Pavonia Cav. SPECIES (MALVACEAE SENSU LATO) AS SOURCE OF NEW DRUGS: A REVIEW

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INTRODUCTION

Medicinal plants constitute the main therapeutic source of folk medicine. Traditional knowledges are passed through generations due to the stark believes that come since primitive folks and healers. Previous ethno-pharmacological-botanical studies form the foundation to the development of new drugs from medicinal herbs.\textsuperscript{1}

Plants provide an essential economic role as they are used as a drug source.\textsuperscript{2} This fact rises in developing countries due to lesser side effects and easy access that low-income populations have to those plants, making them an almost inexhaustible source of remedies for those people.\textsuperscript{3}

Several chemical compounds that act as potential therapeutic agents have been isolated from plant species.\textsuperscript{4} Studies about those compounds are based on ethnomedical, chemical and pharmacological knowledges, aiming to find out new bioactive molecules. On this context, species from Malvaceae sensu lato family arouse major interests of the scientific community due to the fact that those species are important economic sources in agriculture, decorations, manufacturing, food and medicine.\textsuperscript{5}

Among several genus belonging to Malvaceae sensu lato, we highlight Pavonia Cav., which has several biological and pharmacological activities described in literature about folk medicine. Those activities have been confirmed through the isolation, identification and characterization of secondary metabolites, as well as several pharmacological activities described for those compounds.\textsuperscript{6}

The genus Pavonia Cav. includes approximately 271 species distributed worldwide, being more diverse in America and Africa, with only two species being recorded for Asia. A lot of chemical and pharmacological studies with species P. odorata and P. zeylanica are described in literature, mostly for India, due to the traditional medicine system Ayuverda.\textsuperscript{7}

Approximately 224 species can be found in America, ranging from USA to Uruguay, including the Antilles and excluding Chile.\textsuperscript{8}

In Africa, approximately 46 species can be found.\textsuperscript{9} In Brazil, 136 species of Pavonia can be found, ranging from Amazon rainforest, Caatinga, Cerrado, Atlantic Forest, Pampas and Pantanal wetlands.\textsuperscript{9}

Based on presented data, this review aims to accomplish a bibliographical survey about traditional uses of Pavonia species and evaluate the chemical and pharmacological potential of this genus in order to drive future researches based on natural products as a source of new drugs.

METHODOLOGY

Information about the use of plants by folk medicine, phytochemical studies, botanic characteristics and pharmacological activities of genus Pavonia have been based and collected from scientific data banks such as: ‘Web of Science’, ‘Scifinder’, ‘Pubmed’ and ‘Scholar Google’, using papers, books, dissertation and thesis from the year 1918 until April 2021 and searching for the keyword ‘Pavonia’. Following this methodology, we consulted 156 scientific articles, having, as inclusion criteria, the presence of information regarding the use of Pavonia genus in traditional medicine, phytochemical studies, pharmacological and/or biological activities. The exclusion criteria of the articles involved repetition of those in different databases, review articles that contained references used in the manuscript, information with the keyword ‘Pavonia’ that do not concerns the genus, articles with only botanical data or articles not available for access on the platforms used. A single patent referring to the species P. schiedeana (JP 2001181172A (2001)) was found as part of a cosmetic composition.

The development of this revision paper aimed the study of this genus in order to expand the scientific interest through knowledge of isolated compounds with several biological activities, as those are the candidates to new drugs isolated from Pavonia species.

The present study and data have been extracted by the author (JBLA) and confirmed by other (DAF, CMS, PIVS, MFVS). All data are resumed in tables and their descriptions have been resumed as updated information.
RESULTS AND DISCUSSION

Botanical description

*Pavonia* comprises species of herbs, shrubs and bushes. Its flowers are, generally, solitary, composed by four epicalyces, several free bracteoles, a tubulous and cupuliform calyx composed by five petals, carpels uniovulate and stigma capitate (Figure 1). The fruits are schizocarp, formed by five mericarps with a nervous-reticulate dorsal face, smooth lateral faces and smooth or striated obovoid or reniform seeds.

Some species of *Pavonia* possess floral nectaries formed by multicellular glandular trichomes, providing a thick area located near the internal base of calyx. This characteristic attracts hummingbirds, which are pollinators of tubulous flowers, such as *P. glazioviana* and *P. multiflora*. Species that possesses flowers with twisted corolla and short staminal tube formed by free stamens, such as *P. malacophylla*, *P. varians*, *P. zeylanica* and *P. distinguenda*, are pollinated by bees.

Ethnopharmacological relevance

Different species of *Pavonia* Cav. are related in folk medicine as a treatment for several diseases. Among the most used parts of those plants used by some tribes in therapeutics are flowers, bark, roots, rhizomes and flowers (Table 1).

Juice of *P. odorata* leaves is used by traditional medicine Ayurveda as a treatment for dysentery, gonorrhea and halitosis, whereas leaves macerate as a paste are used as a treatment for rheumatism, foot infections and antipyretic.

Powder from seeds of *P. senegalensis* is used as a contraceptive. Decoct of *P. urens* roots is largely used as a treatment for toothache. Brewing of roots and leaves of *P. zeylanica*, as well as decocts, powder and pastes are largely used by eastern communities as a treatment for osteoarthritis, joint pain, bone fractures, cough with discharge and healing of wounds. Leaves’ juice and the entire plant prepared as infusion are also used for its vermifuge and purgative properties.

Several ethnopharmacological studies regarding *Pavonia* species have been described in literature, which give us basis for deepening the chemical and pharmacological knowledge of those herbs, since many of the pharmacological activities are related to traditional use of medicinal plants, therefore providing essential information to the development of new drugs.

