Review

Bioactive Secondary Metabolites of the Genus *Diaporthe* and Anamorph *Phomopsis* from Terrestrial and Marine Habitats and Endophytes: 2010–2019

Tang-Chang Xu, Yi-Han Lu, Jun-Fei Wang, Zhi-Qiang Song, Ya-Ge Hou, Si-Si Liu, Chuan-Sheng Liu and Shao-Hua Wu *

Yunnan Institute of Microbiology, School of Life Sciences, Yunnan University, Kunming 650091, China; xu2950129@163.com (T.-C.X.); luyihan1995@126.com (Y.-H.L.); wang_junfei@163.com (J.-F.W.); songzhiquan1996@126.com (Z.-Q.S.); houyage@126.com (Y.-G.H.); liusisi1994@126.com (S.-S.L.); liucs313@126.com (C.-S.L.)

* Correspondence: shwu123@126.com

Abstract: The genus *Diaporthe* and its anamorph *Phomopsis* are distributed worldwide in many ecosystems. They are regarded as potential sources for producing diverse bioactive metabolites. Most species are attributed to plant pathogens, non-pathogenic endophytes, or saprobes in terrestrial host plants. They colonize in the early parasitic tissue of plants, provide a variety of nutrients in the cycle of parasitism and saprophytism, and participate in the basic metabolic process of plants. In the past ten years, many studies have been focused on the discovery of new species and biological secondary metabolites from this genus. In this review, we summarize a total of 335 bioactive secondary metabolites isolated from 26 known species and various unidentified species of *Diaporthe* and *Phomopsis* during 2010–2019. Overall, there are 106 bioactive compounds derived from *Diaporthe* and 246 from *Phomopsis*, while 17 compounds are found in both of them. They are classified into polyketides, terpenoids, steroids, macrolides, ten-membered lactones, alkaloids, flavonoids, and fatty acids. Polyketides constitute the main chemical population, accounting for 64%. Meanwhile, their bioactivities mainly involve cytotoxic, antifungal, antibacterial, antiviral, antioxidant, anti-inflammatory, anti-algae, phytotoxic, and enzyme inhibitory activities. *Diaporthe* and *Phomopsis* exhibit their potent talents in the discovery of small molecules for drug candidates.

Keywords: ascomycetes; endophytic fungi; plant pathogens; biological activities; natural products

1. Introduction

*Diaporthe* is an important fungal genus of plant pathogens [1] belonging to the family Diaporthaceae, order Diaporthales, class Sordariomycetes [2]. It is mainly isolated from various hosts distributed in tropical and temperate zones and can cause diseases to a wide range of plant hosts, as well as humans and other mammals [3,4]. The ascomycetes of *Diaporthe* Nitschke 1870 and *Phomopsis* (Sacc.) Bubák 1905 are regarded to form a genus [5,6]. In Index Fungorum (2020), more than 1120 records of *Diaporthe* and 986 of *Phomopsis* are listed (http://www.indexfungorum.org/, accessed December 2020). There is a common understanding that, in these ascomycetes, the teleomorph states are named as *Diaporthe* and the anamorph states called as *Phomopsis* [7–10]. For a long time, a dispute has remained concerning whether the generic name should be defined as *Diaporthe* or *Phomopsis*. Due to the importance of this genus as plant pathogens, the classification of *Diaporthe* has been discussed by many researchers. Since *Diaporthe* was cited earlier and represents most of the species described in nature, more mycologists suggest that the use of *Diaporthe* as a generic name have more priority and is more suitable for the current study of this fungal group [11–13]. In recent years, the previous classification methods based on morphological characteristics are no longer applicable to the genus *Diaporthe* and advanced molecular
techniques will replace them to solve the classification problem of Diaporthe [13,14]. In this review, we use the older name Diaporthe as the generic name.

Based on the existing literature investigations, more secondary metabolites have been separated from Phomopsis than Diaporthe. To date, a large number of compounds have been isolated from endophytic fungi of terrestrial plants in Diaporthe and Phomopsis, some of which originate from the marine environment (mainly mangroves and sediments). Most of compounds are classified as polyketides, which is the main structural type of secondary metabolites in this genus. The reported compounds showed various bioactivities, such as cytotoxic [15], antifungal [16], antibacterial [17], antiviral [18], antioxidant [19], anti-inflammatory [20], phytotoxic [21], and enzyme inhibition [22]. Up to now, there are 26 known species and various unidentified species of Diaporthe and Phomopsis have been studied for their metabolites. Our current review comprehensively summarize a total of 335 bioactive natural products from Diaporthe and Phomopsis between 2010 and 2019, covering their detailed chemical structures with classifications in structural types, as well as their bioactivities and habitats.

2. Bioactive Secondary Metabolites from Phomopsis

The Phomopsis fungi are important resource of bioactive compounds in the field of drug discovery, and have remarkable medical application value. According to the literature reports in recent ten years, a total of 246 bioactive compounds are summarized from Phomopsis herein. These substances have rich and diverse biological activities, such as cytotoxic, antifungal, antibacterial, antiviral, antioxidant, anti-inflammatory, phytotoxic, antimalarial, antialgae, antimigratory, pro-apoptotic, accelerating, and inhibiting the growth of subintestinal vessel plexus (SIV) branches, protecting effects on pancreatic \( \beta \)-cells, motility inhibitory and zoosporicidal potential, and enzyme inhibitory activities (Table 1). Among them, some interesting and promising bioactive compounds might be used in pharmaceutical and agricultural fields. The derived habitats of the Phomopsis strains can also be found in Table 1, which shows that there are 174 (accounting for 71%) and 66 (accounting for 27%) compounds obtained from terrestrial and marine environments, respectively, while six compounds (accounting for 2%) were not mentioned their habitats.

| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 1      | Xanthenes       | 1,5-Dihydroxy-3-hydroxyethyl-6-methoxy-carbonylxanthone | Phomopsis sp. | Paris polyphylla var. yunnanensis (T) | Cytotoxic | [23]  |
| 2      |                 | 1-Hydroxy-5-methoxy-3-hydroxyethyl-6-methoxycarbonyl-xanthone | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Cytotoxic | [23]  |
| 3      |                 | 1-Hydroxy-3-hydroxyethyl-8-ethoxycarbonyl-xanthone | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Cytotoxic | [23]  |
| 4      | Pinselin        | 1-Hydroxy-8-(hydroxymethyl)-3-methoxy-6-methylxanthone | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Cytotoxic | [23]  |
| 5      |                 | 2,6-Dihydroxy-3-methyl-9-oxoxanthene-8-carboxylic acid methyl ester | Phomopsis sp. (No. SK7RN3G1) | Sediment (M) | Cytotoxic | [24]  |
| 6      |                 | 4,5-Dihydroxy-3-(2-hydroxyethyl)-1-methoxy-8-methoxy-carbonylxanthone | P. amygdali | Paris axialis (T) | Cytotoxic | [25]  |
| 7      |                 | 1,8-Dihydroxy-4-(2-hydroxyethyl)-3-methoxycarboxylic acid | P. amygdali | P. axialis (T) | Cytotoxic | [25]  |
| 8      |                 | Hydroxyvertixanthone | Phomopsis sp. YM 355364 | Aconitum carmichaelii (T) | Antimicrobial | [26]  |
| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|------------------|-----------|---------|-----------------|------------|-------|
| 10     |                  | Dalianxanthone A | Phomopsis sp. | Paris daliensis (T) | Cytotoxic | [27] |
| 11     |                  | Dalianxanthone B | Phomopsis sp. | P. daliensis (T) | Cytotoxic | [27] |
| 12     |                  | Dalianxanthone C | Phomopsis sp. | P. daliensis (T) | Cytotoxic | [27] |
| 13     | Paucinervin E    | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [28] |
| 14     | 1,3-Dihydroxy-4-(1,3,4-trihydroxybutan-2-yl)-8-methoxy-9H-xanthen-9-one | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 15     | 8-Methoxy-1,3,4-trihydroxy-5-(1′,3′,4′-trihydroxybutan-2′-yl)-xanthone | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 16     | 3,8-Dihydroxy-4(2,3-dihydroxy-1-hydroxymethylpropyl)-1-methoxyxanthone | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 17     | 1,7-Dihydroxy-2-methoxy-3-(3-methylbut-2-enyl)xanthone | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 18     | 6-O-Methyl-2-deprenylhidrodiannthone B | P. amygdi | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 19     |                  | Oliganths E | Phomopsis sp. | P. daliensis (T) | Cytotoxic | [27] |
| 20     |                  | Dihydrosterigmatocystin | Phomopsis sp. | P. amygdi | Cytotoxic | [27] |
| 21     |                  | Veilardixanthone | Phomopsis sp. | P. amygdi | Cytotoxic | [27] |
| 22     | 1,7-Dihydroxy-2-methoxy-3-(3-methylbut-2-enyl)xanthone | Phomopsis sp. | P. amygdi | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 23     | 1-Hydroxy-4,7-dimethoxy-6-(3-oxobutyl)-xanthone | Phomopsis sp. | (ZH76) | Excoecaria agallocha (M) | Antioxidant | [30] |
| 24     |                  | Asperxanthone | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Cytotoxic | [29] |
| 25     |                  | Cratoxylumxanthone D | Phomopsis sp. | P. daliensis (T) | Cytotoxic | [27] |
| 26     |                  | Cratoxylumxanthone D | Phomopsis sp. | P. daliensis (T) | Cytotoxic | [27] |
| 27     |                  | Phomoxanthone A | Phomopsis sp. IM 41-1 | Sonneratia cascatoria (M) | Pro-apoptotic | [31] |
| 28     |                  | Phomoxanthone A | Phomopsis sp. IM 33# | Rhizophora mucronata (M) | Inhibiting | [32] |
| 29     |                  | 12-O-Deacetylphomoxanthone A | Phomopsis sp. IM 41-1 | Rhizophora stylosa (M) | Inhibiting | [33] |
| 30     |                  | Dicerandrol A | Phomopsis sp. | Acanthus ilicifolius (M) | Antimicrobial | [32] |
| 31     |                  | Dicerandrol B | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Cytotoxic | [34] |
| 32     |                  | Dicerandrol C | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Cytotoxic | [34] |
| 33     |                  | Deacetylphomoxanthone B | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Cytotoxic | [34] |
| 34     |                  | Penexanthone A | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Cytotoxic | [34] |
| 35     |                  | (+)-Phomopsichin A | Phomopsis sp. 33# | R. stylosa (M) | Antimicrobial, Antioxidant, Inhibiting | [32] |
| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 36     | (-)-Phomopsichin B | Phomopsis sp. 33# | R. stylosa (M) | Antimicrobial, Antioxidant, Inhibiting acetylcholinesterase and α-glucosidase | [33] |
| 37     | Phomopsichin C   | Phomopsis sp. 33# | R. stylosa (M) | Antimicrobial, Antioxidant, Inhibiting acetylcholinesterase and α-glucosidase | [33] |
| 38     | Phomopsichin D   | Phomopsis sp. 33# | R. stylosa (M) | Antimicrobial, Antioxidant, Inhibiting acetylcholinesterase and α-glucosidase | [33] |
| 39     | Chaetocyclinone B | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Cytotoxic | [36] |
| 40     | Pestalotiopsone F | Phomopsis sp. IFB-ZS1-S4 | Scaevola hainanensis (M) | Inhibiting neuraminidase | [37] |
| 41     | Phomoxanthone F  | Phomopsis sp. xy21 | Xylacarpus granatum (M) | Anti-HIV | [38] |
| 42     | 5-Hydroxy-3-hydroxymethyl-2-methyl-7-methoxycromone | Phomopsis sp. (No. Gx-4) | Sediment (M) | Cytotoxic, Inhibiting the growth of SIV branch | [39] |
| 43     | Phomochromone A  | Phomopsis sp. | Cistus monspeliensis (T) | Antimicrobial, Antialgal | [40] |
| 44     | Phomochromone B  | Phomopsis sp. | C. monspeliensis (T) | Antimicrobial, Antialgal | [40] |
| 45     | Phomochromalone A | Phomopsis sp. CGMCC No. 5416 | Achyranthes bidentata (T) | Cytotoxic, Anti-HIV | [41] |
| 46     | Phomochromalone B | Phomopsis sp. CGMCC No. 5416 | A. bidentata (T) | Cytotoxic, Anti-HIV | [41] |
| 47     | 5-Hydroxy-6,8-dimethoxy-2-benzyl-4H-naphtho[2,3-b]pyran-4-one | Phomopsis sp. ZSU-H26 | E. agallocha (M) | Cytotoxic | [42] |
| 48     | Phomopsichin H76 A | Phomopsis sp. (#su-H76) | E. agallocha (M) | Accelerating the growth of SIV branch | [43] |
| 49     | Chromanones      | Phomopsis sp. (No. ZH-111) | Sediment (M) | Accelerating the growth of SIV branch, Cytotoxic, Motility inhibitory and zoosporicidal potential, Inhibiting DnaG primase | [44] |
| 50     | Chaetocyclinone B | Phomopsis sp. (No. Gx-4) | Sediment (M) | Cytotoxic, Inhibiting the growth of SIV branch, Cytotoxic, Motility inhibitory and zoosporicidal potential, Inhibiting DnaG primase | [39] |
| 51     | Chromanones      | Phomopsis sp. (No. Gx-4) | Sediment (M) | Cytotoxic, Inhibiting the growth of SIV branch, Cytotoxic, Motility inhibitory and zoosporicidal potential, Inhibiting DnaG primase | [39] |
| 52     | 5,8-Dihydroxy-4-methylcoumarin | Phomopsis sp. (No. Gx-4) | Sediment (M) | Cytotoxic, Inhibiting the growth of SIV branch | [39] |
| 53     | (10S)-Diaporthin | Phomopsis sp. sh917 | Isodon ericicalyx var. laxiflora (T) | Antiangiogenic | [45] |
| 54     | Cytosporone D    | Phomopsis sp. CMU-LMA | Alpinia malacensis (T) | Antimicrobial, Inhibiting DnaG primase | [46] |
| 55     | Alternariol      | Phomopsis sp. A240 | Taxus chinensis var. nuirei (T) | Cytotoxic | [47] |
| 56     | Alternariol-5-O-methyl ether | Phomopsis sp. CAFT69 | E. calyphiloides (T) | Motility inhibitory and zoosporicidal potential | [48] |
| Number | Structural Types | Compounds | Activities | Refs. |
|--------|------------------|-----------|------------|-------|
| 57     | 5′-Hydroxyalternariol | Phomopsis sp. A240, A123 | Antioxidant | [47] |
| 58     | Phomochromanone C | Phomopsis sp. CGMCC No. 5416 | Cytotoxic, Pro-apoptotic | [41] |
| 59     | Benzofuranones | 7-Methoxy-6-methyl-3-oxo-1,3-dihydroisobenzofuran-4-carboxylic acid | Cytotoxic, Antifungal, Antioxidant | [50] |
| 60     | Diaporthelactone | Phomopsis sp. A123 | Cytotoxic, Antifungal, Antioxidant | [50] |
| 61     | 7-Hydroxy-4,6-dimethy-3H-isobenzofuran-1-one | Phomopsis sp. A123 | Cytotoxic, Antifungal, Antioxidant | [50] |
| 62     | 7-Methoxy-4,6-dimethy-3H-isobenzofuran-1-one | Phomopsis sp. A123 | Cytotoxic, Antifungal, Antioxidant | [50] |
| 63     | Excelsione | Phomopsis sp. (No. ZH-111) | Inhibiting the growth of SIV branch, Cytotoxic | [44] |
| 64     | Cytosporone E | Phomopsis sp. BCC 45011 | Cytotoxic, Antimalarial | [51] |
| 65     | Cytosporone P | Phomopsis sp. BCC 45011 | Antimalarial | [51] |
| 66     | Phomopsidone A | Phomopsis sp. A123 | Cytotoxic, Antifungal, Antioxidant | [50] |
| 67     | Excelsional | Phomopsis sp. CAFT69 | Cytotoxic, Antifungal, Antioxidant | [50] |
| 68     | Lithocarol A | P. lithocarpus FS508 | Cytotoxic | [52] |
| 69     | Lithocarol B | P. lithocarpus FS508 | Cytotoxic | [52] |
| 70     | Lithocarol C | P. lithocarpus FS508 | Cytotoxic | [52] |
| 71     | Lithocarol D | P. lithocarpus FS508 | Cytotoxic | [52] |
| 72     | Lithocarol E | P. lithocarpus FS508 | Cytotoxic | [52] |
| 73     | Lithocarol F | P. lithocarpus FS508 | Cytotoxic | [52] |
| 74     | Isoprenylisobenzofuran A | P. lithocarpus FS508 | Cytotoxic | [52] |
| 75     | 7-Methoxy-2-(4-methoxyphenyl)-3-methyl-5-(3-prenyl)-benzofuran | Phomopsis sp. P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 76     | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 77     | 2-(4′-Hydroxy-3,5-dimethoxyphenyl)-3-methyl-5-(3-prenyl)-benzofuran-7-ol | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 78     | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 79     | Moracin N | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 80     | 2-(2′-Methoxy-4′-hydroxy)-aryl-3-methyl-6-hydroxybenzofuran | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 81     | Itaefuranal B | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
| 82     | Moracin P | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-TMV | [53] |
Table 1. Cont.

| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 83     | Pyrones         | Phomaspynone A | P. asparagi SWUKJ5.2020 | Kadsura angustifolia (T) | Cytotoxic | [54]  |
| 84     |                 | Macommelin-8,9-diol | P. asparagi SWUKJ5.2020 | K. angustifolia (T) | Cytotoxic | [54]  |
| 85     |                 | Phomaspynone B | P. asparagi SWUKJ5.2020 | K. angustifolia (T) | Cytotoxic | [54]  |
| 86     |                 | Phomaspynone C | P. asparagi SWUKJ5.2020 | K. angustifolia (T) | Cytotoxic | [54]  |
| 87     |                 | Phomaspynone D | P. asparagi SWUKJ5.2020 | K. angustifolia (T) | Cytotoxic | [54]  |
| 88     |                 | Phomaspynone E | P. asparagi SWUKJ5.2020 | K. angustifolia (T) | Cytotoxic | [54]  |
| 89     |                 | Macommelin-9-ol | P. asparagi SWUKJ5.200 | K. angustifolia (T) | Cytotoxic | [54]  |
| 90     |                 | Phomaspynone B | P. asparagi SWUKJ5.200 | K. angustifolia (T) | Cytotoxic | [54]  |
| 91     |                 | Macommelin | P. asparagi SWUKJ5.200 | C. salvifolius (T) | Antifungal, Antibacterial, Algicidal | [55]  |
| 92     |                 | Pyrenocine J | Phomopsis sp. | C. salvifolius (T) | Cytotoxic | [55]  |
| 93     |                 | Pyrenocine K | Phomopsis sp. | C. salvifolius (T) | Cytotoxic | [55]  |
| 94     |                 | Pyrenocine L | Phomopsis sp. | C. salvifolius (T) | Cytotoxic | [55]  |
| 95     |                 | Pyrenocine M | Phomopsis sp. | C. salvifolius (T) | Cytotoxic | [55]  |
| 96     | Quinones        | Anhydrojavanicin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 97     |                 | Dihydroanhydrojavanicin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 98     |                 | Fusarubin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 99     |                 | Javanicin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 100    |                 | 2-Acetonyl-3-methyl-5-hydroxy-7-methoxy-naphthazarin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 101    |                 | Bostrycoidin | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| 102    |                 | Altersolanol B | P. longicolla HL-2223 | Bruguiera sexangula var. rhizophorata (M) | Antibacterial | [57]  |
| 103    |                 | Altersolanol A | Phomopsis sp. (PM0409092) | Nectanthes arbor-tristis (T) | Cytotoxic | [58]  |
| 104    |                 | (2R,3S)-7-Ethyl-1,2,3,4-tetrahydro-2,3,8-trihydroxy-6-methoxy-3-methyl-9,10-anthracenedione | Phomopsis sp. PSU-MA214 | Rhuizoflora apiculata (M) | Cytotoxic, Antibacterial | [60]  |
| 105    |                 | Altersolanol J | P. foeniculi | F. vulgare (T) | Phytotoxic, Antibacterial | [59]  |
| 106    |                 | 2-Hydroxymethyl-4β,5α,6β-trihydroxy-cyclohex-2-en | Phomopsis sp. | Notobus syrriaca (T) | Antibacterial, Algicidal | [61]  |
| 107    |                 | (−)-Phyllostine | Phomopsis sp. | N. syrriaca (T) | Antibacterial, Algicidal | [61]  |
| 108    |                 | (+)-Epipoxydon | Phomopsis sp. | N. syrriaca (T) | Antibacterial, Algicidal | [61]  |
| 109    |                 | (+)-Epipoxydon monoacetate | Phomopsis sp. | N. syrriaca (T) | Antibacterial, Algicidal | [61]  |
| 110    |                 | Phomonaphthalenone A | Phomopsis sp. HCCB04730 | Radix Stephaniae japonicae (T) | Cytotoxic, Anti-HIV | [56]  |
| Number | Strains | Activities | Refs. |
|--------|---------|------------|-------|
| 111    | A.  Ilicifolius (M) | Antibacterial | [62]  |
| 112    | N. syriaca (T) | Antibacterial | [61]  |
| 113    | L. vulgare (T) | Antibacterial | [63]  |
| 114    | L. vulgare (T) | Antibacterial | [63]  |
| 115    | L. vulgare (T) | Antibacterial | [63]  |
| 116    | L. vulgare (T) | Antibacterial | [63]  |
| 117    | L. vulgare (T) | Antibacterial | [63]  |
| 118    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [64]  |
| 119    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [64]  |
| 120    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [65]  |
| 121    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [65]  |
| 122    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [65]  |
| 123    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [66]  |
| 124    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [66]  |
| 125    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [66]  |
| 126    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [66]  |
| 127    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [67]  |
| 128    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [68]  |
| 129    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [68]  |
| 130    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [68]  |
| 131    | P. polypylla var. yunnanensis (T) | Anti-MRSA | [69]  |
| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|------------------|-----------|---------|-----------------|------------|-------|
| 132    | 2-(Hydroxymethyl)-5-methoxy-7-(3-methyl-2-oxobut-3-enyl)-1-naphthaldehyde | Phomopsis sp. | P. polyphylla var. yunnanensis (T) | Anti-MRSA | [69] |
| 133    | Tenellone H      | P. lithocarpus FS508 | Sediment (M) | Cytotoxic | [70] |
| 134    | 16-Acetoxycytosporone B | Phomopsis sp. YM 35364 | A. carmichaelii (T) | Antifungal | [71] |
| 135    | Cytosporone B    | Phomopsis sp. PSU-H188 | P. polyphylla var. yunnanensis (T) | Inhibiting lipase Protecting pancreatic β-cells | [72] [73] |
| 136    | Dothiorelone A   | Phomopsis sp. 0391 | P. polyphylla var. yunnanensis (T) | Inhibiting lipase | [72] |
| 137    | Lithocarpinol A  | P. lithocarpus FS508 | Sediment (M) | Cytotoxic | [74] |
| 138    | Lithocarpinol B  | P. lithocarpus FS508 | Sediment (M) | Cytotoxic | [74] |
| 139    | Phomoindene A    | Phomopsis sp. (No. GX7-4A) | Sediment (M) | Cytotoxic | [75] |
| 140    | 4-Hydroxybenzaldehyde | Phomopsis sp. YM 35364 | A. carmichaelii (T) | Antimicrobial | [26] |
| 141    | 5,5′-Dimethoxybiphenyl-2,2′-diol | P. longicolla HL-2232 | B. sexangula var. rhynchoptera (M) | Antibacterial | [57] |
| 142    | Phomoniitroester | Phomopsis sp. PSU-MA214 | R. apiculate (M) | Cytotoxic | [60] |
| 143    | Cytosporone U    | Phomopsis sp. FJBR-11 | Bruea javanica (T) | Anti-TMV | [76] |
| 144    | Altenusin        | Phomopsis sp. CAFT69 | E. calophyloides (T) | Motility inhibitory and zoosporicidal potential Cytotoxic, Growth-inhibition activity | [48] |
| 145    | Cosmochlorin D   | Phomopsis sp. N-125 | Ficus ampelas (T) | Cytotoxic, Growth-inhibition activity | [77] |
| 146    | Cosmochlorin E   | Phomopsis sp. N-125 | F. ampelas (T) | Cytotoxic, Growth-inhibition activity | [77] |
| 147    | Oblongolides     | Phomopsis sp. BCC 9789 | Musa acuminate (T) | Cytotoxic, Anti-HSV-1 | [78] |
| 148    | Oblongolide Y    | Phomopsis sp. BCC 9789 | M. acuminate (T) | Cytotoxic | [78] |
| 149    | Oblongolide Cl   | Phomopsis sp. XZ-01 | Camptotheca acuminata (T) | Cytotoxic | [79] |
| 150    | Oblongolide P1   | Phomopsis sp. XZ-01 | C. acuminate (T) | Cytotoxic | [79] |
| 151    | Oblongolide X1   | Phomopsis sp. XZ-01 | C. acuminate (T) | Cytotoxic | [79] |
| 152    | 6-Hydroxyphomodiol | Phomopsis sp. XZ-01 | C. acuminate (T) | Cytotoxic | [79] |
| 153    | Oblongolide C    | Phomopsis sp. XZ-01 | C. acuminate (T) | Cytotoxic | [79] |
| 154    | 2-Deoxy-4α-hydroxyoblongolide | Phomopsis sp. BCC 9789 | M. acuminate (T) | Cytotoxic, Anti-HSV-1 | [78] |
| 155    | Unclassified polyketides | Phomoxydiene C | X. granatum (M) | Cytotoxic, Antimalarial | [51] |
| 156    | 1893 A           | Phomopsis sp. BCC 45011 | X. granatum (M) | Cytotoxic | [51] |
| 157    | Mycoepoxydiene   | Phomopsis sp. BCC 45011 | X. granatum (M) | Cytotoxic, Antimalarial | [51] |
| 158    | Deacetylmycoepoxydiene | Phomopsis sp. BCC 45011 | X. granatum (M) | Cytotoxic, Antimalarial | [51] |
| 159    | Phomoxydiene A   | Phomopsis sp. BCC 45011 | X. granatum (M) | Cytotoxic, Antimalarial | [51] |
| Number | Structural Types | Compounds | Strains | Habits (T/M *) | Activities | Refs. |
|--------|------------------|-----------|---------|---------------|-----------|-------|
| 160    |                  | Phomopsis A | Phomopsis sp. YE3250 | Paeonia delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 161    |                  | Phomopsis B | Phomopsis sp. YE3250 | P. delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 162    |                  | Phomopsis C | Phomopsis sp. YE3250 | P. delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 163    |                  | Phomopsis D | Phomopsis sp. YE3250 | P. delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 164    |                  | Phomopsis E | Phomopsis sp. YE3250 | P. delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 165    |                  | Phomopsis F | Phomopsis sp. YE3250 | P. delavayi (T) | Cytotoxic, Antifungal, Inhibiting α-glycosidase | [80] |
| 166    |                  | Phomentrioloxin | Phomopsis sp. | Carthamus lanatus (T) | Phytotoxic | [81] |
| 167    |                  | Phomotenone | Phomopsis sp. | C. monspeliensis (T) | Antifungal, Antibacterial, Antiaggl | [40] |
| 168    |                  | Phomopsolidone B | Phomopsis sp. DC275 | Vitis vinifera (T) | Antibacterial, Phytotoxic | [82] |
| 170    |                  | Phomopsolidone A | Phomopsis sp. DC275 | V. vinifera (T) | Antibacterial, Phytotoxic | [82] |
| 171    |                  | Phomopsolidone B | Phomopsis sp. DC275 | V. vinifera (T) | Antibacterial, Phytotoxic | [82] |
| 172    | Monoterpenoids   | Acropyrene | Phomopsis sp. HNY29-2B | A. ilicifolius (M) | Antibacterial | [62] |
| 173    |                  | Nectriapirone | Phomopsis sp. DC275 | F. vulgare (T) | Phytotoxic | [59] |
| 174    |                  | (15,25,4S)-Trihydroxy-p-methane | Phomopsis sp. | C. monspeliensis (T) | Antibacterial, Antiaggl | [40] |
| 175    | Sesquiterpenoids | Phomophyllin A | Phomopsis sp. TJ507A | Phyllanthus glaucus (T) | Inhibiting BACE1 | [83] |
| 176    |                  | Phomophyllin B | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 177    |                  | Phomophyllin C | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 178    |                  | Phomophyllin D | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 179    |                  | Phomophyllin E | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 180    |                  | Phomophyllin F | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 181    |                  | Phomophyllin G | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 182    |                  | Radulone B | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 183    |                  | Phomophyllin I | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 184    |                  | Onitin | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 185    |                  | (7R,9S,10R)-3,9-Di-hydroxicalamene | P. cassiae | Cassia spectabilis (T) | Inhibiting acetylcholinesterase, Antifungal | [84] |
| 186    |                  | (7R,9S,10R)-3,9-Di-hydroxicalamene | P. cassiae | C. spectabilis (T) | Inhibiting acetylcholinesterase, Antifungal | [84] |
| 187    |                  | (7S,10R)-3-Hydroxicalamen-8-one | P. cassiae | C. spectabilis (T) | Inhibiting acetylcholinesterase, Antifungal | [84] |
Table 1. Cont.

| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|------------------|-----------|---------|-----------------|------------|-------|
| 188    |                  | Aristelegone-A | P. cassiae | C. spectabilis (T) | Inhibiting acetylcholinesterase, Anti- fungal | [84] |
| 189    |                  | Phomoarcherin A | P. archeri | Vanilla albida (T) | Cytotoxic | [85] |
| 190    |                  | Phomoarcherin B | P. archeri | V. albida (T) | Cytotoxic, Antimalarial | [85] |
| 191    |                  | Phomoarcherin C | P. archeri | V. albida (T) | Cytotoxic | [85] |
| 192    |                  | Kampanol A | P. archeri | V. albida (T) | Cytotoxic | [85] |
| 193    |                  | (+)-5,6-Dihy- drox-10-oxodehydro- dihydrotryrdial | Phomopsis sp. TJ507A | P. glaucus (T) | Inhibiting BACE1 | [83] |
| 194    |                  | Curcumol | P. castaneae-mollissimae GQH87 | Artemisia annua (T) | Cytotoxic | [87] |
| 195    |                  | 9-Hydroxyphomopside | Phomopsis sp. CAFT69 | E. calophyloides (T) | Motility inhibitory and zoosporicidal potential | [48] |
| 196    |                  | Phomopsidin | Phomopsis sp. CAFT69 | E. calophyloides (T) | Motility inhibitory and zoosporicidal potential | [48] |
| 197    |                  | AA03390 | P. lithocarpus FS508 | Sediment (M) | Cytotoxic | [70] |
| 198    | Diterpenoids     | Libertellenone J | Phomopsis sp. S12 | Illigera rhodantha (T) | Anti-inflammatory | [88] |
| 199    |                  | Libertellenone C | Phomopsis sp. S12 | Diospyros caronaria (T) | Anti-inflammatory | [89] |
| 200    |                  | Libertellenone T | Phomopsis sp. S12 | Diospyros caronaria (T) | Anti-inflammatory | [89] |
| 201    |                  | Pedinophyllol K | Phomopsis sp. S12 | Diospyros caronaria (T) | Anti-inflammatory | [89] |
| 202    |                  | Pedinophyllol L | Phomopsis sp. S12 | Diospyros caronaria (T) | Anti-inflammatory | [89] |
| 203    |                  | Fusicoicin J | P. amygdalii | C. midge (T) | Antibacterial | [86] |
| 204    |                  | 3a-Hydroxyfusicoicin J | P. amygdalii | C. midge (T) | Antibacterial | [86] |
| 205    | Triterpenoids    | 3β,26,22E-Eupha- dien-11-one | Phomopsis sp. P. chimonanthii (T) | Tanaxis chinensis (T) | Cytotoxic | [90] |
| 206    |                  | Betulinic acid | Phomopsis sp. SNB-LAP1-7-32 | Diospyros caronaria (T) | Antiviral, Cytotoxic | [91] |
| 207    |                  | Oleaneolic acid | castaneae-mollissimae GQH87 | A. annua (T) | Cytotoxic | [87] |
| 208    | Steroids        | (14β,22E)-9,14, 15,26-Dihydroxyergosta-4,7,22- triene-3,6-dione | Phomopsis sp. | A. carmicheili (T) | Antifungal | [92] |
| 209    |                  | (5α,6β,15β,22E)-6-Ethoxy- 5,15-dihydroxyergosta-7,22- dien-3-one | Phomopsis sp. | A. carmicheili (T) | Antifungal | [92] |
| 210    |                  | Calvasterol A | Phomopsis sp. | A. carmicheili (T) | Antifungal | [92] |
| 211    |                  | Calvasterol B | Phomopsis sp. | A. carmicheili (T) | Antifungal | [92] |
| 212    |                  | Ganodermaside D | Phomopsis sp. | A. carmicheili (T) | Antifungal | [92] |
| 213    |                  | Dankaisterone A | Phomopsis sp. YM 355364 | A. carmicheili (T) | Anti-influenza | [71] |
| 214    |                  | 3β,5α,9α,12- Dihydroxy- (22E,24R)-ergosta-7,22-dien-6- one | Phomopsis sp. YM 355364 | A. carmicheili (T) | Anti- fungal | [71] |
| 215    |                  | Phomopsterone B | Phomopsis sp. TJ507A | P. glaucus (T) | Anti-inflammatory | [93] |
| 216    |                  | Cyathisterol | Phomopsis sp. YM 355364 | A. carmicheili (T) | Anti- fungal | [93] |
| 217    | Macrolides       | Sch-642305 | Phomopsis sp. CMU-LMA | Alpinia malaccensis (T) | Cytotoxic, Anti- microbial | [94] |
| 218    |                  | LMA-P1 | Phomopsis sp. CMU-LMA | A. malaccensis (T) | Cytotoxic | [94] |
| 219    |                  | Benquoine | Phomopsis sp. CMU-LMA | A. malaccensis (T) | Cytotoxic, Anti- microbial | [94] |
| 220    |                  | Aspergillide C | Phomopsis sp. IFB-Z51-54 | S. hainanensis (M) | Inhibiting neuraminidase | [37] |
Table 1. Cont.

| Number | Structural Types | Compounds               | Strains                        | Habitats (T/M *) | Activities                     | Refs. |
|--------|------------------|-------------------------|--------------------------------|------------------|--------------------------------|-------|
| 223    |                  | Lithocarpin A           | P. lithocarpus FS508           | Sediment (M)     | Cytotoxic                      | [95]  |
| 224    |                  | Lithocarpin B           | P. lithocarpus FS508           | Sediment (M)     | Cytotoxic                      | [95]  |
| 225    |                  | Lithocarpin C           | P. lithocarpus FS508           | Sediment (M)     | Cytotoxic                      | [95]  |
| 226    |                  | Lithocarpin D           | P. lithocarpus FS508           | Sediment (M)     | Cytotoxic                      | [95]  |
| 227    | Alkaloids        | Phomopchalasin B        | Phomopsis sp. shj2             | I. eriocalyx var. laxiflora (T) | Antimigratory                     | [96]  |
| 228    |                  | Phomopsisichalin G      | P. spp. xy21 and xy22          | X. granatum (M)  | Cytotoxic                      | [97]  |
| 229    |                  | 18-Metoxycytochalasin J| Phomopsis sp.                   | G. kola (T)      | Cytotoxic, Antifungal          | [98]  |
| 230    |                  | Cytochalasin H          | Phomopsis sp.                  | Gossypium hirsutum (T) | Inhibiting acetylcholinesterase, Anti-inflammatory | [96]  |
| 231    |                  | Cytochalasin J          | Phomopsis sp.                  | S. spectabilis (T) | Cytotoxic, Antifungal, Anti-inflammatory, Antioxidant | [98]  |
| 232    |                  | Phomopchalasin C        | Phomopsis sp. shj2             | I. eriocalyx var. laxiflora (T) | Anti-inflammatory, Antimigratory | [96]  |
| 233    |                  | Cytochalasin N          | Phomopsis sp. By254            | G. hirsutum (T)  | Antifungal                     | [99]  |
| 234    |                  | Epoxyctychalasin H      | Phomopsis sp. By254            | G. hirsutum (T)  | Antifungal                     | [99]  |
| 235    |                  | Diaporthalasin          | Phomopsis sp. PSU-H188         | H. brasiensis (T) | Anti-MRSA                      | [73]  |
| 236    |                  | (+)-Tersone E           | P. tersa FS441                 | Sediment (M)     | Antibacterial, Cytotoxic       | [101] |
| 237    |                  | ent-Citrudone A         | P. tersa FS441                 | Sediment (M)     | Antibacterial                  | [101] |
| 238    |                  | Phychrodine C           | Phomopsis sp. 33#              | R. stylosa (M)   | Anti-inflammatory              | [102] |
| 239    |                  | Phychrodine D           | Phomopsis sp. 33#              | R. stylosa (M)   | Anti-inflammatory              | [102] |
| 240    |                  | PM181110                | P. glabrae                     | Pongania pinnata (T) | Anticancer                      | [103] |
| 241    |                  | Fusaristatin A          | P. longicolla S1B4             | Sediment (M)     | Antibacterial                  | [34]  |
| 242    |                  | Exumolide A             | Phomopsis sp. (No. ZH-111)     | Sediment (M)     | Accelerating the growth of SIV branch, Cytotoxic | [44]  |
| 243    | Flavonoids       | Quercetin               | P. castaneae-mollissimae       | A. annua (T)     | Cytotoxic                      | [87]  |
| 244    |                  | Luteolin                | P. castaneae-mollissimae       | A. annua (T)     | Cytotoxic                      | [87]  |
| 245    |                  | Naringenin              | P. castaneae-mollissimae       | A. annua (T)     | Cytotoxic                      | [87]  |
| 246    |                  | Luteolin-7-O-glucoside  | P. castaneae-mollissimae       | A. annua (T)     | Cytotoxic                      | [87]  |

* T: terrestrial environment; M: marine environment; b The habitat was not mentioned.

2.1. Polyketides

Polyketides are a large and diverse family of natural products, containing various chemical structures and biological activities [104]. In this review, 171 polyketides are summarized from Phomopsis, accounting for 70% of the total compounds from Phomopsis.
The main bioactivities involve cytotoxic, antibacterial and antifungal activities. Herein, we classify these polyketides into xanthones, chromones, chromanones, benzofuranones, pyrones, quinones, phenols, oblongolides, and unclassified polyketides.

2.1.1. Xanthones

Xanthones are a kind of compounds with the framework of 9H-xanthen-9-one, which mainly have anti-inflammatory, antimicrobial, antioxidant and cytotoxic activities [105]. A series of xanthones were obtained from the fermentation products of _Phomopsis_ sp. isolated from _Paris polyphylla_ var. _yunnanensis_, including three new compounds, 1,5-dihydroxy-3-hydroxyethyl-6-methoxycarbonyl-7xanthone (1), 1-hydroxy-5-methoxy-3-hydroxyethyl-6-methoxycarbonyl-7xanthone (2), 1-hydroxy-3-hydroxyethyl-8-ethoxy-carbonyl-xanthone (3), and seven known ones, pinselin (4), 1-hydroxy-8-(hydroxymethyl)-3-methoxy-6-methylxanthone (5), secosterigmatocystin (17), 1,7-dihydroxy-2-methoxy-3-(3-methylbut-2-enyl)xanthone (22), 1-hydroxy-4,7-dimethoxy-6-(3-oxobutyl)xanthone (23), asperxanthone (24) and 6-O-methyl-2-deprenylhediaxanthone B (25). The cytotoxicities of all compounds to five human tumor cells (NB4, A549, SHSY5Y, PC3, and MCF7) were evaluated by using paclitaxel as positive control. The results showed that compounds 1 and 3 displayed cytotoxic activities and provided the IC\(_{50}\) values of 3.6 and 2.5 \(\mu\)M against A549 cells, and 1 gave an IC\(_{50}\) value of 2.7 \(\mu\)M against MCF7 cells. Compounds 22–23 showed weak activities and offered IC\(_{50}\) values greater than 10 \(\mu\)M for five tested cells. The others gave IC\(_{50}\) values between 3.8–10 \(\mu\)M against tested cells [23]. A new compound, 2,6-dihydroxy-3-methyl-9-oxo-xanthen-8-carboxylic acid methyl ester (6), was isolated from _Phomopsis_ sp. (No. SK7RN3G1) of mangrove sediment in the Shankou, Hainan, China. It showed cytotoxicity towards HEP-2 (IC\(_{50}\) = 8 \(\mu\)g/mL) and HepG2 (IC\(_{50}\) = 9 \(\mu\)g/mL) cancer cells [24]. Three secondary metabolites were characterized from fermentation products of _P. amygdali_, isolated from _Paris axialis_: 4.5-dihydroxy-3-[(2-hydroxyethyl)-1-methoxy-8-methoxy-carbonyl]xanthone (7), 1,8-dihydroxy-4-(2-hydroxyethyl)-3-methoxynanthone (8), and paucinervin E (13). Compound 7 was active against A549 (IC\(_{50}\) = 2.6 \(\mu\)M) and PC3 (IC\(_{50}\) = 2.4 \(\mu\)M) cell lines. Compounds 8 and 13 displayed moderate activities with IC\(_{50}\) values in the range of 5.2–9.2 \(\mu\)M against one or more cell lines of NB4, A549, SHSY5Y, PC3 and MCF7 [25]. Hydroxyverticillane (9) was obtained from the endophytic fungus _Phomopsis_ sp. YM 355364, originated from Chinese medicinal plant _Aconitum carmichaelii_. It showed antitumor activity with minimal inhibitory concentration (MIC) values of 256, 256, 128, and 64 \(\mu\)g/mL against _Escherichia coli_, _Bacillus subtilis_, _Pyricularia oryzae_, and _Candida albicans_, respectively [26]. The fermentation of fungus _Phomopsis_ sp. derived from _Paris dalienensis_, led to the isolation of six xanthones and identified as dalienxanthones A–C (10–12), 3,8-dihydroxy-4-(2,3-dihydroxy-1-hydroxymethylpropyl)-1-methoxynanthone (18), oliganthins E (19), and cratoxylumxanthone D (26). These compounds were evaluated for cytotoxicities of five cancer cell lines (NB4, A549, SHSY5Y, PC3 and MCF-7). Compounds 12 and 18 were active to SHSY5Y with IC\(_{50}\) values of 3.8 and 3.5 \(\mu\)M, respectively, and the remaining compounds provided IC\(_{50}\) values in the range of 4.6–9.2 \(\mu\)M [27]. An investigation of extracts from fungus _P. amygdali_ derived from the rhizome of _Paris polyphylla_ var. _yunnanensis_ afforded a new xanthone, 1,3-dihydroxy-4-(1,3,4-trihydroxybutan-2-yl)-8-methoxy-9H-xanthen-9-one (14). The bioactive results showed that 14 exhibited significant cytotoxic activity against A549 (IC\(_{50}\) = 5.8 \(\mu\)M) and PC3 (IC\(_{50}\) = 3.6 \(\mu\)M) [28].

An endophytic fungus _P. amygdali_ associated with the rhizome of _Paris axialis_ was cultured to obtain five xanthones: 3-methoxyl-1,4,8-trihydroxy-5-(1′,3′,4′-trihydroxybutan-2'-yl)-xanthone (15), 8-methoxy-1,3,4-trihydroxy-5-(1′,3′,4′-trihydroxybutan-2'-yl)-xanthone (16), secosterigmatocystin (17), dihydrosterigmatocystin (20), and vieillardixanthone (21). The cytotoxic assay for NB4, A549, SHSY5Y, PC3 and MCF7 cancer cells were evaluated. The IC\(_{50}\) values of compound 15 against A549 and 16 against SHS5Y were 3.6 and 4.2 \(\mu\)M, respectively. Compounds 17 and 20–21 displayed moderate activities with IC\(_{50}\) values in the range of 5.4–8.8 \(\mu\)M [29]. Studies of an endophytic fungus _Phomopsis_ sp. (ZFH76) from the stems of the mangrove tree _Excoecaria agallocha_ contained a new O-glycoside
compound, 3-O-(6-O-α-L-arabinopyranosyl)-β-D-glucopyranosyl-1,4-dimethoxyxanthone (27). The IC₅₀ values of cytotoxicity for compound 27 on HEp-2 and HepG2 cells were 9 and 16 µmol/mL, respectively [30]. Phomoxanthone A (28), a dimeric tetrahydroxanthone, was extracted from *P. longicolla* of the mangrove tree *Sonneratia caseolaris*. Compound 28 had the strongest pro-apoptotic activity on human cancer cell lines and cisplatin-resistant cells, and its activity on healthy blood cells was reduced by more than 100 times. It was the most effective activator of mouse T lymphocytes, NK cells, and macrophages [31]. The study on secondary metabolites from fungus *Phomopsis* sp. IM 41-1 of mangrove plant *Rhizophora mucronata* afforded phomoxanthone A (28) and 12-O-deacetyl-phomoxanthone A (29). When the concentration was 30 µg/disk, compounds 28 and 29 showed moderate antimicrobial activities against *Botrytis cinerea*, *Sclerotinia sclerotiorum*, *Diaporthe medusaea*, and *Staphylococcus aureus*, but were inactive against *Pseudomonas aeruginosa* [32]. Four bioactive metabolites, dicerandrols A-C (30–32) and deacetylphomoxanthone B (33), were derived from *P. longicolla* S1B4. All compounds exhibited strong antibacterial activities against *Xanthomonas oryzae* KACC 10331. Dicerandrol A (30) also displayed notable antimicrobial activity against *S. aureus*, *B. subtilis*, and *C. albicans* with MIC values of 0.25, 0.125 and 2 µg/mL [34]. *Phomopsis* sp. HNY29-2B, isolated from mangrove plant *Acanthus ilicifolius*, produced four xanthone derivatives, 30–31, 33 and penexanthone A (34). Compounds 30–31 and 33–34 displayed cytotoxicities and provided IC₅₀ values of 1.76–42.82 µM against MDA-MB-435, HCT-116, Calu-3, Huh7, and MCF-10A human cancer cell lines [35]. The structures of xanthenes (1–34) are shown in Figure 1.

