Metabolites from *Alternaria* Fungi and Their Bioactivities

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**Abstract:** *Alternaria* is a cosmopolitan fungal genus widely distributing in soil and organic matter. It includes saprophytic, endophytic and pathogenic species. At least 268 metabolites from *Alternaria* fungi have been reported in the past few decades. They mainly include nitrogen-containing metabolites, steroids, terpenoids, pyranones, quinones, and phenolics. This review aims to briefly summarize the structurally different metabolites produced by *Alternaria* fungi, as well as their occurrences, biological activities and functions. Some considerations related to synthesis, biosynthesis, production and applications of the metabolites from *Alternaria* fungi are also discussed.

**Keywords:** metabolites; *Alternaria* fungi; biological activities; phytotoxins; mycotoxins; endophytes; plant pathogens

1. Introduction

*Alternaria* fungi, belonging to the Dematiaceae of the Hyphomycetes in the Fungi Imperfecti, have a widespread distribution in Nature. They act as plant pathogens, weak facultative parasites, saprophytes and endophytes [1]. Some metabolites from *Alternaria* fungi are toxic to plants and animals, and are designated as phytotoxins and mycotoxins, respectively [2–4]. *Alternaria* metabolites exhibit a variety of biological activities such as phytotoxic, cytotoxic, and antimicrobial properties, which have drawn the attention of many chemists, pharmacologists, and plant pathologists in research programs as well as in application studies [5,6]. For examples, porritoxin (21, Table 1) from endophytic *Alternaria* species has been studied as the candidate of cancer chemopreventive agent [7].
Depudecin (257), an inhibitor of histone deacetylase (HDAC) from *A. brassicicola*, also showed its antitumor potency [8,9]. Some *Alternaria* metabolites such as tenuazonic acid (15), maculosin (43) and tentoxin (53) have been studied as the herbicide candidates [10–12].

In the early 1990s, about 70 metabolites from *Alternaria* fungi were reviewed [13]. Several reviews on *Alternaria* phytotoxins have been published over the last few decades [6,14,15]. In recent years, more and more metabolites with bioactivities from *Alternaria* fungi have been isolated and structurally characterized. This review mainly presents classification, occurrences, biological activities and functions of the metabolites from *Alternaria* fungi. We also discussed and prospected the synthesis, biosynthesis, production and applications of the metabolites from *Alternaria* fungi.

2. Classification and Occurrence

The metabolites from *Alternaria* fungi can be grouped into several categories which include nitrogen-containing compounds, steroids, terpenoids, pyranones (pyrones), quinones, phenolics, etc. Several metabolites are unique to one *Alternaria* species, but most metabolites are produced by more than one species. Occurrences of the isolated metabolites from *Alternaria* fungi are listed in Table 1 [16–135]. The most widespread metabolite is alternariol (157) which has been isolated from a few *Alternaria* fungi [25,27,84,85]. Some metabolites were also isolated from other genus fungi and even from higher plants. Typical examples included AAL toxins 3–10 from *Fusarium* species [5,136,137], helvolic acid (117) from *Aspergillus* species [138] and *Pichia* species [139], paclitaxel (taxol, 61) from yew trees (*Taxus* spp.) [140], resveratrol (252) from a variety of plant species such as *Vitis vinifera*, *Polygonum cuspidatum* and *Glycine max* [141], besides these metabolites from *Alternaria* species [43,53,130].

| Metabolite class       | Metabolite name | *Alternaria* species       | Reference     |
|------------------------|-----------------|---------------------------|---------------|
| Nitrogen-containing    | AAL-toxin TA₁   | *A. alternata* f.sp. lycopersici | [16,17]       |
| Metabolites            | AAL-toxin TA₂   | *A. alternata* f.sp. lycopersici | [16,17]       |
|                        | AAL-toxin TB₁   | *A. alternata* f.sp. lycopersici | [16,17]       |
|                        | AAL-toxin TB₂   | *A. alternata* f.sp. lycopersici | [16,17]       |
|                        | AAL-toxin TC₁   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | AAL-toxin TC₂   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | AAL-toxin TD₁   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | AAL-toxin TD₂   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | AAL-toxin TE₁   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | AAL-toxin TE₂   | *A. alternata* f.sp. lycopersici | [18]          |
|                        | Fumonisin B₁    | *A. alternata*             | [19]          |
|                        | Altersetin (12) | *Alternaria* sp.           | [21]          |
|                        | *N*-Acetyltiramine (13) | *A. tenuissima* | [22]          |
|                        | Pyrophen (14)   | *A. alternata*             | [23]          |
| Metabolite class                  | Metabolite name                                         | Alternaria species          | Reference    |
|----------------------------------|---------------------------------------------------------|----------------------------|--------------|
| Tenuazonic acid = TeA = TA       | A. alternata                                            | [24–28]                    |
| = AAC-toxin (15)                 | A. citri                                                | [29]                       |
|                                  | A. crassa                                               | [30]                       |
|                                  | A. linicola                                             | [31]                       |
|                                  | A. tenuissima                                           | [24]                       |
| Deprenylzinnimide (16)           | A. porri                                                | [32]                       |
| Zinnimide (17)                   | A. porri                                                | [32]                       |
| Cichorine (18)                   | A. cichorii                                             | [33]                       |
| Zinnimidine (19)                 | A. cichorii                                             | [33]                       |
|                                  | A. porri                                                | [32,34,35]                 |
| Z-Hydroxyzinnimidine (20)        | A. cichorii                                             | [33]                       |
| Porritoxin (21)                  | A. porri                                                | [7,36]                     |
| Porritoxin sulfonic acid (22)    | A. porri                                                | [35]                       |
| ACT-toxin I (23)                 | A. alternata                                            | [37,38]                    |
| ACT-toxin II (24)                | A. alternata                                            | [37,38]                    |
| AK-toxin I (25)                  | A. kikuchiana (A. alternata)                           | [39]                       |
| AK-toxin II (26)                 | A. kikuchiana (A. alternata)                           | [39]                       |
| AS-I toxin (27)                  | A. alternata                                            | [40]                       |
| Octadecane-1,3,4-triol (28)      | Alternaria sp.                                          | [41]                       |
| Cerebroside B (29)               | Alternaria sp.                                          | [41]                       |
| Cerebroside C (30)               | Alternaria sp.                                          | [41]                       |
| AI-77-B (31)                     | A. tenuis                                               | [42]                       |
| AI-77-F (32)                     | A. tenuis                                               | [42]                       |
| Sg17-1-4 (33)                    | A. tenuis                                               | [42]                       |
| Cyclo-(Pro-Ala-) (34)            | A. alternata                                            | [10]                       |
|                                  | A. tenuissima                                           | [22]                       |
| Nitrogen-containing Metabolites  | Cyclo-(Pro-Pro-) (35)                                   | A. tenuissima               | [22]         |
|                                  | Cyclo-(Phe-Ser-) (36)                                   | Alternaria sp. FL25         | [43]         |
|                                  | Cyclo-(L-Leu-trans-4-hydroxy-L-Pro-) (37)               | A. alternata                | [44]         |
|                                  | A. tenuissima                                           | [22]                       |
|                                  | Cyclo-(S-Pro-R-Val-) (38)                              | A. alternata                | [10]         |
|                                  | A. tenuissima                                           | [22]                       |
|                                  | Cyclo-(Pro-Leu-) (39)                                   | A. tenuissima               | [22]         |
|                                  | Cyclo-(Pro-Homoleucine-) (40)                           | A. alternata                | [10]         |
|                                  | A. tenuissima                                           | [22]                       |
|                                  | Cyclo-(S-Pro-R-Ile-) (41)                               | A. alternata                | [22]         |
|                                  | Cyclo-(Pro-Phe-) (42)                                   | A. alternata                | [10]         |
|                                  | A. tenuissima                                           | [22]                       |
|                                  | Maculosin =                                             | A. alternata                | [10]         |
|                                  | Cyclo-(L-Pro-L-Tyr-) (43)                               |                            |              |
Table 1. Cont.

| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|-----------------|--------------------|-----------|
| Cyclo-(L-Phe-trans-4-hydroxy-L-Pro-) (44) | A. alternata | [44] |
| Cyclo-(L-Ala-trans-4-hydroxy-L-Pro-) (45) | A. alternata | [44] |
| AM-toxin I (46) | A. mali (A. alternata) | [39] |
| AM-toxin II (47) | A. mali (A. alternata) | [39] |
| AM-toxin III (48) | A. mali (A. alternata) | [39] |
| Destruxin A (49) | A. linicola | [31] |
| Destruxin B (50) | A. brassicaceae | [45] |
| AM-toxin I (46) | A. mali (A. alternata) | [39] |
| AM-toxin II (47) | A. mali (A. alternata) | [39] |
| AM-toxin III (48) | A. mali (A. alternata) | [39] |
| Destruxin A (49) | A. linicola | [31] |
| Destruxin B (50) | A. brassicaceae | [45] |
| Homodestruxin B (51) | A. brassicaceae | [46] |
| Desmethyldestruxin B (52) | A. brassicaceae | [46] |
| Tentoxin (53) | A. alternata | [47] |
| Isotentoxin (54) | A. porri | [47] |
| Dihydrotentoxin (55) | A. citri | [47] |
| Uridine (56) | A. alternata | [49] |
| Adenosine (57) | A. alternata | [49] |
| Brassicicolin A (58) | A. brassicicola | [50,51] |
| Fumitremorgin B (59) | Alternaria sp. FL25 | [52] |
| Fumitremorgin C (60) | Alternaria sp. FL25 | [52] |
| Paclitaxel = Taxol (61) | A. alternata var. monosporus | [53] |
| Steroids | Ergosterol (62) | A. alternata | [27,54] |
| Ergosta-4,6,8(14),22-tetraen-3-one (63) | A. alternata | [27,54] |
| Ergosta-4,6,8(9),22-tetraen-3-one (64) | A. alternata | [49] |
| Ergosta-7,24(28)-dien-3-ol (65) | A. alternata | [49] |
| 3β-Hydroxy-ergosta-5,8(9),22-trien-7-one (66) | A. brassicicola ML-P08 | [55] |
| 3β,5α-Dihydroxy-ergosta-7,22-dien-6-one (67) | A. brassicicola ML-P08 | [55] |
| Cerevisterol (68) | A. brassicicola ML-P08 | [55] |
| Terpenoids | Bicycloalternarene 1 (69) | A. alternata | [56] |
| Bicycloalternarene 11 (70) | A. alternata | [56] |
| Bicycloalternarene 2 (71) | A. alternata | [56] |
| Bicycloalternarene 3 = ACTG toxin A (72) | A. alternata | [56] |
| Bicycloalternarene 4 (73) | A. alternata | [56] |
| Bicycloalternarene 10 (74) | A. alternata | [56] |
| Metabolite class       | Metabolite name            | Alternaria species | Reference  |
|-----------------------|----------------------------|--------------------|------------|
| Bicycloalternarene 5  |                           | A. alternata       | [56]       |
| Bicycloalternarene 8  |                           | A. alternata       | [56]       |
| Bicycloalternarene 9 =| ACTG toxin B (77)          | A. alternata       | [56]       |
| Bicycloalternarene 6  |                           | A. alternata       | [56]       |
| Bicycloalternarene 7  |                           | A. alternata       | [56]       |
| Tricycloalternarene 1a|                           | A. alternata       | [57]       |
| Tricycloalternarene 1b|                           | A. alternata       | [57,58]    |
| Tricycloalternarene 11a|                          | A. alternata       | [59]       |
| Tricycloalternarene 11b|                          | A. alternata       | [59]       |
| Tricycloalternarene 2a|                           | A. alternata       | [57]       |
| Tricycloalternarene 2b|                           | A. alternata       | [57,58]    |
| Tricycloalternarene 3a|                           | A. alternata       | [57]       |
| Tricycloalternarene 3b|                           | A. alternata       | [57,60]    |
| ACTG toxin H (88)     |                           | A. citri           | [61]       |
| Tricycloalternarenal  (89)|                      | A. alternata       | [60]       |
| Tricycloalternarene 4a|                           | A. alternata       | [57]       |
| Tricycloalternarene 4b|                           | A. alternate       | [57]       |
| Tricycloalternarene 10b|                          | A. alternate       | [59]       |
| Tricycloalternarene 5a|                           | A. alternate       | [57]       |
| Tricycloalternarene 5b|                           | A. alternate       | [57]       |
| Tricycloalternarene 8a|                           | A. alternate       | [59]       |
| Tricycloalternarene 9b|                           | A. alternate       | [59]       |
| Tricycloalternarene 6a|                           | A. alternate       | [59]       |
| Tricycloalternarene 6b|                           | A. alternate       | [59]       |
| Tricycloalternarene 7a|                           | A. alternate       | [59]       |
| Tricycloalternarene 7b|                           | A. alternate       | [59]       |
| Tricycloalternarene A  |                           | A. alternata Ly83  | [58]       |
| Tricycloalternarene B  |                           | A. alternata Ly83  | [58]       |
| Tricycloalternarene C  |                           | A. alternata Ly83  | [58]       |
| Tricycloalternarene D  |                           | A. alternata Ly83  | [58]       |
| Tricycloalternarene E  |                           | A. alternata Ly83  | [58]       |
| Brassicicene A (106)   |                           | A. brassicicola    | [62]       |
| Brassicicene B (107)   |                           | A. brassicicola    | [62]       |
| Brassicicene C (108)   |                           | A. brassicicola    | [62]       |
| Brassicicene D (109)   |                           | A. brassicicola    | [62]       |
| Brassicicene E (110)   |                           | A. brassicicola    | [62]       |
| Brassicicene F (111)   |                           | A. brassicicola    | [62]       |
| Brassicicene G (112)   |                           | A. brassicicola    | [51]       |
| Brassicicene H (113)   |                           | A. brassicicola    | [51]       |
| Brassicicene I (114)   |                           | A. brassicicola    | [51]       |
| Abscisic acid = ABA (115)|                             | A. brassicae      | [63]       |
| Metabolite class | Metabolite name | Alternaria species | Reference |
|-----------------|----------------|--------------------|-----------|
| Pyranones       | Radicinin (118) | A. chrysanthemi     | [64,65]   |
|                 |                | A. helianthi        | [66]      |
|                 |                | A. radicina         | [67]      |
| Deoxyradicinin (119) | Alternaria sp. CIB 108 | A. helianthi | [68]       |
| Radicinol (120) |                | A. chrysanthemi     | [64,65]   |
|                 |                | A. helianthi        | [66,69]   |
| Deoxyradicinol (121) | A. chrysanthemi | A. helianthi | [66]      |
| 3-Epiradicalin (122) | A. helianthi | A. chrysanthemi     | [65]    |
|                 |                | A. radicina         | [67]      |
| 3-Epideoxyradicinol (123) | Alternaria sp. CIB 108 | A. helianthi | [68]     |
| 3-Methoxy-3-epiradicalin (124) | A. chrysanthemi | A. helianthi | [65]     |
| 9,10-Epoxy-3-methoxy-3-epiradicalin (125) | A. chrysanthemi | A. helianthi | [66]     |
| Radianthin (126) |                | A. chrysanthemi     | [65]      |
| 3-Butyryl-6-[rel-(1S,2S)-1,2-dihydroxypropyl]-4-hydroxy-2H-pyrano-2-one (127) | Alternaria sp. CIB 108 | A. helianthi | [68] |
| Phomapyrone A = Phomenenin A (128) | A. brassicicola | A. infectoria | [51] |
| Phomenenin B (129) | A. infectoria | A. brassicicola | [71] |
| Phomapyrone G (130) | A. arbusi | A. conjuncta | [72] |
| Infectopyrone (131) | A. conjuncta | A. infectoria | [72] |
|                 |                | A. intercepta       | [72]      |
|                 |                | A. metachromatica   | [72]      |
|                 |                | A. novae-zelandiae  | [72]      |
|                 |                | A. oregonensis      | [72]      |
|                 |                | A. triticimaculae   | [72]      |
|                 |                | A. viburni          | [72]      |