Chemical composition

Based on literature data, 29 references in the area of phytochemistry have been found to species of the genus *Pavonia*: 10 papers referred to species *P. odorata* (06) and *P. zeylanica* (04); 9 papers referred to species *P. malacophylla* (03), *P. glazioviana* (03) and *P. sepium* (03), and; 2 papers referred to *P. cancelatta*. Besides, several other papers have been related in this field with the species *P. varians*, *P. xanthogloea*, *P. sepioides*, *P. distinguenda*, *P. multiflora*, *P. hastata*, *P. lasiopetala*, *P. schiedeana* and *P. alnifolia*. 169 compounds have been isolated and/or identified in the genus *Pavonia* (Table 2), comprehending the most diverse classes of secondary metabolites ever related.

Fatty acids are molecule that consists of the most diverse lipids and, by enzymatic action, become free fatty acids, presenting powerful biological activities.

Table 1. Species of *Pavonia* genus and their uses in folk medicine

| Scientific name/ Popular name | Used plant part | Traditional Use | Therapeutic Properties | References |
|-------------------------------|-----------------|-----------------|------------------------|------------|
| *Pavonia cancellata* | LV | Poultice | Boils | 31 |
| *Pavonia distinguenda* | AP * | * | Antitumor and antibacterial | 32 |
| *Pavonia lasiopetala* | WP | Decoction | Antipyretic and common cold | 33 |
| *Pavonia rosa* | LV * | Breaks and disintegrates kidney and urinary stones; Diuretic | 34 |
Table 1. Species of *Pavonia* genus and their uses in folk medicine (cont.)

| Species                        | Uses                                                                 | References |
|--------------------------------|----------------------------------------------------------------------|------------|
| **RH**                         | Dysentry, anti-inflammatory, anti-hemorrhagic; Antipyretic, digestive and astringent | 35,36      |
| **RH and LV**                  | Antipyretic, stomachic, dysentry and antiurolytic                      | 37,38      |
| **WP**                         | Antipyretic, stomachic, dysentry; Rheumatism; Antiemetic; Anti-hemorrhagic; Demulcent, carminative, diaphoretic, diuretic, anti-inflammatory, spasmyotic and astringent | 29,39-45   |
| **ST and RT**                  | Antipyretic                                                           | 7          |
| **ST**                         | Bone fractures                                                         | 46         |
| **AP**                         | Colds, diaphoretic, diuretic, demulcent; Antipyretic, anti-inflammatory and anti-hemorrhagic | 47-49      |
| **P**                          | Antipyretic, stomachic, dysentry; Anti-hemorrhagic; Skin diseases, anti-inflammatory, spasmyotic; Nervous weakness | 3,35,50-54 |
| **LV**                         | Leaf juice, Dysentry; Gonorrhoea; Anti-halitosis                       | 12-15      |
| **RT**                         | Stomachache, anti-inflammatory, anti-hemorrhagic; Antipyretic, diuretic; Carminative, diaphoretic, polydipsia, burning when urinating, demulcent astringent, stomachic, haemorrhages from intestines; bleeding disorders, dysentry and antiulcerogenic; appetizer | 4,29,52,55-58 |
| **Pavonia odorata/ Sugandhibala** |                                                                       |            |
| **LV**                         | Paste, Athlete’s foot                                                 | 1,159      |
| **RT**                         | Decoction, Athlete’s foot                                             | 1,59       |
| **Powder**                     | Dislocations of bone joints; Osteoarthritis                           | 21,22      |
| **Decoction**                  | Dysentry and carminative                                               | 60,61      |
| **Pavonia procumbens**         | Antiulcerogenic, fumigation, vermifuge, analgesic and skin infections | 2,51,62-64 |
| **Pavonia schiedeana/ Cadillo**| Decoction, Retained placenta and prevention of miscarriage            | 65         |
| **RT and WP**                  | Poultice, Antipyretic                                                 | 66         |
| **LV**                         | Infusion, Hypoglycemic; retained placenta and prevention of miscarriage | 65,67      |
| **Pavonia senegalensis**       | Aqueous extract, Bone and soft tissue infections                       | 68,69      |
| **RT**                         | Inhalation and infusion, Diarrhea and induce labour                   | 70,71      |
| **SD**                         | Powder, Contraceptive                                                 | 18         |
| **Pavonia spinifex**           | Infusion, Analgesic and skin problems                                 | 72,73      |
| **FL**                         | Infusion, Stomach problems, gallstones and liver pain                 |            |
| **LV**                         | Infusion, Hepatoprotection, antioxidant, anticancer, antifungal and antibacterial | 74         |
| **AP**                         | Inhalation and decoction, Antipyretic                                 | 75         |
| **RT**                         | Decoction, Toothache                                                  | 19,20      |
| **Pavonia urens**              | Boils, Repellent for mosquitoes and house flies                       | 78         |
| **Pavonia varians/ Malva-peluda** | Infections of the digestive system, and anti-inflammatory              | 82         |
| **Pavonia xanthogloeal/ Erva-de-ovelha** | Antimicrobial and antitumor                                           | 83,84      |
| **Pavonia zeylanica/ Citramutti** | Eczema; Eye diseases; Antipyretic, Anthelmintic, anti-inflammatory, analgesic, toothache; Dysentry, anti-hemorrhagic and emollient | 43,85-91  |
| **LV**                         | Decoction, Cough with phlegm                                          | 23         |
| **Ground**                     | Constipation in animals                                               | 92         |
| **Paste**                      | Bone fractures; Healing of acute and chronic wounds                   | 24,25      |
| **Smoke**                      | Skin diseases, anthelmintic, leprosy, scabies, ringworm, dermatitis, acne, wounds and antiulcerogenic; Blood circulation | 3,93       |
**Table 1. Species of *Pavonia* genus and their uses in folk medicine (cont.)**