2.1.2. Chromones

Chromones are a class of bioactive compounds with a benzo-γ-pyrone skeleton, which have been reported to have various activities, such as anti-tumor, anti-viral, antimicrobial, anti-inflammatory, and antioxidant [106]. *Phomopsis* sp. 33#, a mangrove endophytic fungus isolated from the bark of *Rhizophora stylosa*, produced four new chromone derivatives, (+)-phomopsichin A (35), (−)-phomopsichin B (36), phomopsichins C (37) and D (38), along with a known phomoxanthone A (28). These metabolites displayed low effects on inhibitions of acetylcholinesterase and α-glucosidase, radical scavenging function on DPPH and OH, and antimicrobial activities [33]. A cytotoxic chromone, chaetocyclin B (39), was characterized from a culture of *Phomopsis* sp. HNY29-2B, an endophytic fungus obtained from the mangrove plant *A. ilicifolius* Linn. Compound 39 had cytotoxic activity against PC-3 (IC₅₀ = 8.13 µmol/L) and DU145 (IC₅₀ = 3.59 µmol/L) [36]. The fungus *Phomopsis* sp. IFB-ZS1-S4 isolated from *Scaevola hainanensis* Hance extracted a known pestalotiopsone F (40), which showed moderate inhibition on neuraminidase in vitro with IC₅₀ value of 9.90 ± 0.42 µM [37]. Cultivation of *Phomopsis* sp. xy21 derived from the mangrove *Xylocarpus granatum* afforded a new xanthone-derived polyketide, phomoxanthone F (41). It showed inhibitory effects on VSV-G pseudotyped viral supernatant (HIV-1) with the inhibitory rate of 16.48 ± 6.67% at a concentration of 20 µM, which was higher than that of the positive control, efavirenz with a rate of 88.54 ± 0.45% [38]. 5-Hydroxy-3-hydroxymethyl-2-methyl-7-methoxyxanthone (42) was separated from the extracts of *Phomopsis* sp. (No. Gx-4) derived from mangrove sediment in ZhuHai, Guangdong, China. It showed low cytotoxic activity with IC₅₀ values greater than 50 µmol/mL towards Hep-2 and HepG2. Moreover, it also significantly inhibited the growth of subintestinal vessel plexus (SIV) branches [39]. According to the bioassay-guided fractionation, two new chromones, phomochromones A (43) and B (44) were obtained from an endophytic fungus *Phomopsis* sp. of *Cistus monspeliensis*. They displayed remarkable antifungal, antibacterial, and antialgal activities against *Microbotryum violaceum*, *E. coli*, *Bacillus megaterium*, and *Chlorella fusca* [40]. Chemical investigation of *Phomopsis* sp. CGMCC No. 5416 isolated from *Achyranthes bidentata* led to the identification of two novel chromanones, phomochromones A (45) and B (46). They showed anti-HIV activities with IC₅₀ values of 20.4 and 32.5 µg/mL, and exhibited moderate cytotoxic activities towards A549, MDA-MB-231, and PAN-1 with CC₅₀ values between 62.5–79.3 µg/mL [41]. A new naphtho-γ-pyrone compound, 5-
hydroxy-6,8-dimethoxy-2-benzyl-4H-naphtho[2,3-b]-pyran-4-one (47), was obtained from *Phomopsis* sp. ZSU-H26 of the mangrove tree *E. agallocha*. This compound showed cytotoxic activity against HEP-2 (IC$_{50}$ = 10 µg/mL) and HepG2 (IC$_{50}$ = 8 µg/mL) [42]. The following work on the similar strain *Phomopsis* sp. (#ZSU-H76) from the same host additionally obtained phomopsis-H76 A (48), which significantly promoted the growth of the branches of SIV [43]. The structures of chromones (35–48) are shown in Figure 2.

![Chemical structures of compounds 1–34 from *Phomopsis*.](image-url)
2.1.3. Chromanones

Chromanones have been widely studied due to their structural characteristics. They always have important biological and pharmacological activities, including cytotoxic, antimicrobial, antiviral, antioxidant, etc [107]. The culture of a marine fungus *Phomopsis* sp. (No. ZH-111) from mangrove sediment of Zhuhai, Guangdong, China, obtained a new isochroman, (3R,4S)-3,4-dihydro-4,5,8-trihydroxy-3-methylisocoumarin (49). It could promote the growth of SIV branches and exhibited low cytotoxic activity against Hep-2 and HepG2 cells with IC$_{50}$ values above 50 mg/mL [44]. Three compounds were separated from *Phomopsis* sp. (No. Gx-4), including (3R,4S)-3,4-dihydro-8-hydroxy-4-methoxy-3-methylisocoumarin (50), 3,4-dihydro-8-hydroxy-3-methyl-1H-2-benzopyran-1-one-5-carboxylic acid (51), and 5,8-dihydroxy-4-methylcoumarin (52). All isolated compounds showed weak cytotoxic activities against Hep-2 and HepG2 cells with IC$_{50}$ values above 50 µmol/mL. In addition, compounds 50 and 51 significantly promoted the growth of SIV branches, while 52 inhibited their growth [39]. The endophytic fungus *Phomopsis* sp. sh917 found in stems of *Isodon eriocalyx* var. *laxiflora* obtained (10S)-diaporthin (53), showing antiangiogenic activity that inhibited the angiogenesis process induced by vascular endothelial growth factor (VEGF) [45]. From agar-supported fermentation culture of *Phomopsis* sp. CMU-LMA derived from *Alpinia malacensis*, a trihydroxybenzene lactone, cytosporone D (54) was isolated. It showed antimicrobial activity and inhibited *E. coli* DnaG primase with an IC$_{50}$...
value of 0.25 mM [46]. Alternariol (55) and 5′-hydroxyalternariol (57) were isolated from the endophytic fungus *Phomopsis* sp. A240 of *Taxus chinensis* var. *mairei*. Compound 55 showed low cytotoxicity against SF-268 (IC\(_{50}\) = 88.1 \(\mu\)M), MCF-7 (IC\(_{50}\) = 94.36 \(\mu\)M), and NCI-H460 (IC\(_{50}\) = 81.35 \(\mu\)M). Moreover, compound 57 had antioxidant activity with IC\(_{50}\) values of 42.83 \(\mu\)M [47]. Three compounds were sourced from *Endodesmia calophylloides* associated with *Phomopsis* sp. CAFT69, including alternariol (55), alternariol-5-O-methyl ether (56) and 5′-hydroxyalternariol (57). In the range of 1–10 \(\mu\)g/mL, compounds 55–57 had certain motility inhibition and lytic activities on the zoospores of grapevine downy mildew pathogen *P. viticola* in dose- and time-dependent manner [48]. Phomochromanone C (58) was extracted from *Phomopsis* sp. CGMCC No. 5416. The bioactivity assay revealed that compound 58 showed cytotoxicity towards A549, MDA-MB-231, and PANC-1 with CC\(_{50}\) values of 69.4, 53.5, and 36.5 \(\mu\)g/mL, and it induced early apoptosis of PANC-1 cancer cells with the rate of 10.52% [41]. The structures of chromanones (49–58) are shown in Figure 2.

2.1.4. Benzofuranones

Benzofuranones are an important intermediate of pharmacophores and drug molecules in natural products. Due to the furan ring being unstable and easy to open and crack, benzofuranones as a pharmaceutical intermediate have been widely concerned by pharmaceutical chemists [108]. The endophytic fungus *Phomopsis* sp. A123 isolated from mangrove plant *Kandelia candel* (L.) Druce, produced a novel depsidone, phomopsidone A (66), a known excelsione (67), and four known isobenzofuranones (59–62). All compounds showed different degrees of cytotoxicities against Raji and MDA-MB-435 tumor cells with IC\(_{50}\) values above 18 \(\mu\)M, displayed low antioxidant activities through DPPH radical scavenging effects, and exhibited antifungal activities [50]. The research on bioactive metabolites of marine fungus *Phomopsis* sp. (No. ZH-111) led to the isolation of 4-(hydroxymethyl)-7-methoxy-6-methyl-1(3\(H\))-isobenzofuranone (63). Compound 63 inhibited the growth of SIV branches and exhibited low cytotoxic activity with IC\(_{50}\) values above 50 mg/mL against Hep-2 and HepG2 cells [44]. Chemical investigations of secondary metabolites from *Phomopsis* sp. BCC 45011 of *X. granatum* resulted in the identification of two known metabolites, cytosporones E (64) and P (65). Compounds 64 and 65 showed antimalarial activities against *Plasmodium falciparum* K1 with IC\(_{50}\) values of 2.02 and 3.65 \(\mu\)g/mL, and 64 exhibited cytotoxicity against MCF-7, NCI-H187, and Vero cells with IC\(_{50}\) values at 29.66, 5.84, and 4.53 \(\mu\)g/mL, respectively [51]. Cultivation of *Phomopsis* sp. CAFT69 afforded excelsional (68). In the range of 1–10 \(\mu\)g/mL, compound 68 had certain motility inhibition and lytic activities on the zoospores of grapevine downy mildew pathogen *P. viticola* in dose- and time-dependent manner [48]. Lithocarols A-F (69–74), with highly-oxygenated isobenzofuran skeleton, and isoprenylisobenzofuran A (75), were derived from *P. lithocarpus* FS508 isolated from a deep-sea sediment collected from the Indian Ocean. These metabolites were cytotoxic and provided IC\(_{50}\) values between 10.5–87.7 \(\mu\)M against HepG-2, MCF-7, SF-268, and A549 cells [52]. The endophytic fungus *Phomopsis* sp., separated from *Paris polyphylla* var. *yunnanensis*, gave three new arylbenzofurans (76–78) and four known compounds, moracin N (79), 2-(2′-methoxy-4′-hydroxy)-aryl-3-methy-6-hydroxybenzofuran (80), iteafuranal B (81), and moracin P (82). Compounds 76–82 showed inhibitory effects on tobacco mosaic virus (TMV) with inhibition rates of 18.6–35.2% [53]. The structures of benzofuranones (59–82) are shown in Figure 3.
2.1.5. Pyrones

Pyrones are a kind of polyketides with six membered oxygen-containing heterocycles. As the precursor of many plants, animals, and microorganisms’ biosynthetic reactions, as well as its outstanding anti-tumor and antibacterial activities, researchers have shown strong interest [109]. Eight compounds were identified from the strain *P. asparagi* SWUKJ5.2020 isolated from medicinal plant *Kadsura angustifolia*, including five new 2-pyrone compounds, phomaspyrones A-E (83 and 85–88), along with three known metabolites, macommelin-8,9-diol (84), macommelin-9-ol (89), and macommelin (90). All isolated metabolites showed significant cytotoxic activities against six tested tumor cells (A549, Raji, HepG2, MCF-7, HL-60 and K562) with IC\textsubscript{50} values of 1.0–26.8 µg/mL. However, phomaspyrone C (86) display better activity than the other compounds with IC\textsubscript{50} values of 1.0–2.2 µg/mL against all tested cells [54]. The endophytic fungus *Phomopsis* sp. isolated from the plant *Cistus salvifolius*, yielded four new pyrenocines, pyrenocines J-M
They exhibited antibacterial and algicidal activities against *E. coli, B. megaterium,* and *C. fuscus.* The antifungal assay showed that 92 and 94 were active against *M. violaceum,* and compounds 91–92, and 94 were active against *Septoria tritici* [55]. An unusual pyrone metabolite, phomopsis-H76 C (95), was isolated from *Phomopsis* sp. (#zsus-H76), which inhibited the growth of SIV branch [43]. The structures of pyrones (83–95) are shown in Figure 3.

2.1.6. Quinones

Quinones are natural bioactive molecules with unsaturated cyclic diketones, such as cytotoxic, antimicrobial, antiviral and anti-inflammatory activities. In recent years, the development of new anti-tumor quinones and their derivatives as lead compounds has become a hot topic [110,111]. Studies of the endophytic fungus *Phomopsis* sp. HCCB04730 associated with stems of *Radix Stephaniae japonicae* obtained six known naphthoquinones 96–101. These metabolites showed cytotoxic activities against A549, MDA-MB-231 and PANC-1 cancer cells with IC$_{50}$ values of 1.1–120.5 µg/mL, and anti-HIV activities with IC$_{50}$ values between 1.6–26.8 µg/mL [56]. Altersolanol B (102) was separated from *P. longicolla* HL-2232 of leaves of *Bruguiera sexangula* var. *rhynchopetala* collected from the South China Sea. Compound 102 showed antibacterial activity against *Vibrio parahaemolyticus* (MIC = 2.5 µg/mL) and *Vibrio anguillarum* (MIC = 5 µg/mL) [57]. A cytotoxic anthraquinone described as altersolanol A (103), was extracted from *Phomopsis* sp. (PM0409092) isolated from *Nyctanthes arbor-tristis.* Compound 103 had cytotoxic activity to 34 human cancer cells in vitro and gave the mean IC$_{50}$ (IC$_{70}$) value of 0.005 µg/mL (0.024 µg/mL) [58]. A new tetrahydroanthraquinone, named (2R,3S)-7-ethyl-1,2,3,4-tetrahydro-2,3,8-trihydroxy-6-methoxy-3-methyl-9,10-anthracenedione (104), was separated from *Phomopsis* sp. PSU-MA214 associated with mangrove plant *Rhizophora apiculata.* Compound 104 was found to have low cytotoxic activity against MCF-7 and antibacterial activity against *S. aureus* ATCC25923 and methicillin-resistant *Staphylococcus aureus* SK1 [60]. The extraction of fungus *P. foeniculi* associated with *Foeniculum vulgare* in Bulgaria, resulted in the isolation of two octaketides anthracenones, altersolanols A (103) and J (105). They exhibited phytotoxic activities by leaf puncture bioassay [59]. Four known compounds were isolated from *Phomopsis* sp. derived from *Notobasis syriaca,* including 2-hydroxymethyl-4β,5α,6β-trihydroxycyclohex-2-en (106), (−)-phyllostine (107), (+)-epiepoxydon (108), and (+)-epoxydon monoacetate (109). All metabolites exhibited antifungal (*M. violaceum*), antibacterial (*E. coli, B. megaterium*), and algicidal activities (*C. fuscus*), but 106 and 108 were inactive against *M. violaceum* [61]. A novel dihydroanthalenone, phonaphthalenone A (110), was derived from *Phomopsis* sp. HCCB04730. In terms of bioactive evaluation, compound 110 showed weak cytotoxic activity and moderate inhibitory activity on HIV with IC$_{50}$ value of 11.6 µg/mL [56]. Ampelanol (111) was extracted from *Phomopsis* sp. HNY29-2B isolated from mangrove plant *A. ilicifolius.* Compound 111 showed antibacterial activity towards *B. subtilis* and *S. aureus* with MIC of 25 and 50 µM [62]. The structures of quinones (96–111) are shown in Figure 4.

2.1.7. Phenols

Phenols are a kind of secondary metabolites which are widely distributed and have important physiological functions. They normally have antioxidant activity and play an important role in food industry [112]. Phomosine K (112) isolated from a *Phomopsis* strain showed remarkable antibacterial activity against *Legionella pneumophila* Corby and *E. coli* K12 [61]. Five known metabolites, phomosines A-D (113–116) and phomosine I (117) were isolated from a *Phomopsis* strain derived from *Ligustrum vulgare.* They had antibacterial and antifungal activities against *B. megaterium* and *M. violaceum,* except 116 was not active against *B. megaterium.* Moreover, compounds 113 and 116 inhibited the growth of algae [63]. Two new diphenyl ethers (118–119) were obtained from the culture of *P. asparagi* isolated from the rhizome of *Paris polyphylla* var. *yunnanensis,* collected in Kunming, Yunnan, China. These compounds displayed anti-methicillin-resistant *S. aureus* (anti-MRSA) activities with inhibition zone diameters (IZD) 10.8 ± 2.0 and 11.4 ± 1.8 mm, respectively [64].
new diphenyl ethers, 4-(3-methoxy-5-methylphenoxy)-2-(2-hydroxyethyl)-6-methylphenol (120), 4-(3-hydroxy-5-methylphenoxy)-2-(2-hydroxyethyl)-6-methylphenol (121), and 4-(3-methoxy-5-methylphenoxy)-2-(3-hydroxypropyl)-6-methylphenol (122), were extracted from \textit{P. fukushii} of \textit{Paris polyphylla} var. \textit{yunnanensis}. Compounds 120–122 showed anti-MRSA activities and provided an IZD of 20.2 ± 2.5 mm, 17.9 ± 2.2 mm, and 15.2 ± 1.8 mm, respectively [65]. An endophytic fungus \textit{P. fukushii}, separated from the rhizome of \textit{Paris polyphylla} var. \textit{yunnanensis}, gave three new isopentylated diphenyl ethers (123–125). Compounds (123–125) had notable anti-MRSA activities, and their IZD were 21.8 ± 2.4 mm, 16.8 ± 2.2 mm, and 15.6 ± 2.0 mm, respectively [66]. Two new diphenyl ethers (126–127) were obtained from the fermentation products of \textit{P. fukushii} isolated from \textit{Paris polyphylla} var. \textit{yunnanensis}. The results of the anti-MRSA activities assay revealed that compounds 126 and 127 gave IZD of 13.8 ± 1.5 mm and 14.6 ± 1.6 mm, respectively [67]. Three new naphthalene derivatives (128–130) were separated from \textit{P. fukushii}, an endophytic fungus isolated from \textit{Paris polyphylla} var. \textit{yunnanensis}. Compounds 128–130 showed anti-MRSA activities with MCI values of 4, 4 and 6 mg/mL [68]. From fermentation products of the fungus \textit{Phomopsis} sp. associated with \textit{Paris polyphylla} var. \textit{yunnanensis}, two new naphthalene derivatives (131–132) were obtained. Compounds 131–132 displayed anti-MRSA activities with IZD of 14.5 ± 1.2 and 15.2 ± 1.3 mm [69]. A culture of the marine fungus \textit{P. lithocarpus} FS508 isolated from deep-sea sediment collected from Indian Ocean, obtained a new benzophenone, tenellone H (133). It showed cytotoxicity against HepG-2 (IC\textsubscript{50} = 16 µM) and A549 (IC\textsubscript{50} = 17.6 µM) [70].

\textbf{Figure 4.} Chemical structures of compounds 96–111 from \textit{Phomopsis}.

The new metabolite, 16-acetoxycytosporone B (134), was sourced from \textit{Phomopsis} sp. YM 355364 associated with \textit{Aconitum carmichaeli}. In the bioassay, compound 134
had remarkable antifungal activity towards Cl. albicans, Hormodendrum compactum, and Trichophyton gypseum with MIC values of 32, 128, and 512 μg/mL [71]. Cultivation of Phomopsis sp. 0391 isolated from the stems of Paris polyphylla var. yunnanensis afforded cytosporone B (135) and dothiorelone A (136). These two compounds showed notable lipase inhibition and gave IC₅₀ values of 115 and 275 μg/mL with Orlistat (IC₅₀ = 43 μg/mL) as positive control [72]. Cytosporone B (135) was extracted from the cultivation of Phomopsis sp. PSU-H188, an endophytic fungus from Hevea brasiliensis. 135 showed protective effect on INS-1 832/13 pancreatic β-cells (IC₅₀ = 11.08 μM) [73]. Two diastereomeric antineoplastic tenellone derivatives identified as lithocarinols A (137) and B (138), were isolated from P. lithocarpus FS508, a deep-sea derived fungus derived from a sediment collected in the Indian Ocean. During the cytotoxic assay, compounds 137–138 showed inhibitory effects against HepG-2, MCF-7, SF-268, and A549 cancer cells with IC₅₀ values ranging from 9.4 to 35.9 μmol/L [74]. Phomoindene A (139), a new indene derivative, was produced by Phomopsis sp. (No. GX7-4A) from the mangrove sediment of BeiHai, GuangXi, China. Compound 139 showed weak cytotoxicity against KB, KBv 200, and MCF-7 cancer cells with IC₅₀ values greater than 50 μmol/mL [75]. Then, 4-Hydroxybenzaldehyde (140) was extracted from a strain of Phomopsis sp. YM 35536. The antimicrobial activities of 140 provided MIC values at 256 and 128 μg/mL against B. subtilis and P. oryzae [26]. An investigation of the extracts from P. longicolla HL-2232, afforded a new biphenyl derivative, 5,5′-dimethoxybiphenyl-2,2′-dion (141). Compound 141 displayed antibacterial activity against V. parahaemolyticus with MIC value of 10 μg/mL [57]. A known phenylethyl alcohol, phonomitroester (142), was derived from Phomopsis sp. PSU-MA214, exhibiting cytotoxicity with IC₅₀ value of 43 μg/mL against KB [60]. Cytosporone U (143) was isolated from the fermentation products of Phomopsis sp. FJBR-11. This compound displayed inhibitory effect on TMV with IC₅₀ value of 144.6 μg/mL [76]. Altenusin (144) was extracted from Phomopsis sp. CAFT69, possessing a certain motility inhibitory and lytic activity against the zoospores of grapevine downy mildew pathogen P. viticola between 1–10 μg/mL [48]. Cosmochlorins D (145) and E (146) produced by the endophytic fungus Phomopsis sp. N-125 of Ficus ampelast, showed significant cytotoxic activities against HL60 cells with IC₅₀ values of 6.1 and 1.8 μM, and displayed growth-inhibition activities [77]. The structures of phenols (112–146) are shown in Figure 5.

