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Review of compounds and activities from mangrove *Sonneratia* genus and their endophytes

Bin Liu [a,b,1], Xin Wang [c,1], Yiming Wang [a,b], Xiaohong Chen [a,b], Xiaobao Jin [a,b,*], Xiongming Luo [a,b,**]

[a] *School of Life Sciences and Biopharmaceutics, Guangdong Pharmaceutical University, Guangzhou, 510006, China*
[b] *Guangdong Provincial Key Laboratory of Pharmaceutical Bioactive Substances, Guangzhou, 510006, China*
[c] *School of Basic Medical Sciences, Guangdong Pharmaceutical University, Guangzhou, 510006, China*

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ABSTRACT

Sonneratia is an important mangrove plant, and its fruit has been used as traditional medicine and food in southeast China. With recent research focusing on its compounds and activities, an increasing number of compounds with novel structures and excellent antitumor, antioxidant, and other activities have been discovered. This review covered the compounds and activities of six species of the genus *Sonneratia* and their endophytes. To date, 116 compounds of *Sonneratia* have been reported, including 26 terpenoids, 9 flavonoids, 17 phenols, 9 lignans, 27 acid lipids, 16 steroids, and 12 other compounds. The main activities of the compounds in *Sonneratia* are antioxidant, antitumor, liver protection, antibacterial, and antidiabetic. Research on the compounds of endophytes from *Sonneratia* was first reported in 2009, and 56 compounds have been isolated, which mainly include sesquiterpenes, peptides, phenanthropyran ring-structured acids, pyrones, and anthracene derivatives. Individual compounds have been produced in *Sonneratia* and their endophytes that have the same structural fragments, and their interactions with small molecules and sources require further study. Recent advances in the bioactivities and compounds in the *Sonneratia* genus and their endophytes were summarized in this review, which is useful for the future isolation and discovery of active compounds and research regarding chemical ecology from the perspective of secondary metabolites.

1. Introduction

Mangrove plants are the woody plants that grow in the tropical and subtropical coastal intertidal zones, and are mainly distributed between the north and south tropics. There are a total of six species and three varieties of *Sonneratia*, including *Sonneratia apetala* (*S. apetala*), *Sonneratia caesolaris* (*S. caesolaris*), *Sonneratia hainanensis* (*S. hainanensis*), *Sonneratia alba* (*S. alba*), *Sonneratia paracaseolaris* (*S. paracaseolaris*), *Sonneratia ovata* (*S. ovata*), as well as *Sonneratia urama* (*S. urama*), *Sonneratia griffithii* (*S. griffithii*) and *Sonneratia lanceolata* (*S. lanceolata*).[1] In China, *Sonneratia* includes the first six species and is mainly distributed in the Hainan, Guangdong, and Guangxi provinces. *Sonneratia,* attributed to the order *Myrtle* and family *Sonneratia*, grows all year round at the confluence of the land and sea. Because of factors like serious soil hypoxia, salinization, and intense ultraviolet radiation, *Sonneratia* has developed a unique biological environment adaptation and metabolic system (such as high osmotic pressure, developed roots, and salt secretion mechanisms). This system enables *Sonneratia* to survive in a hostile environment and produce unusual secondary metabolites.[2]

In tropical and subtropical coastal areas, the fruit and seeds of *S. apetala* are widely used as food and to treat various diseases because of their rich nutritional value and pharmacologically active ingredients. *S. apetala* is rich in nutrients, and the content of the dry fruit peel of *S. apetala* includes carbohydrates, proteins, lipids, and ash account for 29.6%, 8.8%, 2.8%, and 25.5%, while the proportion in seeds is 28.3%, 11.5%, 4.2%, and 22.7% respectively. Linoleic acid (29.9%), palmitic acid (23.2%), ascorbic acid palmitate (21.2%), and stearic acid (10.5%) are the main components in the *S. apetala* seeds.[3–5]

This review offers comprehensive insight into the research on the compounds and activities of *Sonneratia* since 1950 (1950–2023) and

* Corresponding author. School of Life Sciences and Biopharmaceutics, Guangdong Pharmaceutical University, Guangzhou, 510006, China.
** Corresponding author. School of Life Sciences and Biopharmaceutics, Guangdong Pharmaceutical University, Guangzhou, 510006, China.
E-mail addresses: jinxf2001@163.com (X. Jin), qxjun312xx@gdpu.edu.cn (X. Luo).
[1] These authors contributed equally to this manuscript and worked as co-first authors.

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Table 1
Terpenoids in *Sonneratia*.

No.	Compound	Plant species	Plant site	Refs.
1	Sonneratiosides C	*S. alba*	leaves	[6]
2	Sonneratiosides D	*S. alba*	leaves	[6]
3	Sonneratiosides A	*S. alba*	leaves	[6]
4	Sonneratiosides B	*S. alba*	leaves	[6]
5	Sonneratiosides E	*S. alba*	leaves	[6]
6	9-Oxonerolidol	*S. paracaseolaris*	whole plant	[7]
7	3,7,11-trimethyldodeca-1,7(*E*),10-trien-3-ol-9-one	*S. paracaseolaris*	whole plant	[7]
8	Gibberllinum A1	*S. apetala*	leaves	[8]
9	Gibberllinum A2	*S. apetala*	leaves	[9]
10	Gibberllinum A3	*S. apetala*	leaves	[9]
11	Taraxerol	*S. apetala*	whole plant	[10]
12	*β*-Amyrin	*S. apetala*	whole plant	[10]
13	Betulinic acid	*S. apetala*	aerial parts	[11]
14	Lupenone	*S. apetala*	aerial parts	[11]
15	Betulin	*S. ovata*	trunk	[12]
16	Lupeol	*S. apetala*	aerial parts	[11]
17	Oleanicacid	*S. apetala*	leaves	[8]
18	Ursolic acid	*S. ovata*	trunk	[12]
19	Maslinic acid	*S. paracaseolaris*, *S. ovata*	fruits	[13]
20	Corosolic acid	*S. ovata*	leaves	[14]
21	3-*O*-acetylursolic acid	*S. ovata*	leaves	[14]
22	Paracaseolin E	*S. paracaseolaris*	aerial parts	[15]
23	Paracaseolin A	*S. paracaseolaris*	aerial parts	[15]
24	Paracaseolin B	*S. paracaseolaris*	aerial parts	[15]
25	Paracaseolin C	*S. paracaseolaris*	aerial parts	[15]
26	Paracaseolin D	*S. paracaseolaris*	aerial parts	[15]

