

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

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Revisão

Pavonia Cav., is a genus in the Malvaceae *sensu lato* family, containing 271 species with worldwide distribution, although with a higher diversity in America and Asia. Species from this genus are traditionally used in folk medicine with several biological activities, arousing scientific interest on the search for the substances responsible for such activities. This review aimed to provide and expand the scientific interest through phytochemical and pharmacological studies and the utilization of those plants in folk medicine. Species *P. odorata* and *P. zeylanica* are described in literature, specially at India, following the traditional medicine system Ayuverda, while the other species are studied mostly at Africa and America. There have been around 169 compounds isolated and characterized for such genus, most of them from the metabolic classes fat acids, terpenoids, flavonoids and phenolic compounds. Those species have shown *in vivo*, *in vitro* and *in silico* significant pharmacological activities, which include anti-inflammatory, analgesic, antimicrobial, cytotoxic, antitumoral, antidiabetic and antioxidant properties. Based on those informations, the search for new sources of plant based biologic prototypes with potential for the treatment of several diseases is of major scientific, economical and medicinal interest.

Keywords: *Pavonia* Cav.; ethnopharmacological relevance; natural products; biological studies.

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-pharmaceutical-botanical studies form the foundation to the development of new drugs from medicinal herbs.¹

Plants provide an essential economic role as they are used as a drug source.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.³

Several chemical compounds that act as potential therapeutic agents have been isolated from plant species.⁴ Studies about those compounds are based on ethnobotanical, 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.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.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.⁷

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

In Africa, approximately 46 species can be found.⁸ In Brazil, 136 species of *Pavonia* can be found, ranging from Amazon rainforest, Caatinga, Cerrado, Atlantic Forest, Pampas and Pantanal wetlands.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.

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RESULTS AND DISCUSSION

Botanical description

Pavonia comprises species of herbs, shrubs and bushes. Its flowers are, generally, solitary, composed by four epicalyxes, 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.¹⁰

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*¹¹ 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.¹²

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 Ayuverda 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.¹³⁻¹⁸

Powder from seeds of *P. senegalensis* is used as a contraceptive.¹⁹ Decoct of *P. urens* roots is largely used as a treatment for toothache.^{20,21} 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.²²⁻²⁶ Leaves' juice and the entire plant prepared as infusion are also used for its vermifuge and purgative properties.²⁷⁻³⁰

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 find 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. lasiopetalata*, *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.

Fat acids, terpenoids, steroids, flavonoids, phenolics and other compounds such as pheophytins, hydrocarbons and volatile oils are some of the substances that can be found in the genus *Pavonia*. A broad profile of such compounds within has been detected in a study of the chemical composition of oils in the aerial parts of the species *Pavonia odorata* through hyphenated gas chromatography techniques coupled with mass spectrometry.¹⁰⁵ All compounds and their chemical structures are related in Table 2 and Figure 2, respectively.

Fatty acids

Fatty acids are molecule that consists of the most diverse lipids and, by enzymatic action, become free fatty acids, presenting powerful biological activities.¹²²

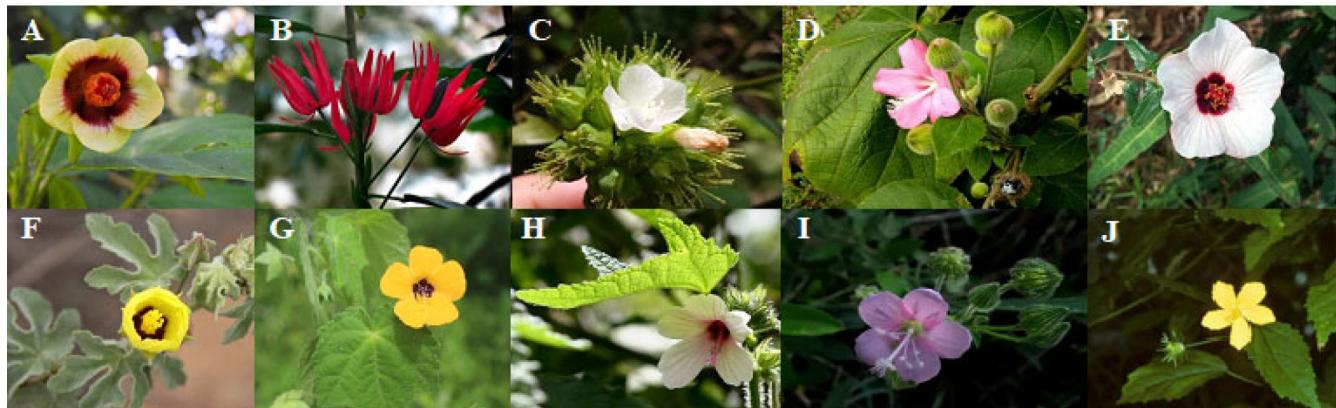


Figure 1. *Pavonia* plants. A) *P. alnifolia*, B) *P. multiflora*, C) *P. fruticosa*, D) *P. malacophylla*, E) *P. hastata*, F) *P. varians*, G) *P. procumbens*, H) *P. urens*, I) *P. odorata*, J) *P. spinifex*

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

Scientific name/ Popular name	Used plant part	Traditional Use	Therapeutic Properties	References
<i>Pavonia cancellata</i> /Malva- rasteira	LV	Poultice	Boils	31
<i>Pavonia distinguenda</i>	AP	*	Antitumor and antibacterial	32
<i>Pavonia fruticosa</i> /Anamu	WP	Decoction	Antipyretic and common cold	33
<i>Pavonia lasiopetalata</i> / <i>Pavonia rosa</i>	LV	*	Breaks and disintegrates kidney and urinary stones; Diuretic	34