Table 1. Cont.
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| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|-----------------|--------------------|-----------|
| Pyranones        | Herbarin A (132) | *A. brassicicola* ML-P08 | [55]      |
|                  | Alternaric acid (133) | *A. solani* |          |
| Novae-zelandin A (134) | *A. cetera* | | [72] |
|                  | A. *infectioria* | | [72] |
|                  | A. *intercepta* | | [72] |
|                  | *A. novae-zelandiae* | | [72] |
|                  | *A. triticmaculans* | | [72] |
|                  | *A. viburni* | | [72] |
| Novae-zelandin B (135) | *A. cetera* | | [72] |
|                  | A. *infectioria* | | [72] |
|                  | A. *intercepta* | | [72] |
|                  | *A. novae-zelandiae* | | [72] |
|                  | *A. triticmaculans* | | [72] |
|                  | *A. viburni* | | [72] |
| 4Z-Infectopyrone (136) | *A. arbusti* | | [72] |
|                  | A. *conjecta* | | [72] |
|                  | A. *infectioria* | | [72] |
|                  | A. *intercepta* | | [72] |
|                  | *A. metachromatica* | | [72] |
|                  | *A. novae-zelandiae* | | [72] |
|                  | *A. oregonensis* | | [72] |
|                  | *A. triticmaculans* | | [72] |
|                  | *A. viburni* | | [72] |
| Pyrenocine A (137) | *A. infectioria* | | [72] |
| Pyrenocine B (138) | *A. infectioria* | | [72] |
| Pyrenocine C (139) | *A. infectioria* | | [72] |
| ACRL toxin I (140) | *A. citri* | | [75] |
| ACRL toxin II (141) | *A. citri* | | [76] |
| ACRL toxin III (142) | *A. citri* | | [76] |
| ACRL toxin IV (143) | *A. citri* | | [76] |
| ACRL toxin IV’ (144) | *A. citri* | | [76] |
| Solanapyrone A (145) | *A. solani* | | [77] |
| Solanapyrone B (146) | *A. solani* | | [77] |
| Solanapyrone C (147) | *A. solani* | | [77] |
| Solanapyrone D (148) | *A. solani* | | [78] |
| Solanapyrone E (149) | *A. solani* | | [78] |
| Tenuissimasatin (150) | *A. tenuissima* | | [22] |
| Altechromone A (151) | *A. brassicicola* ML-P08 | | [55] |
| 2,5-Dimethyl-7-hydroxychromone (152) | *Alternaria* sp. | | [79] |
| Phomapyrone F (153) | *A. brassicicola* | | [51] |
| Altenusiol (154) | *Alternaria* sp. | | [80] |
| Altertenuol (155) | *A. tenuis* | | [81] |
| Dehydroaltenusin (156) | *A. tenuis* | | [82] |
Table 1. Cont.

| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|----------------|-------------------|-----------|
| Alternariol =AOH (157) | *Alternaria* sp. | [41,84] |
| | *A. alternata* | [25,27,85] |
| Alternariol 5-O-sulfate (158) | *Alternaria* sp. | [84] |
| Alternariol 9-methyl ether = AME | *Alternaria* sp. | [41,84,86] |
| | = Djalonensone (159) | *A. alternata* | [25,27,85] |
| | | *A. linicola* | [31] |
| | | *A. tenuis* | [87] |
| | | *A. tenuissima* | [86] |
| Alternariol 5-O-methyl ether-4'-O-sulfate (160) | *Alternaria* sp. | [84] |
| 3'-Hydroxylinterariol (161) | *Alternaria* sp. | [84] |
| Altenuene = ATL (162) | *Alternaria* sp. | [84] |
| | *A. alternata* | [85] |
| Isoaltenuene (163) | *A. alternata* | [88] |
| 4'-Epialtenuene (164) | *Alternaria* sp. | [84] |
| 5'-Epialtenuene (165) | *A. alternata* | [89] |
| Neoaltenuene (166) | *A. alternata* | [89] |
| Rubrofusarin B (167) | *A. alternata* | [23] |
| Fonsecin (168) | *A. alternata* | [23] |
| Fonsecin B (169) | *A. alternata* | [23] |
| Aurasperone A (170) | *A. alternata* | [23] |
| Aurasperone B (171) | *A. alternata* | [23] |
| Aurasperone C (172) | *A. alternata* | [23] |
| Aurasperone F (173) | *A. alternata* | [23] |
| Quinones | Macrosporin (174) | *Alternaria* sp. ZJ-2008003 | [90] |
| | | *A. porri* | [32] |
| | | *A. solani* | [91] |
| | Demethylmacrosporin (175) | *A. porri* | [32] |
| | Dihydroaltersolanol A (176) | *Alternaria* sp. ZJ-2008003 | [90] |
| | Tetrahydroaltersolanol B (177) | *Alternaria* sp. ZJ-2008003 | [90] |
| | | *A. solani* | [92] |
| | Tetrahydroaltersolanol C (178) | *Alternaria* sp. ZJ-2008003 | [90] |
| | Tetrahydroaltersolanol D (179) | *Alternaria* sp. ZJ-2008003 | [90] |
| | Tetrahydroaltersolanol E (180) | *Alternaria* sp. ZJ-2008003 | [90] |
| | Tetrahydroaltersolanol F (181) | *Alternaria* sp. ZJ-2008003 | [90] |
| | Bostry cin (182) | *A. eichhorniae* | [93] |
| | 4-Deoxybostry cin (183) | *A. eichhorniae* | [93] |
| | Hydroxybostry cin (184) | *A. solani* | [94] |
| | Altersolanol A = Stemphylin (185) | *A. porri* | [95] |
| | | *A. solani* | [94,96,97] |
| | Altersolanol B = Dactylarin (186) | *Alternaria* sp. ZJ-2008003 | [90] |
| | | *A. porri* | [95] |
| | | *A. solani* | [94,96,97] |
Table 1. Cont.

| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|-----------------|--------------------|-----------|
| Quinones         | Altersolanol C = Dactylariol (187) | *Alternaria* sp. ZJ-2008003 | [90]       |
|                  |                 | *A. porri*         | [95,98]   |
|                  |                 | *A. solani*        | [94,96,97]|
|                  | Altersolanol D (188) | *A. solani*        | [94,96,97]|
|                  | Altersolanol E (189) | *A. solani*        | [94,96,97]|
|                  | Altersolanol F (190) | *A. solani*        | [94,96,97]|
|                  | Altersolanol G (191) | *A. solani*        | [94]      |
|                  | Altersolanol H (192) | *A. solani*        | [94]      |
|                  | Altersolanol L (193) | *Alternaria* sp. ZJ-2008003 | [90]     |
|                  | Ampelanol (194) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterporriol A/B (195) | *A. porri*       | [32]     |
|                  |                 | *A. solani*        | [94,99]   |
|                  | Alterporriol C (196) | *Alternaria* sp. ZJ-2008003 | [90]     |
|                  |                 | *A. porri*         | [32]     |
|                  |                 | *A. solani*        | [99]     |
|                  | Alterporriol D/E (197) | *A. porri*       | [32]     |
|                  | Alterporriol F (198) | *A. porri*         | [32]     |
|                  | Alterporriol K (199) | *Alternaria* sp. ZJ9-6B | [100]   |
|                  | Alterporriol L (200) | *Alternaria* sp. ZJ9-6B | [100]   |
|                  | Alterporriol M (201) | *Alternaria* sp. ZJ9-6B | [100]   |
|                  | Alterporriol N (202) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterporriol O (203) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterporriol P (204) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterporriol Q (205) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterporriol R (206) | *Alternaria* sp. ZJ-2008003 | [90] |
|                  | Alterperylenol (207) | *Alternaria* sp. | [79,101] |
|                  |                 | *Alternaria* sp. M6 | [102]   |
|                  |                 | *A. alternata*     | [27]     |
|                  |                 | *A. cassiae*       | [103]    |
|                  |                 | *A. tenuissima*    | [22]     |
|                  | 8β-Chloro-3,6aa,7β,9β,10-pentahydroxy-9,8,7,6a-tetrahydroperylen-4(6aH)-one (208) | *Alternaria* sp. M6 | [102] |
|                  | Dihydroalterperylenol (209) | *Alternaria* sp. | [101]   |
|                  |                 | *Alternaria* sp. M6 | [102]   |
|                  |                 | *A. alternate*     | [104]    |
|                  | Stemphyperylenol (210) | *Alternaria* sp. | [79]    |
|                  |                 | *A. alternata*     | [105]    |
|                  |                 | *A. cassiae*       | [103]    |
|                  | 6-Epi-stemphytriol (211) | *A. alternata*   | [105]    |
Table 1. Cont.

| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|-----------------|--------------------|-----------|
| Quinones         | Altertoxin I = ATX-I (212) | Alternaria sp. | [79,80,106] |
|                  | A. alternata    | [26,27,104,105,107] |
|                  | A. cassiae      | [103]              |
|                  | A. tenuissima   | [22]               |
|                  | Alteichin (213) | A. alternata       | [26,107]  |
|                  | A. eichorniae   | [108]              |
|                  | Alterlosin I (214) | A. alternata | [26]       |
|                  | Alterlosin II (215) | A. alternata | [26]       |
| Phenolics        | p-Hydroxybenzoic acid (219) | A. tagetica | [109]      |
|                  | Tyrosol (220)   | A. tagetica        | [109]      |
|                  | α-Acetylcorcinol (221) | A. tenuissima | [22]       |
|                  | 2-Carboxy-3-(2-hydroxypropanyl) | Alternaria sp. HS-3 | [110] |
|                  | phenol (222)    |                     |           |
|                  | Methyl eugenol (223) | Alternaria sp. | [111]     |
|                  | Tagetolone (224) | A. tagetica        | [109]     |
|                  | Tagetenolone (225) | A. tagetica | [109]     |
|                  | Zinniol (226)   | A. earthami        | [112,113] |
|                  | A. cichorii     | [33]               |
|                  | A. cirsinoxia   | [114]              |
|                  | A. dauci        | [115]              |
|                  | A. macrospora   | [113]              |
|                  | A. porri        | [113,116]          |
|                  | A. solani       | [113,117,118]      |
|                  | A. tagetica     | [113,116,119]      |
|                  | A. zinniae      | [120]              |
|                  | 8-Zinniol 2-(phenyl)-ethyl ether (227) | A. solani | [118]     |
|                  | A. tagetica     | [116]              |
|                  | A. solani       | [118]              |
|                  | A. tagetica     | [116]              |
|                  | 8-Zinniol acetate (229) | A. tagetica | [116]     |
|                  | 7-Zinniol acetate (230) | A. tagetica | [116]     |
|                  | Homozinniol (231) | A. solani | [117]     |
|                  | Zinnol (232)    | A. cichorii        | [33]      |
|                  | A. solani       | [118]              |
|                  | A. tagetica     | [116]              |
|                  | A. cichorii     | [33]               |
|                  | 8-Zinniol methyl ether (233) | A. solani | [118]     |
|                  | A. tagetica     | [116]              |
|                  | A. cichorii     | [33]               |
|                  | Zinnidiol (234) | A. solani         | [118]     |
|                  | 2-(2''-3''-dimethyl-but-1-enyl)-Zinniol (235) | A. solani | [118]     |
|                  | Bis-7-O-8''-8-O-7''-zinniol (236) | A. tagetica | [121]     |
|                  | Bis-7-O-7''-8-O-8''-zinniol (237) | A. tagetica | [121]     |
|                  | 4-Acetyl-5-hydroxy-3,6,7-trimethylbenzofuran-2(3H)-one (238) | Alternaria sp. HS-3 | [110] |
|                  | 5-Methyl-6-hydroxy-8-methoxy-3-methylisochroman (239) | Alternaria sp. HS-3 | [110] |
| Metabolite class | Metabolite name | Alternaria species | Reference |
|------------------|----------------|--------------------|-----------|
| Phenolics        | Alternarian acid (240) | Alternaria sp. | [79] |
|                  | Altenusin (241) | Alternaria sp. | [79,84,122,123] |
|                  | A. mali | | [124] |
|                  | A. tenuis | | [82] |
|                  | Desmethylaltenusin (242) | Alternaria sp. | [84] |
|                  | Porrnic acid D (243) | Alternaria sp. | [123] |
|                  | Alterlactone (244) | Alternaria sp. | [84] |
|                  | Alternethanoxin A (245) | A. sonchi | [125] |
|                  | Alternethanoxin B (246) | A. sonchi | [125] |
|                  | Alternarienonic acid (247) | Alternaria sp. | [79,84] |
|                  | Talaroflavone (248) | Alternaria sp. | [84] |
|                  | Curvularin (249) | A. cinerariae | [126] |
|                  | A. tomato | | [127] |
|                  | (4S)-α,β-Dehydrocurvularin (250) | Alternaria sp. | [86] |
|                  | A. cinerariae | | [126,128] |
|                  | A. tenuissima | | [86] |
|                  | A. tomato | | [127] |
|                  | A. zinniae | | [129] |
|                  | β-Hydroxycurvularin (251) | A. tomato | [127] |
|                  | Resveratrol (252) | Alternaria sp. MG1 | [130] |
|                  | 6-(3’,3’-dimethylallyloxy)-4-Methoxy-5-methylphthalide (253) | A. porri | [7] |
|                  | A. solani | | [117] |
|                  | A. tagetica | | [116] |
|                  | A. porri | | [131] |
|                  | 5-(3’,3’-dimethylallyloxy)-7-Methoxy-6-methylphthalide (255) | A. porri | [7,32,34] |
|                  | A. solani | | [118] |
|                  | A. tagetica | | [116] |
|                  | A. porri | | [7,32] |
| Miscellaneous    | Depudecin (257) | A. brassicicola | [132] |
| Metabolites      | Altenin (258) | A. kikuchiana | [133] |
|                  | Brefeldin A (259) | A. carthami | [112] |
|                  | A. zinniae | | [129] |
|                  | 7-Dehydrobrefeldin A (260) | A. carthami | [112] |
|                  | α-Linoleic acid (261) | A. infectia | [71] |
|                  | α-Linolenic acid (262) | A. infectia | [71] |
|                  | AF-toxin I (263) | A. alternata | [134,135] |
|                  | AF-toxin II (264) | A. alternata | [134,135] |
|                  | AF-toxin III (265) | A. alternata | [134] |
|                  | Xanalteric acid I (266) | Alternaria sp. | [79] |
|                  | Xanalteric acid II (267) | Alternaria sp. | [79] |
|                  | Cladosporol (268) | A. alternate var. monosporus | [53] |
2.1. Nitrogen-Containing Metabolites

The nitrogen-containing compounds such as amides, amines, and cyclopeptides have been isolated from *Alternaria* fungi. Some of them belong to the host-selective phytotoxins in host-parasite interactions [39].