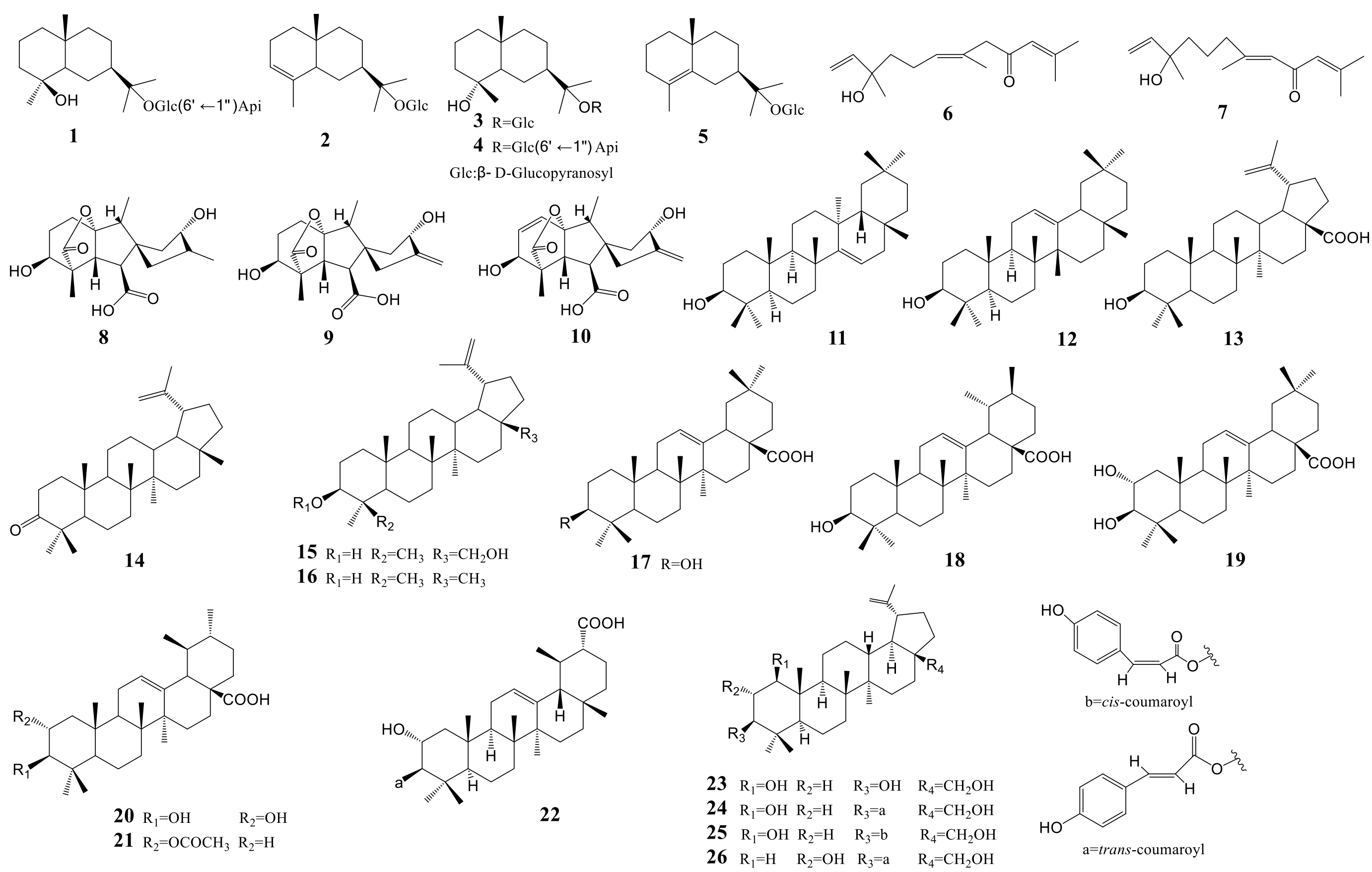

Fig. 1. Chemical structure of terpenoids in *Sonneratia*.

Table 2
Aromatics in *Sonneratia*.

No.	Compound	*S*Plant speciess	PPlant site	[Refs.
27	Luteolin	*S. caesolaris*	leaves	16
28	Luteolin 7-*O*-Glucoside	*S. caesolaris*	leaves	16
29	Aromadendrol	*S. ovata*	trunk	12
30	Isoaromadendrol	*S. ovata*	trunk	12
31	Diosmetin	*S. paracaseolaris*	aerial parts	17
32	Ticin	*S. paracaseolaris*	aerial parts	17
33	5,3′,5′-Trihydroxy-7,4′-dimethoxyflavone	*S. paracaseolaris*	aerial parts	17
34	5-Hydroxy-7,4′-dimethoxyflavone	*S. paracaseolaris*	aerial parts	17
35	5-Hydroxyl-7,3′,4′-trimethoxydihydroflavone	*S. paracaseolaris*	aerial parts	17
36	Sonneradons A	*S. apetala*	fruits	5
37	Sonneradons B	*S. apetala*	fruits	5
38	Hovetrichoside C	*S. paracaseolaris, S. ovata*	fruits	13
39	Sonnerphenolic A	*S. ovata*	leaves	14
40	(−)-Rhodolatouchol	*S. ovata*	leaves	14
41	Sonnerphenolic C	*S. ovata*	leaves	14
42	Syringaldehyde	*S. apetala*	fruits	18
43	1,3-Dihydroxyphenyl-4-pentene-1-ketone	*S. apetala*	fruits	18
44	4′-*O*-Methy-hinokiresinol	*S. ovata*	trunk	12
45	Hnokiresinol	*S. apetala*	fruits	18
46	3′-Hydroxyl-4′-methoxy-4′-dehydroxymetaberberine	*S. apetala*	fruits	18
47	Vanillin	*S. ovata*	trunk	12
48	Sonnerphenolic B	*S. ovata*	leaves	14
49	(−)-(*R*)-Nyasol	*S. ovata*	leaves	14
50	4′-*O*-Methy-*cis*-hinokiresinol	*S. ovata*	trunk	12
51	Acetovanillone	*S. ovata*	trunk	12
52	Abutin	*S. alba*	leaves	6
53	(7*S*,8*R*)-Dehydroconiferyl alcohol	*S. ovata*	leaves	14
54	(7*S*,8*R*)-5-Methoxydehydroconiferyl alcohol	*S. ovata*	leaves	14
55	(7*S*,8*R*)-Urolignoside	*S. ovata*	leaves	14
56	Lingueresinol	*S. ovata*	leaves	14
57	(+)-Isolariciresinol	*S. ovata*	leaves	14
58	(+)-Isolariciresinol 9′-*O*-*β*-D-glucopyranoside	*S. ovata*	leaves	14
59	(−)-Isolariciresinol 9′-*O*-*β*-D-glucopyranoside	*S. ovata*	leaves	14
60	(−)-Episyringaresinol	*S. ovata*	leaves	14
61	(+)-Syringaresinol	*S. ovata*	leaves	14

their endophytes since 2009, which provides the base reference data for further isolation and discovery of active components in *Sonneratia* and its endophytes.

2. Compounds

2.1. Terpenoids

Terpenoids with isoprene as the base structural unit of the molecular skeleton were derived from the methylglutaric acid biosynthetic pathway. *Sonneratia* contains abundant terpenoids with diverse structural types, and the probability of discovering novel compounds is high. The 28 reported terpenoids include 9 sesquiterpenes, 3 diterpenes, and 16 triterpenes. Terpenoids in *Sonneratia* are mainly derived from *S. apetala*, *S. paracaseolaris,* and *S. ovata*. Specific information about the terpenoids is shown in Table 1, and the chemical structure is shown in Fig. 1.

2.2. Aromatics

2.2.1. Flavonoids

There are nine flavonoids reported in *Sonneratia*, which include flavonols, flavonoid glycosides, and other flavonoids. Specific information about the flavonoids is shown in Table 2, and the chemical structure is shown in Fig. 2.

2.2.2. Phenols

Fifteen phenols (**36**–**52**) have been reported in *Sonneratia*. The structure of sonnerphenolic A (**39**) is a 1,4-dihydroxycyclopentane ring with two 4-hydroxyphenyl groups at the C-2 and C-3 positions. The specific information about the phenols is shown in Table 2, and the chemical structure is shown in Fig. 3.

2.2.3. Lignans

Lignans are natural products that are formed through the oxidative polymerization of phenylpropanoid and usually refer to their dimers; however, a few exist as trimers and tetramers. There are 9 previously reported lignans (**53**–**61**) in *Sonneratia*, and all have been isolated from *S. ovata*, including 3 simple lignans, 4 cyclolignans, and 2 bicyclic lignans. The specific information about the lignans is shown in Table 2, and the chemical structure is shown in Fig. 4.