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

	RH	*	Dysentery, anti-inflammatory, anti-hemorrhagic; Antipyretic, digestive and astringent	35,36
	RH and LV	*	Antipyretic, stomachic, dysentery and antiulolytic	37,38
	WP	*	Antipyretic, stomachic, dysentery; Rheumatism; Antiemetic; Anti-hemorrhagic; Demulcent, carminative, diaphoretic, diuretic, anti-inflammatory, spasmolytic 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
<i>Pavonia odorata</i> / Sugandhibala	*	*	Antipyretic, stomachic, dysentery; Anti-hemorrhagic; Skin diseases, anti-inflammatory, spasmolytic; Nervous weakness	3,50-54
	LV	Leaf juice	Dysentery; Gonorrhea; Anti-halitosis	12-15
		Paste	Rheumatism; Foot infection, and antipyretic	16,17
	RT	*	Stomachache, anti-inflammatory, anti-hemorrhagic; Antipyretic, diuretic; Carminative, diaphoretic, polydipsia, burning when urinating, demulcent astringent, stomachic, haemorrhages from intestines; bleeding disorders, dysentery and antiulcerogenic; appetizer	4,29,52,55-58
		Paste	Athlete's foot	1,59
		Powder	Dislocations of bone joints; Osteoarthritis	21,22
		Decoction	Dysentery and carminative	60,61
<i>Pavonia procumbens</i>	*	*	Antiulcerogenic, fumigation, vermifuge, analgesic and skin infections	2,51,62-64
	RT	Decoction	Retained placenta and prevention of miscarriage	65
<i>Pavonia schiedeana</i> / Cadillo	RT and WP	Poultice	Antipyretic	66
	LV	Infusion	Hypoglycemic; retained placenta and prevention of miscarriage	65,67
	LV	Aqueous extract	Bone and soft tissue infections	68,69
<i>Pavonia senegalensis</i>	RT	Inhalation and infusion	Diarrhea and induce labour	70,71
	SD	Powder	Contraceptive	18
	FL	Infusion	Analgesic and skin problems	72,73
<i>Pavonia spinifex</i>	LV and TW	Infusion	Stomach problems, gallstones and liver pain	
	LV	*	Hepatoprotection, antioxidant, anticancer, antifungal and antibacterial	74
	AP	Inhalation and decoction	Antipyretic	75
	RT	*	Pneumonia and stomachic	76,77
<i>Pavonia urens</i>		Decoction	Toothache	19,20
	LV	*	Boils	78
		Smoke	Repellent for mosquitoes and house flies	79-81
<i>Pavonia varians</i> / Malva-peluda	*	*	Infections of the digestive system, and anti-inflammatory	82
<i>Pavonia xanthogloea</i> / Erva-de-ovelha	*	*	Antimicrobial and antitumor	83,84
	LV	*	Eczema; Eye diseases; Antipyretic, Anthelmintic, anti-inflammatory, analgesic, toothache; Dysentery, anti-hemorrhagic and emollient	43,85-91
		Decoction	Cough with phlegm	23
<i>Pavonia zeylanica</i> / Citraramutti		Ground	Constipation in animals	92
		Paste	Bone fractures; Healing of acute and chronic wounds	24,25
	*	*	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
<i>Pavonia zeylanica</i> / Citramutti	WP	Inhalation	Wound dressing	94
		*	Antipyretic and anthelmintic; Paralysis; Joint pain	4,95,96
		Infusion and leaf juice	Vermifuge and purgative	26-29
	RT	*	Demulcent, carminative, diaphoretic, diuretic, astringent, tonic, anti-hemorrhagic and anti-inflammatory;	88,97
			Antiulcerogenic	
		Powder	Dislocations of bone joints; Osteoarthritis	21,22

* not reported in the literature. AP: Aerial Parts; FL: Flowers; FR: Fruits; LV: Leaves; RH: Rhizomes; RT: Roots; SD: Seeds; ST: Stems; TW: Twigs; WP: Whole Plant.

Table 2. Isolated compounds from *Pavonia* genus

Nº	Name	Source	Reference	Nº	Name	Source	Reference
Fatty acids							
1	Malvalic acid	SD of <i>P.sepiu.</i> and <i>P.z.</i>	98-101	32	Cedran-diol,8S,13		
2	Sterculic acid			33	Cedrol		
3	Palmitic acid			34	S-guaiazulene		
4	Stearic acid	SD of <i>P.z.</i> , RT and	48,101-105	35	Pinocarveol	RT of <i>P.o.</i>	48,102-
5	Oleic acid	AP of <i>P.o.</i>		36	α -terpinene		104,106
6	Linoleic acid			37	Pavonenol*		
7	Dihydrosterculic acid	SD of <i>P.z.</i>	101	38	β -pinene		
8	(9Z,12Z,15Z)-9,12,15- Octadecatrienoic acid 2,3-bis(trimethylsilyloxy) propyl-ester	RT of <i>P.o.</i>	48,102- 104,106	39	<i>p</i> -cymene		
9	Isovaleric acid			40	1,8-cineole		
10	Caproic acid			41	(Z)-linalooloxide		
11	Dodecanoic acid			42	(E)-linalooloxide		
12	Methyl tetradecanoate			43	Linalool		
13	Tetradecanoic acid			44	(E)-pinocarveol		
14	Methyl-(2E,6E)-farnesate	AP of <i>P.o.</i>	105	45	Borneol		
15	Pentadecanoic acid			46	Menthol		
16	Methyl palmitate			47	Terpinen-4-ol		
17	Methyl linoleate			48	<i>p</i> -cymen-8-ol		
18	Methyl oleate			49	α -terpineol		
Terpenoids							
19	α -amirine	AP of <i>P.mal.</i>	107	50	Carvone		
20	β -amirine			51	Geraniol	AP of <i>P.o.</i>	105
21	Lupeol	AP of <i>P.mal.</i> and <i>P.d.</i>	31,108	52	Thymol		
22	Blumenol C			53	Eugenol		
23	Vomifoliol			54	β -damascenone		
24	4,5-dihydroblumenol A	LV of <i>P.mul.</i>	109	55	β -caryophyllene		
25	3-oxo- α -ionol			56	β -eudesmol		
26	Loliolide			57	Muurolane		
27	Taraxerol <i>p</i> -methoxybenzoate			58	Farnesyl acetone		
28	Cycloart-23Z-en-3 β , 25-diol	AP of <i>P.g.</i>	110	59	Phytol		
29	Cycloart-25Z-en-3 β , 24-diol			60	β -caryophyllene oxide		
30	Taraxerol	AP of <i>P.d.</i>	31	61	Guaiol		
31	Germanicol			62	γ -eudesmol		
Steroids							
65	Sitosterol-3-O- β -D- glucopyranoside	AP of <i>P.c.</i> , <i>P.mal.</i> and <i>P.g.</i>	107,110-112				
66	Stigmasterol-3-O- β -D- glucopyranoside						

