, and eight species in Africa. Among the studied species, 31 species have ethnopharmacological/pharmacological information, 23 species were chemically investigated, and only eighteen species were chemically and biologically studied, mainly in the last decade. The most studied species are *Justicia pectoralis* Jacq., *Justicia procumbens* L., *Justicia gendarussa* Burm. f., and *Justicia anselliana* (Nees) T. Anderson. Consequently, the phytochemical and biological potential of other species of *Justicia* have yet to be fully explored.

Material and Methods

An extensive search in original and review articles was carried out in this work. The keywords used for this review were *Justicia*, Acanhaceae and Medicinal Plants. The search was performed accessing SciFinder, ScienceDirect, Web of Science, and Scielo web sites, updated to May 2011. From the literature search, all plants/herbal of *Justicia* preparations that are used ethnomedically were included in this review. More than 90% of the references obtained were later consulted.

Ethnopharmacological information for the species of *Justicia*

Several species of Justicia are widely used in folk medicine (as shown in Table 2) for the treatment of respiratory and gastrointestinal diseases (thirteen and ten occurrences, respectively) as well as inflammation (ten occurrences, including applications in rheumatism and arthritis). The plants are also utilized for their effects on the central nervous system as hallucinogens, somniferous agents, sedatives, depressors, and treatments for epilepsy and other mental disorders, with eleven occurrences. Other species are popularly used in the treatment of headache and fever (eight occurrences, which may be associated with their sedative and analgesic properties), cancer (seven occurrences), diabetes (three occurrences), and HIV (two occurrences).

Whole plant and aerial parts are usually used in folk medicine. Extracts made from only the leaves are the most used (nineteen occurrences), followed by those extracts made from only the roots (five occurrences). Some species are used as mixtures (three occurrences). For example, traditional physicians around Kotagiri village near Ootacamund use a mixture of the powdered roots of Cassia occidentalis L., Caesalpineae, Derris brevipes var. coriacea, Papillionaceae, and Justicia simplex D. Don, Acanthaceae, to control fertility. Administration of this mixture for a few days after menstruation prevents conception without any toxic effects. The number of pregnancies among treated women was significantly less than that of the control group. These results indicate the abortifacient nature of the roots of these plants (Badami et al., 2003). The species Justicia pectoralis Jacq. is used as the major component in a mixture to treat various diseases. Moreover, Justicia insularis T. Anderson is used as an infusion mixed with the leaves of Ambrosia maritime L., Compositae.

Pharmacological tests of species of Justicia

Table 3 shows the pharmacological activities of the species of *Justicia* described in the literature. Some species show antitumoral activity against different cancer cell lines (seven occurrences). An ethanol extract of *Justicia neesii* Ramamoorthy (Acanthaceae) exhibited anticancer activity against P388 lymphocytic leukemia in mice. A methanol extract of the whole plant of *Justicia procumbens* L. showed significant inhibitory activity *in vivo* against P-388 lymphocytic leukemia growth and *in vitro* cytotoxicity in the 9-KB (human nasopharyngeal carcinoma) cell culture assay (Chen et al., 1995). Some species also showed inhibition of human cancer cell lines, mainly toward human cervical carcinoma (*Justicia ciliata* Jaqc.), T 47D and HeLa human cell lines (*Justicia spicigera* Schltdl.), and human ovarian cancer cell line (*Justicia rhodoptera* Baker), as well as prevention of some tumoral cell growth (*Justicia patentiflora* Hemsl.). The activity of popularly used whole-plant extracts of *J. procumbens* and *J. nesii* and leaf extracts of *J. specigera* as anticancer agents (Table 2) was confirmed by employing the same parts of the plant, as seen in Table 3. However, the anticancer properties of *Justicia adhatoda* L. have not yet been confirmed pharmacologically.

The whole-plant extract of *J. spicigera* contains cytotoxic factors for leukemic cells and has no proliferative activity on normal hematopoietic progenitor cells. The plant extract induces apoptosis in the human leukemia cell line TF-1, but not in the bcl-2 transfectant cell line TB-1. These data suggest a strong correlation between the cytotoxic effect and cell proliferation. The results indicate that the infusion of the aerial parts of *J. spicigera* does not contain any hematopoietic activity, induces apoptosis inhibited by bcl-2, and is linked to cell proliferation.

Some species show antiviral activity (five occurrences, *i.e., Justicia extensa* T. Anderson, *Justicia gendarussa* Burm. f., *J. procumbens, Justicia reptans* Sw., and *Justicia valida* Ridl.) against *in vitro* HIV type 1 reverse transcriptase, HIV replication, and vesicular stomatitis virus (Table 3). However, the species popularly used as antiviral agents, *Justicia betonica* L. and *Justicia flava* (Vahl) Vahl (see Table 2), were either not included in pharmacological studies, or were tested but did not show antiviral activity. Crude water extracts of the aerial parts of *J. gendarussa* proved to be strongly active against *in vitro* HIV type 1 reverse transcriptase (as shown in Table 3). Based on these observations, this species might be further explored for its antiviral indications.

J. pectoralis showed high antibacterial activity against *E. coli, E. faecalis,* and *S. epidermidis.* Moreover, this species shows positive antimosquito tests, which were observed on the growth and development of IV-stage larvae of *Aedes aegypti* mosquitoes. A brief exposure to concentrations of 0.05 to 0.50 mg/mL of the plant extract is required to produce 100% larvicidal activity. The extracts of *J. pectoralis* were found to be the most toxic larvicide among the species of *Justicia* extracts tested. Extracts of *J. pectoralis* have estrogenic, progestagenic, and anti-inflammatory effects, explaining the plant's traditional use in menopause and PMS therapies.

The methanol extract of the whole plant of *J. procumbens* exhibited 50% inhibitory activity toward the arachidonic acid-induced aggregation of rabbit platelets (Chen et al., 1995; Chen et al., 1996). The antiplatelet aggregation activity can be related to the popular use of extracts obtained from *Justicia* *ansellian*a (Nees) T. Anderson in the treatment of heart disease (Table 2).