| Scientific name/ Popular name | Medicinal Parts | Traditional Use | Therapeutic Properties | References |
|-------------------------------|----------------|-----------------|------------------------|------------|
| *Pavonia zeylanica*/*Citramutti* | WP | Inhalation | * Antipyretic and anthelmintic; Paralysis; Joint pain | 94, 4, 95, 96 |
|                               | RT | Infusion and leaf juice | * Demulcent, carminative, diaphoretic, diuretic, astringent, tonic, anti-hemorrhagic and anti-inflammatory; Antiulcerogenic | 88, 97 |
|                               | AP: Aerial Parts; FL: Flowers; FR: Fruits; LV: Leaves; RH: Rhizomes; RT: Roots; SD: Seeds; ST: Stems; TW: Twigs; WP: Whole Plant. |

*not reported in the literature.*

**Table 2. Isolated compounds from *Pavonia* genus**

| Nº  | Name                  | Source                  | Reference |
|-----|-----------------------|-------------------------|-----------|
| 1   | Malvalic acid         | SD of *P. sepium* and *P. zeylanica* | 98-101    |
| 2   | Sterculic acid        |                         |           |
| 3   | Palmitic acid         |                         |           |
| 4   | Stearic acid          | SD of *P. zeylanica*, RT and AP of *P. oleracea* | 48, 101-105 |
| 5   | Oleic acid            | AP of *P. oleracea*     |           |
| 6   | Linoleic acid         |                         |           |
| 7   | Dihydrosterculic acid | SD of *P. zeylanica*    | 101       |
| 8   | (9Z,12Z,15Z)-9,12,15-Octadecatrienoic acid | RT of *P. oleracea* | 48, 102-104, 106 |
| 9   | Isovaleric acid       |                         |           |
| 10  | Caproic acid          |                         |           |
| 11  | Dodecanoic acid       |                         |           |
| 12  | Methyl tetradecanoate |                         |           |
| 13  | Tetradecanoic acid    |                         |           |
| 14  | Methyl-(2E,6E)-farnesate | AP of *P. oleracea* | 105       |
| 15  | Pentadecanoic acid    |                         |           |
| 16  | Methyl palmitate      |                         |           |
| 17  | Methyl linoleate      |                         |           |
| 18  | Methyl oleate         |                         |           |
| 19  | α-amirine             | AP of *P. malaba*       | 107       |
| 20  | β-amirine             |                         |           |
| 21  | Lupeol                | AP of *P. malaba* and *P. doistionii* | 31, 108 |
| 22  | Blumenol C            |                         |           |
| 23  | Vomifoliol            |                         |           |
| 24  | 4,5-dihydroxalbumenol A | LV of *P. malaba*       | 109       |
| 25  | 3-oxo-α-ionol         |                         |           |
| 26  | Loliolide             |                         |           |
| 27  | Taraxerol p-methoxybenzoate |                 |           |
| 28  | Cycloart-23Z-en-3β, 25-diol | AP of *P. gularia* | 110       |
| 29  | Cycloart-25Z-en-3β, 24-diol |                         |           |
| 30  | Taraxerol             | AP of *P. dianthus*     | 31        |
| 31  | Germanicol            |                         |           |

**Terpenoids**

| Nº  | Name                  | Source                  | Reference |
|-----|-----------------------|-------------------------|-----------|
| 32  | Cedran-diol,8S,13     |                         |           |
| 33  | Cedrol                |                         |           |
| 34  | S-guaiazulene         |                         |           |
| 35  | Pinocarveol           |                         |           |
| 36  | α-terpinene           | RT of *P. oleracea*    | 48, 102-104, 106 |
| 37  | Pavonanol*            |                         |           |
| 38  | β-pinene              |                         |           |
| 39  | p-cymene              |                         |           |
| 40  | 1,8-cineole           |                         |           |
| 41  | (Z)-linalooloxide     |                         |           |
| 42  | (E)-linalooloxide     |                         |           |
| 43  | Linalool              |                         |           |
| 44  | (E)-pinocarveol       |                         |           |
| 45  | Borneol               |                         |           |
| 46  | Menthol               |                         |           |
| 47  | Terpinen-4-ol         |                         |           |
| 48  | p-cymen-8-ol          |                         |           |
| 49  | α-terpineol           |                         |           |
| 50  | Carvone               |                         |           |
| 51  | Geraniol              | AP of *P. oleracea*    | 105       |
| 52  | Thymol                |                         |           |
| 53  | Eugenol               |                         |           |
| 54  | β-damascenone         |                         |           |
| 55  | β-caryophyllene       |                         |           |
| 56  | β-eudesmol            |                         |           |
| 57  | Mururolane            |                         |           |
| 58  | Farnesyl acetone      |                         |           |
| 59  | Phytole               |                         |           |
| 60  | β-caryophyllene oxide |                         |           |
| 61  | Guaiole               |                         |           |
| 62  | γ-eudesmol            |                         |           |
| 63  | α-eudesmol            | RT and AP of *P. oleracea* | 48, 102-105 |
| 64  | α-pinene              |                         |           |

**Steroids**

| Nº  | Name                               | Source                  | Reference |
|-----|------------------------------------|-------------------------|-----------|
| 65  | Sitosterol-3-O-β-D-glucopyranoside | AP of *P. oleracea*    | 107, 110-112 |
| 66  | Stigmasterol-3-O-β-D-glucopyranoside | AP of *P. oleracea* and *P. gularia* | 107, 110-112 |
Table 2. Isolated compounds from Pavonia genus (cont.)