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

Nº	Name	Source	Reference	Nº	Name	Source	Reference				
67	β-sitosterol	AP of <i>P.c.</i> , <i>P.mal.</i> and <i>P.d.</i> ; RT of <i>P.o.</i>	31,106, 107,111, 112	100	2-[(1E)-prop-1-en-1-yl] benzoic acid						
68	Stigmasterol	AP of <i>P.c.</i>	111,112	101	3-[(1E)-prop-1-en-1-yl] benzoic acid	LV of <i>P.sepio.</i>	119				
69	Ethyl iso-allocholate	RT of <i>P.o.</i>	106	102	Syringic acid						
Flavonoids											
70	Kaempferol 3-O-(6"-O- <i>p</i> -coumaroyl glucoside (Tiliroside)	AP of <i>P.c.</i> , <i>P.x.</i> , <i>P.mal.</i> , <i>P.v.</i> , <i>P.g.</i> , <i>P.d.</i>	11,31,83, 107, 111-114	103	Protocatechuic acid						
71	3,7-di- <i>O</i> -methylkaempferol	AP of <i>P.c.</i>	111,112	Other compounds							
72	Quercetin	FL of <i>Ph.</i> and <i>P.l.</i> ;	11,83,	104	17 ³ -ethoxy-phaeophorbide <i>a</i>	AP of <i>P.mal.</i>	107,108				
73	2-(3,4-dihydroxyphenyl) chromane-3,5,7-triol (Cyanidin)	AP of <i>P.x.</i> , <i>P.mal.</i> , <i>P.g.</i>	107,115	105	Phaeophytin <i>b</i>						
74	Rutin	AP of <i>P.a.</i> and <i>P.x.</i>	83,116	106	13 ² -S-hydroxy- phaeophytin <i>a</i>						
75	Quercitrin	AP of <i>P.x.</i>	83	107	13 ² -S-hydroxy-17 ³ -ethoxy- phaeophorbide <i>a</i>	AP of <i>P.g.</i> and <i>P.mal.</i>	110				
76	Kaempferol	AP of <i>P.mal.</i> , <i>P.g.</i>	11,107	108	Triacontanol						
77	5,8-dihydroxy-7,4'- dimethoxyflavone	AP of <i>P.mal.</i>	108	109	cis- <i>p</i> -coumaric acid ethyl ester						
78	5,7-dihydroxy-4'- methoxyflavone (Acacetin)			110	Pavophylline	ST of <i>P.z.</i>	26,120				
79	5,7-dihydroxy-3,8,4'- trimethoxyflavone			111	Methyl-19-ketotetracosanoate						
80	5-hydroxy-3,7,8,4'- tetramethoxyflavone	AP of <i>P.g.</i>	11,110, 117	112	12-Methyl-tetracosan-9-one	FL of <i>P.z.</i>	121				
81	5,7,4'-trihydroxy-3,8- dimethoxyflavone			113	Phenyl-alcohol						
82	5,7,4'-trihydroxy-3- methoxyflavone			114	Benzoic acid-2-hydroxy- ethyl-ester						
83	Kaempferol-3-glucoside (Astragalin)	AP of <i>P.d.</i>	31	115	5aH-3a,12-methano- 1H-cyclopropa[5',6'] cyclodeca[1',2',1,5] cyclopenta[1,2-d] [1,3] dioxal-13-one						
84	Dihydrokaempferol (Aromadendrin)	RT of <i>P.o.</i>	48,102-104	116	2,7-diphenyl-1,6- dioxopyridazino[4,5,2',3'] pyrrolo[4',5'-d]pyridazine	RT of <i>P.o.</i>	48,102- 104,106				
85	Aromadendrene			117	Bicyclo [4, 3, 0] nonan-7- one,1-(2-methoxyvinyl)						
Compounds Phenolics											
86	Gossypol	SD of <i>P.sch.</i>	118	118	1,5-bis (3-cyclopentyl- propoxy)-1, 13,3,5,5-hexa- methyltrisiloxane						
87	Gallic acid			119	Pavonene*						
88	Catechin	AP of <i>P.x.</i>	83	120	Isovaleraldehyde						
89	Chlorogenic acid			121	Azulene						
90	Caffeic acid	AP of <i>P.x.</i> ; LV of <i>P.sepio.</i>	83,119	122	Hexahydrofarnesyl-acetone	RT and AP of	48,102-105				
91	Vanillic acid			123	6-methyl-5-hepten-2-one	<i>P.o.</i>					
92	Ferulic acid	LV of <i>P.mul.</i> and <i>P.sepio.</i>	109,119	124	Isopentyl alcohol						
93	<i>p</i> -Hydroxybenzoic acid			125	Pentanol						
94	<i>p</i> -coumaric acid	LV of <i>P.mul.</i>	109	126	Hexanol						
95	Salicylic acid			127	Benzyl alcohol						
96	Cinnamic acid			128	Phenylethyl alcohol						
97	<i>p</i> -Hydroxyphenylacetic acid	LV of <i>P.sepio.</i>	119	129	2-methoxy- <i>p</i> -cresol						
98	Gentisic acid			130	2-methoxy-4-vinylphenol	AP of <i>P.o.</i>	105				
99	4-[(1E)-prop-1-en-1-yl] benzoic acid			131	2,4-bis(1,1-dimethylethyl)- phenol						
				132	Acetophenone						
				133	2-nonanone						
				134	Isophorone						
				135	4-keto-isophorone						
				136	<i>p</i> -menth-4-en-3-one						

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

Nº	Name	Source	Reference	Nº	Name	Source	Reference
137	Dihydro-5-pentyl-2-(3H)-furanone			156	1,3,4-trimethyl-3-cyclohexene-1-carboxyaldehyde		
138	Hexahydropseudoionone			157	2-methyl-3-phenyl-propanal		
139	α -ionone			158	2-hydroxy-4-methoxybenzaldehyde		
140	Dihydro- β -ionone			159	Pentadecanal		
141	Dihydropseudoionone			160	<i>p</i> -ethoxy-ethyl-benzoate		
142	β -ionone			161	Isobutyl-phthalate		
143	4,8,12-trimethyltridecan-4-oxide			162	Naphthalene	AP of <i>P.o.</i>	105
144	Phthalic acid			163	Dodecane		
145	2-pentyl-furan	AP of <i>P.o.</i>	105	164	2-methyl-naphthalene		
146	3-butyl-pyridine			165	Tetradecane		
147	<i>p</i> -allyl-anisole			166	2,3,6-trimethyl-naphthalene		
148	3-phenylpyridine			167	3-(2-methyl-propenyl)-1H-indene		
149	Dihydroactinolide			168	γ -cadinene		
150	Ageratochromene			169	Hexadecane		
151	Hexadecanolactone						
152	Hexanal						
153	Benzaldehyde						
154	Phenylacetaldehyde						
155	(2E)-nonen-1-al						

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.^{123,124} A recent study has shown that *P. malacophylla* and *P. cancellata* have palmitic, oleic and linoleic acids as majoritarian fatty acids.¹²⁵

Eighteen fatty acids have been isolated and identified in species *P. sepium*, *P. odorata* and *P. zeylanica* (Table 2). Palmitic (**3**) and caproic (**10**) fatty acids showed significant activities in preparatory *in silico* studies as having inhibitory properties for the activities of glycerokinase enzyme from the fungus *Epidermophyton floccosum*¹⁰⁴ and inhibitory properties for the alcohol-dehydrogenase enzyme from the protozoan *Entamoeba histolytica*.⁵³

Terpenoids and steroids

Terpenoids can be find in several groups of organisms. In plants, they are present under distinct aspects such as volatile molecules or adhered to resins. Their oxygenated, hydrogenated and dehydrogenated derivates have hydrocarbons as a base-structure, being widely distributed among plant species.¹²⁶

Forty-six terpenoids have been isolated and identified in *P. odorata*, *P. multiflora*, *P. malacophylla*, *P. glazioviana* and *P. distinguenda*, being the last one of the most common of *Pavonia* species. Terpenoids α -amirine (**19**) and β -amirine (**20**) showed *in vitro* antibacterial activities against *Escherichia coli*.¹⁰⁷ The terpenoid cicloart-23Z-en-3 β -25-diol (**28**) also presented *in vitro* antimicrobial activities against *Escherichia coli*, *Pseudomonas aeruginosa*, *Candida tropicalis*, *Candida parapsilopsis* e *Aspergillus fumigatus*.¹¹⁰

Compounds loliolide (**26**) and the taraxerol *p*-methoxybenzoate (**27**) have demonstrated significant *in vitro* activities on the inhibition of electrons flux in photosystem II of plants, therefore allowing those molecules to become future candidates to herbicides as they prevent photosynthesis.¹²⁷

P.a.: *P. alnifolia*; *P.c.*: *P. cancellata*; *P.d.*: *P. distinguenda*; *P.g.*: *P. glazioviana*; *P.h.*: *P. hastata*; *P.l.*: *P. plasiopetala*; *P.mal.*: *P. malacophylla*; *P.mul.*: *P. multiflora*; *P.o.*: *P. odorata*; *P.sch.*: *P. schiedeana*; *P.sep.*: *P. sepium*; *P.v.*: *P. varians*; *P.x.*: *P. xanthogloea*; *P.z.*: *P. zeylanica*. AP: Aerial Parts; FL: Flowers; LV: Leaves; SD: Seeds; ST: Stems; RT: Roots. *chemical structures not reported in the literature.

