Non-Volatile Metabolites from *Trichoderma* spp.

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Abstract: The genus *Trichoderma* is comprised of many common fungi species that are distributed worldwide across many ecosystems. *Trichoderma* species are well-known producers of secondary metabolites with a variety of biological activities. Their potential use as biocontrol agents has been known for many years. Several reviews about metabolites from *Trichoderma* have been published. These reviews are based on their structural type, biological activity, or fungal origin. In this review, we summarize the secondary metabolites per *Trichoderma* species and elaborate on approximately 390 non-volatile compounds from 20 known species and various unidentified species.

Keywords: bioactivity; metabolites; *Trichoderma*

1. Introduction

*Trichoderma* is a genus of fungi of the family Hypocreaceae. It is distributed in soils worldwide across various habitats [1]. *Trichoderma* is a valuable resource for structurally novel natural products with diverse bioactivities [2]. Among well-studied fungi, *Trichoderma* species are known for their ability to produce bioactive secondary metabolites, including polyketides, alkaloids, terpenoids, and peptaibols [3]. Many species have been extensively investigated due to their application as biological control agents [4]. In this article, we reviewed the origin, structure, and bioactivity of non-volatile secondary metabolites from *Trichoderma* spp. and grouped them per species.

2. Results

2.1. Metabolites from *Trichoderma arundinaceum*

A series of peptaibols were isolated from the scaled-up fermentation of *T. arundinaceum* MSX70741: three new compounds [prealamethicin F50 (1); Glu(OMe)18-alamethicin F50 (2); and trichobrevin BIII-D (3)], and four known compounds [alamethicin F50 (4); atroviridin J (6); and trichobranchin D-I (7)]. The cytotoxic activity of compounds 2, 3, 4, and 6 were evaluated against a panel of cancer cell lines: HCT 116, DLD-1, HT-29, SW948, Hep-G2, Huh-7, and HeLa. Compound 2 was the most active compound with IC\textsubscript{50} values ranging from 2.5 through 6.5 mM. Compound 3 exhibited moderate activity against HCT 116 and HT-29, with IC\textsubscript{50} values of 6.8 and 6.7 mM, respectively [3].

2.2. Metabolites from *Trichoderma asperellum*

Nine compounds were isolated from the fungus *T. asperellum*: trichodermaerin (8) [5]; 6-amyl alpha-pyrone (9) [6]; aspereline G (10); aspereline H (11); aspereline A (12); aspereline C (13); aspereline D (14); aspereline E (15); and aspereline F (16) [7]. Among them, compounds 10 and 11 were two new peptaibols.
Eight new compounds were isolated from the marine-derived fungus *T. asperellum* cf.44-2: bisabolane sesquiterpene bisabolan-1,10,11-triol (17); norbisabolane sesquiterpene 12-nor-11-acetoxybisabolen-3,6,7-triol (18); two naturally occurring monoterpenes ([7S]-1-hydroxy-3-p-methylen-9-oic acid (19) and (7R)-1-hydroxy-3-p-methylen-9-oic acid (20)); trichodenone dechlorotrichodenone C (21); chlorine-containing trichodenone 3-hydroxytrichodenone C (22); diketopiperazine methylcordysinin A (23); and oxazole derivative 4-oxazolopropanoic acid (24). Compounds 17, 18, 21 and 22 were evaluated for the inhibition of four marine phytoplankton species (*Chattonella marina, Heterosigma akashiwo, Karlodinium veneficum*, and *Prorocentrum donghaiense*) and four marine-derived pathogenic bacteria (*Vibrio parahaemolyticus, V. anguillarum, V. harveyi*, and *V. splendidus*). All exhibited growth inhibition of the four phytoplankton species, and compound 18, with IC₅₀ values ranging from 4.2 to 8.5 µg/mL, was more active than the others. Additionally, compounds 17, 18, 21 and 22 showed weak antibacterial activities against the four *Vibrio* species, with inhibitory zone diameters of 6.2–8.5 mm at 20 µg/disk. Among them, compound 18 had the highest antibacterial activity [8].

From the cultures of *T. asperellum* dl-34, eighteen compounds were identified: a new diterpenoid, wickerol A (25); a known diterpenoid, harziandione (26); ten known steroids [ergosterol endoperoxide (27); 5α,8α-epidioxyergosta-6,9(11),22-trien-3β-ol (28); 5β,5α,6β-trihydroxyergosta-7,22-diene (29); 3β,5α-di-hydroxy-6β-methoxyergosta-7,22-diene (30); 3β,5α,9α-trihydroxyergosta-7,22-dien-6-one (31); (22E,24R)-ergosta-4,6,8(14),22-tetraen-3-one (32); (22E,24R)-5α,6α-epoxyergosta-8,22-diene-3β,7α-diol (33); ergosta-7,22-dien-3β-ol (34); (22E,24R)-ergosta-5,7,22-trien-3β-ol (35); and 3β-sitosterol (36)]; two diketopiperazines, [(L)-Pro-(L)-Leu (37) and (L)-4-OH-Pro-(L)-Leu (38); one nucleotide, adenine nucleoside (39); and three polyketides, [cis-4-hydroxy-6-deoxyscytalone (40); 2,4-dihydroxy-3,6-dimethylbenzaldehyde (41); and dihydrocitrinone (42)]. Most of these compounds were screened for biological activities, only compounds 25 and 26 were toxic to *Artemia salina*, with LC₅₀ values of 12.0 and 38.2 µg/mL, respectively [9].

### 2.3. Metabolites from Trichoderma atroviride

Eleven compounds were obtained from the marine-derived fungus *T. atroviride*: three novel compounds [3-amino-5-hydroxy-5-vinyl-2-cyclopenten-1-one dimer atrichodermone A (43); cyclopentenone derivative atrichodermone B (44), and sesquiterpene atrichodermone C (45) [10]] and eight known compounds [atrichodermone D (46); trichodermone A (47); (5R)-5-hydroxy-3-[(methoxy carbonyl)-amino]-5-vinyl-2-cyclopenten-1-one (48); 4H-1,3-dioxin-4-one-2,3,6-trimethyl (49); 1,3-dione-5,5-dimethylcyclohexane (50); 2-enone-3-hydroxy-5,5-dimethylcyclohex (51) [11]; 6-pentylpyran-2-one (52); and 6-pent-1-enyl-pyran-2-one (53) [1]]. Among these, compounds 43–45 were evaluated for their cytotoxicity against HL60 and U937 cell lines, as well as anti-inflammatory effect against the production of the pro-inflammatory cytokines TNF-α and IL-1β; but none showed notable cytotoxicity or anti-inflammatory activity. Compound 49 significantly inhibited the growth of *Helicobacter pylori* and Shigella toxin-producing *Escherichia coli*, and it also induced cell death and cytotoxicity.

Five new compounds were isolated from the marine-derived fungus *T. atroviride* G20-12: 2-hydroxybutan-3-yl5′-(2′″-hydroxy-N’-2′″-oxobutan-3′″-yl)propanamido)butanoate (54); 3-hydroxy-5-(4-hydroxybenzyl)dihydrofuran-2(3H)-one (55) [12]; 4′-(4,5-dimethyl-1,3-dioxolan-2-yl)methyl-phenol (56); 3′-hydroxybutan-2′-yl)5-oxopyrrolidine-2-carboxylate (57) and atroviridetide (58) [13].