2.1.8. Oblongolides

Oblongolides are a kind of natural active products with novel norsesquiterpene γ-lactone. At present, oblongolides are relatively less reported than other kinds of polyketides. Most of them exist in the fungi of Phomopsis, and mainly have cytotoxic activities [113]. Three new oblongolides, oblongolides Z (147) and Y (148) and 2-deoxy-4α-hydroxyoblongolide X (154), were extracted from Phomopsis sp. BCC 9789 isolated from a wild banana (Musa acuminata) leaf. Compound 147 was found to have inhibitory effect on anti-herpes simplex virus type 1 (HSV-1) with IC₅₀ value of 14 μM and showed cytotoxicities with IC₅₀ values of 26–60 μM towards KB, BC, NCI-H187, and Vero cancer cells. Compound 148 was cytotoxic against BC (IC₅₀ = 48 μM) and 154 showed anti-HSV-1 activity with IC₅₀ value of 76 μM [78]. Five metabolites, oblongolides C1 (149), P1 (150), X1 (151), and C (153), along with 6-hydroxyphomodiol (152), were separated from the strain Phomopsis sp. XZ-01, an endophytic fungus of Camptotheca acuminata. Compounds 149–153 displayed different degrees of selective inhibition in cytotoxicities against HepG2 and A549 [79]. The structures of oblongolides (147–154) are shown in Figure 5.
2.1.9. Unclassified Polyketides

Five compounds were obtained from *Phomopsis* sp. BCC 45011, including phomoxydiene C (155), 1893 A (156), mycoepoxydiene (157), deacetylmycoepoxydiene (158), and phomoxydiene A (159). All metabolites, except 156, showed strong antimalarial activities against *P. falciparum* K1 with IC$_{50}$ values at 2.41–3.52 µg/mL and cytotoxicities against KB, MCF-7, NCI-H187, and Vero with IC$_{50}$ values between 1.49–45.5 µg/mL [51]. Seven new polyoxygenated cyclohexenoids, phomopoxides A-G (160–166) were obtained from the fermentation products of *Phomopsis* sp. YE3250 isolated from *Paeonia delavayi*. All compounds exhibited α-glycosidase inhibition with IC$_{50}$ values from 1.47 to 3.16 mM, cytotoxic activities against Hela, MCF-7, and NCI-H460 cancer cell lines, and moderate antifungal activities against *C. albicans*, *Aspergillus niger*, *P. oryzae*, *Fusarium avenaceum*, *Fusarium oxysporum*, *Fusarium solani*, *Fusarium moniliforme*, and *Fusarium fujikuroi*. 

Figure 5. Chemical structures of compounds 112–154 from *Phomopsis*. 
and *H. compactum* [80]. A new geranylcylohexenetriol, named phomentrioloxin (167), was obtained from *Phomopsis* sp. of the plant *Carthamus lanatus*. This compound showed phytotoxic activity and might be considered a potential mycoherbicide [81]. A new natural cyclopentenone, phomotenone (168) was produced by *Phomopsis* sp. Compound 168 displayed remarkable antifungal, antibacterial, and antialgal activities against *M. violaceum*, *E. coli*, *B. megaterium*, and *C. fusca* [40]. The cytotoxicity-guided investigation of the fungus *Phomopsis* sp. DC275 of *Vitis vinifera* yielded two new furanones, phomopsolidones A (170) and B (171), and a known phomopsolide B (169). All these metabolites showed weak phytotoxic and antibacterial activities [82]. The structures of unclassified polyketides (155–171) are shown in Figure 6.

![Figure 6. Chemical structures of compounds 155–171 from Phomopsis.](image)

### 2.2. Terpenoids

Terpenoids are a kind of natural bioactive substances with isoprene as scaffold, which are widely distributed and rich in species [114,115]. Herein, a total of 38 terpenoids, including three monoterpenoids, 25 sesquiterpenoids, seven diterpenoids, and three triterpenoids, were isolated from various *Phomopsis* strains, accounting for 15% of all the described metabolites, second only to polyketides. It is worth noting that some terpenoids showed interesting bioactivities, such as enzyme inhibitory and anti-inflammatory activities.

#### 2.2.1. Monoterpenoids

Monoterpenoids and their derivatives have a variety of biological activities, such as cytotoxic, antimicrobial, and anti-inflammatory, which have potential application value in clinical medicine [116]. Acropyrone (172) was extracted from culture of *Phomopsis* sp.
HNY29-2B. Compound 172 showed antibacterial activity towards *B. subtilis* (MIC = 25 µM) and *P. aeruginosa* (MIC = 50 µM) [62]. A phytotoxic pentaketide monoterpenoid, nectriapyrone (173), was produced by the fungus *P. foeniculi* [59]. According to bioassay-guided procedure, a known compound, (15,25,45)-trihydroxy-α-methane (174) was obtained from *Phomopsis* sp., displaying antialgal activity against *C. fusca* and antibacterial activity against *E. coli* and *B. megaterium* [40]. The structures of monoterpenoids (172–174) are shown in Figure 7.

**Figure 7.** Chemical structures of compounds 172–199 from *Phomopsis*. 
2.2.2. Sesquiterpenoids

Sesquiterpenoids are the most abundant members of natural terpenoids because of their various structures and notable bioactivities. The chemical components of sesquiterpenoids had been found in plants, animals, microorganisms and marine organisms [117,118]. A series of sesquiterpenoids (175–184 and 195) were isolated from a strain of *Phomopsis* sp. TJ507A obtained from *Phyllanthus glaucus*. All compounds exhibited the inhibitory rates in the range of 19.4% to 43.8% against β-site amyloid precursor protein cleaving enzyme 1 (BACE1) at the concentration of 40 µM [83]. From the endophytic fungus *P. cassia* associated with *Cassia spectabilis*, two new diastereoisomeric cadinanes sesquiterpenes (185–186), (7S,10R)-3-hidroxicalamen-8-one (187), and aristelegone-A (188) were isolated. Compounds 185–188 showed antifungal activities towards *Cladosporium cladosporioides* and *Cladosporium sphaerospermum*, and acetylcholinesterase inhibitory activities [84]. Four metabolites were separated from *P. archeri* of *Vanilla albidia*, including three new sesquiterpenes, phomoarcherins A-C (189–191), and a known kampanol A (192). The cytotoxic activites of 189–192 provided IC50 values from 0.1 to 19.6 µg/mL against five cholangiocarcinoma cells (KKU-100, KKU-M139, KKU-M156, KKU-M213, and KKU-M214), and 189–190 showed little activities against the KB with IC50 values at 42.1 and 9.4 µg/mL. Compound 190 displayed antimalarial activity against *P. falciparum* (IC50 = 0.79 µg/mL) [85]. A new sesquiterpene, (+)-S-1-methyl-abscisic-6-acid (193), and a known (+)-S-abscisic acid (194), were extracted from *P. amygdali* of *Call midge*. Compounds 193–194 showed antibacterial activities against *P. aeruginosa* 2033E with MIC at 30 and 58 µg/mL [86]. Curcumol (196), isolated from *P. castaneae-mollissimae* GQH87 derived from medicinal plant *Artemisia annua*, showed cytotoxicity against MCF-7, HepG2, and A549 with IC50 values of 25.73, 65.18, and 178.32 µg/mL, respectively [87]. The cultivation of fungus *Phomopsis* sp. CAFT69, afforded two bioactive compounds, 9-hydroxyphomopsidin (197) and phomopsidin (198). Both of them showed motility inhibition and lytic activities on the zoospores of grapevine downy mildew pathogen *P. viticola* [48]. AA03390 (199) was isolated from a strain of *P. lithocarpus* FS508. The compound had low cytotoxicity with IC50 values of 25.5–29.6 µM against HepG-2, MCF-7, SF-268, and A549 [70]. The structures of sesquiterpenoids (175–199) are shown in Figure 7.

2.2.3. Diterpenoids

Diterpenoids are a kind of terpenoids with various skeletons. They possess significant pharmacological activities, such as cytotoxic, antimicrobial, and anti-inflammatory activities [119]. A new diterpenes, libertellenone J (200), was derived from fungus *Phomopsis* sp. S12 isolated from *Iligera rhodantha*. This compound showed anti-inflammatory activity by reducing the production of NO, IL-1β, IL-6 and TNF-α, and inhibiting MAPKs and NF-κB pathways [88]. Four metabolites were extracted from *Phomopsis* sp. S12, including three new pimaranes, libertellenone T (202), pedinophyllols K (203) and L (204), together with a known compound, libertellenone C (201). Compounds 201–204 showed different degrees of anti-inflammatory activities against inhibiting the production of inflammatory factors (IL-1β, IL-6) by lipopolysaccharide in macrophages [89]. Secondary metabolites from fungus *P. amygdali* contained two known compounds, fusicoccin J (205) and 3α-hydroxyfusicoccin J (206). Biologically, compounds 205–206 showed antibacterial activities against *P. aeruginosa* 2033E with MICs at 26 µg/mL [86]. The structures of diterpenoids (200–206) are shown in Figure 8.
2.2.4. Triterpenoids

Triterpenoids are a kind of organic compounds widely found in nature. They have attracted the attention of researchers because their structural diversity and rich bioactivities [120]. A new euphane triterpenoid, 3\text{S},22\text{R},26-trihydroxy-8,24\text{E}-euphadien-11-one (207), was isolated from \textit{P. chimonanthi} obtained from medicinal plant \textit{Tamarix chinensis} in the yellow river delta, Dongying. Compound 207 exhibited cytotoxicity against A549, MDA-MB-231, and PANC-1 cancer cells with IC\textsubscript{50} values of 20.32, 19.87 and 30.45 \textmu M, respectively [90]. The fungus \textit{Phomopsis} sp. SNB-LAPI-7-32, occurring from plant \textit{Diospyros carbonaria}, produced a first lupane-type triterpenoid, betulinic acid (208). Compound 208 displayed antiviral activity on inhibiting RNA-dependant RNA polymerase with IC\textsubscript{50} values of 4.3 \textmu M and cytotoxicity against HCT-116 and MRC-5 [91]. Oleanolic acid (209) was extracted from \textit{P. castanea-mollissimae} GQH87, which showed cytotoxicity against MCF-7, HepG2, and A549 with IC\textsubscript{50} values of 16.61, 39.53, and 40.08 \textmu g/mL, respectively [87]. The structures of triterpenoids (207–209) are shown in Figure 8.

2.3. Steroids

Steroids are secondary metabolites with a variety of chemical structures and biological activities. At present, many researchers try to find steroidal metabolites as potential lead compounds in drug design [121]. Till now, only nine steroids were isolated from \textit{Phomopsis} and showed antifungal, anti-inflammatory, and antiviral activities. Five steroids were derived from culture of \textit{Phomopsis} sp., an endophytic fungus separated from \textit{A. carmichaeli}, including (14\text{β},22\text{E})-9,14-dihydroxyergosta-4,7,22-triene-3,6-dione (210), (5\text{α},6\text{β},15\text{β},22\text{E})-6-ethoxy-5,15-dihydroxyergosta-7,22-dien-3 one (211), calvasterols A (212) and B (213), and ganodermaside D (214). All isolated compounds displayed different degrees of selective...
antifungal activities against \( C. \) albicans, \( A. \) niger, \( P. \) oryzae, \( F. \) avenaceum, \( H. \) compactum, and \( T. \) gypseum with MIC values between 64–512 \( \mu \)g/mL [92]. Dankasterone \( A \) (215) and \( 3\beta,5\alpha,9\alpha\)-trihydroxy-(22E,24R)-ergosta-7,22-dien-6-one (216) were isolated from \( Phomopsis \) sp. YM 355364. Compound 215 showed anti-influenza activity against H5N1 pseudovirus (IC\(_{50} = 3.56 \mu M\)). Compounds 215–216 showed antifungal activities against \( C. \) albicans, \( P. \) oryzae, \( H. \) compactum, and \( T. \) gypseum with MIC values of 64–512 \( \mu \)g/mL [71]. A new functionalized ergostane-type steroid, named phomosterone \( B \) (217), was obtained from \( Phomopsis \) sp. TJ507A isolated from medicinal plant \( P. \) glaucus. Compound 217 showed anti-inflammatory activity by inhibiting iNOS enzyme with an IC\(_{50}\) value of 1.49 \( \mu M\) [93]. Cyathisterol (218) was extracted from \( Phomopsis \) sp. YM 355364, displaying moderate antifungal activity toward \( P. \) oryzae (MIC = 128 \( \mu \)g/mL) [26]. The structures of steroids (210–218) are shown in Figure 9.

![Chemical structures of compounds 210–218 from Phomopsis.](image)

**Figure 9.** Chemical structures of compounds 210–218 from \( Phomopsis \).

### 2.4. Macrolides

Macrolides are a class of medicinal compounds containing macrolactone ring structures, many of which are used as antifungal and antibacterial drugs in clinic, such as erythromycins [122]. Nowadays, a large number of macrolide antibiotics are widely used in the treatment of human diseases. Eight secondary metabolites were obtained from \( Phomopsis \) and showed cytotoxic, antimicrobial, and enzyme inhibitory activities. Three cytotoxic polyketides, Sch-642305 (219), LMA-P1 (220), and benquoine (221), were found in the endophytic fungus \( Phomopsis \) sp. CMU-LMA of \( Alpinia \) malaccensis. Compounds 219 and 221 also displayed antimicrobial activities [94]. The endophytic fungus \( Phomopsis \)
sp. IFB-ZS1-S4 provided a known aspergillide C (222), which had moderate inhibitory effect on neuraminidase in vitro with IC\textsubscript{50} value of 5.59 µM [37]. Four highly oxygenated tenellone-macrolide conjugated dimers, lithocarpins A-D (223–226), were obtained from \textit{P. lithocarpus} F5508 isolated from the deep-sea sediment sample collected in the Indian Ocean. All metabolites (223–226) showed cytotoxic activities against three human tumor cells (SF-268, MCF-7, and HepG-2) with IC\textsubscript{50} values in the range of 17.0–52.2 µM [95]. The structures of macrolides (219–226) are shown in Figure 10.

![Figure 10. Chemical structures of compounds 219–226 from \textit{Phomopsis}.](image)

2.5. Alkaloids

Alkaloids are important nitrogen-containing organic compounds widely existing in microorganisms. At present, some alkaloids have been used to treat human diseases [123]. A total of 16 alkaloids have been isolated from \textit{Phomopsis} and display various important bioactivities, such as cytotoxic, antibacterial, anti-inflammatory activities. Two compounds with special carbon skeleton, named phomopchalasins B (227) and C (232) were isolated from \textit{Phomopsis} sp. shj2, an endophytic fungus obtained from the stems of \textit{Isodon eriocalyx} var. \textit{laxiflora}. Compound 232 showed cytotoxic activity against HL-60, SMMC-7721, and A-549 with IC\textsubscript{50} values of 14.9, 22.7, and 21.1 µM, and displayed anti-inflammatory activity by reducing NO production (IC\textsubscript{50} = 11.2 µM). In addition, compounds 227 and 232 showed antimigratory activities against MDA-MB-231 with IC\textsubscript{50} values of 19.1 and 12.7 µM [96]. Chemical investigation of \textit{Phomopsis} spp. xy21 and xy22 obtained from leaves of the mangrove tree \textit{X. granatum}, collected in Trang Province, Thailand, led to the isolation of a new cytochalasin, phomopsichalasin G (228). It showed cytotoxicities against HCT-8, HCT-8/T, A549, MDA-MB-231, and A2780 cancer cells with IC\textsubscript{50} values between 3.4–8.6 µM [97]. Three known compounds, namely 18-metoxycytochalasin J (229), cytochalasins H (230) and J (231), were obtained from \textit{Phomopsis} sp. isolated from the nut of \textit{Garcinia kola}. These three compounds exhibited cytotoxicities against HeLa (LC\textsubscript{50} = 3.66–35.69 µg/mL) and Vero (LC\textsubscript{50} = 73.88–129.10 µg/mL), and different degrees of antibacterial activities against six bacterial pathogens (\textit{Vibrio cholera} SG24, \textit{V. cholera} CO6, \textit{V. cholera} NB2, \textit{V. cholera} PC2, \textit{Shigella flexneri} SDINT, and \textit{S. aureus} ATCC 25923) [98]. The cytochalasins, epoxycytochalasin H (234) and cytochalasin N (233) and H (230), were extracted from \textit{Phomopsis} sp. By254 derived from the root of \textit{Gossypium hirsutum}. They showed remarkable antifungal activities with IC\textsubscript{50} values between 0.1–50 µg/mL against \textit{S. sclerotiorum}, \textit{Bipolaris maydis}, \textit{Fusarium oxysporum}, \textit{B. cinerea}, \textit{Bipolaris sorokiniana}, \textit{Gaumannomyces graminis} var. \textit{tritici} and \textit{Rhizoctonia cerealis} [99]. Cytochalasins H (230) and J (231), and alternariol (55) were extracted from \textit{Phomopsis} sp. of \textit{Senna spectabilis} and showed anti-inflammatory activities by inhibiting the production of reactive oxygen species (ROS). Compound 230 also showed antifungal and acetylcholinesterase enzyme (AChE) inhibitory activities [49]. Cytochalasin J
(231) was derived from *P. asparagi* of plant *Peperomia sui* and exhibited antiandrogen activity (IC$_{50}$ = 6.2 µM) [100]. The antibacterial diaporthalasin (235) was extracted from *Phomopsis* sp. PSU-H188, showing anti-MRSA activity with MIC of 4 µg/mL [73]. A phenylfuropyridone racemate, (+)-tersone E (236), and a known ent-citrione A (237), were separated from *P. tersa* FS441 derived from deep-sea sediment in the Indian Ocean. Compound 236 showed cytotoxicity with IC$_{50}$ values at 32.0, 29.5, 39.5 and 33.2 µM towards SF-268, MCF-7, HepG-2, and A549 cancer cells. Compounds 236–237 had antibacterial activities against *S. aureus* with MIC value of 31.2 and 31.5 µg/mL [101]. Two new chromenopyridine derivatives, phochrodines C (238) and D (239) with 5H-chromeno[4,3-b]pyridine, were isolated from *Phomopsis* sp. 33# associated with the bark of *R. stylosa* in the South China Sea. Compounds 238–239 displayed anti-inflammatory activities with IC$_{50}$ values of 49 and 51 µM by inhibiting nitric oxide production. Moreover, compound 239 also showed antioxidant activity with IC$_{50}$ value at 34 µM [102]. A novel depsipeptide, PM181110 (240), was obtained from *P. glabrae* of *Pongamia pinnata*. It showed anticancer activity towards 40 human cancer cells in vitro (mean IC$_{50}$ = 0.089 µM) and 24 human tumor xenografts ex vivo (mean IC$_{50}$ = 0.245 µM) [103]. Fusaristatin A (241) was separated for the first time from *P. longicolla* S1B4, showing antibacterial activity against *X. oryzae* [34]. Exumolide A (242) from the strain *Phomopsis* sp. (No. ZH-111) significantly promoted the growth of SIV branches and showed low cytotoxic activity against Hep-2 and HepG2 [44]. The structures of alkaloids (227–242) are shown in Figure 11.

Figure 11. Chemical structures of compounds 227–242 from *Phomopsis*. 
2.6. Flavonoids

Flavonoids are a kind of natural active substances of polyphenols. They are relatively less occurred in fungi [124]. In this review, only four flavonoids, quercetin (243) (Figure 12), luteolin (244), naringenin (245), and luteolin-7-O-glucoside (246) were isolated from P. castaneae-mollissimae GQH87. They displayed cytotoxic activities against MCF-7, HepG2, and A549 with IC\textsubscript{50} values between 18.7 and 169.8 µg/mL [87].