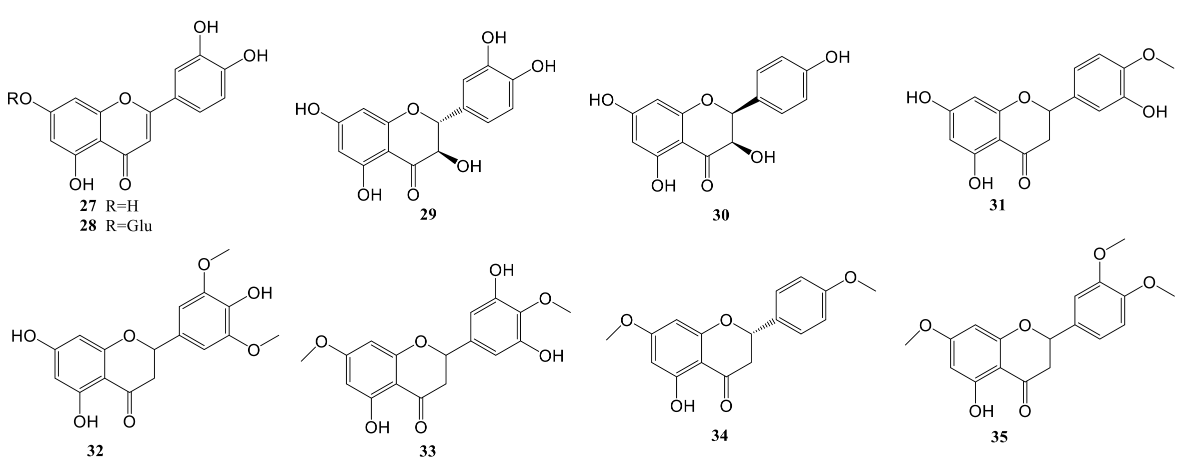

Fig. 2. Chemical structure of flavonoids in *Sonneratia*.

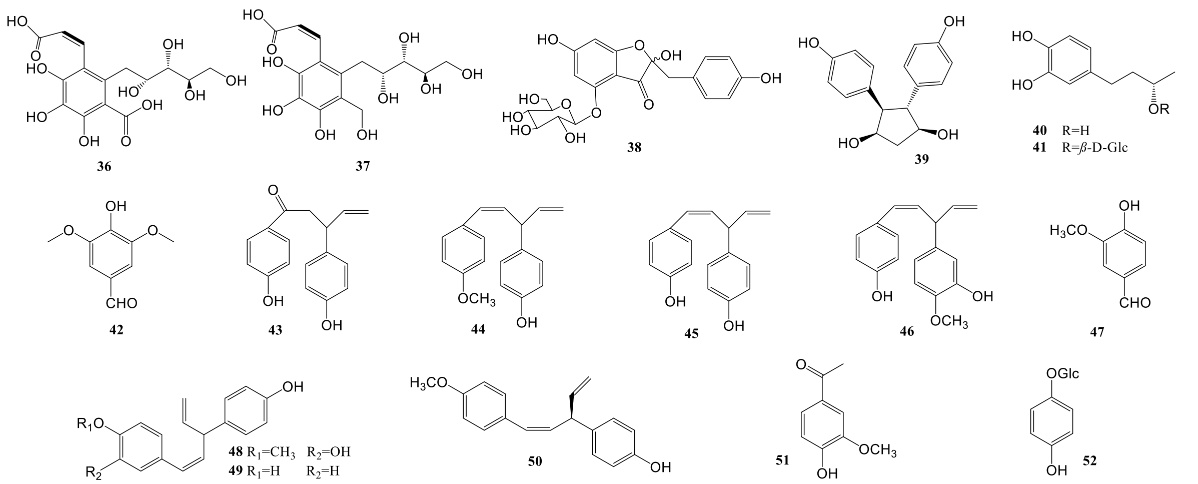

Fig. 3. Chemical structure of phenols in *Sonneratia*.

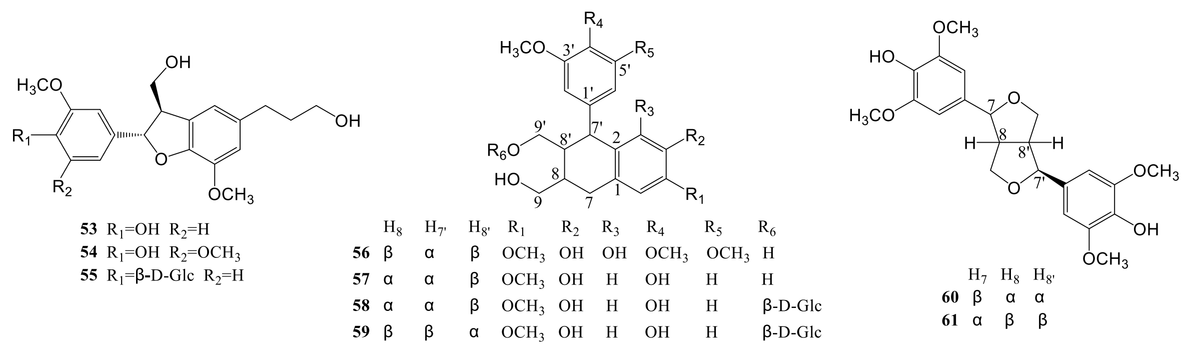

Fig. 4. Chemical structure of lignans in *Sonneratia*.

2.3. Acids and lipids

In *Sonneratia,* there are 27 acids and lipids (**62**–**88**), which mainly include phenolic acids, aliphatic acids, and their derivatives. The specific information about the acids and lipids is shown in Table 3, and their chemical structures are shown in Fig. 5.

2.4. Steroids

Steroids are compounds with a cyclopentane polyhydrophenanthrene carbon frame structure. There are 16 reported steroid compounds (**89**–**104**) in *Sonneratia*, mainly originating from *S. caesolaris*, *S. paracaseolaris*, *S. ovata,* and *S. apetala*. The structural types include sterols, sterones, and other steroids. The specific information about the steroids is shown in Table 4, and the chemical structure is shown in Fig. 6.

2.5. Other compounds

There are 12 compounds (**105**–**116**) reported in *Sonneratia* that include three anthraquinone compounds (**109**–**111**), namely emodin methyl ether, chrysophanol, and emodin. These three compounds were isolated and structurally determined from *S. caesolaris* by Chaudhry in 1950, which marks the first report of the compounds from *S. caesolaris*.[21] The R-alkylbutenolide substructure is frequently encountered in a variety of pharmacologically active natural compounds, such as the anti-leukemic/neuroprotective labdane pinusolide, novel antimalarial clerodane gomphostinin, and substantial antitumor acetogenin (annomolon A). In addition, *R*-substituted butenolides are also important intermediates in the synthesis of other important targets, including a host of antimicrobial and herbicidal lactones. Paracaseolide A (**106**) is an *R*-alkylbutenolide dimer that is characterized by an unusual tetraquinane oxa-cage bislactone skeleton bearing two linear alkyl chains, which was isolated from *S. paracaseolaris*.[22] Sonnercerebroside (**113**) is a novel cerebroside, and its structure is 1-*O*-*β*-D-glucopyranosyl-(2*S*,3*R*,20*R*,4*E*,13*E*)-2-*N*-(20-hydroxyhexadecanoylamino)octadeca-4,13-dien-3-ol.[15] Sonneratine A (**115**) is a diphenacyl-piperidine alkaloid and was the first 2,6-disubstituted piperidine alkaloid isolated from *S. hainanensis*.[23] The specific information about the other compounds is shown in Table 5, and the chemical structure is shown in Fig. 7.