Eight compounds were isolated from the solid culture of endophytic fungus *T. atroviride* S361: a pair of novel N-furanone amide enantiomers [(+)trichodermadione A (59a) and (+)-trichodermadione A (59b)]; a new cyclohexenone sesquiterpene, trichodermadione B (60); and six known compounds [4′-(2-formyl-5-(methoxymethyl)-1H-pyrrol-1-yl)butanoic acid (61); 5-methoxymethyl-1H-pyrrole-2-carbaalde-hyde (62); 3′-(1-carbaalde)-6-methyl-2H-pyran-2,4(3H)-dione (63); lignoren (64); ascortic acid (65); and cateniolbin C (66). Compounds 59 and 60 were also evaluated for their cytotoxicity against DU145 and PC3 cell lines, as well as inhibitory effects against the production of NO in
lipopolysaccharide (LPS)-stimulated RAW264.7 cells. However, none of them showed notable cytotoxicity or anti-inflammatory activity [14].

The compound 6-pentyl-α-pyrone (67), which was isolated from T. atroviride UST1 and UST2, it was involved in Trichoderma-pathogen interactions on grapevine pruning wounds [15].

2.4. Metabolites from Trichoderma aureoviride

A new compound, koninginin G (68), and a known compound, Koninginin G triacetate (69), were obtained from a strain of T. aureoviride. Compound 68 significantly inhibited the growth of etiolated wheat coleoptiles by 56% at 10−3 M concentration [16].

2.5. Metabolites from Trichoderma brevicompactum

The bioactive compound trichodermin (70) was isolated from the endophytic fungus T. brevicompactum. It displayed significant inhibitory activity on Rhizoctonia solani and Botrytis cinerea, with an EC50 of 0.25 µg/mL and 2.02 µg/mL, respectively. However, a relatively poor inhibitory effect was shown against Colletotrichum lindemuthianum (EC50 = 25.60 µg/mL) [17].

2.6. Metabolites from Trichoderma citrinoviride

Fifteen compounds were isolated from the T. citrinoviride: four new compounds [(R)-vertinolide (71) [1]; trichoderol C (72); citrinoviric acid (73); and penicillenol D (74)] and twelve known compounds [lignoren (64); trichotetronine (75); bisvertinol (76); spirosorbidillinol A (77); spirosorbidillinol B (78); spirosorbidillolin C (79); trichoderol A (80); penicillenol B1 (81); penicillenol B2 (82); cyclo-(Leu-Pro) (83); cyclo-(Ile-Pro) (84); and cyclo-(Phe-Pro) (85)] [18]. Among them, compounds 73 and 74 showed moderate cytotoxic effects against the A-375 cell line, with IC50 values of 85.7 and 32.6 µM, respectively.

From T. citrinoviride cf-27, twenty-two metabolites were obtained: a new diterpene, trichocitrin (86), and twenty-one known compounds [ergosterol endoperoxide (27); (22E,24R)-ergosta-4,6,8,14,22-tetraen-3-one (32); (22E,24R)-ergosta-5,7,22-trien-3β-ol (35); 24-methylene cycloartanol (87); cycloecalenol (88); citrostadienol (89); euphorbol (90); 24-methylene-lanost-8-en-3β-ol (91); cyclonerodiol (92); (22E,24R)-7β,8β-epoxy-3β,5α,9α-tri hydroxyergosta-22-en-6-one (93); nafuredin (94); harzianolide (95); 5-hydroxy-2,3-dimethyl-7-methoxychromone (96); 5-hydroxy-3-hydroxymethyl-2-methyl-7-methoxychromone (97); methyl 8-hydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate (98); methyl 2,8-dihydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate (99); stachyline B (100); trans-3,4-dihydro-2,4,8-trihydroxynaphthalene-1(2H)-one (101); pyrazole-3-carboxylic acid (102); pyrrole-2-carboxylic acid (103); and dibutyl phthalate (104)]. Most of the isolated compounds were screened for biological activities, and the results showed that compounds 86 and 94 exhibited 54.1% and 36.7% inhibition, respectively, of P. donghaiense at 100 µg/mL [9].

2.7. Metabolites from Trichoderma cremenum

A new 10-member lactone, cremenolide (105), was isolated from T. cremenum. In vitro tests showed that cremenolide inhibited the radial mycelium growth of Fusarium oxysporum, B. cinerea, and R. solani, and it significantly promoted tomato seedling growth [19].

2.8. Metabolites from Trichoderma gamsii

Two new cytochalasans, trichoderones A (106) and B (107), and three known analogues, aspochalasins D (108), J (109), and I (110), were isolated from the endophytic fungus T. gamsii. Compound 106 possesses an unprecedented 7/6/6/5/5 pentacyclic system, whereas compound 107 contains the rare 6/5/6/6/5 pentacyclic skeleton with a 12-oxatricyclo [6.3.1.02,7] moiety. Compounds 108 and 109 displayed cytotoxic activity against the HeLa cell line [20].
2.9. Metabolites from Trichoderma harzianum

Fourteen compounds were identified from the cultures of *T. harzianum* R5: ergosterol endoperoxide (27); 5α,8α-epidioxyergosta-6,9(11),22-trien-3β-ol (28); 3β,5α,6β-trihydroxyergosta-7,22-diene (29); adenine nucleoside (39); trichoharzianolide (111); 3β-hydroxyergosta-8,24(28)-diene-7-one (112); (22E,24R)-24-methylcholaeta-5,22-dien-3β-ol (113); 5,7-dihydroxy-2,3-dimethylchromone (114); (22E,24R)-3β,5α-dihydroxy-ergosta-7,22-dien-6-one (115); 5-hydroxy-2-hydroxymethyl-3-methyl-7-methoxychromone (116); indole-3-carboxaldehyde (117); 3-indol acetic acid (118); 2,4-dimethylbenzene-1,3,5-triol (119); and 5′-o-acetyltarcal nucleoside (120). Compound 111 was a new terpenoid that showed significant lethal activity against *A. saline*, and the LC50 value was 68.6 μg/mL [9].

Five terpenoids [cyclonerodiol (92); wickerol B (121); 15-hydroxyacorenone (115,45,55)-8-hydroxyethyl-1-isopropyl-4-methyl spiro[4.5]dec-8-en-7-one (122); epicycloneodiol oxide (123); and cycloneodiol oxide (124)], one lactone [5,6-dihydro-4-methyl-2*H*-pyran-2-one (125)], and one steroid [demethylincisterol A3 (126)] from *T. harzianum* R5-1 were studied. Three bacterial strains (*V. splendidus*, *V. anguillarum* and *B. cinerea*) were tested for resistance to these compounds. Compounds 92, 121, 122, 123, and 124 showed an inhibitory effect on *V. anguillarum* [21].

Six compounds were isolated from *T. harzianum* T-4: β-sitosterol (36); palmitic acid (127); 1,8-dihydroxy-3-methylanthraquinone (128); 6-pentyl-2*H*-pyran-2-one (129); 2(5H)-furanone (130); and stigmasterol (131). While seven were isolated from *T. harzianum* strain T-5: palmitic acid (127); 6-pentyl-2*H*-pyran-2-one (129); 1-hydroxy-3-methylanthraquinone (132); 8-decanolactone (133); ergosterol (134); harzianopyridone (135); and 6-methyl-1,3,8-trihydroxyanthraquinone (136). These compounds were screened for antifungal activity; compound 135 was the most active, with an EC50 of 35.9-50.2 mg/mL [22].

Harzianolide (95); 1,8-dihydroxy-3-methylenanthraquinone (128); 1-hydroxy-3-methylenanthraquinone (132); harzianopyridone (135); T22azaphilone (137); and T39butenolide (138) were obtained from the broth of *T. harzianum* T22 and *T. harzianum* T39. In antifungal assays, compounds 135 and 137 inhibited the growth of *Leptosphaeria maculans*, *Phytophthora cinnamomi*, and *B. cinerea* even at low doses (1–10 μg per plug), while high concentrations of compounds 95 and 138 were needed (>100 μg per plug) for inhibition [23].