![Figure 12. Chemical structures of compounds 243–246 from Phomopsis.](image)

3. Bioactive Secondary Metabolites from Diaporthe spp.

In the last ten years, a total of 106 bioactive secondary metabolites have been isolated from the genus Diaporthe (Table 2). These compounds exhibit various bioactivities, such as cytotoxic, antifungal, antibacterial, antiviral, antioxidant, anti-inflammatory, phytotoxic, antitubercular, antifibrotic, antidiabetic, antimigratory, antiangiogenic, antihyperlipidemic, inhibiting leishmanicidal, activating the NF-κB pathway, enzyme inhibition, inhibitory effects on osteoclastogenesis, antifeedant, contact toxicity, and oviposition deterrent activities. The habitats of the Diaporthe strains were also shown in Table 2, which revealed that there are 73 (accounting for 69%) and 32 (accounting for 30%) compounds isolated from terrestrial and marine environments, respectively, while only one compound (1%) was not mentioned with its habitat.

| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 247    | Xanthones       | 3,8-Dihydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate | Diaporthe sp. SCSIO 41011 | Rhizophora stylosa (M) | Anti-IAV | [125] |
| 248    | Chromones       | Penialidin A | Diaporthe sp. GZU-1021 | Chiromanteshaematochir (M) | Anti-inflammatory | [126] |
| 249    | (−)-Phomopsichin A | (+)-Phomopsichin B | D. phaseolorum SKS09 | Acanthus ilicifolius (M) | Inhibitory effects on osteoclastogenesis | [128] |
| 250    | (−)-Phomopsichin B | (+)-Phomopsichin B | D. phaseolorum SKS09 | A. ilicifolius (M) | Inhibitory effects on osteoclastogenesis | [128] |
| 251    | Diaporchromanone C | Diaporchronmanone D | SCSIO 41011 | A. ilicifolius (M) | Inhibitory effects on osteoclastogenesis | [128] |
| 253    | Pestalotiopsone F | Pestalotiopsone B | Diaporthe sp. SCSIO 41011 | R. stylosa (M) | Anti-IAV | [125] |
|        |                 |           | D. pseudomangiferae | Tylophora ouata (T) | Antifibrotic | [129] |

Table 2. The bioactive secondary metabolites of the genus Diaporthe during 2010–2019.
| Number | Structural Types | Compounds | Strains | Habitats (T/M a) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 254    | Diaportheone A  | Diaporthe sp. P133 | Pandanus amaryllifolius (T) | Antitubercular | [130] |
| 255    | Diaportheone B  | Diaporthe sp. P133 | P. amaryllifolius (T) | Antitubercular | [130] |
| 53     | Chromanones     | (105)-Diaporthin | Orthosporin | D. terebinthifolii LGMF907 | Antitubercular | [131] |
| 54     | Cytosporone D   | D. terebinthifolii LGMF907 | T. ouata (T) | Cytotoxic, Antioxidant, Antidiabetic | [129] |
| 256    | Orthosporin     | Diaporthe sp. SXZ-19 | Schinus terebinthifolius (T) | Antibacterial | [131] |
| 53     | Chromanones     | (105)-Diaporthin | Orthosporin | D. terebinthifolii LGMF907 | Antibacterial | [131] |
| 54     | Cytosporone D   | D. terebinthifolii LGMF907 | T. ouata (T) | Cytotoxic, Antioxidant, Antidiabetic | [129] |
| 257    | Mucorisorcoumarin A | Diaporthe sp. SXZ-19 | Schinus terebinthifolius (T) | Antibacterial | [131] |
| 258    | Butyl 5-[(1R)-1-hydroxymethyl]-[2,2′-bifuran]-5(2H)-one | Diaporthe sp. SXZ-19 | Schinus terebinthifolius (T) | Antibacterial | [131] |
| 259    | Biatriosporin N | Diaporthe sp. SXZ-19 | Schinus terebinthifolius (T) | Antibacterial | [131] |
| 260    | Pyrones Phomopsolide A | Diaporthe sp. SXZ-19 | Carthamus lanatus (T) | Cytotoxic | [134] |
| 261    | Pyrones Phomopsolide B | D. maritima Picea mariana (T) | Picea rubens (T) | Antibacterial | [136] |
| 262    | Pyrones Phomopsolide C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 263    | Pyrones Phomopsolide C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 264    | Phyllostyrone acetate A | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 265    | Phyllostyrone acetate B | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 266    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 267    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 268    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 269    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 270    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 271    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 272    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 273    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 274    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 275    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |
| 276    | Phyllostyrone acetate C | D. maritima Picea mariana (T) | P. mariana (T) | Antibacterial | [136] |

a T: terrestrial, M: marine.
| Number | Structural Types | Compounds | Strains | Habitats (T/Ma) | Activities | Refs. |
|--------|------------------|-----------|---------|----------------|------------|-------|
| 277    | Phenols          | Tyrosol   | D. helianthin | Luehea divaricate (T) | Antagonistic | [141] |
|        |                  | 2,5-Dihydroxybenzyl alcohol | D. vochysiae | Vitis vinifera (T) | Phytotoxic | [142] |
| 278    |                  | 4-Hydroxybenzaldehyde | D. eres | V. vinifera (T) | Phytotoxic | [142] |
| 279    |                  | 4-Hydroxybenzoic acid | D. eres | V. vinifera (T) | Phytotoxic | [142] |
| 280    |                  | Arbutin | D. lithocarpus | A. heterophyllus (T) | Cytotoxic | [137] |
| 113    |                  | Phomosine A | Diaporthole sp. F2934 | Siparana gesnerioides (T) | Antibacterial | [144] |
| 115    |                  | Phomosine C | Diaporthole sp. F2934 | S. gesnerioides (T) | Antibacterial | [144] |
| 282    |                  | Flavomannin-6,6'-di-O-methyl ether | D. melonis | Annona squamosa (T) | Antimicrobial | [145] |
| 283    |                  | Acetoxydothiorelone B | D. pseudomangiferae | T. ouata (T) | Anti-inflammatory | [130] |
| 284    |                  | Dothiorelone B | D. pseudomangiferae | T. ouata (T) | Anti-inflammatory | [130] |
| 285    |                  | Dothiorelone L | D. pseudomangiferae | T. ouata (T) | Anti-inflammatory | [130] |
| 286    |                  | Dothiorelone G | D. pseudomangiferae | T. ouata (T) | Anti-inflammatory | [130] |
| 287    |                  | Diaporthol A | Diaporthole sp. ECN-137 | Phellodendron amurense (T) | Anti-migration | [146] |
| 288    |                  | Diaporthol B | Diaporthole sp. ECN-137 | P. amurense (T) | Anti-migration | [146] |
| 289    |                  | Tenellone C | Diaporthole sp. SYSU-HQ3 | Excococia gallocha (M) | MptP inhibitory | [147] |
| 290    |                  | Tenellone D | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
| 291    |                  | Diaporindene A | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
| 292    |                  | Diaporindene B | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
| 293    |                  | Diaporindene C | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
| 294    |                  | Diaporindene D | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
| 295    |                  | Isoprenylisobenzofuran A | Diaporthole sp. SYSU-HQ3 | E. gallocha (M) | Anti-inflammatory | [148] |
|        |                  | Unclassified polyketides | Phomentrioxin B | D. gulyae | C. lanatus (T) | Phytotoxic | [149] |
| 300    |                  | epi-Isochromophilone II | Diaporthole sp. SC1011 | R. stylosa (M) | Cytotoxic | [150] |
| 301    |                  | Isochromophilone D | Diaporthole sp. SC1011 | R. stylosa (M) | Cytotoxic | [150] |
| 302    |                  | Monoterpenoids | (1R,2R,4R)-Trihydroxy-p-methane | Diaporthole sp. SXZ-19 | C. lanatus (T) | Cytotoxic | [134] |
| 303    |                  | Gullypyrone A | Diaporthole sp. SXZ-19 | C. lanatus (T) | Phytotoxic | [149] |
| 304    |                  | Gullypyrone B | Diaporthole sp. SXZ-19 | C. lanatus (T) | Phytotoxic | [149] |
| 173    |                  | Nectriaprynone | D. Kongii | C. lanatus (T) | Phytotoxic | [153] |
| 305    |                  | Sesquiterpenoids | Diaporol R | Diaporthole sp. SXZ-19 | R. stylosa (M) | Cytotoxic | [151] |
| 306    |                  | Eremofortin F | Diaporthole sp. SNB-GSS10 | Sabicea cinerea (T) | Cytotoxic | [152] |
| 307    |                  | Lithocarin B | Diaporthole sp. SXZ-19 | A. heterophyllus (T) | Morinda offcinalis (T) | Cytotoxic | [153] |
| Number | Structural Types | Compounds | Strains | Habitats (T/M *4) | Activities | Refs. |
|--------|------------------|-----------|---------|------------------|------------|-------|
| 308    | Triterpenoids    | Lithocarin C | D. lithocarypus A740 | M. officinalis (T) | Cytotoxic | [153] |
| 309    | Steroids         | Triterpenoids | Diaporthe sp. LG23 | Maltonia fortunei (T) | Antibacterial | [154] |
| 216    | Steroids         | 3β,5α,9α-Trihydroxy-(22E,24R)-ergosta-7,22-dien-6-one | Diaporthe sp. LG23 | M. fortunei (T) | Antibacterial | [154] |
| 310    | Steroids         | Chaxine C | Diaporthe sp. LG23 | M. fortunei (T) | Antibacterial | [154] |
| 311    | Ten-membered lactones | Phomolide C | Diaporthe sp. | Aucuba japonica var. boralis (T) | Inhibitory of proliferation of human colon adenocarcinoma cells | [155] |
| 312    | Alkaloids        | Xylarolide | D. terebinthifolii Glycyrrhiza glabra (T) | | Antimicrobial, Cytotoxic | [156] |
| 313    | Alkaloids        | Phomolide G | D. terebinthifolii G. glabra (T) | Cytotoxic | | [156] |
| 314    | Alkaloids        | Xylarolide A | Diaporthe sp. | D. inoxia (T) | Cytotoxic, Antioxidant | [133] |
| 315    | Alkaloids        | 18-Des-hydroxy cytochalasin H | D. phaseolorum-92C | Combretum lanceolatum (T) | Inhibiting leishmaniacid, Antioxidant, Cytotoxic | [157] |
| 316    | Alkaloids        | 21-Acetoxytocchalasin J2 | Diaporthe sp. GDG-118 | Sophora tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 317    | Alkaloids        | 21-Acetoxytocchalasin J3 | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 318    | Alkaloids        | Cytochalasin J3 | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 319    | Alkaloids        | Cytochalasin H | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 320    | Alkaloids        | 7-Acetoxytocchalasin H | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 321    | Alkaloids        | Cytochalasin J | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 322    | Alkaloids        | Cytochalasin E | Diaporthe sp. GDG-118 | S. tonkinensis (T) | Antifungal, Antibacterial | [158] |
| 323    | Alkaloids        | 21-O-Decetyl-L-696,474 | Diaporthe sp. | Chiromanteshae matohir (M) | Anti-inflammatory | [126] |
| 324    | Alkaloids        | Cordysinin A | Diaporthe sp. GZU-1021 | Kandelia oburate (M) | | [159] |
| 325    | Alkaloids        | 5-Deoxybostrycoidin | Diaporthe sp. GDG-118 | A. ilicifolius (M) | Cytotoxic | [160] |
| 326    | Alkaloids        | Fusaristatin A | D. phaseolorum DE-2 | A. ilicifolius (M) | Cytotoxic | [160] |
| 327    | Alkaloids        | Diapolic acid A | D. phaseolorum SYSU-HQ3 | V. divergens (T) | Antimicrobial, Cytotoxic | [143] |
| 328    | Alkaloids        | Diapolic acid B | Diaporthe sp. SYSU-HQ3 | E. agallocha (M) | Anti-inflammatory | [148] |
| 329    | Alkaloids        | Cordysinin A | Diaporthe sp. SYSU-HQ3 | E. agallocha (M) | Anti-inflammatory | [148] |
| 330    | Fatty acids      | Fusaristatin A | D. phaseolorum DE-2 | A. ilicifolius (M) | Cytotoxic | [160] |
| 331    | Fatty acids      | Diapolic acid A | D. phaseolorum SYSU-HQ3 | V. divergens (T) | Antimicrobial, Cytotoxic | [143] |
| 332    | Fatty acids      | Diapolic acid B | Diaporthe sp. SYSU-HQ3 | E. agallocha (M) | Anti-inflammatory | [148] |
| 333    | Fatty acids      | Protein A | D. phaseolorum SYSU-HQ3 | E. agallocha (M) | Anti-inflammatory | [148] |

*T/M* denotes the temperature and medium conditions used during the experiment.
Table 2. Cont.

| Number | Structural Types | Compounds | Strains | Habitats (T/M *) | Activities | Refs. |
|--------|-----------------|-----------|---------|-----------------|------------|-------|
| 334    | Diaporthin E    | Diaporthe sp. JC-J7 | Dendrobium nobile (T) | Antihyperlipidemic | [163] |
| 335    | 3-Hydroxy-5-methoxyhex-5-ene-2,4-dione | Diaporthe sp. ED2 | Orthosiphon stamineus (T) | Antifungal | [164] |

* T: terrestrial environment; M: marine environment; † The habitat was not mentioned.

3.1. Polyketides

There are 67 polyketides reviewed from *Diaporthe* and they exhibit rich biological activities. Here, we classify these polyketides into the following structural types: xanthones, chromones, chromanones, furanones, pyrones, quinones, phenols, oblongolides, and unclassified polyketides.

3.1.1. Xanthones

Chemical investigation of *Diaporthe* sp. SCSIO 41011 derived from mangrove plant *R. stylosa* led to identification of a known compound, 3,8-dihydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate (247) (Figure 13). It showed influenza A virus (IAV) inhibition against A/Puerto Rico/8/34 H274Y (H1N1), A/FM-1/1/47 (H1N1), and A/Aichi/2/68 (H3N2) with IC\(_{50}\) values of 9.40, 4.80, and 5.12 \(\mu\text{M}\), respectively [125]. Phomoxanthone A (28) with novel carbon skeleton was isolated from the fungus *Diaporthe* sp. GZU-1021 derived from a red-clawed crab *Chiromantes haematochir* and *D. phaseolorum* FS431 of deep-sea sediment from the Indian Ocean. This compound showed anti-inflammatory activity by inhibiting nitric oxide (NO) production in RAW 264.7 cells with an IC\(_{50}\) value of 6.1 \(\mu\text{M}\) [126], and it displayed good cytotoxicity against MCF-7, HepG-2, and A549 with IC\(_{50}\) values of 2.60, 2.55, and 4.64 \(\mu\text{M}\), respectively [127].

3.1.2. Chromones

Chemical analysis of *Diaporthe* sp. GZU-1021 associated with *Chiromantes haematochir* resulted in the identification of penialidin A (248) and (−)-phomopsichin B (36). They showed inhibitory effects on NO production with IC\(_{50}\) values at 11.9 and 16.5 \(\mu\text{M}\) [126]. Six bioactive metabolites were separated from *D. phaseolorum* SKS019 derived from mangrove plant *A. ilicifolius*, including four new compounds, (−)-phomopsichin A (249), (+)-phomopsichin B (250), diaporchromanones C (251) and D (252), along with two known compounds, (+)-phomopsichin A (35) and (−)-phomopsichin B (36). These metabolites showed moderate inhibition on osteoclastogenesis by inhibiting RANKL-induced NF-κB activation [128]. Pestalotiopsones F (40) and B (253) were isolated from *Diaporthe* sp. SCSIO 41011. The two compounds exhibited remarkable anti-IAV activities with IC\(_{50}\) values between 2.52–39.97 \(\mu\text{M}\) [125]. Two new benzopyranones, diaportheones A (254) and B (255), were extracted from *Diaporthe* sp. P133 derived from *Pandanus amaryllifolius*. They showed moderate antitubercular activities and provided MIC values of 100.9 and 3.5 \(\mu\text{M}\) against *Mycobacterium tuberculosis* H\(_{37}\)Rv with Rifampin (MIC = 0.25 \(\mu\text{M}\)) as the positive control [130]. The structures of chromones (248–255) are shown in Figure 13.

3.1.3. Chromanones

Two isocoumarins, (10S)-diaporthin (53) and orthosporin (256), were extracted from *D. terebinthifolii* LGMF907 isolated from *Schinus terebinthifolius*. They showed antibacterial activities against the methicillin-sensitive *Staphylococcus aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) [131]. Cytosporone D (54) and mucorisorcomarin A (257) were isolated from the endophytic fungus *D. pseudomangiferinae* of *Tylophora ovata*. Compound 257 displayed anti-fibrosis activity with the inhibitory rate of 52.1% on the activation of human lung fibroblasts MRC-5 cells induced by TFG-β at 10 \(\mu\text{M}\). Cytosporone D (54) showed cytotoxicity toward BGC-823 (IC\(_{50} = 8.1 \mu\text{M}\)) and antioxidant activity with the inhibition rate of...
63.3% by releasing MOA at the concentration of 10 µM, and moderate antidiabetic activity against protein tyrosine phosphatase 1B (PTP1B) [129]. The fungus D. erez derived from pathogen-infected leaf of Hedera helix produced an isocoumarin, 3,4-dihydro-8-hydroxy-3,5-dimethylisocoumarin (258), showing phytotoxic activity in Lemma paucicostata growth [132]. A novel metabolite, diportharine A (259), was obtained from the culture of Diaporthe sp. isolated from Datura inoxia. It showed notable antioxidant activity through DPPH radical scavenging effects (EC$_{50}$ = 10.3 µM) [133]. The structures of chromanones (256–259) are shown in Figure 13.

![Chemical structures of compounds 247–269 from Diaporthe](image)

**Figure 13.** Chemical structures of compounds 247–269 from Diaporthe.

### 3.1.4. Furanones

Furanones are widely used in the field of synthesis, and the synthesized products have important pharmacological activities, such as antiviral, antitumor and antimicrobial [165]. Four bioactive furanones were derived from Diaporthe sp. SXZ-19 of C. acuminate, including the new (1R,2E,4S,5R)-1-[(2R)-5-oxotetrahydrofuran-2-yl]-4,5-dihydroxy-hex-2-en-1-yl(2E)-2-methylbut-2-enoate (260) and three linear furanopolyketides (261–263). These compounds had weak cytotoxicities against HCT 116 cells with the concentration at 10 µM [134]. A new 3-substituted-5-diazenylcyclopentendione, named kongiidiazadione (264), was separated from D. kongii of plant C. lanatus, which was phytotoxic component and showed low antibacterial activity against Bacillus amyloliquefaciens [135]. The structures of furanones (260–264) are shown in Figure 13.

### 3.1.5. Pyrones

Four secondary metabolites were isolated from D. maritima of healthy Picea mariana and Picea rubens needles collected from the Acadian forest of Eastern Canada, including three dihydropyrones, phomopsolides A (265), B (169), and C (266), and a stable α-pyrone, (S,E)-6-(4-hydroxy-3-oxopent-1-en-1-yl)-2H-pyran-2-one (267). All compounds showed antifungal
and antibiotic activities against *M. violaceum, Saccharomyces cerevisiae,* and *B. subtilis* [136]. Two known metabolites, 7-hydroxy-6-methoxycoumarin (268) and coumarin (269), were isolated from the endophytic fungus *D. lithocarpus* obtained from *Artocarpus heterophyllus*. Compounds 268 showed significant antifungal activity against *Sporobolomyces salminocolor* with the of 12.2 ± 0.3 mm, and 269 had a diameter inhibition zone of 12.3 ± 0.3 mm against the bacteria *B. subtilis* [137]. The structures of pyrones (265–269) are shown in Figure 13.

### 3.1.6. Quinones

Two cyclohexeneoxidedione derivatives, phyllostine acetate (270) and phyllostine (107), showing strong antifeedant activities on *Plutella xylostella*, were extracted from culture of *D. miricariae* of plant *Cyperus iria*. Compounds 270 and 107 had the feeding inhibition of 100% at 50 µg/cm² and the 50% feeding deterrence (DC₅₀) values of 9 and 4.7 µg/cm², displayed contact toxicities with the median lethal concentration (LC₅₀) values of 4.38 and 6.54 µg/larva, and exhibited oviposition deterrent activities with the indexes of 100% and 28.6% at 50 µg/cm², respectively [138]. The new biatroisporin N (271) was isolated from the marine-derived fungus Diaporthe sp. GZU-1021 and displayed anti-inflammatory activity by inhibiting NO production in RAW 264.7 cells with an IC₅₀ value of 11.5 µM [126]. Two anthraquinone derivatives, emodin (272) and 1,2,8-trihydroxyanthraquinone (273), were isolated from an endophytic fungus *D. lithocarpus*. Emodin (272) exhibited notable cytotoxic activity against murine leukemia P-388 cells (IC₅₀ = 0.41 µg/mL) and antibacterial activity against *B. subtilis, M. luteus, Pseudomonas fluorescences, E. coli,* and *S. cerevisiae* with the diameter of inhibition zones of 14.7, 13.2, 13.7, 12.7, and 11.7 mm, respectively. Compound 273 also displayed antibacterial activity against *B. subtilis, E. coli,* and *S. cerevisiae* at 14.2, 11.3, and 10.7 mm, respectively [137]. A bis-anthraquinone derivative, named (+)-2,2′-epicytoskyrin A (274), was isolated from *Diaporthe* sp. GNBP-10 of *Uncaria gambir* Roxb. It showed antifungal activity against 22 yeast strains and 3 filamentous fungi with MICs between 16–128 µg/mL [139]. Two cytoskyrin type bisanthraquinones, cytoskyrin C (275) and (+)-epicytoskyrin (276), were isolated from *Diaporthe* sp., an endophytic fungus obtained from *Anoectochilus roxburghii*. Compounds 275–276 could activate NF-κB pathway and increase the relative activity of luciferase at the concentration of 50 µM, and showed cytotoxicities against SMMC-7721 cells in dose-dependent manner [140]. The structures of quinones (270–276) are shown in Figure 14.

**Figure 14.** Chemical structures of compounds 270–276 from *Diaporthe.*

### 3.1.7. Phenols

The phenolic metabolite, tyrosol (277), was extracted from *D. helianthi* isolated from *Luehea divaricate*. Tyrosol showed significant antagonistic activity against the tested pathogenic bacteria (*Enterococcus hirae, E. coli, M. luteus, Salmonella typhi, S. aureus,* and *Xanthomonas*)
Microorganisms 2021, 9, 217

asc. Phaseoli) [141]. 2,5-Dihydroxybenzyl alcohol (278) was derived from D. vochysiae LGMF1583 of medicinal plant Vochysia divergens, which showed cytotoxic activity against A549 (IC_{50} = 54.8 µM) and PC3 (IC_{50} = 9.45 µM) [143]. Four phytotoxic compounds, 4-hydroxybenzaldehyde (140), p-cresol (279), 4-hydroxybenzoic acid (280), and tyrosol (277), were isolated from D. erez of grapevine (V. vinifera) wood. In the leaf disk and leaf absorption bioassay, phytotoxicities of all compounds increased with the concentration ranging in 0.1–1 mg/mL [142]. Arbutin (281), obtained from an endophytic fungus D. lithocarpus, had moderate cytotoxicity against murine leukemia P-388 cells and gave an IC_{50} value of 2.91 µg/mL [137]. Two antibacterial metabolites, phomosines A (113) and C (115), were extracted from Diaporthe sp. F2934 of plant Siparuna gesnerioides. They were active against S. aureus, M. luteus, Streptococcus oralis, Enterococcus fecalis, Enterococcus cloacae, and Bordetella bronchiseptica with inhibition zone diameter from 6 ± 0.62 to 12 ± 1.18 mm at the concentration of 4 µg/µL [144]. Flavomannin-6,6′-di-O-methyl ether (282) was extracted from an endophytic strain of D. melonis from Annona squamosal, which showed antimicrobial activity against S. aureus 25697, S. aureus 29213, and Streptococcus pneumoniae ATCC 49619 with MIC values of 32, 32, and 2 µg/mL, respectively [145]. Four secondary metabolites, acetoxydothiorelone B (283), and dothiorelones B (284), L (285) and G (286), were isolated from D. pseudomangiferae. All of them displayed antifibrotic activities with the inhibitory rates of 17.4, 62.9, 59.2 and 41.1% on the activation of human lung fibroblasts MRC-5 cells induced by TGF-β at 10 µM, with pirfenidone (53.2%) as positive control at 1 mM [129]. Two diphenyl ether derivatives, diaporthols A (287) and B (288), were extracted from Diaporthe sp. ECN-137 isolated from the leaves of Phellodendron amurense. Compounds 287–288 exhibited anti-migration effects on TGF-β1-elicited MDA-MB-231 breast cancer cells with an concentration at 20 µM [146]. Tenellone C (289) was obtained from Diaporthe sp. SYSU-HQ3 of mangrove plant E. agallocha, displaying inhibitory effect on M. tuberculosis protein tyrosine phosphatase B (MptpB) (IC_{50} = 5.2 µM) [147]. Six compounds were isolated from endophytic fungus Diaporthe sp. SYSU-HQ3 derived from the branches of E. agallocha, including a new benzophenone derivative, tenellone D (290), four special 2,3-dihydro-1H-indene isomers, diaporindenes A-D (291–294), and isoprenylsobenzofuran A (75). All isolated compounds showed anti-inflammatory activities by LPS-Induced NO production in RAW 264.7 cells with IC_{50} values of 4.2–18.6 µM [148]. The structures of phenols (277–294) are shown in Figure 15.