The ethanol extract of the leaves of *J.* gendarussa showed a higher paw edema inhibition than aspirin-treated rats in the FCA-induced and the collagen-induced arthritic models (Table 3). These pharmacological results align with the popular use of *J.* gendarussa in the treatment of arthritis and rheumatism (see Table 2). The species *J. spicigera* is popularly used as an anti-inflammatory agent (Table 2), and this activity was also pharmacologically confirmed (see Table 3).

The popular use of J. pectoralis in the treatment of epilepsy and anxiety (as shown in Table 2) was confirmed with the ethanol extract of the leaves (Table 3). The ethanol extracts of J. pectoralis, Justicia aurea Schltdl., and Justicia albobracteata Leonard were tested in vitro for their ability to inhibit GABAtransaminase (GABA-T) or to bind to the GABAAbenzodiazepine receptor, two principal drug targets in epilepsy and anxiety. A significant positive correlation between GABA-T inhibition and the relative frequency of use for epilepsy was observed. Moreover, an even stronger correlation between GABAA binding and the relative frequency of use for shock was observed. Thus the Q'eqchi' traditional knowledge of J. pectoralis, J. aurea, and J. albobracteata is associated with the plant's antiepileptic and anxiolytic activities.

The pharmacological studies of some species were not based on their use in folk medicine. Extracts of the whole plant of Justicia prostrata Gamble showed antiulcer activity (Table 3). The aqueous extract was more active than the alcoholic extract when tests were made using the aspirin-induced pylorus ligated rat model. The antiulcerogenic activities of both extracts were compared with the drug Rantidine, an H2-receptor antagonist. Alcoholic extracts of J. anselliana showed allelopathic properties (Table 3). The aerial part of the plant produced more significant effects on the growth parameters of the cowpea plant (Vigna unguiculata (L.) Walp., Leguminosae), such as germination, elongation, and the weight, than extracts of the root (Ahanchede et al., 2004). Likewise, the popular use of the leaves of Justicia schimperiana (Hochst. ex Nees) T. Anderson in the treatment of liver disease (Table 2) may be related to the hepatoprotective activity of the leaf extracts of the plant (Table 3). However, the hepatoprotective activity of J. adhatoda (Table 3) was not studied despide its popular use. In addition, some other species, such as J. betonica, Justicia calycina (Nees) V.A.W.Graham, Justicia diffusa Willd., Justicia dumetorum Morong, J. flava, Justicia ghiesbreghtiana Lem., Justicia ideogenes, J. insularis, Justicia plectrantus, Justicia purpurea L., Justicia secunda Vahl, Justicia sericea Ruiz & Pav., and J. simplex, showed a variety of popular

uses and have no yet been studied pharmacologically.

Compounds isolated from species of Justicia

A great diversity of chemical classes is found in the species of Justicia, mainly alkaloids, lignans, flavonoids, and terpenoids (iridods, diterpenoids, and triterpenoids). Other chemical classes have been isolated from species of Justicia, such as essential oils, vitamins, fatty acids (docosanoic acid), and salicylic acid (Angonese et al., 1992; Al-Juaid & Abdel-Mojib, 2004). The steroids campesterol, stigmasterol, sitosterol, and sitosterol-D-glucoside were isolated from the leaves and roots of J. flava, J. spicigera, and J. gendarussa (Olaniyi, 1980; Wahi et al., 1974; Domínguez et al., 1990; Amborabé et al., 2002; Deepak et al., 2002; Rajakumar & Shivana, 2009). The literature describes the allelopathy effect of the sterols and triterpenes. Both of the chemical classes isolated from the alcoholic extract of the aerial parts of J. anselliana showed allelopathic effects on cowpea plants (Kpoviessi et al., 2006). The allelopathic effects of the leaf and root extracts of J. anselliana have also been described, as shown in Table 3.

Table 4 shows a coumarin, flavonoids, alkaloids, and triterpenoidal glycosides isolated from the species of *Justicia*. Only one coumarin, umbeliferone (1), and a small variety of flavonoids (2-5), alkaloids (6-13), and triterpenoidal glycosides (14-21) were identified.

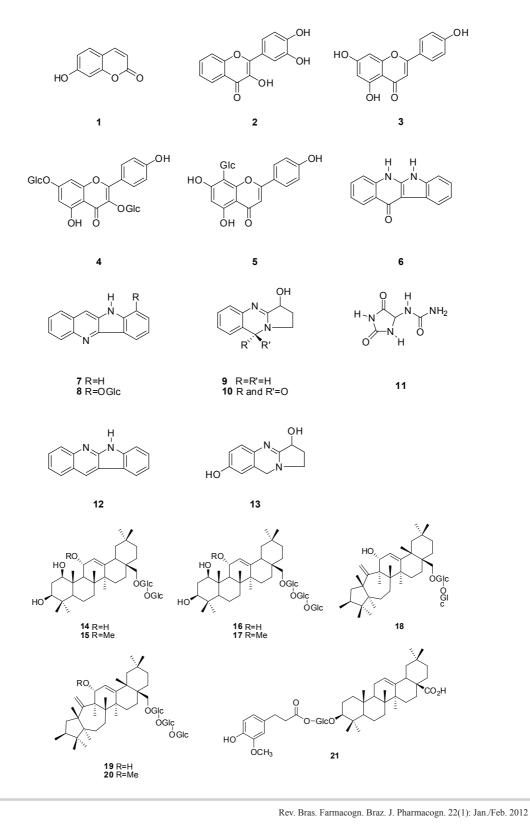
Leaf extracts from *J. reptans* display a clear virucidal effect on HIV, which was attributed to two glycosylated flavonoids that have not yet been identified (Bedoya, 2008). Compounds of this chemical class have been previously reported to display anti-HIV properties including reverse transcriptase or integrase inhibition, but this is the first time that they are described as virucides (Kumar et al., 2005). Pharmacological tests using the ethanol extract from *J. reptans* indicated inhibition of HIV replication (Table 3).

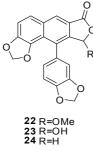
A large variety of lignans has been isolated from species of *Justicia* (Table 5). Lignans are a large group of natural products that show diverse biological effects. Lignans may serve as lead compounds for the development of new therapeutic agents with cytotoxic activity (Fukamiya & Lee, 1986; Hui et al., 1986). For example, lignans obtained from *J. pectoralis* are cytotoxic to leukemia and solid tumor cell lines (Hui et al., 1986).