Six compounds were isolated from *T. harzianum* dl-36: 5α,8α-epidioxyergosta-6,9(11),22-trien-3β-ol (28); 3β,5α,9α-trihydroxyergosta-7,22-dien-6-one (31); (22E,24R)-ergosta-5,7,22-trien-3β-ol (35); harzianolide (95); (22E,24R)-5α,8β-epidioxyergosta-6,22-dien-3-β-ol (139); and ergosta-7,22-dien-3β,5α,6β-triol (140) [24].

Thirty-two compounds were obtained from *T. harzianum*: 6-pentyl-pyran-2-one (52); trichodermin (70) [25,26]; cyclonerodiol (92); harzianic acid (141) [27]; 15-hydroxyacorenone (142) [28]; 2460A (143) [29]; trichokindins I–VII (144–150) [30]; trichorozins I–IV (151–154) [31]; octaketide keto diol (155) [32]; oxidized analog (156) [1]; 2-phenylethanol (157); tyrosol (158); 6-n-pentyl-●pyrone (159) [33]; cyclo-(R-Pro-Gly) (160); cyclo-(R-Pro-R-Ala) (161); cyclo-(S-Pro-R-Ala) (162); cyclo-(4-methyl-R-Pro-S-Nva) (163); cyclo-(R-Pro-R-Leu) (164); cyclo-(R-Pro-R-Phe) (165); cyclo-(4-hydroxy-S-Pro-S-Leu) (166); uraci (167); p-hydroxylphenylethanol (168); and m-hydroxylphenylactic acid (169) [34]. Compound 70 exhibited antifungal activity against the mycelial growth of *F. oxysporum*, *C. lindemuthianum*, *C. gloeosporoides*, *Thanatephorus cucumeris*, *R. solani*, *B. cinerea*, and *Cochliobolus miyabeanus*. It also prevented the spore germination of pathogenic fungi *T. cucumeris* and *R. solani*. Compound 141 showed antibiotic activity against *Pythium irregulare*, *Sclerotinia sclerotiorum*, and *R. solani* and a plant-growth-enhancing effect was observed at low concentrations. The anti-tumor activities of the new compound 143 was demonstrated on CM126 and HT-29 cell lines, with an IC50 of 2.17 × 10⁻⁵ mol/L and 1.8 × 10⁻⁵ mol/L respectively; and the compound somewhat affected the HT-29 cell cycle at S phase. Seven new peptaibols, compounds 144–150, induced Ca²⁺-dependent catecholamine secretion from bovine adrenal medullary cells. Compound 159 showed antifungal and antibacterial activity and completely inhibited the growth of fungus *Armillaria mellea* at a concentration of 200 ppm. Compounds 160–169 were isolated from *T. harzianum* for the first time.
In addition, compound 6-pentyl-α-pyrone (67) was also found from T. harzianum T77 and SQR-T037. It is used for the control of grapevine trunk diseases [15], and it effectively controlled F. oxysporum and may control Fusarium wilt in cucumber, in continuously cropped soil [35].

2.10. Metabolites from Trichoderma koningii

An unstable antifungal compound, 3-dimethylamino-5-hydroxy-5-vinyl-2-cyclopenten-1-one (170), which was a new cyclopentenone derivative, was obtained from the marine-derived fungus T. koningii [36]. From another marine fungus T. koningii, five new polyketide derivatives, 7-O-methylkoninginin D (171) and trichodermaketones A–D (172–175), together with four known compounds, konginginin A (176); konginginin D (177); konginginin E (178); and konginginin F (179), were identified [36]. Compound 172 showed synergistic antifungal activity against Candida albicans with 0.05 µg/mL ketoconazole [37].

Four compounds were isolated from T. koningii T-8: palmitic acid (127); 8-decanolactone (133); 6-pentyl-α-pyrone (180); and 6-(4-oxopentyl)-2H-pyran-2-one (181). Two compounds, stigmasterol (131) and 6-pentyl-α-pyrone (180), were obtained from T. koningii T-11. These compounds were evaluated for antifungal activity against soilborne pathogenic fungi R. solani, Sclerotium rolfsii, Macrophomina phaseolina, and F. oxysporum. Compounds 180 and 181 exhibited excellent antifungal activity against S. rolfsii [38].

Fourteen metabolites were derived from T. koningii: which included a new sesquiterpene alcohol, tricho-acorenone (182) [39], and thirteen other compounds: cyclonerodiol (92); uracil (167); methyl benzoate (183); cyclo-(L-Pro-L-Leu) (184); 4-hydroxyphenethylalcohol (185); ceramide (186); and trichokonins-V, VI, II, III, Ia, Ib, and IX (187–193) [40,41].

2.11. Metabolites from Trichoderma koningiopsis

Four konginginin compounds were characterized from T. koningiopsis [1]: trikoningin KAV (194); 11-residue lipopeptabols (195); trikoningin KB I (196); and trikoningin KB II (197).

Five polyketides were isolated from T. koningiopsis YIM PH30002. Their structures were elucidated as konginginin A (198); konginginin B (199); konginginin D (200); konginginin F (201); and konginginin M (202) [42]. Among them, compounds 198–201 showed siderophoric activity. Compound 199 presented higher activity with a maximum tolerable concentration of 300 µg/mL, in the iron (Fe III) acquisition tests. Compounds 198–202 exhibited weak antimicrobial activity against Acinetobacter baumannii, Staphylococcus aureus, F. oxysporum, F. solani and Alternaria panax.

Twenty-four compounds were identified from T. koningiopsis Y10-2 [43]: wickerol A (25); harziandione (26); cyclonerodiol (92); wickerol B (121); epicyclerodiol oxide (123); cycloneodiol oxide (124); konginginin A (176); konginginin D (177); 3-acetyl-6-methyl-2H-pyran-2,4(3H)-dione (203); lutildecarboxylic acid (204); cyclonertriol (205); 2-hydroxypipelopterol (206); verrucosidin (207); neoechinulin A (208); isoecchinulin A (209); echinuline (210); cyclo-trans-4-OH-(D)-Pro-(D)-Phe (211); fructigenine A (212); 3-O-methylviridicatin (213); cyclopelen (214); olemolide (215); ethyl 4-hydroxyphenylacetate (216); 4-hydroxyphenylethanol (217); and m-methoxyphenol (218). A preliminary evaluation on antibacterial and antimicrobial activities, as well as brine shrimp lethality of some compounds were carried out. The results showed that compound 214 displayed excellent activity against Pseudoalteromonas citrea, V. parahaemolyticus, V. splendidus, V. anguillarum, and V. harveyi, with IC50 values ranging from 8 to 32 µg/mL. Compounds 209, 210, and 212 showed potent inhibitory activity against C. marina, P. donghaiense, H. akashiwo, and K. veneficum, with IC50 values ranging from 0.040 to 12 µg/mL.

2.12. Metabolites from Trichoderma lignorum

Lignoren (64), a new sesquiterpenoid, was first isolated from T. lignorum HKI 0257. It showed moderate antimicrobial activity against Bacillus subtilis ATCC 6633, Mycobacterium smegmatis SG 987, and Pseudomonas aeruginosa K 599/WT [44].
2.13. Metabolites from Trichoderma longibrachiatum

Eight known compounds were identified from the marine-derived endophytic *T. longibrachiatum*: β-sitosterol (36); ergosterol (134) [33]; sorbicillin (219); ergosterol peroxide (220); 2-anhydromevalonic acid (222); squalene (223) [45]; and ergokonin A (224) [46]. Biological activity indicated that compound 219 exhibited moderate activity against *Bacillus brevis*, *B. subtilis*, *Sarcina lutea*, and *Enterobacter dissolvens*. Compound 224 exhibited activity against *Candida* and *Aspergillus* species but was inactive against *Cryptococcus* species; and it induced alterations in the hyphal morphology of *Aspergillus fumigatus*.

Two new tetronic acid derivatives were isolated from *T. longibrachiatum* Rifai aggr, 5-hydroxyvertinolide (225) and bislongiquinolide (226), which were antagonistic to the fungus *Mvcena citricolor* [47].

