



The Genus *Alternanthera*: Phytochemical and Ethnopharmacological Perspectives

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Ethnopharmacological relevance: The genus *Alternanthera* (*Amaranthaceae*) comprises 139 species including 14 species used traditionally for the treatment of various ailments such as hypertension, pain, inflammation, diabetes, cancer, microbial and mental disorders.

Aim of the review: To search research gaps through critical assessment of pharmacological activities not performed to validate traditional claims of various species of *Alternanthera*. This review will aid natural product researchers in identifying *Alternanthera* species with therapeutic potential for future investigation.

Materials and methods: Scattered raw data on ethnopharmacological, morphological, phytochemical, pharmacological, toxicological, and clinical studies of various species of the genus *Alternanthera* have been compiled utilizing search engines like SciFinder, Google Scholar, PubMed, Science Direct, and Open J-Gate for 100 years up to April 2021.

Results: Few species of *Alternanthera* genus have been exhaustively investigated phytochemically, and about 129 chemical constituents related to different classes such as flavonoids, steroids, saponins, alkaloids, triterpenoids, glycosides, and phenolic compounds have been isolated from 9 species. Anticancer, antioxidant, antibacterial, CNS depressive, antidiabetic, analgesic, anti-inflammatory, and immunomodulator effects have been explored in the twelve species of the genus. A toxicity study has been conducted on 3 species and a clinical study on 2 species.

Conclusions: The available literature on pharmacological studies of *Alternanthera* species reveals that few species have been selected based on ethnobotanical surveys for scientific validation of their traditional claims. But most of these studies have been conducted on uncharacterized and non-standardized crude extracts. A roadmap of research needs to be developed for the isolation of new bioactive compounds from *Alternanthera* species, which can emerge out as clinically potential medicines.

Keywords: *alternanthera*, anticancer, antidiabetic, antimicrobial, flavonoids, triterpenoid saponins, natural products (NP)

INTRODUCTION

The family *Amaranthaceae* comprises 65 genera and about 850 species (Hundiwale et al., 2012; Chandrashekhar, 2019). These species are mainly distributed in tropical regions of the United States of America, Africa, and India. Amongst 65 genera and 850 species, only 17 genera and 50 species have been recorded to be found in India. The plants from this family include herbs, shrubs, and universal weeds. The genus *Alternanthera*, a significant delegate of the family *Amaranthaceae* was coined by Forsskal in 1775. The genus *Alternanthera* comprises roughly 139 species which are distributed in India, China, Sri Lanka, the United States of America, and Africa (**Figure 1**). Though not complete and exhaustive, but phytochemical characterization was found to be reported that of *Alternanthera sessilis* (L.) R.Br. ex DC., *Alternanthera philoxeroides* (Mart.) Griseb., *Alternanthera brasiliana* (L.) Kuntze, *Alternanthera hirtula* (Mart.) R.E.Fr., *Alternanthera praelonga* A.St.-Hil., *Alternanthera littoralis* P.Beauv., *Alternanthera bettzickiana* (Regel) G.Nicholson, and *Alternanthera pungens* Kunth (**Table 1** with complete details).

The present review emphasizes traditional uses, chemical constituents, pharmacological actions, clinical potential, and safety profile of *Alternanthera* species. The current work has been compiled to fulfill the following goals: 1) to explore if traditional claims of *Alternanthera* species have been scientifically justified by pharmacological and clinical studies, and also to assess critically if their mechanism of actions is established, 2) to explore whether detailed phytochemical investigations have been conducted to detect and isolate main/bioactive constituents of various species, 3) to reveal whether appropriate analytical methods have been developed for standardization of plant materials based on marker compounds, 4) to analyze whether isolated compounds from *Alternanthera* species have potential to be developed as lead

molecules unaltered or needs derivatization to develop semisynthetic drugs through proper SAR studies and 5) to check if the safety and toxicity profiles of *Alternanthera* species have been studied. The scattered raw data has been compiled from online databases such as SciFinder, Google Scholar, PubMed, Science Direct, and Open J-Gate for 100 years up to April 2021 and offline databases such as Aromatic Plants Abstract, scientific journals, and books from different libraries of National repute. Keywords selected were based on various species of *Alternanthera* genus, and different biological activities. The articles which were in English and available with full text were included. Manuscript written in non-English versions were excluded. A total of 156 articles related to *Alternanthera* genus were finally studied and cited. But the cross-sectional literature review led us to cover a total of around 500 articles in this review article. The review article is categorized into six sections: 1) morphology emphasizes morphological characters of different *Alternanthera* species; 2) ethnopharmacology covers traditional uses of different *Alternanthera* species; 3) phytoconstituents includes name and structure of chemicals constituents isolated from various species of the genus; 4) biological activities focus on different pharmacological activities reported in various species and presented in the table; 5) toxicity studies include scientific reports of toxicity studies of different *Alternanthera* species and 6) clinical studies describe clinical trials conducted on humans.

Morphology

The morphological profile of various species of the genus was found to be similar with some variations. *A. brasiliana* (L.) Kuntze (a perennial herb mainly distributed in Brazil) is prostrate, 7.5–45 cm long branches, introducing a round stem, long internodes, and swollen nodes, at which inverse leaves connect (Kumar S. et al., 2011). Branches are glabrous, two

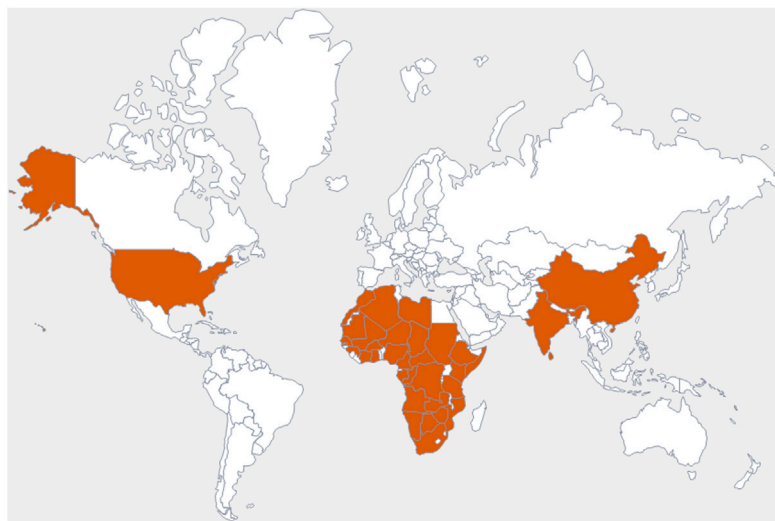


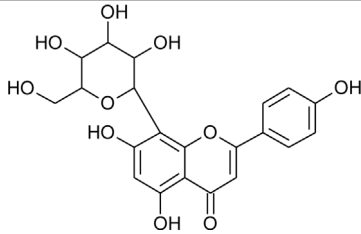
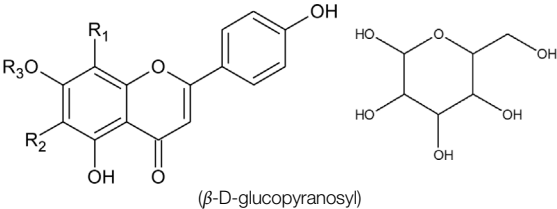
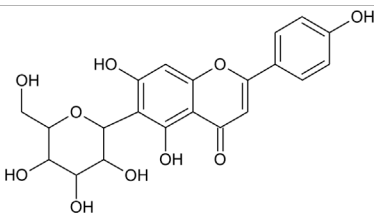
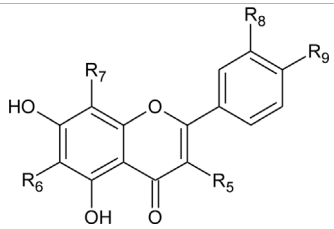
FIGURE 1 | Commonly observed geographical distribution of *Alternanthera* species, indicated in dark orange.

TABLE 1 | Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
Benzopyran					
1	3,3'-(Propane-2,2diyl)-bis-3,4,5,6,7,8-hexahydro-1H-isochromene		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Sundar et al. (2019)
Flavonoids					
2	Luteolin-6-C- β -D-boivinopyranosyl-3'-O- β -D-glucopyranoside		$R_1 = \text{Glu}; R_2 = \text{H}$ <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Not specified	Li et al. (2016)
3	Chrysoeriol-6-C- β -D-boivinopyranosyl-4'-O- β -D-glucopyranoside		$R_1 = \text{CH}_3; R_2 = \text{Glu}$ <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Not specified	Li et al. (2016)
4	Luteolin-6-C- β -D-boivinopyranosyl-4'-O- β -D-glucopyranoside		$R_1 = \text{H}; R_2 = \text{Glu}$ <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Not specified	Li et al. (2016)
5	Luteolin-6-C- β -D-boivinopyranoside or Alternanthin B or Demethyl-torosaf flavone B		$R_1 = \text{H}; R_2 = \text{H}$ <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Khampukdee et al. (2018)
6	Chrysoeriol-6-C- β -D-boivinopyranoside or Alternanthin A		$R_1 = \text{CH}_3; R_2 = \text{H}$ <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Zhou et al. (1988) Fan, (2008) Li et al. (2016) Khampukdee et al. (2018)
7	Chrysoeriol 6-C- β -boivinopyranosyl-7-O- β -glucopyranoside		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)

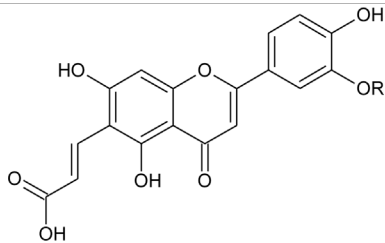
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
8	2''-O-Ramnosylvitexin	$R_1 = \text{Glucosyl (1} \rightarrow 6) \text{ ramnoside; } R_2 = R_3 = R_4 = \text{H}$	<i>Alternanthera brasiliana</i> (L.) Kuntze	Aerial parts	Araujo et al. (2014)
9	4',5,7-trimethoxy-2''-O-ramnosylvitexin	$R_1 = \text{Glucosyl (1} \rightarrow 6) \text{ ramnoside; } R_2 = R_3 = R_4 = \text{CH}_3$	<i>Alternanthera brasiliana</i> (L.) Kuntze	Aerial parts	Araujo et al. (2014)
10	Ligustroflavone	$R_1 = \text{H; } R_2 = \text{Glucosyl (2} \rightarrow 1) \text{ ramnoside, (6} \rightarrow 1) \text{ ramnoside; } R_3 = R_4 = \text{H}$	<i>Alternanthera brasiliana</i> (L.) Kuntze	Aerial parts	Araujo et al. (2014)
11	Vitexin or Apigenin-8-C-glucoside		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera philoxeroides</i> (Mart.) Griseb., <i>Alternanthera hirtula</i> (Mart.) R.E.Fr., <i>Alternanthera praelonga</i> A.St.-Hil., <i>Alternanthera littoralis</i> P.Beauv	Aerial parts; Leaves	Salvador and Dias, (2004) Correa et al. (2016) Deladino et al. (2017)
		 <p>(β-D-glucopyranosyl)</p>			
12	7-O- β -D-glucopyranosyl-6-C- β -D-glucopyranosyl-apigenin	$R_1 = \text{H; } R_2 = R_3 = \beta\text{-D-glucopyranosyl}$	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Flower	Petrus et al. (2014b)
13	6-C- β -D-glucopyranosyl-apigenin	$R_1 = R_3 = \text{H; } R_2 = \beta\text{-D-glucopyranosyl}$	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Flower	Petrus et al. (2014b)
14	8-C- β -D-glucopyranosyl-apigenin	$R_1 = \beta\text{-D-glucopyranosyl; } R_2 = R_3 = \text{H}$	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Flower	Petrus et al. (2014b)
15	5,7,4'-trihydroxyflavone	$R_1 = R_2 = R_3 = \text{H}$	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Flowers	Petrus et al. (2014a)
16	Isovitexin		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Salvador and Dias, (2004)
					
17	Kaempferol	$R_5 = R_9 = \text{OH; } R_6 = R_7 = R_8 = \text{H}$	<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; Leaves; Whole Plant	Salvador and Dias, (2004) Salvador et al. (2006) Salvador et al. (2009) Deladino et al. (2017)

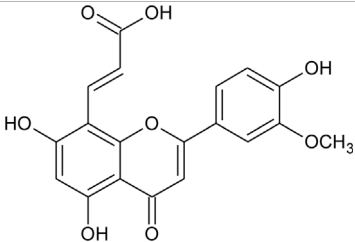
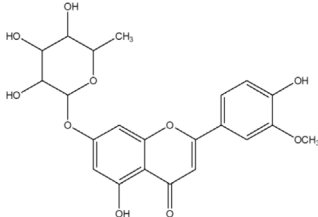
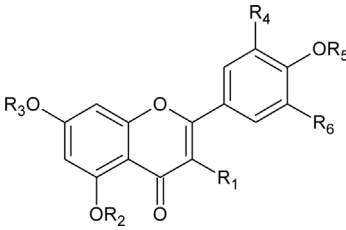
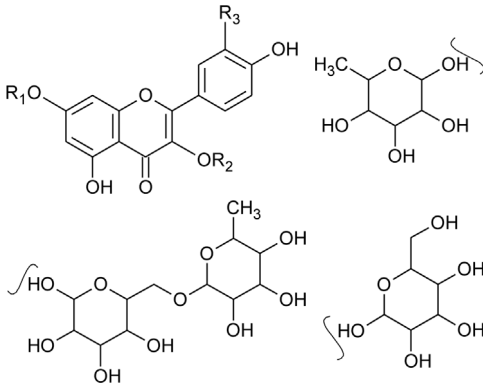
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
18	Quercetin-3-methyl ether	$R_5 = \text{OCH}_3; R_6 = R_7 = \text{H}; R_8 = R_9 = \text{OH}$	<i>Alternanthera littoralis</i> P.Beauv.; <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts	Salvador and Dias, (2004) Souza et al. (2007) Salvador et al. (2009)
19	Quercetin	$R_5 = R_8 = R_9 = \text{OH}; R_6 = R_7 = \text{H}$	<i>Alternanthera brasiliensis</i> (L.) Kuntze, <i>Alternanthera littoralis</i> P.Beauv.; <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.; <i>Alternanthera hirtula</i> (Mart.) R.E.Fr.; <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts; Whole plant	Salvador and Dias, (2004) Salvador et al. (2006) Souza et al. (2007) Fan, (2008) Salvador et al. (2009) Correa et al. (2016) Deladino et al. (2017) Vani et al. (2018) Zhang et al. (2018)
20	Luteolin	$R_5 = R_6 = R_7 = \text{H}; R_8 = R_9 = \text{OH}$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
21	2''-O- α -L-rhamnopyranosyl vitexin	$R_5 = R_6 = R_8 = \text{H}; R_7 = \text{C-Glu}''' \rightarrow 2'' \text{ Rha (d)}; R_9 = \text{OH}$	<i>Alternanthera brasiliensis</i> (L.) Kuntze, <i>Alternanthera littoralis</i> P.Beauv.; <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; whole plant	Salvador and Dias, (2004) Salvador et al. (2006) Souza et al. (2007) Salvador et al. (2009) Deladino et al. (2017)
22	2''-O- β -D-glucopyranosyl vitexin	$R_5 = R_6 = R_8 = \text{H}; R_7 = \text{C-Glu}''' \rightarrow 2'' \text{ Glu (d)}; R_9 = \text{OH}$	<i>Alternanthera brasiliensis</i> (L.) Kuntze, <i>Alternanthera littoralis</i> P.Beauv.; <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; whole plant	Salvador and Dias, (2004) Salvador et al. (2006) Souza et al. (2007) Salvador et al. (2009) Deladino et al. (2017)
23	Acacetin 8-c-[α -L-rhamnopyranoyl-(1 \rightarrow 2)- β -D-glucopyranoside]	$R_5 = R_6 = R_8 = \text{H}; R_7 = \text{C-Glu}''' \rightarrow 2'' \text{ Rha (d)}; R_9 = \text{OCH}_3$	<i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; whole plant	Salvador et al. (2006) Souza et al. (2007) Salvador et al. (2009)
24	Quercetin 3-O- α -L-rhamnosyl-(1 \rightarrow 6)- β -D-glucopyranoside	$R_5 = \text{d}; R_6 = \text{H}; R_7 = \text{H}; R_8 = \text{OH}; R_9 = \text{OH}$	<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Souza et al. (2007)
25	Isorhamnetin 3-O- α -L-rhamnosyl-(1 \rightarrow 6)- β -D-glucopyranoside	$R_5 = \text{d}; R_6 = \text{H}; R_7 = \text{H}; R_8 = \text{OH}; R_9 = \text{OCH}_3$	<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Souza et al. (2007)
					
26	Torosafllavone E	$R = \text{CH}_3$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Khamphukdee et al. (2018)
27	Demethyl torosafllavone D	$R = \text{H}$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Khamphukdee et al. (2018)

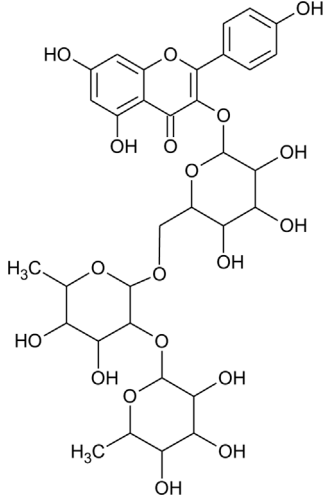
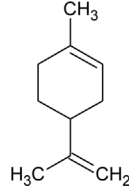
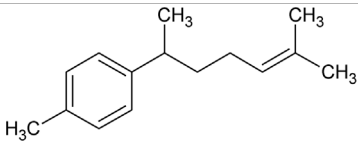
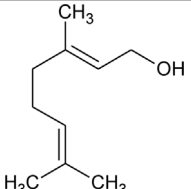
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
28	Luteolin-8-C-E-propenoic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Khamphukdee et al. (2018)
29	Chrysoeriol-7-O-rhamnoside		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Khamphukdee et al. (2018)
					
30	Crysoeriol (5,7,4'-trihydroxy-3'-methoxyflavone)	$R_1 = R_2 = R_3 = R_4 = R_5 = H; R_6 = OCH_3$	<i>Alternanthera brasiliiana</i> (L.) Kuntze	Flowers	Facundo et al. (2012)
31	Tricin (5,7,4'-trihydroxy-3',5'-dimethoxyflavone)	$R_1 = R_2 = R_3 = R_5 = H; R_4 = R_6 = OCH_3$	<i>Alternanthera brasiliiana</i> (L.) Kuntze	Flowers	Facundo et al. (2012)
32	7-O- β -D-glucopyranoside-5,4'-dihydroxy-3'-methoxyflavone	$R_1 = R_2 = R_4 = R_5 = H; R_6 = OCH_3; R_3 = O-\beta$ -D-glucopyranoside	<i>Alternanthera brasiliiana</i> (L.) Kuntze	Flowers	Facundo et al. (2012)
					
33	Kaempferol-3-O-robinobioside-7-O- α -L-rhamnopyranoside or Robinin or Kaempferol-3-O-rutinoside-7-O- α -L-rhamnopyranoside	$R_1 = a; R_2 = b; R_3 = H$	<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Brochado et al. (2003) Deladino et al. (2017)
34	Kaempferol-7-O-glucoside	$R_1 = c; R_2 = H; R_3 = H$	<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)

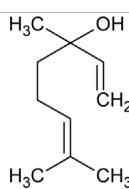
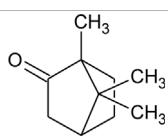
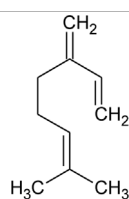
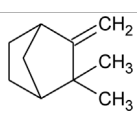
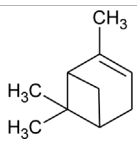
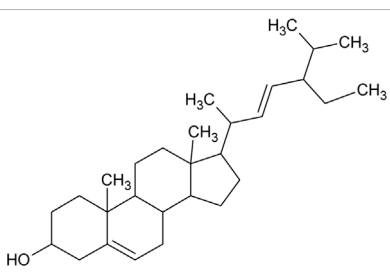
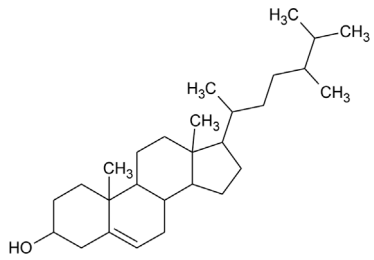
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
35	Quercetin-3-β-D-glucoside	R ₁ = H; R ₂ = c; R ₃ = H	<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
36	Quercetin-3-O-robinobioside-7-O-α-L-rhamnopyranoside or Clovin	R ₁ = a; R ₂ = b; R ₃ = OH	<i>Alternanthera brasiliana</i> (L.) Kuntze	Leaves	Brochado et al. (2003)
37	Quercetin-3-O-robinobioside or Quercetin-3-O-rutinoside or Rutin	R ₁ = H; R ₂ = b; R ₃ = OH	<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves; Aerial parts	Brochado et al. (2003) Salvador and Dias, (2004) Deladino et al. (2017)
38	Kaempferol-3-O-robinobioside or Kaempferol-3-O-rutinoside	R ₁ = H; R ₂ = b; R ₃ = H	<i>Alternanthera brasiliana</i> (L.) Kuntze	Leaves	Brochado et al. (2003)
39	Isorhamnetin-3-O-robinobioside or Isorhamnetin-3-O-rutinoside	R ₁ = H; R ₂ = b; R ₃ = OCH ₃	<i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves; Aerial parts	Salvador and Dias, (2004) Deladino et al. (2017)
40	Kaempferol-rhamnosyl- rhamnosyl-glycoside		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
Volatile oil					
41	Limonene		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
42	α-Curcumene		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
43	Geraniol		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)

