

## *Justicia secunda* Vahl species : Phytochemistry, Pharmacology and Future Directions: A mini-review



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### ABSTRACT

The aim of this review was to provide knowledge on Phytochemistry and Pharmacology of *Justicia secunda* Vahl. and *Justicia species* from various electronic databases (Science Direct, PubMed Central, PubMed and Google scholar). The scientific names of those plants species were used as a keyword for the search, along with the terms phytochemistry and pharmacology. The chemical structures of the *Justicia* species naturally occurring compounds were drawn using ChemBioDraw Ultra 12.0 software package. Results revealed those plants are traditionally used for the treatment of respiratory and gastrointestinal diseases and as well as inflammation. Those 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. Other species are popularly used in the treatment of headache and fever, sedative, analgesic properties, cancer, diabetes, and HIV. Those plants are reported to possess various biological properties like antitumoral activity against different cancer cell lines, anticancer activity against P388 lymphocytic leukemia in

mice, inhibitory activity *in vivo* against P-388 lymphocytic leukemia growth and *in vitro* cytotoxicity in the 9-KB (human nasopharyngeal carcinoma) an cell lines (*Justicia spicigera* Schltdl.), antioxidant, antibacterial, antifungal, antiangiogenic, anthelmintic, and hepatoprotective activities, human ovarian cancer cell line (*Justicia rhodoptera* Baker), as well as prevention of some tumoral cell growth (*Justicia patentiflora* Hemsl), bronchitis, arthritis, vaginal discharges, dyspepsia and eye disease. These properties are due to the presence of numerous naturally occurring phytochemicals like phenols, flavonoids, alkaloids, tannins, glycosides, saponins, coumarins, terpenes and Phytochemical studies on leaves from *J. gendarussa* revealed the presence of flavonoids, alkaloids, triterpenes, amino acids, aromatic amines, stigmasterol, lupeol and steroids. The results of the present review of literature makes an interesting candidate for advanced antisickling pharmacological investigations such as *Justicia secunda* Vahl antisickling, anti-hemolytic and membrane stabilizing effects of this plant.

**Keyword :** Sick cell Disease, phytochemistry, pharmacology, *Justicia secunda* Vahl.

### INTRODUCTION

The World Health Organization (WHO) recognizes that traditional and complementary medicines (TCM) are a vital part of the global health care system.<sup>1</sup> In Africa, it is estimated that over 80% of the population continues to rely on medicinal plant species to meet their basic health care needs.<sup>2</sup> *Justicia* is the largest genus of Acanthaceae. Its species are widespread in tropical regions of the world<sup>3</sup> and are poorly represented in temperate regions.<sup>4</sup> *Justicia* this genus of Acanthaceae, its species are found in Asia, America and Africa. They are cultivated in Democratic Republic of the Congo (DRC). Many parts of those plants are used in traditional medicine to treat several diseases include, diabetes, cancers, respiratory and gastrointestinal diseases and as well as inflammation, central nervous system as hallucinogens, somniferous agents,

sedatives, depressors and treatments for epilepsy and other mental disorders. Other species are used in the treatment of headache and fever, sedative, analgesic, bronchitis, arthritis, vaginal discharges, dyspepsia, and eye disease. Biological activities of different extracts of *Justicia* are well documented and a considerable amount of phytochemicals was isolate from different parts of those plants.

### Botany description and Geographical Distribution

The Acanthaceae family, order Scrophulariales, superorder Lamiflorae (sensu Dahlgren), comprises almost 250 genus with 2500 species. These plants are distributed over the tropical and sub-tropical regions<sup>3</sup> and are poorly represented in temperate regions.<sup>4</sup> *Justicia secunda* Vahl. (Acanthaceae), a native tropical herbaceous plant originating

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**Cite This Article:** Kitadi, J.M.,  
Lengbiye, E.M., Gbolo, B.Z.,  
Inkoto, C.L., Muanyishay, C.L.,  
Lufuluabo, G.L., Tshibangu, D.S.T.,  
Tshilanda, D.D., Mbala, B.M.,  
Ngbolua, K., Mpiana, P.T. 2019.  
*Justicia secunda* Vahl species :  
Phytochemistry, Pharmacology and  
Future Directions: A mini-re-  
view. *Discovery Phytomedicine*  
6(4): 157-171. DOI: [10.15562/  
phytomedicine.2019.93](https://doi.org/10.15562/phytomedicine.2019.93)

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from South America, is nowadays grown in other tropical or subtropical African countries such as Democratic Republic of the Congo. *Justicia* is the largest genus of Acanthaceae, with approximately 600 species that are found in pantropical and tropical regions. 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. Infl orescences are in spikes or panicles cimas, and the species rarely has solitary, terminal, or axillary fl owers. 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.<sup>5</sup>

### Ethnobotany

*Justicia secunda* Vahl (Acanthaceae), a native tropical herbaceous plant originating from South America, is nowadays grown in other tropical or subtropical African countries such as Democratic Republic of the Congo. In the past, this plant was grown in the local surroundings as an ornamental until locals discovered its medicinal properties. The leaves of this plant were subsequently used to cure various illnesses such as anemia or hypertension and are now widely used for many other medicinal applications. The phytochemical composition of various cultivar leaf extracts revealed the presence of polyphenols such as flavonoids, tannins, leuco-anthocyanins and anthocyanins.<sup>6</sup> Flavonoids were the largest class of phenolic compound found. Several species of *Justicia* are widely used in folk medicine (as shown in Table 1) for the treatment of respiratory and gastrointestinal diseases as well as inflammation. 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 fever, analgesic properties, cancer, diabetes, and HIV. Whole plant and aerial parts are used in folk medicine. Extracts made from only the leaves are the most used, followed by those extracts made from only the roots. Some species are used as mixtures. For example, traditional physicians around Kotagiri village near Ootacamund use a mixture of the powdered roots of *Cassia occidentalis* L., *Caesalpinia*, *Derris brevipes* var. *Coriacea*, *Papilionaceae*, 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.<sup>7</sup> 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*.

### METHODOLOGY

A literature search was conducted to obtain information about the phytochemistry and pharmacognosy of *Justicia* species and *Justicia secunda* Vahl. from various electronic databases (PubMed Central, PubMed, Science Direct and Google scholar). The scientific name of this plant species was used as the keyword for the search, along with the terms phytochemistry and pharmacognosy. The chemical structures of the *Justicia* species naturally occurring compound were drawn using ChemBioDraw Ultra 12.0 software package.