A new sesquiterpene, 10,11-dihydrocyclonerotriol (227), together with two known compounds, catenioblin C (66) and sohirnone A (228), were identified from the endophytic fungus *T. longibrachiatum* YM311505. Compounds 66, 227 and 228 exhibited antifungal activities against *Pyricularia oryzae* and *C. albicans* [48].

Two compounds, trichokonins A (229) and B (230), were obtained from *T. longibrachiatum* SMF2. Compound 229 exhibited a variety of biological activities: antimicrobial, antiviral, anti-tumor, and inducing plant resistance [49].

2.14. Metabolites from Trichoderma polysporum

A new minor metabolite valinotricin (231) was reported from *T. polysporum*, along with cyclonerodiol oxide (232) and epi-cyclonerodiol oxide (233) [50]. From another strain of *T. polysporum*, two antibiotic peptides, trichosporin Bs (234) [51] and trichosporin B-V (235) [52], were obtained.

2.15. Metabolites from Trichoderma reesei

Six compounds were isolated from the marine fungus *T. reesei*: cyclonerodiol (92); 8,9-dihydroxy-megastigmatrienone (236); harzialactone A (237); 3,6-dibenzylpiperazine-2,5-dione (238); 3-isobutyl-8-hydroxyl-pyrrolopiperazine-2,5-dione (239); and 3-benzyl-8-hydroxyl-pyrrolopiperazine-2,5-dione (240) [53].

2.16. Metabolites from Trichoderma saturnisporum

Fourteen compounds were isolated from *T. saturnisporum*: bislongiquinolide (226), cerebroside A (241); cerebroside D (242); sorbicillin A (243); sorbicillin B (244); bisvertinolone (245) [54]; and new sorbicillinoid-based saturnispols A–H (246–253) [55]. Among these, compounds 226, 241, 242, and 245 showed the potential for antibacterial activity. Compound 251 exerted significant inhibition against a panel of bacteria strains, including vancomycin-resistant enterococci (VRE), with MIC ranging from 1.63 to 12.9 µg/mL, while compound 253 showed selective effects against VRE and *B. subtilis*.

2.17. Metabolites from Trichoderma spirale

Two compounds were isolated from the endophytic fungus *T. spirale* A17: tyrosol (158) and trichodemic acid (254). Compound 254 showed significant inhibitory activity against tumor cells SF-268, MCF-7, and NCI-H460, while compound 158 displayed weak hyperplasia inhibition activity against tumor cells [56].

2.18. Metabolites from Trichoderma virens

Four toxins were isolated from *T. virens* ITC-4777: gliotoxin (255); dimethyl gliotoxin (256); viridin (257); and viridiol (258). Compound 255 was active against *Rhizoctonia bataticola* (with ED50 0.03 µg/mL), *M. phaseolina* (with ED50 1.76 µg/mL), *Pythium debaryanum* (with ED50 29.38 µg/mL),
Pythium aphanidermatum (with ED\textsubscript{50} 12.02 µg/mL), S. rolfsii (with ED\textsubscript{50} 2.11 µg/mL), and R. solani (with ED\textsubscript{50} 3.18 µg/mL) [57].

Twenty-three compounds were identified from T. viridescens Y13-3: fourteen new compounds [trichorenins A–C (259–261); trichocarotins A–H (262–269); trichocadinin A (270); (3S,6R)-6-(para-hydroxybenzyl)-1,4-dimethyl-3,6-bis(methylthio)piperazine-2,5-dione (271); and dehydroxymethylbis (dethio)bis(methylthio)gliotoxin (272)] and nine known compounds [demethylincisterol A3 (126); CAF-603 (273); 14-hydroxy CAF-603 (274); 7-β-hydroxy CAF-603 (275); trichocaraneA (276); 3[4′-hydroxyxyphenyl]methyl]-1,4-dimethyl-3,6-bis(methylthio)piperazine-2,5-dione (277); bis(dethio)bis (methylthio)gliotoxin (278); bisdethiobis(methylthio)-dehydrogliotoxin (279); and chromosome (280)] [43]. Bioassays showed that compound 280 could remarkably inhibit Pseudoalteraria citrea with an IC\textsubscript{50} value of 8 µg/mL; and compounds 270 and 276 showed potential brine shrimp lethality, with IC\textsubscript{50} values of 17 and 21 µg/mL, respectively. In the experiment on growth inhibition of microalgaes, compounds 259–261 had significant inhibitory effects on C. marina and K. veneficum, with IC\textsubscript{50} values ranging from 0.41 to 1.0 µg/mL. Compounds 264, 265, 266, 269 and 276 showed potent inhibitory activity against C. marina, P. donghaiense, H. akashiwo, and K. veneficum, with IC\textsubscript{50} values ranging from 0.24 to 12 µg/mL.

2.19. Metabolites from Trichoderma viride

T. viride is widely used as a fungal antagonist. Twenty-eight compounds have been reported from T. viride: seventeen new antibiotic peptaibols [trichodecenins (281); trichorovins (282); trichocellins (283) [58]; and trichorovins I–XIV (284–297) [59]]; one new pyranone derivative, trichopyrone (298); and ten known compounds [bisvertinol (76); bislongiquinolide (226); trichodermanones A–D (299–302); rezishanone (303); vertinolide (304); trichodimerol (305); and 2-furancarboxylic acid (306)] [60].

2.20. Metabolites from Trichoderma viridescens

Two bioactive compounds were elucidated from T. viridescens TS0404: 6-pentyl-2H-pyran-2-one (129) and α-phenylcinnamic acid (307). Compound 129 had significant inhibitory activity against hyphal growth of Phytophthora capsici, Phytophthora melonis, R. solani, and F. oxysporum (with EC\textsubscript{50} 115.26, 99.58, 126.46, and 315.75 µg/mL, respectively). The inhibitory effect on P. melonis was the best among them, and hyphal growth was completely inhibited when its concentration reached 300 µg/mL. Similarly, compound 129 had a conspicuous inhibitory effect on the zoosporangial germination of P. capsici and P. melonis, but the inhibitory effect on P. melonis was the most profound; and zoosporangial germination of P. melonis was completely inhibited at 400 µg/mL. In addition, compound 129 had a significant inhibitory effect on the conidial germination of F. oxysporum (with EC\textsubscript{50} 151.81 µg/mL) and sclerotial germination of R. solani with complete inhibitory concentration 300 µg/mL [61].

2.21. Metabolites from Trichoderma spp.

A novel cyclopentenone, trichoderone (308), and a known compound, cholesta-7,22-diene-3β,5α,6β-triol (309), were identified from a marine Trichoderma sp. Compound 308 displayed potent cytotoxicity against A549, NCI-H460, MCF-7, MDA-MB-435s, HeLa-229, DU-145, and HLF. Compounds 308 and 309 also exhibited bioactivity against HIV protease and Taq DNA polymerase [62]. Four compounds were elucidated from mycelia of Trichoderma sp.: cyclonerodiol (92); 5α,8α-epidioxygosta-6,22-dien-3β-ol (310); 1-monooelen (311); and methyl elaidate (312). Compound 92 showed weak nematicidal activity against Panagrellus redivivus, with 35.6% mortality at 800 mg/L in 72 h, and antimicrobial activity against Pseudomonas syringae, with an inhibition zone of 1.2 cm at 1 mg/disc [63]. One new compound, trichoderol A (313), was isolated from Trichoderma sp. cultures. Compound 313 was evaluated for antibacterial activity against Pseudomonas putida, Nocardioids brasiliensis, and Kocuria rhizophila. The results showed compound 313 had antibacterial activity against the three pathogenic bacteria, with a MIC value of 5 µmol/L [64].
Two compounds were obtained from *Trichoderma* sp.: 6-pentyl-2H-pyran-2-one (129) and harzianic acid (141). Compounds 129 and 141 showed potential to improve plant growth and protect plant health [65].

