http://dx.doi.org/10.21577/0100-4042.20230028 *Quim. Nova,* Vol. 46, No. 5, 460-469, 2023

Revisão

PHYTOCHEMICAL AND PHARMACOLOGICAL ASPECTS OF THE ALKALOIDS OF MALVACEAE *sensu lato* SPECIES: A REVIEW

Ana Laura de Cabral Sobreira[a], Janderson Barbosa Leite de Albuquerque[a], Wallace Amorim Machado de Queiroz[a], Pedro Isaac Vanderlei de Souza[b], Diégina Araújo Fernandes[c] and Maria de Fátima Vanderlei de Souza[a,d,*]

[a]Centro de Ciências da Saúde, Universidade Federal da Paraíba, 58051-900 João Pessoa – PB, Brasil
[b]Instituto de Biociências, Universidade Federal do Mato Grosso do Sul, 79070-900 Campo Grande – MS, Brasil
[c]Instituto de Pesquisas de Produtos Naturais, Universidade Federal do Rio de Janeiro, 21941-902 Rio de Janeiro – RJ, Brasil
[d]Departamento de Ciências Farmacêuticas, Universidade Federal da Paraíba, 58051-900 João Pessoa – PB, Brasil

Recebido em 25/07/2022; aceito em 23/12/2022; publicado na web 02/03/2023

Malvaceae *sensu lato* is a family containing about 245 genera and 4,465 species mainly distributed across tropical and subtropical regions worldwide. Species of this family usually contain alkaloids with anti-inflammatory, antinociceptive, antiparasitic, antimicrobial and anticancer properties due to its secondary metabolites. In this context, this review aims to checklist the alkaloids isolated from Malvaceae *sensu lato* species, evaluating their chemical profile and pharmacological potential, providing a broad and concise overview of these secondary metabolites. The results were collected from scientific databases such as Web of Science, Scifinder, Pubmed, ScienceDirect and Google Scholar, using the keywords "Alkaloids" and "Malvaceae". Several pharmacological/biological activities are reported in literature for the most varied alkaloid nuclei, such as: vasorelaxation of the mesentery of rats (cryptolepinone), antitrypanosomal activity (waltherione) and anti-inflammatory and bronchodilator activity (vasicine), which highlights a succession of activities related to this class of secondary metabolites. Presented data report the importance of the Malvaceae *sensu lato* family, demonstrating the biological relevance of its alkaloids, in order to contribute to scientific knowledge and the development of new drugs.

Keywords: Malvaceae *sensu lato*; alkaloids; natural products.

INTRODUCTION

Natural products are of great importance in the health studies: about 68.8% of all active principles found in drug formulations originate directly or indirectly from a plant-based product.[1,2]

Malvaceae *sensu lato* is a family comprising about 245 genera and 4,465 species distributed mainly in tropical and subtropical regions and, less commonly, in temperate regions.[3,4] In Brazil, it is part of one of the most varied families represented with about 80 genera and 859 native species, of these 7 genera and 457 species are endemic to the country.[5]

Several species belonging to this family are part of the botanical arsenal of traditional medicine in the northeast region of Brazil: *Helicteres baruensis* Jacq. is used in folk medicine to treat dysmenorrhea, renal failure and as an analgesic; *Guazuma ulmifolia* Lamarck is used to treat bursitis, arthritis and hemorrhoids; *Hibiscus esculentus* L. is used in the prevention of hair loss, constipation, and asthma; and *Cavanillesia umbellata* Ruiz & Pav. is used to treat appendicitis, skin mycoses, as analgesics, to suppress gynecological inflammation and breast tumors.[6]

The family Malvaceae *sensu lato* comprises a rich source of alkaloids that present significant pharmacological effects and scientifically proven described in the literature, as seen in the species *Waltheria douradinha* (vanessine), *Sida rhombifolia* (cryptolepinone), *Tilia cordata* (trigonelline), *Triumfetta grandidens* (waltherione A) etc., reporting cytotoxic, antimicrobial, anti-inflammatory, analgesic, antispasmodic, hepatoprotective and antiparasitic activities, thus demonstrating the pharmacological potential that alkaloids have after being isolated from natural products.[7-10]

Based on the data presented, the objective of this review was to carry out a bibliographic survey about the alkaloids reported in species of the Malvaceae *sensu lato* family, to evaluate their chemical and pharmacological potential, encouraging and reinforcing the importance of research on natural products as a source of new drugs.

METHODOLOGY

Available information on traditional use, phytochemical studies, and biological activities of alkaloids of Malvaceae *sensu lato* were collected from scientific databases: Web of Science, Scifinder, Pubmed, ScienceDirect and Google Scholar. Through this methodology, 99 works involving the subject were consulted, which were described in articles, books, dissertations, and thesis from 2010 to May 2022, using the keywords "Alkaloids" and "Malvaceae".

Articles with isolated and identified alkaloids from the Malvaceae *sensu lato* family, phytochemical studies, pharmacological and/or biological activities of these metabolites were used as inclusion criteria. Repeated articles, papers containing information on protoalkaloids, pseudoalkaloids and other nitrogen compounds, as well as articles with only botanical data or articles not available for access on consulted platforms were excluded.

The present study and data have been extracted by the author (A. L. C. S.) and confirmed by others (J. B. L. A., W. A. M. Q., D. A. F., P. I. V. S., M. F. V. S.). The interest in scientific studies with alkaloids present in the Malvaceae *sensu lato* has increased over the years due to favorable results of research on its biological activity. Data obtained were arranged in the form of tables and figures and a narrative description was performed to provide a summary of the information.