Steroids are a minority class in *Pavonia* genus, with only five isolated compounds (**65-69**). Phytosteroids share as common structure ciclopentanoperidofenoterne as carbonic skeleton, being β -sitosterol and stigmasterol the most common steroids of this genus and commonly encountered attached to sugar monomers.¹²⁸

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.¹²⁹

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'-trimethoxyflavone (**79**) has demonstrated *in vitro* antimicrobial, *in silico* anticancer, *in vitro* antineoplastic, *in vitro* antiprotozoal and *in vitro* photoprotective activities.^{130,131}

The compound tiliroside (**70**) has demonstrated *in vitro* and *in vivo* antihypertensive activities, leading to reduction of peripheric vascular and vasorelaxant resistances by blocking the Calcium channels dependent of voltage (Ca_V) in cells of vascular smooth muscle (VSMCs);¹³² *in vitro* antimicrobial activity;^{31,107} *in silico* antidiabetic activity through interaction with human pancreatic α -amylase enzyme;¹¹⁴ *in vitro* anticancer and anticolinesterasic activities.³¹

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

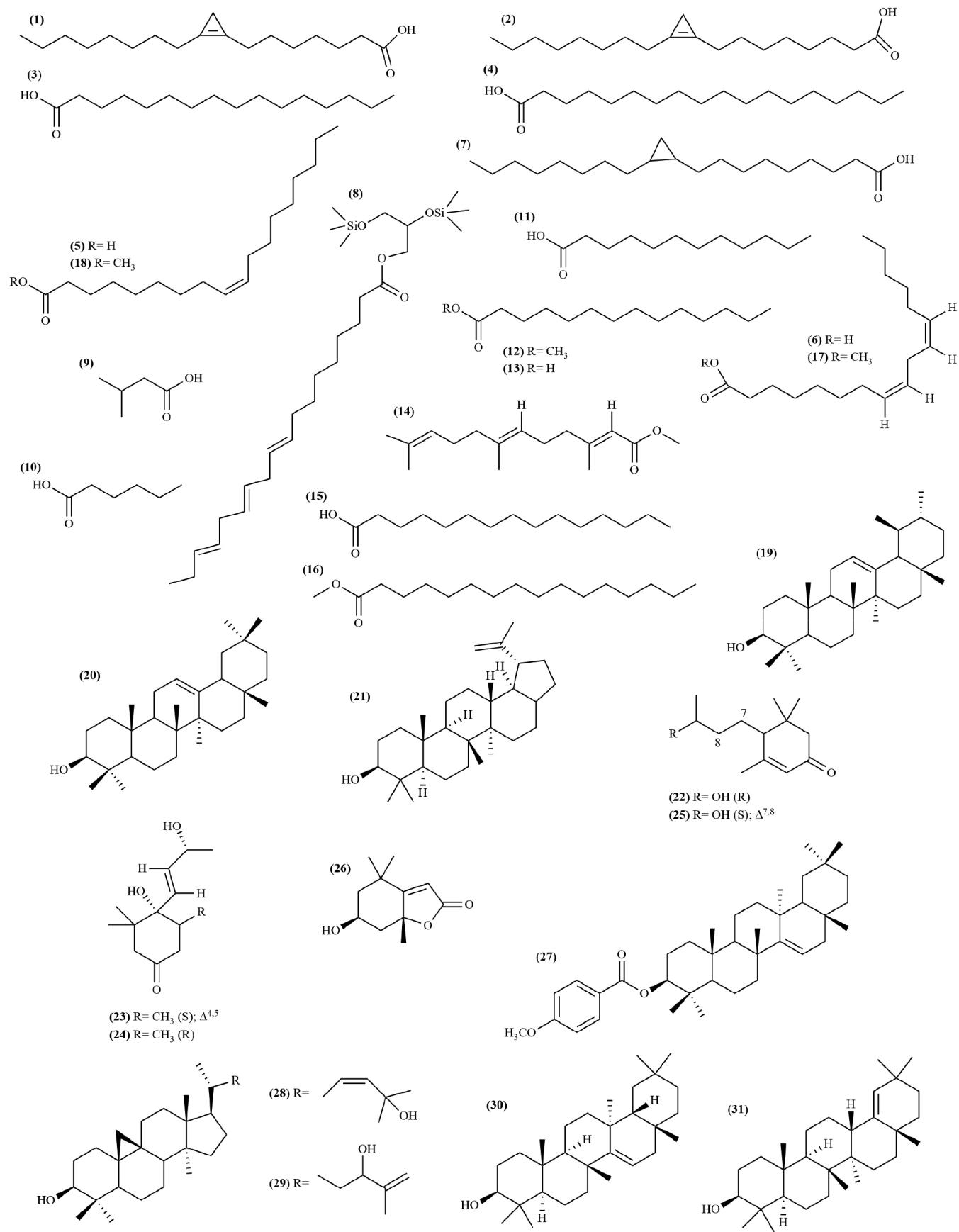


Figure 2. Compounds isolated from *Pavonia* species

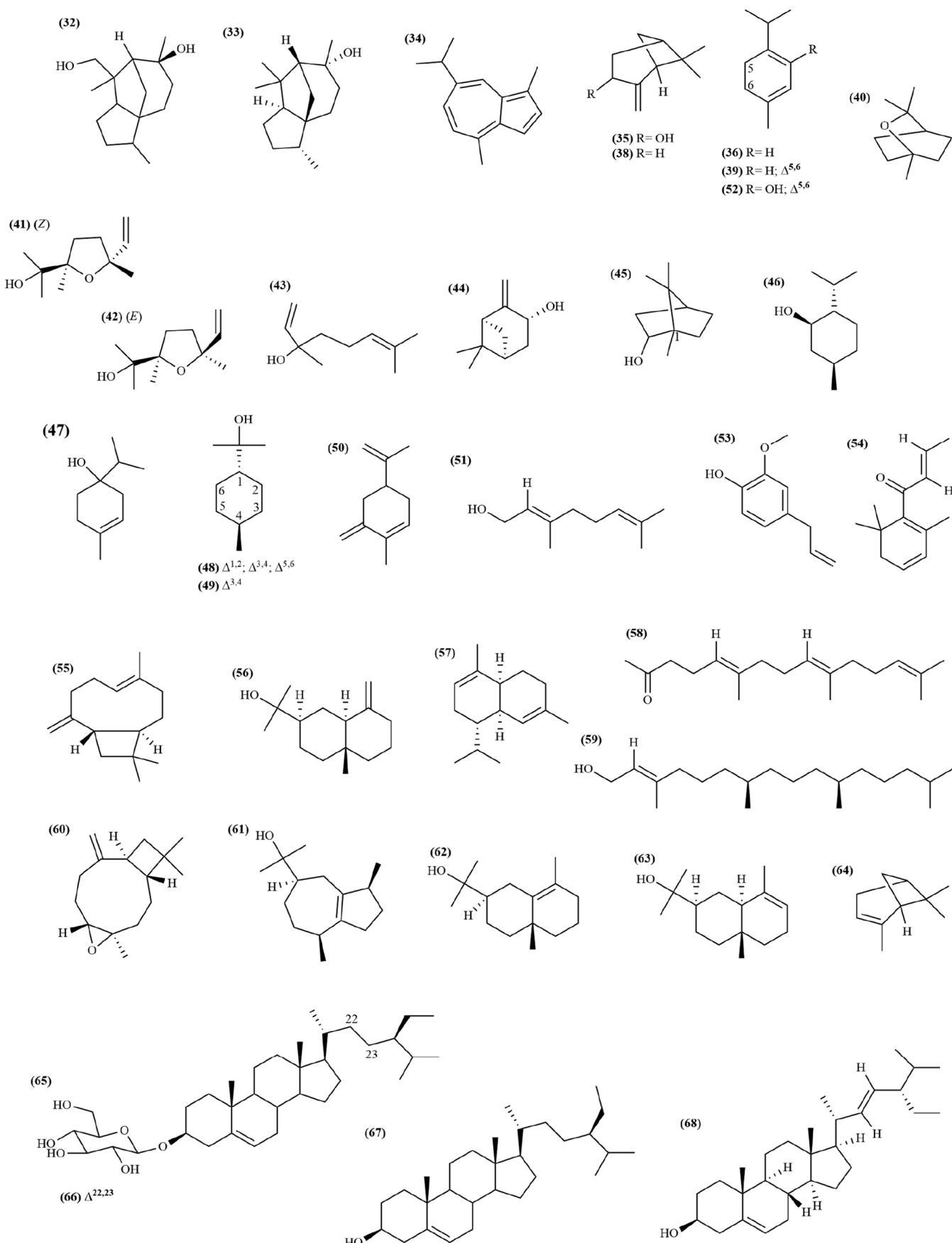
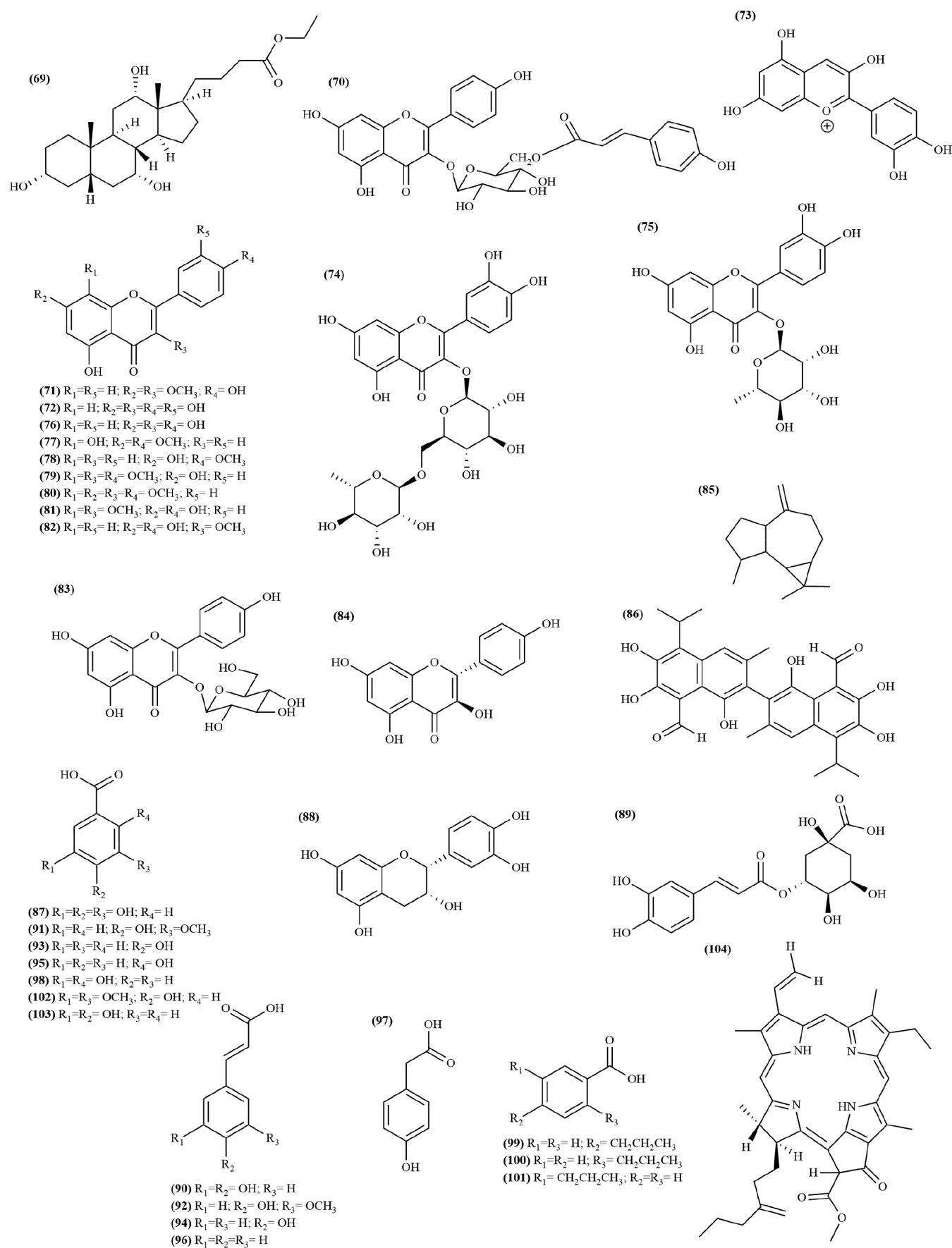
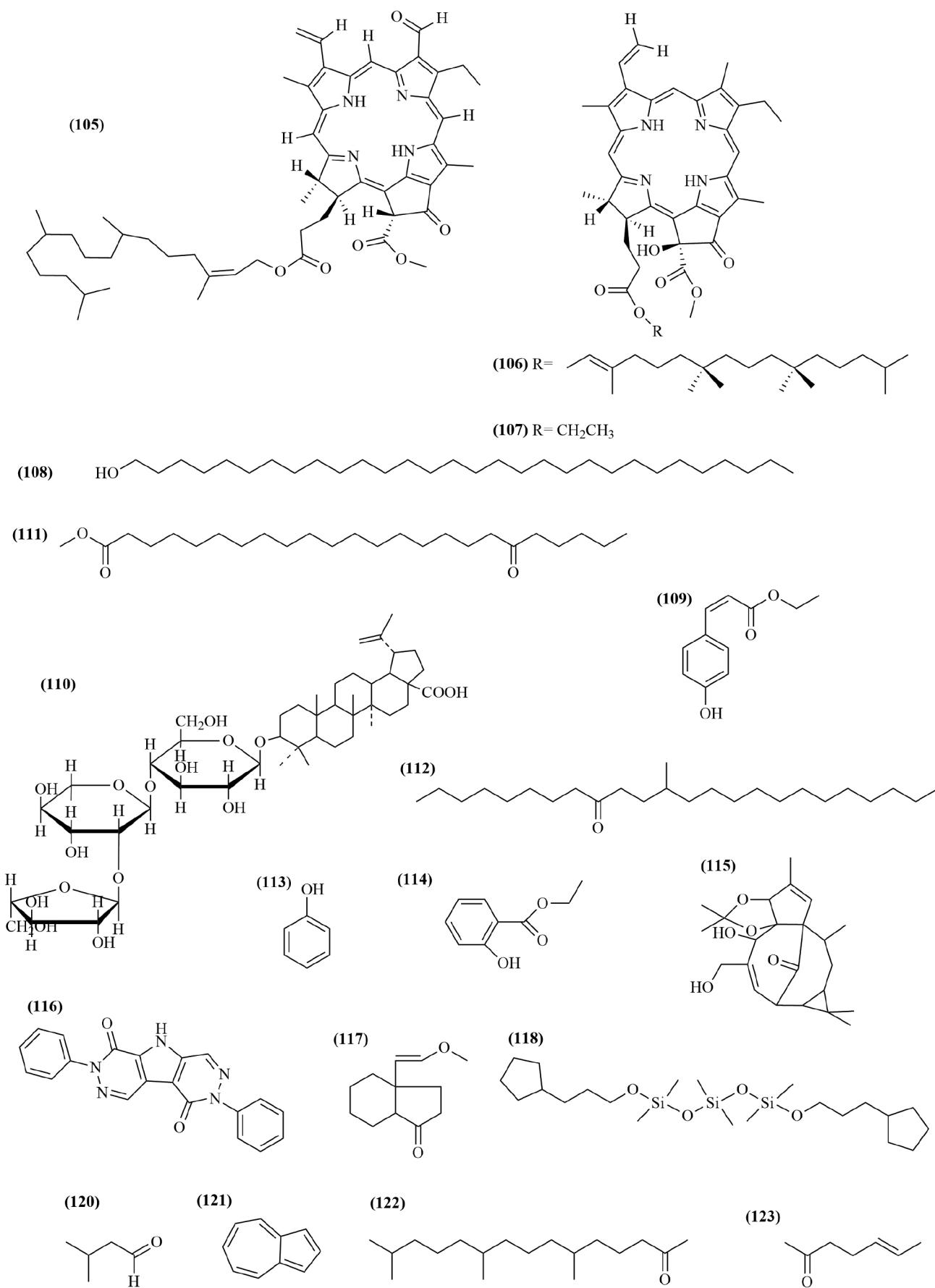