Nine compounds were isolated from a sponge-derived *Trichoderma* sp. SCsIO41004: three new polyketides, [trichbenzoisochromen A (314), 5,7-dihydroxy-3-methyl-2-(2-oxopropyl)naphthalene-1,4-dione (315); and 7-acetyl-1,3,6-trihydroxyanthracene-9,10-dione (316)], and six known compounds [ZSU-H85 A (317); 1,3,6-trihydroxy-8-methylanthraquinone (318); 2,5-dimethyl-7-hydroxy-chromone (319); 7-hydroxy-2-(2’5-hydroxypropyl)-5-methylchromone (320); cyclonerotriol (321); and adenosine (322)] [66]. Compound 317 exhibited significant inhibitory activity against EV71 with an IC$_{50}$ value of 25.7 µM.

Seventeen compounds were obtained from the endophytic fungus *Trichoderma* sp. 307 [64]: two new sesquiterpenes, microsphaeropsisins B (323) and C (324); two new de-o-methylasiddiolipdsins, (3R,7R)-7-hydroxy-de-o-methylasiddiolipdin (325) and (3R)-5-oxo-de-o-methylasiddiolipdin (326); one new metabolite, (3R)-7-oxo-de-o-methylasiddiolipdin (327); and twelve known compounds [microsphaeropsisins (328), (3R)-5-oxolasiapldiolopin (329); (3S)-6-oxo-de-o-methylasiddiolipdin (330); (3R)-de-o-methylasiddiolipdin (331); (3R,4R)-4-hydroxy-de-o-methylasiddiolipdin (332); (3R,5R)-5-hydroxy-de-o-methylasiddiolipdin (333); (3R,6R)-6-hydroxy-de-o-methylasiddiolipdin (334); (3R-lasiapldiolipdin (335); (3S)-ozoroalide (336); (3S,5R)-5-hydroxylasiddiolipdin (337); (E)-9-ethenolasiapldiolipdin (338); and (3R)-nordinone (339)]. The isolated compounds were tested for their α-glucosidase inhibitory activity and cytotoxicity. Only compounds 325 and 326 exhibited potent α-glucosidase inhibitory activity with IC$_{50}$ values of 25.8 and 54.6 µM, respectively [67].

An active antifungal compound, 2,5-cyclohexadiene-1,4-dione-2,6-bis(1,1-dimethylethyl) (340), was reported from *Trichoderma* sp. T-33 [68].

Three compounds were separated from *Trichoderma* sp. KK19L1: 5-hydroxy-3-hydroxymethyl-2-methyl-7-methoxychromone (97); (E)-3-acetylbenzylbut-2-enoate (341); and 1-hydroxy-6-methyl-9,10-anthraquinione (342)]. Compound 341 was a new compound [69].

Six compounds were isolated from *Trichoderma* sp. 09: methyl hexadecanoate (343); N-2'-hydroxy-3'E-octadecenoyl-1-o-β-D-glucopyranosyl-9-methyl-4E,8E-sphingadiene (344); (4E,8E)-1-o-(β-D-glucopyranosyl)-2-(2'-hydroxyl-(E)-3'-heptadecenylamido)-3-hydroxyl-9-methyl-4,8-nonadecadiene (345); ergosta-7,24(28)-diene-3-β-ol (346); cholest-4-ene-3-ol (347); and methyl decanoate (348). Primary bioassay showed that compound 344 exhibited moderate inhibitory activity against *Fusarium graminearum*, *Calletotrichum musae*, and *Penicillium italicum*; and compound 345 exhibited moderate inhibitory activity against *F. graminearum* and *C. musae* and low inhibitory activity against *P. italicum* at a concentration of 0.5 µmol/mL [70].

Two unusual pyridines, trichodins A (47) and B (350), together with a known compound, pyridoxatin (351), were extracted from the marine *Trichoderma* sp. MF106. Compounds 349 and 351 showed antibiotic activities against the clinically relevant microorganism *Staphylococcus epidermidis*, with IC$_{50}$ values of 24 µM and 4 µM, respectively [71].

A nematicidal compound, trichodermin (70), was isolated from the ethyl acetate extract of *Trichoderma* sp. YMF1.02647. Compound 70 killed more than 95% of both *Panagrellus redivivus* and *Caenorhabditis elegans* in 72 h at 0.4 g/L [72].

Two new cyclopentenones, trichodermones A (47) and B (352), together with a known compound, 3-(3-oxocyclopent-1-enyl)propanoic acid (353), were obtained from *Trichoderma* sp. YLF-3. These compounds were assayed for antibacterial activity, and compound 353 showed activity against *Staphylococcus aureus* and *Bacillus cereus* [73].

Two novel compounds were isolated from *Trichoderma* sp. USF-2690: demethylsorbicillin (354) and oxosorbidicillin (355). In a 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical-scavenging assay, compound 355 gave an ED$_{50}$ value of 87.7 µM [74].

Thirteen compounds were obtained from the fermentation broth of *Trichoderma* sp. Jing-8: a new natural mycotoxin, alternariol 1'-hydroxy-9-methyl ether (356), and twelve known compounds
[ergosterol (134); and cereviseterol (221); alternariol 9-methyl ether (357); alternariol (358); altechromone A (359); altenuene (360); 4′-epialtenuene (361); scytalone (362); α-acetylorcinol (363); cerebroside C (364); α-palmitoyl-β-linoleoyl-α′-linoleoyl glycerol (365); and 1,2-benzenedicarboxylic acid bis(2S-methyl heptyl) ester (366)]. Compounds 356, 363, and 364 showed an inhibitory effect against cabbage seed germination (MIC < 3 µg/mL). Compound 356 showed antibacterial activity against *B. subtilis* and *S. aureus* (with MIC 64 µg/mL). Compounds 356 and 358 showed significant DPPH radical-scavenging activity (with IC₅₀ 12 µg/mL) [75].

Eight known compounds were isolated from *Trichoderma* sp. TA26-28: nafuredin (94); 5-hydroxy-2,3-dimethyl-7-methoxychromene (96); cerebroside D (242); cerebroside C (364); pachybasin (367); chrysophanol (368); 8-o-methylchrysophanol (369); and soya-cerebroside I (370). In the research, MIC (µM) values of eight compounds were evaluated against a panel of pathogenic bacteria: six Gram-positive bacteria [*S. aureus*, *Sardine albus*, *B. cereus*, *B. subtilis*, *Micrococcus tetragenus*, and *K. rhizophila*] and four Gram-negative bacteria [*E. coli*, *V. paraahaemolyticus*, *V. anguillarum*, and *P. putida*]. Compound 96 showed pronounced antibacterial activity against all the tested bacteria, with MIC values ranging from 0.78 to 6.25 M. In addition, compounds 242 and 364 showed selective antibacterial activity against Gram-negative bacteria, and compound 94 showed weak antibacterial activity against *B. cereus* and *P. putida* [76].

Nine compounds were obtained from *Trichoderma* sp. YM311505: 3β,5α,9α-trihydroxyergosta-7,22-dien-6-one (31); ergosterol (134); trichodimerol (305); 5α,6α-epoxyergosta-8(14),22-diene-3β,7α-diol (371); campesterol (372); 7-methoxy-4,6-dimethyl phthalide (373); 7-hydroxy-4,6-dimethyl phtalide (374); daidzein (375); and cinnamic acid (376). Compound 31 exhibited the most potent antifungal activities against *P. oryzae*, *C. albicans*, Aspergillus *niger*, and *Alternaria alternata* with MIC value at 32 µg/mL. Compound 373 showed antimicrobial activity against *E. coli*, *B. subtilis*, *P. oryzae*, *A. niger* and *A. alternata* with MIC 64 µg/mL. Compounds 373 and 375 exhibited antibacterial activity against *E. coli* with MIC 64 µg/mL. Compound 305 showed antifungal activity against *P. oryzae*, *C. albicans*, and *A. niger* with MIC values of 32, 32, and 64 µg/mL, respectively [77].