3.1.8. Oblongolides

Four lovastatin analogues, oblongolides D (295), H (296), P (297) and V (298), were obtained from the endophytic fungus Diaporthe sp. SXZ-19. These metabolites showed weak cytotoxic activities against HCT 116 cells with the concentration of 10 µM [134]. The structures of oblongolides (295–298) are shown in Figure 16.

3.1.9. Unclassified Polyketides

Phomentrioloxin B (299) was obtained from a strain of D. gulyae isolated from C. lana-tus, which had low phytotoxic effect to cause small necrosis against several weedy and crop plant species [149]. The fungus Diaporthe sp. SC51011 derived from mangrove plant R. styllosa, afforded two metabolites, epi-isochromopholine II (300) and isochromopholine D (301). Compound 300 displayed cytotoxicities against ACHN, OS-RC-2, and 786-O cells with IC_{50} values between 3.0 and 4.4 µM, and 301 had an IC_{50} of 8.9 µM against 786-O cancer cells [150]. The structures of unclassified polyketides (299–301) are shown in Figure 16.
Figure 15. Chemical structures of compounds 277–294 from *Diaporthe*.

Figure 16. Chemical structures of compounds 295–301 from *Diaporthe*. 
3.2. Terpenoids

(1R,2R,4R)-Trihydroxy-p-menthane (302) was isolated from Diaporthe sp. SXZ-19, and displayed weak cytotoxicity on HCT 116 cells [134]. Two new α-pyriones, gulypyrones A (303) and B (304), were extracted from D. gulyae. Both of them showed phytotoxic activities and gulypyrone A caused necrosis against Helianthus annuus plantlets [149]. A pentaketide monoterpenoid, nectriapyrone (173), was isolated from culture of D. Kongii, showing phytotoxic activity [135]. A new brasilane-type sesquiterpenoid, diaporol R (305) was produced by an endophytic fungus Diaporthe sp. isolated from leaves of R. stylosa. Diaporol R had moderate cytotoxic effect on SW480 cancer cells and provided an IC\textsubscript{50} value at 8.72 ± 1.32 µM [151]. Eremofortin F (306) was obtained from endophytic fungus Diaporthe sp. SNB-GSS10 of Sabicea cinerea. It showed cytotoxic activity against KB and MRC5 cells with IC\textsubscript{50} values of 13.9 and 12.2 µM [152]. Two new eremophilanes, lithocarins B (307) and C (308), were extracted from D. lithocarpus A740, an endophytic fungus isolated from Morinda officinalis. These compounds displayed low cytotoxicities against SF-268, MCF-7, HepG-2, and A549 tumor cells with IC\textsubscript{50} values between 37.68–97.71 µM [153]. The new triterpenoid, 19-nor-lanosta-5(10),6,8,24-tetraene-1α,3β,12β,22S-tetraol (309), was obtained from Diaporthe sp. LG23 of the Chinese medicinal plant Mahonia fortunei, and displayed antibacterial activity against both Gram-positive and Gram-negative bacteria [154]. The structures of terpenoids (302–309) are shown in Figure 17.

![Figure 17. Chemical structures of compounds 302–314 from Diaporthe.](image)

3.3. Steroids

Only two steroids, 3β,5α,9α-trihydroxy-(22E,24R)-ergosta-7,22-dien-6-one (216) and chaxine C (310) (Figure 17), were isolated from Diaporthe sp. LG23, showing antibacterial activities against B. subtilis with streptomycin as a positive control [154].
3.4. Ten-Membered Lactones

Ten-membered lactones always have anti-tumor, anti-inflammatory, anti-viral, antibacterial and other pharmacological activities, exhibiting important medical value in clinical practice [166]. Phomolide C (311) from Diaporthe sp. of Aucuba japonica var. borealis, inhibited the proliferation of colon adenocarcinoma cells with concentration of 50 µg/mL [155]. The endophytic fungus D. terebinthifoliolus GG3F6 derived from medicinal plant Glycyrrhiza glabra, afforded two known compounds, xylarolide (312) and phomolide G (313). Compound 312 had cytotoxicity in vitro against cancer cells MIA PaCa-2, HCT-116 and T47D cancer cells with IC50 values of 38, 100, and 7 µM and showed notable antimicrobial activity against C. alibans and Yersinia enterocolitica with IC50 values at 78.8 and 72.1 µM. Moreover, Compound 313 showed an IC50 value of 69.2 µM against Y. enterocolitica [156]. A novel metabolite, named xylarolide A (314), was isolated from the fungus Diaporthe sp. of D. inoxia. Compound 314 had remarkable cytotoxicities against MIA PaCa-2 and PC-3 cancer cells with IC50 values between 14–32 µM, and also showed antioxidant activity on DPPH radical scavenging effect (EC50 = 10.3 µM) [133]. The structures of four ten-membered lactones (311–314) are shown in Figure 17.

3.5. Alkaloids

18-Des-hydroxy cytochalasin H (315) was obtained from endophytic fungus D. phaseolorum-92C of Combretum lanceolatum. This compound inhibited leishmanicidal activity, displayed moderate antioxidant activity, and had cytotoxic activity against the breast cancer cells MDA-MB-231 and MCF-7 [157]. A series of the cytochalasins were extracted from Diaporthe sp. GDG-118 of Sophora tonkinensis, including 21-acetoxycytochalasins J1 (316) and J3 (317), 7-acetoxycytochalasin H (319), and cytochalasins J1 (318), H (230), J (231), and E (320). All isolated metabolites showed different degrees of antifungal activities against Alternaria oleracea, Pestalotiopsis theae, Colletotrichum capsici, and Ceratocystis paradoxa with MIC values of 1.56–100 µg/mL, and antibacterial activities against Gram-positive bacteria (B. subtilis, B. megaterium and Bacillus anthraci) and Gram-negative bacteria (Proteus vulgaris, E. coli and Salmonella paratyphi B) with MIC values in the range of 12.5–100 µg/mL [158]. The fungus Diaporthe sp. GZU-1021 yielded cytochalasin H (230) and 21-O-deacetyl-L-696,474 (321), which showed anti-inflammatory activities by inhibiting NO production in RAW 264.7 cells with IC50 values of 1.94 and 7.35 µM [126]. Cordysinin A (322) was derived from endophytic fungus D. arecae of Kandelia obovata. It showed anti-angiogenic activity against the human endothelial progenitor cells (EPCs) with IC50 value of 15.1 ± 0.2 µg/mL [159]. Further research led to the identification of 5-deoxybostrycoidin (323) and fusaristatin A (241) from D. phaseolorum SKS019 of mangrove plant A. ilicifolius. Compound 323 showed cytotoxic activity against MDA-MB-435 and NCI-H460 with IC50 values at 5.32 and 6.57 µM, and the IC50 value of 241 was 8.15 µM on MDA-MB-435 [160]. A new carboxamide, vochysiae (324), was extracted from new species D. vochysiae LGMF1583, which displayed antibacterial activity on the Gram-negative bacterium Klebsiella pneumoniae (KPC) with MIC value at 80 µg/mL and showed cytotoxic activity against A549 (EC50 = 86.4 µM) and PC3 (EC50 = 40.25 µM) [143]. Four compounds, diaporisoindoles A (325), B (326), D (327), and E (328), were obtained from an endophytic fungus Diaporthe sp. SYSU-HQ3. They all showed anti-inflammatory activities by reducing NO production with IC50 values of 22.7, 18.2, 8.9, and 8.3 µM, respectively [148]. Diaporisoindole D (327) also exhibited inhibitory activity towards M. tuberculosis protein tyrosine phosphatase B (MptpB) (IC50 = 4.2 µM) [147]. Phomospin F (329) was isolated from D. toxica, and showed cytotoxic activity against HepG2 cells [161]. The structures of alkaloids (315–329) are shown in Figure 18.
Figure 18. Chemical structures of compounds 315–329 from Diaporthe.

3.6. Fatty Acids

Fatty acids are simple linear compounds that play an important role in the synthesis and catabolism of organisms [167]. Over here, six fatty acids are reported from Diaporthe. The fungus D. phaseolorum derived from Laguncularia racemose, afforded 3-hydroxypropionic acid (330), which showed antimicrobial activity against S. aureus and S. typhi [162]. A phytotoxic metabolite, 3-nitropropionic acid (331), was isolated from D. gulyae. Compound 331 was notably active in causing necroses on several weedy and crop plant species [149]. Two new fatty acids, diapolic acids A and B (332 and 333), were isolated from endophytic fungus D. terebinthifolii. They had moderate antibacterial activities against Y. enterocolitica with IC$_{50}$ values of 78.4 and 73.4 µM [156]. Studies of the strain Diaporthe sp. JC-J7 from stems of Dendrobium nobile led to the isolation of a new compound, diaporthsin E (334). It showed low antihyperlipidemic activity on triglycerides (TG) in steatotic L-02 cells with the inhibition rate of 26% at the concentration of 5 µg/mL [163]. The novel anti-candidal metabolite, 3-hydroxy-5-methoxyhex-5-ene-2,4-dione (335), was derived from Diaporth sp. ED2 of medicinal herb Orthosiphon stamieus Benth. It showed antifungal activity against C. albicans with MIC value of 3.1 µg/mL [164]. The structures of fatty acids (330–335) are shown in Figure 19.
4. Characteristics of Bioactive Secondary Metabolites from the Genus *Diaporthe* and Anamorph *Phomopsis*

In this paper, a total of 335 bioactive compounds from the genus *Diaporthe* and *Phomopsis* are summarized. There are 106 secondary metabolites from *Diaporthe* and 246 ones from *Phomopsis*, in which 17 compounds were obtained from both of *Diaporthe* and *Phomopsis*. These compounds are classified into polyketides, terpenoids, steroids, macrolides, ten-membered lactones, alkaloids, flavonoids, and fatty acids. As seen in Figure 20, about two thirds of all compounds reported from *Diaporthe* and *Phomopsis* are refered to polyketides, accounting for 63% and 70%, respectively. Moreover, terpenoids (8%, 15%), alkaloids (17%, 6%), and steroids (2%, 4%) were also produced by both of *Diaporthe* and *Phomopsis*. It is worth noting that fatty acids (6%) and ten-membered lactones (4%) are only reported from *Diaporthe*, while flavonoids (2%) and macrolides (3%) are only found in *Phomopsis*. Polyketides, as the largest member of the metabolites, are widely used in the field of medicine and play an important role in the treatment of cancer diseases.

![Figure 19](image1.png)

**Figure 19.** Chemical structures of compounds 330–335 from *Diaporthe*.

![Figure 20](image2.png)

**Figure 20.** (a) The proportion of structural types of bioactive compounds from *Diaporthe*; (b) The proportion of structural types of bioactive compounds from *Phomopsis*. 
The various bioactivities of the compounds isolated from *Diaporthe* and *Phomopsis* are presented in Figure 21, mainly containing cytotoxic, antibacterial, antifungal, anti-inflammatory, antioxidant, antialgae, enzyme inhibition, and phytotoxic activities. Most of compounds have at least one kind of bioactivities. As seen in Figure 21 and Tables 1 and 2, secondary metabolites of *Diaporthe* and *Phomopsis* mainly exhibit cytotoxic, antibacterial and antifungal activities, accounting for 73% of all compounds, with 56 in *Diaporthe* and 200 from *Phomopsis*. Interestingly, in recent years, more and more compounds with anti-inflammatory, antioxidant and enzyme inhibitory activities have been studied in important human diseases.

![Figure 21](image-url)

Figure 21. The distribution of main bioactivities of compounds isolated from *Diaporthe* and *Phomopsis*.

5. Conclusions

This review presents the diverse chemical structures and bioactivities of 335 compounds isolated from 26 known species and various unidentified species of the genus *Diaporthe* and its anamorph *Phomopsis* between 2010–2019. Here, we can see from Tables 1 and 2, among all of the reported compounds, there are 236 (accounting for about 70%) and 92 (about 27%) compounds derived only from terrestrial and marine environments (including mangroves, sediments, deep-sea fungi and marine animals), respectively. In addition, only one compound is obtained from both of terrestrial and marine environments. In contrast, six compounds are not mentioned with their habitats in the literature. Polyketides represent the main chemical population, accounting for 64%. About 73% of all metabolites possess cytotoxic, antibacterial, and antifungal activities. The species named as *Phomopsis* significantly produce much more compounds than *Diaporthe*, and most strains have not yet been identified at the species level. In conclusion, these results illustrate that the metabolic resources of *Diaporthe* and *Phomopsis* are of great value and deserved to conduct further research. Interestingly, in the past three years, there have been more reports on the secondary metabolites of the fungi in *Diaporthe* and *Phomopsis* than before, displaying an increasing trend, which indicates that *Diaporthe* and *Phomopsis* are regarded as important sources for discovering new natural bioactive substances.

In the past many years, lots of interesting fungal bioactive metabolites had been widely developed into new drugs, like antibiotics. Although most compounds obtained from *Diaporthe* and *Phomopsis* fungi had been studied on their isolation, structures, and activities, the in-depth research on pharmacological mechanisms and development of potent active
compounds in drugs are still less. According to current studies, some compounds with remarkable bioactivities may serve as potential drug candidates in the future, such as cytotoxic altersolanol A and PM181110, and antimicrobial dicerandrol A. In order to ascertain the therapeutic potential of these compounds, further studies of pharmacological and producing mechanisms are required.

The fungal species in Diaporthe and Phomopsis have been considered to be important sources that can produce diverse and novel bioactive metabolites, which has attracted many natural product chemists and pharmacologists to study in recent years. The metabolites produced by Diaporthe and Phomopsis have rich biological activities, which is enough to show the importance of its metabolic resources. Nowadays, many fungi produce interesting bioactive metabolites that have been studied for their biosynthesis pathway, while similar studies in Diaporthe and Phomopsis are performed relatively less often. In the following work, the microbial biosynthesis pathway might be considered for further developing valuable products from Diaporthe or Phomopsis, which are hoped to be used as drug molecules for disease treatment. However, it cannot be ignored that Diaporthe or Phomopsis are important plant pathogens which might cause a wide range of plant host diseases and even serious human pathogens. In the future work, we should also focus on the role of metabolites produced by these pathogens, as well as the relationships with their hosts.

Author Contributions: Manuscript preparation, T.-C.X.; prepared figures, tables, and analyzed data, Y.-H.L.; data proofreading and manuscript revision, J.-F.W., Z.-Q.S., Y.-G.H., S.-S.L., and C.-S.L.; manuscript conception and revision, S.-H.W. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the National Natural Science Foundation of China (No. 81860634), Applied Basic Research Key Project of Yunnan Province (No. 202001BB050029), Major Science and Technology Projects of Yunnan Province (Digitalization, development and application of biotic resource, 202002AA100007), and Project of Innovative Research Team of Yunnan Province (202005AE160005).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: All data in this article is openly available without any restrictions.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Guarnaccia, V.; Groenewald, J.Z.; Woodhall, J.; Armengol, J.; Cinelli, T.; Eichmeier, A.; Ezra, D.; Fontaine, F.; Gramaje, D.; Gutierrez-Aguirregabiria, A.; et al. Diaporthe diversity and pathogenicity revealed from a broad survey of grapevine diseases in Europe. Persoonia 2018, 40, 135–153. [CrossRef]
2. Dissanayake, A.J.; Chen, Y.Y.; Liu, J.K.J. Unravelling Diaporthe species associated with woody hosts from karst formations (Guizhou) in China. J. Fungi 2020, 6, 251. [CrossRef]
3. Gomes, R.R.; Glienke, C.; Videira, S.I.R.; Lombard, L.; Groenewald, J.Z.; Crous, P.W. Diaporthe: A genus of endophytic, saprobic and plant pathogenic fungi. Persoonia 2013, 31, 1–41. [CrossRef]
4. Udayanga, D.; Castlebury, L.A.; Rossman, A.Y.; Chukiatirote, E.; Hyde, K.D. Insights into the genus Diaporthe: Phylogenetic species delimitation in the D. ceras species complex. Fungal Divers. 2014, 67, 203–229. [CrossRef]
5. Gao, Y.; Liu, F.; Duan, W.; Crous, P.W.; Cai, L. Diaporthe is paraphyletic. IMA Fungus 2011, 27, 9–19. [CrossRef] [PubMed]
6. Zhou, H.; Hou, C.L. Three new species of Diaporthe from China based on morphological characters and DNA sequence data analyses. Phytotaxa 2019, 422, 157–174. [CrossRef]
11. Leon, M.; Berbegal, M.; Rodriguez-Reina, J.M.; Elena, G.; Abad-Campos, P.; Ramon-Albalat, A.; Olmo, D.; Vicent, A.; Luque, J.; Miamau, X.; et al. Identification and characterization of Diaporthe spp. associated with twig cankers and shoot blight of almonds in Spain. *Agronomy* 2020, 10, 1062. [CrossRef]

12. Rossman, A.Y.; Adams, G.C.; Cannon, P.F.; Castlesbury, L.A.; Crous, P.W.; Gryzenhout, M.; Jaklitsch, W.M.; Mejia, L.C.; Stoykov, D.; Udayanga, D.; et al. Recommendations of generic names in Diaporthales competing for protection or use. *IMA Fungus* 2015, 6, 145–154. [CrossRef] [PubMed]

13. Udayanga, D.; Liu, X.; McKenzie, E.H.C.; Chukeatirote, E.; Bahkali, A.H.A.; Hyde, K.D. The genus Phomopsis: Biology, applications, species concepts and names of common phytopathogens. *Fungal Divers*. 2011, 50, 189–225. [CrossRef]

14. Santos, L.; Alves, A.; Alves, R. Evaluating multi-locus phylogenies for species boundaries determination in the genus Diaporthe. *PeerJ* 2017, 5. [CrossRef]

15. Lin, X.; Huang, Y.J.; Fang, M.J.; Wang, J.F.; Zheng, Z.H.; Su, W.J. Cytotoxic and antimicrobial metabolites from marine lignicolous fungi, Diaporthaceae sp. *FEBS Microbiol. Lett.* 2005, 251, 53–58. [CrossRef]

16. Silva, G.H.; Teles, H.L.; Zanardi, L.M.; Marx Young, M.C.; Eberlin, M.N.; Hadad, R.; Pfennig, L.H.; Costa-Neto, C.M.; Castro-Gamboa, I.; Bolzani, V.d.S.; et al. Cadinane sesquiterpenoids of *Phomopsis cassiae*, an endophytic fungus associated with *Cassia spectabilis* (Leguminosae). *Phytochemistry* 2006, 67, 1964–1969. [CrossRef]

17. Niaz, S.I.; Khan, D.; Naz, R.; Safdar, K.; Ul Abidin, S.Z.; Khan, I.U.; Gul, R.; Khan, W.U.; Khan, M.A.U.; Lan, L. Antimicrobial and antioxidant chlorinated azaphilones from mangrove *Diaporthaceae* sp. isolated from the stem of Chinese mangrove *Pongamia pinnata*. *J. Asian Nat. Prod. Res.* 2020. [CrossRef]

18. Yang, Z.J.; Zhang, Y.F.; Wu, K.; Xu, Y.X.; Meng, X.G.; Jiang, Z.T.; Ge, M.; Shao, L. New azaphilones, homophones A-C with biological activities from an endophytic fungus *Phomopsis* sp. CGMCC No.5416. *Fitoterapia* 2020, 145. [CrossRef]

19. Da Rosa, B.V.; Kuhn, K.R.; Ugalde, G.A.; Zabot, G.L.; Kuhn, R.C. Antioxidant compounds extracted from *Diaporthella schini* using supercritical CO₂ plus cosolvent. *Bioprocess Biosyst. Eng.* 2020, 43, 133–141. [CrossRef]

20. Fan, M.M.; Xiang, G.; Chen, J.W.; Gao, J.; Xue, W.W.; Wang, Y.X.; Li, W.H.; Zhou, L.; Jiao, R.H.; Shen, Y.; et al. Libertellenone M, a diterpene derived from an endophytic fungus *Phomopsis* sp. S12, protects against DSS-induced colitis via inhibiting both nuclear translocation of NF-κB and NLRP3 inflammasome activation. *Int. Immunopharmacol.* 2020, 80. [CrossRef]

21. Tsantrizos, Y.S.; Ogilvie, K.K.; Watson, A.K. Phytotoxic metabolites of *Phomopsis convolvuli*, a host-specific pathogen of field bindweed. *Can. J. Chem.* 1992, 70, 2276–2284. [CrossRef]

22. Zhang, C.W.; Ondeyka, J.G.; Herath, K.B.; Guan, Z.Q.; Collado, J.; Platgas, G.; Pelaest, F.; Leavitt, P.S.; Gurnett, A.; Nare, B.; et al. Tenellones A and B from a Diaporthaceae sp.: Two highly substituted benzophenone inhibitors of parasite cGMP-dependent protein kinase activity. *J. Nat. Prod.* 2005, 68, 611–613. [CrossRef] [PubMed]

23. Yang, H.Y.; Gao, Y.H.; Niu, D.Y.; Yang, L.Y.; Gao, X.M.; Du, G.; Hu, Q.F. Xanthone derivatives from the fermentation products of an endophytic fungus *Phomopsis* sp. *Fitoterapia* 2013, 91, 189–193. [CrossRef] [PubMed]

24. Yang, J.X.; Qiu, S.X.; She, Z.G.; Lin, Y.C. A new xanthone derivative from the marine fungus *Phomopsis* sp. (No. SK7RN3G1). *Chem. Nat. Compd.* 2013, 49, 31–33. [CrossRef] [PubMed]

25. Yuan, L.; Huang, W.; Du, G.; Gao, X.; Yang, H.; Hu, Q.; Ma, Y. Isolation of xanthones from the fermentation products of the endophytic fungus *Phomopsis amygdali*. *Chem. Nat. Compd.* 2015, 51, 460–463. [CrossRef]

26. Huang, R.; Ma, K.X.; Xie, X.S.; Wang, T.; Wu, S.H. Secondary metabolites of an endophytic fungus *Phomopsis* sp. *Chem. Nat. Compd.* 2015, 51, 392–394. [CrossRef]

27. Yuan, L.; Huang, W.Z.; Zhou, K.; Wang, Y.D.; Dong, W.; Lou, J.; Li, L.M.; Du, G.; Yang, H.Y.; Ma, Y.H.; et al. Xanthones from the fermentation products of an endophytic fungus *Phomopsis* sp. *Heterocycles* 2015, 91, 381–387. [CrossRef]