### RESULTS AND DISCUSSION

#### Phytochemical Screening and Pharmacology

The phytochemistry screening of *Justicia* species revealed the presence of various secondary metabolites including the phenols, flavonoids,<sup>7,8</sup> alkaloids,<sup>8,9</sup> terpenes, tannins, glycosides,<sup>10,11</sup> saponins, coumarins, saponins, amino acids, aromatic amines, stigmasterol, and lupeol. Lignans also show antifeedant,<sup>11</sup> antiangiogenic, antileishmanial, antifungal, hypolipidemic, cardioprotective, antipressant,<sup>12</sup> analgesic, hepatoprotective activities,<sup>13</sup> antiplatelet,<sup>14</sup> antiasthmatic, antiviral,<sup>15</sup> antineoplastic,<sup>16</sup> insecticidal, and anti-inflammatory.

Different chemical structures of various compounds isolated from the *Justicia* genus (*Acanthaceae*) are given in Figure 1.

Nur-Aqidah et al.<sup>84</sup> in Malaysia reported the concentration of mineral nutrients in the selected medicinal plants, the mean concentration level of iron (Fe) varied between 0.14 and 0.21 mg/kg. Fe is important for the formation of haemoglobin and plays an essential role oxygen and electron transfer in a human body.<sup>85</sup> In cellular respiration, it functions as an important component of enzymes involved in biological oxidation.<sup>86</sup> Mn is an important element as a structural component of some enzymes as stated by.<sup>95</sup> Mn is an essential trace element for the growth of plants and animals. Specifically, it is important in normal reproductive functions and normal functioning of the central nervous system.<sup>95</sup> *Justicia gendarussa* and *S. crispa*

**Table 1** Geography Distribution, Part used, Popular use, Preparation/Administration, ethnopharmacology activities from *Justicia* genus

| Species                         | Part used                  | Preparation/<br>administration                  | Ethnopharmacology activities                                                                                                     | Geography Distribution                                                         | Reference  |
|---------------------------------|----------------------------|-------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------|
| <i>J. adhatoda</i>              | Root                       | Teaspoonful of root<br>Paste                    | Bronchitis                                                                                                                       | Nepal, India, and Pakistan                                                     | 17,18      |
|                                 | Flower, fruit,<br>and root | Juice                                           | Cold, whooping cough, asthma,<br>and helminthic                                                                                  | India                                                                          | 17,19      |
|                                 | Leaf                       | Juice                                           | Diarrhoea, dysentery, and<br>glandular tumor                                                                                     | India                                                                          | 17         |
|                                 | Leaf and<br>root           |                                                 | Expectorant, tuberculosis,<br>abortifacient, antimicrobial,<br>antitussive, and anticancer                                       |                                                                                | 20         |
| <i>J. albobracteata</i> L.      |                            |                                                 |                                                                                                                                  | Guatemala                                                                      | 21         |
| <i>J. anselliana</i>            |                            |                                                 |                                                                                                                                  | Tropical Africa (Mali,<br>Guinea, Liberia, Ghana,<br>Nigeria, Togo, and Benin) | 22         |
| <i>J. aurea</i> Schltdl.        |                            |                                                 |                                                                                                                                  | Guatemala                                                                      | 21         |
| <i>J. betonica</i>              |                            | MeOH                                            | -                                                                                                                                | Northeast of Thailand                                                          | 23, 24, 26 |
| <i>J. calycina</i> Nees         | Whole plant                | Deconction                                      | Stimulant                                                                                                                        | Suriname                                                                       | 27         |
| <i>J. cataractae</i>            |                            |                                                 |                                                                                                                                  | Venezuela                                                                      | 28         |
| <i>J. ciliata</i>               | Whole plant                | Deconction                                      | Fever and pain                                                                                                                   | Taiwan, China                                                                  | 29         |
| <i>J. comata</i> L.             |                            |                                                 |                                                                                                                                  | Peru                                                                           | 30         |
| <i>J. diffusa</i> Willd         | Leaf                       | Paste                                           | Skin disease                                                                                                                     | India                                                                          | 26         |
| <i>J. dumetorum</i>             | Leaf and<br>flower         | Juice                                           | Eye infection                                                                                                                    | Bolivia                                                                        | 15         |
| <i>J. extensa</i>               | Whole plant                | Crushed bark, leaf,<br>and fruit                | Ichthyotoxic (affect the fish<br>respiratory system by paralysis)                                                                | Gabon                                                                          | 33         |
| <i>J. flava</i> Vahl            | Seed                       | Powder                                          | Smear on gingival, teeth<br>pain, and nausea                                                                                     | Tropical and Southern<br>Africa                                                | 34         |
|                                 | Leaf and<br>flower         |                                                 | Haemorrhoids and stomach<br>Disorders                                                                                            | Ghana                                                                          | 35         |
|                                 | Leaf                       |                                                 | HIV/AIDS                                                                                                                         | Uganda                                                                         | 36         |
| <i>J. gendarussa</i><br>Burm F  | Leaf                       | Deconction                                      | Fever, hemiplegia, rheumatism,<br>arthritis, headache, earache, muscle<br>pain, respiratory disorders, and<br>digestive troubles | China, India, Sri Lanka,<br>and Malaysia                                       | 18, 37, 38 |
|                                 |                            | Paste warmed<br>applied<br>on the affected area | Muscle pain and treatment of<br>fractured bone                                                                                   | Malaysia                                                                       | 39         |
|                                 |                            | Poultice                                        | Rheumatism and arthritis                                                                                                         | Vietnam                                                                        | 39         |
|                                 |                            | Deconction                                      | Analgesic to treat hemiplegia,<br>rheumatism, arthritis, headache,<br>and earache                                                | Sri Lanka                                                                      | 20         |
|                                 | Twig                       | Deconction                                      | Herbal bath during childbirth                                                                                                    | Malaysia                                                                       | 39         |
| <i>J. ghiesbreghtiana</i>       | Leaf                       | Deconction                                      | Stimulant and dysentery                                                                                                          | Mexico                                                                         | 40         |
| <i>J. ideogenes</i>             | Whole plant                | Warm decoctions                                 | Treatment of limb trembling                                                                                                      | Brazil                                                                         | 7          |
| <i>J. insularis</i>             | Leaf                       | Cooked as soup                                  | Tooth ache, digestive, weaning<br>agent, and laxative                                                                            | Nigeria                                                                        | 41         |
| <i>J. neesii</i><br>Ramamoorthy | Whole plant                | Ethanol extract                                 | Anticancer                                                                                                                       | India                                                                          | 42         |