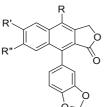
Lignans also show antiangiogenic, antileishmanial, antifungal, hypolipidemic, antiasthmatic (Vasilev & Ionkova, 2005), antiviral (Asano et al., 1996), antineoplastic (Gordaliza et al., 2000), antifeedant (Bedoya et al., 2008), insecticidal, cardiotonic, antidepressant (Ghosal et al., 1979), analgesic, antiplatelet (Chen et al., 1996), and anti-inflammatory (Navarro et al., 2004) indications, as well as activity as lipid peroxidation inhibitors. Potent anti-inflammatory activities were described for lignan glycosides isolated from *J. ciliata* (Day et al., 2000) and phenolic compounds isolated from *J. prostrata* (Sanmugapriya et al., 2005b).

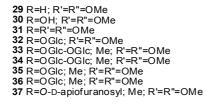
Many lignans contain an arylnaphthalide

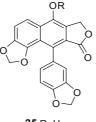
skeleton (22-54) and are found in relatively high proportions (Rajasekhar & Subbaraju, 2000). For example, jusmicranthin (22) was isolated from a chloroform extract of *J. neesii*, giving a mass yield of 0.025%. The dry leaves of *J. extensa* contain approximately 1% of justicidin P (47), which exists at



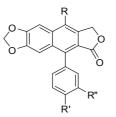




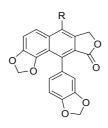




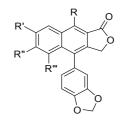
25 R=H 26 R=Me



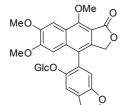
38 R=H; R'=R"=OMe **39** R=OMe; R'=OH; R"=OGIc **40** R=R"=OMe; R'=OH **41** R=OH; R'=R"=OMe



27 R=H 28 R=OMe

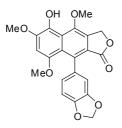


42 R=R'=H; R"=OH; R"'=OGIc **43** R=R'=R"OMe; R"'=H

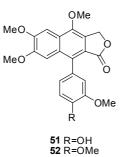


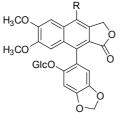


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45 R=H 46 R=OMe

OGIc

49 R=CH₂-O- β -D-xylopyranosyl

C

OH

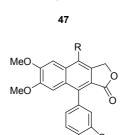
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R.

MeO

MeO

50 R=CH₂OH

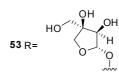


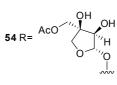
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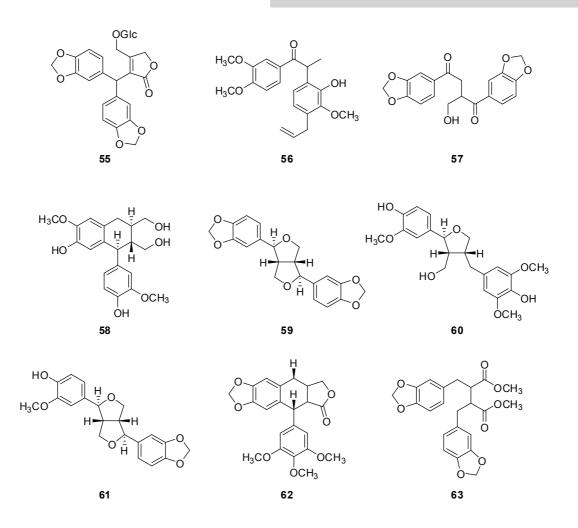
OMe

OCH₃

ò







25 °C as two rotamers (Wang & Ripka, 1983). Some arylnaphthalide lignans are glycosylated derivatives (**32-37**, **39**, **42**, and **49**). Other miscellaneous-type lignans are also found in species of *Justicia* (**55-63**).

Biological activity of compounds isolated from species of *Justicia*

Some compounds show biological activities related to those observed in the species from which they are isolated. Coumarin umbeliferone (1), isolated from hydroalcoholic extract of the leaves of *J. pectoralis* (Table 4), showed anti-inflammatory, antinociceptive, and bronchodilator activities, which are related to the estrogenic, progestogenic, and antiinflammatory activities of this species (Table 3) and its popular use in the treatment of bronchitis (Table 2). This species is also popularly used in the treatment of respiratory diseases (Table 2). The vasodilator activity of the flavonoid **2** is related to the anti-hypertensive activity of the *Justicia cataractae* Leonard, as shown in Table 3. Apigenin (**3**) has been reported to exert antiinflammatory effects such as lowering oxidative stress and forestalling the expression of several inflammatory factors (Sawatzky et al., 2006). The flavonoid vitexin (5) is a potent anti-inflammatory agent, inhibiting the 5-lipoxygenase pathway, which, together with the COX-2 pathway, is very important in producing and maintaining inflammation (Sridhar et al., 2006). Compounds 3 and 5 were isolated from the ethanol extract of J. gendarussa, which is used in the treatment of inflammation, rheumatism, and arthritis in folk medicine (see Table 2). The antimicrobial and antiinflammatory activities of flavonoid 4 (Table 4), as well as its effects on macrophage regulation and reduction in blood glucose levels are related to the popular uses of J. spicigera in giardicidal, anti-inflammatory, anticancer, and antidiabetes therapies (Tables 2 and 3). Alkaloid 11, also isolated from J. spicigera, is used as an antiinflammatory agent (Table 2).

Alkaloids 9, 10, and 13 show bronchodilator activity (Table 4) and were isolated from *J. adhatoda*, which is popularly used in the treatment of bronchitis (Table 2). The antifertility activity of triterpenoidal glycoside 21 (Table 4) is related to the popular use of *J. simplex* as an abortifacient and to control fertility (Table 2). Alkaloids 7 and 8 show antitumor activity (Table 4) and were isolated from *J. betonica*, however, this species is popularly used in the treatment of diarrhea, inflammations, and HIV/AIDS (Table 2), not toward cancer.