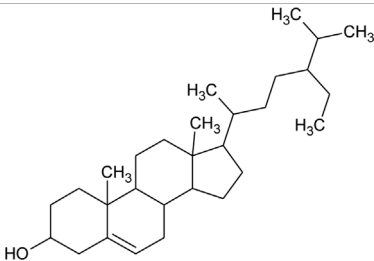
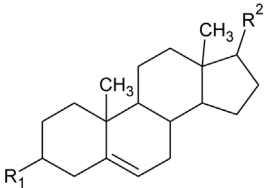
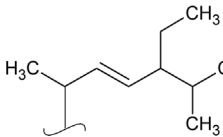
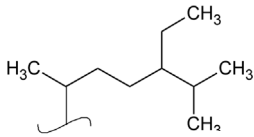
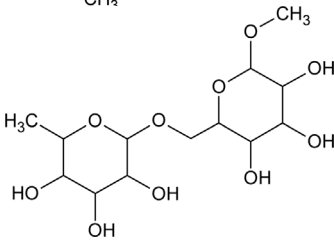
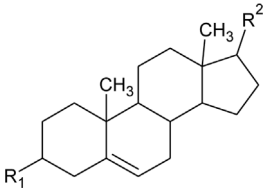
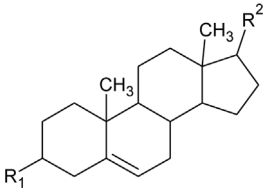
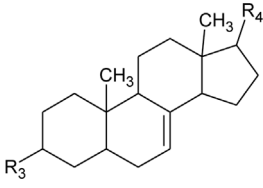
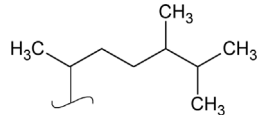
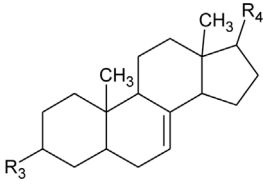
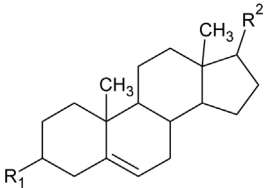
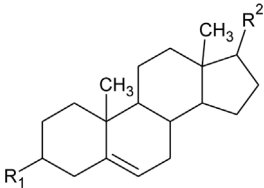
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
44	Linalool		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
45	Camphor		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
46	Myrcene		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
47	Camphene		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
48	α -pinene		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
Sterols					
49	Stigmasterol		<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera</i> <i>sessilis</i> (L.) R.Br. ex DC.	Leaves	Pereira et al. (2013) Walter et al. (2014)
50	Campesterol		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	—	Walter et al. (2014)

(Continued on following page)

TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
51	β -Sitosterol		<i>Alternanthera brasiliensis</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Leaves	Fang et al. (2006) Gupta and Singh, (2012b) Pereira et al. (2013)
52	Δ^5 -Stigmasterol or Stigmasteryl or Stigmasta-5, 22-dien-3- β -ol	   	<i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts; Whole plant	Salvador and Dias, (2004) Fan, (2008) Salvador et al. (2009)
53	β -Sitosterol		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Salvador et al. (2009)
54	Campesterol		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Salvador et al. (2009)
55	Δ^7 -Spinasterol or α -Spinasterol	 	<i>Alternanthera brasiliensis</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts; Whole plant	Salvador and Dias, (2004) Fang et al. (2006) Fan, (2008) Salvador et al. (2009) Pereira et al. (2013) Walter et al. (2014)
56	Δ^7 -Stigmasterol or Stigmast-7en-3- β -ol		<i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; Whole plant	Salvador and Dias, (2004) Salvador et al. (2009)
57	Stigmast-7enyl-3- β -ol-3-O- β -D-glucopyranoside or 3-O- β -D-Glucopyranosyl β -sitosterol		<i>Alternanthera littoralis</i> P.Beauv., <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts; Whole plant	Salvador and Dias, (2004) Salvador et al. (2009)
58	3-O- β -D-Glucopyranosyl stigmasterol		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Salvador et al. (2009)

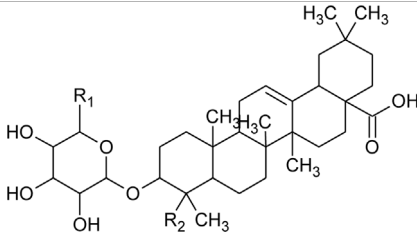
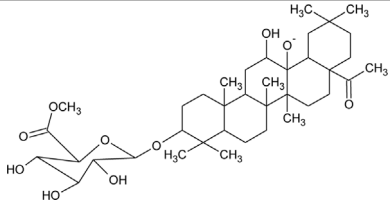
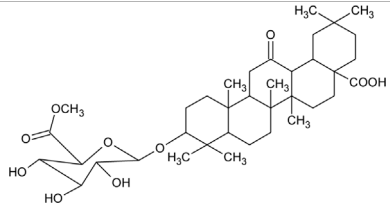
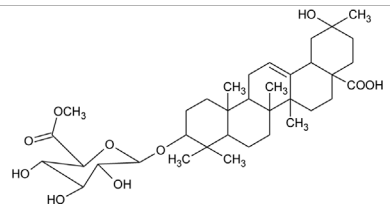
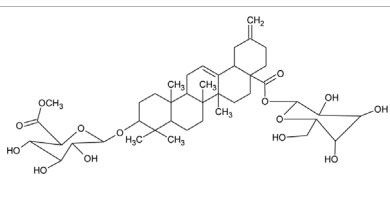
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
59	3-O- β -D-Glucopyranosyl Δ^7 -stigmasterol	R ₃ = O-Glu; R ₄ = b	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Salvador et al. (2009)
60	3-O- β -D-Glucopyranosyl spinasterol	R ₃ = O-Glu; R ₄ = a	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Salvador et al. (2009)
61	6S,7E,9R-6,9-Di-hydroxymegastigma-4,7-dien-3-one-9-O-beta-D-glucopyranoside		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)
62	3 β -Hydroxystigmast-5-en-7-one		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
63	Sitosterol-3-O- β -D-glucopyranoside	R = β -D-glucopyranoside	<i>Alternanthera brasiliana</i> (L.) Kuntze	Flowers	Facundo et al. (2012)
Triterpenoid/Saponins					
64	Ursolic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
65	Oleanolic acid 28-O-beta-D-glucopyranoside		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)

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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
					
66	Oleanolic acid 3-O-beta-D-glucuronopyranoside-6'-O-methyl ester	$R_1 = \text{CH}_3\text{COO}; R_2 = \text{CH}_3$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)
67	Hederagenin 3-O-beta-D-glucuronopyranoside-6'-O-methyl ester	$R_1 = \text{CH}_3\text{COO}; R_2 = \text{CH}_2\text{OH}$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)
68	Hederagenin-3-O-beta-D-glucuronopyranoside (HN-Saponin K)	$R_1 = R_2 = \text{CH}_2\text{OH}$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Guo et al. (2011)
69	Philoxeroideside A		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2009a)
70	Philoxeroideside B		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2009a)
71	Philoxeroideside C		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2009a)
72	Philoxeroideside D		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2009a)

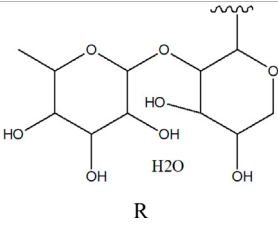
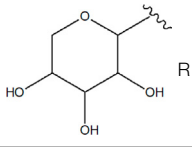
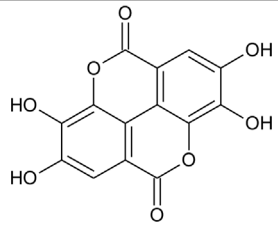
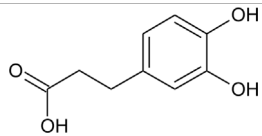
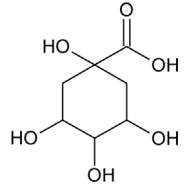
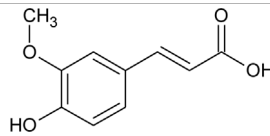
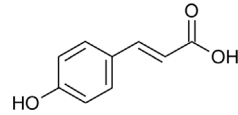
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
73	Chikusetsusaponin IVa or Oleanolic acid-3-O-beta-D-glucopyranosyl-28-O-beta-D-glucopyranosyl ester	$R_1 = H; R_2 = a$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Whole plant	Rattanathongkom et al. (2009)
74	Chikusetsusaponin IV a methyl ester	$R_1 = CH_3; R_2 = a$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)
75	Oleanolic acid 3-O-beta-D-glucuronopyranoside or Calenduloside E	$R_1 = R_2 = H$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Whole plant	Fang et al. (2009b) Rattanathongkom et al. (2009) Guo et al. (2011)
76	Oleanolic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2006)
77	2 α , 3 β -dihydroxyurs-12,20(30)-dien-28-oic acid		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts	Sanoko et al. (1999)

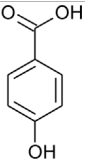
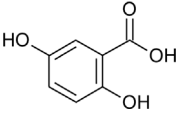
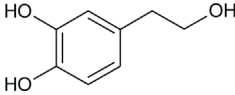
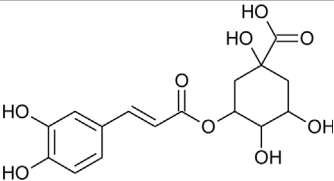
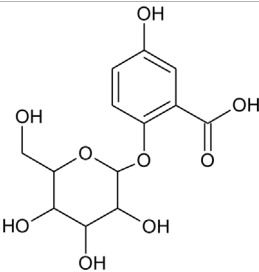
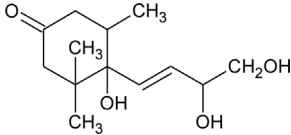
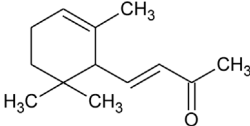
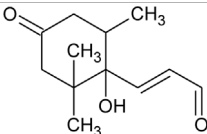
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
78	2 α ,3 β -dihydroxy urs-12,20(30)-dien-28-oic acid 3-O-([O- β -D-quinovopyranosyl-(1 \rightarrow 2)-O- α -L-arabinopyranosyl-(1 \rightarrow 2)-O- β -D-xylopyranosyl-(1 \rightarrow 3)] β -D-glucopyranoside)		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts	Sanoko et al. (1999)
79	2 α ,3 β -dihydroxy urs-12,20(30)-dien-28-oic acid 3-O-([O- α -L-arabinopyranosyl-(1 \rightarrow 2)-O- β -D-xylopyranosyl-(1 \rightarrow 3)] β -D-glucopyranoside)		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts	Sanoko et al. (1999)
80	2 α ,3 β -dihydroxy urs-12,20(30)-dien-28-oic acid 3-O-([O- β -D-xylopyranosyl-(1 \rightarrow 3)] β -D-glucopyranoside)	R = H	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aerial parts	Sanoko et al. (1999)
Phenolic compounds					
81	Ellagic acid		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Whole plant	Mondal et al. (2015)
82	Caffeic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb., <i>Alternanthera hirtula</i> (Mart.) R.E.Fr., <i>Alternanthera praelonga</i> A.St.-Hil	Whole plant	Correa et al. (2016)
83	Quinic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb., <i>Alternanthera hirtula</i> (Mart.) R.E.Fr., <i>Alternanthera praelonga</i> A.St.-Hil	Whole plant	Correa et al. (2016)
84	Ferulic acid		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera hirtula</i> (Mart.) R.E.Fr., <i>Alternanthera praelonga</i> A.St.-Hil	Whole plant; leaves	Correa et al. (2016) Deladino et al. (2017)
85	<i>p</i> -Coumaric acid		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC., <i>Alternanthera philoxeroides</i> (Mart.) Griseb	Leaves; Aerial parts	Fan, (2008) Deladino et al. (2017)

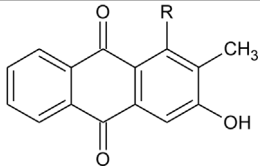
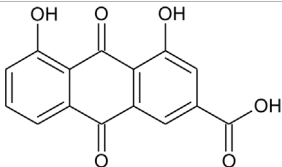
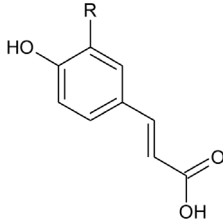
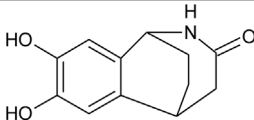
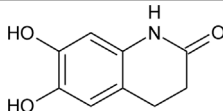
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
86	4-Hydroxybenzoic acid		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
87	2,5-Dihydroxybenzoic acid or gentisic acid		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
88	Hydroxytyrosol		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
89	Chlorogenic acid		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
90	2,5-Dihydroxybenzoic acid 5-O-β-D-glucoside		<i>Alternanthera brasiliana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
	Ionone				
91	Ionone (Alcoholic derivative)		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Ragasa et al. (2010)
92	α-Ionone		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Ragasa et al. (2010)
93	Ionone (Aldehyde derivative)		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Ragasa et al. (2010)

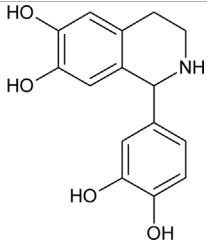
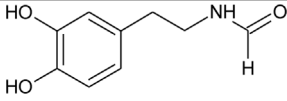
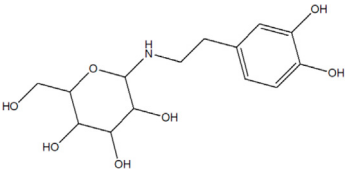
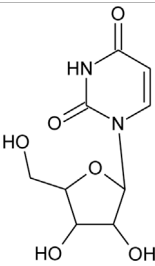
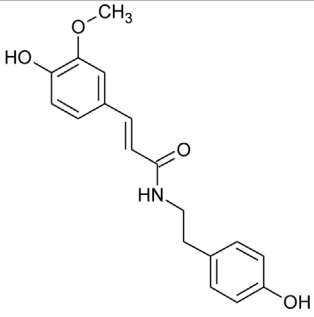
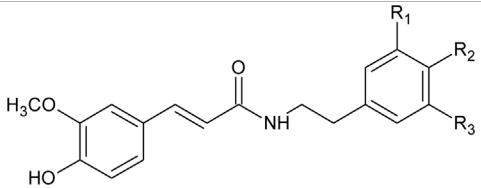
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
Anthraquinone					
					
94	Rubiadin	R = OH	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008) Collett and Taylor, (2019)
95	Rubiadin 1-methyl ether	R = OCH ₃	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
96	2-Hydroxy-3-methylantraquinone	R = H	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
97	Rhein		<i>Alternanthera pungens</i> Kunth	Flowers	Gupta and Saxena, (1987)
Hydroxycinnamic acids					
					
98	(E)-3-(4-hydroxyphenyl)prop-2-enoic acid	R = H	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Leaves	Petrus et al. (2014a)
99	(E)-3-(3,4-dihydroxyphenyl) prop-2-enoic acid	R = OH	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Leaves	Petrus et al. (2014a)
100	(E)-3-(4-hydroxy-3-methoxyphenyl) prop-2-enoic acid	R = OCH ₃	<i>Alternanthera betzickiana</i> (Regel) G.Nicholson	Leaves	Petrus et al. (2014a)
Alkaloids					
101	Alternamide A (7,8-dihydroxy-1,2,4,5-tetrahydro-3H-1,5-ethano [c]azepin-3-one)		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
102	Alternamide B (6,7-dihydroxy-3,4-dihydroquinoline-1-one)		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)

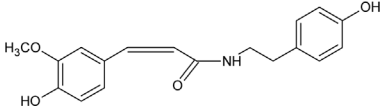
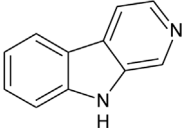
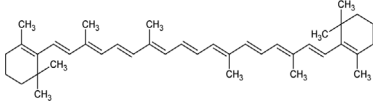
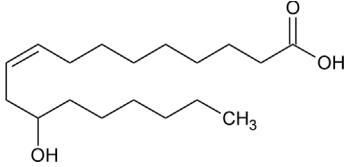
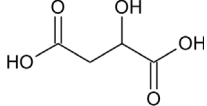
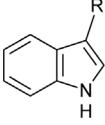
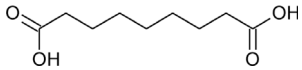
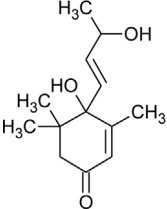
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
103	Alternamine A [(R)-1-(3,4-dihydroxyphenyl)-1,2,3,4-tetrahydroisoquinoline-6,7-diol]		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
104	N-(3,4-Dihydroxyphenethyl) formamide		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
105	Alternamine B [4-(2-aminoethyl) benzene-1,2-diol-4-(2-aminoethyl) benzene-1,2-diol-b-D -glucopyranose]		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
106	Uridine		<i>Alternanthera littoralis</i> P.Beauv	Aerial parts	Koolen et al. (2017)
107	N-trans-feruloyl tyramine		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
					
108	N-trans-feruloyl-3,5-dimethoxytyramine	R ₁ = OCH ₃ ; R ₂ = OH; R ₃ = OCH ₃	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2007)
109	N-trans-feruloyl-3-methyltyramine	R ₁ = OCH ₃ ; R ₂ = OH; R ₃ = H	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2007)

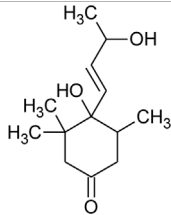
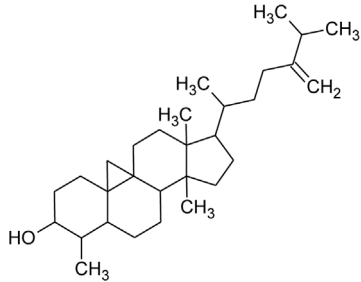
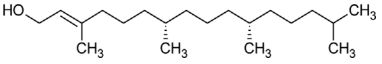
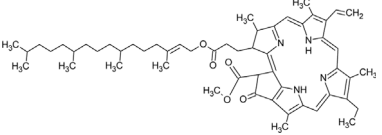
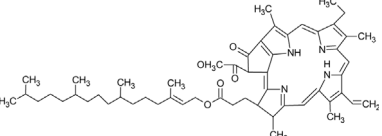
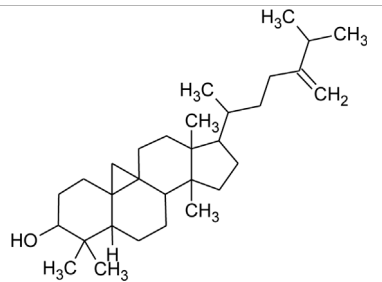
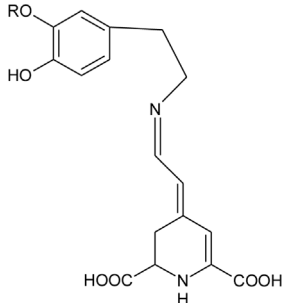
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
110	N-trans-feruloyl tyramine	$R_1 = H; R_2 = OH; R_3 = H$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2007)
111	N-cis-feruloyl tyramine		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fang et al. (2007)
112	β -Carboline		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Leaves	Zhang et al. (2018)
Miscellaneous					
113	β -Carotene		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	—	Walter et al. (2014)
114	Ricinoleic acid		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Seeds	Hosamani et al. (2004)
115	Malic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb., <i>Alternanthera hirtula</i> (Mart.) R.E.Fr	Leaves	Correa et al. (2016)
					
116	Indole-3-carboxaldehyde	$R = CHO$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
117	Indole-3-carboxylic acid	$R = COOH$	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
118	Azelaic acid		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)
119	Blumenol A		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	Aerial parts	Fan, (2008)

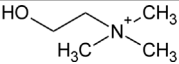
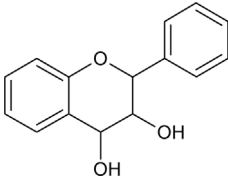
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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
120	4,5-Dihydroblumenol		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2009b)
121	Cycloeucaenol		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2006)
122	Phytol		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2006)
123	Phaeophytin A		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2006)
124	Pheophytin A		<i>Alternanthera philoxeroides</i> (Mart.) Griseb	—	Fang et al. (2006)
125	24-Methylene-cycloartanol	 	<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)

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TABLE 1 | (Continued) Chemical constituents isolated from genus *Alternanthera*.

S.No	Name	Structure	Source	Plant part	References
126	Dopamine-betaxanthin R = H		<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
127	3-Methoxytyramine-betaxanthin R = CH ₃		<i>Alternanthera brasiliiana</i> (L.) Kuntze, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Leaves	Deladino et al. (2017)
128	Choline		<i>Alternanthera pungens</i> Kunth	—	De Ruiz et al. (1993)
129	Leucoantocyanidin		<i>Alternanthera pungens</i> Kunth	Aerial parts	Petrus and Seetharaman, (2005)

lines of hair, nodes frequently villous; leaves are 2.5–7.5 cm, considerably longer when developing in watery spots, rather plump, at some point indefinitely denticulate; flowers are white, found in the form of bunches; seeds are 1.25–1.5 mm, sub-orbicular.

A. denticulata R. Br. and *A. nahui* Heenan and de Lange comprise stem of 100 mm height and located in an upright position (Heenan et al., 2009). The uniform spreading of minute hairs is present on the stems of both plants. The dark green-colored leaves (length—30 mm and breadth—6 mm) of both plants are linear, entire, narrow, elliptic, denticulate margins, and oblong in appearance. The abaxial surface of the tepals (length: 2.0–4.2 mm) is described by keeled, a character that is presented at the base of mature and dried tepals.

A. philoxeroides (Mart.) Griseb., a perennial herb, has stems crawling or gliding rising towards pinnacle, establishing at the lower hubs, branched, empty, with a longitudinal hairy groove score on two inverse sides (Pulipati et al., 2015). The fresh and delicious stems can develop on a level plane and float on the outside of the water, framing pontoons, or structure tangled bunches that develop onto banks. The leaves are inverse two by two, with an unmistakable midrib, and ranges from 5–10 cm. The plant consists of leaf, lanceolate shape, intense pinnacle, whole edge, glabrous surface, graduate base, and short strong petiole.

A. pungens Kunth is a perennial herb with a stem of 10–15 cm long with hair. The leaves are green in color and ovate in a shape of about 0.5–4.5 cm long and 0.3–2 cm in width (Naidu, 2012). It is native to the Southern American continent generally found in South Carolina, Florida, and California spreading around the road sides (Gupta et al., 2012). In 1918 it was first reported in the Southern parts of India (Rao, 2000).

A. sessilis (L.) R.Br. ex DC. is a perennial herb with purple-colored and glabrous branches grown from the root bases about 50 cm in length (Anitha and Kanimozhi, 2012). The fresh leaves are shiny, 1.3–3.0 cm long and 0.5–1.0 cm wide however the

leaves are bigger in wet living spaces, direct elliptic, oval or obovate, zenith adjusted and base cuneate. The blossoms are subtle, white, borne in little, axillary heads; bracts are obovate and 1 mm long. The bracteoles are shorter, persevering; subequal, and intense. Utricleare cordi-structure and are unequivocally compacted. The seeds are orbicular. The plant bears blossoms and natural products consistently.

Ethnopharmacology and Traditional Uses

The infusion of inflorescences of *A. Brasiliiana* (L.) Kuntze with water is used in headaches, coughs, colds, and grippe (Hundiwale et al., 2012). The infusion of leaves with a cup of water has been used in the treatment of fever while a decoction of roots is used in diarrhea. Traditionally, the various plant parts (stems, leaves, flowers, roots) of *A. caracasana* Kunth have been used to treat dysentery, diarrhea, and fever. The infusion of the plant is used as lavage or beverage in the traditional system of medicines (Canales-Martínez et al., 2008). The aerial parts of *A. Brasiliiana* (L.) Kuntze are indicated in the treatment of inflammation, pain, and various infections (Hundiwale et al., 2012). The leaves of *A. ficoidea* (L.) P.Beauv. has been used in the treatment of heart and cancer problems (Patil and Kore, 2019). *A. littoralis* P. Beauv. has a long tradition of use in the treatment of infectious and inflammatory diseases (Koolen et al., 2017). The old texts indicated the use of *A. littoralis* P. Beauv. in the treatment of inflammatory, infectious diseases (de Santana Aquino et al., 2015), viral infections, immunity problems, cancer, malaria, and diarrhea (Hundiwale et al., 2012; Sekar, 2012). *A. nodiflora* R.Br. has been in the treatment of skin, degenerative and microbial infections (Feka et al., 2014). *A. paronychioides* A.St.-Hil. has been used in the treatment of hyperuricemia, rheumatic arthritis, uremia, nephritis, gout, cystitis, diabetes, and systemic neuralgia in TCM (Wu et al., 2013). In Ayurveda, the syrup of the whole

TABLE 2 | (Continued) Pharmacological activities of genus *Alternanthera*.