RESULTS AND DISCUSSION

Alkaloids are often classified by some authors by their chemical structure as protoalkaloids, pseudoalkaloids, and true alkaloids.

*e-mail: mfvanderlei@ltf.ufpb.br

Protoalkaloids and pseudoalkaloids do not follow the same biosynthetic route as alkaloids themselves[11] but are considered part of this group by some authors because they are nitrogenous substances. Considering these biosynthetic and biogenetic data, this review lists only the alkaloids themselves isolated from Malvaceae *sensu lato*, which may have the pyrrolidine, pyridine, piperidine, tropane, pyrrolizidine, quinolizidine, quinoline, indoquinoline, indole, and imidazole types as basic nuclei, among others found in the Malvaceae *sensu lato* family.[12-13]

Alkaloids are secondary metabolites produced mainly by plants, although they can also be found in fungi, bacteria and animals.[14] Therefore, alkaloids are one of the most diverse, efficient and therapeutically significant plant substances and are primarily involved in the defense of plants against herbivores, pathogens and even other plants.[15]

Traditional use of alkaloid-rich species

The traditional use of medicinal plants that have alkaloids has been reported over the centuries. Malvaceae *sensu lato* comprises species rich in these compounds, such the ones in the genera *Waltheria*, *Sida*, *Hibiscus*, *Melochia*, *Helicteres*, among others. Several species have great pharmacological importance, since they are widely used in traditional medicine for the treatment of diseases such as asthma, ulcers, parasitic infections, headaches, bacterial infections, inflammatory diseases, respiratory and urinary diseases.[16-21] Regarding Ethnobotany, several studies have been developed by the scientific community in order to investigate which compounds would be responsible for those activities reported by people, highlighting the scientific evidence of the biological and pharmacological activities of alkaloids.[17-19]

Some species are commonly present in the field of phytochemical studies. *Sida rhombifolia* can be listed as an example, being used in folk medicine against hypertension, diabetes and the treatment of gout.[4,12] *Waltheria indica* is used by traditional medicine to treat malaria and other parasitic diseases.[22] *Helicteres angustifolia* is reported by traditional medicine to have analgesic, antibacterial, anti-inflammatory and anticancer activities.[23]

Several cytotoxic assays were performed with alkaloids isolated from *Waltheria indica*, *Microcos paniculata*, *Sida acuta*, *Sida cordifolia*, *Kleinhovia hospita*, among others, which were described throughout this review.

Alkaloids from Malvaceae *sensu lato*

Among plant extracts, we can mention those alkaloids that are identified in the species that belong to the Malvaceae *sensu lato* family (Table 1 and Figure 1), which are distributed in different genera and are found in different parts of plants.

Biological activities of alkaloids

Alkaloids play essential and specific roles on the treatment of various diseases through different mechanisms of action, including anti-inflammatory, analgesic, antifungal, antimicrobial, anticancer, antiparasitic and several other biological activities (Table 2).

Analgesic and anti-inflammatory activities

Anti-inflammatory activity of alkaloids is directly linked to their chemical structure. As an example of secondary metabolites with proven pharmacological activities we can quote antidesmone (**33**) isolated from the roots of the species *Melochia chamaedrys* A. St.-Hil., a tetrahydroquinolone alkaloid that showed an anti-inflammatory effect by suppressing the production of inflammatory cytokines, including tumor necrosis factor-α, interleukin-6 and interleukin-1β in RAW264.7 cells on mouse macrophages induced by lipopolysaccharides (LPS), exerting an apparently anti-inflammatory effect in acute lung injury, regulated by two signaling pathways, being the protein pathway mitogen-activated kinase (MAPK) and nuclear factor kappa β (NF-κβ).[21]

A study with the quinazoline alkaloid 5'-hydroxymethyl-1'-(1,2,3,9-tetrahydropyrrolo[2,1-*b*]-quinazolin-1-yl)-heptan-1-one (**28**) isolated from aerial parts of *Sida cordifolia* showed that this secondary metabolite acted in the inflammatory process induced by carrageenan, acting in an inhibitory way on the cyclooxygenase enzyme, leading to the inhibition of prostaglandin synthesis. An acetic acid induced writhing test also demonstrated the peripheral analgesic evaluation of drugs, showing responses mediated through peritoneal mast cells, acid-sensitive ion channels and prostaglandin pathway. The antinociceptive activity was also significant by the evaluation of the same signaling pathway, where the tested compound increased the stress tolerance capacity of the animals involved in the study.[24]

Furthermore, other studies with the alkaloids vasicine (**84**) and vasicinol (**85**) isolated from the species *Sida cordifolia* L.[98] also showed anti-inflammatory and analgesic activities.