**Table 1** Continue

| Species                       | Part used     | Preparation/<br>administration                | Ethnopharmacology activities                                                                                                         | Geography Distribution | Reference |
|-------------------------------|---------------|-----------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------|------------------------|-----------|
| <i>J. patentiflora</i> Hemsl. |               | EtOAc                                         |                                                                                                                                      | North Vietnam          | 58        |
| <i>J. pectoralis</i> Jacq.    | Leaf          | Syrup                                         | Asthmas, cough, bronchitis, and Expectorant                                                                                          | Tropical America       | 43, 44    |
|                               | Leaf          | Aqueous infusion                              | Menstruation pain, diuretic, cold, and cough                                                                                         | Ecuador                | 45        |
|                               | Aerial part   | Infusion, major component of mixtures         | Catarrh, allergic eruptions, somniferous, nervousness, sedative, and hypotensive                                                     | Cuba                   | 44        |
|                               | Leaf and Stem |                                               | Diabetes, smooth muscle relaxant in respiratory diseases, prostate diseases, antibacterial, and sedative                             | Colombia               | 46        |
| <i>J. plectratus</i>          | Leaf          | Bath                                          | Headache                                                                                                                             | Brazil                 | 47        |
| <i>J. procumbens</i> L.       | Leaf          | Deconction                                    | Asthmas                                                                                                                              | Taiwan and India       | 48        |
|                               | Whole plant   | Juice                                         | Fever, pain due to pharyngolaryngeal swelling, and cancer                                                                            | Taiwan                 | 14        |
| <i>J. purpurea</i> L.         | Root          | -                                             | Insanity and other mental Disorders                                                                                                  | India                  | 25        |
| <i>J. reptans</i> Swatz       | Leaf          | Infusion                                      | Colic                                                                                                                                | Brazil                 | 49        |
| <i>J. schimperiana</i>        | Leaf          | Juice of crushed fresh Leaf                   | Diarrhoea, dysentery, and other stomach disorders                                                                                    | Ethiopia               | 50        |
| <i>J. secunda</i>             | Leaf          | Infusion                                      | Depression and anaemia                                                                                                               | Ghana                  | 51        |
|                               | Whole plant   | Decoction                                     | Anaemia                                                                                                                              | Suriname and Congo     | 52        |
| <i>J. sericea</i>             | Aerial part   | -                                             | Vaginitis and inflammation                                                                                                           | Peru                   | 20        |
| <i>J. simplex</i>             | Root          | Mixture of powdered roots of different plants | Control fertility and Abortifacient                                                                                                  | India                  | 53        |
| <i>J. spicigera</i>           | Leaf          | Deconctio                                     | Stimulant, colic, inflammation, acabies (skin infection caused by the itch mite), gastrointestinal disorders, and source of blue dye | Mexico                 | 30        |
|                               | Aerial part   | Deconction                                    | Kidney infection, stimulant, dysentery, menstruation, uterine cancer and diabetes                                                    | Mexico                 | 9,54      |
| <i>J. valida</i>              |               |                                               |                                                                                                                                      | Taiwan                 | 55        |

**Table 2** Biological activity of coumarin (1), flavonoids (2-5), alkaloids (6-13), triterpenes (14-21) and Lignans (22-63) isolated from the species of *Justicia*

| Species              | Extract           | Compound                    | Bioactivity                                                                                     | Reference |
|----------------------|-------------------|-----------------------------|-------------------------------------------------------------------------------------------------|-----------|
| <i>J. pectoralis</i> | EtOH              | Umbeliferone (1)            | Anti-inflammatory, antinociceptive, and bronchodilator                                          | 56        |
| <i>J. cataractae</i> | EtOH              | 3',4'-Dihydroxyflavonol (2) | Antioxidant, prevents diabetes, and vasodilator                                                 | 57        |
| <i>J. gendarussa</i> | EtOH              | Apigenin (3)                | Anti-inflammatory and antitumor                                                                 | 58        |
| <i>J. spicigera</i>  | CHCl <sub>3</sub> | Kaempferitrin (4)           | Antimicrobial, anti-inflammatory, regulators of macrophages, and reduce the blood glucose level | 59        |
| <i>J. gendarussa</i> | EtOH              | Vitexin (5)                 | Anti-inflammatory and antinociceptive                                                           | 60        |

**Table 2** Continue

| Species                | Extract                         | Compound                                       | Bioactivity                                                                                                                                               | Reference |
|------------------------|---------------------------------|------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| <i>J. betonica</i>     | EtOAc                           | 5 <i>H</i> ,6 <i>H</i> Quinindolin-11-one (6)  | -                                                                                                                                                         | 61        |
| <i>J. betonica</i>     | EtOAc                           | 10 <i>H</i> -Quindoline (7)                    | Antitumor                                                                                                                                                 | 61        |
| <i>J. betonica</i>     | MeOH                            | Jusbetonin (8)                                 | Antitumor                                                                                                                                                 | 61        |
| <i>J. adhatoda</i>     | EtOH                            | Vasicine (9)                                   | Bronchodilator, uterotonic, and anti-inflammatory                                                                                                         | 62        |
| <i>J. adhatoda</i>     | EtOH                            | Vasicinone (10)                                | Bronchodilator                                                                                                                                            | 62        |
| <i>J. spicigera</i>    | -                               | Allantoin (11)                                 | Anti-inflammatory and anti-ulcer                                                                                                                          | 63        |
| <i>J. betonica</i>     | EtOAc                           | 6 <i>H</i> -Quinindoline (12)                  | -                                                                                                                                                         | 61        |
| <i>J. adhatoda</i>     | EtOH                            | Vasicinol (13)                                 | Bronchodilator                                                                                                                                            | 62        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside A (14)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside B (15)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside C (16)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside D (17)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside E (18)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside F (19)                            | -                                                                                                                                                         | 64        |
| <i>J. betonica</i>     | EtOH/H <sub>2</sub> O           | Justicioside G (20)                            | -                                                                                                                                                         | 64        |
| <i>J. simplex</i>      | MeOH                            | Justicisaponin (21)                            | Antifertility                                                                                                                                             | 65        |
| <i>J. neesii</i>       | EtOH                            | Jusmicranthin (22)                             | -                                                                                                                                                         | 66        |
| <i>J. neesii</i>       | EtOH                            | Jusmicranthin methyl ether (23)                | -                                                                                                                                                         | 66        |
| <i>J. flava</i>        | EtOH                            | Helioxanthin (24)                              | Inhibition human hepatitis B viral replication and antitumor                                                                                              | 67        |
| <i>J. procumbens</i>   | EtOH                            | Taiwanin E (25)                                | Antiplatelet aggregation and antitumor                                                                                                                    | 68        |
| <i>J. purpurea</i>     | MeOH                            | Taiwanin E methyl ether (26)                   | Antiplatelet aggregation                                                                                                                                  | 69        |
| <i>J. procumbens</i>   | MeOH                            | Justicidin E (27)                              | Inhibition of leukotriene biosynthesis by human leukocytes                                                                                                | 70        |
| <i>J. procumbens</i>   | EtOH and MeOH                   | Neojusticin A (28)                             | Antiplatelet aggregation                                                                                                                                  | 71        |
| <i>J. purpurea</i>     | MeOH                            | Justicidin B (29)                              | Anti-inflammatory, antiplatelet aggregation, cytotoxicity, antiviral, fungicidal, antiprotozoal against <i>T. cruzi</i> , antimalarial, and antirheumatic | 72        |
| <i>J. extensa</i>      | EtOH                            | Diphyllin (30)                                 | Cytotoxicity and antiviral                                                                                                                                | 73        |
| <i>J. extensa</i>      |                                 | Justicidin A (31)                              | Cytotoxicity, antiviral, 'fish killing' properties, and induced apoptosis in human hepatoma cells                                                         | 73        |
| <i>J. purpurea</i>     | MeOH                            | Cleistanthin B (32)                            | Antitumor                                                                                                                                                 | 69        |
| <i>J. neesii</i>       | MeOH                            | Neesiinoside A (33)                            | -                                                                                                                                                         | 61        |
| <i>J. patentiflora</i> | EtOAc                           | 4''-O-Acetylpatentiflorin B (34)               | -                                                                                                                                                         | 74        |
| <i>J. patentiflora</i> | EtOAc                           | Patentiflorin A (35)                           | Cytotoxicity against human carcinoma cells                                                                                                                | 74        |
| <i>J. patentiflora</i> | EtOAc                           | Patentiflorin B (36)                           | Cytotoxicity against human carcinoma cells                                                                                                                | 74        |
| <i>J. ciliata</i>      | MeOH                            | Tuberculatin (37)                              | Antitumor                                                                                                                                                 | 75        |
| <i>J. ciliata</i>      | CH <sub>2</sub> Cl <sub>2</sub> | Chinensinaphthol methyl ether (38).            | Antiplatelet aggregation                                                                                                                                  | 76        |
| <i>J. ciliata</i>      | CH <sub>2</sub> Cl <sub>2</sub> | 4'-Dimethyl chinensinaphthol methyl ether (40) | Antiplatelet aggregation                                                                                                                                  | 76        |