S. No.	Pharmacological activity	Species	Extract/fraction/isolate	Dose tested/route of administration	Biocactive dose (mg/kg, IC50, etc.)	Positive control	Negative control	Animals	Experimental model (in vivo/vitro)	Mechanism of action	References
9	Anticancer	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Methanolic extract of leaves	10, 20, 40, 80, 160 mg/ml	160 mg/ml	—	Cardiomyocyte apoptosis induced by doxorubicin	H162 cell line	In vivo—MTT assay and Annexin V/PI-FITC/R staining assay	Decreased the cell apoptosis induced by doxorubicin	Zhang et al. (2019)
			Ethiolic extract of the whole plant	0.25, 0.5, 2.5, 25 and 250 µg/ml	Ethiolic mild activity	Doxorubicin	DMSO	UACC-62 (mammary), MCF-7 (breast), 786O (hepatocellular), HCT116 (colorectal), OVCAR3 (ovary), HT29 (colorectal), H1975 (glioma), Non cancer cell line (Vero), Human cell line from monkey (Hep2), Vero cell line	In vivo—MTT assay	Toxicity against cell lines	Correa et al. (2019)
10	Anticonvulsant	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Methanolic extract of leaves	0.05–10 mg/ml	IC50 = 6.5 mg/ml	—	—	PC12 human prostate cancer cell line	In vivo—4, 5-dimethylthiazolyl-2,5-diphenyltetrazolium bromide assay method	Apoptosis dependent pathway	Jahid et al. (2016)
			Silver nanoparticles of the aqueous extract	1.56, 3.12, 6.25, 12.5, 25 µg/ml	IC50 = 0.85 µg/ml	—	Normal saline/DMSO	HeLa cervical cancer cell line	In vivo—MTT assay	Act as modulating intrinsic apoptotic mechanisms in cervical cancer cells	Influencia and Laffra (2013)
11	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Cold nanoparticles of the aqueous extract of leaves	1–15 mg/ml	10–15 mg/ml	—	A group without extracting	SIRC rabbit corneal cell line	In vivo—MTT assay	Act as inhibiting cytochrome c of the pathway causing ocular diseases	Chen et al. (2018)
			Aqueous extract of leaves and stems	20–100 µg/ml	20–100 µg/ml	—	DMSO (2.5 ml)	—	In vivo Ethio Shrimp lethality assay	—	—
12	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	n-hexane and methanolic extracts of aerial parts	7.51, 15.025, 31.25, 62.5, 125 and 250 µg/ml	LC50 values of methanol and n-hexane extracts are 255.4 and 0.2548 µg/ml respectively	—	—	Male albino Swiss mice	In vivo—lipid peroxidation and Na ⁺ /K ⁺ ATPase assays	Significant increase in the activity of Na ⁺ /K ⁺ ATPase in the lens tissue	Koza et al. (2017)
			Ethiolic extract of aerial parts	200, 400, 800 and 1000 mg/kg p.o.	IC50 = 136 µg/ml	—	—	—	—	—	—
13	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic 70% ethanol, 80% methanolic, ethiolic and aqueous extracts of the whole plant	25 and 50 µg/ml	Ethiolic and water extracts exhibited power activity in a concentration-dependent manner	Quercetin	Group without extracting	Human liver adenocarcinoma (Hep-2) cell line	In vitro—MTT assay	Act as decreasing expression of MMP-9 in the cancer cells and inhibit cancer cell migration and reduce the chances of metastasis in human breast cancer	Sahihshahar et al. (2016)
			Silver nanoparticles of the aqueous extract of leaves	25 and 50 µg/ml	IC50 = 42.5 µg/ml	—	—	—	—	—	—
14	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of aerial parts, stem, and leaves	25–500 µg/ml	25–500 µg/ml	—	—	Male albino Swiss mice	In vivo—MTT assay and colony formation assay	Act as damaging plasma membrane causing necrosis of cancer cell	Guerra et al. (2020)
			Aqueous extract of aerial parts	5 and 50 mg/kg p.o.	50 mg/kg p.o.	—	Normal saline	—	—	—	Act as potentially reducing the number of tumor cells
15	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of leaves	100, 200, and 400 mg	100, 200, and 400 mg	Metformin (100 mg/kg) and thiazolidine Phosphatase	Control induced lenses	Lenses tissue	In vivo—lipid peroxidation and Na ⁺ /K ⁺ ATPase assays	—	Koza et al. (2017)
			Ethiolic extract of leaves	250, 500 and 1,000 mg/kg p.o.	Mild activity at a higher dose	Diacem (1 mg/kg, i.p.), Phenytoin sodium (25 mg/kg, i.p.)	—	Albino mice	In vivo—Pentylenetetrazol (PTZ) induced convulsions, Strychnine induced convulsions, and maximal electroshock seizures	Act as inhibition of blocking GABA _A receptor-mediated neurotransmission, regulation of stimulation of glycine in the spinal cord and blockade of entry of Ca ²⁺ into the cell	—
16	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of leaves	20 mg/kg p.o.	20 mg/kg p.o.	—	Dark water (10–100 mg, p.o.) and PTZ (60 mg/kg, i.p.)	Water rats	In vivo—Pentylenetetrazol induced seizures in rats test	Act as activation of GABAergic system	Schlesinger et al. (2017)
			Methanolic extract of leaves	100, 300 and 600 mg/kg p.o.	100, 300 and 600 mg/kg p.o.	—	Dark water (10–100 mg, p.o.) and PTZ (60 mg/kg, i.p.)	Adult male Swiss albino mice	In vivo—Alloxan electroshock induced seizures and pentylenetetrazol induced seizures	Act as enhancing GABA-mediated inhibition in the brain	Barua et al. (2013)
17	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of leaves	250 and 500 mg/kg p.o.	250 and 500 mg/kg p.o.	17β-Estradiol (1 µg/kg, i.p.)	Dark water (52–100 mg, p.o.)	Female (C3H) mice	In vivo—forced swimming and tail suspension tests	Act as estrogenic activity	Khanolkande et al. (2018)
			Methanolic extract of leaves	100 and 200 mg/kg p.o.	100 and 200 mg/kg	Diacem (2 mg/kg)	Dark water	Adult Swiss albino Water mice	In vivo—Tail suspension test and Food swim test	Act as interaction with adrenergic, dopaminergic, serotonergic and GABAergic system	—
18	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of stem and leaves	200 and 400 mg/kg p.o.	200 and 400 mg/kg p.o.	Metformin (100 mg/kg, p.o.)	Dark water (1 ml, p.o.)	Male Swiss albino mice	In vivo—alloxan induced diabetes model	Significantly decreased the elevated levels of blood glucose, lipid peroxidation, and various levels in diabetic experimental animals	Raza et al. (2019)
			Methanolic extract of whole plant	50, 100, 200 and 400 mg/kg p.o.	200 and 400 mg/kg p.o.	Glibenclamide (10 mg/kg, p.o.)	1% Tween (0.1 ml water, 10 ml/kg)	Swiss albino mice	In vivo—oral glucose tolerance test	Act as normalization of β-cells of the pancreas and act as increasing insulin sensitivity	Act as normalization of β-cells of the pancreas and act as increasing insulin sensitivity
19	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Meth and soluble fraction	20, 40 and 60 µg/ml	00 µg/ml	—	—	Water rats	In vivo—glucosylase inhibitory test	Act as inhibition of glucosylase enzyme	Ebrahimi et al. (2016)
			Aqueous and ethiolic extracts of the whole plant	200 and 400 mg/kg p.o.	Dose-dependent activity	Metformin (100 mg/kg, p.o.)	Dark water	Water rats	In vivo—Alloxan induced hyperglycemia	—	—
20	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aqueous and ethiolic extracts of aerial parts	125, 250 and 500 mg/kg p.o.	125, 250 and 500 mg/kg p.o.	Glibenclamide (0.6 mg/kg, p.o.)	1% Acacia solution, p.o. and alloxan monohydrate (10 mg/kg, p.o.)	Male Water albino rats	In vivo—Alloxan induced diabetes model	Act as preserving the existing β-cells of islets of Langerhans in diabetic rats	Kumar et al. (2017b)
			Hot ethiolic, aqueous and aqueous fractions of aerial parts	500 mg/kg p.o.	500 mg/kg p.o. of ethiolic fraction	Glibenclamide (10 mg/kg, p.o.)	1% CMC (2 ml/kg, p.o.) and streptozotocin monohydrate (40 mg/kg, i.p.) and pargoline (20 mg/kg, i.p.)	Male Sprague-Dawley rats	In vivo—Streptozotocin induced diabetic rat test	Act as preserving pancreatic insulin secretion or by increasing glucosylase	Act as preserving pancreatic insulin secretion or by increasing glucosylase
21	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Methanolic extract of aerial parts	50, 100, 200 and 400 mg/kg p.o.	200 and 400 mg/kg p.o.	Glibenclamide (10 mg/kg, p.o.)	1% Tween (0.1 ml water, 10 ml/kg, and Glucose (2 g/kg, p.o.)	Swiss albino mice	In vivo—oral glucose tolerance tests	Act as preservation on β-oxidation, enhancing effects on cellular antioxidant defense and protection against oxidative damage	Sarker et al. (2019)
			Petiole ether extract of leaves	200 mg/kg p.o.	25 mg/kg p.o.	—	Saline (0.1 ml/kg, p.o.) and streptozotocin monohydrate (50 mg/kg, i.p.)	Water albino rats	In vivo—Streptozotocin induced diabetes	—	—
22	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of the whole plant	200 mg/kg p.o.	200 mg/kg p.o.	Glibenclamide (10 mg/kg, p.o.)	Tween 20 (0.2 ml, p.o.) and streptozotocin monohydrate (50 mg/kg, i.p.)	Male Albino Water rats	In vivo—Streptozotocin induced diabetes	Reduction in blood glucose levels	Ravi et al. (2011)
			n-hexane, ethiolic, and water fractions of the aqueous extract of leaves	Up to 20 mg/ml	Ethiolic fraction IC50 = amylinase=0.025 mg/ml, IC50 = glucosylase=0.38 mg/ml	Metformin (100 mg/kg, p.o.)	Saline (10 ml/kg, p.o.)	Female Swiss albino mice	In vivo—Alloxan induced hyperglycemia	—	—
23	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethiolic extract of aerial parts	200 mg/kg p.o.	200 mg/kg p.o.	—	—	Female Swiss albino mice	In vivo—Alloxan induced hyperglycemia	—	Mohammed et al. (2020)
			Juice	20 and 100 µl	100 µl	Ascorbic acid	—	Male adult Water rats	In vivo—pancreatic-amylinase inhibition assay and insulin-α-glucosylase inhibition assay	Act as values of cell membrane and inhibiting protein synthesis	Act as values of cell membrane and inhibiting protein synthesis
24	Antidiabetic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Hexane, ethiolic, ethiolic fractions, and aqueous fractions of methanolic extracts of leaves and stems	—	Leaf ethiolic fraction and Culture ethiolic fraction exhibited potent anti-glucosylase	Ascorbic acid	—	—	In vivo—glucosylase inhibitory test	Act as inhibition of α-glucosylase enzyme	Choi et al. (2016)
			Hexane, ethiolic, methanolic, and aqueous extracts of the whole plant	50 and 100 mg/kg p.o. of each extract	Mild and potent activity	Diphencylhydrazine (2.5 mg/kg), Phenytoin sodium (25 mg/kg), and Metformin (2 mg/kg)	—	Male Water rats and C57BL/6J strain mice	In vivo—Diabetes induced by streptozotocin and NPY/SSA	Inhibition of water and electrolyte transport through the renal mucosa or an anti-proliferative in carcinoma	—

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TABLE 2 | (Continued) Pharmacological activities of genus *Alternanthera*.

S. No.	Pharmacological activity	Species	Extract/fraction/isolate	Dose tested/route of administration	Bioactive dose (mg/kg, IC ₅₀ , etc)	Positive control	Negative control	Animals	Experimental model (in vitro/vivo)	Mechanism of action	References
14	Anti-gout	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Methanolic extract of aerial parts	100–1,000 µg/ml	IC ₅₀ = 57.7 µg/ml	Allopurinol (IC ₅₀ = 3.1 µg/ml)	DMSO	—	In vivo: Uricemic oxidase inhibitory assay	Xanthine oxidase inhibition	Cheng and Liu, (2023)
15	Anti-HEV	<i>Alternanthera phoeniceoides</i> (Mart.) Gleason	Isolate: 6-C ₂ D-biotinylpenicillinyl-3'-O ₂ -β-D-glucopyranoside, chrysoene 6-C ₂ -β-D-biotinylpenicillinyl-4'-O ₂ -β-D-glucopyranoside, 6-C ₂ -β-D-biotinylpenicillinyl-4'-O ₂ -β-D-glucopyranoside, isolate: 6-C ₂ D-biotinylpenicillinyl and chrysoene 6-C ₂ -β-D-biotinylpenicillinyl	—	—	—	DMSO with 0.2% DMSO	HepG2.2.15 cells	In vitro—Inhibition of HEVAg and HEVAg secretions, HcAg and MTI assay	Act inhibiting the secretion of HEVAg in HepG2.2.15	Li et al. (2018)
16	Anti-hypertensive	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	70% Ethanolic extract of the whole plant and its dichloromethane and aqueous fractions	1–10 mg/kg, ip	Ethanol extract: 1–10 mg/kg, ip	Vegapant (1–10 m. g/kg, ip)	Amlodipine (1 µg/kg)	Spontaneous/Albino rats	In vivo—Isradipine (0.5–80 mg/kg, po) + clonazepam (6 mg/kg, po) anesthetized normotensive rats	Decreased both systolic and diastolic blood pressure of the anesthetized rats	Saib and Jambou, (2018)
17	Anti-inflammatory	<i>Alternanthera baselliana</i> (L.) Kuruba	Aqueous extract of leaves	200 or 400 mg/kg, p.o	400 mg/kg, p.o	Indomethacin (10 mg/kg, p.o)	Distilled water (10 mg/kg, p.o)	Male adult Wistar rats	In vivo—Carrageenan induced edema	Reduction of polyphosphonuclear cells and the increase of mononuclear cells in the exudate of animals	Pulast Formiga et al. (2012)
		<i>Alternanthera thalictroides</i> P. Bavar	Methanolic extract of leaves	300, 600 and 900 mg/kg, p.o	600 mg/kg, p.o	Sulfasalazine (300 mg/kg, p.o)	Normal saline and 4% acetic acid (1 mL, i.p.)	Adult Wistar albino rats	In vivo—Acetic acid induced colitis model of inflammatory bowel disease	Significantly reduced colon weight and decreased macroscopic and microscopic scores	P et al. (2019)
		<i>Alternanthera phoeniceoides</i> (Mart.) Gleason, <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethranolic extract of leaves	100–500 µg/ml, p.a. 1–10, 20 mg/kg, p.o	100, 300 mg/kg, p.o. 1, 10, 20 mg/kg, p.o	Dexamethasone (1 mg/kg, s.c.)	0.6% saline solution	Adult male and female Swiss mice	In vivo—Carrageenan induced paw edema and carrageenan induced uterine spasm	Act as inhibiting TNF-α, oxidative stress, cytokines	on Santoro Aquino et al. (2015)
		<i>Alternanthera racemosa</i> Kuruba	Aqueous extract of leaves	200 mg/kg, ip	200 mg/kg, ip	Indomethacin (10 mg/kg, ip)	—	Wistar strain rats	In vivo—% Nitric oxide inhibition and % Hemorrhagic	Act as inhibiting hydrolytic induced risk of endothelial nitric oxide and inhibition of the release of proinflammatory	Srinivas et al. (2014)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	80% ethanolic extract of stems	25, 50, 100, 200, 300, 400 and 600 µg/ml	200 or 600 µg/ml	Dexamethasone (0.5 µg/ml)	1% Carrageenan (0.1 mL, ip)	Wistar strain rats	In vivo—Carrageenan induced inflammatory test	Decreased level of release of histamine, serotonin and 5-HT, prostaglandin, prostaglandin, leukotrienes, and protein C-reactive	Frank et al. (2018)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Petroleum ether and methanolic extracts of leaves	100, 200 and 300 µg/ml	Methanol extract (100 µg/ml)	Aspirin (100, 200 and 300 µg/ml)	Group without coagulation	—	In vitro—platelet coagulation method	Reduced the level of proinflammatory cytokines and proinflammatory cytokine production, nuclear translocation of NF-κB p65, and protein expression analysis	Murthy et al. (2018a)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethranolic extract of whole plant (ESW) 7:2:1 (β-D-glucopyranosyl:albin)	100, 200 and 300 mg/kg, p.o. 0.1–1 and 10 mg/kg, p.o	100 mg/kg, p.o. 1 mg/kg, p.o	Phenothiazine (0 mg/kg, p.o)	Group without coagulation	Swiss mice	In vivo—Platelet coagulation method	Significantly inhibited (platelet activation) by hydrolysis in carrageenan induced paw edema, (platelet aggregation and protein expression) in carrageenan induced edema; (β) platelet activation; (γ) platelet aggregation; and leukocyte migration in arterial inflammation induced by Zymosan	Koshy et al. (2021)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Aqueous extract of the whole plant	200 and 400 mg/kg, ip	200 and 400 mg/kg, ip	Indomethacin (6 mg/kg, ip)	Stere saline (0.2 mL, ip)	Male BALB/c mice	In vivo—Carrageenan induced edema method	Cyclooxygenase-1 and -2 inhibition	Bali et al. (2018)
18	Antimicrobial	<i>Alternanthera baselliana</i> (Pugh) Gleason	Hexane, chloroform, ethyl acetate, methanolic and aqueous extracts of leaves	125, 250, 500 and 1,000 µg/ml	Mitl activity	Control: 25 µg/disc, Chloramphenicol (30 µg/disc) and Penicillin (100 µg/disc)	Sterile distilled water	Various bacterial strains	In vitro—100% Disc diffusion method	Act against of bacterial cell wall and inhibiting protein synthesis	Vidya et al. (2018)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Aqueous extract of leaves and stem nanoparticles and Ayurvedic medicinal (MCO) nanocomposite	5–100 µg/ml	100 µg/ml of Silver nanoparticles and Ayurvedic medicinal (MCO) nanocomposite	—	DMSO	Various bacterial strains	In vitro—Agar well diffusion assay	Act as inhibition of DNA replication and blocking cell wall respiration	John Ramalingam et al. (2017)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Aqueous extract of leaves (Au-NP)	10, 20, 30 or 40 µg	10, 20, 30 or 40 µg	—	—	Various bacterial strains	In vitro—Agar well diffusion method	Act as inhibiting DNA gyrase, topoisomerase II, topoisomerase IV	Nagalingam et al. (2018)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Ethranolic extract of leaves	MC = 51,024 µg/ml	MC = 51,024 µg/ml	Clotrimazole	—	Various bacterial strains	In vitro—disk diffusion method	Act as modification of the arabinoside binding site and target mutations in the 3'5S ribosomal subunit	Chaitra et al. (2017)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Ethranolic extract of aerial parts	75–1,000 µg/ml	Isobavoside	Amphotericin B	DMSO	Various marine microorganisms and fungi strains	In vitro—broth microdilution method	—	John et al. (2018)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Hexane, chloroform, methanolic, acetone, and ethyl acetate extract of aerial parts and 7-methoxycurcumin	—	Azobenzene/ethyl acetate extracts and 7-methoxycurcumin	Kanamycin and chloramphenicol (25 µg)	DMSO	Various bacterial strains	In vitro—disk diffusion method	Act against of microbial cell wall and inhibiting protein synthesis	Chaitra et al. (2018)
		<i>Alternanthera baselliana</i> (L.) Kuruba	Ethranolic extract of leaves	200 mg	Mitl activity	Clotrimazole	—	Various bacterial strains	In vitro—disk diffusion method	Act against of microbial cell wall and inhibiting protein synthesis	Abulhasan and Ullah et al. (2018)
		<i>Alternanthera thalictroides</i> P. Bavar	Silver nanoparticles from aqueous extract of leaves	20–100 µg/ml	20–100 µg/ml	—	DMSO	Various bacterial strains	In vitro—Agar well diffusion assay	Act as inhibition of DNA replication and blocking cell wall respiration	Kumar et al. (2014)
		<i>Alternanthera thalictroides</i> P. Bavar	Hexane and ethranolic extract of leaves	25 mg/ml (Final active concentration: 2,025 µg)	25 mg/ml (Final active concentration: 2,025 µg)	Isotomycin (0.20 mg/ml) and methylerythritol (0.05 mg/ml)	Physiologic glycodistilled sterilized water (5%)	Various fungal strains	In vitro—agar well diffusion method	Mitochondrial membrane synthesis and protein degradation	Chaitra et al. (2018)
		<i>Alternanthera thalictroides</i> P. Bavar	Aqueous and methanolic extracts of the whole plant	100 µg/ml	100 µg/ml	—	—	Various bacterial and fungal strains	In vitro—agar well diffusion method	Act against of microbial cell wall and inhibiting protein synthesis	Felix et al. (2014)
		<i>Alternanthera thalictroides</i> P. Bavar	Methanolic and ethanolic extracts of leaves	20–40 and 60 µg/ml	Methanol extract (100 mg/ml)	—	—	Various bacterial strains	In vitro—disc diffusion assay	Act against of bacterial cell wall and inhibiting protein synthesis	Chaitra et al. (2018)
		<i>Alternanthera thalictroides</i> P. Bavar	Aqueous and chloroform: methanol (1:1) extracts of leaves	35.25–50 µg/ml	35.25–50 µg/ml	—	Distilled water and DMSO	Various bacterial strains	In vitro—disc diffusion method	—	Ravens et al. (2011)
		<i>Alternanthera thalictroides</i> P. Bavar	Ethranolic extract of leaves	500, 750 and 1,000 µg/ml	1,000 µg/ml	Terbufosin (50 µg/ml) for bacteria and Miconazole (100 µg/ml) for fungi	DMSO	Various bacterial and fungal strains	In vitro—Agar well diffusion assay	Act against of microbial cell wall and inhibiting protein synthesis	Pulast et al. (2016)
		<i>Alternanthera thalictroides</i> P. Bavar	Methanolic extract of leaves, stem and roots in hexane, chloroform and ethyl acetate fractions	100 mg/ml	100 mg/ml	Penicillin (100 µg/ml)	DMSO (100 µL)	Bacterial phytopathogens (white rot, brown rot, and stem rot) and various fungi strains	In vitro—Disk diffusion method in hexane fraction maximum zone of inhibition	—	Ahler et al. (2021)
		<i>Alternanthera thalictroides</i> P. Bavar	Methanolic extract of leaves	500, 750 and 1,000 µg/ml	1,000 µg/ml	Nidularin (500 µg/disc)	DMSO	Xenopus laevis oocytes	In vitro—Agar well diffusion method in methanolic fraction maximum zone of inhibition	Act against of bacterial cell wall and inhibiting protein synthesis	Pulast and Sibal, (2020)
		<i>Alternanthera thalictroides</i> P. Bavar	Aqueous extract of leaves	—	Both strains exhibited antibacterial only	—	—	Various bacterial and fungal strains	In vitro—Agar well diffusion method	Act against of microbial cell wall and inhibiting protein synthesis	Kumar and Krishnan, (2016)
		<i>Alternanthera thalictroides</i> P. Bavar	Ethranolic extract of leaves	10, 25, and 50 µg	10, 25, and 50 µg	Genentech-Nystatin	Ethanol	Various bacterial and fungal strains	In vitro—Vial diffusion assay	—	—