| Nº  | Name                                      | Source              | Reference       |
|-----|-------------------------------------------|---------------------|-----------------|
| 67  | β-sitosterol                               | AP of P.c., P.mal., and P.d.; RT of P.o. | 31,106, 107,111, 112 |
| 68  | Stigmasterol                               | AP of P.c.          | 111,112         |
| 69  | Ethyl iso-allocholate                      | RT of P.o.         | 106             |

**Flavonoids**

| Nº  | Name                                      | Source              | Reference       |
|-----|-------------------------------------------|---------------------|-----------------|
| 70  | Kaempferol-3-O-(6''-O-p-coumaroyl)-glucoside (Tiliroside) | AP of P.c., P.x., P.mal., P.v., P.g., P.d. | 11,31,83, 107, 111-114 |
| 71  | 3,7-di-O-methylkaempferol                  | AP of P.c.          | 111,112         |
| 72  | Quercetin                                  | FL of P.h. and Pl.; AP of P.x., P.mal., P.g. | 11,83, 117, 107,115 |
| 73  | 2-(3,4-dihydroxyphenyl) chromane-3,5,7-triol (Cyanidin) | AP of P.x.         | 83,116         |
| 74  | Rutin                                      | AP of P.a. and P.x. | 83              |
| 75  | Quercitin                                  | AP of P.x.          | 83              |
| 76  | Kaempferol                                 | AP of P.mal., P.g. | 11,107         |
| 77  | 5,8-dihydroxy-7,4'-dimethoxyflavone        | AP of P.mal.        | 108             |
| 78  | 5,7-dihydroxy-4'-methoxyflavone (Acacetin) |                     |                 |
| 79  | 5,7-dihydroxy-3,8,4'-trimethoxyflavone     | AP of P.g.          | 11,110, 117     |
| 80  | 5-hydroxy-3,7,8,4'-tetramethoxyflavone     | AP of P.mal., P.g.  |                 |
| 81  | 5,7,4'-trihydroxy-3,8-dimethoxyflavone     |                     |                 |
| 82  | 5,7,4'-trihydroxy-3-methoxyflavone         |                     |                 |
| 83  | Kaempferol-3-glucoside (Astragalin)        | AP of P.d.          | 31              |
| 84  | Dihydrokaempferol (Aromadendrin)          | RT of P.o.         | 48,102-104      |
| 85  | Aromadendrene                              |                     |                 |

**Compounds Phenolics**

| Nº  | Name                                      | Source              | Reference       |
|-----|-------------------------------------------|---------------------|-----------------|
| 86  | Gossypol                                   | SD of P.sch.        | 118             |
| 87  | Gallic acid                                |                     |                 |
| 88  | Catechin                                   | AP of P.x.          | 83              |
| 89  | Chlorogenic acid                           |                     |                 |
| 90  | Caffeic acid                               | AP of P.x.; LV of P.sepio. | 83,119         |
| 91  | Vanillic acid                              |                     |                 |
| 92  | Ferulic acid                               | LV of P.mal. and P.sepio. | 109,119       |
| 93  | p-Hydroxybenzoic acid                      |                     |                 |
| 94  | p-coumaric acid                           | LV of P.mal.        | 109             |
| 95  | Salicylic acid                             |                     |                 |
| 96  | Cinnamic acid                              |                     |                 |
| 97  | p-Hydroxyphenylacetic acid                 | LV of P.sepio.      | 119             |
| 98  | Gentisic acid                              |                     |                 |
| 99  | 4-[(1E)-prop-1-en-1-yl] benzoic acid       |                     |                 |

**Other compounds**

| Nº  | Name                                      | Source              | Reference       |
|-----|-------------------------------------------|---------------------|-----------------|
| 100 | 2-[(1E)-prop-1-en-1-yl] benzoic acid      |                     |                 |
| 101 | 3-[(1E)-prop-1-en-1-yl] benzoic acid      | LV of P.sepio.      | 119             |
| 102 | Syringic acid                             |                     |                 |
| 103 | Protocatechelic acid                      |                     |                 |

**Phenyl alcohol**

| Nº  | Name                                      | Source              | Reference       |
|-----|-------------------------------------------|---------------------|-----------------|
| 114 | Benzoic acid-2-hydroxy-ethyl-ester        |                     |                 |
| 115 | 5αH-3α,12-methano-1H-cyclopropane [5,6'] cyclodecane [1'-2',1,5] cyclopenta [1,2-d] [1,3] dioxal-13-one |                     |                 |
| 116 | 2,7-diphenyl-1,6 dioxypyridazinol[4,5,2,3'] pyrrolo[4',5'-p]pyridazine |                     |                 |
| 117 | Bicyclo [4, 3, 0] nonan-7-one,1-(2-methoxyvinyl) 1,5-bis (3-cyclopentyl-propoxy)-1, 13,3,5,5-hexamethylsiloxane |                     |                 |
| 118 | Pavenone*                                 |                     |                 |
| 119 | Isovaleraldehyde                          |                     |                 |
| 121 | Azulene                                   |                     |                 |
| 122 | Hexahydrofarnesyl-acetone                 | RT and AP of P.o.   | 48,102-104, 104,106 |
| 123 | 6-methyl-5-hepten-2-one                   |                     |                 |
| 124 | Isopentyl alcohol                         |                     |                 |
| 125 | Pentanol                                  |                     |                 |
| 126 | Hexanol                                   |                     |                 |
| 127 | Benzyl alcohol                            |                     |                 |
| 128 | Phenylethyl alcohol                       |                     |                 |
| 129 | 2-methoxy-p-cresol                        |                     |                 |
| 130 | 2-methoxy-4-vinylphenol                   |                     |                 |
| 131 | 2,4-bis(1,1-dimethylethyl)-phenol          |                     | 105             |
| 132 | Acetophenone                              |                     |                 |
| 133 | 2-nonanone                                |                     |                 |
| 134 | Isophorone                                |                     |                 |
| 135 | 4-keto-isophorone                         |                     |                 |
| 136 | p-menth-4-en-3-one                        |                     |                 |
Studies described in literature review that activities of those compounds depend on the level of unsaturation and the size of hydrocarbons chain, resulting antibacterial, antifungal and antimycobacterial activities. A recent study has shown that P. malacophylla and P. cancellata have palmitic, oleic and linoleic acids as majoritarian fatty acids.