Elenoside (42), isolated from Justicia hyssopifolia L., is the most pharmacologically studied arylnaphthalene lignan in the genus Justicia. This compound shows sedative, muscle relaxant, cytotoxic, antiviral, insecticidal, cardiotonic, analgesic, lipid peroxidation inhibitory, anti-inflammatory, and stimulant activities and exhibits significant central nervous system depressant properties in rats. Its anxiolytic action, inducing sedation and muscle relaxation (Navarro et al., 2001a), is similar to other tranquilizer drugs (Irwin, 1968) such as the action of sedative-hypnotic barbiturates (Navarro et al., 2004). The cytotoxic activity of 42 was verified in human cancer cell lines in a range of concentrations from 10⁻⁵ to 10⁻⁴ M, with an LD50 of 305 mg/kg in mice and central depressive properties at doses of 25, 50, and 100 mg/kg. No lethality was observed for five days following administration of this compound (Alonso et al., 1997). As a consequence, this compound behaves as a sedative with broad-spectrum cytotoxicity (Navarro et al., 2001b), also showing cytotoxic effects toward leukemia cell lines (Navarro et al., 2001a).

Other lignans isolated from species of *Justicia* show a smaller spectrum of biological activity. The antiplatelet aggregation activity of lignans **25**, **26**, **28**, **29**, **38**, **40**, and **52** are related to the pharmacological tests of the methanol extract of *J. procumbens* (Table 3). Lignans **29**, **30**, **31**, **53**, and **54** showed strong antiviral activity against vesicular stomatitis virus and low cytotoxicity against cultured rabbit lung cells (RL-33) (Asano et al., 1996). Lignans **29** and **43** showed inhibition of secondary aggregation induced by adrenaline (Wu et al., 2007). Moreover, these compounds showed an inhibitory effect on cyclooxygenase-1 (COX-1), with an antiplatelet effect partially due to the suppression of COX-1 activity and reduced thromboxane formation.

Lignan **24** inhibits human hepatitis B viral replication. This compound is isolated from *J. flava*, which is popularly used in the treatment of HIV/AIDS

in Uganda. Lignans **29**, **30**, **31**, **44**, **45**, **46**, **53**, and **54** show antiviral activities. These compounds were isolated from *J. extensa*, *J. betonica*, and *J. procumbens*, and also show the same biological activities (Tables 2 and 3). Conversely, lignans **29**, **30**, **31**, **35**, **36**, and **42** show antiviral activity, but were isolated from species that did not show this activity (Tables 2 and 3). A larger investigation of the extracts of these species is required to explore their antiviral activities.

The antitumor activity of lignans 25, 27, 29, 30, 31, 35, 36, 37, 50, 51, 53, and 54 are related to the popular uses of J. procumbens, J. ciliata, J. rhodoptera, and J. patentiflora as anticancer therapies (Tables 2 and 3). Lignans 30, 31, and 37, isolated from J. ciliata, showed significant citotoxic effects toward a number of cancer cell types (human hepatomacellular carcinoma, human cervical carcinoma, human colorectal adenocarcinoma, human colorectal carcinoma, and human breast cancer) (Day et al., 2002). Lignan 31 also displayed potent cytotoxic effects against T-24, CaSki, SiHa, HT-3, PLC/PRF/5, and 212 cells in vitro (Day et al., 1999). Lignan 60 exhibited low cytotoxicity against three human tumor cell lines: A-549 (human lung carcinoma), MCF-7 (human breast carcinoma), and HT-29 (human colon adenocarcinoma) (Subbaraju et al., 1991). Lignan 62 is included in a wide variety of cancer chemotherapy protocols and was used as a precursor for the semi-synthesis of anticancer therapeutics (Canel et al., 2000). Lignans 24, 26, 29, 30, 31, 32, 37, 42, 51, 60, 61, and 62 show antitumoral activity, but they were isolated from species that did not show this activity (see Tables 2, 3, and 5). The data warrant a larger exploration of the extracts of these species for their anticancer properties.

Conclusion

Although the genus *Justicia* contains only a few species that have been chemically and biologically studied, a broad range of biological applications was observed. Lignans are the major components of the active extracts of the species of *Justicia*, exhibiting important pharmacological properties, such as antiviral, antitumoral, anti-inflamatory, and

Table 1. Synonymy, popular name, and geographical distribution of the species of *Justicia* with previous chemical and biological information.

Species	Synonymy (local name)	Geographical distribution	Chemical information	Biological information	Reference
J. adhatoda L.	Adhatoda vasica Ness (malabar nut and vasaka)	Nepal, India, and Pakistan	Yes	Yes	Aswal et al., 1984; Kumar et al., 2005; Rajakumar & Shivanna, 2009
J. albobracteata L.	(No reported)	Guatemala	No	Yes	Awad et al., 2009
J. anselliana	Adhatoda anseliana Ness (damandojé)	Tropical Africa (Mali, Guinea, Liberia, Ghana, Nigeria, Togo, and Benin)	Yes	Yes	Kpoviessi et al., 2006