2.1.1. Amines and Amides

Amines and amides 1–33 are the common nitrogen-containing metabolites produced by *Alternaria* fungi (Figure 1). Ten sphinganine analogs designated AAL toxins 1–10 with an amino polyol backbone were isolated from *A. alternata* f.sp. *lycopersici* [16–18]. AAL toxins belong to host-specific phytotoxins. Very interestingly, AAL-toxins TB1 (3), TB2 (4), TC1 (5), TC2 (6), TD1 (7), TD2 (8), TE1 (9) and TE2 (10) have also been isolated from *Fusarium moniliforme* [136] and *F. verticillioides* [137]. Three amide alkaloids, AI-77-B (31), AI-77-F (32) and Sg17-1-4 (33), containing an isocoumarin structure were isolated from the marine fungus *Alternaria tenuis Sg17-1* [42]. Other *Alternaria* amines and amides along with their distributions in *Alternaria* fungi are shown in Table 1.

**Figure 1.** Amines and amides isolated from *Alternaria* fungi.
2.1.2. Cyclopeptides

Some Alternaria fungi can produce cyclopeptides 34–55 which are shown in Figure 2. Seven cyclopeptides, namely cyclo-(Pro-Ala-) (34), cyclo-(Pro-Pro-) (35), cyclo-[L-Leu-trans-4-hydroxy-L-Pro-] (37), cyclo-(S-Pro-R-Val-) (38), cyclo-(Pro-Leu-) (39), cyclo-(S-Pro-R-Ile-) (41), and cyclo-(Pro-Phe-) (42) were isolated from the endophytic fungus A. tenuissima derived from the bark of Erythrophleum fordii Oliver (Leguminosae) [22].

Three diketopiperazine dipeptides, namely cyclo-[L-Leu-trans-4-hydroxy-L-Pro-] (37), cyclo-(L-Phe-trans-4-hydroxy-1-Pro-) (44), and cyclo-(L-Ala-trans-4-hydroxy-L-Pro-) (45) were extracted from culture broth of the grapevine endophyte A. alternata [44].

Two cyclopeptides destruxins A (49) and B (50) were isolated from A. linicola [31]. Destruxin B (50) was also found in A. brassicaceae as the major phytotoxin [45]. Other cyclopeptides along with their distributions in Alternaria fungi are shown in Table 1.
2.1.3. Other Nitrogen-Containing Metabolites

Other nitrogen-containing metabolites isolated from *Alternaria* fungi are shown in Figure 3. Two nucleosides namely uridine (56) and adenosine (57) were isolated from *A. alternata* [49].
Brassicicolin A (58), an isocyanide metabolite, was isolated as a mixture of epimers from *A. brassicicola* which was the pathogen of Brassica species [50,51]. Two indole alkaloids fumitremorgins B (59) and C (60) were produced by the endophytic fungus *Alternaria* sp. FL25 from *Ficus carica* (Moraceae) [52]. Paclitaxel (taxol, 61), a diterpenoid alkaloid with antitumor activity, was isolated from the endophytic fungus *A. alternata* var. monosporus obtained from the inner bark of *Taxus yunnanensis* (Taxaceae) [53]. Paclitaxel has also been isolated from yew trees (*Taxus* spp.) and their cell cultures [140,142].

**Figure 3.** Other nitrogen-containing metabolites isolated from *Alternaria* fungi.

2.2. Steroids

Some steroids (62–68) have been isolated from *Alternaria* fungi (Figure 4 and Table 1). These findings are consistent with the considerations that ergosterol (62) and their derivatives are common to all fungi and occur widely among the fungi [143].

**Figure 4.** Steroids isolated from *Alternaria* fungi.
Figure 4. Cont.

2.3. Terpenoids

Most of terpenoids from *Alternaria* fungi have been found as the mixed terpenoids which have a multiple biogenesis (69–105). Other *Alternaria* terpenoids include diterpenoids 106–114, sesquiterpenoids 115,116 and a triterpenoid 117, which are shown in Figure 5.

Eleven bicycloalternarenes (BCAs, 69–79) were isolated and characterized from the culture filtrate of the phytopathogenic fungus *A. alternata* [56].

Nineteen tricycloalternarenes (TCAs) were isolated from the culture filtrate of the phytopathogenic fungus *A. alternata* from *Brassica sinensis* (Cruciferae). Tricycloalternarenes are closely related to ACTG toxins 87,88. Structural differences mainly occur in the isoprenoid side chain and the substitution pattern of the C-ring of the tricycloalternarenes [57–60].

Two tricycloalternarenes, ACTG toxins G (TCA 3b, 87) and H (88), along with a sesquiterpene (1aS,2S,6R,7R,7aR,7bR)-1a,2,4,5,6,7,7a,7b-octahydro-7,7a-dimethyl-1a-(1-methylethenyl)-napth[1,2-b]oxiren-2,6-diol (116) were isolated from culture broth of *A. citri*, the pathogen causing brown spot disease of mandarin (*Citrus reticulata*) [61].

Nine fusicoccane diterpenes designated brassicicenes A-I 106–114 were isolated from the culture filtrate of the canola pathogen *A. brassicicola* [51–62].

Abscisic acid (ABA, 115), a sesquiterpenoid with plant growth regulation activity, was isolated from *A. brassicacea*, a black spot pathogen of *Brassica* species (Cruciferae) [63].

Helvolic acid (117), a nortriterpenoid, was isolated from *Alternaria* sp. FL25, an endophytic fungus from *Ficus carica* (Moraceae) [43]. This metabolite (117) has also been isolated from *Aspergillus fumigatus* [138] and *Pichia guilliermondii* [139].

Figure 5. Terpenoids isolated from *Alternaria* fungi.

69. Bicycloalternarene (BCA) 1, R = OH
70. BCA 11, R = OCH₃
71. BCA 2, R₁ = OH, R₂ = CH₃OH
72. BCA 3, R₁ = OH, R₂ = OH
73. BCA 4, R₁ = OCH₃, R₂ = CH₃
74. BCA 10, R₁ = OCH₃, R₂ = CH₂OH
75. BCA 5, R₁ = OCH₃, R₂ = CH₃
76. BCA 8, R₁ = OH, R₂ = CH₂OH
77. BCA 9, R₁ = OH, R₂ = CH₃
Figure 5. Cont.

78. BCA 6, R = OH
79. BCA 7, R = OCH₃

80. Tricycloalternarene (TCA) 1a, R₁ = OH, R₂ = H
81. TCA 1b, R₁ = H, R₂ = OH
82. TCA 11a, R₁ = OCH₃, R₂ = H
83. TCA 11b, R₁ = H, R₂ = OCH₃

84. TCA 2a, R₁ = OH, R₂ = H, R₃ = CH₂OH
85. TCA 2b, R₁ = H, R₂ = OH, R₃ = CH₂OH
86. TCA 3a, R₁ = OH, R₂ = H, R₃ = CH₃
87. TCA 3b, R₁ = H, R₂ = OH, R₃ = CH₃
88. ACTG toxin H, R₁ = H, R₂ = OH, R₃ = CHO
89. Tricycloalternarenal, R₁ = OH, R₂ = H, R₃ = CHO
90. TCA 4a, R₁ = OCH₃, R₂ = H, R₃ = CH₃
91. TCA 4b, R₁ = H, R₂ = OCH₃, R₃ = CH₃
92. TCA 10b, R₁ = H, R₂ = OCH₃, R₃ = CH₂OH

93. TCA 5a, R₁ = OCH₃, R₂ = H, R₃ = CH₃
94. TCA 5b, R₁ = H, R₂ = OCH₃, R₃ = CH₃
95. TCA 8a, R₁ = OH, R₂ = H, R₃ = CH₂OH
96. TCA 9b, R₁ = H, R₂ = OH, R₃ = CH₃

97. TCA 6a, R₁ = OH, R₂ = H
98. TCA 6b, R₁ = H, R₂ = OH
99. TCA 7a, R₁ = OCH₃, R₂ = H
100. TCA 7b, R₁ = H, R₂ = OCH₃

101. TCA A
102. TCA B
103. TCA C, R = COOH
104. TCA D, R = CH₂OAc
105. TCA E

106. Brassicicene A
107. Brassicicene B
108. Brassicicene C, R = H
109. Brassicicene F, R = OH
110. Brassicicene D
2.4. Pyranones

Pyranones are also called pyrones which include α-, β- and γ-pyranones. Most of the pyranones isolated from Alternaria fungi belong to α-pyranones.

2.4.1. Simple Pyranones

The pyranones that do not contain benzene ring structure are defined as simple pyranones which belong to polyketides. Simple pyranones 118–149 from Alternaria fungi are shown in Figure 6. Three phytotoxins, ACRL toxins I (140), II (141) and III (142), with an α-dihydropyrone ring were isolated from A. citri, the causal agent of lemon (Citrus limon) [75,76].

Four metabolites namely novae-zelandins A (134) and B (135), 4Z-infectopyone (136), and infectopyrone (131) isolated from A. infectoria were thought to be important chemotaxonomic markers in the species group of A. infectoria [72].

Figure 6. Simple pyranones isolated from Alternaria fungi.
Figure 6. Cont.

126. Radianthin

127. 3-Butyryl-6-[rel-(1S,2S)-1,2-dihydroxypropyl]-4-hydroxy-2H-pyran-2-one

128. Phomapyrone A

129. Phomenenin B

130. Phomapyrone G

131. Infectopyrone

132. Herbarin A

133. Alternaria acid

134. Novae-zelandin A

135. Novae-zelandin B

136. 4Z-Infectopyrone

137. Pyrenocine A

138. Pyrenocine B

139. Pyrenocine C

140. ACRL toxin I

141. ACRL toxin II

142. ACRL toxin III

143. ACRL toxin IV

144. ACRL toxin IV'

145. Solanapyrone A, R1 = CHO, R2 = OCH3

146. Solanapyrone B, R1 = CH2OH, R2 = OCH3

147. Solanapyrone C, R1 = CHO, R2 = NH(CH2)2OH

148. Solanapyrone D, R = CHO

149. Solanapyrone E, R = CH2OH
2.4.2. Monobenzopyranones

Both benzo-α-pyranones and benzo-γ-pyranones have been found in *Alternaria* species (Figure 7 and Table 1). Benzo-α-pyranones are also called coumarin or isocoumarin derivatives. Four monobenzopyranones namely tenuissimassatin (150), altechromone A (151), 2,5-dimethyl-7-hydroxychromone (152) and phomapyrone F (153) were isolated from *Alternaria* fungi [22,55,79].

**Figure 7.** Monobenzopyranones isolated from *Alternaria* fungi.

![Monobenzopyranones](image)

2.4.3. Dibenzopyranones

A few dibenzo-α-pyranones 154–166 have been found in *Alternaria* fungi so far. They are shown in Figure 8. Both alternariol (AOH, 157) and alternariol 9-methyl ether (AME, 159) represent the main toxic metabolites of *Alternaria* fungi.

**Figure 8.** Dibenzopyranones isolated from *Alternaria* fungi.

![Dibenzopyranones](image)
2.4.4. Naphthopyranones

Seven naphtha-γ-pyranones 167–173 were found in *A. alternata* isolated from the marine soft coral *Denderonephthya hemprichi* (Figure 9). Among them, aurasperones A (170), B (171), C (172) and F (173) were dimeric naphtha-γ-pyranones [23].

**Figure 9.** Naphthopyranones isolated from *Alternaria* fungi.

![Naphthopyranones](image)

2.5. Quinones

Two groups of quinones, anthraquinone and perylenequine derivatives have been isolated in *Alternaria* fungi so far.

2.5.1. Anthraquinones

Figure 10 shows the structures of twenty-one simple anthraquinones 174–194 and twelve bianthraquinones 195–206 from *Alternaria* fungi. Nine tetrahydroanthraquinones 174–183, hydroxybostrycin (184) along with altersolanols A (185), B (186), C (187), D (188), E (189), F (190), G (191) and H (192) were isolated from *A. solani*, a causal pathogen of black spot disease on tomato (*Lycopersicon esculentum*) leaves [94,96].

Four bianthraquinones, alterporriols A/B (195), C (196), D/E (197), and F (198) were isolated from *A. porri*, the critical pathogen associated with the purple blotch disease of onion (*Allium cepa*) [32]. Three other bianthraquinones, alterporriols K (199), L (200) and M (201) were obtained from the mangrove endophytic fungus *Alternaria* sp. ZJ9-6B [100].

**Figure 10.** Anthraquinones isolated from *Alternaria* fungi.

![Anthraquinones](image)
Figure 10. Cont.
2.5.2. Perylenequinones

The perylenequinones are a class of metabolites characterized by a pentacyclic conjugated chromophore. *Alternaria* fungi produce a variety of partially reduced perylenequinone derivatives. A monochloridated perylenequinone namely 8β-chloro-3,6α,7β,9β,10-pentahydroxy-9,8,7,6α-tetrahydroperylen-4(6aH)-one (208) along with alterperylenol (207) and dihydroalterperylenol (209) were isolated from a halotolerant fungus *Alternaria* sp. M6 obtained from the solar salt field at the beach of Bohai Bay in China [102]. Other perylenequinones 207–218 are shown in Figure 11.