Cytotoxic and anticancer activities

Cancer is one of the most serious health problems today, being responsible for 7.6% of deaths around the world. About 75-80% of the world population use medicinal herbs to treat cancer.[99]

One of the most responsible factors for tumor promotion and progression is the activation of the NF-κβ transcription. A phytochemical study carried out with the aerial parts and roots of *Waltheria indica* resulted in the isolation of the quinoline alkaloids waltherione A (**88**) and waltherione C (**90**), which showed inhibitory properties of the nuclear factor NF-κβ (56.1 ± 11.9 μmol L^{-1} and 55.5 ± 8.4 μmol L^{-1}, respectively). Those bioactive compounds that have inhibitory activity can act as chemopreventives and chemotherapeutics in tumor suppression.[41]

The cryptolepine indoquinoline alkaloid (**36**), isolated from the species *Sida acuta* Burm. and *S. cordifolia*, showed anticancer activity through the activation of the caspases-3/7 cascade inducing apoptosis in gastric adenocarcinoma cells[82] and the arrest of G_2/M cell cycle in osteosarcoma cells, activating p53-independent p21WAF1/CIP1 promoter genes, making this drug a promising chemotherapeutic candidate.[45]

The quinoline alkaloid waltherione C (**90**) isolated from *Melochia umbellata* (Houtt.) Stapf has demonstrated significant cytotoxic activity against murine leukemic cell lines. The alkaloid waltherione C isolated from *Melochia odorata* L.f. has demonstrated an LC_{50} activity of 0.29 mg mL^{-1} in the salt brine shrimp assay and toxicity against CEM-TART cells showing an LC_{50} of 3.8 mg mL^{-1}.[72]

A study by Zhang *et al.*[60] showed that microcosamine A (**55**) and microcosamine C (**57**) piperidine alkaloids isolated from the species *Microcos paniculata* L. showed cytotoxic activity *in vitro* against murine macrophage tumor cell lineage (RAW 264.7), with values of 31.5 μmol L^{-1} and 39.8 μmol L^{-1}, respectively.

The alkaloids microgrewiapine A (**58**) isolated from *Microcos paniculata*[54] and quindolinone (**75**) isolated from *Sida acuta* showed cytotoxic activity.[39]

Antibacterial and antifungal activities

The quinoline alkaloid vanessine (**83**) isolated from the *Sida acuta* showed antibacterial activity against strains of