3. Activities

Plants from the genus *Sonneratia* mainly have antioxidant, antitumor, liver protection, antibacterial, antidiabetic, antidiarrheal, kidney protection, and lung protection activity. Most of these activity experiments are based on the extracts from different parts of the *S. apetala* plant. There are a few reports on the activities of monomer compounds, which mainly focus on antitumor activity research. Some compounds have outstanding activities that are deserving of further research. For example, paracaseolide A (**106**) was reported in 2011 and showed significant inhibitory activity against bispecific phosphatase Recombinant Cell Division Cycle Protein 25B (CDC25B) and achieved full synthesis the following year.[26]

3.1. Antioxidant

Research on the antioxidant activities of *Sonneratia* has mainly focused on its extracts. Ethanol extracts from the branches and leaves of *S. caesolaris* have high antioxidant and anti-Methicillin resistant

Table 3
Acidic and lipids in *Sonneratia*.

No.	Compound	Plant species	Plant site	Refs.
62	Vanillic acid	*S. apetala*	fruits	18
63	Methyl gallate	*S. apetala*	fruits	18
64	3,4-Dihydroxy-5-methoxybenzoic acid	*S. apetala*	fruits	18
65	Syringate	*S. apetala*	fruits	18
66	Methyl 4-hydroxybenzoate	*S. apetala*	fruits	18
67	Gallic acid	*S. ovata*	trunk	12
68	Sonneradon C	*S. apetala*	fruits	5
69	3,3′-Dimethoxy ellagic acid	*S. ovata*	trunk	12
70	3,3′,4-Trirnethoxy-4′-hydroxydiphenic acid dilactone	*S. paracaseolaris*	aerial parts	17
71	Decanoic acid	*S. caesolaris*	whole plant	19
72	Gallic acid 3-*O*-*β*-D-glucopyranoside	*S. ovata*	leaves	14
73	Sonneradon D	*S. apetala*	fruits	5
74	6-*O*-Galloyl-D-glucopyranose	*S. ovata*	leaves	14
75	1-*O*-Benzyl-6-*O*-galloyl-*β*-D-glucopyranose	*S. ovata*	leaves	14
76	4-Ethoxy-3-hydroxy-4-oxobutanoic acid	*S. apetala*	fruits	18
77	Dimethyl malate	*S. apetala*	fruits	18
78	Ethylmethyl malate a	*S. apetala*	fruits	18
79	Ethylmethyl malate b	*S. apetala*	fruits	18
80	Butylethyl malate a	*S. apetala*	fruits	18
81	Butylethyl malate b	*S. apetala*	fruits	18
82	Bibutyl malate	*S. apetala*	fruits	18
83	Butylmethyl malate a	*S. apetala*	fruits	18
84	Butylmethyl malate b	*S. apetala*	fruits	18
85	(*E*)-Ethyl 3-(4-hydroxyphenyl) acrylate	*S. paracaseolaris*	aerial parts	17
86	3-Monopalmitin	*S. caesolaris*	whole plant	19
87	Salicylic acid	*S. paracaseolaris*	aerial parts	17
88	3,4,5-Trimethyl ether gallic acid	*S. paracaseolaris*	aerial parts	17

Table 4
Steroids in *Sonneratia*.

No.	Compound	Plant species	Plant site	Refs.
89	*β*-Sitosterol	*S. caesolaris*	stems, twigs	20
90	*β*-Sitosterol palmitate	*S. caesolaris*	stems, twigs	20
91	Stigmast-5-en-3*β*-*O*-(6-*O*-hexadecanoyl-*β*-D-glucopyranoside	*S. caesolaris*	stems, twigs	20
92	6′-Acetyl-*β*-daucosterol	*S. caesolaris*	stems, twigs	20
93	Daucosterol	*S. caesolaris*	stems, twigs	20
94	*β*-Daucosterol	*S. ovata*	trunk	12
95	Cholesterol	*S. caesolaris*	stems, twigs	20
96	Cholest-5-en-3*β*,7*α*-diol	*S. caesolaris*	stems, twigs	20
97	20*S*,24*R* epoxy damamane-3*β*,25-diol	*S. ovata*	trunk	12
98	Stigmaster-4-alkene-3-ketone	*S. ovata*	trunk	12
99	(22*E*,24*R*)-5*α*,*α*-Peroxyergosterol-23-methyl-6,22-diene-3*β*-alcohol	*S. caesolaris*	whole plant	7
100	(22*E*)-5*α*,8*α*-Peroxyergosterol-23-methyl-6,9,22-triene-3*β*-alcohol	*S. caesolaris*	whole plant	7
101	(22*E*)-5*α*,8*α*-Peroxyergosterol-6,22-diene-3*β*-alcohol	*S. caesolaris*	whole plant	7
102	Stigmast-5-en-3*β*-*O*-(6-*O*-acetyl-*β*-D-glucopyranoside)	*S. caesolaris*	whole plant	19
103	Stigmaster-4-alkene-3,6-diketone	*S. paracaseolaris*	aerial parts	17
104	Stigmaster-4,22-diene-3,6-diketone	*S. paracaseolaris*	aerial parts	17

Staphylococcus aureus (MRSA) activity. Antioxidant activity measurements have shown that the extract exhibited antioxidant activity comparable to that of ascorbic acid, with IC_{50} values of 4.2499 and 5.2456 ppm, respectively.[27,28] The ethyl acetate extract of *S. caesolaris* showed excellent antioxidant activity in four evaluation systems (e.g., antioxidant activity test system for superoxide anion radicals, 1,1-diphenyl-2-picrylhydrazyl (DPPH) radicals, 2,2′-azino-bis(3-ethylbenzothiazoline-6-sulfonic acid) diammonium salt (ABTS) radical scavenging ability, and reducing ability). The DPPH radical scavenging activity (IC_{50} = 1.69 μM) is significantly stronger than that of the positive control vitamin E (VE) (IC_{50} = 6.06 μM),