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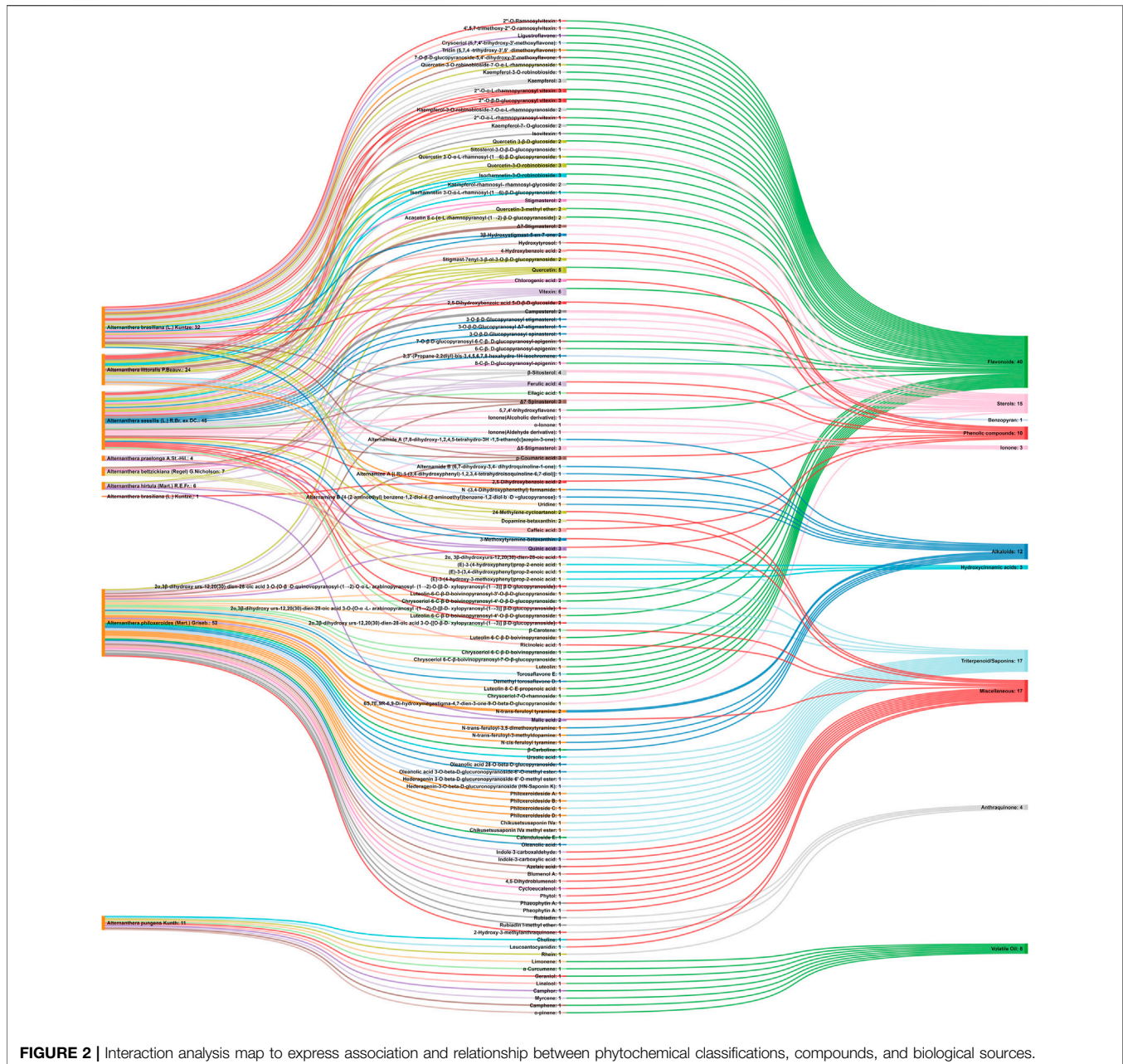
TABLE 2 | (Continued) Pharmacological activities of genus *Alternanthera*.

S. No.	Pharmacological activity	Species	Extract/fraction/substrate	Dose tested/route of administration	Biocactive dose (mg/kg, IC ₅₀ , etc)	Positive control	Negative control	Animals	Experimental model (in vitro/ in vivo)	Mechanism of action	References
			Ethanic and aqueous extracts of aerial parts	100–1000 µg/ml	β-carotene, ascorbic acid, Trolox, iron (II) sulfate heptahydrate	Solution of stable free radicals	–	–	In vitro – β-carotene bleaching assay, 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay, 2,2'-azobis(2-amidinopropane) dihydrochloride (ABTS) assay, and Oxygen radical absorbance capacity (ORAC) assay, and In vitro – 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay, 2,2'-azobis(2-amidinopropane) dihydrochloride (ABTS) assay, hydrogen peroxide (H ₂ O ₂) scavenging assay, ferric chloride reducing assay	Inhibition of stable free radical	Murthy et al. (2018) Chinnai et al. (2018)
			Juice	25, 50, and 100 µl	Ascorbic acid	Solution of stable free radicals	–	–	In vitro – 2,2-Diphenyl-1-picrylhydrazyl (DPPH) assay, 2,2'-azobis(2-amidinopropane) dihydrochloride (ABTS) assay, hydrogen peroxide (H ₂ O ₂) scavenging assay, ferric chloride reducing assay	Inhibition of stable free radical	Tiwari et al. (2013)
			Ethanic extract of leaves	10, 50, 100, 250 and 500 µg/ml	IC ₅₀ = 396, 522 µg/ml	Solution of stable free radicals	–	–	In vitro – DPPH radical scavenging assay, ABTS radical cation-scavenging assay, and Reducing power assay	Inhibition of stable free radical	Rajmangum et al. (2013)
			Methanolic extract of leaves	100–1200 µg/ml	IC ₅₀ = 400 µg/ml	Solution of stable free radicals	–	–	In vitro – DPPH radical scavenging method	Inhibition of stable free radical	Jain et al. (2016)
			Aqueous extract of leaves and stems	10–100 µg/ml	Quercetin (10–100 µg/ml)	Solution of stable free radicals	–	–	In vitro – DPPH radical scavenging and Ferric reducing antioxidant power assay	Inhibition of stable free radical	Sudhakar et al. (2018)
			Hexane, ethyl acetate, ethanolic, and aqueous extracts of leaves and stem	0–1000 µg/ml	The ethanolic extract exhibited potent activity	Solution of stable free radicals	–	–	In vitro–DPPH test, Trolox equivalent antioxidant capacity, and Ferric reducing antioxidant power assay	Inhibition of stable free radical	Mohi-ud-din et al. (2018)
			Sliver methanolic from aqueous extract of leaves	100–500 µg/ml	IC ₅₀ = 30.6 µg/ml	Solution of stable free radicals	–	–	In vitro–DPPH test	Inhibition of stable free radical	Prasanna et al.
			100% Ethanolic, 70% ethanolic, 80% methanolic, ethyl acetate, and aqueous extracts of the whole plant	0–1000 µg/ml	Ethanic extract exhibited maximum activity (IC ₅₀ = 95.0 µg/ml, TEAC = 0.51 mmol TEAC/mg FRAP = 1.06 mmol Fe ²⁺ /g)	Solution of stable free radicals	–	–	In vitro–DPPH test, Trolox equivalent antioxidant capacity, and Ferric reducing antioxidant power assay	Inhibition of stable free radical	Yog et al. (2019)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Petroleum ether, ethyl acetate, chloroform, and methanolic extract of leaves	100–500 µg/ml	Ascorbic acid (100–500 µg/ml)	Solution of stable free radicals	–	–	In vitro – Reducing power and DPPH assay	Inhibition of stable free radical	Koza et al. (2017)
			Petroleum ether and methanolic extracts of leaves	50, 100 and 150 µg/ml	Ascorbic acid (50–150 µg/ml)	Solution of stable free radicals	–	–	In vitro – Reducing power and DPPH assay	Inhibition of stable free radical	Sun et al. (2019)
			n-hexane and methanolic extracts of aerial parts	10, 30, 50, 70, 90 and 110 µg/ml	Methanolic extract (IC ₅₀ = 71.10 µg/ml) n-hexane extract (IC ₅₀ = 92.54 µg/ml)	Solution of stable free radicals	–	–	In vitro DPPH assay	–	Pantik et al. (2020)
			The volatile oil of leaves and flowers	50–250 µg/ml	Flower (IC ₅₀ = 170 µg/ml) and leaves (IC ₅₀ = 170 µg/ml)	Solution of stable free radicals	–	–	In vitro–DPPH assay	Inhibition of stable free radical	Khan et al. (2018)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ether (fractanolic), ethyl acetate, Acetone, n-hexane, methanolic (1:1–3:1), chloroform, 20% Chloroform, L-Ascorbic acid, ethanolic, 20% Chloroform, propylene glycol, and water	–	Bulked hydroxytolerone (IC ₅₀ = 80 µg/ml) Catechin, resveratrol, caffeic acid and epigallocatechin gallate	Solution of stable free radicals	–	–	In vitro–ORAC assay	Inhibition of stable free radical	Selvaraj et al. (2020)
20	Antibacterial/ Antidiarrhea	<i>Alternanthera phillyoides</i> (Mart.) Chab.	Ethanic extract of the whole plant	In vivo (body, 700 and 500 mg/kg, p.o. once daily for 8 weeks) Intracaudal: 100 µg/ml	Dose dependently improved cognitive deficits in the rat of the corticosterone induced mice	Distilled water	Distilled water	OVX Female CD-1 mice	In vivo: Memory recall task, novel object recognition task and Y-maze task	Inhibition of lipid peroxidation in the whole brain, decrease in the level of malondialdehyde (MDA), IL-6, and TNF-α and upregulation of estrogen receptor-mediated factors (p-ERK and Akt) in hypothalamic cortex and hippocampus	Shen-Hou et al. (2021)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Silver nanoparticles and ethanolic extract of the whole plant	20 and 200 mg/kg, p.o.	Syndapin (10 mg/kg, p.o.) (1.5 mg/kg, s.c.)	Distilled water and Potassium	Distilled water and Potassium (1.5 mg/kg, s.c.)	Male Wistar rats	In vitro–cortisone model of pain/analgesia In vivo–cortisone model of pain/analgesia	Act as the reduction in the lipid peroxidation, increase in reduced glutathione, and reduction in oxidative stress in the brain of animals	Myrathi and Harwood (2015)
21	Antiproliferative	<i>Alternanthera ficoidea</i> P.Bonn.	Alternanthera A.B, Alternanthera A.B	–	Alternanthera A (IC ₅₀ = 0.16 µM) and Alternanthera B (IC ₅₀ = 0.02 µM)	DMBS	DMBS	Various probatal strains	In vitro – Tyrosinase and tyrosinase-like assays	–	Kouon et al. (2017)
22	Antispasmodic	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aqueous, hexane, methanolic extract, and fractions of meth and extract (F ₁) of leaves	–	Methanolic extract and fractions of the methanolic extract (F ₁ , F ₂)	–	–	Adult male Wistar rats	In vitro – Smooth muscle preparation. Inhibition of dose-response curves to CaCl ₂ . Relaxant effect on K ⁺ induced contractions. Inhibition of dose response curve to 5-HT ₂ and inhibition of concentration response curve to acetylcholine (ACh)	Act as inhibiting serotonergic and Ca ²⁺ influx. Inhibits the postsynaptic movement of the cell wall, and reduction of the intestinal transit of food in rats	Ganti-Agilar et al. (2013)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	70% Ethanolic extract of the whole plant and its dichloromethane, aqueous fractions	–	Ethanic extract (0.01–1.0 mg/ml), aqueous fraction (0.01–0.3 mg/ml) and dichloromethane (0.01–0.1 mg/ml)	Venquel (1–10 mg/kg, p.o.)	–	White albino rabbits	In vivo – Isolated rabbit tissue preparations (i.e., ileum, trachea, and aorta)	Decreased the contractions in terms of both frequency and magnitude	Saib and Jambuk (2018)
23	Antiviral	<i>Alternanthera phillyoides</i> (Mart.) Chab.	Chloroform (V/a)	–	IC ₅₀ = 26, 30, 70, 23, and 25	–	No drug group	HSR-1, HSR-2, human cytomegalovirus, measles virus, mumps virus, and Female BALB/c mice	In vitro – various viral cell In vivo – mouse model of genital herpes caused by HSV-2	Suppressed both the intracellular virus levels and the release of the virus in a concentration dependent manner and prevent the viral protein synthesis	Ratnantharam et al. (2020)
24	Central-stimulating	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Ethanic extract of leaves	250 and 500 mg/kg, p.o.	Cefixime (20 mg/kg, p.o.)	Pentobarbitone (50 mg/kg, i.p.)	–	Young Swiss Albino mice	In vivo – Pentobarbitone induced sleeping time, open field and hot cross tests	Act as stimulating the inhibitory neurotransmitter gamma-aminobutyric acid (GABA) mediated postsynaptic inhibition through allosteric modification of GABA-A receptors	Moual et al. (2016)
25	Gastrointestinal protective	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aqueous and ethanolic extract of the whole plant	1–300 mg/kg, p.o.	Alcogel (1 mg/kg)	–	–	Swiss mice	In vitro – charcoal meal method	Act as decreasing gastrointestinal content	Asadi-Saeed et al. (2020)
26	Hepatoprotective	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aqueous extract of entire plant	300 mg/kg, p.o.	–	Com (0.03 g/kg, Physiological saline) polyethylene glycol 400 Carbon tetrachloride (0.125 µL/kg, i.p.) or acetaminophen (800 mg/kg, i.p.) in mice and D-xylozamine (180 mg/kg, i.p.) in rats 2% w/v Curcuma suspension (1 ml/kg, p.o.) and carbon tetrachloride (1.25 mg/kg, i.p.)	–	Male CRJ strain mice and male Wistar strain albino rats	In vivo – Carbon tetrachloride induced hepatotoxicity	Act as inhibition of cytochrome P450, or promotion of its gluconidation	Lin et al. (1996)
		<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Methanolic extract of the whole plant	50, 200 and 250 mg/kg, p.o.	Silymarin (100 mg/kg, p.o.)	–	–	Male Wistar rats	In vivo – carbon tetrachloride-induced hepatotoxicity	Act as agonist (measured of degradation) marked by a prominent decrease of glucose, cell integrity restoration	Bhujun et al. (2017)
27	Immunomodulatory	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.	Aqueous extract of the whole plant	50, 100 and 200 mg/kg, i.p.	Sheep blood cell (SBC) 1 mL/20% suspension in saline, (p.o.)	Sheep blood cell (SBC) 1 mL/20% suspension in saline, (p.o.)	–	Male BALB/c mice, adult guinea pigs, and adult sheep	In vivo – Enzyme fixed immunosorbent assay	Act as increasing production of interferon induced antibodies and inhibiting the production of antibody T-helper antigens	Bali et al. (2018)

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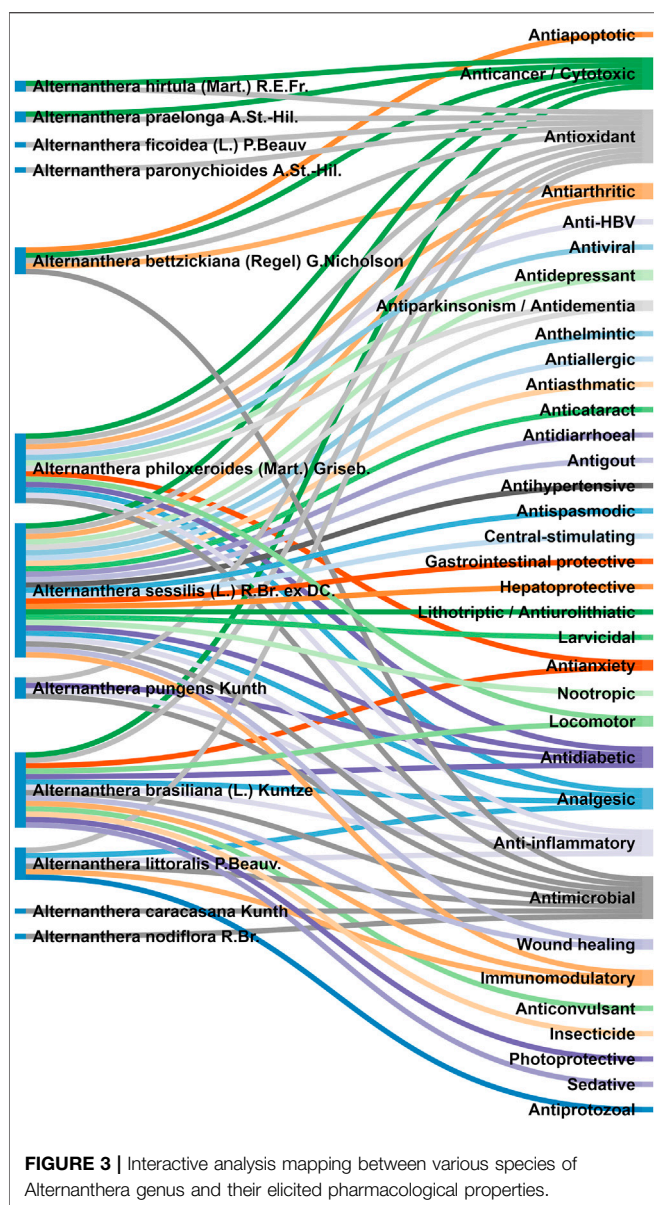
TABLE 2 | (Continued) Pharmacological activities of genus *Alternanthera*.

S. No.	Pharmacological activity	Species	Extract/fraction/isolate	Dose/tenfold dose administration	Biocative dose (mg/kg, µg/g, etc)	Positive control	Negative control	Animals	Experimental model (in vivo/in vitro)	Mechanism of action	References
28	Insecticide	<i>Alternanthera brassicae</i> (L.) Kuntze	Ethanol extract of leaves	10, 20 and 40 µg/ml	–	–	Normal saline	Male albino Swiss mice	In vivo—Mice immunized with sheep red blood cell (SRBC) 10% (p.i.) as T-dependent antigens, or in mice stimulated with mitogens (10 µg, <i>E. coli</i> , <i>Concanavalin A</i> lipopolysaccharide, LPS, Lp)	Act via immune activation either by inhibiting or stimulating antibody production, depending on its concentration	Gurus et al. (2013)
29	Lithotropic/Aniturbid	<i>Alternanthera sessilis</i> (L.) HBK. ex DC., <i>Alternanthera brassicae</i> (L.) Kuntze and <i>Alternanthera rhomboides</i> (L.) Poir.	Aqueous extract of leaves; Interferon- γ , interferon- β , interferon- α , aqueous potassium ether soluble fraction	0–200 µg/ml	–	–	–	Purified blood mononuclear cells	In vitro—Natural killer Assay	Inhibition of lymphocyte activation Act via activation of the cells of the immune system	Moses et al. (1994)
30	Larvicidal	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Ethanol extract of leaves	10, 20 and 40 µg/ml	–	–	1% sucrose	Adult fish (<i>Drosopila melanogaster</i>) locomotor assays	In vivo—Toxicity against <i>Drosopila melanogaster</i> and locomotor assays	Act via inhibition of nucleic acid synthesis, DNA gyrase	Coufiro et al. (2017)
31	Lithotropic/Aniturbid	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Kulka - the paste of macerated fresh plant material	0.054, 0.109, 0.216 g/100g, 0.432, 0.864, 1.728 g/100g, and 3.456 g/100g	Oxytetracycline (0.25 mg/kg)	Oxytetracycline (0.25 mg/kg)	0.75% (v/v) ethylene glycol in drinking water and coconut water (0.8% mg/200 g)	Healthy adult albino rats	In vivo—Ethylene glycol induced urolithiasis	Act via diuretic activity, crystallization inhibition activity, improving renal function and antioxidant activity of the drug	Chenya et al. (2017)
32	Larvicidal	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Ethanol extract of the whole plant	10, 20, and 40 mg	–	–	–	–	In vitro, <i>Thermus</i> , simultaneous flow state model, turbidimetry, and gravimetric methods	–	Eblouat et al. (2021)
33	Larvicidal	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Ethanol extract of the whole plant	20, 40, 60, 80 and 100 µg/ml	LC ₅₀ = 69.94 µg/ml	–	–	–	Percent mortality	–	Eblouat et al. (2021)
34	Larvicidal	<i>Alternanthera brassicae</i> (L.) Kuntze	Aqueous extract of leaves	100, 200 and 400 mg/kg, p.o.	–	–	Distilled water (10 mg/kg, p.o.)	Male adult Wistar rats	In vivo—Open field exposure test	Act via an increase in their exploratory activities	Pisak Formigo et al. (2012)
35	Larvicidal	<i>Alternanthera brassicae</i> (L.) Kuntze	Ethanol extract of leaves	250, 500 and 1,000 mg/kg, p.o.	Diapsam (1 mg/kg, i.p.)	Diapsam (1 mg/kg, i.p.)	Saline (10 mg/kg, p.o.)	Albino mice	In vivo—Neurally induced behaviors	Act via regulation of different neurotransmitters such as GABA, ACh, noradrenaline, serotonin, glutamate, and dopamine	Oyemba et al. (2015)
36	Larvicidal	<i>Alternanthera pflaenderi</i> (Horn) (Craib)	Ethanol extract of leaves	250 and 500 mg/kg/day	Inactive	17-Estradiol (1 µg/kg, i.p.)	Distilled water (0.2 ml/kg, p.o.)	Female C57 mice	In vivo—Y-maze test	–	Kiranprabha et al. (2018)
37	Nootropic	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Methanol extract of leaves	100 or 200 mg/kg, p.o.	200 mg/kg, p.o.	–	Scopolamine (0.4 mg/kg, i.p.)	Adult Swiss albino Wistar mice	In vivo—Rectangular maze and Y-maze tests	Act via evoking pronounced alteration behavior and better learning assessments	Gupta and Singh (2012a)
38	Phytoremediative	<i>Alternanthera brassicae</i> (L.) Kuntze	5% w/v oil form extract enriched with flavonoids	–	5% w/v flavonoid rich gel	–	Gel base	–	In vitro—Mineral method	Act via the ability to stabilize reactive oxygen species, due to the presence of thiol groups attached to the aromatic rings, allowing the resonance	Akcoro Fito et al. (2020)
39	Sedative	<i>Alternanthera brassicae</i> (L.) Kuntze	Ethanol extract of leaves	250, 500 and 1,000 mg/kg, p.o.	Diapsam (1 mg/kg, i.p.) Mianserin (100 mg/kg, i.p.)	Diapsam (1 mg/kg, i.p.) Mianserin (100 mg/kg, i.p.)	Saline (10 mg/kg, p.o.)	Albino mice	In vivo—Kearney-induced hypotensive test	Act via stimulatory or central excitatory effect	Oyemba et al. (2015)
40	Wound healing	<i>Alternanthera brassicae</i> (L.) Kuntze	Methanol extract of leaves	5% ointment applied topically, 200 and 400 µg	5% ointment applied topically, 400 µg	–	–	–	In vivo—Excision and ligation wound model and Chromalobar membrane model	Act via an increase in collagen concentration and stabilization of fibers	Ebra et al. (2008)
41	Wound healing	<i>Alternanthera brassicae</i> (L.) Kuntze	Methanol extract of leaves	5% w/w ointment applied topically	5% w/w ointment applied topically	–	–	–	In vivo—Burn wound model	Act via formation of the epidermis with keratin layer and deposition of collagen fibers	Ebra et al. (2012a)
42	Wound healing	<i>Alternanthera brassicae</i> (L.) Kuntze	Methanol extract of leaves	2.5, 5.0 and 7.5% (w/w) ointment	2.5, 5.0 and 7.5% (w/w) ointment	–	–	–	In vivo—Immunocompromised wound model	Act via collagen deposition, fibroblast proliferation, angiogenesis and development of granulation membrane	Ebra et al. (2012b)
43	Wound healing	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Methanol extract of leaves	5% w/w ointment	5% w/w ointment	–	–	–	In vivo—Excision wound model	Act via stimulation of fibroblasts with keratin layer and deposition of collagen fibers	Ebra et al. (2012c)
44	Wound healing	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	90% hydroethanolic extract of stem	12.5–500 µg/ml	60 and 300 µg/ml	–	–	–	In vivo—Wound excision and RTT assay	Act via formation of the epidermis with keratin layer and deposition of collagen fibers	Makrooy et al. (2018)
45	Wound healing	<i>Alternanthera sessilis</i> (L.) HBK. ex DC.	Chitosan extract of leaves	200 µg/ml	200 µg/ml	–	–	–	In vivo—Excision wound, incision wound, and dead space wound model	Act via increase collagen content, degree of collagen cross-linkage within the wound and promote cell division, growth of bone, cartilage, and other connective tissues	Jalilov et al. (2009)