Figure 2. Compounds isolated from *Pavonia* species (cont.)

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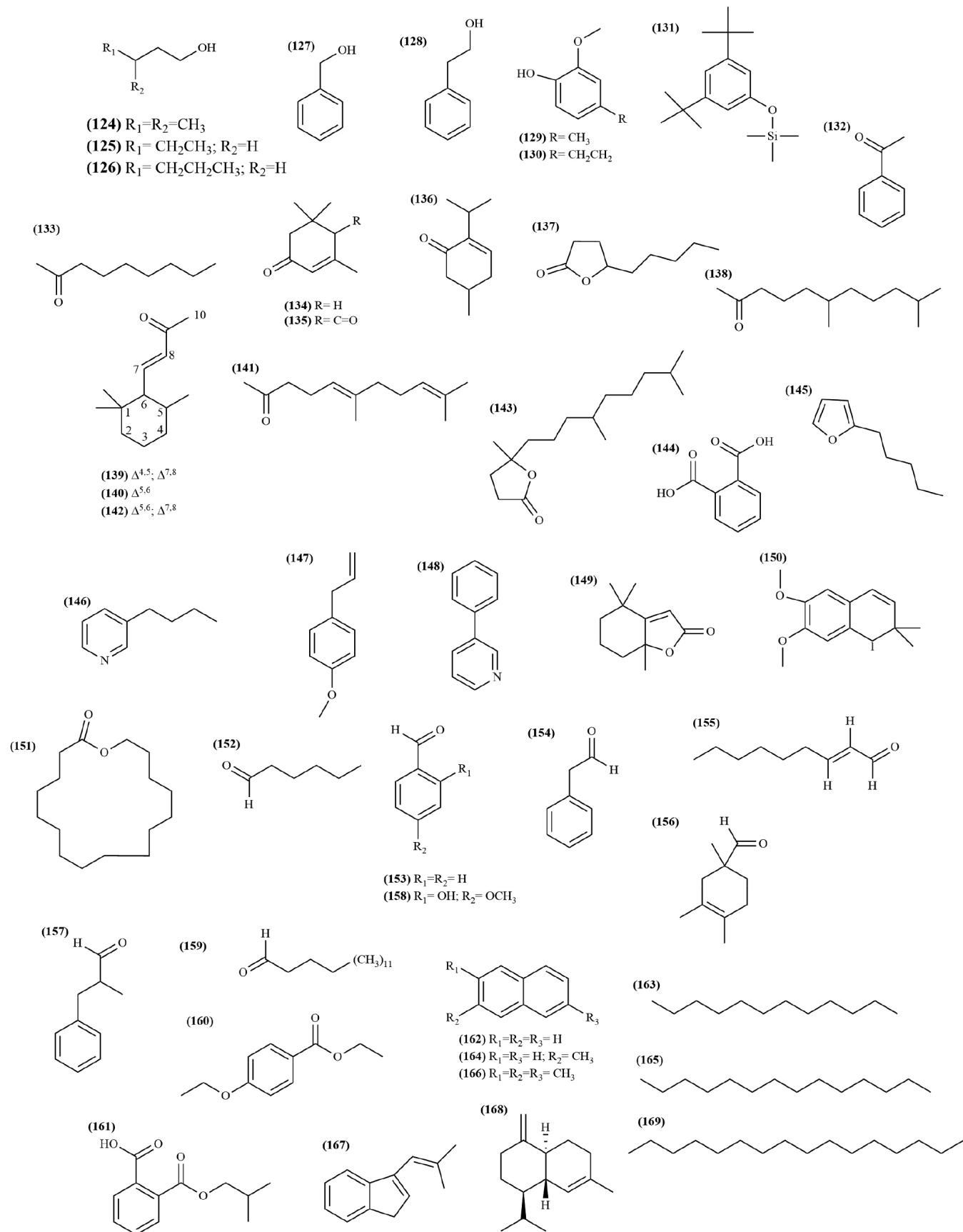


Figure 2. Compounds isolated from *Pavonia* species (cont.)

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*.^{31,44,82,83,90,105,117,133-135}

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 17³-ethoxy-phaeophorbide A (**104**), which has presented *in vitro* antibacterial activity against *Staphylococcus aureus* and *Escherichia coli*.