Eighteen fatty acids have been isolated and identified in species P. sepium, P. odorata and P. zeylanica (Table 2). Palmitic (3) and capric (10) fatty acids showed significant activities in preparatory studies as having inhibitory properties for the activities of glycerol kinase enzyme from the fungus Epidermophyton floccosum and inhibitory properties for the alcohol-dehydrogenase enzyme from the protozoan Entamoeba histolytica.

Table 2. Isolated compounds from Pavonia genus (cont.)

| N° | Name                           | Source | Reference |
|----|--------------------------------|--------|-----------|
| 137| Dihydro-5-pentyl-2-(3H)-furanone | AP of P.o | 105       |
| 138| Hexahydropseudoionone          |        |           |
| 139| α-ionone                       |        |           |
| 140| Dihydro-β-ionone               |        |           |
| 141| Dihydropseudoionone            |        |           |
| 142| β-ionone                       |        |           |
| 143| 4,8,12-trimethyltridecan-4-olide |        |           |
| 144| Phthalic acid                  |        |           |
| 145| 2-pentyl-furan                 |        |           |
| 146| 3-butyl-pyridine               |        |           |
| 147| p-vallyl-anisole               |        |           |
| 148| 3-phenylpyridine               |        |           |
| 149| Dihydroacinnolide              |        |           |
| 150| Ageratocromene                 |        |           |
| 151| Hexadecanolactone              |        |           |
| 152| Hexanal                        |        |           |
| 153| Benzaldehyde                   |        |           |
| 154| Phenylacetaldehyde             |        |           |
| 155| (2E)-nonen-1-al                |        |           |

Steroids are a minority class in Pavonia genus, with only five isolated compounds (65-69). Phyto steroids share as common structure ciclopentanoperidrofenaterne as carbonic skeleton, being β-sitosterol and stigmasterol the most common steroids of this genus and commonly encountered attached to sugar monomers.

Flavonoids and phenolic compounds

Flavonoids are the most important and diversified class of phenolic compounds among natural products, being relatively abundant secondary metabolites and responsible for several functions in plants’ organisms.

Seventeen flavonoids have been isolated from Pavonia species, being sixteen of those members of subclass flavone (70-84) and one, to flavanonol subclass (85). Many isolated flavonoids have glycosids attached to their structures.

Among the isolated compounds, flavonoid 5,7-dihydroxy-3,8,4’-trimethoxy flavone (79) has demonstrated in vitro antimicrobial, in silico anticancer, in vitro antineoplastic, in vitro antiprotozoal and in vitro photoprotective activities.

The compound tiliroside (70) has demonstrated in vitro and in vivo antihypertensive activities, leading to reduction of peripheral vascular and vasorelaxant resistances by blocking the Calcium channels dependent of voltage (CaV) in cells of vascular smooth muscle (VSMCs); in vitro antimicrobial activity; in silico antidiabetic activity through interaction with human pancreatic α-amylase enzyme; in vitro anticancer and anticolinesterasic activities.

Nineteen phenolic compounds (87-105) have been identified and isolated from the species P. xanthogloea, P. sepioides, P. multiflora and P. schiedeana. Studies demonstrated that those compounds presented different activities. Gross ethanolic extract and fractions of ethyl acetated from extractive process of P. sepioides leaves have shown a large quantity of phenolic compounds present on the samples, which...
Figure 2. Compounds isolated from Pavonia species
Figure 2. Compounds isolated from Pavonia species (cont.)
Figure 2. Compounds isolated from Pavonia species (cont.)
Figure 2. Compounds isolated from Pavonia species (cont.)
Figure 2. Compounds isolated from Pavonia species (cont.)
explains the antioxidant activity of those substances against free radicals inhibitions tests through the methods of DPPH and ABTS.119

Besides that species, other studies have shown a large potential of antioxidant activity as a primordial activity of those phenolic compounds such as described for P. xanthogloea, P. zeylanica, P. odorata, P. distinguenda, P. varians, P. glazioviana and P. procumbens.31,44,82,83,90,117,133-135

Other compounds

Differently from previously mentioned compounds, other classes of secondary metabolites have been isolated and identified in a lesser frequency on Pavonia species. Among those compounds, we can list alcohols, aldehydes, ketones, pheophytins and hydrocarbons (106-171) (Table 2, Figure 2).

Chaves107 has conducted a phytochemical study of P. malacophylla, isolating and identifying the compound 17α-ethoxy-phaeophorbide A (104), which has presented in vitro antibacterial activity against Staphylococcus aureus and Escherichia coli.