Figure 11. Perylenequinone derivatives isolated from *Alternaria* fungi.

2.6. Phenolics

The phenolic metabolites 219–256 from *Alternaria* fungi are shown in Figures 12 and 13. Most of them have a polyketide origin. One phenylpropanoid component was identified as methyl eugenol (223) by GC-MS from the volatile oil obtained by hydrodistillation from the *Alternaria* species isolated as the endophyte of rose (*Rosa damascena*) [111]. Methyl eugenol (223) has been used as a flavouring agent in jellies, baked goods, non-alcoholic beverages, chewing gum, candy, pudding, relish, and ice cream [144].

Zinniol (226) along with its two analogues, bis-7-O-8\".8-O-7\"-zinniol (237) and bis-7-O-7\".8-O-8\"-zinniol (238), were isolated from the culture filtrate of *A. tagetica*, which was the causal agent of early blight in marigold (*Tagetes erecta*) [121].
One *Alternaria* species MG1 as the endophytic fungus from *Vitis vinifera* L. cv. Merlot could produce resveratrol (3,5,4'-trihydroxystilbene, 252) [130]. Resveratrol has been known for preventing and slowing the occurrence of some human diseases, including cancer, cardiovascular disease, and ischemic injuries. It has also been shown that resveratrol (252) can enhance stress resistance and extend the lifespan of various organisms ranging from yeasts to vertebrates [145]. Resveratrol has been found in a variety of plant species such as *Vitis vinifera*, *Polygonum cuspidatum*, and *Glycine max* [141]. Endophytic *Alternaria* species for producing plant-derived resveratrol should be an important and novel resource with its potential application in pharmaceutical industry [146].

**Figure 12.** Phenolic metabolites isolated from *Alternaria* fungi.
Figure 12. Cont.

Phthalides are considered as a special group of phenolic compounds. Four phthalates 253–256 were isolated from Alternaria fungi that are shown in Figure 13, and their occurrences are shown in Table 1.

Figure 13. Phthalides isolated from Alternaria fungi.

2.7. Miscellaneous Metabolites

The miscellaneous metabolites 257–268 isolated from Alternaria fungi are shown in Figure 14. Depudecin (257) was an eleven-carbon linear polyketide isolated from A. brassicicola [132]. Two carboxylic acids namely xanalteric acids I (266) and II (267) were isolated from the endophytic fungus Alternaria sp. from the mangrove plant Sonneratia alba (Sonneratiaceae) [79].
3. Biological Activities and Functions

*Alternaria* metabolites with diverse chemical properties have been clarified (Figures 1–14, Table 1). Some of them act as phytotoxins to plants or as mycotoxins to humans and animals. They have been examined to have a variety of biological activities and functions, which mainly include the effects on plants, cytotoxic and antimicrobial activities.

3.1. Effects on Plants

Plant pathogenic *Alternaria* species can affect cereals, vegetables and fruit crops in the field and during storage. *Alternaria* fungi contamination is responsible for some of the world’s most devastating plant diseases, causing serious reduction of crop yields and considerable economic losses. The metabolites from plant pathogenic fungi are usually toxic to plants and are called phytotoxins. They were further divided into host-specific and host non-specific toxins. The host-specific toxins (HSTs) are toxic only to host plants of the fungus that produces the toxin [6,13]. Another definition seems to be more acceptable that the host-specific toxins are toxic to plants that host the pathogen, but have lower phytotoxicity on non-host plants [147,148]. Most HSTs are considered to be pathogenicity factors, which the fungi producing them require to invade tissue and induce disease [149] All isolates of the pathogen that produce an HST are pathogenic to the specific host. All isolates that fail to produce HSTs lose pathogenicity to the host plants. Plants that are susceptible to the pathogen are
sensitive to the toxin. Such correlations between HST production and pathogenicity in the pathogens, and between toxin sensitivity and disease susceptibility in plants provide persuasive evidence that HSTs can be responsible for host-specific infection and disease development. Johnson and coworkers revealed that the genes involved in HST synthesis such as the cyclopeptide synthetase gene, whose product catalyzed AM toxin production in \textit{A. alternata} apple pathotype, might reside on a conditionally dispensable (CD) chromosome. The loss of the CD chromosome led to loss of both toxin production and pathogenicity without affecting fungal growth [150]. On the other hand, the exact roles of non-specific toxins in pathogenesis are largely unknown, but some are thought to contribute to the features of virulence, such as the symptom development and \textit{in planta} pathogen propagation [6]. The virulence and host-specificity of these pathogens are based on production of the distinctive HSTs [13]. For \textit{Alternaria} pathogens, there are now at least nine diseases caused by \textit{Alternaria} species in which HSTs are responsible for fungal pathogenicity (Table 2). Most of \textit{Alternaria} HSTs are nitrogen-containing metabolites.

Table 2. Host-specific phytotoxins from \textit{Alternaria} fungi.

| Phytotoxin name | \textit{Alternaria} species | Host plant | Plant disease | Reference |
|-----------------|-----------------------------|------------|---------------|-----------|
| AAL-toxins TA1 (1), TA2 (2), TB1 (3), TB2 (4), TC1 (5), TC2 (6), TD1 (7), TD2 (8), TE1 (9), TE2 (10) | \textit{A. alternata} f.sp. \textit{lycopersici} | Tomato (\textit{Solanum lycopersicum}) | Stem canker disease of tomato | [16–18] |
| ACT-toxins I (23) and II (24) | \textit{A. citri} (\textit{A. alternata}) | Mandarins and tangerine (\textit{Citrus} spp.) | Brown spot of tangerine | [37,38] |
| AK-toxins I (25) and II (26) | \textit{A. kikuchiana} (\textit{A. alternata}) | Japanese pear (\textit{Pyrus serotina}) Sunflower (\textit{Helianthus annuus}) | Black spot disease | [39,135] |
| AS-I toxin (27) | \textit{A. alternata} | | Necrotic spots on sunflower leaves | [40] |
| Maculosin (43) | \textit{A. alternata} | Spotted knapweed (\textit{Centaurea maculosa}) | Black leaf blight | [10,26] |
| AM-toxins I (46), II (47) and III (48) | \textit{A. mali} (\textit{A. alternata}) | Apple (\textit{Malus pumila}) | \textit{Alternaria} blotch of apple | [39] |
| Destruxin A (49), Destruxin B (50), Homodestruxin B (51), Desmethyldestruxin B (52) | \textit{A. brassicae} | \textit{Brassica juncea}; \textit{Brassica napus}; \textit{Brassica rapa} | \textit{Alternaria} blackspot disease of \textit{Brassica} | [46,148] |
| ACRL toxins I (140), II (141), III (142), IV (143), IV’ (144) | \textit{A. citri} | Rough lemon (\textit{Citrus limon}) | Brown spot disease of \textit{Citrus} \textit{Alternaria} baleck spot of strawberry | [75,76,134,135] |
| AF-toxins I (263), II (264) and III (265) | \textit{A. alternata} | Strawberry (\textit{Fragaria} spp.) | \textit{Alternaria} baleck spot of strawberry | |

Among the HSTs, AAL toxins from tomato stem canker pathogen (\textit{A. alternata} f.sp. \textit{lycopersici}) have received a special attention. They were toxic to all tissues of sensitive tomato cultivars at low
concentrations and induced apoptosis in sensitive tomato plants [151], and were found to inhibit de novo sphingolipid (ceramide) biosynthesis in vitro. Therefore, AAL toxins are called sphinganine-analog mycotoxins (SAMs). It has been reported that the tomato Alternaria stem canker locus mediated resistance to SAMs-induced apoptosis [152].

Destruxins are another group of HSTs produced both in vitro and in planta by A. brassicae, the causal agent of Alternaria blackspot disease of rapeseed and canola [148]. These cyclodepsipeptides exhibited a wide variety of biological activities such as antitumor, antiviral, insecticidal, cytotoxic, immunosuppressant, and antiproliferative effects except their phytotoxicity [153].

Interactions between Alternaria species and cruciferous plants were studied in detail by the Pedras group [51]. Nectrophic phytopathogens such as A. alternata and A. brassicae are known to synthesize phytotoxins that damage plant tissues and facilitate colonization, while in response to pathogen attack crucifers biosynthesize phytoanticipins and phytoalexins. Phytoalexins are secondary metabolites produced de novo by plants in response to diverse forms of stress including microbial infection, UV irradiation, and heavy metal salts, whereas phytoanticipins are constitutive defenses whose concentrations can increase upon stress [154]. To the detriment of cruciferous plants, the phytopathogens can overcome phytoanticipins and phytoalexins by producing detoxifying enzymes. For example, the phytoalexin brassinin (269) was detoxified into 3-indolylmethanamine (270) and \( N^\prime\)-acetyl-3-indolylmethanamine (271) by the pathogen A. brassicae (Figure 15) [51]. Very interestingly, cruciferous plants (i.e., Brassica napus and Sinapis alba) can convert host-specific toxins destruxin B (50) and homodestruxin B (51) into less phytotoxic hydrodestruxin B (272) and hydroxyhomodestruxin B (273), respectively (Figure 16) [155,156].

**Figure 15.** Detoxification pathway of the phytoalexin brassinin (269) by the pathogen A. brassicicola [51].

\[
\text{269. Brassinin} \xrightarrow{A. brassicicola} \text{270. 3-Indolylmethanamine, } R = H \\
\text{271. } N^\prime\text{-Acetyl-3-indolylmethanamine, } R = \text{Ac}
\]

**Figure 16.** Detoxification pathway of the phytotoxins destruxin B (50) and homodestruxin B (51) by the hosts Brassica napus and Sinapis alba [155,156].

\[
\text{50. Destruxin B} \xrightarrow{\text{Brassica napus}} \text{HO} \\
\text{272. Hydroxydestruxin B} \xrightarrow{\text{Sinapis alba}} \text{HN}
\]
Host non-specific *Alternaria* phytotoxins can affect many plants regardless of whether they are a host or non-host of the pathogen [6,13]. Host non-specific nitrogen-containing phytotoxins include tenuazonic acid (15), porritoxin (21) and tentoxin (53). Tentoxin (53), a cyclic tetrapeptide from *A. alternata*, inhibited chloroplast development, which phenotypically manifests itself as chlorotic tissue [157]. Tentoxin (53) was suggested to exert its effect on chlorophyll accumulation through overenergization of thylakoids [158]. Tenuazonic acid (TeA, 15) was investigated in *Chlamydomonas reinhardtii* thylakoids which revealed that TeA inhibited photophosphorylation with the action site at Qb level [159].

Host non-specific pyranone phytotoxins include radicinin (118), deoxyradicinin (119), alternaric acid (133), alternuisol (154), altertenuol (155), dehydroaltenusin (156), alternariol (AOH, 157), alternariol 9-methyl ether (AME, 159), and alternuene (162). They are very common non-specific phytotoxic metabolites of *Alternaria* species [64–69,74,80–85].

Host non-specific quinone phytotoxins included bostrycin (182), 4-dexoybostrycin (183), and altersolanols A (185), B (186) and C (187) [93–95]. Alternsolanol A (185), a tetrahydroanthraquinone phytotoxin from the culture broth of *A. solani*, inhibited the growth of cultured cells of *Nicotiana rustica*. It acted as a potent stimulator of NANH oxidation in the mitochondria isolated from *N. rustica* cells. Alternsolanols acted as electron acceptors in an enzyme preparation of diaphorase. The capacity of altersolanols A, B, C, D, E and F to act as electron acceptors was in the order of A > E > C > B > F > D [160].

Host non-specific phenolic phytotoxins include zinniol (226) and its analogues 227–237. Zinniol (226) from the liquid cultures of *A. tagetica* induced leaf tissue necrosis in a number of unrelated plant species (*Avena sativa*, *Cucumis sativus*, *Daucu carota*, *Hordeum vulgare*, *Triticum aestivum*) from different families which demonstrated that zinniol acted as a non host-specific phytotoxin [161]. However, Qui *et al.* evaluated the effects of zinniol at the cellular level and showed that pure zinniol was not obviously phytotoxic at concentrations known to induce necrosis in leaves of *Tagetes erecta*, which indicated that the classification of zinniol as a host non-specific phytotoxin should be further investigated [162].
Other host non-specific phytotoxins include α,β-dehydrocurvularin (250) and brefeldin A (259) from A. zinniae. They showed phytotoxic activity on Xanthium occidentale, a widespread noxious weed of Australian summer crops and pastures. The fungus A. zinniae and its toxins may be used as the mycoherbicides in integrated weed management programs [129].

Some fungal phytotoxins were toxic to weed species to show their herbicidal potentials in agriculture and forestry [10,163–165]. Some examples are shown in Table 3. Weed pathogens should be a very promising source of bioactive natural products for weed control. Tentoxin (53) was transformed to isotentoxin (54) by UV irradiation. Isotentoxin (54) had stronger wilting effects than tentoxin against the weed Galium aparine [11].

Table 3. Some examples of Alternaria phytotoxins which are toxic to weed species.

| Phytotoxin name                  | Alternaria species | Target weed species             | Reference |
|----------------------------------|--------------------|---------------------------------|-----------|
| AAL-toxins (1–10)                | A. alternata       | Jimson weed (Datura stramonium) | [166]     |
| Tenuazonic acid (15)             | A. alternata       | Lantana camara                  | [12]      |
| Maculosin (43)                   | A. alternata       | Spotted knapweed (Centaurea maculosa) | [10]    |
| Tentoxin (53)                    | A. alternata       | Galium aparine                  | [11]      |
| Isotentoxin (54)                 | A. alternata       | Galium aparine                  | [11]      |
| Alteichin (213)                  | A. eichorniae      | Water hyacinth (Eichhornia crassipes) | [108]  |
| Alternethanoxin A (245)          | A. sonchi          | Sonchus arvensis                | [125]     |
| Alternethanoxin B (246)          | A. sonchi          | Sonchus arvensis                | [125]     |
| Brefeldin A (259)                | A. zinniae         | Xanthium occidentale            | [129]     |

3.2. Cytotoxic Activity

Some Alternaria metabolites have been screened to show cytotoxic activity. They were thought as the potential sources for possible cancer chemopreventive agents. Porritoxin (21) was examined to have anti-tumor-promoting activity [7]. Three amides, AI-77-B (31), AI-77-F (32) and Sg17-1-4 (33), from a marine fungus A. tenuis Sg17-1 exhibited cytotoxic activity. AI-77-B (31) exhibited the cytotoxic activity on human malignant A375-S2 and human cervical cancer Hela cells with IC50 values of 0.1 and 0.02 mM, respectively. AI-77-F (32) showed a weak activity to Hela cells with an IC50 value of 0.4 mM. Sg17-1-4 (33) showed moderate activity with IC50 values of 0.3 and 0.05 mM, on malignant A375-S2 and Hela cells, respectively [42].