Seventeen compounds were isolated from the endophytic fungus *Trichoderma* sp. Xy24: cloneronadiol (92); ergosterol (134); trichodimerol (305); trichoacoreol (377) [78]; trichocage B (378); 1α-isopropyl-4α,8-dimethylspirod[4.5]-dec-8-ene-2β,7α-diol (379); 1α-isopropyl-4α,8-dimethylspirod[4.5]-dec-8-ene-3β,7α-diol (380); 10,11-dihydroxy-cycloneradiol (381); 14-hydroxy-trichoacoreol (382); harzianone (383); (9R,10R)-dihydro-harzianone (384); ergokonin B (385); methyl stearate (386) [79]; harzianelactone (387); trichoacoreol B (388); trichoacoreol C (389); and cloneronadiol B (390) [80]. Among them, compounds 381, 382, and 384 were new. Compound 305 exhibited medium inhibitory activity (with IC₅₀ 74.6 µM), using a neuraminidase (H7N9)/methylumbelliferyl-N-acetylneuraminic acid model. Compound 384 showed cytotoxic activity against the HeLa with IC₅₀ 30.1 µM and MCF-7 cell line with IC₅₀ 30.7 µM. Compound 390 inhibited LPS-induced NO production in BV2 cells by 75.0% (0.1 µM) and had good neuro-anti-inflammatory activity.

All secondary metabolites from *Trichoderma* are summarized in Table 1.
Table 1. Non-volatile metabolites and their biological activities from *Trichoderma*.

| Metabolites                     | Species           | Activity | Refs. | Metabolites                     | Species           | Activity | Refs. |
|---------------------------------|-------------------|----------|-------|---------------------------------|-------------------|----------|-------|
| prealamethicin F50 (1)          | *T. arundinaceum* | -        | [3]   | trikoningin KB I (196)          | *T. koningiopsis* | -        | [1]   |
| Glu(OMe)β-alamethicin F50 (2)   | *T. arundinaceum* | Anti-tumor | [3]   | trikoningin KB II (197)         | *T. koningiopsis* | -        | [1]   |
| trichobrevin BIII-D (3)         | *T. arundinaceum* | Anti-tumor | [3]   | konginginin A (198)             | *T. koningiopsis* | YIM PH30002 Siderophoric | [42] |
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Table 1. Cont.

| Metabolites                               | Species                        | Activity                          | Refs. | Metabolites                               | Species                        | Activity                          | Refs. |
|-------------------------------------------|--------------------------------|-----------------------------------|-------|-------------------------------------------|--------------------------------|-----------------------------------|-------|
| 3-hydroxytrichodenone C (22)              | *T. asperellum* cf44-2         | Antibacterial Growth inhibiting   | [8]   | 4-hydroxyphenylethanol (217)              | *T. koningiopsis* Y10-2       | -                                 | [43]  |
| methylocordysinin A (23)                  | *T. asperellum* cf44-2         | -                                 | [6]   | m-methoxyphenol (218)                    | *T. koningiopsis* Y10-2       | -                                 | [43]  |
| 4-oxazolepropanoic acid (24)              | *T. asperellum* cf44-2         | -                                 | [6]   | sorbicillin (219)                        | *T. longibrachiatum*           | Antibacterial                     | [45]  |
| wickerol A (25)                           | *T. asperellum* dl-34          | Nematicidal                       | [9]   | ergosterol peroxide (220)                | *T. longibrachiatum*           | -                                 | [45]  |
| harzianidione (26)                        | *T. asperellum* dl-34          | Nematicidal                       | [9]   | cerevisterol (221)                       | *T. longibrachiatum*           | -                                 | [45]  |
| ergosterol endoperoxide (27)              | *T. asperellum* dl-34          | -                                 | [9]   | 2-anhydroximevalonic acid (222)          | *T. longibrachiatum*           | -                                 | [45]  |
| 5α,8α-epidioxyergosta-6,9(11),22-trien-3β-ol (28) | *T. asperellum* dl-34          | -                                 | [9]   | squalene (223)                           | *T. longibrachiatum*           | -                                 | [45]  |
| 3β,5α,6β-trihydroxyergosta-7,22-diene (29) | *T. asperellum* dl-34          | -                                 | [9]   | ergokonin A (224)                        | *T. longibrachiatum*           | Antifungal                        | [46]  |
| 3β,5α-dihydroxy-6β-methoxyergosta-7,22-diene (30) | *T. asperellum* dl-34          | -                                 | [9]   | 5-hydroxyximevalonic acid (225)          | *T. longibrachiatum* Rifai    | Antagonism                        | [47]  |
| 3β,5α,9α-trihydroxyergosta-7,22-diene-6-one (31) | *T. asperellum* dl-34          | Antifungal                        | [9]   | bislongiquinolide (226)                  | *T. longibrachiatum* Rifai    | T. saturnisporum                  | [47]  |
| (22E,24R)-ergosta-4,6,8(14),22-tetraen-3-one (32) | *T. asperellum* dl-34          | -                                 | [9]   | 10,11-dihydroximevalonic acid (227)      | *T. longibrachiatum* YM311505 | Antifungal                        | [48]  |
| (22E,24R)-5α,6α-epoxyergosta-8,22-diene-3β,7α-diol (33) | *T. asperellum* dl-34          | -                                 | [9]   | sohirnone A (228)                        | *T. longibrachiatum* YM311505 | Antifungal                        | [48]  |
| ergosta-7,22-dien-3β-ol (34)              | *T. asperellum* dl-34          | -                                 | [9]   | trichokonin A (229)                      | *T. longibrachiatum* SMF2     | Antiviral                         | [49]  |
| (22E,24R)-ergosta-5,7,22-trien-3β-ol (35) | *T. asperellum* dl-34          | -                                 | [9]   | trichokonin B (230)                      | *T. longibrachiatum* SMF2     | -                                 | [49]  |
| β-sitosterol (36)                         | *T. asperellum* dl-34          | -                                 | [9]   | valinotricin (231)                       | *T. polysporum*               | -                                 | [50]  |
| (L)-Pro-(L)-Leu (37)                      | *T. asperellum* dl-34          | -                                 | [9]   | cyclenerodiol oxide (232)                | *T. polysporum*               | -                                 | [50]  |
| (L)-4-OH-Pro-(L)-Leu (38)                 | *T. asperellum* dl-34          | -                                 | [9]   | epi-cyclenerodiol oxide (233)            | *T. polysporum*               | -                                 | [50]  |
| Metabolites | Species | Activity | Refs. | Metabolites | Species | Activity | Refs. |
|-------------|---------|----------|-------|-------------|---------|----------|-------|
| adenine nucleoside (39) | T. asperellum dl-34 T. harzianum R5 | - | [9] | trichosporin Bs (234) | T. polysporum | - | [51] |
| cis-4-hydroxy-6-deoxyscytalone (40) | T. asperellum dl-34 | - | [9] | trichosporin B-V (235) | T. polysporum | - | [52] |
| 2,4-dihydroxy-3,6-dimethylbenzaldehyde (41) | T. asperellum dl-34 | - | [9] | 8,9-dihydroxy-megastigmatriene (236) | T. reesei | - | [53] |
| dihydrocitrinone (42) | T. asperellum dl-34 | - | [9] | harzialactone A (237) | T. reesei | - | [53] |
| atrichodermone A (43) | T. atroviride | Cytotoxic Anti-inflammatory | [10] | 3,6-dibenzylpiperazine-2,5-dione (238) | T. reesei | - | [53] |
| atrichodermone B (44) | T. atroviride | Cytotoxic Anti-inflammatory | [10] | 3-isobutyl-8-hydroxy-pyrrolopiperazine-2,5-dione (239) | T. reesei | - | [53] |
| atrichodermone C (45) | T. atroviride | Cytotoxic Anti-inflammatory | [10] | 3-benzyl-8-hydroxy-pyrrolopiperazine-2,5-dione (240) | T. reesei | - | [53] |
| atrichodermone D (46) | T. atroviride | - | [11] | cerebroside A (241) | T. saturnisporum | Antibacterial | [54] |
| trichoderma A (47) | T. atroviride | - | [11] | cerebroside D (242) | T. saturnisporum | Antibacterial | [54] |
| (5R)-5-hydroxy-3-[(methoxycarbonyl)-amino]-5-vinyl-2-cyclopenten-1-one (48) | T. atroviride | - | [11] | sorbicillin A (243) | T. saturnisporum | - | [54] |
| 4H-1,3-dioxin-4-one-2,3,6-trimethyl (49) | T. atroviride | Antibacterial Cytotoxic | [11] | sorbicillin B (244) | T. saturnisporum | - | [54] |
| 1,3-dione-5,5-dimethylcyclohexane (50) | T. atroviride | - | [11] | bisvertinolone (245) | T. saturnisporum | Antibacterial | [54] |
| 2-enone-3hydroxy-5,5-dimethylcyclohex (51) | T. atroviride | - | [11] | saturnispol A (246) | T. saturnisporum | - | [55] |
| 6-pentyl-pyran-2-one (52) | T. atroviride | - | [11] | saturnispol B (247) | T. saturnisporum | - | [55] |
| 6-pent-1-etyl-pyrene-2-one (53) | T. atroviride | - | [12] | saturnispol D (248) | T. saturnisporum | - | [55] |
| 2-hydroxybutan-3-yl(2‘-hydroxy-N-(2‘‘-oxobutan-3’‘-yl)propanamido)butanoate (54) | T. atroviride G20-12 | - | [12] | saturnispol E (250) | T. saturnisporum | - | [55] |
| 3-hydroxy-5-(4-hydroxybenzyl)dihydrofuran-2(3H)-one (55) | T. atroviride G20-12 | - | [12] | saturnispol F (251) | T. saturnisporum | - | [55] |
| 4’-(4,5-dimethyl)-1,3-dioxolan-2-ylmethylene-phenol (56) | T. atroviride G20-12 | - | [12] | saturnispol G (252) | T. saturnisporum | - | [55] |
| (3’-hydroxybutan-2’-yl)(2‘-oxopyrrolidin-2-carboxylate (57) | T. atroviride G20-12 | - | [12] | saturnispol H (253) | T. saturnisporum | Antibacterial | [55] |