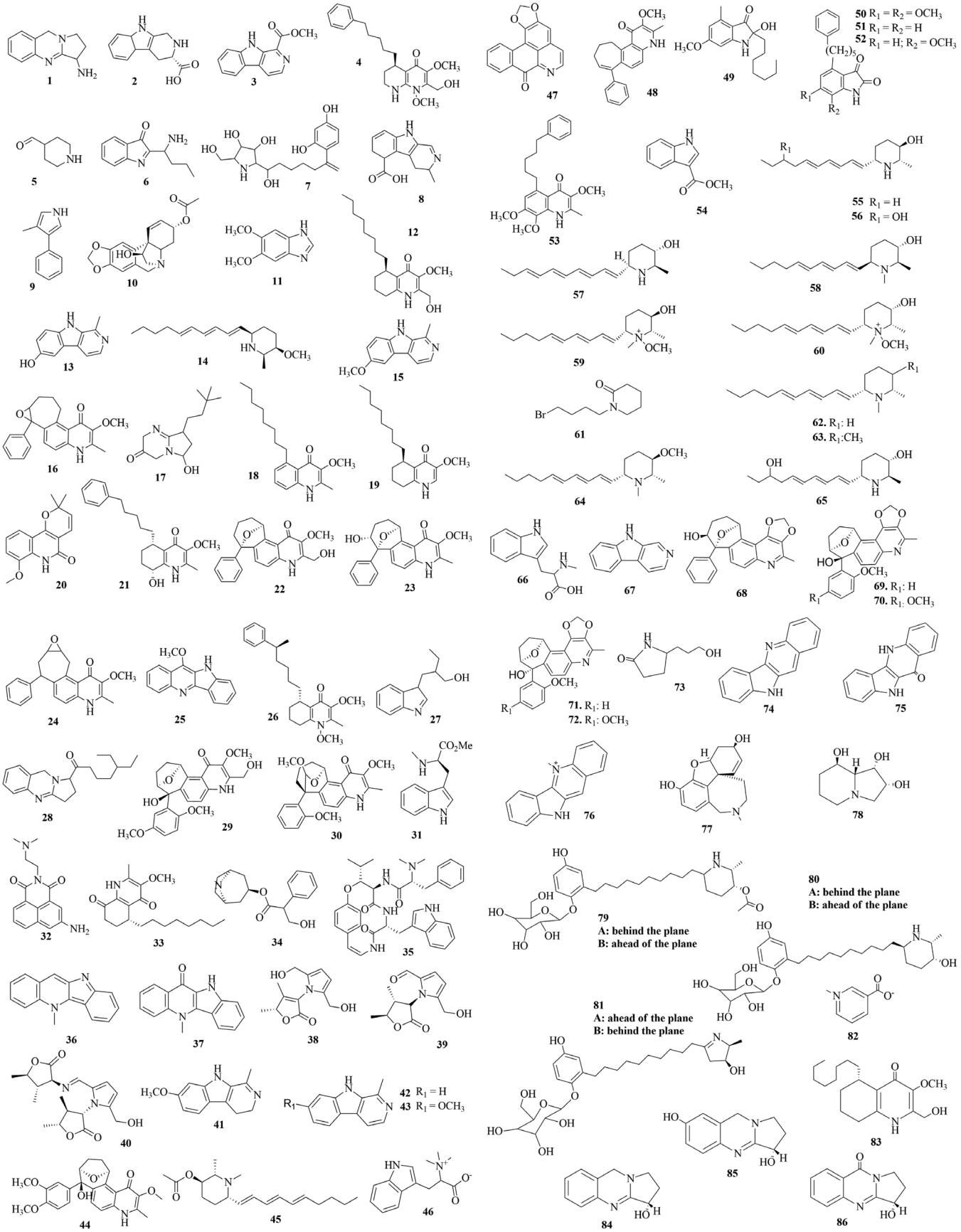

Figure 1. *Alkaloids from Malvaceae sensu lato family*

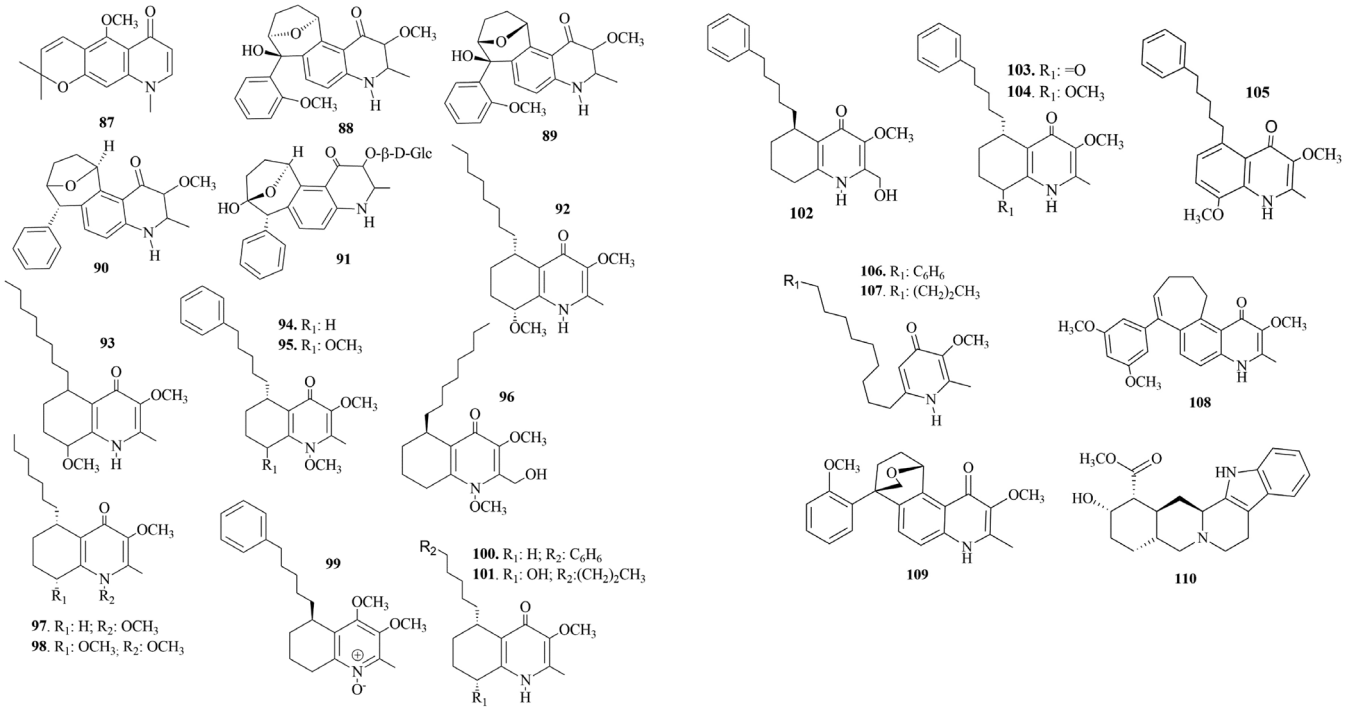

Figure 1. *Alkaloids from Malvaceae sensu lato family (cont.)*

Table 1. Alkaloids from species of the Malvaceae *sensu lato* family

Compound	Trivial name	Species	Plant parts	References
1	1,2,3,9-tetrahydro-pyrrol [2,1-*b*] quinazolyn-3-ylamine	*Sida cordifolia* L. and *Sida glutinosa* Comm. ex Cav.	AP	24, 25
2	1-lycoperodine	*Abutilon indicum* (L.) Sweet	WP	26
3	1-methoxycarbonil-β-carboline			
4	1-methoxywaltherione O	*Waltheria indica* L.	AP, RT, LV	7
5	1-piperazinecarboxaldehyde	*Hibiscus asper* Hook f.	LV	27
6	2-(1'amino-butyl)indol-3-one	*Sida cordifolia* L.	AP	24
7	2,6-dihydroxy-3,4-dihydroxymethylpyrrolidine	*Hibiscus moscheutos* L. and *Hibiscus sabdariffa* L.	PT	28
8	3,4,5,6-tetrahydro-3-methyl-β-carboline-5carboxylic	*Sida szechuensis* Matsuda	**	29
9	3-methyl-4-phenyl-1H-pyrrole	*Hibiscus asper* Hook f.	LV	27
10	3-*O*-Acetylhamayne	*Abutilon figarianum* Webb	**	30
11	5,6-dimethoxybenzimidazole	*Hibiscus asper* Hook f.	LV	27
12	5-(*R*)-vanessine	*Waltheria indica* L.	AP, RT, LV	31, 32
13	6-hydroxyharmane	*Grewia bicolor* Juss.	RT	33
14	6-(deca-1',3',5'-trimethyl)3-methoxy-2-methylpiperidine	*Microcos paniculata* L.	**	34
15	6-methoxyharmane	*Grewia bicolor* Juss.	RT	33
16	7,8-epoxy-melochinon	*Melochia umbellata* L.	RT	35
17	8-(3',3'-dimethylbutyl)-6-hydroxy-2,6,7,8-tetrahydropyrrolo[1,2-*a*]pyrimidin-3-one	*Sida rhombifolia* L.	AP	36
18	8-dimethoxywaltherione F	*Waltheria indica* L.	AP, RT, LV	7
19	8-deoxoantidesmone	*Waltheria indica* L.	AP, RT, LV	32
20	8-methoxyflindersine	*Waltheria brachypetala* Turcz.	ST, LV	37
21	(8*R*)-8-hydroxywaltherione M	*Waltheria indica* L.	AP, RT, LV	7
22	(9*S*,13*S*)-2-hydroxymethylwaltherione C			
23	(9*S*,10*S*,13*S*)-10-hydroxywaltherione C			
24	9,10-epoxy-melochinon	*Melochia umbellata* L.	RT	38
25	11-methoxyquindoline	*Sida acuta Burm.fil.* and *Sida rhombifolia* L.	RT, WP, AP	8, 39
26	15-hydroxywaltherione G	*Waltheria indica* L.	AP, RT, LV	7
27	2'-(3*H*-indol-3-ylmethyl)-butan1'-ol	*Sida cordifolia* L. and *Sida glutinosa* Comm. ex Cav.	AP	24
28	5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-1-yl)-heptan-1-one			
29	5'-methoxywaltherione A	*Waltheria indica* L.	AP, RT, LV	7
30	(*S*)-13-methoxywaltherione V			