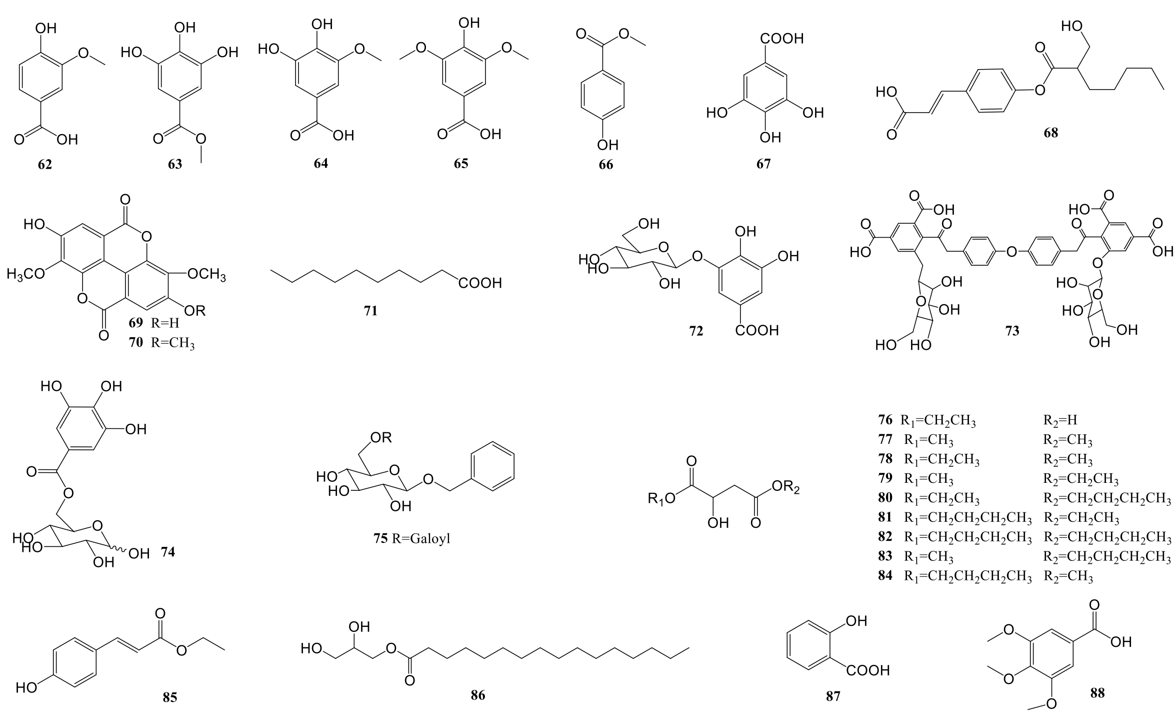

Fig. 5. Chemical structure of acids and lipids in *Sonneratia*.

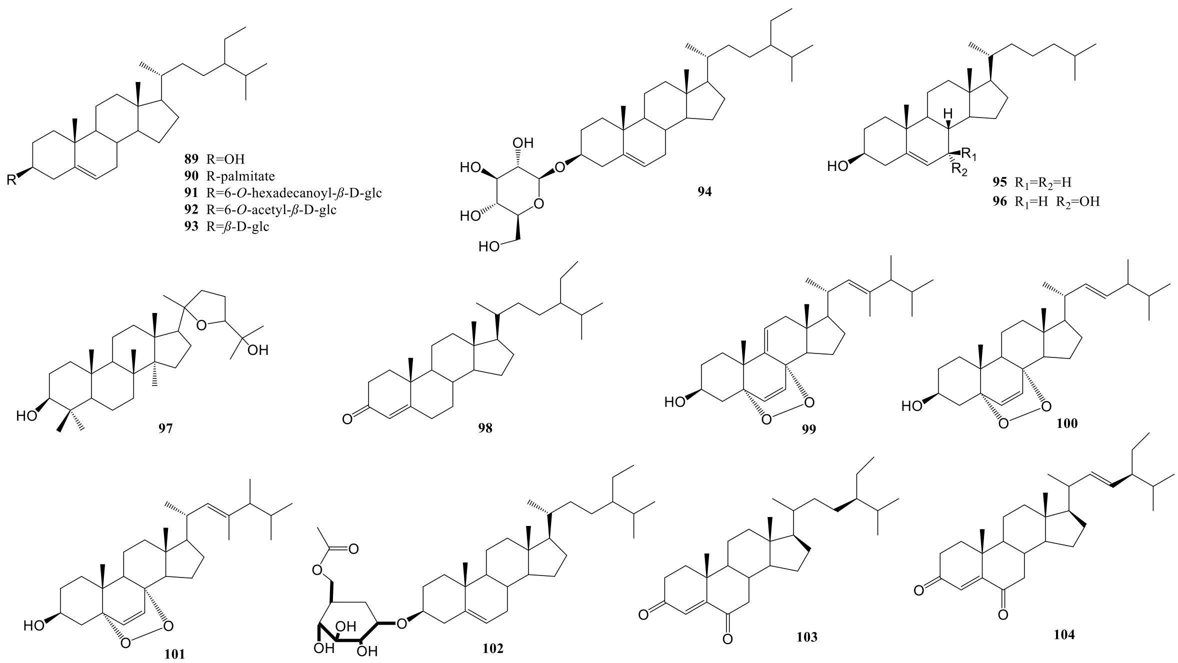

Fig. 6. Chemical structure of steroids in *Sonneratia*.

while the superoxide anion radical scavenging activity ($IC_{50} = 0.35$ μM) and positive control vitamin C (VC) ($IC_{50} = 0.30$ μM) were similar.[29] The ethanol extract of *S. apetala* showed good antioxidant activity in the evaluation of DPPH free radical scavenging and reducing ability. The IC_{50} values of DPPH free radical, hydrogen peroxide free radical, hydroxyl radical, and superoxide anion scavenged by the extract were 71.77, 97.27, 79.62, and 108.89 μM, respectively. Some studies have revealed that the extract of *S. apetala* fruit can effectively improve the activity of superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) in the bodies of aging mice induced by D-neneneba galactose and reduced the content of malondialdehyde (MDA) ($P < 0.05$). This indicates that the extract can effectively improve antioxidant activity in the bodies of aging mice induced by D-galactose, thus achieving the effect of delayed aging.[30]

Table 5
Other compounds in *Sonneratia*.

No.	Compound	Plant species	Plant site	Refs.
105	Triacontanol	*S. apetala*	leaves	24
106	Paracaseolide A	*S. paracaseolaris*	stem bark	23
107	Benzyl-*O*-*β*-glucopyranoside	*S. paracaseolaris, S. ovata*	fruits	13
108	Bis(2-ethylhexyl)benzene-1,2-dicarboxylate	*S. caesolaris*	stems, twigs	20
109	Rheochrysidin	*S. apetala*	aerial parts	11
110	Chrysophanic acid	*S. caesolaris*	whole plant	21
111	Frangula emodin	*S. caesolaris*	whole plant	21
112	2-Nitro-4-(2-nitroethenyl) phenol	*S. caesolaris*	whole plant	23
113	Sonnercerebroside	*S. ovata*	leaves	15
114	(−)-Lobeline	*S. hainanensis*	leaves, stems	25
115	Sonneratine A	*S. hainanensis*	leaves, stems	25
116	(±)1-(2-Piperidyl)-4-(*p*-methoxyphenyl)-butanone-2	*S. hainanensis*	leaves, stems	25

3.2. Antitumor

Antitumor activity is one of the most important compound activities of *Sonneratia*, and multiple reported compounds have exhibited good inhibitory effects on different tumor cell lines. Luteolin (**27**) that was isolated from *S. caesolaris* showed significant cytotoxicity test *in vitro* activity against SMMC-7721 human liver cancer cells, with an IC_{50} value of 2.8 μM.[17] Paracaseolin D (**26**) exhibited significant cytotoxicity against A549 cells with an IC_{50} value of 1.89 μM. Paracaseolin A (**23**) exhibited significant anti-H1N1 virus activity with an IC_{50} of 28.4 μM[16] 3′-Hydroxy-4′-methoxy-4′-dehydroxymetaberberine (**46**) has strong cytotoxic activity against the K562 and HL-60 cell lines, with IC_{50} values of 1.99 and 3.13 μM, respectively.[19] (7*S*,8*R*)-Dehydroconiferol alcohol (**53**) and (7*S*, 8*R*)-5-methoxydehydroconiferol alcohol (**54**) has been reported in *S. ovata* and shows cytotoxic activity against MCF-7 cell lines, with IC_{50} values of 146.9 ± 9.0 μM and 114.5 ± 7.2 μM, respectively. Sonnerphenolic C (**41**) demonstrated cytotoxicity against MCF-7 cells, with an IC_{50} value of 112.8 μM.[15] The methanol extract from *S. apetala* showed an inhibitory effect on EAC cells in Swiss Albino mice with an inhibition rate of 34%.[31]