Table 1. Cont.
| Metabolites                        | Species            | Activity | Refs. | Metabolites                        | Species       | Activity       | Refs. |
|-----------------------------------|--------------------|----------|-------|-----------------------------------|---------------|----------------|-------|
| trichodermadione A (59)           | *T. atroviride* S361 | -        | [14]  | trichodemic acid (254)            | *T. spirale* A17 | Anti-tumor     | [56]  |
| trichodermadione B (60)           | *T. atroviride* S361 | -        | [14]  | gliotoxin (255)                   | *T. virens* ITC-4777 | Antifungal    | [57]  |
| 4-(2-formyl-5-(methoxymethyl)-1H-pyrrol-1-yl)butanoic acid (61) | *T. atroviride* S361 | -        | [14]  | dimethyl gliotoxin (256)           | *T. virens* ITC-4777 | -     | [57]  |
| 5-methoxymethyl-1H-pyrole-2-carboxaldehyde (62) | *T. atroviride* S361 | -        | [14]  | viridin (257)                      | *T. virens* ITC-4777 | -     | [57]  |
| 3-(1-carboxaldehyde)-6-methyl-2H-pyran-2,4(3H)-dione (63) | *T. atroviride* S361 | -        | [14]  | viridol (258)                      | *T. virens* ITC-4777 | -     | [57]  |
| lignoren (64)                     | *T. atroviride* S361 | Antibacterial | [14], [18], [44] | trichorenin A (259) | *T. virens* Y13-3 | Antimicroalgal | [43] |
| ascotrichic acid (65)             | *T. atroviride* S361 | -        | [14]  | trichorenin B (260)               | *T. virens* Y13-3 | Antimicroalgal | [43] |
| catenioblin C (66)                | *T. atroviride* S361 | Antifungal | [14]  | trichorenin C (261)               | *T. virens* Y13-3 | Antimicroalgal | [43] |
| 6-pentyl-α-pyrone (67)            | *T. atroviride* UST1 | Plant resistance | [15], [35] | trichocarotin A (262)           | *T. virens* Y13-3 | -     | [43] |
| roaringinin G (68)                | *T. atroviride*     | Growth inhibiting | [16]  | trichocarotin B (263)            | *T. virens* Y13-3 | -     | [43] |
| Koningin G triacetate (69)        | *T. atroviride*     | -        | [16]  | trichocarotin C (264)             | *T. virens* Y13-3 | Antimicroalgal | [43] |
| trichodermin (70)                 | *T. brevicompactum* | Antifungal | [17]  | trichocarotin D (265)            | *T. virens* Y13-3 | Antimicroalgal | [43] |
| (R)-vertinolide (71)              | *T. citrinoviride*  | -        | [1]   | trichocarotin E (266)            | *T. virens* Y13-3 | Antimicroalgal | [43] |
| trichoderinol C (72)              | *T. citrinoviride*  | -        | [18]  | trichocarotin F (267)            | *T. virens* Y13-3 | -     | [43] |
| citrinoviric acid (73)            | *T. citrinoviride*  | Cytotoxic | [18]  | trichocarotin G (268)            | *T. virens* Y13-3 | -     | [43] |
| penicillenol D (74)               | *T. citrinoviride*  | Cytotoxic | [18]  | trichocarotin H (269)            | *T. virens* Y13-3 | Antimicroalgal | [43] |
| trichotetronine (75)              | *T. citrinoviride*  | -        | [18]  | trichocadim A (270)              | *T. virens* Y13-3 | -     | [43] |
| bisverinol (76)                   | *T. citrinoviride*  | -        | [6]   | (3S,6R)-6-(para-hydroxybenzyl)-1,4-dimethyl-3,6-bis(methylthio)piperazine-2,5-dione (271) | *T. virens* Y13-3 | -     | [43] |
| spirodendrinol A (77)             | *T. citrinoviride*  | -        | [18]  | dehydroxymethylbis(dethio)bis(methylthio)gliotoxin (272) | *T. virens* Y13-3 | -     | [43] |
| spirodendrinol B (78)             | *T. citrinoviride*  | -        | [18]  | CAF-603 (273)                     | *T. virens* Y13-3 | -     | [43] |
Table 1. Cont.