Table 1. Alkaloids from species of the Malvaceae *sensu lato* family (cont.)

Compound	Trivial name	Species	Plant parts	References
31	(*S*)-(+)N_b-methyltryptophan methyl-ester	*Sida cordifolia* L.	RT	40
32	Amonafide	*Hibiscus asper* Hook f.	LV	27
33	Antidesmone	*Waltheria brachypetala* Turcz., *Waltheria douradinha* A.St.-Hil. and *Waltheria indica* L.	LV, RT, AP, ST	31, 41, 42
34	Atropine	*Sida cordifolia* L. and *Waltheria indica* L.	AP	43
35	Chamaedrine	*Melochia chamaedrys* A.St.-Hil. and *Waltheria indica* L.	AP, RT	44
36	Cryptolepine	*Sida acuta Burm.fil.*, *Sida cordifolia* L. and *Sida tuberculata* R.E.Fr.	AP, LV, WP, ST, BK	45-48
37	Cryptolepinone	*Sida acuta* Burm.fil. and *Sida rhombifolia* L.	WP, RT, BK, LV	4, 39
38	Funebradiol	*Quararibea funebris* (La Llave) Vischer	FL	49, 50
39	Funebral			
40	Funebrine			
41	Harmaline	*Grewia bicolor* Juss.	**	51
42	Harmane			
43	Harmine			
44	Helicterone A	*Helicteres angustifolia* L.	RT	22
45	Homomicrogrewiapine	*Grewia nervosa* (Lour.) Panigrahi	RT	52
46	Hypaphorine	*Sida cordifolia* L. and *Sida spinosa* L.	RT, WP, AP	53
47	Liriodenine	*Microcos paniculata* L.	LV, BK, BR	54
48	Melochinone	*Melochia tomentosa* L.	RT	55
49	Melochicorine	*Melochia corchorifolia* L.	AP	56
50	Melosatin A	*Melochia tomentosa* L.	RT	57
51	Melosatin B			
52	Melosatin C			
53	Melovinone	*Melochia tomentosa* L. and *Waltheria indica* L.	AP, LV, RT	7, 58
54	Methyl indole-3-carboxylate	*Abutilon indicum* (L.) Sweet	WP	26
55	Microcosamine A	*Microcos paniculata* L.	LV, BK, BR	54, 59, 60
56	Microcosamine B			
57	Microcosamine C			
58	Microgrewiapine A	*Grewia nervosa* (Lour.) Panigrahi and *Microcos paniculata* L.	RT, LV, BK, BR	52, 54
59	Microgrewiapine B	*Microcos paniculata* L.	LV, BK, BR	54
60	Microgrewiapine C			
61	*N*-[4-bromo-*n*-butyl]-2-piperidinone	*Sida cordata* (Burm.fil.) Borss.Waalk.	WP	61
62	*N*-methyl-6-(deca-1',3',5'-trimethyl)-2-methylpiperidine	*Microcos paniculata* L.	**	34
63	*N*-methyl-6-(deca-1',3',5'-trimethyl)-2,3-dimethylpiperidine			
64	*N*-methyl-6β-(deca-1',3',5'-trimethyl)-3β-methoxy-2β-methylpiperidine	*Microcos paniculata* L.	BK	34
65	*N*-Methyl-microcosamine	*Grewia nervosa* (Lour.) Panigrahi	RT	52
66	*N*-methyl-tryptofan	*Sida cordifolia* L.	RT, SD, LV, BK	62
67	Norharman	*Sida cordifolia* L.	AP	63
68	Paliasanine A	*Melochia umbellata* (Houtt.) Stapf	LV	64
69	Paliasanine B			
70	Paliasanine C			
71	Paliasanine D			
72	Paliasanine E			
73	Pyrrolidine-5-one,2-[3-hydroxypropyl]	*Hibiscus asper* Hook f.	LV	27
74	Quindoline	*Sida acuta* Burm.fil. and *Sida rhombifolia* L.	AP	8, 45
75	Quindolinone	*Sida rhombifolia* L. and *Sida acuta* Burm.fil.	AP, RT, WP	8, 39
76	Salt of cryptolepine	*Sida rhombifolia* L.	AP	8
77	Sanguinine	*Sida rhombifolia* L.	WP	65
78	Swainsonine	*Sida carpinifolia* L. and *Sida rodrigoi* Monteiro	SD	66
79	Tilacetine A and B	*Tilia platyphyllos* Scop. and *Tilia cordata* Mill.	FL	10, 67
80	Tiliamine A and B			
81	Tiliine A and B			
82	Trigonelline	*Tilia cordata* Mill.	BK, NB	68
83	Vanessine	*Waltheria douradinha* A.St.-Hil.	ST, BK	31

Table 1. Alkaloids from species of the Malvaceae *sensu lato* family (cont.)