28. Yang, Y.; Yang, H.; Li, Y.; Ye, Y.; Hu, Q.; Gao, X.; Du, G. A new xanthone from the fermentation products of endophytic fungus *Phomopsis* species. *Asian J. Chem.* 2014, 26, 4591–4593. [CrossRef]

29. Hu, Q.; Yang, Y.; Yang, S.; Cao, H.; Chunyang, M.; Yang, H.; Gao, X.; Du, G. Xanthones from the fermentation products of the endophytic fungus of *Phomopsis* sp. *Chem. Nat. Compd.* 2015, 51, 456–459. [CrossRef]

30. Huang, Z.; Yang, J.; Lei, F.; She, Z.; Lin, Y. A new xanthone O-glycoside from the mangrove endophytic fungus *Phomopsis* sp. *Chem. Nat. Compd.* 2013, 49, 27–30. [CrossRef]

31. Roensberg, D.; Debbab, A.; Mandi, A.; Vasylyeva, V.; Boehler, P.; Stork, B.; Engelke, L.; Hamacher, A.; Sawadogo, R.; Diederich, M.; et al. Pro-apoptotic and immunostimulatory tetrahydroxanthone dimers from the endophytic fungus *Phomopsis longicolla*. *J. Org. Chem.* 2013, 78, 12409–12425. [CrossRef] [PubMed]

32. Shiono, Y.; Sasaki, T.; Shibuya, F.; Yasuda, Y.; Koseki, T.; Supratman, U. Isolation of a phomoxanthone A derivative, a new metabolite of tetrahydroxanthone, from a *Phomopsis* sp. isolated from the mangrove, *Rhizophora mucronata*. *Nat. Prod. Commun.* 2013, 8, 1735–1737. [CrossRef] [PubMed]

33. Meixiang, H.; Jing, L.; Lan, L.; Sheng, Y.; Jun, W.; Yongcheng, L.J.M.D. Phomopsichinin A–D; four new chromone derivatives from mangrove endophytic fungus *Phomopsis* sp. 338. *Mar. Drugs* 2016, 14, 215. [CrossRef]

34. Lim, C.; Kim, J.; Choi, J.N.; Ponnsamy, K.; Jeon, Y.; Kim, S.U.; Kim, J.G.; Lee, C.H. Identification, fermentation, and bioactivity against xanthomonas oryzae of antimicrobial metabolites isolated from *Phomopsis longicolla* S1B4. *J. Microbiol. Biotechnol.* 2010, 20, 494–500. [CrossRef]
35. Ding, B.; Yuan, J.; Huang, X.; Wen, Z.; Zhu, X.; Liu, Y.; Li, H.; Lu, Y.; He, L.; Tan, H.J.M.D. New dimeric members of the phomoxanthone family: Phomolactonexanthones A, B and deacetylphomoxanthone C isolated from the fungus Phomopsis sp. Mar. Drugs 2015, 11, 4961–4972. [CrossRef]

36. Ding, B.; Wang, Z.; Xia, G.; Huang, X.; Xu, F.; Chen, W.; She, Z. Three new chromone derivatives produced by Phomopsis sp. HNY29-2B from Acanthus ilicifolius linn. Chin. J. Chem. 2017, 35, 1889–1893. [CrossRef]

37. Wu, Q.; Guo, Y.; Guo, Z.K.; Chu, Y.L.; Wang, T.; Tan, R.X. Two new cytosporones from the culture of endophytic Phomopsis sp. Chem. Nat. Compd. 2013, 48, 938–941. [CrossRef]

38. Hu, H.B.; Luo, Y.F.; Wang, P.; Wang, W.J.; Wu, J. Xanthone-derived polyketides from the Thai mangrove endophytic fungus Phomopsis sp. xy21. Fitoterapia 2018, 131, 265–271. [CrossRef]

39. Yang, J.X.; Qiu, S.; She, Z.; Lin, Y. A new isochroman derivative from the marine fungus Phomopsis sp. (No. Gx-4). Chem. Nat. Compd. 2014, 50, 424–426. [CrossRef]

40. Ahmed, I.; Hussain, H.; Schulz, B.; Draeger, S.; Padula, D.; Pescitelli, G.; van Ree, T.; Krohn, K. Three new antimicrobial metabolites from the endophytic fungus Phomopsis sp. Eur. J. Org. Chem. 2011, 2011, 2867–2873. [CrossRef]

41. Yang, Z.; Wu, K.; Xu, Y.; Xia, X.; Wang, X.; Ge, M.; Shao, L. Three novel chromanones with biological activities from the endophytic fungus Phomopsis CGMC No. 5416. J. Antibiot. 2020, 73, 194–199. [CrossRef] [PubMed]

42. Huang, Z.; Yang, R.; Guo, Z.; She, Z.; Lin, Y. A new naphtho-γ-pyrone from mangrove endophytic fungus ZSU-H26. Chem. Nat. Compd. 2010, 46, 15–18. [CrossRef]

43. Yang, J.; Xu, F.; Huang, C.; Li, J.; She, Z.; Pei, Z.; Lin, Y. Metabolites from the endophytic fungus Phomopsis sp. (Zsus-H76). Eur. J. Org. Chem. 2010, 2010, 3692–3695. [CrossRef]

44. Yang, J.X.; Chen, Y.; Huang, C.; She, Z.; Lin, Y. A new isochroman derivative from the marine fungus Phomopsis sp. (No. ZH-111). Chem. Nat. Compd. 2011, 47, 13–16. [CrossRef]

45. Tang, J.W.; Wang, W.G.; Li, A.; Yan, B.C.; Chen, R.; Li, X.N.; Du, X.; Sun, H.D.; Pu, J.X. Polyketides from the endophytic fungus Phomopsis sp. sf917 by using the one strain/many compounds strategy. Tetrahedron 2017, 73, 3577–3584. [CrossRef]

46. Adelin, E.; Martin, M.T.; Cortial, S.; Retailleau, P.; Lumyong, S.; Ouazzani, J. Bioactive polyketides isolated from agar-supported fermentation of Phomopsis sp. CMU-LMA, taking advantage of the scale-up device, Platotex. Phytochemistry 2013, 93, 170–175. [CrossRef]

47. Tao, M.H.; Chen, Y.C.; Wei, X.Y.; Tan, J.W.; Zhang, W.M. Chemical constituents of the endophytic fungus Phomopsis sp. A240 isolated from Taxus chinensis var. mairei. Hett. Chim. Acta 2019, 97, 426–430. [CrossRef]

48. Talontsi, F.M.; Islam, M.T.; Facey, P.; Douanla-Meli, C.; von Tiedemann, A.; Laatsch, H. Depsidones and other constituents from Phomopsis sp. CAFT69, a strain isolated from diseased Bulgarian fennel. Eur. J. Plant Pathol. 2013, 130, 173–182. [CrossRef]

49. Chapla, V.M.; Zeraik, M.L.; Ximenes, V.F.; Zanardi, L.M.; Bolzani, V.S.; et al. Bioactive secondary metabolites from Phomopsis sp., an endophytic fungus from Senma spectabilis. Molecules 2014, 19, 6597–6608. [CrossRef]

50. Zhang, W.; Xu, L.; Yang, L.; Huang, Y.; Li, S.; Shen, Y. Phomopsisidone A, a novel depsidone metabolite from the mangrove endophytic fungus Phomopsis sp. A123. Fitoterapia 2014, 96, 146–151. [CrossRef]

51. Kornsakulkarn, J.; Somyong, W.; Supothina, S.; Boonyuen, N.; Thongpanchor, C. Bioactive oxygen-bridged cyclooctadienes from endophytic fungus Phomopsis sp. BCC 45011. Tetrahedron 2015, 71, 9112–9116. [CrossRef]

52. Xu, J.L.; Liu, Z.M.; Chen, Y.C.; Tan, H.B.; Li, H.H.; Li, S.N.; Guo, H.; Huang, Z.L.; Gao, X.X.; Liu, H.X.; et al. Lithocarols A-F, six tenellone derivatives from the deep-sea derived fungus Phomopsis lithocarpus. Bioorg. Chem. 2019, 87, 728–735. [CrossRef] [PubMed]

53. Du, G.; Wang, Z.C.; Hu, W.Y.; Yan, K.L.; Wang, X.L.; Yang, H.M.; Yang, H.Y.; Gao, Y.H.; Liu, Q.; Hu, Q.F. Three new 3-methyl-2-arylenzofurans from the fermentation products of an endophytic fungus Phomopsis sp. and their anti-TMV activity. Phytochem. Lett. 2017, 21, 287–290. [CrossRef]

54. Song, H.C.; Qin, D.; Han, M.J.; Wang, L.; Zhang, K.; Dong, J.Y. Bioactive 2-pyrene metabolites from an endophytic Phomopsis asparagi SWUKJ5.2020 of Kadsura angustifolia. Chin. J. Nat. Prod. 2020, 35, 217–220. [CrossRef]

55. Hussain, H.; Ahmed, I.; Schulz, B.; Draeger, S.; Krohn, K. Pyrenocines J-M: Four new pyrenocines from the endophytic fungus, Phomopsis sp. Fitoterapia 2012, 83, 523–526. [CrossRef]

56. Yang, Z.; Ding, J.; Ding, K.; Chen, D.; Cen, S.; Ge, M. Phomonaphthalenone A: A novel dihydroxyphthalenone with anti-HIV activity from Phomopsis sp. HCCB04730. Tetrahedron 2013, 69, 2264–2267. [CrossRef]

57. Li, X.B.; Chen, G.Y.; Liu, R.J.; Zheng, C.J.; Song, X.M.; Han, C.R. A new bifenyl derivative from the mangrove endophytic fungus Phomopsis longicolla HL-2232. Nat. Prod. Res. 2017, 31, 2264–2267. [CrossRef]

58. Mishra, P.D.; Verekar, S.A.; Deshmukh, S.K.; Joshi, K.S.; Fiebig, H.H.; Kelter, G. Altersolanol A: A selective cytotoxic anthraquinone from a Phomopsis sp. Lett. Appl. Microbiol. 2015, 60, 387–391. [CrossRef]

59. Evidente, A.; Rodeva, R.; Andolfi, A.; Stoyanova, Z.; Perrone, C.; Mota, A. Phytotoxic polyketides produced by Phomopsis foeniculi, a strain isolated from diseased Bulgarian fennel. Eur. J. Plant Pathol. 2011, 130, 173–182. [CrossRef]

60. Klaikey, S.; Rukachaisirikul, V.; Phongpaichtai, S.; Pakawatchai, C.; Saithong, S.; Buatong, J.; Preedanon, S.; Sakayaroj, J. Anthraquinone derivatives from the mangrove-derived fungus Phomopsis sp. PSU-MA214. Phytochem. Lett. 2012, 5, 738–742. [CrossRef]
Hussain, H.; Tchimene, M.K.; Ahmed, I.; Meier, K.; Steinert, M.; Draeger, S.; Schulz, B.; Krohn, K. Antimicrobial chemical constituents from the endophytic fungus Phomopsis sp. from Notobasis syriaca. Nat. Prod. Commun. 2011, 6, 1905–1906. [CrossRef] [PubMed]

Cai, R.; Chen, S.; Liu, Z.; Tan, C.; Huang, X.; She, Z. A new α-pyrene from the mangrove endophytic fungus Phomopsis sp. HNY29-2B. Nat. Prod. Res. 2017, 31, 124–130. [CrossRef] [PubMed]

Krohn, K.; Farooq, U.; Hussain, H.; Ahmed, I.; Rheinheimer, J.; Draeger, S.; Schulz, B.; van Ree, T. Phomosines H-J, novel highly substituted biaryl ethers, isolated from the endophytic fungus Phomopsis sp. from Ligustrum vulgare. Nat. Prod. Commun. 2011, 6, 1907–1912. [CrossRef] [PubMed]

Hu, S.S.; Liang, M.J.; Mi, Q.L.; Chen, W.; Ling, J.; Chen, X.; Li, J.; Yang, G.Y.; Hu, Q.F.; Wang, W.G.; et al. Two new diphenyl ether derivatives from the fermentation products of the endophytic fungus Phomopsis asparagi. Chem. Nat. Compd. 2019, 55, 843–846. [CrossRef]

Gao, Y.H.; Zheng, R.; Li, J.; Kong, W.S.; Liu, X.; Ye, L.; Mi, Q.L.; Kong, W.S.; Zhou, M.; Yang, G.Y.; et al. Three new diphenyl ether derivatives from the fermentation products of an endophytic fungus Phomopsis fukushii. J. Asian Nat. Prod. Res. 2019, 21, 316–322. [CrossRef]

Li, Z.J.; Yang, H.Y.; Li, J.; Liu, X.; Ye, L.; Kong, W.S.; Tang, S.Y.; Du, G.; Liu, Z.H.; Zhou, M.; et al. Isopentylated diphenyl ether derivatives from the fermentation products of an endophytic fungus Phomopsis fukushii. J. Antibiot. 2018, 71, 359–362. [CrossRef]

Yang, H.Y.; Duan, Y.Q.; Yang, Y.K.; Liu, X.; Ye, L.; Mi, Q.L.; Kong, W.S.; Zhou, M.; Yang, G.Y.; Hu, Q.F.; et al. Two new diphenyl ether derivatives from the fermentation products of an endophytic fungus Phomopsis fukushii. Chem. Nat. Compd. 2019, 55, 428–431. [CrossRef]

Yang, H.Y.; Duan, Y.Q.; Yang, Y.K.; Li, J.; Liu, X.; Ye, L.; Mi, Q.L.; Kong, W.S.; Zhou, M.; Yang, G.Y.; et al. Three new naphthalene derivatives from the endophytic fungus Phomopsis fukushii. Phytochem. Lett. 2017, 22, 266–269. [CrossRef]

Li, X.M.; Zeng, Y.C.; Chen, J.H.; Yang, Y.K.; Li, J.; Ye, L.; Du, G.; Zhou, M.; Hu, Q.F.; Guangyu, Y.; et al. Two new naphthalene derivatives from the fermentation products of an endophytic fungus Phomopsis sp. Chem. Nat. Compd. 2019, 55, 618–621. [CrossRef]

Xu, J.L.; Liu, H.X.; Chen, Y.C.; Tan, H.B.; Guo, H.; Xu, L.Q.; Li, S.N.; Huang, Z.L.; Li, H.H.; Gao, X.X.; et al. Highly substituted benzophenone aldehydes and eremophilane derivatives from the deep-Sea derived fungus Phomopsis lithocarpus FSS08. Mar. Drugs 2018, 16, 329. [CrossRef]

Ma, K.X.; Shen, X.T.; Huang, R.; Wang, T.; Xie, X.S.; Liu, S.W.; Wu, S.H.; He, J. Bioactive metabolites produced by the endophytic fungus Phomopsis sp. YM355364. Nat. Prod. Commun. 2014, 9, 669–670. [CrossRef] [PubMed]

Sheng, S.L.; Li, Y.P.; Xiang, H.Y.; Liu, Y.; Wang, Y.D.; Kong, L.P.; Du, G.; Hu, Q.F.; Chen, Y.J.; Wang, W.G. Histone deacetylase inhibitor induced lipase Inhibitors from endophytic Phomopsis sp. 0391. Rec. Nat. Prod. 2020, 14, 42–47. [CrossRef]

Kongprapan, T.; Xu, X.; Rukachaisirikul, V.; Phongpaichit, S.; Sakayaroj, J.; Chen, J.; Shen, X. Cytosporone derivatives from the endophytic fungus Phomopsis sp. PSU-H188. Phytochem. Lett. 2017, 22, 219–223. [CrossRef]

Xu, J.; Tan, H.; Chen, Y.; Li, S.; Guo, H.; Huang, Z.; Li, H.; Gao, X.; Liu, H.; Zhang, W. Lithocarpinols A and B, a pair of diastereomeric antineoplastic terelline derivatives from the deep-sea derived fungus Phomopsis lithocarpus FSS08. Chin. Chem. Lett. 2019, 30, 439–442. [CrossRef]

Chen, Y.G.; Pan, J.H.; Xu, F.; Liu, F.; Yang, J.X.; Huang, C.H.; Xu, C.L.; Lu, Y.J.; Cai, X.L.; She, Z.G.; et al. A new indene derivative from the marine fungus Phomopsis sp. (No. GX7-4A). Chem. Nat. Compd. 2010, 46, 230–232. [CrossRef] [PubMed]

Tan, Q.W.; Fang, P.H.; Ni, J.C.; Gao, F.; Chen, Q.J. Melobolites Produced by an Endophytic Phomopsis sp. and Their Anti-TMV Activity. Molecules 2017, 22, 2073. [CrossRef]

Shiono, Y.; Muslihah, N.I.; Suzuki, T.; Ariefta, N.R.; Anwar, C.; Nurjanto, H.H.; Aboshi, T.; Murayama, T.; Tawaraya, K.; Koseki, T.; et al. New eremophilane and dichlororesorcinol derivatives produced by endophytes isolated from Notobasis syriaca. J. Antibiot. 2017, 70, 1133–1137. [CrossRef]

Bunyaipaiboonsri, T.; Yoiprommarat, S.; Srikittikulchai, P.; Srichomthong, K.; Lumyong, S. Obolongolides from the endophytic fungus Phomopsis sp. BCC 9789. J. Nat. Prod. 2010, 73, 55–59. [CrossRef]

Lin, T.; Wang, G.H.; Lin, X.; Hu, Z.Y.; Chen, Q.C.; Xu, Y.; Zhang, X.K.; Chen, H.F. Three new obolongolides from Phomopsis sp. XZ-01, an endophytic fungus from Ficus delavayi. Phytochemistry 2019, 8602–8607. [CrossRef] [PubMed]

Bunyapaiboonsri, T.; Yoiprommarat, S.; Srikitikulchai, P.; Srichomthong, K.; Lumyong, S. Obolongolides from the endophytic fungus Phomopsis sp. BCC 9789. J. Nat. Prod. 2010, 73, 55–59. [CrossRef]

Cimmino, A.; Andolfi, A.; Zonno, M.C.; Troise, C.; Santini, A.; Tuzi, A.; Vurro, M.; Ash, G.; Evidente, A. Phomentrioloxin: A phytotoxic pentasubstituted geranylcyloxenol produced by Phomopsis sp., a potential mycoherbicide for Carthamus lanatus Biocontrol. J. Nat. Prod. 2012, 75, 1130–1137. [CrossRef] [PubMed]

Goddard, M.L.; Mottier, N.; Jeanneret-Gris, J.; Christen, D.; Tabacchi, R.; Abou-Mansour, E. Differential production of phytotoxins from Phomopsis sp. from grapevine plants showing esca symptoms. J. Agric. Food Chem. 2014, 62, 8602–8607. [CrossRef] [PubMed]

Xie, S.S.; Wu, Y.; Qiao, Y.B.; Guo, Y.; Wang, J.P.; Hu, Z.X.; Zhang, Q.; Li, X.N.; Huang, J.F.; Zhou, Q.; et al. Protoilludane, illudalane, and botryane sesquiterpenoids from the endophytic fungus Phomopsis sp. TJ507A. J. Nat. Prod. 2018, 81, 1311–1320. [CrossRef] [PubMed]
84. Zanardi, L.M.; Bolzani, V.d.S.; Cavalheiro, A.J.; Siqueira Silva, D.H.; Trevisan, H.C.; Araujo, A.R.; Silva, G.H.; Teles, H.L.; Young, M.C.M. Sesquiterpenes produced by endophytic fungus Phomopsis cassiae with antifungal and acetylcholinesterase inhibition activities. Quim. Nova 2012, 35, 2233–2236. [CrossRef]

85. Hemtasin, C.; Kanokmedhakul, S.; Kanokmedhakul, K.; Hahnvajanawong, C.; Soytong, K.; Prabpai, S.; Kongsaeere, P. Cytotoxic pentacyclic and tetracyclic aromatic sesquiterpenes from Phomopsis archeri. J. Nat. Prod. 2011, 74, 609–613. [CrossRef]

86. Ma, X.; Wang, W.; Li, E.; Gao, F.; Guo, L.; Pei, Y. A new sesquiterpene from the entomogenous fungus Phomopsis amygdali. Nat. Prod. Res. 2016, 30, 276–280. [CrossRef]

87. Qian, Y.X.; Kang, J.C.; Luo, Y.K.; He, J.; Wang, L.; Li, Q.R. Secondary metabolites of an endophytic fungus Phomopsis castaneae-mollissimae. Chem. Nat. Compd. 2016, 54, 346–347. [CrossRef]

88. Wei, W.; Gao, J.; Shen, Y.; Chu, Y.L.; Xu, Q.; Tan, R.X. Immunosuppressive diterpenes from Phomopsis sp. S12. Eur. J. Org. Chem. 2014, 2014, 5728–5734. [CrossRef]

89. Xu, K.; Zhang, X.; Chen, J.W.; Shen, Y.; Jiang, N.; Tan, R.X.; Jiao, R.H.; Ge, H.M. Anti-inflammatory diterpenoids from an endophytic fungus Phomopsis sp. S12. Tetrahedron Lett. 2019, 60. [CrossRef]

90. Zhang, Y.; Hao, F.; Liu, N.; Xu, Y.; Jia, A.; Yang, Z.; Xia, X.; Liu, C. Stereochemical determination of a new and cytotoxic euphane triterpenoid from the plant endophytic fungus Phomopsis chimonanthi. J. Antibiot. 2013, 66, 679–682. [CrossRef]

91. Peyrat, L.A.; Ep-parvier, V.; Eydoux, C.; Guillemot, J.C.; Litaudon, M.; Stien, D. Betulinic acid, the first lupane-type triterpenoid isolated from both a Phomopsis sp. and its host plant Diospyros carbonaria benoist. Chem. Biodivers. 2017, 14. [CrossRef][PubMed]

92. Wu, S.H.; Huang, R.; Miao, C.P.; Chen, Y.W. Two new steroids from an endophytic fungus Phomopsis sp. Chem. Biodivers. 2013, 10, 1276–1283. [CrossRef][PubMed]

93. Hu, Z.X.; Xie, S.S.; Sun, W.G.; Guo, Y.; Li, X.N.; Liu, J.J.; Li, H.; Wang, J.P.; Luo, Z.W.; et al. Phomopsterones A and B, two functionalized ergostane-type steroids from the endophytic fungus Phomopsis sp. TS07A. Org. Lett. 2017, 19, 258–261. [CrossRef][PubMed]

94. Adelin, E.; Servy, C.; Cortial, S.; Levaique, H.; Martin, M.T.; Retailleau, P.; Le Goff, G.; Bussaban, B.; Lumyong, S.; Ouazzani, J. Isolation, structure elucidation and biological activity of metabolites from Sch-642305-producing endophytic fungus Phomopsis sp. CMU-LMA. Phytochemistry 2011, 72, 2406–2412. [CrossRef][PubMed]