**Table 2** Continue

| Species                | Extract                         | Compound                          | Bioactivity                                                                                                                                               | Reference |
|------------------------|---------------------------------|-----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|
| <i>J. betonica</i>     | MeOH                            | Chinensinaphthol (41)             | -                                                                                                                                                         | 76        |
| <i>J. hyssopifolia</i> | EtOAc                           | Elenoside (42)                    | Sedative, muscle relaxant, cytotoxic, antiviral, insecticidal, cardiogenic, analgesic, inhibition of lipid peroxidation, anti-inflammatory, and stimulant | 77        |
| <i>J. ciliata</i>      | CH <sub>2</sub> Cl <sub>2</sub> | Neojustin B (43)                  | Antiplatelet aggregation                                                                                                                                  | 76        |
| <i>J. procumbens</i>   | MeOH                            | Justicidin A (44)                 | Antiviral                                                                                                                                                 | 78        |
| <i>J. procumbens</i>   | MeOH                            | Justicidin C (45)                 | Antiviral                                                                                                                                                 | 78        |
| <i>J. procumbens</i>   | MeOH                            | Justicidin B (46)                 | Antiviral                                                                                                                                                 | 78        |
| <i>J. extensa</i>      | EtOH                            | Justidin P (47)                   | -                                                                                                                                                         | 73        |
| <i>J. patentiflora</i> | EtOAc                           | Justicinol (48)                   | Mild effect on the CNS 74                                                                                                                                 |           |
| <i>J. ciliata</i>      | MeOH                            | Ciliatoside A (49)                | Anti-inflammatory 71                                                                                                                                      |           |
| <i>J. procumbens</i>   | MeOH                            | Procumbenoside A (50)             | Antitumor                                                                                                                                                 | 75        |
| <i>J. betonica</i>     | MeOH                            | Cilinaphthalide A (51)            | Antitumor                                                                                                                                                 | 75        |
| <i>J. betonica</i>     | MeOH                            | Cilinaphthalide B (52)            | Antiplatelet aggregation induced by adrenaline                                                                                                            | 1<br>76   |
| <i>J. procumbens</i>   | MeOH                            | Diphyllin apioside (53)           | Cytotoxicity and antiviral                                                                                                                                | 78        |
| <i>J. procumbens</i>   | MeOH                            | Diphyllin apioside-5-acetate (54) | Cytotoxicity and antiviral                                                                                                                                | 78        |
| <i>J. purpurea</i>     | MeOH                            | Juspurpurin (55)                  | -                                                                                                                                                         | 69        |
| <i>J. patentiflora</i> | EtOAc                           | Carinatone (56)                   | -                                                                                                                                                         | 71        |
| <i>J. patentiflora</i> | EtOAc                           | Justiflorinol (57)                |                                                                                                                                                           | 71        |
| <i>J. flava</i>        | EtOH                            | (+)-Isolariciresinol (58)         | Anti-inflammatory                                                                                                                                         | 65        |
| <i>J. purpurea</i>     | MeOH                            | Sesamin (59)                      | Angiogenic                                                                                                                                                | 82        |
| <i>J. glauca</i>       | EtOAc                           | Justiciresinol (60)               | Cytotoxicity                                                                                                                                              | 66        |
| <i>J. purpurea</i>     | MeOH                            | Xanthoxylol (61)                  | Antitumor effect on mouse, skin, and pulmonary carcinogenesis                                                                                             | 03<br>67  |
| <i>J. flava</i>        | EtOH                            | Podophyllotoxin (62)              | Cancer chemotherapy                                                                                                                                       |           |
| <i>J. ciliata</i>      | CH <sub>2</sub> Cl <sub>2</sub> | Heliobupthalmin (63)              | Antineoplastic 83                                                                                                                                         | [         |

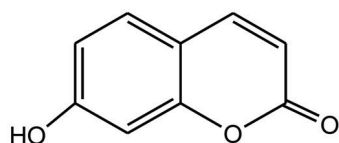
**Table 3** Concentration levels of mineral nutrients (mg/kg) in the selected medicinal plants.