Compound	Trivial name	Species	Plant parts	References
84	Vasicine	*Sida acuta Burm.fil.*, *Sida cordifolia* L., *Sida rhombifolia* L., *Sida humilis* Cav., *Sida spinosa* L. and *Sida tuberculata* R.E.Fr.	RT, LV, BK, AP	40, 69
85	Vasicinol	*Sida cordifolia* L. and *Sida humilis* Cav., *Sida rhombifolia* L. and *Sida spinosa* L.	RT, SD, LV, BK, AP	40, 62
86	Vasicinone	*Sida acuta Burm.fil.*, *Sida cordifolia* L., *Sida spinosa* L., *Sida humilis Cav.* and *Sida rhombifolia* L.	RT, SD, AP, BK	40, 62
87	Vitiquinolone	*Hibiscus vitifolius* L.	RT	70
88	Waltherione A	*Melochia chamaedrys* A.St.-Hil, *Melochia odorata* L.fil., *Waltheria indica* L., *Waltheria douradinha* A.St.-Hil, *Triumfetta grandidens* Hance, *Waltheria brachypetala* Turcz. and *Waltheria viscosissima* A.St.-Hil	RT, AP, BR, ST, LV, BK	9, 37, 41, 44, 31, 71-75
89	Waltherione B	*Waltheria brachypetala* Turcz., *Waltheria douradinha* A.St.-Hil and *Waltheria viscosissima* A.St.-Hil	LV, ST, AP	31, 37
90	Waltherione C	*Melochia umbellata* (Houtt.) Stapf and *Melochia odorata* L.fil.	IT, RT, BR, AP	21, 41, 71, 72, 75, 76
91	Waltherione D	*Melochia odorata* L.fil.	RT, BR	72
92	Waltherione E	*Triumfetta grandidens* Hance and *Waltheria indica* L.	AP, RT	9, 41
93	Waltherione F			
94	Waltherione G			
95	Waltherione H			
96	Waltherione I			
97	Waltherione J			
98	Waltherione K			
99	Waltherione L			
100	Waltherione M			
101	Waltherione N	*Waltheria indica* L.	AP, RT, LV	7, 41, 77, 78
102	Waltherione O			
103	Waltherione P			
104	Waltherione Q			
105	Waltherione R			
106	Waltherione S			
107	Waltherione T			
108	Waltherione U			
109	Waltherione V			
110	Yohimbine	*Helicteres isora* L.	FR	79

**not reported in the literature. (AP): aerial parts. (BK): barks. (BR): branches. (FL): flowers. (FR): fruits. (IT): inner trunck. (LV): leaves. (NB): nibs. (PT): petals. (RT): roots. (SD): seeds. (ST): stems. (WP): whole plant.

Table 2. Biological activities of alkaloids found in Malvaceae *sensu lato*

Species	Alkaloids	Biological activity	References
	Analgesic and anti-inflammatory activities		
Melochia chamaedrys A.St.-Hil.	Antidesmone (**33**)	*In vitro* and *in vivo* - inhibition of lipopolysaccharide-induced inflammatory cytokines	21
Sida cordata (Burm.f.) Borss.Waalk.	*N*-[4-bromo-*n*-butyl]-2-piperidinone (**61**)	Anti-inflamatory activity	80
Sida acuta (Burm.f.)	Cryptolepine (**36**) Quindoline (**74**)	Anti-inflamatory activity	16, 81-85
Sida cordifolia (L.)	*N*-methyl-tryptofan (**66**) 1,2,3,9-tetrahydropyrrolo [2,1-*b*]-quinazolin-3-ylamine (**1**) 5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-1-yl)-heptan-1-one (**28**)	Analgesic and anti-inflammatory activities	86-88
	Cytotoxic and anticancer activities		
Melochia umbellata (Houtt.) Stapf	Waltherione C (**90**)	Cytotoxic activity against CEM-TART cells and against leukemic cells	72

Table 2. Biological activities of alkaloids found in Malvaceae *sensu lato* (cont.)