3.3. Liver protection

Previous studies have shown that the crude polysaccharide of *S. apetala* fruit (SAP) can significantly inhibit the increase of liver index and serum transaminase levels caused by acetaminophen (APAP) and alleviate liver tissue damage caused by excessive APAP, i.e., the polysaccharides of *S. apetala* fruit can alleviate the hepatotoxicity of APAP.[32] *S. caesolaris* fruit extract (SAFE) has a potential protective effect on acute liver injury induced by APAP. Experimental results have shown that it significantly improved the survival rate of mice and reduced the serum levels of alanine transaminase and aspartate aminotransferase exposed to APAP. SAFE treatment also increased the levels of glutathione (GSH) and activity of GSH-Px, enhanced the activity of catalase (CAT) and total antioxidant capacity (T-AOC), and reduced the level of MDA in the liver. These results indicate that *S. apetala* and its fruits can serve as a new source of functional foods with liver protection effects.[33]

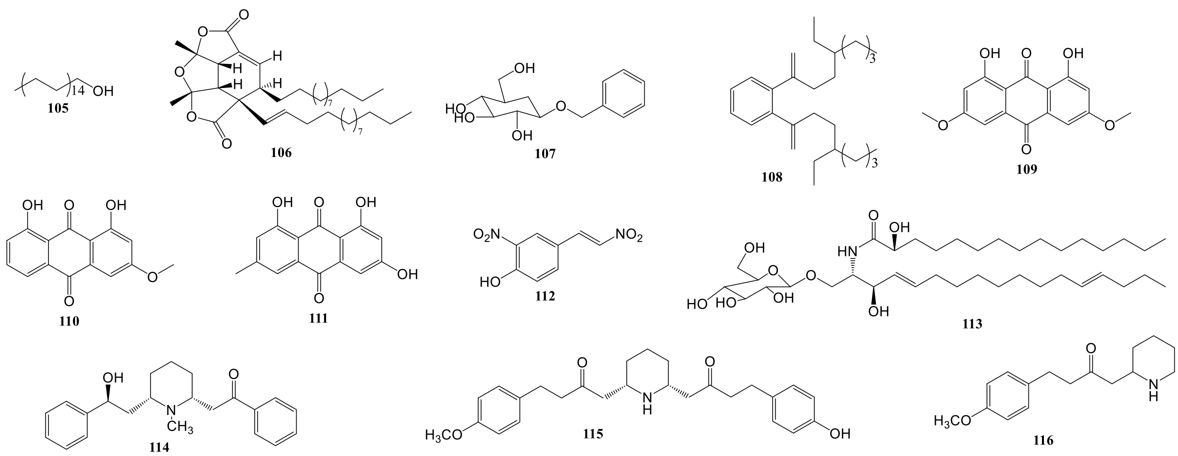

Fig. 7. Chemical structure of other compounds in *Sonneratia*.

3.4. Antibacterial

Reports on the antibacterial activity of *Sonneratia* have involved *S. caesolaris* and *S. alba*. The extract from *S. caesolaris* branches and leaves contains high levels of antibacterial polyphenols, of which 12.4% is composed of non-toxic flavonoids. Liquid chromatography with tandem mass spectrometry (LC-MS/MS) results have shown that phenolic compounds such as azelaic acid and aspirin, as well as flavonoid glycosides such as isovitexin and quercetin, were found in the extract. The minimum inhibitory concentration of ethanol extract from *S. caesolaris* on MRSA was approximately 5000 ppm.[34] The methanol extract from *S. apetala* seeds has a strong inhibitory effect on *Escherichia coli*, *Salmonella paratyphi A*, *Salmonella typhi*, *Shigella dysenteriae,* and *Staphylococcus aureus*. The IC_{50} values of 500 μg/disc for the above strains were 0.59, 0.28, 1.63, 0.83, and 1.1 μM, respectively. Therefore, the methanol extract from *S. apetala* seeds may inhibit all bacteria except *Vibrio cholerae*.[35] The methanol extract of *S. caesolaris* has a good inhibitory effect on *E. coli*, *S. aureus,* and *Bacillus cereus*, with an inhibition ring diameter of 17.5, 12.5, and 12.5 mm, respectively. However, no inhibition rings were observed for *Pseudomonas aeruginosa* or *Candida albicans*.[36] In summary, *S. alba*, *S. apetala,* and *S. caesolaris* may have an excellent therapeutic effect in the treatment of infectious bacterial diseases and can be used as a source of related drug compounds.

3.5. Antidiabetic

Research has found that the acetone, ethanol, methanol, and water extracts from *S. apetala* all exhibited significant effects on dose-dependent α-glucosidase inhibitory activity. Seeds of *S. apetala* contained a large amount of polyphenols (300 ± 8.2 mg GAE/g extract), flavonoids (30.6 ± 0.7 CE/g extract), anthocyanin (2.3 μM/g extract), and VC (4.0 mg/g extract). In type 2 diabetic rats induced through streptozotocin (STZ), the blood glucose in the seed extract treatment group was 13.75 μM (30 min) that dropped to 10.3 μM (135 min), and the blood sugar in the peel treatment group decreased from 14.36 to 11.32 μM. Compared with the peel treatment group, the area under the glucose curve of the seed treatment group was significantly reduced. The fruit and seed extracts of *S. apetala* have significant antidiabetic activity, and the seeds are especially rich in phenols, flavonoids, and antidiabetic compounds.[3,31]

3.6. Other activities

Studies have shown that the *n*-hexane, ether, chloroform, ethyl acetate, and methanol extracts of *S. apetala* seed powder at 500 mg/kg strongly inhibited the onset and onset time of diarrhea induced by castor oil in mice ($P < 0.001$). At the same concentration, the methanol extract had the strongest inhibitory activity on diarrheal episodes in mice, while the *n*-hexane extract significantly prolonged the duration of the diarrheal episodes compared to the positive control group ($P < 0.05$).[36] A study on acute biological toxicity revealed that under the condition of 5000 mg/kg, the extract of the fruit, branches, and leaves of *S. apetala* did not produce toxicity in rats; the mortality rate was 0 at 14 days; and the median lethal dose was greater than 5000 mg/kg body weight, which is considered a non-toxic substance. Within the same fish species, the toxicity of fruit water extract is stronger than that of leaf water extract, and with the same water extract, the sensitivity of marbled fish to the toxicity was greater than that of zebrafish. *S. apetala* is thus a low-toxicity substance.[37] The 10 mg/kg 90% ethanol extract of *S. apetala* fruit alleviated neutrophil elastase-induced alveolar collapse in a mouse model, which indicates that *S. apetala* fruit extract has the potential to inhibit human neutrophil elastase.[38] In addition, ethanol, ethyl acetate, and *n*-butanol extracts of *S. apetala* fruit can improve learning and memory ability by increasing the activity of endogenous antioxidant enzymes (SOD, GSH-Px) in the brains of aging mice induced by D-galactose and reducing the content of NO and MAO activity in the brain.[39] Paracaseolide A (**106**) has significant pharmacological activity against the bispecific phosphatase CDC25B, with an IC_{50} value of 6.44 μM.[23] Sonneradon A (**36**) exhibited the most potent effect in the anti-heat stress assay and significantly attenuated the age-related decrease in the pumping and bending of nematodes in the health span assay. Molecular docking studies have shown that sonneradon A (**36**) binds to the DNA binding domain of HSF-1, which promotes the conformation of HSF-1 and strengthens the interaction between HSF-1 and related DNA.[5]