| Element (mg/kg) | Plants                  |                            |                            |                          |
|-----------------|-------------------------|----------------------------|----------------------------|--------------------------|
|                 | <i>Murraya koenigii</i> | <i>Strobilantes crista</i> | <i>Justicia gendarussa</i> | <i>Centella Asiatica</i> |
| Ca              | 5.16 ± 0.00             | 5.76 ± 0.00                | 5.26 ± 0.00                | 5.71 ± 0.00              |
| Cu              | 0.01 ± 0.00             | 0.01 ± 0.00                | 0.01 ± 0.00                | 0.01 ± 0.00              |
| Fe              | 0.15 ± 0.00             | 0.14 ± 0.00                | 0.15 ± 0.00                | 0.21 ± 0.00              |
| Mg              | 1.37 ± 0.02             | 1.13 ± 0.00                | 1.72 ± 0.00                | 1.49 ± 0.02              |
| Mn              | 0.00 ± 0.00             | 0.00 ± 0.00                | 0.00 ± 0.02                | 0.00 ± 0.00              |
| Mo              | 0.00 ± 0.00             | ND                         | 0.01 ± 0.00                | 0.01 ± 0.00              |
| Zn              | 0.02 ± 0.00             | 0.03 ± 0.00                | 0.03 ± 0.00                | 0.01 ± 0.00              |

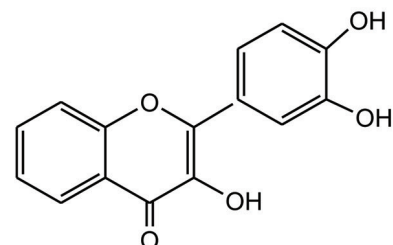
contained the highest zinc (Zn) concentration level of 0.03 mg/kg followed by *M. koenigii* (0.02 mg/kg) and *C. asiatica* (0.01 mg/kg). Zinc is essential to all organisms and has an important role in metabolism, growth, development and general well-being, as well as become a crucial co-factor for numerous enzymes in the body.<sup>85</sup>

### Insecticidal, anti-inflammatory and antiviral activities

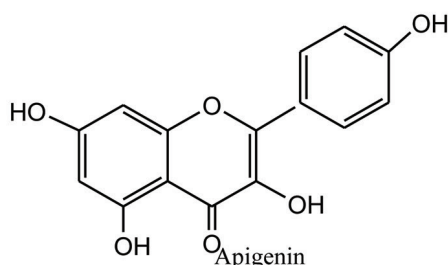
Some species show antiviral activity (*Justicia extensa* T. Anderson, *Justicia gendarussa* Burm f., *J. procumbens*, *Justicia reptans* Sw., and *Justicia valida* Ridl.) against *in vitro* HIV type 1 reverse transcriptase, HIV replication, and vesicular stomatitis virus.



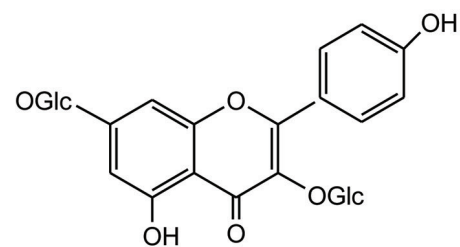
Umbeliferone



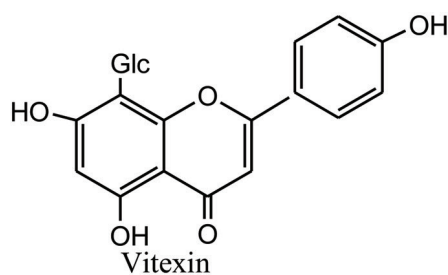
3',4'-Dihydroxy Flavonol



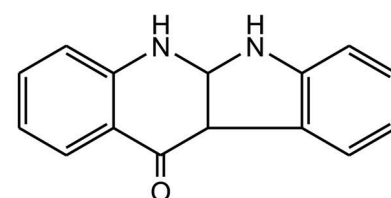
Apigenin



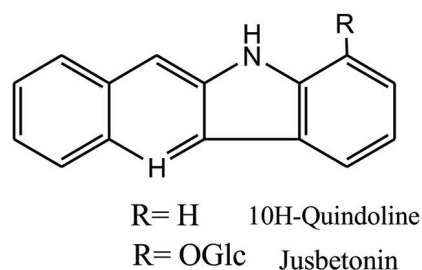
Kaempferitrin



Vitexin

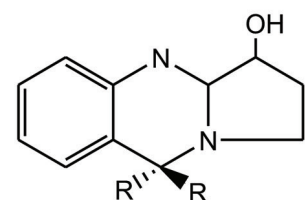


5H,6H-Quinindolin-11-one



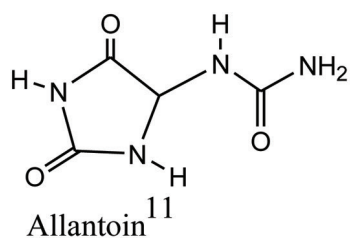
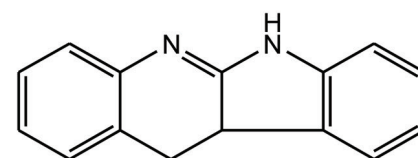
R= H 10H-Quindoline