Of Alternaria dibenzopyranones, alternariol (157) was the most active metabolite to have cytotoxic activity on L5178Y mouse lymphoma cells [84], as well as to have inhibitory activity on protein kinase and xanthine oxidase [55]. Further investigation showed that alternariol (157) has been identified as a topoisomerase I and II poison which might contribute to the impairment of DNA integrity in human colon carcinoma cells [167]. It induced cell death by activation of the mitochondrial pathway of apoptosis in human colon carcinoma cells [168]. Alternariol and its 9-methyl ether induced cytchrome P450 1A1 and apoptosis in murine hepatoma cells dependent on the aryl hydrocarbon receptor [169]. Other alternariol derivatives such as alternariol 5-O-sulfate (158), alternariol 9-methyl ether (159), 3'-hydroxylaturnariol (161), altenuene (162), 4'-epialtenuene (164) and dehydroaltenuenin (156) were also screened to be cytotoxic [84]. Dehydroaltenuenin (165), isolated from A. tenuis, was
found to be a specific inhibitor of eukaryotic DNA polymerase α to show its strong cytotoxic activity on tumor cells [83,170].

Some screened *Alternaria* anthraquinones displayed cytotoxic activity. Demethylmacrosorin (175) was cytotoxic to Hela and KB cells with IC₅₀ values of 7.3 µg/mL and 8.6 µg/mL, respectively [32]. Altersolanol C (187) was also screened to show cytotoxic activity on a few tumor cells [90]. A few bianthraquinones including alterporriols A/B (195), C (196), D/E (197), F (198), K (199), L (200), and P (204) showed strong cytotoxic activity on a few tumor cells [32,90,100,171]. Alterporriol L (200), a bianthraquinone derivative isolated from a marine fungus *Alternaria* sp. ZJ9-6B, inhibited the growth and proliferation of the MDA-MB-435 breast cancer cells through destroying the mitochondria [171].

Some *Alternaria* phenolic metabolites also have cytotoxic activity. Alterlactone (244) from *Alternaria* sp. was toxic on L5178Y mouse lymphoma cells [84]. Alternethanoxins A (245) and B (246) from *A. sonchi* displayed growth inhibitory activity on six cancer cell lines [172]. Both 6-(3',3'-dimethylallyloxy)-4-methoxy-5-methylphthalalide (253) and 5-(3',3'-dimethylallyloxy)-7-methoxy-6-methylphthalalide (255) were proved to have anti-tumor promoting activity [7]. 5-(3',3'-dimethylallyloxy)-7-methoxy-6-methylphthalalide (255) had the cytotoxicity on Hela cells and KB cells with IC₅₀ values as 36.0 µg/mL and 14.0 µg/mL, respectively. Porriolide (256) had the cytotoxicity on KB cells with IC₅₀ value as 59.0 µg/mL [32]. Depudecin (257), an eleven-carbon linear polyketide from *A. brassicicola*, is an inhibitor of histone deacetylase (HDAC) to show its potential in cancer therapy [9].

### 3.3. Antimicrobial Activity

Three diketopiperazine dipeptides namely cyclo-[L-Leu-trans-4-hydroxy-L-Pro-] (37), cyclo-(L-Phe-trans-4-hydroxy-L-Pro-) (44), and cyclo-(L-Ala-trans-4-hydroxy-L-Pro) (45) extracted from broth culture of the grapevine endophyte *A. alternata* showed effectiveness by inhibiting sporulation of the pathogen *Plasmopara viticola* at concentrations of 10⁻³, 10⁻⁴, 10⁻⁵ and 10⁻⁶ mol/L. This indicated that endophytic fungus *A. alternata* can be used as biocontrol agent to control fungal disease in grapevine cultivation [44]. Cyclo-(Phe-Ser-) (36) from *Alternaria* sp. FL25 showed antifungal activity on *Fusarium graminearum*, *F. oxysporum* f.sp. *cucumernum*, *F. oxysporum* f.sp. *neverum*, *Phytophthora capsici*, *Colletotrichum gloesporioides* with MICs from 6.25 to 25.00 µg/mL [43]. Tenuazonic acid (15) was found to be an active compound in *A. alternata* against *Mycobacterium tuberculosis* H37Rv with MIC value of 250 µg/mL. This compound was thought as a promising antitubercular principle [28]. Other nitrogen-containing metabolites with antimicrobial activity included altersetin (12), pyrophophen (14), tenuazonic acid (15) and brassicicolin A (58) [21,23,28,50,51,159].

Helvolic acid (117) from *Alternaria* sp. FL25, an endophytic fungus in *Ficus carica*, showed the strong antifungal activity on all tested phytopathogenic fungi (*Alternaria alternata*, *A. brassicicola*, *Botrytis cinerea*, *Colletotrichum gloesporioides*, *Fusarium graminearum*, *F. oxysporum*, *F. oxysporum* f.sp. *fragariae*, *F. oxysporum* f.sp. *niveum*, *Phytophthora capsici*, *Val sa mali*) with MICs of 1.56–12.50 µg/mL [43].

Herbarin A (132) and altechromone A (151) from *A. brassicicola* ML-P08 exhibited antimicrobial activity on *Trichophyton rubrum*, *Candida albicans*, *Apergillus niger*, *Bacillus subtilis*, *Escherichia*
coli, Pseudomonas fluorescens with MICs ranged from 1.8 to 62.5 μg/mL [55]. Rubrofusarin B (167) from A. alternata showed antifungal activity on Candida albicans [23].

Some anthraquinone metabolites, e.g., macrosporin (174), hydroxybostrycin (184), alternosolanol A (185), alternosolanol B (186), alternosolanol C (187), alternosolanol G (191), and alterporriol C (196) from A. solani and Alternaria sp. showed antibacterial activity on Bacillus subtilis, Escherichia coli, Micrococcus luteus, Pseudomonas aeruginosa, Staphylococcus albus, Staphylococcus aureus, Vibrio parahemolyticus [90,94,97]. Two perylenequinones alterperyleneol (207) and dihydroalterperyleneol (209) from Alternaria sp. had antifungal activity on Valsa ceratosperma [101].

Altenusin (241) and porric acid D (243) from Alternaria sp. showed inhibitory activity against Staphylococcus aureus with MICs of 100 μg/mL and 25 μg/mL, respectively [123]. (4S)-α,β-Dehydrocurvularin (250) from Alternaria sp. showed inhibitory activity on appressorium formation of Magnaporthe oryzae [86], and antibacterial activity on Proteus vulgaris and Salmonella typhimurium with MICs as 25 μg/mL [129].

3.4. Other Bioactivities

Altenusin (241) isolated from the endophytic fungus Alternaria sp. (UFMGCB55) in Trixis vauthieri (Compositae) was screened to show inhibitory activity on trypanothione reductase (TR), which is an enzyme involved in the protection of the parasitic Trypanosoma and Leishmania species against oxidative stress, and has been considered to be a validated drug target. Altenusin (241) had an IC50 value of 4.3 μM in the TR assay [122].

The association of mycotoxins from Alternaria fungi with human and animal health is not a recent phenomenon. Alternaria toxins have been linked to a variety of adverse effects (i.e., genotoxic, mutagenic, and carcinogenic) on human and animal health [173]. Tenuazonic acid (15) has been studied in detail for its toxicity to several animal species, e.g., mice, chickens, dogs. In dogs, it caused haemorrhages in several organs at daily doses of 10 mg/kg, and in chickens, sub-acute toxicity was observed with 10 mg/kg in the feed. In particular, increasing tenuazonic acid in chicken feed from sublethal to lethal levels progressively reduced feed efficiency, suppressed weight gain and increased internal haemorrhaging. Tenuazonic acid (15) is more toxic than AOH (157), AME (159) and ALT (162) [25,167]

There were a few reports about the toxicity of Alternaria metabolites on brine shrimp (Artemia salina L.) [23,107,174,175]. The LC50 values of tenuazonic acid (15), alternariol (157), altenuene (162) and altertoxin-I (212) were 75, 100, 375 and 200 μg/mL, respectively, to brine shrimp larvae by using the disk method of inoculation and an exposure period of 18 h [175]. Tenuazonic acid (15), alternariol (157), alternariol 9-methyl ether (159), altenuene (162), altertoxin I (212) were also verified to toxic to brine shrimp by other investigators [27,174,175]. Six naphthopyranones, namely rubrofusarin B (167), fonsecin (168), aurasperone A (170), aurasperone B (171), aurasperone C (172) and aurasperone F (173) from the marine-derived fungal strain A. alternata were screened to show inhibitory activity on brine shrimp (Artemia salina L.) at 10 μg/mL [23].
4. Conclusions and Future Perspectives

We just clarified one part of metabolites from the known *Alternaria* fungi. The rest of metabolites in *Alternaria* species need to be investigated in detail. In fact, many other *Alternaria* species remain unexplored for their metabolites. In most cases, both the biological activities and modes of action of the metabolites from *Alternaria* fungi have been studied very primarily. The structure-activity relationship has been established only for a few classes of *Alternaria* metabolites. This review mainly focused on the metabolites with low molecular weight from *Alternaria* fungi. Bioactive proteins, saccharides and glycoproteins are also important metabolites. Typical examples included a lipase from *A. brassicicola* [176], an endopolypolygalacturonase from the rough lemon pathotype of *A. alternata* [177], a protein elicitor (Hrip1) from *A. tenuissima* [178], and a polyketide synthase from *A. alternata* [179]. Some bioactive saccharides and glycoproteins have also been isolated such as β-1,3-, 1,6-oligoglucan elicitor from *A. alternata* [180] and a glycoprotein elicitor from *A. tenuissima* [181].

The potential applications of *Alternaria* metabolites as antitumor agents, herbicides, and antimicrobials as well as other promising bioactivities have led to considerable interest within the pharmaceutical community. Chemical syntheses have been achieved for a few bioactive metabolites such as AAL-toxin TA1 (1) [182], maculosin (43) [183], AM-toxin I (46) [184], alternariol (157) [185], alternariol 9-methyl ether (159) [185], altenuene (162) [186], isoaltenuene (163) [186], neoaltenuene (166) [187], altertoxin III (218) [188], zinniol (226) [189], altensusin (241) [190] and alterlactone (244) [190].

In recent years, more and more *Alternaria* fungi have been isolated as plant endophytic fungi from which large amounts of bioactive compounds have been structurally characterized. Another approach is to discovery novel bioactive compounds from the *Alternaria* fungi isolated from marine organisms. These *Alternaria* fungi could be the rich sources of biologically active compounds that are indispensable for medicinal and agricultural applications [191].

After comprehensive understanding of biosynthetic pathways of some *Alternaria* metabolites in the next few years, we can effectively not only increase yields of the bioactive metabolites, but also prohibit biosynthesis of some toxic metabolites (*i.e.*, phytotoxins and mycotoxins) by treatment with some special fungicides.

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Conflict of Interest

The authors declare no conflict of interest.

References

1. Thomma, B.P.H.J. *Alternaria* spp.: From general saprophyte to specific parasite. *Mol. Plant Pathol.* 2003, 4, 225–236.
2. Strange, R.N. Phytotoxins produced by plant pathogens. *Nat. Prod. Rep.* 2007, 24, 127–144.
3. Mobius, N.; Hertweck, C. Fungal phytotoxins as mediators of virulence. Curr. Opin. Plant Biol. 2009, 12, 390–398.

4. Duke, S.O.; Dayan, F.E. Modes of action of microbially-produced phytotoxins. Toxins 2011, 3, 1038–1064.

5. Brase, S.; Encinas, A.; Keck, J.; Nising, C.F. Chemistry and biology of mycotoxins and related fungal metabolites. Chem. Rev. 2009, 109, 3903–3990.

6. Tsuge, T.; Harimoto, Y.; Akimitsu, K.; Ohtani, K.; Kodama, M.; Akagi, Y.; Egusa, M.; Yamamoto, M.; Otani, H. Host-selective toxins produced by the plant pathogenic fungus Alternaria alternata. FEMS Microbiol. Rev. 2013, 37, 44–66.

7. Horiuchi, M.; Tokuda, H.; Ohnishi, K.; Yamashita, M.; Nishino, H.; Maoka, T. Porritoxins, metabolites of Alternaria porri, as anti-tumor-promoting active compounds. Nat. Prod. Res. 2006, 20, 161–166.

8. Monneret, C. Histone deacetylase inhibitors. Eur. J. Med. Chem. 2005, 40, 1–13.

9. Lakshmi, A.I.; Madhusudhan, T.; Kumar, P.D.; Padmavathy, J.; saravanan, D.; Kumar, P.C. Histone deacetylase inhibitors in cancer therapy: an update. Int. J. Pharm. Sci. Rev. Res. 2011, 10, 38–44.

10. Stierle, A.C.; Cardellina II, J.H.; Strobel, G.A. Maculosin, a host-specific phytotoxin for spotted knapweed from Alternaria alternata. Proc. Natl. Acad. Sci. USA 1988, 85, 8008–8011.

11. Liebermann, B.; Ellinger, R.; Pinet, E. Isotentoxin, a conversion product of the phytotoxin tентоксин. Phytochemistry 1996, 42, 1537–1540.

12. Sanodiya, B.S.; Thakur, G.S.; Baghel, R.K.; Pandey, A.K.; Bhogendra, G.; Prasad, K.S.; Bisen, P.S. Isolation and characterization of tenuazonic acid produced by Alternaria alternata, a potential bioherbicidal agent for control Lantana camara. J. Plant Prot. Res. 2010, 50, 133–139.

13. Montemurro, N.; Visconti, A. Alternaria metabolites—Chemical and biological data. In Alternaria: Biology, Plant Disease and Metabolites; Chelkowski, J., Visconti, A., Eds.; Elsevier: Amsterdam, The Netherlands, 1992; pp. 449–557.

14. Nishimura, S.; Kohmoto, K. Host-specific toxins and chemical structures from Alternaria species. Ann. Rev. Phytopathol. 1983, 21, 87–116.

15. Logrieco, A.; Moretti, A.; Solfrizzo, M. Alternaria toxins and plant diseases: and overview of origin, occurrence and risks. World Mycotoxin J. 2009, 2, 129–140.