Table 3. In vitro, in vivo, and in silico biological studies reported from Pavonia genus

| Species | Material used | Experimental model | Reference |
|---------|---------------|--------------------|-----------|
| **Anti-inflammatory and Analgesic Activity** |
| Pz.     | Leaves alcoholic extract | In vitro - anti-inflammatory and antinociceptive by inhibition the arachidonic acid pathway | 88 |
| Pz.     | Leaves and stems aqueous extract | In vitro - anti-inflammatory and analgesic | 136 |
| Pz.     | Leaves ethanolic extract | In vitro – anti-inflammatory activity by inhibition protein denaturation | 90 |
| Po.     | Roots extract | Anti-inflammatory activity | 137 |
| Po.     | Roots methanolic, chloroform and ethyl acetate extract | In vitro - anti-inflammatory | 106 |

| **Antioxidant Activity** |
|--------------------------|
| Pz.                     | Aerial parts hexane fractions, dichloromethane, ethyl acetate, n-butanol, and water ethanol extract | In vitro – inhibition of DPPH, H₂O₂ and sodium nitroprusside radicals (SNP) | 83 |
| Pz.                     | Aerial parts hydroalcoholic extract | In vitro - stabilization of radicals free DPPH | 82 |
| Pgl.                    | Aerial parts ethanolic extract | In vitro – inhibition of DPPH radicals | 117,134 |
| Ppro.                   | Leaves methanolic extract | In vitro – inhibition of ABTS radicals | 135 |
| Pd.                     | Aerial parts methanolic extract and hexane fraction | In vitro - inhibition of DPPH radicals | 31 |
| Psep.                   | Leaves ethanolic extract, hexane fraction, dichloromethane fraction, ethyl acetate fraction and aqueous fraction | In vitro – inhibition of DPPH and ABTS radicals | 119 |
| Pz.                     | Leaves ethanolic extract | In vitro – inhibition of radicals free | 90 |
| Po.                     | Whole plant methanolic extract, hydroalcoholic fractions and ethyl acetate | In vivo – inhibition of lipoperoxidation | 44 |
| Pa.                     | Aerial parts essencial oils | In vitro – inhibition of ORAC radicals | 105 |
| Po.                     | Leaves aqueous extract | In vitro – inhibition of FRAP; NO radicals and reduction of phosphomolybdenum | 133 |

| **Antitumor and Cytotoxic Activity** |
|--------------------------|
| Pgl.                    | 5,7-dihydroxy-3,8,4’-trimethoxy flavone | In silico - uterine and ovarian anticancer; In vitro - antineoplastic activity against sarcoma, carcinoma, melanoma and squamous cells | 130,131 |
| Pd.                     | Methanolic extract Hexane fraction Dichloromethane fraction Tiliroside | In vitro – anticancer activity against leukemia, ovary, colon, prostate, kidney, breast, resistant breast, lung and melanoma; cytotoxic for Artemia salina larvae | 31 |
| Po.                     | Whole plant methanolic extract, hydroalcoholic and ethyl acetate fractions | In vitro – Erlich’s ascites carcinoma (EAC) and cytotoxic | 44 |
| Po.                     | Whole plant methanolic extract | In vitro – lung and human breast cancers | 138 |

| **Antidiabetic Activity** |
|--------------------------|
| Pz.                     | Tiliroside | In silico – interaction by the human pancreatic α-amylase enzyme | 114 |

Pharmacological study

Several pharmacological activities involving Pavonia species have been arousing interest of scientific community hence there is a large collection of reports of their use in folk medicine. Researches have been developed to confirm the anti-inflammatory, analgesic, antioxidant, cytotoxic, antitumoral, antidiabetic, antimicrobial and antiviral potential of Pavonia species through scientific analysis (Table 3).

Anti-inflammatory and analgesic activities

Plants constitute a vast and precious source of natural products, which are essential to human health as they play several biological roles such as anti-inflammatory and analgesic activities, as it has been demonstrated by some studies over extracts and isolated compounds.306

Alcoholic extract of P. zeylanica leaves has shown in vivo anti-inflammatory activity in rat foot edema induced by carrageenan and...
Table 3. *In vitro, in vivo, and in silico* biological studies reported from *Pavonia* genus (cont.)