J. aurea Schltdl.	Cyrtanthera aurea Schltdl., Jacobina aurea Schltdl., and Justicia umbrosa Benth. (yellow justicia and yellow jacobina)	Guatemala	No	Yes	Awad et al., 2009
J. betonica	Nicoteba betonica (white shrimp plant)	Northeast of Thailand	Yes	Yes	Day et al., 1999; Kanchanapoom et al., 2004; Subbaraju et al., 2004
J. calycina Nees	J. acuminatissima (sara-tudo)	Suriname	No	Yes	Ruysschaert et al., 2009
J. cataractae	(No reported)	Venezuela	Yes	Yes	Jiménez et al., 2001
J. ciliata	Dianthera ciliate	Taiwan	Yes	Yes	Day et al., 1999; Day et al., 2000
J. comata L.	(Marsh water-willow)	Peru	No	Yes	McKenna et al., 2011
J. diffusa Willd	J. procumbens L.	India	No	Yes	Ignacimuthu et al., 2008
J. dumetorum Morong	Justicia squalida	Bolivia	No	Yes	Bourdy et al., 2004
J. extensa	Justicia talbotii (castellana Hiern)	Gabon	Yes	Yes	Wang & Ripka, 1983; Ibrahim et al., 2000
<i>J. flava</i> Vahl	Adhatoda flava (yellow justicia)	Tropical and Southern Africa	Yes	Yes	Olaniyi, 1980
J. gendarussa Burm F	<i>Gendarussa vulgaris</i> Ness (daun rusa and gandarusa)	China, India, Sri Lanka, and Malaysia	Yes	Yes	Wahi et al., 1974; Hadi & Bremner 2001; Sridhar et al., 2006; Mruthunjaya & Hukkeri, 2007
J. ghiesbreghtiana	<i>J. spicigera</i> (muitle, muicle, and mexican honeysuckle)	Mexico	Yes	No	Euler & Alam, 1982; Ismail et al., 1998
J. glauca	(Glaucous justicia)	Mexico	Yes	No	Subbaraju et al., 1991; Vega-Avila et al., 2009
J. hayatai	<i>Justicia procumbens</i> L. var. hayatai Yamamoto	Taiwan	Yes	No	Fukamiya & Lee, 1986
J. heterocarpa T. Anders.	J. dinteri S. Moore	Angola, Namibia, Malawi, Mozambique, Zambia, Zimbabwe, and South Africa	Yes	No	Al-Juaid & Abdel-Mojib, 2004; Ssegawa & Kasenene, 2007
J. hyssopifolia L.	(Mataprieta)	Canary Islands	Yes	No	Navarro et al., 2001a; Woradulayapinij et al., 2005
J. ideogenes	(No reported)	Brazil	No	Yes	Schultes, 1993; Adams et al., 2007
J. insularis	(Mmeme, kpahunmarogu)	Nigeria	No	Yes	Ajibesin et al., 2008
J. neesii Ramamoorthy	J. micrantha Wall	India	Yes	Yes	Chariandy et al., 1999; Rajasekhar & Subbaraju, 2000
J. patentiflora Hemsl.	Mananthes patentiflora Bremek.	North Vietnam	Yes	Yes	Susplugas et al., 2005
J. pectoralis Jacq.	(Tilia, chambá, and papa uwii)	Tropical America	Yes	Yes	Moreno et al., 1994; Lino et al., 1997; Leal et al., 2000; Cano & Volpato, 2004
J. plectrantus	(No reported)	Brazil	No	Yes	Leão et al., 2007
J. procumbens L.	(Ramakrishna theertham)	Taiwan and India	Yes	Yes	Chen et al., 1995; Chen et al., 1996 Asano et al., 1996; Savithramma et al., 2007
J. prostrata Gamble	(No reported)	India	Yes	Yes	Sanmugapriya et al., 2005a; Sanmugapriya et al., 2005b
<i>J. purpurea</i> L.	Justicia carnea	India	Yes	Yes	Kavitha et al., 2003
J. reptans Swatz	(Mutuquinha)	Brazil	Yes	Yes	Rodrigues et al., 2010
J. rhodoptera	(No reported)	Madagascar	Yes	Yes	Williams et al., 2003
J. schimperiana	(Sensel, simiza, timisa, and dumoga)	Ethiopia	No	Yes	Umer et al., 2010

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J. secunda	(Brudu uwíi)	Suriname	No	Yes	Teklehaymanot, 2009
J. sericea	(Inca queen)	Peru	No	Yes	Rojas et al., 2003
J. simplex	(No reported)	India	Yes	Yes	Badami et al., 2003
J. spicigera	(Mohintli)	Mexico	Yes	Yes	Meckes et al., 2004
J. valida	(No reported)	Taiwan	No	Yes	Woradulayapinij et al., 2005

Table 2. Ethnopharmacological informations of the species of Justicia	•
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Species	Part used	Popular use	Preparation/ Adminstration	Region	Reference
J. adhatoda	Root	Bronchitis	Teaspoonful of root paste	India	Aswal et al., 1984; Joshi & Joshi, 2000
	Flower, fruit, and root	Cold, whooping cough, asthma, and helminthic	Juice	India	Joshi & Joshi, 2000; Kumar et al., 2005
	Leaf	Diarrhoea, dysentery, and glandular tumor	Juice	India	Kumar et al., 2005
	Leaf and root	Expectorant, tuberculosis, abortificient, antimicrobial, antitussive, and anticancer		India	Roja et al., 2011
J. anselliana	Leaf	Heart diseases	Decoction	Benin	Kpoviéssi et al., 2008
	Root	Heart diseases and testicles inflammation	Decoction	Benin	Kpoviéssi et al., 2008
J. betonica	Aerial part	Diarrhoea and inflammation		India	Kanchanapoon et al., 2004
	Leaf	HIV/AIDS		Uganda	Lamorde et al., 2010
J. calycina	Whole plant	Stimulant	Decoction	Suriname	Ruysschaert et al., 2009
J. ciliata	Whole plant	Fever and pain		China	Day et al., 2000
J. diffusa	Leaf	Skin disease	Paste	India	Ignacimuthu et al., 2008
J. dumetorum	Leaf and flower	Eye infection	Juice	Bolivia	Bourdy et al., 2004
J. extensa	Whole plant	Ichthyotoxic (affect the fish respiratory system by paralysis)	Crushed bark, leaf, and fruit	Gabon	Ibrahim et al., 2000
J. flava	Seed	Smeared on gingival, teeth pain, and nausea	Powder	Sudan	El-Kamali, 2009
	Leaf and flower	Haemorrhoids and stomach disorders		Ghana	Agbovie et al., 2002
	Leaf	HIV/AIDS		Uganda	Lamorde et al., 2010
J. gendarussa	Leaf	Fever, hemiplegia, rheumatism, arthritis, headache, earache, muscle pain, respiratory disorders, and digestive troubles	Decoction	China and India	Ratnasooriya et al., 2007
		Muscle pain and treatment of fractured bone	Paste warmed applied on the affected area	Malaysia	Ahmad & Holdsworth, 2003
		Rheumatism and arthritis	Poultice	Vietnam	Ahmad & Holdsworth, 2003
		Analgesic to treat hemiplegia, rheumatism, arthritis, headache, and earache	Decoction	Sri Lanka	Ratnasooriya et al., 2007
	Twig	Herbal bath during childbirth	Decoction	Malaysia	Ahmad & Holdsworth, 2003
	Whole plant	Haemorrhoids and fever	Decoction	India	Gurib-Fakin et al., 1996
	Whole plant	Fever and pains	Decoction	Brazil	De Albuquerque et al., 2007
J. ghiesbreghtiana	Leaf	Stimulant and dysentery	Decoction	Mexico	Euler & Alam, 1982
J. ideogenes	Whole plant	Treatment of limb trembling	Warm decoctions	South America	Schultes, 1993; Adams et al., 2007