95. Xu, J.; Tan, H.; Chen, Y.; Li, S.; Huang, Z.; Guo, H.; Li, H.; Gao, X.; Liu, H.; Zhang, W. Lithocarpins A–D: Four tenellone-macrolide conjugated [4 + 2] hetero-adducts from the deep-sea derived fungus Coniophora sp. CMU-LMA. Phytochemistry 2016, 135, 114–129. [CrossRef][PubMed]

96. Yan, B.C.; Wang, W.G.; Hu, D.B.; Sun, X.; Kong, L.M.; Li, X.N.; Du, X.; Luo, S.H.; Liu, Y.; Li, Y.; et al. Phomopsterones A and B, two cytochalasans with polycyclic-fused skeletons from the endophytic fungus Phomopsis sp. shj2. Org. Lett. 2018, 20, 1108–1111. [CrossRef]

97. Luo, Y.F.; Zhang, M.; Dai, J.G.; Pedpradab, P.; Wang, W.J.; Wu, J. Cytochalasins from mangrove endophytic fungi Phomopsis sp. xy21 and xy22. Phytochem. Lett. 2016, 17, 162–166. [CrossRef]

98. Jouda, J.B.; Tamokou, J.D.D.; Mbazoa, C.D.; Douala-Meli, C.; Sarkar, P.; Bag, P.K.; Wandji, J. Antibacterial and cytoxic cytochalasins from the endophytic fungus Phomopsis sp. harbored in Garcinia kola (Heckel) nut. BMC Complement. Altern. Med. 2016, 16. [CrossRef]

99. Fu, J.; Zhou, Y.; Li, H.F.; Ye, Y.H.; Guo, J.H. Antifungal metabolites from Phomopsis sp. By254, an endophytic fungus in Gossypium hirsutum. Afr. J. Microbiol. Res. 2011, 5, 1231–1236. [CrossRef]

100. Chang, H.S.; Peng, C.J.; Cheng, M.J.; Wu, H.C.; Chan, H.Y.; Hsieh, S.Y.; Yuan, G.F.; Chen, I.S. Chemical constituents of the endophytic fungus Phomopsis asparagi isolated from the plant Peperomia sui. Chem. Nat. Compd. 2018, 54, 504–508. [CrossRef]

101. Chen, S.C.; Liu, Z.M.; Tan, H.B.; Chen, Y.C.; Li, S.N.; Li, H.H.; Guo, H.; Zhu, S.; Liu, H.X.; Zhang, W.M. Tersone A–G, new functionalized ergostane-type steroids from the endophytic fungus Phomopsis sp. TJ507A. Org. Lett. 2017, 19, 697–701. [CrossRef][PubMed]

102. Chen, S.C.; Liu, Z.M.; Tan, H.B.; Chen, Y.C.; Li, S.N.; Li, H.H.; Guo, H.; Zhu, S.; Liu, H.X.; Zhang, W.M. Tersone A–G, new functionalized ergostane-type steroids from the endophytic fungus Phomopsis sp. TJ507A. Org. Lett. 2017, 19, 697–701. [CrossRef][PubMed]

103. Hu, Z.X.; Xie, S.S.; Sun, W.G.; Guo, Y.; Li, X.N.; Liu, J.J.; Li, H.; Wang, J.P.; Luo, Z.W.; et al. Phomopsterones A and B, two functionalized ergostane-type steroids from the endophytic fungus Phomopsis sp. TS07A. Org. Lett. 2017, 19, 258–261. [CrossRef][PubMed]

104. Katz, L. Manipulation of modular polyketide syntheses. Chem. Rev. 1997, 97, 2557–2575. [CrossRef]

105. Le Pogam, P.; Boustie, J. Xanthones of lichen source: A 2016 update. Molecules 2016, 21, 294. [CrossRef]

106. Duan, Y.D.; Jiang, Y.Y.; Guo, F.X.; Chen, L.X.; Xu, L.L.; Zhang, W.; Liu, B. The antitumor activity of naturally occurring chromones: A review. Fitoterapia 2019, 135, 114–129. [CrossRef]

107. Diwu, B.; Vakili, P.; Basavoji, S.; Bhardavi, G.; Reddy, K.L. Synthesis, structural characterisation and biological evolution of chromanones. J. Mol. Struct. 2017, 1145, 1–9. [CrossRef]

108. Li, Y.; Li, X.; Cheng, J.P. Catalytic asymmetric synthesis of chiral benzofuranones. Adv. Synth. Catal. 2014, 356, 1172–1198. [CrossRef]

109. McGlacken, G.P.; Fairlamb, J.I.S. 2-Pyrone natural products and mimetics: Isolation, characterisation and biological activity. Nat. Prod. Rep. 2005, 22, 369–385. [CrossRef]

110. Bolton, J.L.; Dunlap, T. Formation and biological targets of quinones: Cytotoxic versus cytoprotective effects. Chem. Res. Toxicol. 2017, 30, 13–37. [CrossRef]
111. Jones, T.J.M.; Douglas, C.J. The metabolism and toxicity of quinones, quinonimines, quinone methides, and quinone-thioethers. *Curr. Drug Metab.* **2002**, *3*, 425–438. [CrossRef]

112. Gajera, H.P.; Gevarya, S.N.; Hirpara, D.G.; Patel, S.V.; Golakiya, B.A. Antidiabetic and antioxidant functionality associated with phenolic constituents from fruit parts of indigenous black jamun (*Syzygium cumini* L.) landraces. *J. Food Sci. Technol.* **2017**, *54*, 3180–3191. [CrossRef] [PubMed]

113. Shing, T.K.M.; Yang, J. A short synthesis of natural (−)-oblongolide via an intramolecular or a transannular diels-allyl reaction. *J. Org. Chem.* **1995**, *60*, 5785–5789. [CrossRef]

114. Huang, M.; Lu, J.J.; Huang, M.Q.; Bao, J.L.; Chen, X.P.; Wang, Y.T. Terpenoids: Natural products for cancer therapy. *Expert Opin. Investig. Drugs* **2012**, *21*, 1801–1818. [CrossRef] [PubMed]

115. Thoppill, R.J.; Bishayee, A. Terpenoids as potential chemopreventive and therapeutic agents in liver cancer. *World J. Hepatol.* **2011**, *3*, 228–249. [CrossRef]

116. Zielenksa-Blajet, M.; Feder-Kubis, J. Monoterpenes and their derivatives-recent development in biological and medical applications. *Int. J. Mol. Sci.* **2020**, *21*, 7078. [CrossRef]

117. Chen, D.L.; Wang, B.W.; Sun, Z.C.; Yang, J.S.; Xu, X.D.; Ma, G.X. Natural nitrogenous sesquiterpenoids and their bioactivity: A review. *Molecules* **2020**, *25*, 2485. [CrossRef]

118. Chen, L.; Lu, X.; El-Seedhi, H.; Teng, H. Recent advances in the development of sesquiterpenoids in the treatment of type 2 diabetes. *Trends Food Sci. Technol.* **2019**, *88*, 46–56. [CrossRef]

119. Su, Y.D.; Su, J.H.; Hwang, T.L.; Wen, Z.H.; Sheu, J.H.; Wu, Y.C.; Sung, P.J. Briarane diterpenoids isolated from octocorals between 2014 and 2016. *Mar. Drugs* **2017**, *15*, 44. [CrossRef]

120. Ren, Y.; Kinghorn, A.D. Natural product triterpenoids and their semi-synthetic derivatives with potential anticancer activity. *Planta Med.* **2019**, *85*, 802–814. [CrossRef]

121. Rahman, S.U.; Ismail, M.; Khurram, M.; Ullah, I.; Rabbi, F.; Iriti, M. Bioactive steroids and saponins of the genus Trillium. *Curr. Drug Metab.* **2015**, *16*, 274–285. [CrossRef] [PubMed]

122. Wang, M.; Zhang, J.; He, S.; Yan, X. A review study on macrolides isolated from cyanobacteria. *Mar. Drugs* **2017**, *15*, 126. [CrossRef] [PubMed]

123. Mishra, S.K.; Tripathi, G.; Kishore, N.; Singh, R.K.; Singh, A.; Tiwari, V.K. Drug development against tuberculosis: Impact of alkaloids. *Eur. J. Med. Chem.* **2017**, *137*, 504–544. [CrossRef] [PubMed]

124. Wang, T.Y.; Li, Q.; Bi, K.S. Bioactive flavonoids in medicinal plants: Structure, activity and biological fate. *Asian J. Pharm.* **2018**, *13*, 12–23. [CrossRef]

125. Luo, X.; Yang, J.; Chen, F.; Lin, X.; Chen, C.; Zhou, X.; Liu, S.; Liu, Y. Structurally diverse polyketides from the mangrove-derived fungus *Diaporthe* sp. *SCSIO 41011* with their anti-influenza A virus activities. *Front. Chem.* **2018**, *6*. [CrossRef]

126. Liu, Y.; Ruan, Q.; Jiang, S.; Qu, Y.; Chen, J.; Zhao, M.; Yang, B.; Liu, Y.; Zhao, Z.; Cui, H. Cytochalasins and polyketides from the fungus *Diaporthe* sp. *GZU-1021* and their anti-inflammatory activity. *Fitoterapia* **2019**, *137*. [CrossRef]

127. Niu, Z.; Chen, Y.; Guo, H.; Li, S.N.; Li, H.H.; Liu, H.X.; Liu, Z.; Zhang, W. Cytotoxic polyketides from a deep-sea sediment derived fungus *Diaporthe phaseolorum* FS431. *Molecules* **2019**, *24*, 3062. [CrossRef]

128. Cui, H.; Ding, M.; Huang, D.; Zhang, Z.; Liu, H.; Huang, H.; She, Z. Chroman-4-one and pyrano[4,3-b]chromenone derivatives from the mangrove endophytic fungus *Diaporthe phaseolorum* SKS019. *RSC Adv.* **2017**, *7*, 20128–20134. [CrossRef]

129. Liu, Z.; Zhao, J.; Liang, X.; Lv, X.; Li, Y.; Qu, J.; Liu, Y. Dothiorelone derivatives from an endophyte *Diaporthe pseudomangifericerae* inhibit the activation of human lymphoblast MRC-5 cells. *Fitoterapia* **2018**, *127*, 7–14. [CrossRef]

130. Bungijahan, M.E.; Tan, M.A.; Kitajima, M.; Kogure, N.; Franzblau, S.G.; dela Cruz, T.E.; Takayama, H.; Nonato, M.G. Bioactive metabolites of *Diaporthe* sp. P133, an endophytic fungus isolated from *Pandanus amaryllifolius*. *J. Nat. Med.* **2011**, *65*, 606–609. [CrossRef]

131. De Medeiros, A.G.; Savi, D.C.; Mitra, P.; Shaaban, K.A.; Jha, A.K.; Thorson, J.S.; Rohr, J.; Glienke, C. Bioprospecting of *Diaporthe terebinthifoli* LGMF907 for antimicrobial compounds. *Folia Microbiol.* **2018**, *63*, 499–505. [CrossRef] [PubMed]

132. Meepagala, K.M.; Briscoe, W.E.; Techen, N.; Johnson, R.D.; Clausen, B.M.; Duke, S.O. Isolation of a phytotoxic isocoumarin from *Datura inoxia* induces three novel cytotoxic secondary metabolites in *Diaporthe* sp., an endophytic fungus from *Camptotheca* acuminata. *Nat. Prod. Res.* **2013**, *27*, 2100–2104. [CrossRef] [PubMed]

133. Evidente, M.; Boari, A.; Vergura, S.; Cimmino, A.; Vurro, M.; Ash, G.; Superchi, S.; Evidente, A. Structure and absolute configuration of kongiidiazadione, a new phytotoxic 3-substituted-5-diazenylcyclopentendione produced by *Diaporthe Kogii*. *Chirality* **2015**, *27*, 557–562. [CrossRef]

134. Tanney, J.B.; McMullin, D.R.; Green, B.D.; Miller, J.D.; Seifert, K.A. Production of antifungal and antiinsect metabolites by the *Picea* endophyte *Diapirthe maritima* sp. nov. *Fungal Biol.* **2016**, *120*, 1448–1457. [CrossRef]

135. Riga, R.; Happyan, A.; Quentinmeier, A.; Zammarelli, C.; Kayser, O.; Hakim, E.H. Secondary metabolites from *Diaporthe lithocarpus* isolated from *Artocarpus heterophyllus*. *Nat. Prod. Res.* **2019**. [CrossRef]
138. Ratnaweera, P.B.; Jayasundara, J.M.N.M.; Herath, H.H.M.S.D.; Williams, D.E.; Rajapaksha, S.U.; Nishantha, K.M.D.W.P.; de Silva, E.D.; Andersen, R.J. Antifeedant, contact toxicity and oviposition deterrent effects of phyllostine acetate and phyllostine isolated from the endophytic fungus Diaporthe mirieae against Platella xylostella larvae. Pest Manag. Sci. 2020, 76, 1541–1548. [CrossRef]

139. Wulansari, D.; Julistiono, H.; Nurkanto, A.; Agusta, A. Antifungal activity of (+)-2,2’-epicytoskyrin A and its membrane-disruptive action. Makara J. Sci. 2016, 20, 160–166. [CrossRef]

140. Tian, W.; Liao, Z.; Zhou, M.; Wang, G.; Wu, Y.; Gao, S.; Qiu, D.; Liu, X.; Lin, T.; Chen, H. Cytoskyrin C, an unusual asymmetric bisanthaquinone with cage-like skeleton from the endophytic fungus Diaporthe sp. Fitoterapia 2018, 128, 253–257. [CrossRef]

141. Specian, V.; Sarragiotto, M.H.; Pamphile, J.A.; Clemente, E. Chemical characterization of bioactive compounds from the endophytic fungus Diaporthe helianthi isolated from Luehea dicaricata. Braz. J. Microbiol. 2012, 43, 1174–1182. [CrossRef] [PubMed]

142. Reveglia, P.; Pacetti, A.; Masi, M.; Cinmini, A.; Carella, G.; Marchi, G.; Mugnai, L.; Evidente, A. Phytotoxic metabolites produced by Diaporthe erekae involved in cane blight of grapevine in Italy. Nat. Prod. Res. 2019. [CrossRef] [PubMed]

143. Mandavid, H.; Rodrigues, A.M.S.; Espindola, L.S.; Eparvier, V.; et al. Isolando e identificando bioativos produzidos por um fungo endófito em Luehea divaricata, 2018, 83, 11804–11813. [CrossRef]

144. Roofr, S.A.; Savl, D.C.; Ponomareva, L.V.; Rodrigues, R.; Rohr, J.; Thorsen, J.S.; Glienke, C.; Shaaban, K.A. Vochysiamides A and B: Two new bioactive carboxamides produced by the new species Diaporthe vochysiae. Fitoterapia 2019, 138. [CrossRef] [PubMed]

145. Sousa, J.P.B.; Aguilar-Perez, M.M.; Arnold, A.E.; Rios, N.; Coley, P.D.; Kursar, T.A.; Cubilla-Rios, L. Chemical constituents and their antibacterial activity from the tropical endophytic fungus Diaporthe sp. F2934. J. Appl. Microbiol. 2016, 12, 1501–1508. [CrossRef]

146. Nakashima, K.I.; Tomida, J.; Kamiya, T.; Hirai, T.; Morita, Y.; Hara, H.; Kawamura, Y.; Adachi, T.; Inoue, M. Diaporthols A and B: Two new bioactive carboxamides produced by the new species Diaporthe gulyae. J. Nat. Prod. 2015, 78, 623–629. [CrossRef]

147. Nakashima, K.I.; Tomida, J.; Kamiya, T.; Hirai, T.; Morita, Y.; Hara, H.; Kawamura, Y.; Adachi, T.; Inoue, M. Diaporthols A and B: Two new bioactive carboxamides produced by the new species Diaporthe gulyae. J. Nat. Prod. 2015, 78, 623–629. [CrossRef]

148. Cui, H.; Liu, Y.; Li, J.; Yang, B.; Zhou, X.; Liu, Y.; Long, Y.; She, Z. Dihydroanthracenone metabolites from the marine mangrove endophytic fungus Diaporthe sp. SYSU-HQ3. Org. Lett. 2017, 19, 5621–5624. [CrossRef]

149. Andolfi, A.; Boari, A.; Evidente, M.; Cimmino, A.; Carella, G.; Marchi, G.; Mugnai, L.; Evidente, A. Gulypyrones A and B and phomentrioloxins A and B: Two new bioactive carboxamides produced by the new species Diaporthe vochysiae. J. Nat. Prod. 2015, 78, 623–629. [CrossRef]

150. Luo, X.; Lin, X.; Tao, H.; Wang, J.; Li, J.; Yang, B.; Zhou, X.; Liu, Y. Isochromophilones A-F, cytotoxic chloroazaphilones from the tropical endophytic fungus Diaporthe sp. F2934. J. Appl. Microbiol. 2016, 120, 1501–1508. [CrossRef]

151. Nakashima, K.I.; Tomida, J.; Kamiya, T.; Hirai, T.; Morita, Y.; Hara, H.; Kawamura, Y.; Adachi, T.; Inoue, M. Diaporthols A and B: Two new bioactive carboxamides produced by the new species Diaporthe gulyae. J. Nat. Prod. 2015, 78, 623–629. [CrossRef]

152. Mandavid, H.; Rodrigues, A.M.S.; Espindola, L.S.; Eparvier, V.; Stien, D. Secondary metabolites isolated from the Amazonian endophytic fungus Diaporthe sp. SNB-GSS10. J. Nat. Prod. 2015, 78, 1735–1739. [CrossRef] [PubMed]

153. Liu, H.; Chen, Y.; Li, H.; Li, S.; Tan, H.; Liu, Z.; Li, D.; Liu, H.; Zhang, W. Four new metabolites from the endophytic fungus Diaporthe lithocarpus A740. Fitoterapia 2019, 137. [CrossRef] [PubMed]

154. Li, G.; Kusari, S.; Kusari, P.; Kayser, O.; Spitterler, M. Endophytic Diaporthe sp. LG23 produces a potent antibacterial tetracyclic triterpenoid. J. Nat. Prod. 2015, 78, 2128–2132. [CrossRef]

155. Ito, A.; Maeda, H.; Tonouchi, A.; Hashimoto, M. Relative and absolute structure of phomolide C. Biosci. Biotechnol. Biochem. 2015, 79, 1067–1069. [CrossRef]

156. Yedukondalu, N.; Arora, P.; Wadhwa, B.; Malik, F.A.; Vishwakarma, R.A.; Gupta, V.K.; Riyaz-ul-Hassan, S.; Ali, A. Diapolic acid A from an endophytic fungus, Diaporthe terebinthifoli. a potential mycoherbicide for saffron thistle (Carthamus lanatus). J. Nat. Prod. 2015, 78, 623–629. [CrossRef]

157. Luo, X.; Lin, X.; Tao, H.; Wang, J.; Li, J.; Yang, B.; Zhou, X.; Liu, Y. Isochromophilones A-F, cytotoxic chloroazaphilones from the marine mangrove endophytic fungus Diaporthe sp. SCIOS 4101. J. Nat. Prod. 2018, 81, 934–941. [CrossRef]

158. Cui, H.; Liu, Y.; Luo, M.; Lu, Y.; Huang, X.; She, Z. Dihydroanthracenone metabolites from the marine mangrove endophytic fungus Diaporthe sp. SYSU-HQ3. Org. Lett. 2017, 19, 5621–5624. [CrossRef]

159. Mandavid, H.; Rodrigues, A.M.S.; Espindola, L.S.; Eparvier, V.; Stien, D. Secondary metabolites isolated from the Amazonian endophytic fungus Diaporthe sp. SNB-GSS10. J. Nat. Prod. 2015, 78, 1735–1739. [CrossRef] [PubMed]

160. Liu, H.; Chen, Y.; Li, H.; Li, S.; Tan, H.; Liu, Z.; Li, D.; Liu, H.; Zhang, W. Four new metabolites from the endophytic fungus Diaporthe lithocarpus A740. Fitoterapia 2019, 137. [CrossRef] [PubMed]

161. Schloss, S.; Hackl, T.; Herz, C.; Lamy, E.; Koch, M.; Rohn, S.; Maul, R. Detection of a toxic methylated derivative of phomopsin A produced by the legume-infecting fungus Diaporthe toxica. J. Nat. Prod. 2017, 80, 1930–1934. [CrossRef] [PubMed]

162. Sebastiones, F.L.S.; Cabedo, N.; El Aouad, N.; Valente, A.M.M.P.; Lacava, P.T.; Azavedo, J.L.; Pizzirani-Kleiner, A.A.; Cortes, D. 3-Hydroxypropionic acid as an antibacterial agent from endophytic fungi Diaporthe phaseolorum. Curr. Microbiol. 2012, 65, 622–632. [CrossRef] [PubMed]

163. Hu, M.; Yang, X.Q.; Wan, C.P.; Wang, B.Y.; Yin, H.Y.; Shi, L.J.; Wu, Y.M.; Yang, Y.B.; Zhou, H.; Ding, Z.T. Potential antihyperlipidemic polyketones from endophytic Diaporthe sp. J.C.-J7 in Dendrobium nobile. RSC Adv. 2018, 8, 41810–41817. [CrossRef]
164. Yenn, T.W.; Ring, L.C.; Nee, T.W.; Khairuddin, M.; Zakaria, L.; Ibrahim, D. Endophytic Diaporthe sp. ED2 produces a novel anti-candidal ketone derivative. *J. Microbiol. Biotechnol.* **2017**, *27*, 1065–1070. [CrossRef]

165. El-Helw, E.A.E.; Hashem, A.I. Synthesis and antitumor activity evaluation of some pyrrolone and pyridazinone heterocycles derived from 3-((2-oxo-5-(p-tolyl)furan-3(2H)-ylidene)methyl)quinolin-2(1H)-one. *Synth. Commun.* **2020**, *50*, 1046–1055. [CrossRef]

166. Zheng, C.J.; Shao, C.L.; Chen, M.; Niu, Z.G.; Zhao, D.L.; Wang, C.Y. Merosesquiterpenoids and ten-membered macrolides from a soft coral-derived Lophiostoma sp. fungus. *Chem. Biodivers.* **2015**, *12*, 1407–1414. [CrossRef]

167. Jozwiak, M.; Filipowska, A.; Fiorino, F.; Struga, M. Anticancer activities of fatty acids and their heterocyclic derivatives. *Eur. J. Pharmacol.* **2020**, *871*. [CrossRef]