Species	Alkaloids	Biological activity	References
Microcos paniculata (L.)	Microcosamine A (**55**) Microcosamine C (**57**) Cryptolepine (**36**)	Weak cytotoxic activity against the RAW 264.7 cell line Significant inhibition of 7,12-dimethylbenz-[*a*]-anthracene inducing preneoplastic lesions in a mouse mammary organ culture model	39, 60
Microcos paniculata (L.)	11-methoxyquindoline (**25**) Quindolinone (**75**) Cryptolepine (**36**)	Induction of quinone reductase activity Apoptosis-inducing activity in gastric adenocarcinoma cells	82-85
Sida cordifolia (L.)	Cryptolepine (**36**)	Induction of p21WAF1/CIP1 expression with growth arrest in osteosarcoma, with G_2/M phase arrest of MG63 cells	47, 48
	5'-hydroxymethyl-1'-(1,2,3,9-tetrahydro-pyrrolo [2,1-*b*] quinazolin-1-yl)-heptan-1-one (**28**)	Cytotoxic and antitumor activities	
Waltheria indica (L.)	Waltherione A (**88**) Waltherione C (**90**)	Inhibition of the nuclear factor NF-κβ	41
Grewia bicolor (Juss.)	Harmine (**43**) Harmaline (**41**) Harmane (**42**)	Antiproliferative activity and moderate cytotoxicity against human monocytes	89
		Antibacterial and antifungal activities	
Melochia odorata (L.f.)	Waltherione A (**88**)	*C. albicans*, *C. neoformans* and *S. cerevisiae*	90
Sida acuta (Burm.f.)	Quindoline (**74**) Cryptolepine (**36**) 11-methoxyquindoline (**25**)	*P. vulgaris*, *S. aureus*, *E. faecalis*, *S. boydii*, *S. flexneri*, *S. dysenteriae*, *S. thyphi*, *S. parathyphi*, *E. coli*, *S. carmonum*, *B. cereus* and *L. innocua* *B. subtilis* and *M. phlei*	16, 83, 85
Sida cordata (Burm.f.) Borss.Waalk.	*N*-[4-bromo-*n*-butyl]-2-piperidinone (**61**) Vanessine (**83**)	*E. coli*, *S. setubal* and *K. pneumoniae*	31, 80
Waltheria indica (L.)	Waltherione A (**88**) Waltherione C (**90**) Waltherione E (**92**) Waltherione G (**94**) Waltherione I (**96**) Waltherione N (**101**) Waltherione Q (**104**) 8-deoxoantidesmone (**19**) Waltherione F (**93**) Waltherione J (**97**) Waltherione V (**109**) 5-(*R*)-vanessine (**12**) Antidesmone (**33**)	*C. albicans*, *B. dothidea*, *C. musae*, *P. guepinii*, *C. orbiculare*, *P. nicotianae*, *P. longiseta*, and *S. sclerotiorum*	7, 75, 88, 91
		Antiparasitic activity	
Grewia bicolor (Juss.)	Harmine (**43**) Harmaline (**41**) Harmane (**42**)	Leishmanicidal activity against promastigote forms	89
Sida acuta (Burm.f.)	Quindoline (**74**) Cryptolepine (**36**)	Antimalaric activity *In vitro* and *in vivo* - Antiplasmodial activity	16, 48, 81, 82, 84, 85
Triumfetta grandidens (Hance)	Waltherione A (**88**) Waltherione E (**92**)	*M. incognita*	9
Waltheria indica (L.)	Waltherione A (**88**) Waltherione C (**90**) Waltherione G (**94**) Waltherione H (**95**) Waltherione K (**98**) Waltherione M (**100**) Waltherione P (**103**) Waltherione Q (**104**) Waltherione R (**105**) Waltherione T (**107**) 8-dimethoxywaltherione F (**18**) (8*R*)-8-hydroxywaltherione M (**21**) 5'-methoxywaltherione A (**29**)	*M. incogntia*, *M. arenaria*, *M. hapla* and *B. xylophilus* *T. cruzi* *M. incogntia*, *M. arenaria*, *M. hapla* and *B. xylophilus*	7, 9, 21, 41, 78
		Others activities	
Grewia nervosa (Lour.) Panigrahi	*N*-methyl-microcosamine (**65**)	*In vitro* - α-glucosidase enzyme inhibition activity	52

Table 2. Biological activities of alkaloids found in Malvaceae *sensu lato* (cont.)

Species	Alkaloids	Biological activity	References
Helicteres isora (L.)	Yohimbine (**110**)	*In silico* - Antidiabetic activity through interaction with aldose reductase and insulin receptors	79
Melochia odorata (L.f.)	Waltherione A (**88**)	Anti-HIV activity *in vitro*	72
Melochia umbellata (Houtt.) Stapf	Waltherione C (**90**)	Anti-HIV activity	72
Microcos paniculata (L.)	Microcosamine A (**55**) Microcosamine B (**56**) Microgrewiapine A (**58**) *N*-methyl-6β-(deca-1',3',5'-trimethyl)-3β-methoxy-2β-methylpiperidine (**64**)	Larvicidal activity against the 4th instar of the *C. quinquefasciatus* Cytotoxic activity and muscarinic receptor antagonist Larvicidal activity against the 2nd instar of *Ae. aegypti*	54, 59, 92
Sida carpinifolia (L.f.)	Swainsonine (**78**)	α-mannosidase enzyme inhibition activity	93
Sida rhombifolia (L.)	Cryptolepinone (**37**) Salt of Cryptolepine (**76**) Quindolinone (**75**)	Vasorelaxant activity in rodent mesenteric arteries	4, 8
Waltheria brachypetala (Turcz)	Antidesmone (**33**)	Herbicidal activity against *P. ixacarpa*	94
Sida acuta (Burm.f.)	Quindoline (**74**) Vasicinone (**86**) Vasicine (**84**) Cryptolepine (**36**)	Antipyretic activity and antiulcer Bronchodilator activity and asthmatic Hypotensive, antipyretic and antiulcer	85, 95
Sida cordifolia (L.)	*N*-methyl-tryptofan (**66**) Vasicine (**84**) Vasicinol (**85**) Vasicinone (**86**)	Bronchodilator activity and asthmatic Hypotensive, hepatoprotective and hypoglycemic activities Hypotensive, hepatoprotective, hypoglycemic and vasoconstrictor activities	88, 95-98
Tilia platyphyllos (Scop.) and *Tilia cordata* (Mill.)	Tiliine A (**81**) Tiliamine B (**80**) Tilacetine A (**79**)	Spasmodic activity on airway smooth muscle involving acetylcholinesterase	10
Sida rhombifolia (L.)	Sanguinine (**76**) Vasicine (**84**) Vasicinol (**85**) Vasicinone (**86**)	*In silico* - Potential inhibition of acetylcholinesterase for the treatment of Alzheimer's disease	65