| Species | Material used | Experimental model | Reference |
|---------|---------------|--------------------|-----------|
| *P. o.* | Roots extract | *In vitro* – reduced blood sugar levels | 139 |
| *P. mal.* | Leaves aqueous extract | *In vitro* – reduced blood sugar levels | 86,136 |
| *P. gila.* | Mixture of α-amirine and β-amirine | *In vitro* – *Staphylococcus aureus*, *Escherichia coli* and *Candida albicans* | 107 |
| *P. pro.* | Hexane:Acetate (9:1) fraction | *In vitro* – *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida tropicalis*, *Candida parapsilosis*, *Aspergillus flavus* and *Aspergillus fumigatus* | 131 |
| *P. spi.* | Hexane:Acetate (1:1) fraction | *In vitro* – *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Klebsiella pneumoniae* and *Proteus mirabilis* | 63 |
| *P. a.* | Tiliroside | *In vitro* – *Escherichia coli* | 76,77 |
| *P. sen.* | Aerial parts methanolic extract | *In vitro* – *Staphylococcus aureus* and *Klebsiella pneumoniae* | 140 |
| *P. pra.* | Aerial parts methanolic extract, hexane, dichloromethane, ethyl acetate and n-butanol fractions | *In vitro* – *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Bacillus subtilis*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Escherichia coli* and *Salmonella setubal* | 31 |
| *P. z.* | Leaves dichloromethane extract | *In vitro* – *Escherichia coli* and *Klebsiella aerogenes* | 85 |
| *P. o.* | Leaves ethyl acetate extract | *In vitro* – *Escherichia coli* | |
| *P. o.* | Leaves diethyl ether extract | | |
| *P. o.* | Leaves methanolic extract | *In vitro* – *Staphylococcus aureus* | |
| *P. o.* | Rhizomes essential oil | *In vitro* – *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Klebsiella pneumoniae*, *Salmonella typhi H*, *Salmonella paratyphi A.*, *Shigella flexneri*, *Vibrio cholerae* Ogawa, *Escherichia coli*, *Klebsiella sp.*, *Helminthosporium* sp., *Fusarium solani*, *Aspergillus flavus*, *Aspergillus niger*, *Aspergillus nidulans*, *Aspergillus fumigatus*, *Botrytis cerealis*, *Alternaria* sp., *Rhizopus nodosus*, *Colletotrichum capsici*, *Trichophyton mentagrophytes*, *Chrysosporium* indicum and *Rhizoctonia* sp. | 35,141-143 |
| *P. o.* | Roots methanolic, chloroform and ethyl acetate extracts | *In vitro* – *Staphylococcus aureus* and *Candida albicans* | 106 |
| *P. o.* | Caproic and palmmitic acids | *In silico* – inhibition of the activity of the glycerol kinase enzyme of *Epidermophyton floccosum* | 104 |
| *P. c.* | Tiliroside | *In vitro* e *in vivo* – antihypertensive activity by reducing resistance peripheral vascular and vasorelaxing by blocking voltage-gated calcium channels (CaV) in vascular smooth muscle cells (VSMCs) | 132 |
| *P. gle.* | Leaves aqueous extract | *In vitro* – phytostaticial activity against termites | 144 |
| *P. l.* | Leaves aqueous extract | *In vitro* - antiurolytic activity (inhibition of calcium oxalate nucleation by disintegrating into smaller particles with increasing fraction concentrations) | 34 |
| *P. pra.* | Leaves ethanolic extract | *In vitro* – inhibition of tyrosinase enzyme | 145 |
| *P. sch.* | Aerial parts methanolic extract | *In vitro* - Antiretroviral activity (reverse transcriptase inhibition) | 146,147 |
| *P. sch.* | Aqueous extract | Promoter of peripheral vascular blood flow; improves dryness and roughness of the skin and stimulates hair growth | 148 |
| *P. sen.* | Leaves aqueous ethanolic extracts | It does not present acute toxicity, however after 28 days the extract becomes nephrotoxic and slightly hepatotoxic | 68 |
| *P. a.* | Stems hydroethanolic extract | *In vivo e in vitro* - dose-dependent hypotensive and ACE inhibitor | 116 |
| *P. a.* | Stems ethanolic extract | *In vivo* - gastroprotective activity | 149 |
| *P. mul.* | Leaves ethanolic extract | *In vitro* - inhibitor of cathepsins K and V | 109 |
Table 3. *In vitro, in vivo, and in silico* biological studies reported from *Pavonia* genus (cont.)

| Species | Material used | Experimental model | Reference |
|---------|---------------|--------------------|-----------|
| *P. mul.* | Lolitide | *In vitro - inhibition of electron flow in photosystem II* | 127 |
| | | Tararexol *p*-methoxybenzoate | |
| *P. gla.* | 5,7-dihydroxy-3,8,4′-trimethoxy flavone | *In vitro – antipROTOzoan (Trichomonas vaginalis)* | 130, 131 |
| | | *In vitro - photoprotective activity with a high level of protection (25.01 FPS)* | |
| *P. d.* | Tiliroside | *In vitro - inhibition of acetylcholinesterase (AChE) activity* | 31 |
| *P. z.* | Leaves methanolic extract | *In vitro - larvicidice against Culex quinquefasciatus* | 150 |
| *P. z.* | Leaves methanolic, hexanic, chloroformic, ethyl acetate and aceton | *In vitro - larvicidice against Anopheles stephensi and Culex quinquefasciatus* | 151 |
| *P. p.* | Leaves and stems ethanolic extract | *In vitro – laxative activity* | 136 |
| *P. o.* | Leaves ethanolic extract | *In vitro - inhibition of denaturation of albumin, stabilization of the erythrocyte membrane and protection against hemolysis* | 90 |
| *P. o.* | Rhizones essential oil | *In vitro – anthelmintic against tapeworms and roundworms* | 35, 141-143 |
| *P. o.* | Rhizones essential oil | *In vitro - Hypotensive, antispasmodic and intestinal relaxant* | 36 |
| *P. o.* | Whole plant extract | Antirheumatic, antiasthmatic/antibronchial activities | 137 |
| *P. o.* | Roots aqueous and alcoholic extracts | *In vitro – anthelmintic against Pheretima postuma* | 152 |
| *P. o.* | Leaves methanolic extract | *In vitro – larvicidal and repellent activity against Aedes aegypti, Anopheles stephensi and Culex quinquefasciatus* | 153 |
| *P. o.* | Caprico, palmitic acids and hexahydropharmesylacetone | *In vitro – inhibition of the activity of the enzyme alcohol dehydrogenase of Entamoeba histolytica* | 53 |
| *P. o.* | Whole plant aqueous extract | *In vitro – inhibits the formation of minerals in urine samples* | 154 |
| *P. o.* | Whole plant aqueous extract | *In vitro – controls human urinary calculogenesis* | 155 |
| *P. o.* | Whole plant extract | Antiparasitic activity against Entamoeba histolytica | 29 |