4. Compounds and bioactivities of *Sonneratia* endophytes

In 2009, Julia et al. isolated the endophytic fungus *Alternaria* from *S. alba* and six compounds (**117**–**122**) were obtained from its extract.[40] In 2011, Li et al. studied the endophytic fungus *Talaromyces flavus* from *S. apetala* and isolated four demethylated sesquiterpene peroxides, talaperoxides A-D (**123**, **125**–**127**). Talaperoxide B (**125**) and talaperoxide D (**127**) exhibited cytotoxicity against the human cancer cell lines MCF7, MDA-MB-435, HepG-2, HeLa, and PC-3, with IC_{50} values ranging from 0.70 to 2.78 μM.[41] In 2012, Weaam Ebrahim et al. studied the ethyl acetate extract of the endophytic fungus *Bionectria ochroluca* from *S. caseolaris*, and two peptide compounds, pullularins E and F (**128**, **129**) and three known compounds (**130**–**132**), were identified.[42] In 2013, Rönsberg et al. isolated the endophytic fungus *Pestalotiopsis virgatula* from *S. caseolaris*, obtained five pyranones (**133**–**137**) from its ethyl acetate extract, and performed a variety of activity tests on the obtained compounds; however, none of them were active.[43] In 2015, torrubiellin B

Table 6
Compounds from endophytes in *Sonneratia*.

No.	Compound	Plant species	Endophytes	Refs.
117	Xanalteric acids I	*S. alba*	*Alternaria*	40
118	Xanalteric acids II	*S. alba*	*Alternaria*	40
119	Altenusin	*S. alba*	*Alternaria*	40
120	Altertoxin I	*S. alba*	*Alternaria*	40
121	Alterperylenol	*S. alba*	*Alternaria*	40
122	Stemphyperylenol	*S. alba*	*Alternaria*	40
123	Talaperoxides A	*S. apetala*	*Talaromyces flavus*	41
124	Steperoxide B	*S. apetala*	*Talaromyces flavus*	41
125	Talaperoxides B	*S. apetala*	*Talaromyces flavus*	41
126	Talaperoxides C	*S. apetala*	*Talaromyces flavus*	41
127	Talaperoxides D	*S. apetala*	*Talaromyces flavus*	41
128	Pullularin E	*S. caseolaris*	*Bionectria ochroleuca*	42
129	Pullularin F	*S. caseolaris*	*Bionectria ochroleuca*	42
130	Pullularins A	*S. caseolaris*	*Bionectria ochroleuca*	42
131	Pullularins C	*S. caseolaris*	*Bionectria ochroleuca*	42
132	Verticillin D	*S. caseolaris*	*Bionectria ochroleuca*	42
133	Pestalotiopyrones I	*S. caseolaris*	*Pestalotiopsis virgatula*	43
134	Pestalotiopyrones J	*S. caseolaris*	*Pestalotiopsis virgatula*	43
135	Pestalotiopyrones K	*S. caseolaris*	*Pestalotiopsis virgatula*	43
136	Pestalotiopyrones L	*S. caseolaris*	*Pestalotiopsis virgatula*	43
137	(6*S*,10*S*,20*S*)-Hydroxypestalotin	*S. caseolaris*	*Pestalotiopsis virgatula*	43
138	Torrubiellin B	*S. caseolaris*	*Acremonium*	44
139	Nectriacids A	*S. ovata*	*Nectria* sp. HN001	45
140	Nectriacids B	*S. ovata*	*Nectria* sp. HN001	45
141	Nectriacids C	*S. ovata*	*Nectria* sp. HN001	45
142	12-Epicitreoisocoumarinol	*S. ovata*	*Nectria* sp. HN001	45
143	Citreoisocoumarinol	*S. ovata*	*Nectria* sp. HN001	45
144	Citreoisocoumarin	*S. ovata*	*Nectria* sp. HN001	45
145	Macrocarpon C	*S. ovata*	*Nectria* sp. HN001	45
146	Peniphenone	*S. apetala*	*Penicillium*	46
147	Methyl peniphenone	*S. apetala*	*Penicillium*	46
148	Conioxanthone A	*S. apetala*	*Penicillium*	46
149	Methyl 8-Hydroxy-6-methyl-9-oxo-9*H*-xanthene-1-carboxylate	*S. apetala*	*Penicillium*	46
150	Pinselin	*S. apetala*	*Penicillium*	46
151	Sydowinin B	*S. apetala*	*Penicillium*	46
152	Sydowinin A	*S. apetala*	*Penicillium*	46
153	Remisporine B	*S. apetala*	*Penicillium*	46
154	Epiremisporine B	*S. apetala*	*Penicillium*	46
155	Acorenone C	*S. apetala*	*Pseudofusicoccum*	47
156	Uracil	*S. apetala*	*Pseudofusicoccum*	47
157	Cyclo(L-Pro-L-Tyr)	*S. apetala*	*Pseudofusicoccum*	47
158	Bis-(2-ethylhexyl) terephthalate	*S. apetala*	*Pseudofusicoccum*	47
159	4-Hydroxybenzaldehyde	*S. apetala*	*Pseudofusicoccum*	47
160	2-Phenylethanol	*S. apetala*	*Pseudofusicoccum*	47
161	4-Hydroxyphenethyl-alcohol	*S. apetala*	*Pseudofusicoccum*	47
162	Estigmast-4-en-6β-ol-3-ona	*S. apetala*	*Pseudofusicoccum*	47
163	Ergosterol	*S. apetala*	*Pseudofusicoccum*	47
164	Ergosterol peroxide	*S. apetala*	*Pseudofusicoccum*	47
165	Cerevisterol	*S. apetala*	*Pseudofusicoccum*	47
166	Cytoindenones A	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
167	3′-Methoxycytoindenone A	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
168	Cytoindenones B	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
169	Cytoindenones C	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
170	Cytosporaphenones E	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
171	Cytorhizophin J	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48
172	(±)-4,6-Dihydroxy-5-methoxy-α-tetralone	*S. caseolaris*	*Cytospora heveae* NSHSJ-2	48

(**138**) was isolated from the branches and leaves of *S. caseolaris*, and the absolute configuration of torrubiellin B (**138**) was established as (50′*R*, 100′*S*,10a′*R*) based on its electronic circular dichroism (ECD) spectra aided with TDDFT-ECD calculations.[44] In 2016, Cui et al. isolated four novel polyketone compounds from the culture medium of *Necria* sp. HN001 of *S. ovata*. Four new polyketides: nectriacids A-C (**139**–**141**) and 12-epicitreoisocoumarinol (**142**), together with three known compounds: citreoisocoumarinol (**143**), citreoisocoumarin (**144**), and macrocarpon C (**145**) were isolated. The absolute configuration of the stereogenic carbons for 12-epicitreoisocoumarinol (**142**) was further assigned using the Mosher ester method.[45] In 2016, Liu et al. isolated nine polyketones from the endophytic fungus *Penicillium* from *S. apetala*, which included two new benzophenone derivatives, peniphenone (**146**) and methyl peniphenone (**147**), along with seven known xanthones (**148**–**154**). Compounds **146**, **148**, **150,** and **152** exhibited strong immunosuppressive activity with IC_{50} values ranging from 5.9 to 9.3 μM.[46] In 2021, Jia et al. isolated the endophytic fungus *Pseudofusicoccum* sp. J003 from *S. apetala* for the first time. Researchers have subsequently conducted chemical studies on the methanol extract of the strain culture medium, and a new sesquiterpenoid named acorenone C (**155**) was isolated along with two alkaloids (**156**, **157**), four phenolics (**158**–**161**), and four sterol derivatives (**162**–**165**). The *in vitro* AChE inhibitory, anti-inflammatory, and cytotoxic activities of selected compounds were evaluated. Compound **155** showed mild AChE inhibitory activity, with an inhibition rate of 23.34% at a concentration of 50 μM. Compound **163** exerted a significant inhibitory effect against NO production in lipopolysaccharide (LPS)-stimulated RAW 264.7 mouse macrophages, with an inhibition rate of 72.89% at a concentration of 25 μM, which was greater than that of the positive control L-NMMA.[47] In 2023, Ge et al. isolated the endophytic fungus *Cytospora heveae* NSHSJ-2 from the fresh stem of *S. caseolaris*. Subsequent research discovered seven new polyketides, including four indenone derivatives, cytoindenones A-C (**166, 168, 169**), 3′-methoxycytoindenone A (**167**), a benzophenone derivative, cytorhizophin J (**171**), and a pair of tetralone enantiomers, (±)-4, 6-dihydroxy-5-methoxy-α-tetralone (**172**), along with a known compound (**170**). Cytoindenones B (**168**) represented the first identified natural indenone monomer substituted by two benzene moieties at the C-2 and C-3 positions. In bioactivity assays, compounds **166, 169**–**171** showed potent DPPH-scavenging activity, with EC_{50} values ranging from 9.5 to 16.6 μM, which was greater than that of the ascorbic acid positive control (21.9 μM). The specific information about the other compounds is shown in Table 6, and the chemical structure is shown in Fig. 8.[48]