plant of *A. philoxeroides* (Mart.) Griseb. has been employed in the treatment of influenza (Hundiwale et al., 2012). The aqueous infusion of leaf and flower of *A. porrigens* (Jacq.) Kuntze has been recorded in old texts for the treatment of hepatic pain, kidney problems, and influenza. *A. pungens* Kunth has been employed as folk medicine in Argentina, commonly known as Yerba del pollo, recorded in the Pharmacopeia National Argentina (1978) for various medicinal purposes. It has been traditionally used in the treatment of swelling, nasopharyngeal infections, as a painkiller in labor pain, and also for lactation stimulus in veterinary-related cases (Burkill, 1985). It is also used in the treatment of gonorrhoea (Semenya and Potgieter, 2014),

menstrual disorder, miscarriage (Lucky and Diame, 2010) and to treat dysentery, cholera, and many parasitic diseases (Grønhaug et al., 2008; Guede et al., 2010). In Sudan, it is used in aqueous form for the treatment of cough. In Brazil, the aerial parts are used against gripe and vermifuge (Agra et al., 2007). It is used for crushing kidney stones or renal calculi in the form of decoction. The whole plant of *A. sessilis* (L.) R.Br. ex DC. has been used as green vegetable for maintain the nutrient balance in body (Astudillo-Vázquez et al., 2008). The roasted leaves and stems (*p.o.*) of *A. sessilis* (L.) R.Br. ex DC. have been in the treatment of stomach pain, ulcer, and gastric problems (Kumar S. M. et al., 2011). The aerial parts of *A. sessilis* (L.) R.Br. ex DC. have been used as a diuretic in the Ayurvedic system of



medicines (Hundiwal et al., 2012). The leaves of *A. sessilis* (L.) R.Br. ex DC. are used as a diuretic, antipyretic and antiseptic and roots are used as amenorrhea, inflammations, ovarian diseases, and female sterility. The young shoots of *A. sessilis* (L.) R.Br. ex DC. have been used as lactagogue and febrifuge (Hosamani et al., 2004). Keeping these in mind, the most common traditional uses for the *Alternanthera* species were recorded for the treatment and management of inflammation, pain, infectious diseases, and gastric problems.

Phytoconstituents Isolated and Identified in *Alternanthera* Species

GC-MS of n-hexane extract of *A. philoxeroides* (Mart.) Griseb. leaves showed the presence of 25 compounds. Among this Acetic acid, 2-(2-methoxycarbonylamino-5-nitrophenylthio)-, methyl

ester (31.92%); 1,4-Benzenediol, 2,5-bis(1,1-dimethylethyl) (15.06%); 4-Pyridinecarboxamide, 6-bromo-4,5-dicyano-1,2,3,4-tetrahydro-3,3-dimethyl-2-[[[(1-methylethylamino) oxy] (8.53%); L-Cysteine, N-(trifluoroacetyl)-, butyl ester, trifluoroacetate (ester) (6.59%); Cyclopentaneundecanoic acid, methyl ester (5.4%) and 3-Bromo-N-(2-thiazolyl) benzamide (3.49%) are dominant (Akbar et al., 2021). LC-MS/MS and GC-MS analysis of an ethanolic extract of *A. brasiliana* (L.) Kuntze aerial parts were performed (Alencar Filho et al., 2019). Five compounds (luteolin-8-C-rhamnosylglucoside, 2''-O-rhamnosylvitexin, 2''-O-rhamnosyl-6-C-glucosyl methyl-luteolin, rutin, and 2''-O-rhamnosylswertisin) were identified by LC-MS/MS whereas twenty-two compounds were identified by GC-MS but major proportions were n-hexadecanoic acid with 16.61% followed by linoleic acid, clonasterol, α -tocopherol, stigmast-7-en-3-ol, and α -amyrin. The GC-MS analysis of volatile oil obtained from leaves of *A. pungens* Kunth showed the presence of 12 compounds and the major compound was β -ionone (42.18%) (Ogunmoye et al., 2020). Other compounds identified were Hexahydrofarnesyl acetone (15.53%), Methyl palmitate (6.13%), 1-Octadecyne (4.72%), Undecane (3.73%), p-Metha-1,3,8-triene (3.65%), Isophytol (3.21%), δ -Cadinene (3.06%), 1,2-Dimethyl cyclooctene (3.05%), p-Cymene (2.96%), Phytol (2.67%) and Neophytadiene (2.50%).

The phytoconstituents—benzopyran, flavonoids, volatile oil, sterols, triterpenoid/saponins, phenolic compounds, ionone, anthraquinone, hydroxycinnamic acids, alkaloids, etc. have been scientifically reported from 9 species of *Alternanthera*. The chemical constituents (along with their structure) isolated from different species of the *Alternanthera* genus are shown in **Table 1**.

Referring to the data tabulated in **Table 1** covering the isolated phytoconstituents from 9 species of *Alternanthera* genus, we have prepared an interactive mapping (**Figure 2**) to give some quick insight about it to the readers. Notably, it has also been observed that some of the phytoconstituents like kaempferol, stigmastrol, quercetin, vitexin, ferulic acid, caffeic acid, etc. have been isolated from various species of *Alternanthera* genus. This somehow lead us to suggest that these phytoconstituents could serve as standardization of these markers could be helpful in identifying *Alternanthera* species, and avoid adulteration. Some of the compounds isolated from the species of *Alternanthera* genus are very common and usually been reported from multiple biological sources and well known for many pharmacological activities. For instance, kaempferol has been isolated from various other sources including *Euonymus alatus* (Thunb.) Siebold (Fang et al., 2008; Singla et al., 2021), *Vachellia nilotica* (L.) P.J.H.Hurter and Mabb.(Singh et al., 2008), etc. with multiple therapeutic potential, including but not limited to antiproliferative (Park et al., 2021), antiviral (Arabyan et al., 2021), hepatoprotective (Alshehri et al., 2021), antioxidant (Sharma et al., 2021), etc. Similarly, chlorogenic acid had been reported from multiple resources, including *Cocos nucifera* L. (Bankar et al., 2011), apple fruit (Hulme, 1953), *Neolamarckia cadamba* (Roxb.) Bosser (Kapil et al., 1995), etc with multiple therapeutic potential like neuroprotective (Hung et al., 2021),

TABLE 3 | Relationship between reported scientific pharmacological activities of *Alternanthera* species and their traditional claims.

Sr No	Species name	Traditional uses	Scientifically validated traditional claims	Traditional claims not validated scientifically	Other pharmacological activities
1	<i>Alternanthera bettzickiana</i> (Regel) G.Nicholson	—	—	—	Antibacterial, anticancer, antimicrobial, antioxidant
2	<i>Alternanthera brasiliana</i> (L.) Kuntze	In the treatment of headaches, cough, colds, grippe, fever, and diarrhea	Analgesic, antioxidant	Antidiarrhoeal, antipyretic	Allelopathic, antianxiety, antibacterial, anticancer, anticonvulsant, antifungal, anti-inflammatory, insecticide, sedative, and wound healing
3	<i>Alternanthera caracasana</i> Kunth	In the treatment of dysentery, diarrhea, and fever	—	Anti-dysentery, antidiarrhoeal, and antipyretic	—
4	<i>Alternanthera dentata</i> (Now reclaimed as <i>Alternanthera brasiliana</i> (L.) Kuntze)	In the treatment of inflammation, pain	—	Analgesic, anti-inflammatory	Antimicrobial, antioxidant
5	<i>Alternanthera ficoidea</i> (L.) P.Beauv	In the treatment of heart and cancer problems	Antioxidant	Anticancer, cardiogenic	—
6	<i>Alternanthera hirtula</i> (Mart.) R.E.Fr	—	—	—	Anticancer, antioxidant
7	<i>Alternanthera littoralis</i> P.Beauv	In the treatment of infectious and inflammatory diseases	Antioxidant	Anti-inflammatory	—
8	<i>Alternanthera maritima</i> (now reclaimed as <i>Alternanthera littoralis</i> P.Beauv.)	In the treatment of inflammation, viral infections, cancer, malaria, and diarrhea	Anti-inflammatory, antimicrobial	Antiviral, antidiarrhoeal, and anticancer	—
9	<i>Alternanthera nodiflora</i> R.Br	In the treatment of skin problems, degenerative and microbial infections	Antimicrobial	Skin protection	—
10	<i>Alternanthera paronychioides</i> A.St.-Hil	In the treatment of hyperuricemia, rheumatic arthritis, nephritis, gout, cystitis, diabetes, and systemic neuralgia	Antioxidant	Antihyperuricemia, antiarthritic, antigout, renal protective, antidiabetic, anti-inflammatory, and analgesic	Antiapoptotic
11	<i>Alternanthera philoxeroides</i> (Mart.) Griseb	In the treatment of influenza	Antioxidant, antiviral	—	α -glucosidase, inhibitory, analgesic, antianxiety, antiarthritic, anticancer, antidepressant, antidiabetic, anti-HBV, anti-inflammatory, antimicrobial
12	<i>Alternanthera porrigens</i> (Jacq.) Kuntze	In the treatment of hepatitis, kidney problems, influenza	—	Hepatoprotective, analgesic, antiviral, renal protective	—
13	<i>Alternanthera praelonga</i> A.St.-Hil	—	—	—	Anticancer, antioxidant
14	<i>Alternanthera pungens</i> Kunth	In the treatment of nasopharyngeal infections, pain, gonorrhoea, menstrual disorder, dysentery, cholera, and many parasitic diseases	Anti-inflammatory, antimicrobial, antioxidant	Analgesic, anti-dysentery	—
15	<i>Alternanthera repens</i> (now reclaimed as <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.)	—	—	—	Antibacterial, antidiarrhoeal, antispasmodic, gastrointestinal protective
16	<i>Alternanthera sessilis</i> (L.) R.Br. ex DC.)	In the treatment of stomach pain, ulcer, and gastric problems	Analgesic, antioxidant	Antiulcer, gastroprotective	α -glucosidase inhibitory, anthelmintic, anti-allergic, antiarthritic, antiasthmatic, antibacterial, anticancer, antidiabetic, antidepressant, antifungal, antihypertensive, anti-inflammatory, antimicrobial, anti-parkinsonism, hepatoprotective, nootropic, and wound healing
17	<i>Alternanthera tenella</i> (Now reclaimed as <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.)	In the treatment of urinary problems, fever, menstruation problem, inflammations, and ovarian diseases	Anti-inflammatory, antimicrobial, antioxidant	Renal protective, antipyretic	Immunomodulatory, inhibition of lymphocyte activation, and anticancer
18	<i>Alternanthera triandra</i> (Now reclaimed as <i>Alternanthera sessilis</i> (L.) R.Br. ex DC.)	In the treatment of fever, lactation problem	—	Antipyretic	—

Pharmacological Activities

Several scientific investigations were conducted to validate traditional claims of various species of *Alternanthera*. Uncharacterized/non-standardized crude extracts of various species of *Alternanthera* were used in most of these scientific pharmacological studies. *Alternanthera* species have been observed to display analgesic, anticancer, anti-inflammatory, antimicrobial, antioxidant, hepatoprotective, hypotensive, allelopathic, α -glucosidase inhibitory, anthelmintic, anti-allergic, anti-anxiety, sedative, antiapoptotic, antiarthritic, antiasthmatic, anticataract, anticonvulsant, antidepressant, antidiabetic, anti-diarrhoeal, antifungal, antibacterial, anti-HBV, antiparkinsonian, antiprotozoal, antispasmodic, antiviral, gastrointestinal protective, immunomodulatory and wound healing activities. The plant species, extract/fraction/isolate, dose tested/route of administration, bioactive dose, positive control, negative control, *In vivo/in vitro* models, and mechanism of action have been summarized in **Table 2**.

Referring to the data tabulated in **Table 2**, and interactive **Figure 3**, it is quite evident that the *Alternanthera* genus is having tremendous potential having polypharmacological effects. 35 different types of pharmacological effects were elicited by different species of *Alternanthera* genus. While the species like *Alternanthera sessilis* (L.) R.Br. ex DC., *Alternanthera brasiliana* (L.) Kuntze, and *Alternanthera philoxeroides* (Mart.) Griseb. were most widely explored, it opens up the opportunity for the researchers to explore other species of this genus.

Analgesic Activity

Pelisoli Formagio and the team had evaluated the aqueous extract from the aerial parts of *Alternanthera brasiliana* (L.) Kuntze for its analgesic potential. 90.35% reduction of acetic acid induced contractions were observed in mice, when treated with 25 mg/kg of the aqueous extract (Pelisoli Formagio et al., 2012). Coutinho and the team had performed the formalin test in mice for assessment of analgesic effect of ethanolic extract from the leaves of *Alternanthera brasiliana* (L.) Kuntze. At 100 mg/kg, ethanolic extract was capable of reducing the edematogenic process by 64.17% (Coutinho et al., 2017). Phytoconstituents like kaempferol (Parveen et al., 2007), quercetin (Anjaneyulu and Chopra, 2003), vitexin (Zhu et al., 2016), etc may be responsible for the analgesic potential of *Alternanthera brasiliana* (L.) Kuntze.

de Santana Aquino and the team had evaluated ethanolic extract as well as isolated compound, 2''-O- α -L-rhamnopyranosylvitexin from the aerial parts of *Alternanthera littoralis* P.Beauv. for analgesic potential. Results suggested that the ethanolic extract as well as 2''-O- α -L-rhamnopyranosylvitexin are capable of exerting significant analgesic effect, most probably through the TNF pathway (de Santana Aquino et al., 2015). Since kaempferol, quercetin, and vitexin were also been reported from *Alternanthera littoralis* P.Beauv. (**Figure 2**), so these compounds could also attribute in analgesic potential of the extract.

Khatun and the team had prepared the methanolic extract from the whole plant part of *Alternanthera philoxeroides* (Mart.) Griseb. and evaluated for its analgesic potential in

the acetic acid induced mice. They found that 400 mg/kg dose of methanolic extract was capable of reducing constrictions by 44.8%. Phytoconstituents like kaempferol (Parveen et al., 2007), quercetin (Anjaneyulu and Chopra, 2003), vitexin (Zhu et al., 2016), caffeic acid (Gamaro et al., 2011), ursolic acid (Vasconcelos et al., 2006), etc may be responsible for the analgesic potential of *Alternanthera philoxeroides* (Mart.) Griseb.

Various research teams have independently assessed the analgesic potential of *Alternanthera sessilis* (L.) R.Br. ex DC.: Mondal and the team used ethanolic extract of the leaves (Mondal et al., 2014); Mohapatra and the team used hydroethanolic extract of leaves (Mohapatra et al., 2018); Hossain and the team used methanolic extract of aerial parts (Hossain et al., 2014); while Mohaimenul and the team used ethanolic extract of aerial parts (Mohaimenul et al., 2020). It is thus quite validated that aerial parts especially leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. have the analgesic potential. Various mechanisms observed by those researchers for this activity. Some of them are like inhibition of interleukins like IL-4, IL-5, and IL-13, dopaminergic and serotonergic pathways, inhibition of lipoxygenase and cyclooxygenase, etc. Along with kaempferol, vitexin, and quercetin, compounds like stigmaterol (Walker et al., 2017) may also be responsible for such analgesic effect.

Anthelmintic Activity

Vennila and Nivetha had prepared various extracts from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. and performed *In vitro*—*Pheretima Posthuma* method for assessment of anthelmintic activity. They observed that methanolic extract was the most potent and active at all the tested concentrations. The possible mechanism proposed by them was membrane lysis which subsequently led to paralysis or death of the worm (Vennila and Nivetha, 2015). On the other hand, Mondal and the team had assessed anthelmintic activity of ethanolic extract of the whole plant as well as the isolated ellagic acid by using *In vitro*—Adult motility test. They had also indicated the disruption of cell permeability, along with various other pathways and found ellagic acid a key responsible compound (Mondal et al., 2015). Other compounds that may be responsible for this pharmacological effects could be quercetin (Borges et al., 2020), β -sitosterol (Deepak et al., 2002), etc.

Antiallergic Activity

Rayees and the team checked the antiallergic activity of 95% ethanolic extract from aerial parts of *Alternanthera sessilis* (L.) R.Br. ex DC. Studies were conducted in rat basophilic leukemia (RBL-2H3) cells. They found that the treatment with ethanolic extract resulted in nuclear factor-KB (NF- κ B) dependent inhibition of cytokines like IL-6, TNF- α , IL-13, and IL-4, along with the decrease in β -hexosaminidase release (Rayees et al., 2013). Compounds like β -sitosterol (Yuk et al., 2007; Mahajan and Mehta, 2011), kaempferol (Oh et al., 2013), quercetin (Mlcek et al., 2016), vitexin (Venturini et al., 2018), stigmaterol (Antwi et al., 2018), etc may be responsible for the antiallergic activity of *Alternanthera sessilis* (L.) R.Br. ex DC.

Antianxiety Property

Various research teams have independently assessed the antianxiety potential of *Alternanthera brasiliana* (L.) Kuntze: Pelisoli Formagio had used the aqueous extract of the leaves (Pelisoli Formagio et al., 2012); Oyemitan and the team had used the ethanolic extract of the leaves (Oyemitan et al., 2015); while Barua and the team had used the methanolic extract of the leaves (Barua et al., 2013). It is thus quite validated that the leaves of *Alternanthera brasiliana* (L.) Kuntze have the antianxiety potential. Various mechanisms observed by those researchers for this activity. Some of them are like activation of GABA receptor and 5-HT partial agonistic action. Phytomolecules like stigmaterol (Karim et al., 2021), kaempferol (Kaur et al., 2017), quercetin (Singh et al., 2013), p-coumaric acid (He Y. et al., 2021), etc may be responsible for this antianxiety property of *Alternanthera brasiliana* (L.) Kuntze.

Khamphukdee and the team had assessed ethanolic extract from the leaves of *Alternanthera philoxeroides* (Mart.) Griseb. for antianxiety potential by performing *In vivo*—Elevated plus-maze test, Light/Dark transition test, and Locomotor activity test in female mice. They observed that both the test doses i.e. 250 and 500 mg/kg/day of the extract was able to reduce the anxiety, most probably through the esterogenic pathway. Quercetin and kaempferol were detected in this plant also, so may be responsible for such antianxiety behavior.

Antiapoptotic Activity

Wu and the team had studied the antiapoptotic potential of ethanolic extract from the whole plant of *Alternanthera bettzickiana* (Regel) G.Nicholson. They found that ethanolic extract has strong tendency to reduce apoptosis which was modulated via multiple mechanisms including reduction of reactive oxygen species, inhibition of caspase-3 and caspase-9 activation, etc. They had reported quercetin as the major compound in that extract, and they found same mechanisms when evaluated quercetin for antiapoptotic potential.

Antiarthritic Activity

Manan and the team had studied antiarthritic potential of the ethanolic extract obtained from the aerial parts of *Alternanthera bettzickiana* (Regel) G.Nicholson using *in silico*, *in vitro* and *in vivo* methodologies. HPLC analysis indicated the presence of catechin, gallic acid, sinapic acid, chlorogenic acid, alpha-tocopherol, gamma-tocopherol, and quercetin. They have found that even the 250 mg/kg/day of the ethanolic extract was able to modulate the parameters suggesting the antiarthritic potential when compared with standard drug and disease control. *In silico* analysis suggested the strong interaction between the HPLC-analysed phytomolecules and cyclooxygenases (Manan et al., 2020).

Sunmathi and the team had studied the antiarthritic activity of ethanolic extracts obtained from the leaves of *Alternanthera philoxeroides* (Mart.) Griseb. and *Alternanthera sessilis* (L.) R.Br. ex DC. using *in vitro* methodologies. They found that 500 µg/ml of ethanolic extract of *Alternanthera philoxeroides* (Mart.) Griseb. and *Alternanthera sessilis* (L.) R.Br. ex DC. were able to stabilize the membrane by 64.92 and 75.43%,

respectively. Phytomolecules like vitexin (Yang et al., 2019) and quercetin (Mamani-Matsuda et al., 2006) may be responsible for the antiarthritic activity of *Alternanthera philoxeroides* (Mart.) Griseb. and *Alternanthera sessilis* (L.) R.Br. ex DC.