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.¹⁰⁶

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

Species	Material used	Experimental model	Reference
Anti-inflammatory and Analgesic Activity			
<i>P.z.</i>	Leaves alcoholic extract	<i>In vitro</i> - anti-inflammatory and antinociceptive by inhibition the arachidonic acid pathway	88
<i>P.z.</i>	Leaves and stems aqueous extract	<i>In vitro</i> - anti-inflammatory and analgesic	136
<i>P.z.</i>	Leaves ethanolic extract	<i>In vitro</i> – anti-inflammatory activity by inhibition protein denaturation	90
<i>P.o.</i>	Roots extract	Anti-inflammatory activity	137
<i>P.o.</i>	Roots methanolic, chloroform and ethyl acetate extract	<i>In vitro</i> - anti-inflammatory	106
Antioxidant Activity			
<i>P.x.</i>	Aerial parts hexane fractions, dichloromethane, ethyl acetate, n-butanol, and water ethanolic extract	<i>In vitro</i> – inhibition of DPPH, H ₂ O ₂ and sodium nitroprusside radicals (SNP)	83
<i>P.v.</i>	Aerial parts hydroalcoholic extract	<i>In vitro</i> - stabilization of radicals free DPPH	82
<i>P.gla.</i>	Aerial parts ethanolic extract	<i>In vitro</i> – inhibition of DPPH radicals	117,134
<i>P.pro.</i>	Leaves methanolic extract	<i>In vitro</i> – inhibition of ABTS radicals	135
<i>P.d.</i>	Aerial parts methanolic extract and hexane fraction	<i>In vitro</i> - inhibition of DPPH radicals	31
<i>P.sep.</i>	Leaves ethanolic extract, hexane fraction, dichloromethane fraction, ethyl acetate fraction and aqueous fraction	<i>In vitro</i> – inhibition of DPPH and ABTS radicals	119
<i>P.z.</i>	Leaves ethanolic extract	<i>In vitro</i> – inhibition of radicals free	90
<i>P.o.</i>	Whole plant methanolic extract, hydroalcoholic fractions and ethyl acetate	<i>In vivo</i> – inhibition of lipoperoxidation	44
<i>P.o.</i>	Aerial parts essencial oils	<i>In vitro</i> – inhibition of ORAC radicals	105
<i>P.o.</i>	Leaves aqueous extract	<i>In vitro</i> – inhibition of FRAP, NO radicals and reduction of phosphomolybdenum	133
Antitumor and Cytotoxic Activity			
<i>P.gla.</i>	5,7-dihydroxy-3,8,4'-trimethoxy flavone	<i>In silico</i> - uterine and ovarian anticancer; <i>In vitro</i> - antineoplastic activity against sarcoma, carcinoma, melanoma and squamous cells	130,131
<i>P.d.</i>	Methanolic extract		
	Hexane fraction	<i>In vitro</i> – anticancer activity against leukemia, ovary, colon, prostate, kidney, breast, resistant breast, lung and melanoma; cytotoxic for <i>Artemia salina</i> larvae	31
	Dichloromethane fraction		
Tiliroside			
<i>P.o.</i>	Whole plant methanolic extract, hydroalcoholic and ethyl acetate fractions	<i>In vitro</i> – Ehrlich's ascites carcinoma (EAC) and cytotoxic	44
<i>P.o.</i>	Whole plant methanolic extract	<i>In vitro</i> – lung and human breast cancers	138
Antidiabetic Activity			
<i>P.v.</i>	Tiliroside	<i>In silico</i> – interaction by the human pancreatic α-amylase enzyme	114