R= OGlc Jusbetonin

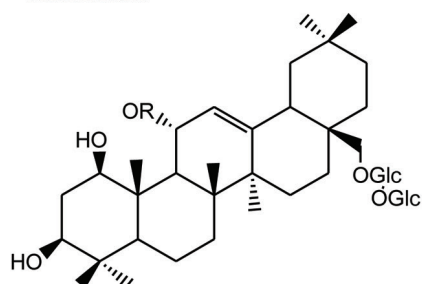


R = R' = H Vasicine

R and R' = O Vasicinone

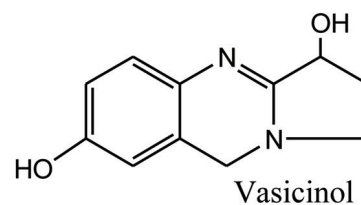
Allantoin<sup>11</sup>

6H-Quinindoline

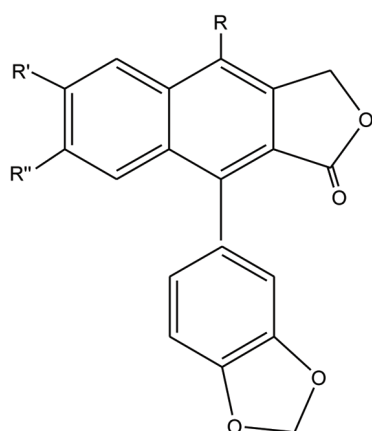
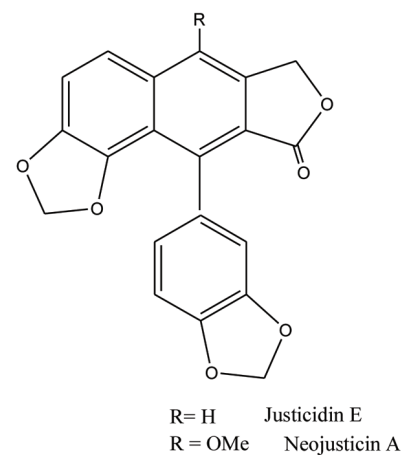
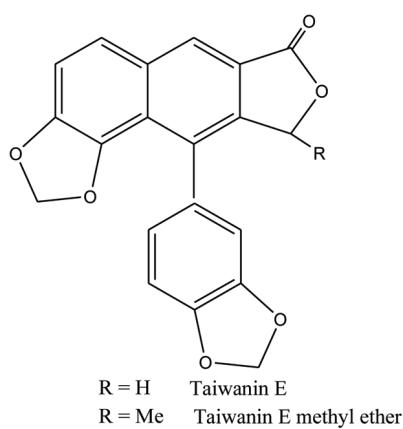
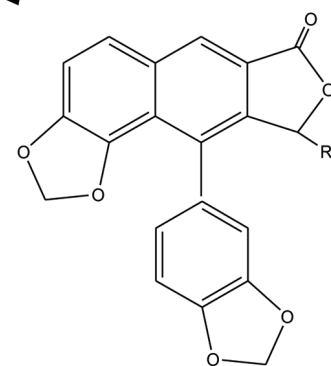
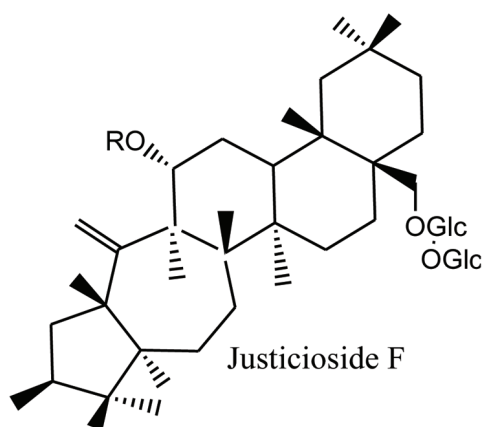
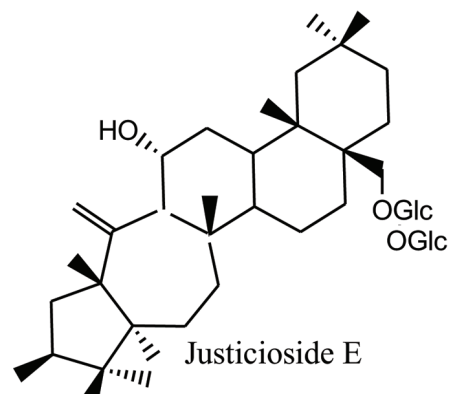
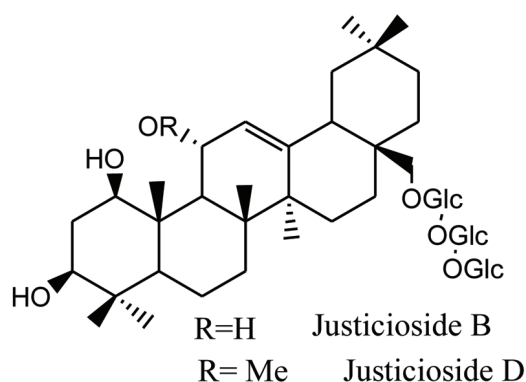


R= H Justicioside A

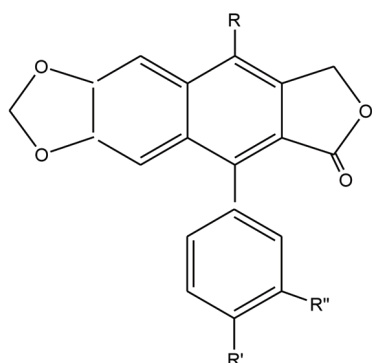
R= Me Justicioside C



Vasicinol

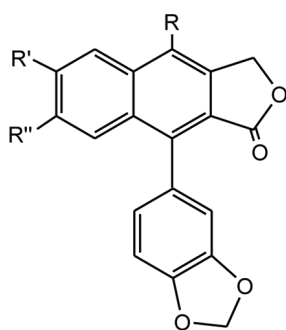


R = H; R' = R'' = OMe Justicidin B  
R = OH; R' = R'' = OMe Diphyllin  
R = R' = R'' = OMe Justicidin A  
R = OGlc; R' = R'' = OMe Cleistanthin B  
R = OGlc-OMe; R' = R'' = OMe Neesiinoside A  
R = OGlc-OMe; R' = R'' = OMe 4''-O-Acetylpatenti?orin B  
R = OGlc; Me; R' = R'' = OMe Patentiflorin A  
R = OGlc; Me; R' = R'' = OMe Patentiflorin B  
R = O-D-apiof uranosyl; Me; R' = R'' = OMe Tuberculatin



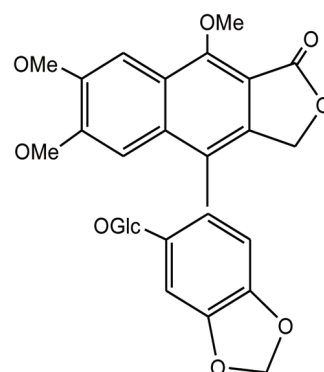
R= H; R'= R'' = OMe  
 R= OMe; R= OH; R''= OGlc  
 R=R''= OMe; R'=OH  
 R= OH; R'= R'' = OMe

Chinensinaphthol methyl ether  
 Justalakonin  
 4'-Dimethyl chinensinaphthol methyl ether  
 Chinensinaphthol