J. insularis	Leaf	Tooth ache, digestive, weaning agent, and laxative	Cooked as soup	Nigeria	Ajibesin et al., 2008
	Leaf	Antimalarial	Infusion mixed with leaves of Ambrosia maritima	Uganda	Adjanohoun et al., 1993; Tabuti, 2008
J. neesii	Whole plant	Anticancer	Ethanolic extract	India	Chariandy et al., 1999; Rajasekhar & Subbaraju, 2000
J. pectoralis	Leaf	Asthmas, cough, bronchitis, and expectorant	Syrup	Brazil	Agra et al., 2007
	Leaf	Menstruation pain, diuretic, cold, and cough	Aqueous infusion	Ecuador	Tene et al., 2007
		Skin rash	Crushed	Caribbean Region	Longuefosse & Nossin, 199
	Aerial part	Catarrh, allergic eruptions, somniferous, nervousness, sedative, and hypotensive	Infusion, major component of mixtures	Cuba	Moreno et al., 1994; Cano & Volpato, 2004
		Pulmonary infections and hallucinogenic snuff		South America	MacRae & Towers, 1984
	Whole plant	Asthmas	Crushed and sap	Suriname	Teklehaymanot, 2009
		Epilepsy		Belize	Awad et al., 2009
	Leaf and stem	Diabetes, smooth muscle relaxant in respiratory diseases, prostate diseases, antibacterial, and sedative		Colombia	Lizcano et al., 2010
J. plectrantus	Leaf	Headache	Bath	Brazil	Leão et al., 2007
J. procumbens	Leaf	Asthmas	Decoction	India	Savithramma et al., 2007
	Root	Fever due to typhoid	Decoction	Nepal	Joshi & Joshi, 2000
	Aerial part	Fish-killing material	Juice	Taiwan	Fukumiya & Lee, 1986; Chen et al., 1996
	Whole plant	Fever, pain due to pharyngolaryngeal swelling, and cancer	Juice	Taiwan	Chen et al., 1996
		Laryngeal disease and cancer		China	Asano et al., 1996
J. purpurea	Root	Insanity and other mental disorders		India	Kavitha et al., 2003
J. reptans	Leaf	Colic	Infusion		Rodrigues et al., 2010
J. schimperiana	Leaf	Diarrhoea, dysentery, and other stomach disorders	Juice of crushed fresh leaf	Ethiopia	Teklehaymanot, 2009
	Leaf	Liver diseases		Ethiopia	Umer et al., 2010
J. secunda	Leaf	Depression and anaemia	Infusion	Ghana	N'Guessan et al., 2010
	Whole plant	Anaemia	Decoction	Suriname and Congo	Teklehaymanot, 2009
J. sericea	Aerial part	Vaginitis and inflammation		Peru	Rojas et al., 2003
J. simplex	Root	Control fertility and abortifacient	Mixture of powdered roots of different plants	India	Badami et al., 2003
J. spicigera	Leaf	Stimulant, colic, inflammation, acabies (skin infection caused by the itch mite), gastrointestinal disorders, and source of blue dye	Decoction	Mexico	Meckes et al., 2004
	Aerial part	Kidney infection, stimulant, dysentery, menstruation, uterine cancer and diabetes	Decoction	Mexico	Vega-Avila et al., 2009; Alonso-Castro et al., 2011
	Leaf	diabetes	Infusion	Mexico	Andrade-Cetto & Heinrich, 2005

Species	Tested Part	Biological Activity	Extract	Reference
J. albobracteata	Leaf	Epilepsy and anxiety	EtOH	Awad et al., 2009
J. adhatoda	Leaf	Hepatoprotective	Aqueous	Bhattacharyya et al., 2005
J. anselliana	Leaf and root	Allellopathy	EtOH	Ahanchede et al., 2004
J. aurea	Leaf	Epilepsy and anxiety	EtOH	Awad et al., 2009
J. cataractae	Whole plant	Anti-hypertensive	EtOH	Jiménez et al., 2001
J. ciliata	Whole plant	Inhibition of human cervical carcinoma	MeOH	Day et al., 1999
J. comata	Whole plant	Cognitive deficits	Aqueous	McKenna et al., 2011
J. extensa	Leaf	Insecticidal and antiviral	EtOH	Wang & Ripka, 1983
J. gendarussa	Leaf	Anti-arthritic	EtOH	Paval et al., 2009
	Aerial part	Inhibition of HIV type 1 reverse transcriptase	Aqueous	Sridhar et al., 2006
	Leaf	Antinociceptive and antioxidant	Aqueous	Ratnasooriya et al., 2007
	Leaf	Immunosuppressive	MeOH	Arokiyaraj et al., 2007
J. neesii	Whole plant	Inhibition of P388 lymphocytic leukaemia in mice	EtOH	Chariandy et al., 1999; Rajasekhar & Subbaraju, 2000
J. patentiflora	Leaf and stem	Inhibition of tumoral cell growth	EtOAc	Susplugas et al., 2005
J. pectoralis	Leaf	Bactericidal and larvicidal	EtOAc	Chariandy et al., 1999
	Aerial part	Estrogenic, progestogenic, and anti-inflammatory	MeOH	Lockleara et al., 2010
	Leaf	Epilepsy and anxiety	EtOH	Awad et al., 2009
J. procumbens	Whole plant	Inhibition of tumoral cell growth and aggregation of rabbit platelets	МеОН	Fukamiya & Lee, 1986; Cher et al., 1996
	Aerial part	Inhibition of vesicular stomatitis virus (VSV).	MeOH	Asano et al., 1996
J. prostrata	Whole plant	Anti-inflammatory, antiulcerogenic, and anti- depressant	Aqueous and EtOH	Stevenson, 1995; Sanmugapriya et al., 2005a
J. reptans	Leaf	Inhibition of HIV replication	EtOH	Bedoya et al., 2008
J. rhodoptera	Leaf	Inhibition of human ovarian cancer cell line		Williams et al., 2003
J. schimperiana	Leaf	Hepatoprotective	Hydroalcoholic	Umer et al., 2010
J. spicigera	Leaf	Inhibition of edema	Hexane, CHCl ₃ , and MeOH	Meckes et al., 2004
	Leaf	Antitumor	Aqueous	Cáceres-Cortés et al., 2001
	Aerial part	Inhibition of human cancer cell lines	Aqueous and EtOH	Vega-Avila et al., 2009; Alonso-Castro et al., 2011
	Aerial part	Giardicidal	MeOH	Peraza-Sanches et al., 2005
J. valida	Aerial part	Inhibition of HIV type 1 reverse transcriptase in vitro	Aqueous	Woradulayapinij et al., 2005