Antiasthmatic Activity

Various research teams have independently assessed the antiasthmatic potential of *Alternanthera sessilis* (L.) R.Br. ex DC.: Fathima and the team had used ethanolic extract of leaves (Fathima et al., 2016) while Saqib and Janbaz had used 70% Ethanolic extract of the whole plant and its dichloromethane and aqueous fractions (Saqib and Janbaz, 2016). This validates the applicability of *Alternanthera sessilis* (L.) R.Br. ex DC. in the treatment management of asthma. Ethanolic extract obtained from the leaves was found to reduce the leucocyte count and significantly inhibited the histamine release (Fathima et al., 2016). 70% ethanolic extract of the whole plant was found to act via calcium channel blocking mechanism (Saqib and Janbaz, 2016). Phytomolecules like kaempferol (Gong et al., 2012), vitexin (Venturini et al., 2018), quercetin (Fortunato et al., 2012), stigmaterol (Antwi et al., 2017a), chlorogenic acid (Kim et al., 2010), etc. may be key components for the antiasthmatic activity of *Alternanthera sessilis* (L.) R.Br. ex DC.

Anticancer/Cytotoxic Property

Various research teams have independently assessed the anticancer property of *Alternanthera bettzickiana* (Regel) G.Nicholson: M Nagalingam and the team had used aqueous extract of the leaves (Nagalingam et al., 2018) while R Jothi Ramalingam and the team had used aqueous extract of leaves and silver nanoparticles and Ag-mesoporous MnO₂ nanocomposite (Jothi Ramalingam et al., 2017). This validates the potential of leaves from *Alternanthera bettzickiana* (Regel) G.Nicholson and their nanoparticles in colon cancer and lung cancer. Apigenin analogues present in the *Alternanthera bettzickiana* (Regel) G.Nicholson may be responsible for the anticancer property (Madunić et al., 2018; Imran et al., 2020).

Similarly, various research teams have independently assessed the anticancer property of *Alternanthera brasiliana* (L.) Kuntze: Brochado and the team had used aqueous fraction of the ethanolic extract from the leaves. They had also isolated 6 bioactive compounds from this fraction viz. robinin, clovin, quercetin 3-O-robinobioside, kaempferol 3-O-robinobioside, kaempferol 3-O-rutinoside-7-O-a-L-rhamnopyranoside, and kaempferol 3-O-rutinoside (Brochado et al., 2003); Samudrala and the team had used ethyl acetate extract obtained from the leaves (Samudrala et al., 2015). These pieces of evidence validates the anticancer potential of *Alternanthera brasiliana* (L.) Kuntze leaves. Brochado and the team found Kaempferol 3-O-robinobioside and kaempferol 3-O-rutinoside as the active phytomolecules (Brochado et al., 2003).

Independently several researches had also been conducted from various labs to assess the potential of *Alternanthera philoxeroides* (Mart.) Griseb. as anticancer agent: Zhang and the team had used the methanolic extract of the leaves and checked cytotoxicity against H9c2 cell lines. They found that

even at 20 mg/ml, the methanolic extract was able to inhibit the doxorubicin induced cardiomyocyte apoptosis by more than 50%. They had also observed the presence of -carboline and quercetin (Zhang et al., 2018). Fang and the team had isolated 5 phytomolecules from the aerial parts of *Alternanthera philoxeroides* (Mart.) Griseb., and checked their inhibitory activity against Hela and L929 cell lines. While N-trans-feruloyl-3,5-dimethoxytyramine, alternanthin, N-trans-feruloyl-3-methyl-dopamine, and N-trans-feruloyl tyramine were found to have more than 50% inhibition at 30 µg/ml against Hela cell line, only Alternanthin B, and alternanthin were having more than 50% inhibition at 30 µg/ml against L929 cell line (Fang et al., 2007). Fang and the team had further isolated 4 more compounds from the aerial parts of *Alternanthera philoxeroides* (Mart.) Griseb. The triterpenoidal saponins, Philoxeroidesides A, B, C, and D were found to inhibit SK-N-SH cell line with an IC50 of 51, 118.69, 60.6, and 37.29 µg/ml, respectively, while inhibited HL60 cell line with an IC50 of 185.29, 185.57, 271.45, and 45.93 µg/ml, respectively. Philoxeroidesides D was found to be quite potential against both the cell lines (Fang J.-B. et al., 2009). In another study performed by Correa and the team where they had used ethanolic extracts obtained from the whole plant of *Alternanthera philoxeroides* (Mart.) Griseb.; *Alternanthera hirtula* (Mart.) R.E.Fr., and *Alternanthera praelonga* A.St.-Hil. They tested the ethanolic extracts against various human cancer cells lines including that from melanoma, breast, kidney, lung, prostate, ovary, colon, leukemia, along with non-cancer cell line from green monkey kidney. Out of all the cancer cell lines, these ethanolic extracts were being able to be found potent only against the leukemia cell line, K562 (Correa et al., 2016).

Several researchers have independently assessed the potential of *Alternanthera sessilis* (L.) R.Br. ex DC. for the management of cancer: Jain and the team had used the methanolic extract of leaves (Jain et al., 2016); Firdhouse and Lalitha had used silver nanoparticles of the aqueous extract (Firdhouse and Lalitha, 2013); Qian and the team had used gold nanoparticles of the aqueous extract of leaves (Qian et al., 2019); D Suganya and the team had used aqueous extract of leaves and stems (Suganya et al., 2019); Pathak and the team had used n-hexane and methanolic extracts of aerial parts (Pathak et al., 2020); Mohaimenul and the team had used ethanolic extract of aerial parts (Mohaimenul et al., 2020); Yap and the team had used ethanolic, 70% ethanolic, 80% methanolic, ethyl acetate, and aqueous extracts of the whole plant (Yap et al., 2019); Sathishkumar and the team had used silver nanoparticles of the aqueous extract of leaves (Sathishkumar et al., 2016); Arulselvan and the team had used ethanolic extract of aerial parts, stem, and leaves (Arulselvan et al., 2018); while Guerra and the team aqueous extract of aerial parts (Guerra et al., 2003). All these studies indicated the true potential of *Alternanthera sessilis* (L.) R.Br. ex DC. for the treatment and management of cancer, with leaving no doubt in it. Phytomolecules present in the *Alternanthera sessilis* (L.) R.Br. ex DC. like kaempferol (Imran et al., 2019), vitexin (Liu et al., 2019; Lee et al., 2020), quercetin (Rauf et al., 2018), stigmasterol (Ali et al., 2015), chlorogenic acid (Barahuie et al., 2017), campesterol (Bae et al., 2021), and β-sitosterol

(Pradhan et al., 2016), etc. may be responsible for this anticancer property.

Anticataract Property

Kota and the team had checked the anticataract property of ethyl acetate extract obtained from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. Cataract induced in eye lenses of the chicks were subjected for the treatment with 100, 200, and 400 mg of ethyl acetate extract, followed by analysis of lipid peroxidation and Na⁺ - K⁺ ATPases. They found that 100 and 200 mg ethyl acetate treatment will lead to decrease in malondialdehyde and increase in the inorganic phosphorous content (Kota et al., 2017). Phytomolecules like quercetin (Lan et al., 2020), chlorogenic acid (Kim et al., 2011), and β-sitosterol (Haroon et al., 2020) may be responsible for this anticataract property of *Alternanthera sessilis* (L.) R.Br. ex DC.

Anticonvulsant Activity

Independently several researches had also been conducted from various labs to assess the potential of *Alternanthera brasiliiana* (L.) Kuntze as anticonvulsant agent: Oyemitan and the team had used the ethanolic extract of leaves (Oyemitan et al., 2015); Schallenberger and the team had also used the ethanolic extract of leaves (Schallenberger et al., 2017); while Barua and the team had used the methanolic extract of leaves (Barua et al., 2013). This had validated the anticonvulsant potential of the leaves of *Alternanthera brasiliiana* (L.) Kuntze. Various mechanisms elucidated by them are like modulation of GABAergic system, controlling the entry of calcium and sodium ions in the cells, and glycine regulation in spinal cord (Oyemitan et al., 2015). Phytomolecules like vitexin (de Oliveira et al., 2020), quercetin (Nassiri-Asl et al., 2014; Nieoczym et al., 2014), stigmasterol (Karim et al., 2021), chlorogenic acid (Aseervatham et al., 2016), and ferulic acid (Hassanzadeh et al., 2017) may be responsible for the antiepileptic effect of *Alternanthera brasiliiana* (L.) Kuntze.

Antidepressant Activity

Khamphukdee and the team had assessed the antidepressant effect of the ethanolic extract obtained from the leaves of *Alternanthera philoxeroides* (Mart.) Griseb. They found that the extract was having significant antidepressant effect modulated through the estrogenic pathway (Khamphukdee et al., 2018). Phytomolecules like quercetin (Anjaneyulu and Chopra, 2003), vitexin (Can et al., 2013), β-sitosterol (Zhao et al., 2016), p-coumaric acid (Lee et al., 2018), caffeic acid (Monteiro et al., 2020), ursolic acid (Machado et al., 2012; Singla et al., 2017), and malic acid (Gómez-Moreno et al., 2013) may be responsible for the antidepressant activity of *Alternanthera philoxeroides* (Mart.) Griseb.

Gupta and K. Singh had evaluated the antidepressant activity of methanolic extract obtained from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. They had observed that the antidepressant effect of the methanolic extract was acting via interaction with adrenergic, dopaminergic serotonergic, and GABAergic system (Gupta and Singh, 2014). Phytomolecules like quercetin, vitexin, and p-coumaric acid had also been reported from *Alternanthera*

sessilis (L.) R.Br. ex DC., along with other antidepressant agents like kaempferol (Park et al., 2010b), ferulic acid (Chen et al., 2014) and chlorogenic acid (Park et al., 2010a). These phytochemicals may be responsible for the antidepressant activity of *Alternanthera sessilis* (L.) R.Br. ex DC.

Antidiabetic Activity

Reza and the team had assessed the antidiabetic potential of 80% ethanolic extracts obtained from the stem and leaves of *Alternanthera brasiliensis* (L.) Kuntze. They found that the ethanolic extracts were being able to significantly modulate the biochemical parameters like blood glucose, lipid peroxidation, and free radicals in the alloxan-induced diabetic Swiss albino mice (Reza et al., 2019). Phytochemicals like kaempferol (Ibitoye et al., 2018), quercetin (Vessal et al., 2003), stigmaterol (Wang et al., 2017; Singla and Shen, 2020), p-coumaric acid (Amalan et al., 2016), ferulic acid (Narasimhan et al., 2015), and chlorogenic acid (Ong et al., 2013) may be responsible for the antidiabetic potential of *Alternanthera brasiliensis* (L.) Kuntze.

Khatun and the team as well as Bhattacharjee and the team had independently assessed the antidiabetic activity of *Alternanthera philoxeroides* (Mart.) Griseb. Various important mechanisms had been observed by them including regeneration of the β -cells of the pancreas, α -glucosidase inhibition, as well as the inhibition of the glucose absorption from the gut wall (Khatun et al., 2012; Bhattacharjee et al., 2014). Compounds like quercetin and p-coumaric acid had been reported from *Alternanthera philoxeroides* (Mart.) Griseb., and may be responsible for such antidiabetic effect.

Mourya and the team had used aqueous and ethanolic extracts obtained from the whole plant of *Alternanthera pungens* Kunth for the assessment of antidiabetic potential. Dose dependent antidiabetic activity was observed by them when studied in alloxan-induced diabetic Wistar rats. Phytochemicals like camphene (Hachlafi et al., 2021), camphor (Drikvandi et al., 2020), geraniol (Babukumar et al., 2017), and limonene (Murali and Saravanan, 2012) may be responsible for such antidiabetic property of *Alternanthera pungens* Kunth.

Independently several researches had also been conducted from various labs to assess the potential of *Alternanthera sessilis* (L.) R.Br. ex DC. as antidiabetic agent: Kumar and the team had used aqueous and ethanolic extracts of aerial parts (Kumar S. M. et al., 2011); Tan and Kim had used hexane, ethyl acetate, and aqueous fractions of aerial parts (Tan and Kim, 2013); Hossain and the team had used methanolic extract of aerial parts (Hossain et al., 2014); Sundar and the team had used petroleum ether extract of leaves (Sundar et al., 2019); Das and the team had used 95% ethanolic extract of the whole plant (Das et al., 2015); Rao and the team had used ethanolic extract of the whole plant (Rao et al., 2011); Manalo and the team had used n-hexane, ethyl acetate, and water fractions of the methanolic extract of leaves (Manalo et al., 2020); Mohaimenul and the team had used ethanolic extract of

aerial parts (Mohaimenul et al., 2020); Tiwari and the team had used the juice (Tiwari et al., 2013); Chai and the team had used hexane, chloroform, ethyl acetate, butanol, and aqueous fractions of methanolic extracts of leaves and callus (Chai et al., 2016). Plenty of evidences obtained from the above researches leaved no doubt in that fact that *Alternanthera sessilis* (L.) R.Br. ex DC. possesses antidiabetic properties. Various mechanisms demonstrated by different preparations from *Alternanthera sessilis* (L.) R.Br. ex DC., including but not limited to modulation of insulin sensitivity, improvement in pancreatic insulin secretion, reduction in blood glucose level, inhibition of α -glucosidase enzyme, etc. Phytochemicals like kaempferol (Ibitoye et al., 2018), quercetin (Vessal et al., 2003), stigmaterol (Wang et al., 2017; Singla and Shen, 2020), 4-hydroxybenzoic acid (Peungvicha et al., 1998), β -sitosterol (Ponnulakshmi et al., 2019), ellagic acid (Fatima et al., 2015), ferulic acid (Narasimhan et al., 2015), and chlorogenic acid (Ong et al., 2013) may be responsible for the antidiabetic potential of *Alternanthera sessilis* (L.) R.Br. ex DC.

Antidiarrheal Activity

Zavala and the team had evaluated the antidiarrheal property of hexane, chloroform, methanolic, and aqueous extracts obtained from the whole plant of *Alternanthera sessilis* (L.) R.Br. ex DC. They had observed that out of all extracts, methanolic and aqueous extracts had shown significant inhibition of castor oil-induced diarrhea. Methanolic extract was further found to inhibit normal defecation in mice also. Peristaltic movement was also modulated by the methanolic extract (Zavala et al., 1998). Phytochemicals like quercetin (Lozoya et al., 1994; Song et al., 2011; Shi et al., 2020), β -sitosterol (Ding et al., 2018), ellagic acid (Chen et al., 2020), ferulic acid (Hu et al., 2021), and chlorogenic acid (Zhang et al., 2017; Chen et al., 2018) may be responsible for the antidiarrheal property of *Alternanthera sessilis* (L.) R.Br. ex DC.

Antigout Activity

Chong and Loh had assessed the antigout potential of methanolic extract obtained from the aerial parts of *Alternanthera sessilis* (L.) R.Br. ex DC. Methanolic extract was able to inhibit xanthine oxidase enzyme with an IC₅₀ of 557.77 μ g/ml (Chong and Loh, 2020). Phytochemicals like kaempferol (Wang et al., 2015d), quercetin (Bindoli et al., 1985), stigmaterol (Chiang and Chen, 2008), ellagic acid (Sun et al., 2021), ferulic acid (Nile et al., 2016), and chlorogenic acid (Wang et al., 2009) may be responsible for the antigout potential of *Alternanthera sessilis* (L.) R.Br. ex DC.

Anti-Hepatitis B Virus Activity

Li and the team had isolated C-boivinopyranosyl flavones from *Alternanthera philoxeroides* (Mart.) Griseb. and found that luteolin-6-C- β -d-boivinopyranosyl-3'-O- β -d-glucopyranoside, chrysoeriol-6-C- β -d-boivinopyranosyl-4'-O- β -d-glucopyranoside, and luteolin-6-C- β -d-boivinopyranosyl-4'-O- β -d-glucopyranoside were strongly inhibiting the viral antigen, HBsAg in HBV-infected

HepG2.2.15 with an IC₅₀ of 28.65, 22.20, and 31.54 μ M, respectively (Li et al., 2016).

Antihypertensive Activity

Saqib and Janbaz had evaluated the antihypertensive effect of 70% Ethanol extract of the whole plant and its dichloromethane and aqueous fractions from *Alternanthera sessilis* (L.) R.Br. ex DC. The *in vivo* studies suggested that the ethanolic extract was capable to reducing both the systolic and the diastolic pressure. Phytomolecules like kaempferol (Ahmad et al., 1993; Binang and Takuwa, 2021), quercetin (Perez-Vizcaino et al., 2009; Binang and Takuwa, 2021), vitexin (Xue et al., 2020), β -sitosterol (Olaiya et al., 2014), ellagic acid (Berkban et al., 2015), ferulic acid (Li et al., 2020), and chlorogenic acid (Zhao et al., 2011) may be responsible for the antihypertensive potential of *Alternanthera sessilis* (L.) R.Br. ex DC.

Anti-Inflammatory Activity

Pelisoli Formagio and the team had performed the *in vivo* studies to assess the anti-inflammatory activity of the aqueous extract obtained from the leaves of *Alternanthera brasiliensis* (L.) Kuntze while P Shivashankar and the team had used the methanolic extract obtained from the leaves. Pelisoli Formagio and the team had observed the significant decrease in the polymorphonuclear cells as well as increase in the mononuclear cells in rat's exudate after treated with the aqueous extract, while P Shivashankar and the team found the reduction in the colon weight in acetic acid-induced colitis model of adult Wistar albino rats after treatment with the methanolic extract (Pelisoli Formagio et al., 2012; P et al., 2016). Phytomolecules like kaempferol (Devi et al., 2015), quercetin (Lesjak et al., 2018), stigmasterol (Morgan et al., 2021), p-coumaric acid (Pragasam et al., 2012), ferulic acid (Ozaki, 1992), and chlorogenic acid (Hwang et al., 2013) may be responsible for the anti-inflammatory potential of *Alternanthera brasiliensis* (L.) Kuntze.

de Santana Aquino and the team had evaluated anti-inflammatory activity of ethanolic extract of aerial parts and the isolated compound, 2''-O- α -L-rhamnopyranosylvitexin from *Alternanthera littoralis* P.Beauv. They found that the ethanolic extract was able to reduce the paw edema as well as capable to reducing leukocyte migration. In addition to these, the isolated compound was also able to reduce protein leakage into the pleural cavity (de Santana Aquino et al., 2015). Other phytomolecules that could be responsible for the anti-inflammatory activity of the ethanolic extract will be kaempferol, quercetin, stigmasterol, etc.

Sunmathi and the team had evaluated anti-inflammatory activity of ethanolic extract obtained from the leaves of *Alternanthera philoxeroides* (Mart.) Griseb. Dose dependent membrane stabilization was observed. Phytomolecules like quercetin (Lesjak et al., 2018), vitexin (Rosa et al., 2016), β -sitosterol (Loizou et al., 2010), p-coumaric acid (Pragasam et al., 2012), caffeic acid (da Cunha et al., 2009), ursolic acid (Baricevic et al., 2001), and malic acid (Obertreis et al., 1996) may be responsible for the anti-inflammatory activity of *Alternanthera philoxeroides* (Mart.) Griseb.

Franck and the team had evaluated the anti-inflammatory activity of aqueous extract obtained from the leaves of

Alternanthera pungens Kunth. They had observed the decreased level of histamine release, serotonin and kinin, prostaglandin, proteases, lysosomes, and protein C-reactive. Phytomolecules like α -pinene (Kim et al., 2015), myrcene (Rufino et al., 2015), limonene (Rufino et al., 2015), choline (Rowley et al., 2010), rhein (Gao et al., 2014), linalool (Peana et al., 2002), geraniol (Ye et al., 2019), and camphor (Ehrnhöfer-Ressler et al., 2013) which were reported earlier in *Alternanthera pungens* Kunth., may be responsible for this anti-inflammatory effect.

Independently several researches had also been conducted from various labs to assess the potential of *Alternanthera sessilis* (L.) R.Br. ex DC. as anti-inflammatory agent: Sunmathi and the team had used ethanolic extract obtained from the leaves (Sunmathi et al., 2016); Muniandy and the team had used 90% ethanolic extract of stems (Muniandy et al., 2018a); Sundar and the team had used petroleum ether and methanolic extracts of leaves (Sundar et al., 2019); Kassuya and the team had used Ethanolic extract of whole plant (EEAT) as well as the isolated molecule, 2''-O- β -D-glucopyranosyl-vitexin (Kassuya et al., 2021); Biella and the team had used aqueous extract of the whole plant (Biella et al., 2008). Plenty of evidences obtained from the above researches leaved no doubt in that fact that *Alternanthera sessilis* (L.) R.Br. ex DC. possesses anti-inflammatory properties. Various mechanisms demonstrated by different preparations from *Alternanthera sessilis* (L.) R.Br. ex DC., including but not limited to cyclooxygenase -1 and -2 inhibition (Biella et al., 2008), modulating NF- κ B pathway (Muniandy et al., 2018a), leukocyte migration (Kassuya et al., 2021), etc. Phytomolecules like kaempferol (Devi et al., 2015; Pizzo et al., 2018), quercetin (Lesjak et al., 2018), vitexin (Rosa et al., 2016), stigmasterol (Morgan et al., 2021), β -sitosterol (Loizou et al., 2010), 4-hydroxybenzoic acid (Winter et al., 2017), ellagic acid (Corbett et al., 2010), ferulic acid (Ozaki, 1992), campesterol (Moreno-Anzúrez et al., 2017), spinasterol (Jeong et al., 2010), β -carotene (Uteshev et al., 2000), p-coumaric acid (Pragasam et al., 2012), ricinoleic acid (Vieira et al., 2001), and chlorogenic acid (Hwang et al., 2013) may be responsible for the anti-inflammatory potential of *Alternanthera sessilis* (L.) R.Br. ex DC.

Antimicrobial Activity

Independently, several research teams had evaluated the antimicrobial effects of the leaves of *Alternanthera bettzickiana* (Regel) G.Nicholson: Vidhya and the team had used hexane, chloroform, ethyl acetate, methanolic, and aqueous extracts of leaves (Vidhya et al., 2015); R, Jothi Ramalingam and the team had used aqueous extract of leaves and silver nanoparticles and Ag-mesoporous MnO₂ nanocomposite (Jothi Ramalingam et al., 2017); Nagalingam and the team had used the aqueous extract obtained from leaves (Au-NP) (Nagalingam et al., 2018). These research were focused on leaves and somehow validated the antimicrobial property of it. Various mechanisms elucidated were like cell wall lysis, protein synthesis inhibition, and topoisomerase inhibition, etc (Vidhya et al., 2015; Jothi Ramalingam et al., 2017; Nagalingam et al., 2018). Phytocompounds like apigenin analogs (Koo, 2003;

Thirukumaran et al., 2019) may be responsible for this antimicrobial property of *Alternanthera bettzickiana* (Regel) G.Nicholson.