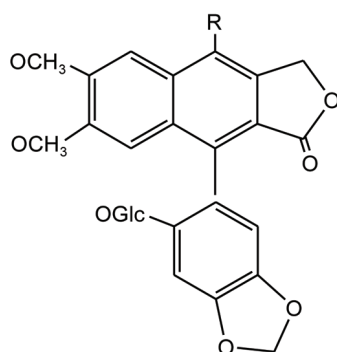


R = R'= H; R''= OH; R''' = OGlc Elenoside

R= R' = R'' OMe; R''' = H Neojustin B

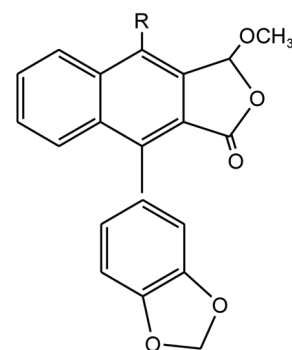


Justicidin A

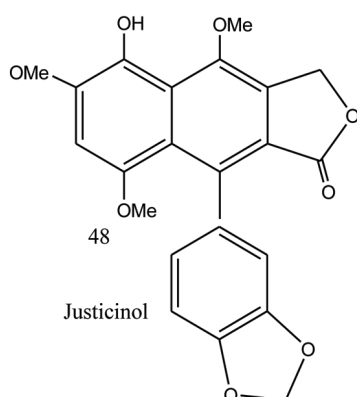


R= H Justicidin C

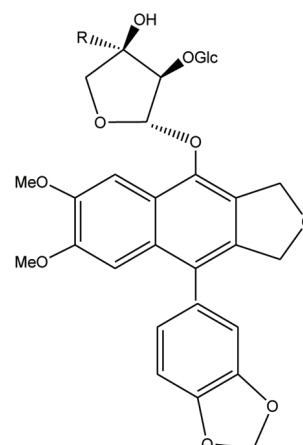
R= OMe Justicidin B



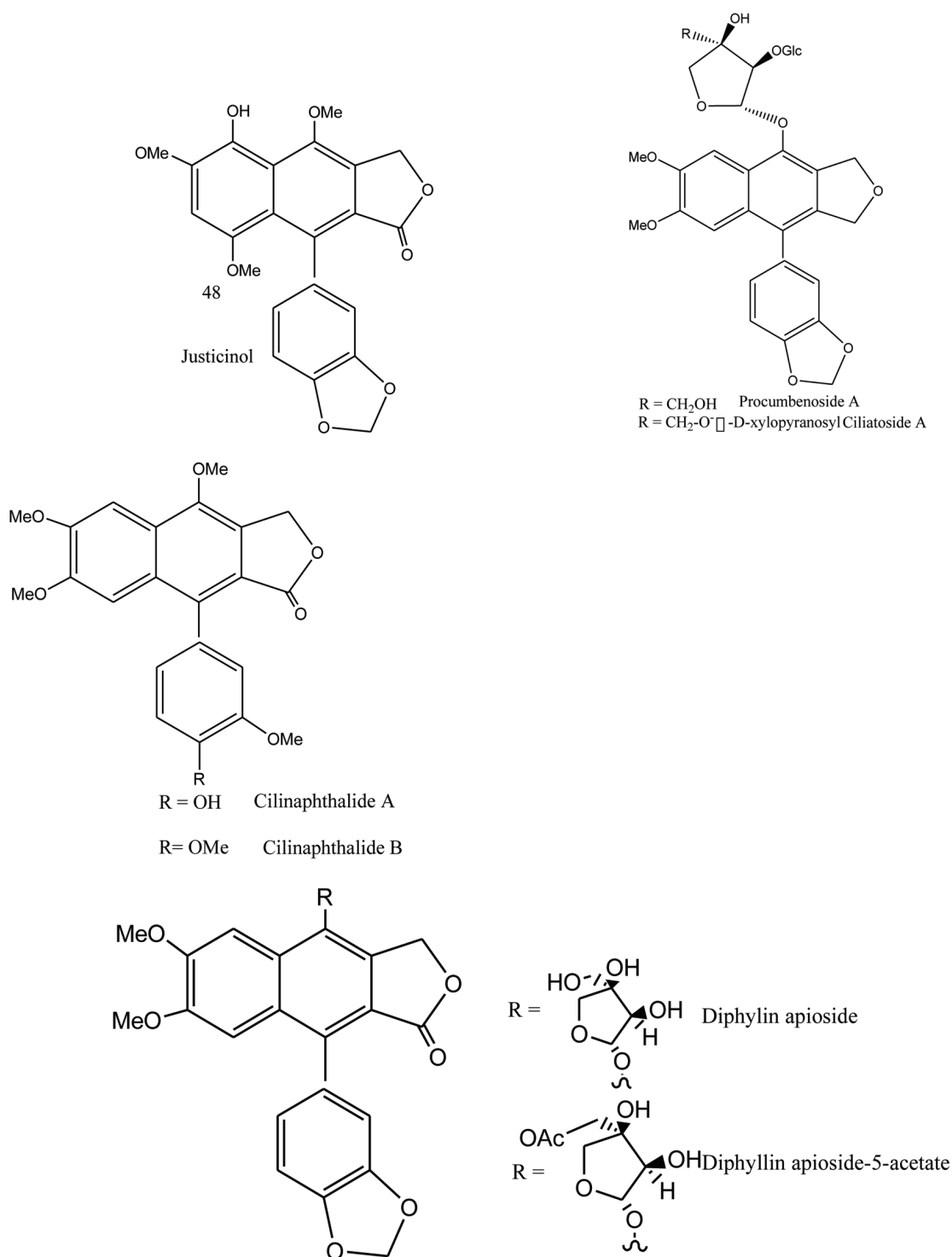
Justicidin P



Justicinol



R = CH<sub>2</sub>OH Procumbenoside A  
 R = CH<sub>2</sub>-O- $\square$ -D-xylopyranosyl Ciliatioside A



However, the species popularly used as antiviral agents, *Justicia betonica* L. and *Justicia flava* (Vahl) Vahl, 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. Based on these observations, this species might be further explored for its antiviral indications. 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,<sup>87</sup>

effects, explaining the plants traditional use in menopause and PMS therapies.

In Uganda. Lignans Justicidin B, Diphyllin, Justicidin A, Justicidin C, Justicidin B, Diphyllin apioside, and Diphyllin apioside-5-acetate show antiviral activities. These compounds were isolated from *J. extensa*, *J. betonica*, and *J. procumbens*, and also show the same biological activities. Conversely, lignans Justicidin B, Diphyllin, Justicidin A, Patentiflorin A, Patentiflorin B, and Elenoside show antiviral activity, but were isolated from species that did not show this activity. A larger investigation of the extracts of these species is required to explore their antiviral activities.<sup>88</sup>

### Cytotoxicity and Antibacterial activity

In Malaysia a total of 300 endophytes were isolated from various parts of plants (*Justicia spp*) from the National Park, Pahang. 3.3% of extracts showed potent ( $IC_{50} < 0.01 \mu\text{g/ml}$ ) cytotoxic activity against the murine leukemic P388 cell line and 1.7% against a human chronic myeloid leukemic cell line K562. *Sporothrix* sp. (KK29FL1) isolated from *Costus speciosus* showed strong cytotoxicity against colorectal carcinoma (HCT116) and human breast adenocarcinoma (MCF7) cell lines with  $IC_{50}$  values of  $0.05 \mu\text{g/ml}$  and  $0.02 \mu\text{g/ml}$ , respectively. Antibacterial activity has been demonstrated for 8% of the extracts. *J. pectoralis* showed high antibacterial activity against *E. coli*, *E. faecalis*, and *S. epidermidis*.<sup>89</sup>