Antioxidant activity

Antioxidants are substances that control the action of free radicals, minimizing the risk of diseases, specially those related to oxidative damage on nervous system. Naturally, some enzymes are responsible for the protection of harmful effects of free radicals, such as catalasis and dismutasis superoxide, as well as natural products with antioxidant action such as ascorbic acid, tocopherol, phenolics and flavonoids.\(^\text{133}\)

The evaluation of antioxidant activity of extracts from the aerial parts of *Pavonia* species has shown the presence of phenolics and flavonoids as its constituents, having those compounds demonstrated a huge antioxidant potential in tests through the methods DPPH (1,1-diphenyl-2-picril-hidrazil), $\text{H}_2\text{O}_2$ (hydrogen peroxide), NO (nitric oxide), ABTS (2,2′-azino-bis(3-ethylbenzotiazoline-6-sulphonic acid), FRAP (Ferric Reduction Antioxidant Power), SNP (Sodium Nitroprussiate radicals), phosphomolybdiumen reduction, ORAC (Oxygen Radical Absorbance Capacity) and TBARS (Thiobarbituric Acid Reactive Substances) (Table 3).

Cytotoxic and anticancer activities

Cancer is one of the most lethal diseases that affects humankind. Some phytochemical studies have demonstrated anticancer potentials in several plants due to their chemoprotective and antioxidant properties, which make plants an option to minimize the adverse effects of conventional cancer treatments.\(^\text{156}\)

Extracts and isolated compounds from *P. glazioviana*, *P. distinguenda* and *P. odorata* have demonstrated anticancer activities. The tiliroside flavonoid isolated from *P. distinguenda* has shown *in vitro* anticancer activity against leukemic, ovarian, colon, prostate, kidney, breast, resistant breast and melanoma cells, besides being cytotoxic to *Artemia salina* larvae.\(^\text{31}\)

Other flavonoid isolated from *P. glazioviana* (5,7-dihydroxy-3,8,4′-trimethoxyflavone) (79) has shown *in silico* anticancer activity against carcinogen uterine and ovarian cells, while having *in vitro* antineoplastic activity against sarcoma, carcinoma, melanoma and squamous cell carcinoma.\(^\text{130, 131}\)

Extracts from the whole plant of *P. odorata* has shown *in vitro* anticancer activity against *Ehrlich* Ascites Carcinoma (EAC), lung and breast cancer.\(^\text{43, 138}\)

Antidiabetics activity

Several plants are used by folk medicine worldwide against diabetes.\(^\text{86}\) Some of the species quoted in literature are *P. zeylanica* and *P. odorata*. Extracts from their leaves, stems and roots have been evaluated regarding their *in vitro* antidiabetic activity, being constated a significant reduction of glucose levels in bloodstream.\(^\text{86, 136, 139}\)

*In silico* hypoglycemic activity of the tiliroside flavonoid isolated from *P. varians* through the interaction of this compound with human pancreatic α-amylase enzyme presented a lesser linking energy of -9.4 kcal/mol, being more stable in its active site when compared to the standard drug acarbose, that presented an energy of -7.6 kcal/mol.\(^\text{144}\)

Antimicrobial activity

Bacterial resistance has been increasing significatively in the last years, which leads to high mortalities caused by generalized infections. This fact is a consequence of ungovernable use of...
antibiotics. For those reasons, the search for new natural compounds with antimicrobial activity and new action mechanisms if necessary for the control of such micro-organisms.

Extracts, fractions and compounds isolated from *Pavonia* species have shown a great antimicrobial potential that has already been described in literature. Among the compounds that were tested against several fungal and bacterial lineages, we have α-amirine (19), β-amirine (20), 17-ethoxy-phaeophorbide A (A104) isolated from *P. malacophylla*, cycloart-23E-en-3β,25-diol (28), 5,7-dihydroxy-3,8,4'-trimethoxyflavone (79) isolated from *P. glazioviana*, tiliroside (70) isolated from *P. malacophylla* and p. distinguenda and caproic (10) and palmitic (3) acids identified in *P. odorata* (Table 3).

Other activities

Other activities have been related for *Pavonia* species. Methyleneic extract from *P. odorata* leaves has shown in vitro larvicidal and repellent activities against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*.153 Researches have shown anti-hypertensive,16,116,132 anti-helminthic,138-141,152 anti-uricemic,16,46 gastroprotective,149 lactic,136 photoprotective,131 antiretroviral146,147 and several other kinds of activities.

Furthermore, a study on *P. senegalensis* has showed that fresh liquid ethanolic extract of leaves has not a very strong toxicity, becoming nephrotoxic and slightly hepatotoxic after 28 days.68

**CONCLUSIONS**

*Pavonia Cav.* is one of the largest genus on Malvaceae *sensu lato* family and has showed different biologic activities amongst its species, which have already been mentioned in literature and scientific proved. Studies have shown that fatty acids, terpenoids, flavonoids and phenolics are the most common classes of secondary metabolites on this genus. Pharmacological *in vivo*, *in vitro* and *in silico* tests have given the researches promissory results due to the presence of those compounds, both isolated and present on the extracts, corroborating the reports of use of those herbs in folk medicine.

Nonetheless, there is a major need of keep exploring chemical and biological potentials of *Pavonia* species, both already and never studied, since medicinal plants are almost inexhaustible sources of bioactive molecules that can help the treatment and cure of several diseases that affect human populations worldwide.

This paper is a database with very relevant information from both phytochemical and biological studies of *Pavonia* species that can be further explored, aiming to understand the use of *Pavonia* by traditional medicine in various diseases, becoming alternatives for therapies by the use of these natural products with emphasis on the benefit of the world population.

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