16. Bottini, A.T.; Gilchrist, D.G. Phytotoxins. I. A 1-aminodimethylheptadecapentol from Alternaria alternata f.sp. lycopersici. Tetrahedron Lett. 1981, 22, 2719–2722.

17. Bottini, A.T.; Bowen, J.R.; Gilchrist, D.G. Phytotoxins. II. Characterization of a phytotoxic fraction from Alternaria alternata f.sp. lycopersici. Tetrahedron Lett. 1981, 22, 2723–2726.

18. Caldas, E.D.; Jones, A.D.; Ward, B.; Winter, C.K.; Gilchrist, D.G. Structural characterization of three new AAL toxins produced by Alternaria alternata f.sp. lycopersici. J. Agric. Food Chem. 1994, 42, 327–333.

19. Abbas, H.K.; Riley, R.T. The presence and phytotoxicity of fumonisins and AAL-toxin in Alternaria alternata. Toxicon 1996, 34, 133–136.

20. Chen, J.; Mirocha, C.J.; Xie, W.; Hogge, L.; Olson, D. Production of the mycotoxin fumonisin B1 by Alternaria alternata f.sp. lycopersici. Appl. Environ. Microbiol. 1992, 58, 3928–3931.
21. Hellwig, V.; Grothe, T.; Mayer-Bartschmid, A.; Endermann, R.; Geschke, F.-U.; Henkel, T.; Stadler, M. Altersetin, a new antibiotic from cultures of endophytic Alternaria spp. taxonomy, Fermentation, Isolation, Structure elucidation and biological activities. *J. Antibi.**ot* 2002, 55, 881–892.

22. Fang, Z.F.; Yu, S.S.; Zhou, W.Q.; Chen, X.G.; Ma, S.G.; Li, Y.; Qu, J. A new isocoumarin from metabolites of the endophytic fungus *Alternaria tenuissima* (Nee & T. Nee: Fr) Wiltshire. *Chin. Chem. Lett.** 2012, 23, 317–320.

23. Shaaban, M.; Shaaban, K.A.; Abdel-Aziz, M.S. Seven naphtho-γ-pyrone s from the marine-derived fungus *Alternaria alternata*: Structure elucidation and biological properties. *Org. Med. Chem. Lett.** 2012, 2, 6.

24. Davis, N.D.; Diener, U.L.; Morgan-Jones, G. Tenuazonic acid production by *Alternaria alternata* and *Alternaria tenuissima* isolated from cotton. *Appl. Environ. Microbiol.** 1977, 34, 155–157.

25. Griffin, G.F.; Chu, F.S. Toxicity of the *Alternaria* metabolites alternariol, Alternariol methyl ether, Altenueene, and tenuazonic acid in the chicken embryo assay. *Appl. Environ. Microbiol.** 1983, 46, 1420–1422.

26. Stierle, A.C.; Cardellina II, J.H.; Strobel, G.A. Phytotoxins from *Alternaria alternata*, a pathogen of spotted knapweed. *J. Nat. Prod.** 1989, 52, 42–47.

27. Qin, J.-C.; Zhang, Y.-M.; Hu, L.; Ma, Y.-T.; Gao, J.-M. Cytotoxic metabolites produced by *Alternaria* no.28, an endophytic fungus isolated from *Ginkgo biloba*. *Nat. Prod. Commun.** 2009, 4, 1473–1476.

28. Sonaimuthu, V.; Parihar, S.; Thakur, J.P.; Luqman, S.; Saikia, D.; Chanotiya, C.S.; Jhonpaul, M.; Negi, A.S. Tenuazonic acid: A promising antitubercular principle from *Alternaria alternata*. *Microbiol. Res.** 2010, 2, 63–65.

29. Kono, Y.; Gardner, J.M.; Takeuchi, S. Nonselective phytotoxins simultaneously produced with host-selective ACTG-toxins by a pathotype of *Alternaria citri* causing brown spot disease of mandarins. *Agric. Biol. Chem.** 1986, 50, 2401–2403.

30. Sattar, A.; Alam, M.; Janardhanan, K.K.; Husain, A. Isolation of tenuazonic acid, a phytotoxin from *Alternaria crassa* (Sacc.) rands causing leaf blight and fruit rot of *Datura stramonium* Mill. *Curr. Sci.** 1986, 55, 195–196.

31. Evans, N.; Mcroberts, N.; Hill, R.A.; Marshall, G. Phytotoxin production by *Alternaria linicola* and phytoalexin production by the linseed host. *Ann. Appl. Biol.** 1996, 129, 415–431.

32. Phuwapraisirisan, P.; Rangsan, J.; Siripong, P.; Tip-pyang, S. New antitumour fungal metabolites from *Alternaria porri*. *Nat. Prod. Res.** 2009, 23, 1063–1071.

33. Stierle, A.; Hershenhorn, J.; Strobel, G. Zinniol-related phytotoxins from *Alternaria cichorii*. *Phytochemistry** 1993, 32, 1145–1149.

34. Suemitsu, R.; Ohnishi, K.; Morikawa, Y.; Nagatomo, S. Zinnimidine and 5-(3’,3’-dimethylallyloxy)-7-methoxy-6-methylphthalide from *Alternaria porri*. *Phytochemistry** 1995, 38, 495–497.

35. Horiuchi, M.; Ohnishi, K.; Iwase, N.; Nakajima, Y.; Tounai, K.; Yamashita, M.; Yamada, Y. A novel isoindoline, porritoxin sulfonic acid, from *Alternaria porri* and the structure-phytotoxicity correlation of its related compounds. *Biosci. Biotechnol. Biochem.** 2003, 67, 1580–1583.
36. Horiuchi, M.; Maoka, T.; Iwase, N.; Ohnishi, K. Reinvestigation of structure of porritoxin, a phytotoxin of *Alternaria porri*. *J. Nat. Prod.* **2002**, *65*, 1204–1205.

37. Kohmoto, K.; Itoh, Y.; Shimomura, N.; Kondoh, Y.; Otani, H.; Kodama, M.; Nishimura, S.; Nakatsuka, S. Isolation and biological activities of two host-specific toxins from the tangerine pathotype of *Alternaria alternata*. *Phytopathology* **1993**, *83*, 495–502.

38. Masunaka, A.; Ohtani, K.; Peever, T.L.; Timmer, L.W.; Tsuge, T.; Yamamoto, M.; Yamamoto, H.; Akimitsu, K. An isolate of *Alternaria alternata* that is pathogenic to both tangerines and rough lemon and produces two host-selective toxins, ACT- and ACR-toxins. *Phytopathology* **2005**, *95*, 241–247.

39. Ueno, T. Secondary metabolites related to host selection by plant pathogenic fungi. *Pure Appl. Chem.* **1990**, *62*, 1347–1352.

40. Liakopoulou-Kyriakides, M.; Lagopodi, A.L.; Thanassoulopoulos, C.C.; Stavropoulos, G.S.; Magafa, V. Isolation and biological activities of two host-specific toxins from the tangerine pathotype of *Alternaria alternata*. *Phytopathology* **1993**, *83*, 495–502.

41. Masunaka, A.; Ohtani, K.; Peever, T.L.; Timmer, L.W.; Tsuge, T.; Yamamoto, M.; Yamamoto, H.; Akimitsu, K. An isolate of *Alternaria alternata* that is pathogenic to both tangerines and rough lemon and produces two host-selective toxins, ACT- and ACR-toxins. *Phytopathology* **2005**, *95*, 241–247.

42. Buchwaldt, L.; Green, H. Phytotoxicity of destruxin B and its possible role in the pathogenesis of *Alternaria brassicae*. *Plant Pathol.* **1992**, *41*, 55–63.

43. Ayer, W.A.; Pena-Rodriguez, L.M. Metabolites produced by *Alternaria brassicae*, the black spot pathogen of canola. Part 1, the phytotoxic components. *J. Nat. Prod.* **1987**, *50*, 400–407.

44. Liebermann, B.; Koeblin, R. A new phytotoxic activity of the cyclic peptides tentoxin and dihydrotentoxin. *J. Phytopathol.* **1992**, *135*, 245–250.

45. Horiuchi, M.; Akimoto, N.; Ohnishi, K.; Yamashita, M.; Maoka, T. Rapid and simultaneous determination of tetra cyclic peptide phytotoxins, tentoxin, isotentoxin and dihydrotentoxin, from *Alternaria porri* by LC/MS. *Chromatography* **2003**, *24*, 109–116.

46. Ma, Y.-T.; Qiao, L.-R.; Shi, W.-Q.; Zhang, A.-L.; Gao, J.-M. Metabolites produced by an endophyte *Alternaria alternata* isolated from *Maytenus hookeri*. *Chem. Nat. Compd.* **2010**, *46*, 504–506.

47. Gloer, J.B.; Poch, G.K.; Short, D.M.; McCloskey, D.V. Structure of brassicicolin A: A novel isocyanide antibiotic from the phylloplane fungus *Alternaria brassicola*. *J. Org. Chem.* **1988**, *53*, 3758–3761.

48. Pedras, M.S.C.; Chumala, P.B.; Jin, W.; Islam, M.S.; Hauck, D.W. The phytopathogenic fungus *Alternaria brassicola*: Phytotoxin production and phytoalexin elicitation. *Phytochemistry* **2009**, *70*, 394–402.
52. Ma, Y.; Feng, C.; Zhang, H.; Zhou, X. Two indole alkaloids produced by endophytic fungus FL25 from Ficus carica. Chem. Res. Appl. 2009, 21, 1173–1175.

53. Chen, J.; Qiu, X.; Wang, R.; Duan, L.; Chen, S.; Luo, J.; Kong, L. Inhibition of human gastric carcinoma cell growth in vitro and in vivo by cladosporol isolated from the paclitaxel-producing strain Alternaria alternata var. monosporus. Biol. Pharm. Bull. 2009, 32, 2072–2074.

54. Seitz, L.M.; Paukstelis, J.V. Metabolites of Alternaria alternata: ergosterol and ergosta-4,6,8(14),22-tetraen-3-one. J. Agric. Food Chem. 1977, 25, 838–841.

55. Gu, W. Bioactive metabolites from Alternaria brassicicola ML-P08, an endophytic fungus residing in Malus halliana. World J. Microbiol. Biotechnol. 2009, 25, 1677–1683.

56. Nussbaum, R.-P.; Gunther, W. Bicycloalternarenes produced by the phytopathogenic fungus Alternaria alternata. Phytochemistry 2000, 55, 987–992.

57. Liebermann, B.; Ellinger, R.; Gunther, W.; Ihn, W.; Gallander, H. Tricycloalternarenes produced by Alternaria alternata related to ACTG-toxins. Phytochemistry 1997, 46, 297–303.

58. Yuan, L.; Zhao, P.-J.; Ma, J.; Li, G.-H.; Shen, Y.-M. Tricycloalternarenes A-E: Five new mixed terpenoids from the endophytic fungal strain Alternaria alternata Ly83. Helv. Chim. Acta 2008, 91, 1588–1594.

59. Nussbaum, R.-P.; Gunther, W.; Heinze, S.; Liebermann, B. New tricycloalternarenes produced by the phytopathogenic fungus Alternaria alternata. Phytochemistry 1999, 52, 593–599.

60. Qiao, L.-R.; Yuan, L.; Gao, J.-M.; Zhao, P.-J.; Kang, Q.-J.; Shen, Y.-M. Tricycloalternarene derivatives produced by an endophyte Alternaria alternata isolated from Maytenus hookeri. J. Basic Microbiol. 2007, 47, 340–343.

61. Kono, Y.; Gardner, J.M.; Suzuki, Y.; Kondo, H.; Takeuchi, S. New minor components of host-selective ACTG-toxin and a novel sesquiterpene produced by a pathotype of Alternaria citri causing brown spot disease of mandarins. Nippon Noyaku Gakkaishi 1989, 14, 223–228.

62. MacKinnon, S.L.; Keifer, P.; Ayer, W.A. Components from the phytotoxin extract of Alternaria brassicicola, a black spot pathogen of canola. Phytochemistry 1999, 51, 215–221.

63. Dahiya, J.S.; Tewari, J.P.; Woods, D.L. Abscisic acid from Alternaria brassicicola. Phytochemistry 1988, 27, 2983–2984.

64. Robeson, D.J.; Gray, G.R.; Strobel, G.A. Production of the phytotoxins radicinin and radicinol by Alternaria chrysanthemi. Phytochemistry 1982, 21, 2359–2362.

65. Sheridan, H.; Canning, A.-M. Novel radicinol derivatives from long-term cultures of Alternaria chrysanthemi. J. Nat. Prod. 1999, 62, 1568–1569.

66. Tal, B.; Robeson, D.J.; Burke, B.A.; Aasen, A.J. Phytotoxins from Alternaria helianthi: radicinin and the structures of deoxyradicinol and radianthin. Phytochemistry 1985, 24, 729–731.

67. Solfrizzo, M.; Vitti, C.; De Girolamo, A.; Visconti, A.; Logrieco, A.; Fanizzi, F.P. Radicinols and radicinin phytotoxins produced by Alternaria radicina on carrots. J. Agric. Food Chem. 2004, 52, 3655–3660.

68. Chen, Q.F.; Zhou, M.; Yang, T.; Chen, X.Z.; Wang, C.; Zhang, G.L.; Li, G.Y. Secondary metabolites from fungus Alternaria sp. CIB108. Chin. Chem. Lett. 2011, 22, 1226–1228.