5. Summary

To date, 172 compounds have been isolated from *Sonneratia* and its endophytes. Interestingly, some compounds or analogs were produced by both plants and their endophytes. The potential allelopathy of the chemical interactions between *Sonneratia* and their endophytes provides ample research opportunities. Compounds in *Sonneratia* are abundant, including terpenoids, steroids, lignans, and alkaloids, some of which exhibit significant activity (e.g., talaperoxide B (**125**) showed cytotoxicity against the PC-3 human cancer cell line with an IC_{50} value of 0.89 μg/mL). In recent years, endophyte compounds from *Sonneratia* have attracted further investigation. Endophyte resources have greatly expanded the sources of natural products, and these resources have the convenience for biosynthetic manufacturing, sustainable resource

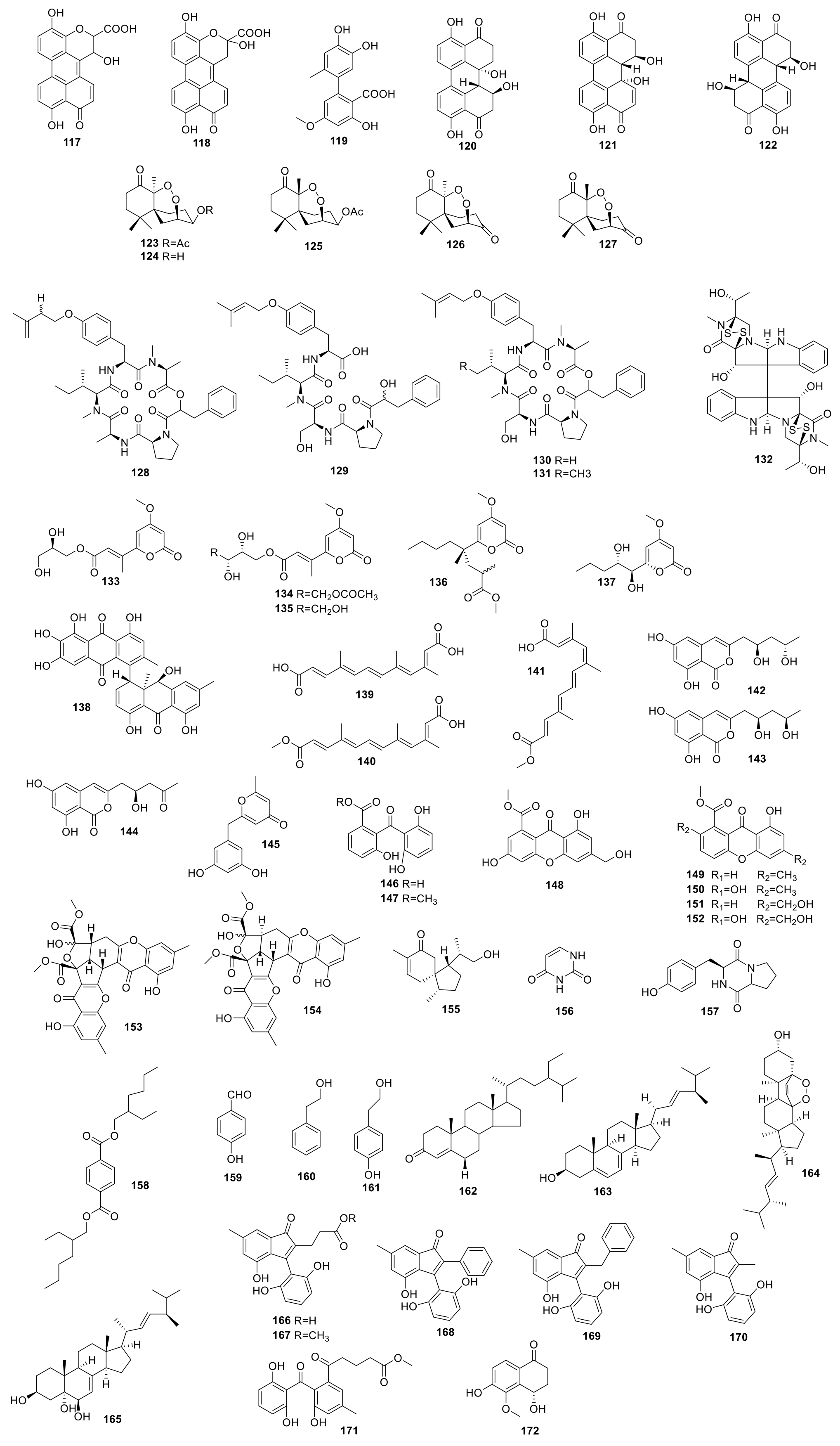

Fig. 8. Chemical structure of compounds of endophytes in *Sonneratia*.

utilization, and feasible genetic manipulation, which provides a broader scope for the development of synthetic biology and its related disciplines.

The study of the natural product of the endophytes of *Sonneratia* was first reported in 2009. In the following years, many compounds with novel structures were identified, including 56 isolated compounds, which were mainly sesquiterpene peroxides, peptides, phenanthropyran ring-structured acids, pyranones, and anthracene derivatives. However, compared to other mangrove plants, most research on *Sonneratia* only considers the ecology and environmental evaluation thereof, with just a few studies focusing on its compounds and activities. For example, as a unique species (*S. hainanensis),* which is distributed in the Hainan province, there has only been one literature report on its compounds.[24] Activity research on *Sonneratia* has mainly focused on the crude extracts, and only a few compounds have been tested for their biological activity. The research depth of the compounds and their activities in *Sonneratia* are insufficient, and further research is required. The genus *Sonneratia* still has a large scope for future investigation. Further research can focus on identifying compounds by using different separation and purification technologies and discovering compounds with enhanced activities, thus contributing to human health.

CRediT authorship contribution statement

Bin Liu: Conceptualization, Data curation, Software, Writing – original draft, Writing – review & editing. **Xin Wang:** Funding acquisition. **Yiming Wang:** Software. **Xiaohong Chen:** Software. **Xiaobao Jin:** Funding acquisition. **Xiongming Luo:** Data curation, Funding acquisition, Methodology, Supervision, Validation.

Declaration of competing interest

All authors have no conflict of interest to declare.

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