Table 3. Pharmacological activities of the species of *Justicia*.

Table 4. Biological activity of coumarin (1), flavonoids (2-5), alkaloids (6-13), and triterpenes (14-21) isolated from the species of *Justicia*.

Compound	Biological Activity	Species	Extract	Reference
Umbeliferone (1)	Anti-inflammatory, antinociceptive, and bronchodilator	J. pectoralis	EtOH	Lino et al., 1997; Leal et al., 2000
3',4'-Dihydroxyflavonol (2)	Antioxidant, prevents diabetes, and vasodilator	J. cataractae	EtOH	Jiménez et al., 2001; Wang et al., 2004; Woodman et al., 2005; Woodman & Malakul, 2009
Apigenin (3)	Anti-inflammatory and antitumor	J. gendarussa	EtOH	Wahi et al., 1974; Sawatzky et al., 2006; Cai et al., 2011
Kaempferitrin (4)	Antimicrobial, anti- inflammatory, regulators of macrophages, and reduce the blood glucose level	J. spicigera	CHCl ₃	Dominguez et al., 1990; Abdel-Ghani et al., 2001; Fang et al., 2005; Cazarolli et al., 2006
Vitexin (5)	Anti-inflammatory and antinociceptive	J. gendarussa	EtOH	Wahi et al., 1974; Sridhar et al., 2006; Gorzalczany et al., 2011

5 <i>H</i> .6 <i>H</i> -Quinindolin-11-one (6)		J. betonica	EtOAc	Subbaraju et al., 2004
	Antitumor	J. betonica	EtOAc	y ,
10 <i>H</i> -Quindoline (7)				Caprio et al., 2000; Subbaraju et al., 2004
Jusbetonin (8)	Antitumor	J. betonica	MeOH	Caprio et al., 2000; Subbaraju et al., 2004
Vasicine (9)	Bronchodilator, uterotonic, and anti-inflammatory	J. adhatoda	EtOH	 Amin & Mehta, 1959; Mehta et al., 1963; Ikram & Huq, 1966; Bhalla et al., 1982; Chakravarthy et al., 1982; Jindal et al., 1988; Ismail et al., 1998; Lorenz et al., 1999; Claeson et al., 2000; Shevyakov et al., 2006; Rachana et al., 2011
Vasicinone (10)	Bronchodilator	J. adhatoda	EtOH	 Amin & Mehta, 1959; Mehta et al., 1963; Ikram & Huq, 1966; Bhalla et al., 1982; Chakravarthy et al., 1982; Ismail et al., 1998; Jindal et al., 1998; Lorenz et al., 1999; Rachana et al., 2011
Allantoin (11)	Anti-inflammatory and anti-ulcer	J. spicigera		Dominguez et al., 1990; Niu et al., 2010
6H-Quinindoline (12)		J. betonica	EtOAc	Subbaraju et al., 2004
Vasicinol (13)	Bronchodilator	J. adhatoda	EtOH	 Amin & Mehta, 1959; Mehta et al., 1963; Ikram & Huq, 1966; Bhalla et al., 1982; Chakravarthy et al., 1982; Ismail et al., 1998; Jindal et al., 1998; Lorenz et al., 1999; Rachana et al., 2011
Justicioside A (14)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2004
Justicioside C (15)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2004
Justicioside B (16)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2004
Justicioside D (17)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2004
Justicioside E (18)		J. betonica	EtOH/H,O	Kanchanapoom et al., 2005
Justicioside F (19)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2005
Justicioside G (20)		J. betonica	EtOH/H ₂ O	Kanchanapoom et al., 2005
Justicisaponin (21)	Antifertility	J. simplex	MeOH	Ghosal et al., 1981; Badami et al., 2003

Table 5. Lignans isolates from the species of Justicia.

Compound	Biological Activity	Species	Extract	Reference
Jusmicranthin (22)		J. neesii	EtOH	Rajasekhar & Subbaraju, 2000
Jusmicranthin methyl ether (23)		J. neesii	EtOH	Rajasekhar & Subbaraju, 2000
Helioxanthin (24)	Inhibition human hepatitis B viral replication and antitumor	J. flava	ETOH	Chang et al., 2000; Tseng et al., 2008;
Taiwanin E (25)	Antiplatelet aggregation and antitumor	J. procumbens	EtOH	Chen et al., 1996; Chang et al., 2000
Taiwanin E methyl ether (26)	Antiplatelet aggregation and	J. purpurea	MeOH	Kavitha et al., 2003
	cytotoxicity against human cervical carcinoma	J. betonica	MeOH	Day et al., 1999
	carcinoma	J. procumbens	EtOH	Chen et al., 1996
Justicidin E (27)	Inhibition of leukotriene biosynthesis by human leukocytes	J. procumbens	МеОН	Fukamiya & Lee, 1986; Thérien et al., 1993
Neojusticin A (28)	Antiplatelet aggregation	J. procumbens	EtOH and MeOH	Fukamiya & Lee, 1986; Chen et al., 1996; Wu et al., 2007
			МеОН	Fukamiya & Lee, 1986; Asano et al., 1996
Justicidin B (29)	Anti-inflammatory, antiplatelet aggregation, cytotoxycity, antiviral, fungicidal, antiprotozoal against T. cruzi, antimalarial, and antirheumatic	J. purpurea	MeOH	Baba et al., 1996; Gertsch et al., 2003; Kavitha et al., 2003 Rao et al., 2006; Wu et al., 2007; Kaur et al., 2009
		J. procumbens	EtOH	Chen et al., 1996
			MeOH	Asano et al., 1996
Diphyllin (30)	Cytotoxycity and antiviral	J. extensa	EtOH	Wang & Ripka, 1983
		J. procumbens	МеОН	Fukamiya & Lee, 1986; Cher et al., 1996; Asano et al., 1996
		J. ciliata	MeOH	Day et al., 1999