69. Robeson, D.J.; Strobel, R.A. Deoxyradicinin, a novel phytotoxin from Alternaria helianthi. Phytochemistry 1982, 21, 1821–1823.
70. Robeson, D.J.; Strobel, G.A. Deoxyradicin and 3-epideoxyradicinol production by the sunflower pathogen Alternaria helianthi. Ann. Appl. Biol. 1985, 107, 409–415.
71. Ivanova, L.; Petersen, D.; Uhlig, S. Phomenins and fatty acids from Alternaria infectoria. Toxicon 2010, 55, 1107–1114.
72. Christensen, K.B.; Van Klink, J.W.; Weavers, R.T.; Larsen, T.O.; Andersen, B.; Phipps, R.K. Novel chemotaxonomic markers of the Alternaria infectoria species-group. J. Agric. Food Chem. 2005, 53, 9431–9435.
73. Larsen, T.O.; Perry, N.B.; Andersen, B. Infectopyrone, a potential mycotoxin from Alternaria infectoria. Tetrahedron Lett. 2003, 44, 4511–4513.
74. Patel, S.J.; Subramanian, R.B.; Jha, Y.S. A simple and rapid method for isolation of alternaric acid from Alternaria solani. Curr. Trends Biotechnol. Pharm. 2011, 5, 1098–1103.
75. Gardner, J.M.; Kono, Y.; Tatun, J.H.; Suzuki, Y.; Takeuchi, S. Plant pathotoxins from Alternaria citri: the major toxin specific for rough lemon plants. Phytochemistry 1985, 24, 2861–2867.
76. Kono, Y.; Gardner, J.M.; Suzuki, Y.; Takeuchi, S. Plant pathotoxins from Alternaria citri: the minor ACRL toxins. Phytochemistry 1985, 24, 2869–2874.
77. Ichihara, A.; Tazaki, H.; Sakamura, S. Solanapyrones A, B and C, phytotoxic metabolites from the fungus Alternaria solani. Tetrahedron Lett. 1983, 24, 5373–5376.
78. Oikawa, H.; Yokota, T.; Sakano, C.; Suzuki, Y.; Naya, A.; Ichihara, A. Solanapyrones, phyto toxins produced by Alternaria solani: Biosynthesis and isolation of minor components. Biosci. Biotechnol. Biochem. 1988, 62, 2016–2022.
79. Kjer, J.; Wray, V.; Edrada-Ebel, R.A.; Ebel, R.; Pretsch, A.; Lin, W.; Proksch, P. Xanalteric acids I and II and related phenolic compounds from an endophytic Alternaria sp. isolated from the mangrove plant Sonneratia alba. J. Nat. Prod. 2009, 72, 2053–2057.
80. Chu, F.S. Isolation of altenuisol and alters toxins I and II, minor mycotoxins elaborated by Alternaria. J. Am. Oil Chem. Soc. 1981, 58, 1006–1008.
81. Pero, R.W.; Harvan, D.; Blois, M.C. Isolation of the toxin, altenuisol, from the fungus, Alternaria tenuis Auct. Tetrahedron Lett. 1973, 12, 945–948.
82. Thomas, R. Biosynthesis of fungal metabolites. IV. Alternariol monomethyl ether and its relation to other phenolic metabolites of Alternaria tenuis. Biochem. J. 1961, 80, 234–240.
83. Maeda, N., Kokai, Y.; Ohtani, S.; Sahara, H.; Kuriyama, I.; Kamisuki, S.; Takahashi, S.; Sakaguchi, K.; Sugawara, F.; Yoshida, H. Anti-tumor effects of dehydroaltenusin, a specific inhibitor of mammalian DNA polymerase α. Biochem. Biophys. Res. Commun. 2007, 352, 390–396.
84. Aly, A.H.; Edrada-Ebel, R.; Indriani, I.D.; Wray, V.; Muller, W.E.G.; Totzke, F.; Zirrgiebel, U.; Schachtele, C.; Kubbutat, M.H.G.; Lin, W.H.; et al. Cytotoxic metabolites from the fungal endophyte Alternaria sp. and their subsequent detection in its host plant Polygonum senegalense. J. Nat. Prod. 2008, 71, 972–980.
85. Watanabe, I.; Kakishima, M.; Adachi, Y.; Nakajima, H. Potential mycotoxin productivity of Alternaria alternata isolated from garden trees. Mycotoxins 2007, 57, 3–9.
86. Jeon, Y.-T.; Ryu, K.-H.; Kang, M.-K.; Park, S.-H.; Yun. H.; QT, P.; Kim, S.-U. Alternariol monomethyl ether and α,β-dehydrocurvularin from endophytic fungi Alternaria spp. inhibit appressorium formation of Magnaporthe grisea. J. Korean Soc. Appl. Biol. Chem. 2010, 53, 39–42.
87. Pero, R.W.; Main, C.E. Chlorosis of tobacco induced by alternariol monomethyl ether produced by *Alternaria tenuis*. *Phytopathology* **1970**, *60*, 1570–1573.

88. Visconti, A.; Bottalico, A.; Solfrizzo, M.; Palmisano, F. Isolation and structure elucidation of *isoaltenuene*, a new metabolite of *Alternaria alternata*. *Mycotoxin Res.* **1989**, *5*, 69–76.

89. Bradburn, N.; Coker, R.D.; Blunden, G.; Turner, C.H.; Crabb, T.A. *5*-Epialtenuene and neoaltenuene, dibenzo-α-pyrones from *Alternaria alternata* cultured on rice. *Phytochemistry* **1994**, *35*, 665–669.

90. Zheng, C.-J.; Shao, C.-L.; Guo, Z.-Y.; Chen, J.-F.; Deng, D.-S.; Yang, K.-L.; Chen, Y.-Y.; Fu, X.-M.; She, Z.-G.; Lin, Y.-C.; *et al*. Bioactive hydroanthraquinones and anthraquinone dimers from a soft coral-derived *Alternaria* sp. fungus. *J. Nat. Prod.* **2012**, *75*, 189–197.

91. Stoessl, A.; Unwin, C.H.; Stothers, J.B. Metabolites of *Alternaria solani*. Part V. Biosynthesis of altersolanol A and incorporation of carbon-13 labeled altersolanol A into altersolanol B and macrosporin. *Tetrahedron Lett.* **1979**, *27*, 2481–2484.

92. Stoessl, A.; Stothers, J.B. Metabolites of *Alternaria solani*. Part VIII. Tetrahydroaltersolanol B, a hexahydroanthronol from *Alternaria solani*. *Can. J. Chem.* **1983**, *61*, 378–382.

93. Huang, C.-H.; Pan, J.-H.; Chen, B.; Yu, M.; Huang, H.-B.; Zhu, X.; Lu, Y.-J.; She, Z.-G.; Lin, Y.-C.; *et al*. Three bianthraquinone derivatives from the mangrove endophytic fungus *Alternaria* sp. ZJ9–6B from the South China Sea. *Mar. Drugs* **2011**, *9*, 832–843.

94. Okuno, T.; Natsume, I.; Sawai, K.; Sawamura, K.; Furusaki, A.; Matsumoto, T. Structure of antifungal and phytotoxic pigments produced by *Alternaria* species. *Tetrahedron Lett.* **1983**, *24*, 5653–5656.
103. Hradil, C.M.; Hallock, Y.F.; Clardy, J.; Kenfield, D.S.; Strobel, G. Phytotoxins from *Alternaria cassiae*. *Phytochemistry* 1989, 28, 73–75.

104. Stack, M.E.; Mazzola, E.P.; Page, S.W.; Pohland, A.E.; Hight, R.J.; Tempesta, M.S.; Corley, D.G. Mutagenic perylenequinone metabolites of *Alternaria alternata*: altertoxins I, II and III. *J. Nat. Prod.* 1986, 49, 866–871.

105. Gao, S.-S.; Li, X.-M.; Wang, B.-G. Perylene derivatives produced by *Alternaria alternata*, an endophytic fungus isolated from *Laurencia* species. *Nat. Prod. Commun.* 2009, 4, 1477–1480.

106. Hu, D.; Liu, M.; Xia, X.; Chen, D.; Zhao, F.; Ge, M. Preparative isolation and purification of altertoxin I from an *Alternaria* sp. by HSCCC. *Chromatographia* 2008, 67, 863–867.

107. Visconti, A.; Sibilia, A.; Sabia, C. *Alternaria alternata* from oilseed rape: mycotoxin production, and toxicity to *Artemia salina* larvae and rape seedlings. *Mycotoxin Res.* 1992, 8, 9–16.

108. Robeson, D.; Strobel, G.; Matusumoto, G.K.; Fisher, E.L.; Chen, M.H.; Clardy, J. Alteichin: An unusual phytotoxin from *Alternaria eichorniae*, a fungal pathogen of water hyacinth. *Experientia* 1984, 40, 1248–1250.

109. Gamboa-Angulo, M.M.; Garcia-Sosa, K.; Alejos-Gonzalez, F.; Escalante-Erosa, F.; Delgado-Lamas, G.; Pena-Rodriguez, L.M. Tagetolone and tagetenolone: two phytotoxic polyketides from *Alternaria tagetica*. *J. Agric. Food Chem.* 2001, 49, 1228–1232.

110. Xia, X.; Qi, J.; Wei, F.; Jia, A.; Yuan, W.; Meng, X.; Zhang, M.; Liu, C.; Wang, C. Isolation and characterization of a new benzofuran from the fungus *Alternaria* sp. (HS-3) associated with a sea cucumber. *Nat. Prod. Commun.* 2011, 6, 1913–1914.

111. Kaul, S.; Wani, M.; Dhar, K.L.; Dhar, M.K. Production and GC-MS trace analysis of methyl eugenol form endophytic isolate of *Alternaria* from rose. *Ann. Microbiol.* 2008, 58, 443–445.

112. Tietjen, K.G.; Schaller, E.; Matern, U. Phytotoxins from *Alternaria carthami* Chowdhury: Structural identification and physiological significance. *Physiol. Plant Pathol.* 1983, 23, 387–400.

113. Cotty, P.J.; Misaghi, I.J. Zinniol production by *Alternaria* species. *Phytopathology* 1984, 74, 785–788.

114. Berestetskii, A.O.; Yuzikhin, O.S.; Katkova, A.S.; Dobrodumov, A.V.; Sivogrivov, D.E.; Kolombet, L.V. Isolation, Identification, and characteristics of the phytotoxin produced by the fungus *Alternaria cirsinoxia*. *Appl. Biochem. Microbiol.* 2010, 46, 75–79.

115. Barasch, I.; Mor, H.; Netzer, D.; Kashman, Y. Production of zinniol by *Alternaria dauci* and its phytotoxic effect on carrot. *Physiol. Plant Pathol.* 1981, 19, 7–16.

116. Gamboa-Angulo, M.M.; Escalante-Erosa, F.; Garcia-Sosa, K.; Alejos-Gonzalez, F.; Delgado-Lamas, G.; Pena-Rodriguez, L.M. Natural zinniol derivatives from *Alternaria tagetica*. Isolation, synthesis, and structure-activity correlation. *J. Agric. Food Chem.* 2002, 50, 1053–1058.

117. Gamboa-Angulo, M.M.; Alejos-Gonzalez, F.; Pena-Rodriguez, L.M. Homozinniol, a new phytotoxic metabolite from *Alternaria solani*. *J. Agric. Food Chem.* 1997, 45, 282–285.

118. Moreno-Escobar, J.; Puc-Carrillo, A.; Ceres-Farfan, M.C.A.; Pena-Rodriguez, L.M.; Gamboa-Angulo, M.M. Two new zinniol-related phytotoxins from *Alternaria solani*. *Nat. Prod. Res.* 2005, 19, 603–607.

119. Cotty, P.J.; Misaghi, I.; Hine, R. Production of zinniol by *Alternaria tagetica* and its phytotoxic effect on *Tagetes erecta*. *Phytopathology* 1983, 73, 1326–1328.
120. Starratt, A.N. Zinniol: a major metabolite of *Alternaria zinniae*. *Can. J. Chem.* 1968, 46, 767–770.

121. Gamboa-Angulo, M.M.; Alejos-Gonzalez, F.; Escalante-Erosa, F.; Garcia-Sosa, K.; Delgado-Lamas, G.; Pena-Rodriguez, L.M. Novel dimeric metabolites from *Alternaria tagetica*. *J. Nat. Prod.* 2000, 63, 1117–1120.

122. Kota, B.B.; Rosa, L.H.; Caligiore, R.B.; Rabello, A.L.T.; Alves, T.M.A.; Rosa, C.A.; Zani, C.L. Altenusin, a biphenyl isolated from the endophytic fungus *Alternaria* sp., inhibits trypanothione reductase from *Trypanosoma cruzi*. *FEMS Microbiol. Lett.* 2008, 285, 177–182.

123. Xu, X.; Zhao, S.; Wei, J.; Fang, N.; Yin, L.; Sun, J. Porric acid D from marine-derived fungus *Alternaria* sp. isolated from Bohai Sea. *Chem. Nat. Compd.* 2012, 47, 893–895.

124. Chadwick, D.J.; Easton, I.W.; Johnstone, R.A.W. Fungal metabolites. Part 9. Isolation and x-ray structure determination of alternarian acid from *Alternaria mali* Sp. *Tetrahedron* 1984, 40, 2451–2455.

125. Evidente, A.; Punzo, B.; Andolfi, A.; Berestetsk iy, A.; Motta, A. Alternethanoxins A and B, polycyclic ethanones produced by *Alternaria sonchi*, potential mycoherbicides for *Sonchus arvensis* biocontrol. *J. Agric. Food Chem.* 2009, 57, 6656–6660.

126. Robeson, D.J.; Strobel, G.A. αβ-Dehydrocurvularin and curvularin from *Alternaria cinerariae*. *Z. Naturforsch., C: J. Biosci.* 1981, 36C, 1081–1083.

127. Hyeon, S.-B.; Ozaki, A.; Suzuki, A.; Tamura, S. Isolation of αβ-dehydrocurvularin and β-hydroxycurvularin from *Alternaria tomato* as sporulation-suppressing factors. *Agric. Biol. Chem.* 1976, 40, 1663–1664.

128. Liu, Y.; Li, Z.; Vederas, J.C. Biosynthetic incorporation of advanced precursors into dehydrocurvularin, a polyketide phytotoxin from *Alternaria cinerariae*. *Tetrahedron* 1998, 54, 15937–15958.

129. Vurro, M.; Evidente, A.; Andolfì, A.; Zonno, M.C.; Giordano, F.; Motta, A. Brefeldin A and α,β-dehydrocurvularin, two phytotoxins from *Alternaria zinniae*, a biocontrol agent of *Xanthium occidentale*. *Plant Sci.* 1998, 138, 67–79.

130. Shi, J.; Zeng, Q.; Liu, Y.; Pan, Z. *Alternaria* sp. MG1, a resveratrol-producing fungus: isolation, identification, and optimal cultivation conditions for resveratrol production. *Appl. Microbiol. Biotechnol.* 2012, 95, 369–379.

131. Suemitsu, R.; Ohnishi, K.; Morikawa, Y.; Ideguchi, I.; Uno, H. Porritoxinol, a phytotoxin of *Alternaria porri*. *Phytochemistry* 1994, 35, 603–605.

132. Matsumoto, M.; Matsutani, S.; Shigeru, S.; Kenji, Y.; Hiroshi, H.; Hayashi, F.; Terui, Y.; Nakai, H.; Uotani, N.; Kawamura, Y. Depudecin: a novel compound inducing the flat phenotype of NIH3T3 cells doubly transformed by ras- and src- oncogene, produced by *Alternaria brassicicola*. *J. Antibiot.* 1992, 45, 879–885.