Escherichia coli (25.0 μg mL^{-1}), *Salmonella setubal* (50.0 μg mL^{-1}) and *Klebsiella pneumoniae* (25.0 μg mL^{-1}).[31]

The plant species *Waltheria indica* L. is extensively studied, having some major quinoline alkaloids in its metabolic composition demonstrated great antifungal activity, such as waltherione N (**101**), 8-deoxoantidesmone (**19**), antidesmone (**33**), waltherione E (**92**), waltherione G (**94**), waltherione I (**96**), waltherione J (**97**), waltherione F (**93**) and 5-(*R*)-vanessine (**12**), which presented a minimum inhibitory concentration MIC ≤ 32 μg mL^{-1}.[78]

Antiparasitic activity

Among the secondary metabolites that present antiparasitic activity, we can highlight the alkaloids. *Waltheria indica* has shown a good anti-chagasic activity, being the alkaloids waltherione R (**105**), (8*R*)-8-hydroxywaltherione M (**21**), waltherione T (**107**), waltherione M (**100**), waltherione P (**103**) and waltherione Q (**104**) prominent for antiparasitic activity against the *Trypanosoma cruzi* parasite with IC_{50} values of 2.1, 0.8, 2.1, 1.3, 0.5 and 0.1 μmol L^{-1}, respectively.[7] In addition, waltherione C (**90**) showed a higher antitrypanosome activity against *Trypanosoma cruzi* (IC_{50} 1.93 μmol L^{-1}) combined with a low cytotoxicity (IC_{50} 101.23 μmol L^{-1}).[21]

Alkaloids waltherione A (**88**) and waltherione E (**92**) have been isolated from *Triumfetta grandidens* Hance and evaluated for nematocidal activity against the worm *Meloidogyne incognita*, known as cotton root nematode, which is considered as vermin in agriculture. These alkaloids showed a potency of inhibition against the egg hatching process of this worm, being 91.9 and 87.4%, respectively, after 7 days of exposure to a concentration of 1.25 μg mL^{-1}.[9]

Other activities

Some other activities of alkaloids are reported as vasorelaxant, hepatoprotective, antioxidant, hypoglycemic, antiviral and larvicide actions.

The vasorelaxant activity of quindolinone alkaloids (**75**), salt of cryptolepine (**76**)[8] and cryptolepinone (**37**)[4] against the mesenteric arteries of rodents were reported for the first time for *Sida rhombifolia*. These results justify the antihypertensive activity reported by Indian folk medicine of the species *Sida rhombifolia*.[4,8]

Aleykutty & Akhila[79] performed a computational study (*in silico*) of the indolalkylamine alkaloid yohimbine (**110**) isolated from *Helicteres isora* L. This compound was designed using the Chem.Sketch software and the molecular docking was performed with the Autodock 4.0 program, making it possible to predict its antidiabetic (hypoglycemic) activity against the interaction with the enzyme aldose reductase, noting a better binding energy to insulin receptors (-10.08 kcal mol^{-1}), when compared to the standard compound pentadecane (-9.4 kcal mol^{-1}).

Studies with alkaloids have also led to promising activities such as antivirals and larvicides.

Alkaloids waltherione A (**88**) and waltherione C (**90**) isolated from *Melochia odorata* L.f. exhibited an *in vitro* anti-HIV antiviral activity, with cytoprotection at concentrations of 56.2 and 0.84 μmol L^{-1} and inhibition of HIV P24 formation of more 50% at concentrations of 1.7 and 0.95 μmol L^{-1}, respectively. Waltherione C isolated from *Melochia umbellata* heartwood has also been reported as having anti-HIV antiviral activity with an EC_{50} of 0.3 mg mL^{-1}.[72]

For larvicidal activity, a study carried out by Feng *et al.*[59] showed that the alkaloids microcosamine A (**55**) and microcosamine B (**56**) isolated from *Microcos paniculata* would present potent activity

against the larval stages of the mosquito *Culex quinquefasciatus* in lethal concentrations CL_{50} of 5.2 and 17.0 μg mL^{-1}, respectively.

CONCLUSION

This review gathered information concerning the alkaloids found in different plant species belonging to the Malvaceae *sensu lato* family. Several medicinal properties come from these species widely used by the population for the treatment of illnesses.

After analyzing the literature, we concluded that the diversity of alkaloid nuclei found in Malvaceae species are responsible for characterizing the different pharmacological activities of these secondary metabolites from different parts of plants, presenting anti-inflammatory, analgesic, antimicrobial, antiparasitic, vasorelaxant and anticancer activities. This implies that such alkaloids, with extreme biological relevance, have great potential to be explored as sources of bioactive molecules, and species of Malvaceae *sensu lato* contribute to such importance.

ACKNOWLEDGMENTS

The authors are grateful to Coordenação de Aperfeiçoamento do Ensino Superior (CAPES) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) for the support to our researches.

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