The antimicrobial activity of biosynthesized AgNP were evaluated against foodborne bacteria (*Bacillus cereus*, *Klebsiella pneumoniae* and *Enterobacter aerogenes*) and phytopathogenic fungi (*Colletotrichum* sp., *Fusarium solani*, *Alternaria alternata* and *Macrophomina phaseolina*). The elemental profile of synthesized nano-particles using *J. spicigera* shows higher counts at 3 keV due to silver, confirming the formation of silver nanoparticles. Scanning electron microscopy (SEM) analysis showed a particle size between 86 and 100 nm with spherical morphology. AgNP showed effective antibacterial and antifungal activity against the tested organisms principally with *B. cereus*, *K. pneumoniae*, *E. aerogenes*, *A. alternata* and *M. phaseolina*. Therefore, further studies are needed to confirm the potential of AgNP from *J. spicigera* in the control of indicator organisms under field conditions.<sup>90</sup>

### Anticancer activity

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.<sup>91</sup> 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. spicigera* as anticancer agents was confirmed by employing the same parts of the plant. However, the anticancer properties of *Justicia adhatoda* L. have not yet been confirmed pharmacologically.<sup>92</sup>

Zahidah *et al.* 2014,<sup>13</sup> report them the methanolic leaf extracts of the *Justicia gendarussa* from five different locations in the Southern region of Peninsular Malaysia and two flavonoids, kaempferol and naringenin, were tested for cytotoxic activity. Kaempferol and naringenin were two flavonoids detected in leaf extracts using gas chromatography-flame ionization detection (GC-FID). The results indicated that highest concentrations of kaempferol and naringenin were detected in leaves extracted from Mersing with 1591.80mg/kg and 444.35mg/kg, respectively. Positive correlations were observed between kaempferol and naringenin concentrations in all leaf extracts analysed with the Pearson method. The effects of kaempferol and naringenin from leaf extracts were examined on breast cancer cell lines (MDA-MB-231 and MDA-MB-468) using MTT assay. Leaf extract from Mersing showed high cytotoxicity against MDA-MB-468 and MDA-MB-231 with  $IC_{50}$  values of  $23 \mu\text{g/mL}$  and  $40 \mu\text{g/mL}$ , respectively, compared to other leaf extracts. Kaempferol possessed high cytotoxicity against MDA-MB-468 and MDA-MB-231 with  $IC_{50}$  values of  $23 \mu\text{g/mL}$  and  $34 \mu\text{g/mL}$ , respectively. These findings suggest that the presence of kaempferol in Mersing leaf extract contributed to high cytotoxicity of both MDA-MB-231 and MDA-MB-468 cancer cell lines.

### Antiepileptic and anxiolytic activities.

The popular use of *J. pectoralis* in the treatment of epilepsy and anxiety has been confirmed with the ethanol extract of the leaves. The ethanol extracts of *J. pectoralis*, *Justicia aurea* Schltdl., and *Justicia albobractea* Leonard were tested *in vitro* for their ability to inhibit GABA transaminase (GABA-T) or to bind to the GABA benzodiazepine 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 GABA Abinding 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 plants antiepileptic and anxiolytic activities.<sup>92</sup>

### Anti-sickling activity

Anthocyanins from *Justicia secunda* were found to possess anti-sickling activity. Treated SS red blood cells recovered a normal, classical biconcave form with a radius of  $3.3 \pm 0.3 \mu\text{m}$ , similar to that of normal erythrocytes.<sup>93</sup> The results obtained indicate that all these three collected species from Kisangani and its surrounding, located at the North-East of the D.R. CONGO, showed an antisickling activity. The chemical screening performed on these plants showed in these three species the presence of polyphenols of which anthocyanins. The tests carried out with anthocyanins extracts showed a significant activity of these metabolites with a normalization rate of the form of the sickle cells of 87% for *Justicia gendarussa*, 92% for *Justicia insularis* and 80% for *Justicia tenella*. The minimal concentrations in anthocyanins necessary to have maximal normalization are respectively of 7.2  $\mu\text{g/mL}$  for *Justicia insularis*, 7.6  $\mu\text{g/mL}$  for *Justicia gendarussa* and 7.7  $\mu\text{g/mL}$  for *Justicia tenella*.<sup>6</sup>

The acute toxicity was performed with up and down method and the highest dose used was 2 g/kg. The anti-inflammatory activity was evaluated using the carrageenan and formalin-induced paw edema models, and antinociceptive activity was evaluated using acetic acid-induced writhing reflex and tail flick test models while the antioxidant activity was evaluated using 2,2-diphenyl-2-picryl hydrazyl (DPPH) and ferric reducing antioxidant power (FRAP) photometric assay. The extract was well tolerated as no signs of toxicity or death were noticed during the period of observation. The extract produced a concentration dependent increase in antioxidant activities in both DPPH and FRAP models. The extract produced its optimum activity at 400 lg/ml in both DPPH (54.07%) assay and FRAP (1.58 lM) assay. The extract produced significant ( $P < 0.05$ ) dose-dependent increase in both anti-inflammatory and antinociceptive activities. The antinociceptive and anti-inflammatory activities of the extract (0.4 g/kg) were comparable with the reference drugs (aspirin and pentazocine) used in the study.<sup>94</sup>

### CONCLUSION

The present mini-review was undertaken with the aim of providing highlight and updated information

on the medically and scientific evidence supporting the multiple uses of *Justicia secunda* Vahl. species in Traditional Medicine. Medicinal plant species are rich in secondary metabolites of pharmaceutical relevance. The advantages of their therapeutic uses in various ailments are their safety besides being economical, effective and available. Justicia species are pharmacologically and chemically much studied but limited to only some activities, although the diversity of secondary metabolites present in the plants species especially alkaloids, saponins tannins, flavonoids, terpenoids, amino acids, aromatic amines, stigmasterol, lupeol, coumarin, steroids, glycosides have already been isolated from there. *Justicia secunda* Vahl. is a good candidate for Tropical Plants Screening Research program for the development of lead compounds against genetic and parasitic diseases such as the antisickling, anti-hemolytic and membrane stabilizing effects.

### ACKNOWLEDGEMENT

The authors gratefully acknowledge and thank the TWAS and the Swedish International Development Agency (SIDA) for the grant

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