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

Species	Material used	Experimental model	Reference
<i>P.z.</i>	Leaves aqueous extract	<i>In vitro</i> – reduced blood sugar levels	86,136
	Leaves and stems aqueous extract		
<i>P.o.</i>	Roots extract	<i>In vitro</i> – reduced blood sugar levels	139
Antimicrobial and Antiviral Activity			
<i>P.mal.</i>	Mixture of α-amirine and β-amirine		
	17 ³ -ethoxy-pheoforbide A		
	Tiliroside		
	Acetate Fraction		
	Hexane:Acetate (9:1) fraction	<i>In vitro</i> – <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> and <i>Candida albicans</i>	107
<i>P.gla.</i>	Hexane:Acetate (1:1) fraction		
	Acetate:Methanol (9:1) fraction		
	Acetate:Methanol (1:1) fraction		
	Aerial parts Crude Ethanolic Extract		
<i>P.pro.</i>	5,7-dihydroxy-3,8,4'-trimethoxy flavone	<i>In vitro</i> – <i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i> , <i>Candida tropicalis</i> , <i>Candida parapsilopsis</i> , <i>Aspergillus flavus</i> and <i>Aspergillus fumigatus</i>	131
	Cicloart-23Z-en-3β, 25-diol		
<i>P.u.</i>	Leaves methanolic extract	<i>In vitro</i> – <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Escherichia coli</i> , <i>Klebsiella pneumoniae</i> and <i>Proteus mirabilis</i>	63
<i>P.spi.</i>	Roots methanolic extract	<i>In vitro</i> – <i>Candida albicans</i> , <i>Aspergillus fumigatus</i> , <i>Fusarium culmorum</i> , <i>Staphylococcus aureus</i> , <i>Pseudomonas syringae</i> and <i>Erwinia amylovora</i> .	76,77
<i>P.d.</i>	Whole plant ethanolic extract	<i>In vitro</i> – <i>Staphylococcus aureus</i> and <i>Klebsiella pneumoniae</i>	140
	Aerial parts methanolic extract, hexane, dichloromethane, ethyl acetate and n-butanol fractions	<i>In vitro</i> – <i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i> , <i>Bacillus subtilis</i> , <i>Klebsiella pneumoniae</i> , <i>Pseudomonas aeruginosa</i> , <i>Escherichia coli</i> and <i>Salmonella setubal</i>	31
	Tiliroside		
	Leaves dichloromethane extract	<i>In vitro</i> – <i>Escherichia coli</i> and <i>Klebsiella aerogenes</i>	85
<i>P.o.</i>	Leaves ethyl acetate extract	<i>In vitro</i> – <i>Escherichia coli</i>	
	Leaves diethyl ether extract	<i>In vitro</i> – <i>Staphylococcus aureus</i>	
	Leaves methanolic extract	<i>In vitro</i> – <i>Bacillus subtilis</i> , <i>Escherichia coli</i> and <i>Klebsiella aerogenes</i>	
	Rhizomes essential oil	<i>In vitro</i> – <i>Staphylococcus aureus</i> , <i>Bacillus subtilis</i> , <i>Bacillus myoides</i> , <i>Diplococcus pneumoniae</i> , <i>Salmonella typhi</i> H, <i>Salmonella paratyphi</i> A., <i>Shigella flexneri</i> , <i>Vibrio cholerae</i> Ogawa, <i>Escherichia coli</i> , <i>Klebsiella sp.</i> ; <i>Helminthosporium sp.</i> , <i>Fusarium solani</i> , <i>Aspergillus flavus</i> , <i>Aspergillus niger</i> , <i>Aspergillus nidulans</i> , <i>Aspergillus fumigatus</i> , <i>Botryodiplodia sp.</i> , <i>Alternaria sp.</i> , <i>Rhizophorus nodosus</i> , <i>Colletotrichum capsici</i> , <i>Trichophyton mentagrophytes</i> , <i>Chrysosporium indicum</i> and <i>Rhizoctonia sp.</i>	35,141-143
<i>P.o.</i>	Roots methanolic, chloroform and ethyl acetate extracts	<i>In vitro</i> – <i>Staphylococcus aureus</i> and <i>Candida albicans</i>	106
<i>P.o.</i>	Caproic and palmitic acids	<i>In silico</i> – inhibition of the activity of the glycerol kinase enzyme of <i>Epidermophyton floccosum</i>	104
Other Activities			
<i>P.c.</i>	Tiliroside	<i>In vitro</i> e <i>in vivo</i> – antihypertensive activity by reducing resistance peripheral vascular and vasorelaxing by blocking voltage-gated calcium channels (CaV) in vascular smooth muscle cells (VSMCs)	132
<i>P.gle.</i>	Leaves aqueous extract	<i>In vitro</i> – phytopesticidal activity against termites	144
<i>P.l.</i>	Leaves aqueous extract	<i>In vitro</i> - antiurolytic activity (inhibition of calcium oxalate nucleation by disintegrating into smaller particles with increasing fraction concentrations)	34
<i>P.pra.</i>	Leaves ethanolic extract	<i>In vitro</i> – inhibition of tyrosinase enzyme	145
<i>P.sch.</i>	Aerial parts methanolic extract	<i>In vitro</i> - Antiretroviral activity (reverse transcriptase inhibition)	146,147
<i>P.sch.</i>	Aqueous extract	Promoter of peripheral vascular blood flow; improves dryness and roughness of the skin and stimulates hair growth	148
<i>P.sen.</i>	Leaves aqueous ethanolic extracts	It does not present acute toxicity, however after 28 days the extract becomes nephrotoxic and slightly hepatotoxic	68
<i>P.a.</i>	Stems hydroethanolic extract	<i>In vivo</i> e <i>in vitro</i> - dose-dependent hypotensive and ACE inhibitor	116
<i>P.a.</i>	Stems ethanolic extract	<i>In vivo</i> - gastroprotective activity	149
<i>P.mul.</i>	Leaves ethanolic extract	<i>In vitro</i> - 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
<i>P.mul.</i>	Loliolide	<i>In vitro</i> - inhibition of electron flow in photosystem II	127
	Taraxerol <i>p</i> -methoxybenzoate		
<i>P.gla.</i>	5,7-dihydroxy-3,8,4'-trimethoxy flavone	<i>In vitro</i> – antiprotozoan (<i>Trichomonas vaginalis</i>) <i>In vitro</i> - photoprotective activity with a high level of protection (25.01 FPS)	130,131
<i>P.d.</i>	Tiliroside	<i>In vitro</i> - inhibition of acetylcholinesterase (AChE) activity	31
<i>P.z.</i>	Leaves methanolic extract	<i>In vitro</i> - larvicide against <i>Culex quinquefasciatus</i>	150
<i>P.z.</i>	Leaves methanolic, hexanic, chloroformic, ethyl acetate and acetonnic	<i>In vitro</i> - larvicide against <i>Anopheles stephensi</i> and <i>Culex quinquefasciatus</i>	151
<i>P.z.</i>	Leaves and stems ethanolic extract	<i>In vitro</i> – laxative activity	136
<i>P.z.</i>	Leaves ethanolic extract	<i>In vitro</i> - inhibition of denaturation of albumin, stabilization of the erythrocyte membrane and protection against hemolysis	90
<i>P.o.</i>	Rhizomes essential oil	<i>In vitro</i> – anthelmintic against tapeworms and roundworms	35,141-143
<i>P.o.</i>	Rhizomes essential oil	<i>In vitro</i> - Hypotensive, antispasmodic and intestinal relaxant	36
<i>P.o.</i>	Whole plant extract	Antirheumatic, antiasthmatic/antibronchial activities	137
<i>P.o.</i>	Roots aqueous and alcoholic extracts	<i>In vitro</i> – anthelmintic against <i>Pheretima postuma</i>	152
<i>P.o.</i>	Leaves methanolic extract	<i>In vitro</i> – larvicidal and repellent activity against <i>Aedes aegypti</i> , <i>Anopheles stephensi</i> and <i>Culex quinquefasciatus</i>	153
<i>P.o.</i>	Caproic, palmitic acids and hexahydro-pharnesyl-acetone	<i>In silico</i> – inhibition of the activity of the enzyme alcohol dehydrogenase of <i>Entamoeba histolytica</i>	53
<i>P.o.</i>	Whole plant aqueous extract	<i>In vitro</i> – inhibits the formation of minerals in urine samples	154
<i>P.o.</i>	Whole plant aqueous extract	<i>In vitro</i> – controls human urinary calculogenesis	155
<i>P.o.</i>	Whole plant extract	Antiparasitic activity against <i>Entamoeba histolytica</i>	29

P.a.: *P. alnifolia*; *P.c.*: *P.cancelata*; *P.d.*: *P.distinguenda*; *P.gla.*: *P.glaioviana*; *P.gle.*: *P.glechomifolia* *P.l.*: *P.lasiopetala*; *P.mal.*: *P.malacophylla*; *P.mul.*: *P.multiflora*; *P.o.*: *Podorata*; *P.pra.*: *P.praemorsa*; *P.pro.*: *P.procumbens*; *P.sch.*: *P.schiedeana*; *P.sen.*: *P.senegalensis*; *P.sep.*: *P.sepoides*; *P.spi.*: *P.spinifex*; *P.u.*: *Purens*; *P.v.*: *P.varians*; *P.x.*: *P.xanthogloea*; *P.z.*: *P.zeylanica*.

in vivo antinociceptive activity by inhibition of arachidonic acid formation.⁸⁸ Methanolic, chloroformic and ethyl acetate extracts of *P. odorata* roots have also demonstrated *in vivo* anti-inflammatory activity in albino rat foot edema induced by carrageenan.¹⁰⁶ (Table 3).

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.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-diphenil-2-picril-hidrazil), H₂O₂ (hydrogen peroxide), NO (nitric oxide), ABTS (2,2'-azino-bis(3-etylbenzotiazoline-6-sulphonic) acid), FRAP (Ferric Reduction Antioxidant Power), SNP (Sodium Nitroprussiate radicals), phosphomolybdenum 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.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.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.^{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.^{44,138}

Antidiabetics activity

Several plants are used by folk medicine worldwide against diabetes.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.^{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.¹¹⁴

Antimicrobial activity

Bacterial resistance has been increasing significantly 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.¹⁴⁰

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 β -ethoxy-phaeophorbide A (**104**)¹⁰⁷ isolated from *P. malacophylla*, cycloart-23Z-en-3 β ,25-diol (**28**), 5,7-dihydroxy-3,8,4'-trimethoxyflavone (**79**)¹¹⁰ isolated from *P. glazioviana*, tiliroside (**70**)^{31,107} isolated from *P. malacophylla* e *P. distinguisenda* and caproic (**10**) and palmitic (**3**)¹⁰⁴ acids identified in *P. odorata* (Table 3).

Other activities

Other activities have been related for *Pavonia* species. Methanolic extract from *P. odorata* leaves has shown *in vitro* larvicide and repellent activities against *Aedes aegypti*, *Anopheles stephensi* and *Culex quinquefasciatus*.¹⁵³ Researches have shown anti-hypertensive,^{36,116,132} anti-helminthic,^{35,141-143,152} anti-urolithic,³⁴ gastroprotective,¹⁴⁹ laxative,¹³⁶ photoprotective,¹³¹ antiretroviral^{146,147} 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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