133. Sugiyama, N.; Kashima, C.; Yamamoto, M.; Mohri, R. Altenin, a new phytopathologically toxic metabolite from *Alternaria kikuchiana*. *Bull. Chem. Soc. Jpn.* 1965, 38, 2028.

134. Maekawa, N.; Nishimura, S.; Kohimoto, K.; Watanabe, Y. Isolation of the host-specific toxins produced by *Alternaria alternata*, Strawberry pathotype. *Ann. Phytopathol. Soc. Jpn.* 1979, 45, 536–537.
135. Hayashi, N.; Tanabe, K.; Tsuge, T.; Nishimura, S.; Kohmoto, K.; Otani, H. Determination of host-selective toxin production during spore germination of *Alternaria alternata* by high-performance liquid chromatography. *Phytopathology* **1990**, *80*, 1088–1091.

136. Abbas, H.K.; Tanaka, T.; Duke, S.O. Pathogenicity of *Alternaria alternata* and *Fusarium moniliforme* and phytotoxicity of AAL-toxin and fumonisin B1 on tomato cultivars. *J. Phytopathol.* **1995**, *143*, 329–334.

137. Yamagishi, D.; Akamatsu, H.; Otani, H.; Kodama, M. Pathological evaluation of host-specific AAL-toxins and fumonisin mycotoxins produced by *Alternaria* and *Fusarium* species. *J. Gen. Plant Pathol.* **2006**, *72*, 323–327.

138. Liu, J.Y.; Song, Y.C.; Zhang, Z.; Wang, L.; Guo, Z.J.; Zou, W.X.; Tan, R.X. *Aspergillus fumigatus* CY018, an endophytic fungus in *Cynodon dactylon* as a versatile producer of new and bioactive metabolites. *J. Biotechnol.* **2004**, *114*, 279–287.

139. Zhao, J.; Mou, Y.; Shan, T.; Li, Y.; Lu, S.; Zhou, L. Preparative separation of helvolic acid from the endophytic fungus *Pichia guilliermondii* Ppf9 by high-speed counter-current chromatography. *World J. Microbiol. Biotechnol.* **2012**, *28*, 835–840.

140. Van Rozendaal, E.L.M.; Kurstjens, S.J.L.; Van Beek, T.A.; Van Den Berg, R.G. Chemotaxonomy of *Taxus*. *Phytochemistry* **1999**, *52*, 427–433.

141. Brisdelli, F.; D’Andrea, G.; Bozzi, A. Resveratrol: a natural polyphenol with multiple chemopreventive properties (review). *Curr. Drug Metabol* **2009**, *10*, 530–546.

142. Zhou, L.G.; Wu, J.Y. Development and application of medicinal plant tissue cultures for production of drugs and herbal medicinals in China. *Nat. Prod. Rep.* **2006**, *23*, 789–810.

143. Dupont, S.; Lemetais, G.; Ferreira, T.; Cayot, P.; Gervais, P.; Beney, L. Ergosterol biosynthesis: a fungal pathway for life on land. *Evolution* **2012**, *66*, 2961–2968.

144. Robison, S.H.; Barr, D.B. Use of biomonitoring data to evaluate methyl eugenol exposure. *Environ. Health Persp.* **2006**, *114*, 1797–1801.

145. Valenzano, D.R.; Terzibasi, E.; Genade, T.; Cattaneo, A.; Domenici, L.; Cellerino, A. Resveratrol prolongs life span and retards the onset of age-related markers in a shortlived vertebrate. *Curr. Biol.* **2006**, *16*, 296–300.

146. Zhao, J.; Shan, T.; Mou, Y.; Zhou, L. Plant-derived bioactive compounds produced by endophytic fungi. *Mini-Rev. Med. Chem.* **2011**, *11*, 159–168.

147. Graniti, A. Phytotoxins and their involvement in plant diseases. *Experientia* **1991**, *47*, 751–755.

148. Pedras, M.S.C.; Biesenthal, C.J.; Zaharia I.L. Comparison of the phytotoxic activity of the phytotoxin destruxin B and four natural analogs. *Plant Sci.* **2000**, *156*, 185–192.

149. Howlett, B.J. Secondary metabolite toxins and nutrition of plant pathogenic fungi. *Curr. Opin. Plant Biol.* **2006**, *9*, 371–375.

150. Johnson, L.J.; Johnson, R.D.; Akamatsu, H.; Salamiah, A.; Otani, H.; Kohmoto, K.; Kodama, M. Spontaneous loss of a conditionally dispensable chromosome from the *Alternaria alternata* apple pathotype leads to loss of toxin production and pathogenicity. *Curr. Genet.* **2001**, *40*, 65–72.

151. Winter, C.K.; Gilchrist, D.G.; Dickman, M.B.; Jones, C. Chemistry and biological activity of AAL toxins. *Adv. Exp. Med. Biol.* **1996**, *392*, 307–316.
152. Brandwagt, B.F.; Mesbah, L.A.; Takken, F.L.W.; Laurent, P.L.; Kneppers, T.J.A.; Hille, J.; Nijkamp, HJ. A longevity assurance gene homolog of tomato mediates resistance to *Alternaria alternata* f.sp. *lycopersici* toxins and fumonisin B1. *Proc. Natl. Acad. Sci. USA* 2000, 97, 4961–4966.

153. Liu, B.-L.; Tzeng, Y.-M. Development and application of destruxins: a review. *Biotechnol. Adv.* 2012, 30, 1242–1254.

154. Pedras, M.S.C.; Yaya, E.E.; Glawischnig, E. The phytoalexins from cultivated and wild crucifers: chemistry and biology. *Nat. Prod. Rep.* 2011, 28, 1381–1405.

155. Pedras, M.S.C.; Zaharia, I.L.; Gai, Y.; Smith, K.C.; Ward, D.E. Metabolism of the host-selective toxins destruxin B and homodestruxin B: probing a plant disease resistance trait. *Org. Lett.* 1999, 1, 1655–1658.

156. Pedras, M.S.C.; Montaut, S.; Zaharia, I.L.; Gai, Y.; Ward, D.E. Transformation of the host-selective toxin destruxin B by wild crucifers: probing a detoxification pathway. *Phytochemistry* 2003, 64, 957–963.

157. Halloin, J.M.; De Zoeten, G.A.; Gaard, G.R.; Walker, J.C. Effects of tentoxin on chlorophyll synthesis and plastid structure in cucumber and cabbage. *Plant Physiol.* 1970, 45, 310–314.

158. Avni, A.; Anderson, J.D.; Hollan, N.; Rochaix, J.D.; Gromet-Elhanan, Z.; Edelman, M. Tentoxin sensitivity of chloroplasts determined by codon 83 of β subunit of proton ATPase. *Science* 1992, 257, 1245–1247.

159. Liu, Y.-X.; Xu, X.-M.; Dai, X.-B.; Qiang, S. *Alternaria alternata* crofton-weed toxin: a natural inhibitor of photosystem II in *Chlamydomonas reinhardtii* thylakoids. *J. Agric. Food Chem.* 2007, 55, 5180–5185.

160. Haraguchi, H.; Abo, T.; Fukuda, A.; Okamura, N.; Yagi, A. Mode of phytotoxic action of altersolanols. *Phytochemistry* 1996, 43, 989–992.

161. Robeson, D.J.; Strobel, G.A. Zinniol induces chlorophyll retention in barley leaves: The selective action of a non-specific phytotoxin. *Phytochemistry* 1984, 23, 1597–1599.

162. Qui, J.A.; Castro-Concha, L.A.; Garcia-Sosa, K.; Miranda-Ham, M.L.; Pena-Rodriguez, L.M. Is zinniol a true phytotoxin? Evaluation of its activity at the cellular level against *Tagetes erecta*. *J. Gen. Plant Pathol.* 2010, 76, 94–101.

163. Kenfield, D.; Bunkers, G.; Strobel, G.A.; Sugawara, F. Potential new herbicides—phytotoxins from plant pathogens. *Weed Technol.* 1988, 2, 519–524.

164. Abbas, H.K.; Duke, S.O. Phytotoxins from plant pathogens as potential herbicides. *Toxin Rev.* 1995, 14, 523–543.

165. Mallik, M.A.B. Selective isolation and screening of soil microorganisms for metabolites with herbicidal potential. *J. Crop Prot.* 2001, 4, 219–236.

166. Abbas, H.K.; Hamed, K.; Vesonder, R.F.; Boyette, C.D.; Peterson, S.W. Phytotoxicity of AAL-toxin and other compounds produced by *Alternaria alternata* to jimson weed (*Datura stramonium*). *Can. J. Bot.* 1993, 71, 155–160.

167. Ostry, V. *Alternaria* mycotoxins: an overview of chemical characterization, producers, toxicity, analysis and occurrence in foodstuffs. *World Mycotoxin J.* 2008, 1, 175–188.

168. Bensassi, F.; Gallerne, C.; Sharaf El Dein, O.; Hajlaoui, M.R.; Bacha, H.; Lemaire, C. Cell death induced by the *Alternaria* mycotoxin alternariol. *Toxicol. In Vitro* 2012, 26, 915–923.
169. Schreck, I.; Deigendesch, U.; Burkhardt, B.; Marko, D.; Weiss, C. The Alternaria mycotoxins alternariol and alternariol methyl ether induce cytochrome P450 1A1 and apoptosis in murine hepatoma cells dependent on the aryl hydrocarbon receptor. *Arch. Toxicol.* 2012, 86, 625–632.

170. Mizushina, Y.; Maeda, N.; Kuriyama, I.; Yoshida, H. Dehydroalternatusin is a specific inhibitor of mammalian DNA polymerase α. *Expert Opin. Inv. Drug.* 2011, 20, 1523–1534.

171. Huang, C.; Jin, H.; Song, B.; Zhu, X.; Zhao, H.; Cai, J.; Lu, Y.; Chen, B.; Lin, Y. The cytotoxicity and anticancer mechanisms of alterporriol L, a marine bianthraquinone, against MCF-7 human breast cancer cells. *Appl. Microbiol. Biotechnol.* 2012, 93, 777–785.

172. Bury, M.; Punzo, B.; Berestetskii, A.; Lallemand, B.; Dubois, J.; Lefranc, F.; Mathieu, V.; Andolfi, A.; Kiss, R.; Evidente, A. Evaluation of the anticancer activities of two fungal polycyclic ethanones, alternmethanoxins A and B, and two of their derivatives. *Int. J. Oncol.* 2011, 38, 227–232.

173. Moreno, M.A.P.; Alonso, I.G.; Martin de Santos, R.; Lacarra, T.G. The role of the genus Alternaria in mycotoxin production and human diseases. *Nutricion Hospitalaria* 2012, 27, 1772–1781.

174. Zajkowski, P.; Grabarkiewicz-Szcesna, J.; Schmidt, R. Toxicity of mycotoxins produced by four Alternaria species to Artemia salina larvae. *Mycotoxin Res.* 1991, 7, 11–15.

175. Panigrahi, S.; Dallin, S. Toxicity of the Alternaria spp metabolites, tenuazonic acid, alternariol, altertoxin-I, and alternariol monomethyl ether to brine shrimp (Artemia salina L.) larvae. *J. Sci. Food Agric.* 1994, 66, 493–496.

176. Berto, P.; Belingheri, L.; Dehorter, B. Production and purification of a novel extracellular lipase from Alternaria brassicicola. *Biotechnol. Lett.* 1997, 19, 533–536.

177. Isshiki, A.; Akimitsu, K.; Nishio, K.; Tsukamoto, M.; Yamamoto, H. Purification and characterization of an endopolygalacturonase from the rough lemon pathotype of Alternaria alternata, the cause of citrus brown spot disease. *Physiol. Mol. Plant Pathol.* 1997, 51, 155–167.

178. Kulye, M.; Liu, H.; Zhang, Y.L.; Zeng, H.M.; Yang, X.F.; Qiu, D.W. Hrip1, a novel protein elicitor from necrotrophic fungus, Alternaria tenuissima, elicits cell death, expression of defence-related genes and systemic acquired resistance in tobacco. *Plant Cell Environ.* 2012, 35, 2104–2120.

179. Saha, D.; Fetzner, R.; Burkhardt, B.; Podlech, J.; Metzler, M.; Dang, H.; Lawrence, C.; Fischer, R. Identification of a polyketide synthase required for alternariol (AOH) and alternariol-9-methyl ether (AME) formation in Alternaria alternata. *PLoS ONE* 2012, 7, e40456.

180. Shinya, T.; Menard, R.; Kozone, I.; Matsuoka, H.; Shibuya, N.; Kauffmann, S.; Matsuoka, K.; Saito, M. Novel beta-1,3-, 1,6-oligoglucan elicitor from Alternaria tenuissima. *World J. Microbiol. Biotechnol.* 2009, 25, 2035–2042.

181. Oikawa, H.; Yamawaki, D.; Kagawa, T.; Ichihara, A. Total synthesis of AAL-toxin TAv1. *Tetrahedron Lett.* 1999, 40, 6621–6625.

182. Bobylev, M.M.; Bobyleva, L.I.; Strobel, G.A. Synthesis and bioactivity of analogs of maculosin, a host-specific phytotoxin produced by Alternaria alternata on spotted knapweed (Centaurea maculosa). *J. Agric. Food Chem.* 1996, 44, 3960–3964.
184. Lee, S.; Aoyagi, H.; Shimohigashi, Y.; Izumiya, N.; Ueno, T.; Fukami, H. Syntheses of cyclotretradepsipeptides, AM-toxin I and its analogs. *Tetrahedron Lett.* **1976**, *17*, 843–846.
185. Koch, K.; Podlech, J.; Pfeiffer, E.; Metzler, M. Total synthesis of alternariol. *J. Org. Chem.* **2005**, *70*, 3275–3276.
186. Altemoller, M.; Podlech, J.; Fenske, D. Total synthesis of altenuene and isoaltenuene. *Eur. J. Org. Chem.* **2006**, *2006*, 1678–1684.
187. Altenoeller, M.; Podlech, J. Total synthesis of neoaltenuene. *Eur. J. Org. Chem.* **2009**, *2009*, 2275–2282.
188. Geiseler, O.; Mueller, M.; Podlech, J. Synthesis of the altertoxin III framework. *Tetrahedron* **2013**, *69*, 3683–3689.
189. Martin, J.A.; Vogel, E. The synthesis of zinniol. *Tetrahedron* **1980**, *36*, 791–794.
190. Cudaj, J.; Podlech, J. Total synthesis of altenusin and alterlactone. *Synlett* **2012**, *23*, 371–374.
191. Beresteskiy, A.O. A review of fungal phytotoxins: from basic studies to practical use. *Appl. Biochem. Microbiol.* **2008**, *44*, 453–465.

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