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Justicidin A (31)	Cytotoxycity, antiviral, 'fish-killing' properties, and induced apoptosis in human hepatoma cells	J. extensa	EtOH	Wang & Ripka, 1983
	a a Fritani	J. betonica	EtOH	Munakata et al., 1965; Day et al., 1999
		J. procumbens	МеОН	Fukamiya & Lee, 1986; Asano et al., 1996; Chen et al., 1996; Su et al., 2006
		J. rhodoptera	EtOH	Williams et al., 2003
Cleistanthin B (32)	Antitumor	J. purpurea	MeOH	Pradheepkumar et al., 2000; Kavitha et al., 2003
Neesiinoside A (33)		J. neesii	MeOH	Subbaraju et al., 2001
4 ^{···} -O-Acetylpatentiflorin B (34)		J. patentiflora	EtOAc	Susplugas et al., 2005
Patentiflorin A (35)	Cytotoxicity against human carcinoma cells	J. patentiflora	EtOAc	Susplugas et al., 2005
Patentiflorin B (36)	Cytotoxicity against human carcinoma cells	J. patentiflora	EtOAc	Susplugas et al., 2005
Tuberculatin (37)	Antitumor	J.ciliata	MeOH	Day et al., 1999; Lu et al., 2008
		J. betonica	MeOH	
Chinensinaphthol methyl ether (38)	Antiplatelet aggregation	J. ciliata	CH ₂ Cl ₂	Day et al., 1999
Justalakonin (39)		J. purpurea	MeOH	Kavitha et al., 2003
4'-Dimethyl chinensinaphthol	Antiplatelet aggregation	J. ciliata	CH_2Cl_2	Day et al., 1999
methyl ether (40)		J. procumbens	EtOH	Chen et al., 1996
Chinensinaphthol (41)		J. betonica	MeOH	Day et al., 1999
		J. procumbens	EtOH	Chen et al., 1996
Elenoside (42)	Sedative, muscle relaxant, cytotoxic, antiviral, insecticidal, cardiotonic, analgesic, inhibition of lipid peroxidation, anti-inflammatory, and stimulant	J. hyssopifolia	EtOAc	Alonso et al., 1997; Navarro et al., 2001a; Navarro et al., 2001b
Neojusticin B (43)	Antiplatelet aggregation	J. ciliata	CH ₂ Cl ₂ / Me ₂ CO	Day et al., 1999
		J. procumbens	EtOH	Fukamiya & Lee, 1986; Asano et al., 1996; Chen et al., 1996
Justicidinoside A (44)	Antiviral	J. procumbens	MeOH	Asano et al., 1996
Justicidinoside C (45)	Antiviral	J. procumbens	MeOH	Asano et al., 1996
Justicidinoside B (46)	Antiviral	J. procumbens	MeOH	Asano et al., 1996
Justicidin P (47)		J. extensa	EtOH	Wang & Ripka, 1983
Justicinol (48)	Mild effect on the CNS	J. patentiflora	EtOAc	Susplugas et al., 2005
Ciliatoside A (49)	Anti-inflammatory	J. ciliata	MeOH	Day et al., 2000; Wu et al., 2007
Procumbenoside A (50)	Antitumor	J. procumbens	MeOH	Day et al., 2002; Lu et al., 2008
Cilinaphthalide A (51)	Antitumor	J. betonica		
		J. ciliata	CH_2Cl_2	Day et al., 1999
Cilinaphthalide B (52)	Antiplatelet aggregation induced by	J. betonica	MeOH	
	adrenaline	J. ciliata	CH_2Cl_2	Day et al., 1999
		J. procumbens	MeOH	Wenga et al., 2004
Diphylin apioside (53)	Cytotoxycity and antiviral	J. procumbens	MeOH	Asano et al., 1996
Diphyllin apioside-5-acetate (54)	Cytotoxycity and antiviral	J. procumbens	MeOH	Asano et al., 1996
Juspurpurin (55)		J. purpurea	MeOH	Kavitha et al., 2003
Carinatone (56)		J. patentiflora	EtOAc	Susplugas eta al., 2005
Justiflorinol (57)		J. patentiflora	EtOAc	Susplugas et al., 2005

(+)-Isolariciresinol (58)	Anti-inflammatory	J. flava	EtOH	Küpeli et al., 2003;
Sesamin (59)	Angiogenic	J. purpurea	MeOH	Kavitha et al., 2003; Chung e al., 2010
Justiciresinol (60)	Cytotoxicity	J. glauca	EtOAc	Subbaraju et al., 1991
Xanthoxylol (61)	Antitumor effect on mouse, skin, and pulmonary carcinogenesis	J. purpurea	МеОН	Konoshima & Atta-Ur- Rahman, 2000; Kavitha et al. 2003
Podophyllotoxin (62)	Cancer chemotherapy	J. flava	EtOH	Canel et al., 2000; Meckes et al., 2004;
Heliobuphthalmin (63)	Antineoplasic	J. ciliata	$\rm CH_2\rm Cl_2$	Day et al., 1999; Duarte et al 2010

antiplatelet aggregations activities, which warrant further exploration. The chemical and pharmacological data shown in the present work should inspire additional study of the species of *Justicia* for their use in therapeutics.

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*Correspondence

Geone M. Corrêa

Departamento de Química, ICEx, Universidade Federal de Minas Gerais 31270-901 Belo Horizonte- MG, Brazil or Instituto de Ciências Exatas e Tecnologia, Universidade Federal do Amazonas 69100-000 Itacoatiara- AM, Brazil geonemaia@ufam.edu.br