Coutinho and the team had evaluated the antimicrobial property of ethanolic extract obtained from the leaves of *Alternanthera brasiliana* (L.) Kuntze. They had observed that though the ethanolic extract as such was having insignificant potential, but it elicited significant synergetic potential when combined with gentamycin and tested against *Staphylococcus aureus*, *Escherichia coli*, and *Pseudomonas aeruginosa* (Coutinho et al., 2017). Johann and the team had also performed the antimicrobial experiments on the ethanolic extract obtained from the aerial parts of *Alternanthera brasiliana* (L.) Kuntze, and they had also observed that the extract was inactive against various murine macrophages and fungal strains (Johann et al., 2010). Other research team like that of Akachukwu and Uchegbu had also reported mild activity of the ethanolic extract obtained from its leaves (Akachukwu and Uchegbu, 2016) while Kumar and the team noticed significant activity elicited by the silver nanoparticles obtained from the leaves aqueous extract (Kumar et al., 2014).

Canales-Martínez and the team had evaluated the antimicrobial effect of the hexane, chloroform, methanolic, acetone, and ethyl acetate extracts obtained from the aerial parts of *Alternanthera caracasana* Kunth and also isolated a bioactive compound, 7-methoxycoumarin. They observed that the ethyl acetate extract as well as 7-methoxycoumarin were active against various Gram-positive and Gram-negative bacterial strains, but inactive against *Candida albicans* (Canales-Martínez et al., 2008). Phytochemical profiling of *Alternanthera caracasana* Kunth is still not done, leaving a scope for the researchers.

Gasparetto and the team had used crude hexane and ethanolic extract obtained from the leaves of *Alternanthera littoralis* P.Beauv., and assessed them for their antimicrobial potential. They noticed that the antifungal activity was exhibited by the crude extracts only when combined with photo-irradiation by a diode laser (Gasparetto et al., 2010). Phytochemicals like kaempferol (del Valle et al., 2016), stigmastanol (Alawode et al., 2021), hydroxytyrosol (Bisignano et al., 1999), quercetin (Gatto et al., 2002), vitexin (Das et al., 2016), and uridine (Wiegmann et al., 2016) which were reported earlier from *Alternanthera littoralis* P.Beauv., may be responsible for such antimicrobial effects.

Feka and the team had studied the antimicrobial property of the aqueous and methanolic extracts obtained from the whole plant of *Alternanthera nodiflora* R.Br. They found that the methanolic extract was having significant antimicrobial activity against bacterial and yeast strains, but inactive against mould test strain (Feka et al., 2014). Phytochemical profiling of *Alternanthera nodiflora* R.Br. is still not done, leaving a scope for the researchers.

Independently several research teams had evaluated the antimicrobial potential of *Alternanthera philoxeroides* (Mart.) Griseb.: Bhattacharjee and the team had used methanol-soluble fraction obtained from the leaves (Bhattacharjee et al., 2014); Rawani and the team had used aqueous and chloroform:

methanol (1:1) extracts of leaves (Rawani et al., 2011); Pulipati and the team had used ethanolic extract obtained from the leaves (Pulipati et al., 2016); Akbar and the team had used methanolic extract of leaves, stem and roots as well as their n-hexane, chloroform and ethyl acetate fractions (Akbar et al., 2021); while Pulipati and Babu had used the methanolic extract of leaves (Pulipati and Babu, 2020). These independent researches left no doubt and validated the antimicrobial feature of *Alternanthera philoxeroides* (Mart.) Griseb. They had reported multiple mechanisms of actions like bacterial cell wall lysis and protein synthesis inhibition (Bhattacharjee et al., 2014; Pulipati et al., 2016; Pulipati and Babu, 2020). Phytochemicals like quercetin (Gatto et al., 2002), vitexin (Das et al., 2016), β -sitosterol (Ododo et al., 2016), stigmastanol (Alawode et al., 2021), p-coumaric acid (Boz, 2015), caffeic acid (Lima et al., 2016), luteolin analogs (Chiruvella et al., 2007; Qian et al., 2020), chrysoeriol analogs (Jang et al., 2020), malic acid (Raybaudi-Massilia et al., 2009), β -carboline (Arshad et al., 2008; Suzuki et al., 2018), ursolic acid (Collins and Charles, 1987), oleanolic acid (Horiuchi et al., 2007), azelaic acid (Leeming et al., 1986), phytol (Pejin et al., 2014), and rubiadin (Marioni et al., 2016) which were earlier reported from *Alternanthera philoxeroides* (Mart.) Griseb., may be responsible for this antimicrobial property.

Jakhar and Dahiya had studied the aqueous, acetone, ethanolic, and petroleum ether extracts obtained from the aerial parts of *Alternanthera pungens* Kunth for assessment of antimicrobial effect against various bacterial and fungal strains. They found that all the extracts were having potential as antibacterial, but the antifungal property was exhibited by only acetone and aqueous extracts. Noticed mechanisms were inhibition of DNA replication as well as blocking of cellular respiration. Phytochemicals like choline (Siopa et al., 2016), rhein (Joung et al., 2012), limonene (Vuuren and Viljoen, 2007), α -curcumene (Santos da Silva et al., 2015), geraniol (Lira et al., 2020), linalool (Park S.-N. et al., 2012), camphor (Masry et al., 2021), myrcene (Chaves-Quirós et al., 2020), and α -pinene (Dhar et al., 2014; Cloeckert et al., 2015) which were earlier reported from *Alternanthera pungens* Kunth, may be responsible for such antimicrobial action.

Plenty of independent researches have been extracted from the literature, covering evaluation of antimicrobial activity of *Alternanthera sessilis* (L.) R.Br. ex DC.: Osuna and the team had used hexane and methanolic extracts obtained from the aerial parts (Osuna et al., 2008); Jalalpure and the team had used petroleum ether (40–60°C), chloroform, acetone, methanolic, and aqueous extracts of leaves (Jalalpure et al., 2008); Monroy and Limsiaco had used aqueous, ethanolic, and acetone extracts obtained from leaves (Monroy and Limsiaco, 2016); Niraimathi and the team had used silver nanoparticles of aqueous extract of leaves (Niraimathi et al., 2013); Rajamurugan and the team had used ethanolic extract obtained from the leaves (Rajamurugan et al., 2013); D Suganya and the team had used aqueous extract of leaves and stems (Suganya et al., 2019); Kota and the team had used petroleum ether, ethyl acetate, chloroform, and methanolic extract obtained from the leaves (Kota et al., 2017); Sundar and the team had used petroleum ether and methanolic extracts of

leaves (Sundar et al., 2019); while Salvador and the team had used hexane and ethanolic extracts obtained from the adult plants (Salvador et al., 2009). These studies clearly concluded that *Alternanthera sessilis* (L.) R.Br. ex DC. possesses antimicrobial properties. Several mechanisms elucidated by them are like cell membrane lysis, prevention of protein synthesis, blocking cellular respiration, inhibition of DNA replication, deprivation of iron for microbial growth, etc (Osuna et al., 2008; Salvador et al., 2009; Rajamurugan et al., 2013; Monroy and Limsiaco, 2016; Kota et al., 2017; Suganya et al., 2019). Phytomolecules like Vitexin (Das et al., 2016), Kaempferol (del Valle et al., 2016), Quercetin (Gatto et al., 2002), Kaempferol-7- O-glucoside (Singh et al., 2011), Stigmasterol (Alawode et al., 2021), β -Sitosterol (Ododo et al., 2016), Ellagic acid (Abuelsaad et al., 2013; De et al., 2018), Ferulic acid (Shi et al., 2016), p-Coumaric acid (Boz, 2015), 4-Hydroxybenzoic acid (Cho J.-Y. et al., 2014), 2,5-Dihydroxybenzoic acid (Kim et al., 2007), Chlorogenic acid (Li et al., 2013; Kabir et al., 2014), Ionone (Mikhlin et al., 1983), β -Carotene (Hayashi et al., 2012), and Ricinoleic acid (Novak et al., 1961) which were earlier reported from *Alternanthera sessilis* (L.) R.Br. ex DC. may be responsible for its antimicrobial property.

Antioxidant Activity

Petrus and the team had evaluated the antioxidant activity of the 80% aqueous methanolic extract obtained from the flowers of *Alternanthera bettzickiana* (Regel) G.Nicholson. They had observed that the extract possessed radical scavenging and ferrous ion chelating properties (Petrus A. et al., 2014). On the other hand, Vidhya and the team had evaluated the antioxidant activity of the hexane, chloroform, ethyl acetate, methanolic, and aqueous extracts obtained from the leaves *Alternanthera bettzickiana* (Regel) G.Nicholson. They observed that out of all, methanolic extract was exhibiting stronger radical scavenging activity (Vidhya et al., 2015). Phytomolecules like apigenin analogs (Prince Vijaya Singh et al., 2004) which were earlier reported from *Alternanthera bettzickiana* (Regel) G.Nicholson, may be responsible for this antioxidant potential.

Independently, several research teams had investigated the antioxidant potential of *Alternanthera brasiliana* (L.) Kuntze: Reza and the team had used 80% ethanolic extract of stem and leaves (Reza et al., 2019); Enechi and the team had used ethanolic extract of leaves (Enechi et al., 2013); Chandran R had used methanolic extract of leaves (Chandran, 2017); Attaugwu and Uvere had used ethanolic extract of leaves (Attaugwu and Uvere, 2017); Pereira and the team had used ethanolic extract and its dichloromethane, ethyl acetate, n-butanolic fractions of leaves (Pereira et al., 2013); Araujo and the team had used ethanolic extract of aerial parts and its hexane, chloroform, and ethyl acetate fractions (Araujo et al., 2014); while Akachukwu and Uchegbu had used ethanolic extract of leaves (Akachukwu and Uchegbu, 2016). These pieces of evidence increase the credibility of *Alternanthera brasiliana* (L.) Kuntze as antioxidant. Phytoconstituents like Ligustroflavone (Kang et al., 2021), Vitexin (An et al., 2012), Kaempferol (Park et al., 2006), Quercetin (Zhang et al., 2011), Tricin (Duarte-Almeida et al., 2007), Quercetin 3- β -D-glucoside (Niranjan Panat et al., 2015), Isorhamnetin-3-O-robinobioside (Boubaker et al., 2012),

Stigmasterol (Liang et al., 2020), β -Sitosterol (Gupta et al., 2011), Ferulic acid (Graf, 1992), p-Coumaric acid (Kiliç and Yeşiloğlu, 2013), 4-Hydroxybenzoic acid (Velika and Kron, 2012), 2,5-Dihydroxybenzoic acid (Calderón Guzmán et al., 2007), Chlorogenic acid (Sato et al., 2011), Dopamine-betaxanthin (Cai et al., 2003), and 3-Methoxytyramine-betaxanthin (Cai et al., 2003) which were earlier reported from *Alternanthera brasiliana* (L.) Kuntze, may be responsible for its antioxidant property.

Patil and Kore had evaluated the antioxidant property of methanolic extracts obtained from different parts viz. leaves, stem, and roots of *Alternanthera ficoidea* (L.) P.Beauv. They had observed that out of all, the methanolic extract from the roots was having most potent antioxidant activity (Patil and Kore, 2019). To the best of our knowledge, the phytochemical characterization of *Alternanthera ficoidea* (L.) P.Beauv. was not yet done, leaving an ample scope for the researchers.

Koolen and the team had isolated seven phytoconstituents from the aerial sections of *Alternanthera littoralis* P.Beauv. and evaluated them for the antioxidant potential using *In vitro*—ORAC assay. They had observed that out of all compounds, Alternamide B was the most significant one as antioxidant. Researchers had further suggested the catechol scaffold as a pharmacophore for this activity (Koolen et al., 2017).

Two independent research teams had evaluated the antioxidant potential of *Alternanthera paronychioides* A.St.-Hil.: Wu and the team had used methanolic, ethanolic, and aqueous extracts of the whole plant (Wu et al., 2013) while Tukun and the team had used aqueous extract obtained from the leaves (Tukun et al., 2014). These preliminary studies signifies the role of *Alternanthera paronychioides* A.St.-Hil. as antioxidant. To the best of our knowledge, the phytochemical characterization of *Alternanthera paronychioides* A.St.-Hil. was not yet done, leaving an ample scope for the researchers.

Bhattacharjee and the team had evaluated the antioxidant activity of methanol soluble fraction obtained from the leaves of *Alternanthera philoxeroides* (Mart.) Griseb. (Bhattacharjee et al., 2014). while Correa and the team had used ethanolic extracts of the whole plant (Correa et al., 2016). These preliminary studies suggested that the *Alternanthera philoxeroides* (Mart.) Griseb. is worthy of further investigation as antioxidant. Phytoconstituents like Luteolin and luteolin analogs (Romanova et al., 2001), Chrysoeriol analogs (Mishra et al., 2003), Vitexin (An et al., 2012), Quercetin (Zhang et al., 2011), β -Sitosterol (Gupta et al., 2011), Δ^5 -Stigmasterol (Liang et al., 2020), Ursolic acid (Bobé et al., 2012; do Nascimento et al., 2014), Oleanolic acid and Oleanolic acid analogs (Wang et al., 2010), Calendulose E (Tang et al., 2019), Caffeic acid (Gulcin, 2006), Quinic acid (Pero et al., 2009), p-Coumaric acid (Kiliç and Yeşiloğlu, 2013), Rubiadin (Tripathi et al., 1997), β -Carboline (Moura et al., 2007), Malic acid (Jin et al., 2016), Azelaic acid (Muthulakshmi and Saravanan, 2013), Cycloeucaenol (Wang W. et al., 2015), Phytol (Santos et al., 2013), and Pheophytin A (Endo et al., 1985) which were previously been reported from *Alternanthera philoxeroides* (Mart.) Griseb., may be responsible for this antioxidant property.

Several research teams have independently assessed the antioxidant potential of *Alternanthera pungens* Kunth: Mourya and the team had used ethanolic and aqueous extracts obtained from the leaves (Mourya et al., 2019); Franck and the team had used aqueous extract of leaves (Franck et al., 2016); while Jakhar and Dahiya had used aqueous, acetone, ethanolic, and petroleum ether extracts of aerial parts (Jakhar and Dahiya, 2017). These studies validated the antioxidant potential of *Alternanthera pungens* Kunth. Various phytochemicals like Limonene (Roberto et al., 2009), Geraniol (Aytac et al., 2016), Linalool (Duarte et al., 2016), Camphor (Drikvandi et al., 2020), Myrcene (Khalili et al., 2020), Camphene (Tiwari and Kakkar, 2009), and α -pinene (Aydin et al., 2013) which were reported earlier from *Alternanthera pungens* Kunth, may be responsible for its antioxidant action.

While going through literature, we have found enough pieces of evidences reporting and validating the antioxidant property of *Alternanthera sessilis* (L.) R.Br. ex DC.: Borah and the team had used 90% methanolic, 70% acetone, 80% ethanolic extracts of leaves and stems (Borah et al., 2011); Chai and the team had used hexane, chloroform, ethyl acetate, butanolic, and aqueous fractions of leaves and callus methanol extracts (Chai et al., 2016); Sharma and the team 30% hydroethanolic extract of the whole plant (Sharma et al., 2013); Khan and the team had used separate Methanolic and hexane extracts of leaves and stems (Khan et al., 2018); Azizah and the team had used ethanolic and aqueous extracts of aerial parts (Azizah et al., 2015); Muniandy and the team had used 90% hydroethanolic extract of stem (Muniandy et al., 2018b); Othman and the team had used ethanolic and aqueous extracts of aerial parts (Othman et al., 2016); Tiwari and the team had used juice (Tiwari et al., 2013); Rajamurugan and the team had used ethanolic extract of leaves (Rajamurugan et al., 2013); Jain and the team had used methanolic extract of leaves (Jain et al., 2016); Suganya and the team had used aqueous extract of leaves and stems (Suganya et al., 2019); Mohd Hazli and the team had used hexane, ethyl acetate, ethanolic, and aqueous extracts of leaves and stem (Mohd Hazli et al., 2019); Niraimathi and the team had used silver nanoparticles from aqueous extract of leaves (Niraimathi et al., 2013); Yap and the team had used 100% ethanolic, 70% ethanolic, 80% methanolic, ethyl acetate, and aqueous extracts of the whole plant (Yap et al., 2019); Kota and the team had used petroleum ether, ethyl acetate, chloroform, and methanolic extract of leaves (Kota et al., 2017); Sundar and the team had used petroleum ether and methanolic extracts of leaves (Sundar et al., 2019); Pathak and the team had used n-hexane and methanolic extracts of aerial parts (Pathak et al., 2020); Khan and the team had used the volatile oil of leaves and flowers (Khan et al., 2016); while Salvador and the team had used ethanolic extract and its four fractions; Acacetin 8-c-[α -L-rhamnopyranoyl-(1 \rightarrow 2)- β -D-glucopyranoside]; 2''-O- α -L-rhamnopyranosyl-vitexin; 2''-O- β -D-glucopyranosyl vitexin and Vitexin (Salvador et al., 2006). Results from these researches left no doubt in the credibility and applicability of *Alternanthera sessilis* (L.) R.Br. ex DC. in reducing oxidative stress. Phytomolecules like Vitexin and vitexin analogs (An et al., 2012), Kaempferol and kaempferol analogs (Park et al., 2006),

Quercetin and quercetin analogs (Zhang et al., 2011), Acacetin analogs (Li et al., 2019), Isorhamnetin-3-O-robinobioside (Boubaker et al., 2012), Stigmasterol (Liang et al., 2020), Campesterol (Yoshida and Niki, 2003), β -Sitosterol (Gupta et al., 2011), Spinasterol (Adebiyi et al., 2018), Ellagic acid (Priyadarsini et al., 2002), Ferulic acid (Graf, 1992), p-Coumaric acid (Kiliç and Yeşiloğlu, 2013), 4-Hydroxybenzoic acid (Velika and Kron, 2012), 2,5-Dihydroxybenzoic acid (Calderón Guzmán et al., 2007), Chlorogenic acid (Sato et al., 2011), Ionone (Liu et al., 2009), β -Carotene (Paiva and Russell, 1999), Ricinoleic acid (Park et al., 2020), Dopamine-betaxanthin (Cai et al., 2003), and 3-Methoxytyramine-betaxanthin (Cai et al., 2003) which were earlier been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for its antioxidant action.

Antiparkinsonism/Antidementia Property

Khamphukdee and the team had evaluated the antidementia activity of the ethanolic extract obtained from the whole plant of *Alternanthera philoxeroides* (Mart.) Griseb. They had noticed various mechanisms behind it like inhibition of lipid peroxidation in the whole brain, downregulation of neuroinflammatory cytokines (IL-1 β , IL-6, and TNF- α), etc (Khamphukdee et al., 2021). Phytomolecules like Luteolin and luteolin analogs (Delgado et al., 2021), Vitexin (Malar et al., 2020; Zhang et al., 2021), Quercetin (Yao et al., 2010), Torosaflavone E (Khamphukdee et al., 2021), Demethyl torosaflavone D (Khamphukdee et al., 2021), β -Sitosterol (Kim et al., 2008), Stigmasterol (Park S. J. et al., 2012; Pratiwi et al., 2021), Ursolic acid (Habtemariam, 2019), Oleanolic acid and oleanolic acid analogs (Lin et al., 2021), Caffeic acid (Khan et al., 2013; Deshmukh et al., 2016), Quinic acid (Liu et al., 2020), p-Coumaric acid (Kim H.-B. et al., 2017), β -Carboline (Zhao et al., 2013; Li et al., 2018), Malic acid (Tian et al., 2021), Blumenol A (Emir et al., 2019), Phytol (Sathya et al., 2020), and Pheophytin A (Park et al., 2014) which were earlier reported from *Alternanthera philoxeroides* (Mart.) Griseb., may be responsible for this antidementia property.

Ittiyavirah and Hameed had evaluated the antiparkinsonian activity of silver nanoparticles and ethanolic extract obtained from the whole plant of *Alternanthera sessilis* (L.) R.Br. ex DC. They had observed that the silver nanoparticles as well as the ethanolic extract were able to impart neuroprotection with decrease in catalepsy as well as in muscle rigidity, along with locomotion improvement (Ittiyavirah and Hameed, 2015). Phytomolecules like Vitexin and vitexin analogs (Hu et al., 2018), Kaempferol and kaempferol analogs (Filomeni et al., 2012), Quercetin-3-methyl ether (Kim et al., 2009), Quercetin (Lv et al., 2012), Acacetin analogs (Kim S. M. et al., 2017), Stigmasterol (Haque and Moon, 2018), β -Sitosterol (Kim et al., 2008), Spinasterol (Jeong et al., 2010), Ellagic acid (Baluchnejadmojarad et al., 2017), Ferulic acid (Haque et al., 2015), p-Coumaric acid (Vauzour et al., 2010), 4-Hydroxybenzoic acid (Winter et al., 2017), Chlorogenic acid (Singh et al., 2018), and Ionone (Ma et al., 2014) which were previously been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for the antiparkinsonian activity.

Antiprotozoal Activity

Koolen and the team had isolated compounds like Alternamide A-B and Alternamine A-B from the aerial parts of *Alternanthera littoralis* P.Beauv. and evaluated for their antiprotozoal activity against protozoal strains viz. *Trypanosoma cruzi* trypomastigotes and *Leishmania amazonensis*. They had observed that out of all the tested compounds, Alternamine A was the most efficient one (Koolen et al., 2017).

Antispasmodic Activity

Garín-Aguilar and the team had antispasmodic activity of aqueous, hexane, methanolic extract, and fractions of methanol extract (F₁-F₆) obtained from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. (Garín-Aguilar et al., 2013). while Saqib and Janbaz had used 70% ethanolic extract of the whole plant and its dichloromethane, aqueous fractions (Saqib and Janbaz, 2016). They had observed that *Alternanthera sessilis* (L.) R.Br. ex DC. possesses significant antispasmodic activity. Phytochemicals like Vitexin and vitexin analogs (Ragone et al., 2007), Quercetin and quercetin analogs (Lozoya et al., 1994; Morales et al., 1994), Acacetin analogs (González-Trujano et al., 2012), Stigmasterol (Ammar et al., 2009), β -Sitosterol (Rehman et al., 2012), and Ellagic acid (Krenn et al., 2011) which were previously been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be the contributors towards the antispasmodic activity of the extracts.

Antiviral Activity

Rattanathongkom and the team had isolated Chikusetsusaponin IVa isolated from the whole plant of *Alternanthera philoxeroides* (Mart.) Griseb. and evaluated antiviral activity against various viral cell lines through *in vitro* and *in vivo* assays. They had observed the dose-dependent activity along with the potential of Chikusetsusaponin IVa in inhibiting the viral protein synthesis (Rattanathongkom et al., 2009).

Central-Stimulating Activity

Mondal and the team had evaluated the central stimulating potential of the ethanolic extract obtained from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. Results were quite significant (Mondal et al., 2014). Phytoconstituents acting on GABA receptors like Ricinoleic acid (Witt et al., 2002), Chlorogenic acid (Hara et al., 2014), p-Coumaric acid (Scheepens et al., 2014), Ferulic acid (Cheng et al., 2010; Sonar et al., 2019), Ellagic acid (Girish et al., 2013), Spinasterol (Socafa et al., 2015), Stigmasterol (Karim et al., 2021), Acacetin analogs (Gálvez et al., 2015), Vitexin and vitexin analogs (Zhu et al., 2016; de Oliveira et al., 2020), and Quercetin and quercetin analogs (Goutman and Calvo, 2004; Kim et al., 2014) which were previously been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be behind this GABA receptor mediated central-stimulating activity.

Gastrointestinal Protective Activity

Astudillo-Vázquez and the team had evaluated the gastrointestinal protective potential of the aqueous and

ethanolic extracts obtained from the whole plant of *Alternanthera sessilis* (L.) R.Br. ex DC. They noticed that the antidiarrheal property i.e. decreasing the gastrointestinal content is the major factor behind the gastrointestinal protective activity of *Alternanthera sessilis* (L.) R.Br. ex DC. (Astudillo-Vázquez et al., 2008). Phytochemicals like Vitexin and vitexin analogs (Figer et al., 2017), Kaempferol and kaempferol analogs (Beber et al., 2017; Campos-Vidal et al., 2021), Quercetin and quercetin analogs (de la Lastra et al., 1994), Stigmasterol (Sánchez-Mendoza et al., 2008), β -Sitosterol (Sánchez-Mendoza et al., 2008), Ellagic acid (Beserra et al., 2011), Ferulic acid (Shahid et al., 2018), p-Coumaric acid (Panda and Suresh, 2015), Chlorogenic acid (Ahmed et al., 2021), and β -Carotene (Mózsik et al., 1996) which were earlier reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for this gastrointestinal protective potential.

Hepatoprotective Activity

Lin and the team had evaluated the hepatoprotective activity of the aqueous extract obtained from the whole plant of *Alternanthera sessilis* (L.) R.Br. ex DC. (Lin et al., 1994). while Bhuyan and the team had evaluated the hepatoprotective potential of the methanolic extract obtained from the whole plant (Bhuyan et al., 2017). Both these independent researches finally concluded that the *Alternanthera sessilis* (L.) R.Br. ex DC. is hepatoprotective. Phytochemicals like Vitexin and vitexin analogs (Duan et al., 2020), Kaempferol and kaempferol analogs (Wang M. et al., 2015; Wang et al., 2015c), Quercetin-3-methyl ether (Tseng et al., 2012), Quercetin and quercetin analogs (Miltonprabu et al., 2017), Acacetin analogs (Cho H.-I. et al., 2014), Stigmasterol (Carter et al., 2007), β -Sitosterol (Abdou et al., 2019), Ellagic acid (Girish and Pradhan, 2012), Ferulic acid (Rukkumani et al., 2004), p-Coumaric acid (Parvizi et al., 2020), 2,5-Dihydroxybenzoic acid (Pujari and Bandawane, 2021), Chlorogenic acid (Chen et al., 2019), and β -Carotene (Manda and Bhatia, 2003) which were previously reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be the contributory constituents towards the elicited hepatoprotective activity.

Immunomodulatory Activity

Several research teams had independently assessed the immunomodulatory potential of *Alternanthera sessilis* (L.) R.Br. ex DC.: Biella and the team had used aqueous extract of the whole plant (Biella et al., 2008); Guerra and the team had used aqueous extract of aerial parts (Guerra et al., 2003); while Moraes and the team had used aqueous and ethanolic extract of leaves as well as tetrahydrofuran, dichloromethane, aqueous, petroleum ether soluble fraction (Moraes et al., 1994). These studies validated the immunomodulatory property of *Alternanthera sessilis* (L.) R.Br. ex DC. Phytochemicals like Vitexin and vitexin analogs (Rosa et al., 2016), Kaempferol and kaempferol analogs (Lin et al., 2011; Swarnalatha et al., 2015), Quercetin-3-methyl ether (Martino et al., 2016), Quercetin and quercetin analogs (Manjunath and Thimmulappa, 2021), Acacetin analogs (Zhao et al., 2014), Stigmasterol (Antwi et al., 2017b), β -Sitosterol

(Desai et al., 2009), Ellagic acid (Abuelsead et al., 2013), Ferulic acid (He F. et al., 2021), p-Coumaric acid (Pragasam et al., 2012), Chlorogenic acid (Guo et al., 2021), and β -Carotene (Jyonouchi et al., 2009) which were previously been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for this immunomodulatory potential.

Moraes and the team had also evaluated the immunomodulatory activity of aqueous and ethanolic extract of leaves as well as tetrahydrofuran, dichloromethane, aqueous, petroleum ether soluble fractions obtained from *Alternanthera brasiliiana* (L.) Kuntze and *Alternanthera littoralis* P.Beauv. (Moraes et al., 1994). Phytomolecules like Vitexin and vitexin analogs (Rosa et al., 2016), Kaempferol and kaempferol analogs (Lin et al., 2011; Swarnalatha et al., 2015), Quercetin and quercetin analogs (Manjunath and Thimmulappa, 2021), Tricin (Santos et al., 2017), Stigmasterol (Antwi et al., 2017b), β -Sitosterol (Desai et al., 2009), Ferulic acid (He F. et al., 2021), p-Coumaric acid (Pragasam et al., 2012), and Chlorogenic acid (Guo et al., 2021) which were previously reported from *Alternanthera brasiliiana* (L.) Kuntze, may be responsible towards its immunomodulatory activity. Phytomolecules like Vitexin and vitexin analogs (Rosa et al., 2016), Kaempferol (Lin et al., 2011; Swarnalatha et al., 2015), Quercetin-3-methyl ether (Martino et al., 2016), Quercetin and quercetin analogs (Manjunath and Thimmulappa, 2021), Acacetin analogs (Zhao et al., 2014), Stigmasterol (Antwi et al., 2017b), and Hydroxytyrosol (Shan and Miao, 2022) which were previously reported from *Alternanthera littoralis* P.Beauv., may be responsible for its immunomodulatory activity.

Insecticidal Property

Coutinho and the team had evaluated the insecticidal potential of the ethanolic extract obtained from the leaves of *Alternanthera brasiliiana* (L.) Kuntze. against *Drosophila melanogaster* (Harwich strain). They found that the tested concentrations of the ethanolic extract were having a mild insecticidal effect, and that too after 24–48 h exposure (Coutinho et al., 2017). Phytomolecules like Kaempferol and kaempferol analogs (Zhang et al., 2016), Quercetin and quercetin analogs (Mesbah et al., 2007), Stigmasterol (Gade et al., 2017), β -Sitosterol (Zolotar et al., 2002), Spinasterol (Ahmed et al., 2020), and Ferulic acid (Yang et al., 2017) which were previously isolated from *Alternanthera brasiliiana* (L.) Kuntze., may be responsible for this insecticidal property.

Lithotriptic/Antiuroolithiatic Activity

Dhanya and the team had evaluated the antiuroolithiatic activity of Kalka—fine paste of macerated fresh plant material of *Alternanthera sessilis* (L.) R.Br. ex DC. while Babu and the team had used ethanolic extract of the whole plant for the assessment of antiuroolithiatic activity (Dhanya et al., 2017; Babu et al., 2021). Results obtained by both these independent studies are quite significant and reflects the potential of *Alternanthera sessilis* (L.) R.Br. ex DC. as lithotriptic agent. Phytomolecules like Kaempferol and kaempferol analogs (Cechinel-Zanchett et al., 2020), Quercetin and quercetin analogs (Dinnimath et al., 2017), Stigmasterol (Lobine et al.,

2020), and Ferulic acid (Zhao et al., 2019) which were previously been reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for this antiuroolithiatic activity.

Larvicidal Activity

Babu and the team had also evaluated the larvicidal property of ethanolic extract obtained from the whole plant of *Alternanthera sessilis* (L.) R.Br. ex DC. They found that the ethanolic extract was having a dose dependent percent mortality against mosquito larvae (Babu et al., 2021). Phytomolecules like Stigmasterol (Gade et al., 2017), β -Sitosterol (Angajala and Subashini, 2018), and Ferulic acid (Pavela, 2011), which were earlier isolated from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible behind this larvicidal activity.

Nootropic Activity

Gupta and Singh had evaluated the nootropic activity of methanolic extract obtained from the leaves of *Alternanthera sessilis* (L.) R.Br. ex DC. And results were quite promising (Gupta and Singh, 2012b). Phytomolecules like Kaempferol and kaempferol analogs (Das et al., 2018), Quercetin and quercetin analogs (Halder et al., 2015), Ellagic acid (Bansal et al., 2017; Kiasalari et al., 2017), and Ferulic acid (Yang et al., 2016; Mhillaj et al., 2017) which had been previously isolated from *Alternanthera sessilis* (L.) R.Br. ex DC., may be the contributing phytomolecules towards this nootropic activity.

Photoprotective Activity

Alencar Filho and the team had evaluated the photoprotective effect of the gel prepared from 5% w/w of extract *Alternanthera brasiliiana* (L.) Kuntze enriched in flavonoids. They had observed that the stabilization of the ROS and resonating permission are the mechanisms behind this photoprotective activity of the gel extract (Alencar Filho et al., 2020). Phytomolecules like Kaempferol and kaempferol analogs (Monici et al., 1994), Quercetin and quercetin analogs (Saija, 2003; Gonçalves et al., 2019), Tricin (Moon et al., 2018), Stigmasterol (Bayer et al., 2011), β -Sitosterol (Bayer et al., 2011), Ferulic acid (Lin et al., 2005; Peres et al., 2018), p-Coumaric acid (Biswas et al., 2021), and Chlorogenic acid (Wang et al., 2021) which were earlier reported from *Alternanthera brasiliiana* (L.) Kuntze, may be responsible for this photoprotective property of the gel extract.

Sedative Property

Oyemitan and the team had evaluated the sedative action of the ethanolic extract obtained from the leaves of *Alternanthera brasiliiana* (L.) Kuntze. They had observed that the ethanolic extract was expressing the sedative property by acting on stimulatory or central excitatory channels (Oyemitan et al., 2015). Phytomolecules like Quercetin and quercetin analogs (Nakhaee et al., 2021), β -Sitosterol (Aguirre-Hernández et al., 2007), and Ferulic acid (Tu et al., 2012) which were previously been reported from *Alternanthera brasiliiana* (L.) Kuntze., may be responsible for this sedative action.

Wound Healing Property

Barua and the team had reported several studies validating the wound healing property of *Alternanthera brasiliana* (L.) Kuntze (Barua et al., 2009; Barua C. et al., 2012; Baru et al., 2012; Barua C. C. et al., 2012). Phytomolecules like Vitexin and vitexin analogs (Bektas et al., 2020), Kaempferol and kaempferol analogs (Petpiroon et al., 2015; Özyay et al., 2019), Quercetin and quercetin analogs (Gomathi et al., 2003), Tricin (Han et al., 2016), β -Sitosterol (Abbas et al., 2019), Ferulic acid (Ghaisas et al., 2014), p-Coumaric acid (Kong et al., 2013; Boeing et al., 2020), and Chlorogenic acid (Bagdas et al., 2015) which had been isolated from *Alternanthera brasiliana* (L.) Kuntze previously, may be responsible for this wound healing property.

Muniandy and the team had evaluated the wound healing action of the 90% hydroethanolic extract obtained from the stem of *Alternanthera sessilis* (L.) R.Br. ex DC. while Jalalpure and the team had used chloroform extract obtained from the leaves *Alternanthera sessilis* (L.) R.Br. ex DC. Both these teams had independently ascertained the wound healing property of *Alternanthera sessilis* (L.) R.Br. ex DC. (Jalalpure et al., 2008; Muniandy et al., 2018b). Phytomolecules like Vitexin and vitexin analogs (Bektas et al., 2020), Kaempferol and kaempferol analogs (Petpiroon et al., 2015; Özyay et al., 2019), Quercetin and quercetin analogs (Gomathi et al., 2003), Acacetin analogs (Bhat et al., 2013), β -Sitosterol (Abbas et al., 2019), Ellagic acid (Mo et al., 2014), Ferulic acid (Ghaisas et al., 2014), p-Coumaric acid (Kong et al., 2013; Boeing et al., 2020), and Chlorogenic acid (Bagdas et al., 2015), β -Carotene (Gerber and Erdman, 1982), and Ricinoleic acid (Nada et al., 2018) which had earlier reported from *Alternanthera sessilis* (L.) R.Br. ex DC., may be responsible for this wound healing property.

After this exhaustive cross-literature review for the bioactive compounds that may be responsible elements behind the potent pharmacological actions elicited by the extracts, we have summarized those in a smart interactive illustration (**Figure 4**).

It is indispensable to confirm if traditional claims of *Alternanthera* species have been proven by systematic scientifically designed pharmacological (preclinical or clinical) studies. Traditional claims and reported pharmacological activities of various species are presented in **Table 3**, and observations are as follows:

a) Traditional claims of some species (*Alternanthera brasiliana* (L.) Kuntze, *Alternanthera caracasana* Kunth, *A. dentata* (now reclaimed as *Alternanthera brasiliana* (L.) Kuntze), *A. ficooides* (now reclaimed as *Alternanthera sessilis* (L.) R.Br. ex DC.), *Alternanthera littoralis* P.Beauv., *A. maritima* (now reclaimed as *Alternanthera littoralis* P.Beauv.), *Alternanthera nodiflora* R.Br., *Alternanthera paronychioides* A.St.-Hil., *Alternanthera porrigens* (Jacq.) Kuntze, *Alternanthera pungens* Kunth, *Alternanthera sessilis* (L.) R.Br. ex DC., *A. tenella* (now reclaimed as *Alternanthera sessilis* (L.) R.Br. ex DC.), and *A. triandra* (now reclaimed as *Alternanthera sessilis* (L.) R.Br. ex DC.)) have not been validated scientifically.

b) Traditionally used species like *Alternanthera caracasana* Kunth and *Alternanthera porrigens* (Jacq.) Kuntze have not been investigated for any pharmacological activities. These species hold great potential for future research intending to validate traditional claims.

c) Species (*Alternanthera brasiliana* (L.) Kuntze, *Alternanthera paronychioides* A.St.-Hil., *Alternanthera philoxeroides* (Mart.) Griseb., and *Alternanthera sessilis* (L.) R.Br. ex DC.) have been screened for those pharmacological actions which are not claimed traditionally. These species may have been chosen following a chemotaxonomical or ecological approach.

d) Literature did not reveal any traditional use of three species (*Alternanthera bettzickiana* (Regel) G.Nicholson, *Alternanthera hirtula* (Mart.) R.E.Fr., and *Alternanthera praelonga* A.St.-Hil.) but evaluated for varied pharmacological activities.

Toxicological Studies

Hydroalcoholic extract of *Alternanthera brasiliana* (L.) Kuntze and *Alternanthera bettzickiana* (Regel) G.Nicholson leaves was orally administered (200 mg/kg dose) for 14 days in mice to observe any change in behavior of animals (Kasthuri and Ramesh, 2018). Further, hematological and histopathological changes were also observed. Sub-acute toxicity study suggested that both extracts samples did not show any harmful side effects. Hydroethanolic leaf extract of *Alternanthera bettzickiana* (Regel) G.Nicholson displayed a progressively powerful cytotoxic impact on DLA cell lines than *Alternanthera brasiliana* (L.) Kuntze extract.

The oral acute toxicity study was conducted on 95% ethanolic extract of *Alternanthera philoxeroides* (Mart.) Griseb. at the dose of 500 mg/kg in male and female rodents (Thanabhorn et al., 2005). The ethanolic extract did not show mortality and gross morphological alterations in the organs of rodents. Oral administration of 1,000 mg/kg/day for 14 days showed no significant changes in the body and inner organs weights, hematological and clinical parameters.

Clinical Studies

The studies have shown antiretroviral activity of *Alternanthera pungens* Kunth herbal tea due to antioxidant potential when administered to HIV patients (Djohan et al., 2009). Blood samples were taken from fasted patients who received an *Alternanthera pungens* Kunth tea for 12 months every day before dinner. The markers of oxidative stress (malondialdehyde and advanced oxidation protein end products), plasma T lymphocytes, transaminases, and creatinine were determined in the blood sample. A significant decrease in concentrations of markers of oxidative stress and an increase in plasma levels of CD4 and CD8 T cells after this period were observed. Further, no signs of hepatic and renal toxicity were seen in HIV patients.

In another case study, the potential of *Alternanthera sessilis* (L.) R.Br. ex DC., *Momordica charantia* L., and *Colocasia esculenta* (L.) Schott were investigated in reducing postprandial blood glucose levels in healthy human subjects and patients with type II diabetes (Bachok et al., 2014). The

results of the clinical report suggested that *Alternanthera sessilis* (L.) R.Br. ex DC. reduced the non-significant glucose level in 3 h in comparison to standard control diet in healthy and diseased subjects. This case study was conducted in India with eight healthy subjects and six diabetic subjects.

CONCLUSION

Scrutiny of available literature reveals that out of 139 species of the genus *Alternanthera*:

- Nine species have been investigated phytochemically,
- Fifteen species possess strong ethnopharmacological records,
- Twelve species have been scientifically evaluated in the *in vitro* or *in vivo* experimental models for various pharmacological activities,
- Three species have been subjected to toxicity studies for establishing safety profiles,
- Two species have been examined for clinical studies.

To date, 129 compounds have been isolated from 9 species of *Alternanthera*. 129 bioactive compounds were classified in 11 phytochemical classes, covering information about 40 flavonoids, 17 triterpenoid/saponins, 15 sterols, 12 alkaloids, 10 phenolic compounds, 3 ionone, 1 benzopyran, 3 hydroxycinnamic acids, 4 anthraquinone, 8 volatile oils and 17 miscellaneous compounds. Flavonoids (~32%) constitute the main class of phytoconstituents in the genus *Alternanthera* followed by triterpenoids (~13%). The isolated triterpenoids such as oleanolic acid, ursolic acid, and flavonoids such as luteolin, apigenin, vitexin, kaempferol, quercetin aglycones and their glycosides from the genus have proven therapeutic value. In terms of the phytochemical exploration, the most explored species of *Alternanthera* genus were *Alternanthera philoxeroides* (Mart.) Griseb. (52 compounds), *Alternanthera sessilis* (L.) R.Br. ex DC. (45 compounds), *Alternanthera brasiliana* (L.) Kuntze (32 compounds), and *Alternanthera littoralis* P.Beauv (24 compounds). *Alternanthera sessilis* (L.) R.Br. ex DC. has so far yielded a diverse class of compounds, like benzopyran, flavonoids, sterols, triterpenoid/saponin, phenolic compounds, ionone, and miscellaneous compounds. Similarly, *Alternanthera philoxeroides* (Mart.) Griseb. has also yielded a diverse class of compounds like flavonoids, sterols, triterpenoid/saponins, phenolic compounds, anthraquinone, alkaloids, and miscellaneous compounds. While volatile oil related compounds were extracted only from *Alternanthera pungens* Kunth, ionone analogues were isolated from *Alternanthera sessilis* (L.) R.Br. ex DC. only and hydroxycinnamic acids were reported only from *Alternanthera bettzickiana* (Regel) G.Nicholson. Researchers could explore rest of the species of *Alternanthera* genus to check if containing ionone analogues, volatile oils, and hydroxycinnamic acids. Further, the species of *Alternanthera* genus which were least explored in terms of phytochemical characterization is also leading for possible opportunities for the researchers.

To the best of our knowledge, the phytochemical characterization of *Alternanthera paronychioides* A.St.-Hil.,

Alternanthera caracasana Kunth, *Alternanthera nodiflora* R.Br., and *Alternanthera ficoidea* (L.) P.Beauv. was not yet done, leaving an ample scope for the researchers.

Some phytoconstituents like quercetin, vitexin, chlorogenic acid, kaempferol, ferulic acid, β -sitosterol, p-coumaric acid, caffeic acid, quinic acid, etc had been reported from more than one species of *Alternanthera*. Probably, we could say that these phytoconstituents may be common secondary metabolites in *Alternanthera* genus. So, we recommend the researchers to explore the rest of the *Alternanthera* species for these common metabolites. These metabolites could serve as biomarkers for them.

As twelve species of *Alternanthera* have been investigated scientifically for pharmacological activities, only 9 species of the genus have been explored phytochemically. Few medicinally promising *Alternanthera* species have not been taken into consideration for phytochemical studies. The existing literature demonstrates that 5 species of genus *Alternanthera* such as:

Alternanthera brasiliana (L.) Kuntze, *Alternanthera caracasana* Kunth, *Alternanthera ficoidea* (L.) P.Beauv., *Alternanthera nodiflora* R.Br., and *Alternanthera paronychioides* A.St.-Hil. have been scientifically reported to exhibit various pharmacological activities, but these species have never been subjected to bioactivity directed fractionation to isolate bioactive phytoconstituents using appropriate chromatographic techniques. Therefore, natural product scientists should expand their research activities on *Alternanthera* species to isolate more bioactive compounds which can be developed as safer and efficacious lead molecules or potent analogs of bioactive markers. Further, it seems necessary to mention a major research gap in phytochemical studies that no emphasis has been given to standardizing these plants based on marker compounds. Appropriate analytical methods need to be developed using HPLC, HPTLC, or LC-MS for the standardization of *Alternanthera* species. Molecular docking and QSAR studies on selective bioactive markers of these species are also lacking. It has been observed that crude uncharacterized extracts of *Alternanthera* species have been used in most pharmacological studies. This observation attracts attention towards the isolation of bioactive compounds from *Alternanthera* following the bioactivity-guided fractionation approach. Highlighting a mechanistic approach for pharmacological activities is another area of research to be covered. Alternamide A-B and Alternamine A-B were evaluated only for antiprotozoal activity while Chikusetsusaponin IVa was checked for antiviral activity only, leaving a wide scope for the researchers.

Amongst 139 species of *Alternanthera*, only 12 species have shown medicinal value in preclinical studies, and out of these only *Alternanthera pungens* Kunth and *Alternanthera sessilis* (L.) R.Br. ex DC. have been investigated clinically for antiretroviral and antidiabetic activities, respectively. The toxicity studies have been conducted on 3 species such as *Alternanthera bettzickiana* (Regel) G.Nicholson, *Alternanthera brasiliana* (L.) Kuntze, and *Alternanthera philoxeroides* (Mart.) Griseb. to establish their safety profile. Please be noted that as per the latest guidelines and recommendations of the ethnopharmacology team, the scientific names of the plants have been reassessed and considered the name

given on <https://mpns.science.kew.org/mpns-portal/>. So the universally recognized name has been mentioned rather than the synonym indicated in the cited articles.

It is finally concluded that a well-planned roadmap of research activities is needed to be designed on traditionally used and medicinally promising plants of genus *Alternanthera*, so that their products and preparations may emerge out to be clinically potential and safe medicines in the treatment of various ailments.

AUTHOR CONTRIBUTIONS

RM and BS contributed to the conception and design of the study. RS, VD, DK, SB, MB, SK, AD, and SS wrote sections of the manuscript. All authors contributed to manuscript revision, read, and approved the submitted version.

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