| Metabolites                               | Species          | Activity | Refs. | Metabolites                               | Species          | Activity | Refs.       |
|-------------------------------------------|------------------|----------|-------|-------------------------------------------|------------------|----------|-------------|
| spirosorbicillinol C (79)                 | T. citrinoviride | -        | [18]  | 14-hydroxy CAF-603 (274)                  | T. virens Y13-3  | -        | [43]        |
| trichoderiol A (80)                      | T. citrinoviride | -        | [18]  | 7-β-hydroxy CAF-603 (279)                 | T. virens Y13-3  | -        | [43]        |
| penicillenol B₁ (81)                     | T. citrinoviride | -        | [18]  | trichocarane A(276)                       | T. virens Y13-3  | - Antimicrobial | [43] |
| penicillenol B₂ (82)                     | T. citrinoviride | -        | [18]  | 3[(4′-hydroxyphenyl)methyl]-1,4-dimethyl- | T. virens Y13-3  | -        | [43]        |
| cyclo-(Leu-Pro) (83)                     | T. citrinoviride | -        | [18]  | bis(dethio)bis(methylthio)gliotoxin (278) | T. virens Y13-3  | -        | [43]        |
| cyclo-(Ille-Pro) (84)                    | T. citrinoviride | -        | [18]  | bisdethiobis(methylthio)-dehydrogliotoxin| T. virens Y13-3  | -        | [43]        |
| cyclo-(Phe-Pro) (85)                     | T. citrinoviride | -        | [18]  | chromone (280)                            | T. virens Y13-3  | Antifungal | [43]        |
| trichocitrin (86)                        | T. citrinoviride cf-27 | Antimicrobial | [9]  | trichodecenins (281)                      | T. viride        | -        | [59]        |
| 24-methylene cycloartanol (87)           | T. citrinoviride cf-27 | -        | [9]   | trichorovins (282)                        | T. viride        | -        | [59]        |
| cycloeucalenol (88)                      | T. citrinoviride cf-27 | -        | [9]   | trichocellins (283)                       | T. viride        | -        | [59]        |
| citrostadienol (89)                      | T. citrinoviride cf-27 | -        | [9]   | trichonovin I (284)                       | T. viride        | -        | [59]        |
| euphorbol (90)                           | T. citrinoviride cf-27 | -        | [9]   | trichonovin II (285)                      | T. viride        | -        | [59]        |
| 24-methylene-lanost-8-en-3β-ol (91)      | T. citrinoviride cf-27 | -        | [9]   | trichonovin III (286)                     | T. viride        | -        | [59]        |
| cyclonerodiol (92)                       | T. citrinoviride cf-27 | -        | [9]   | trichonovin IV (287)                      | T. viride        | -        | [59]        |
| 22E,24R)-7β,8β-epoxy-3β,5α,9α-trihydroxysterost-22-en-6-one (93) | T. citrinoviride cf-27 | -        | [9]   | trichonovin V (288)                       | T. viride        | -        | [59]        |
| nafuredin (94)                           | T. citrinoviride cf-27 | Antimicrobial | [9]  | trichonovin VI (289)                      | T. viride        | -        | [59]        |
| harzianolide (95)                        | T. citrinoviride cf-27 | Antimicrobial | [9]  | trichonovin VII (290)                     | T. viride        | -        | [59]        |
| 5-hydroxy-2,3-dimethyl-1,2-methoxychromone (96) | T. citrinoviride cf-27 | Antimicrobial | [9]  | trichonovin VIII (291)                    | T. viride        | -        | [59]        |
Table 1. Cont.

| Metabolites                                                      | Species                     | Activity | Refs. | Metabolites                      | Species               | Activity | Refs. |
|-----------------------------------------------------------------|-----------------------------|----------|-------|----------------------------------|-----------------------|----------|-------|
| 5-hydroxy-3-hydroxymethyl-2-methyl-7-methoxychromone (97)       | T. citrinoviride cf-27      | -        | [9]   | trichovin IX (292)               | T. viride             | -        | [59]  |
| methyl                                                           | T. citrinoviride cf-27      | -        | [9]   | trichovin X (293)                | T. viride             | -        | [59]  |
| 8-hydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate (98)         | T. citrinoviride cf-27      | -        | [9]   | trichovin XI (294)               | T. viride             | -        | [59]  |
| methyl 2,8-dihydroxy-6-methyl-9-oxo-9H-xanthene-1-carboxylate   | T. citrinoviride cf-27      | -        | [9]   | trichovin XII (295)              | T. viride             | -        | [59]  |
| stachyline B (100)                                              | T. citrinoviride cf-27      | -        | [9]   | trichorovin IX (292)             | T. viride             | -        | [59]  |
| trans-3,4-dihydro-2,4,8-trihydroxynaphthalen-1(2H)-one (101)   | T. citrinoviride cf-27      | -        | [9]   | trichorovin X (293)              | T. viride             | -        | [59]  |
| pyrazole-3-carboxylic acid (102)                                | T. citrinoviride cf-27      | -        | [9]   | trichorovin XIX (294)            | T. viride             | -        | [59]  |
| dibutyl phthalate (104)                                         | T. citrinoviride cf-27      | -        | [9]   | trichodermanone A (299)          | T. viride             | -        | [60]  |
| cremenolide (105)                                               | T. cremenum                 |          | [19]  | trichodermanone B (300)          | T. viride             | -        | [60]  |
| trichoderone A (106)                                            | T. gamsii                   | -        | [20]  | trichodermanone C (301)          | T. viride             | -        | [60]  |
| trichoderone B (107)                                            | T. gamsii                   | -        | [20]  | trichodermanone D (302)          | T. viride             | -        | [60]  |
| aspochalasin D (108)                                            | T. gamsii                   | Cytotoxic| [20]  | rezishanone (303)                | T. viride             | -        | [60]  |
| aspochalasin J (109)                                            | T. gamsii                   | Cytotoxic| [20]  | vertinolid (304)                 | T. viride             | -        | [60]  |
| aspochalasin I (110)                                            | T. gamsii                   | -        | [20]  | trichoderol (305)                | Antifungal Enzyme inhibiting | [60]    |       |
| trichoharzianin (111)                                           | T. harzianum R5             | Antimicrobial | [9]   | 2-furancarboxylic acid (306)     | T. viride             | -        | [60]  |
| 3β-hydroxyergosta-8,24(28)-dien-7-one (112)                     | T. harzianum R5             | -        | [9]   | α-phenylcinnamic acid (307)      | T. viride             | -        | [61]  |
| (22E,24R)-24-methylcholesta-5,22-dien-3β-ol (113)               | T. harzianum R5             | -        | [9]   | trichoderone (308)               | T. viride             | -        | [62]  |
| 5,7-dihydroxy-2,3-dimethylchromone (114)                        | T. harzianum R5             | -        | [9]   | cholesta-7,22-diene-3β,5α,6β-triol (309) | T. viride             | -        | [62]  |
| (22E,24R)-3β,5α-dihydroxy-ergosta-7,22-dien-6-one (115)         | T. harzianum R5             | -        | [9]   | 5α,8α-epidioxyergosta-6,22-dien-3β-ol (310) | T. viride             | -        | [63]  |
| 5-hydroxy-2-hydroxymethyl-3-methyl-7-methoxychromone (116)      | T. harzianum R5             | -        | [9]   | 1-monoolein (311)                | T. viride             | -        | [63]  |
| indole-3-carboxaldehyde (117)                                   | T. harzianum R5             | -        | [9]   | methyl elaidate (312)             | T. viride             | -        | [63]  |
| 3-indol acetic acid (118)                                       | T. harzianum R5             | -        | [9]   | trichoderol A (313)              | T. viride             | -        | [64]  |
Table 1. Cont.

| Metabolites Species Activity Refs. Metabolites Species Activity Refs. |
|------------------------------|------------------------------|
| 2,4-dimethylbenzene-1,3,5-triol (119) T. harzianum R5 - [9] | Trichoschoiizochromen A (314) Trichoderma sp. SCSIO41004 - [66] |
| 5′-o-acetyluracil nucleoside (120) T. harzianum R5 - [9] | 5,7-dihydroxy-3-methyl-2-(2-oxopropyl)naphthalene-1,4-dione (315) Trichoderma sp. SCSIO41004 - [66] |
| T. harzianum R5-1 T. koningiopsis Y10-2 Antibacterial [21] [43] | 7-acetyl-1,3,6-trihydroxyanthraquinone (316) Trichoderma sp. SCSIO41004 | Antibacterial [21] [43] |
| (15,45,55)-8-hydroxymethyl-1-isopropyl-4-methylspino[4.5]dec-8-en-7-one (122) T. harzianum R5-1 | 5′-o-acetyluracil nucleoside (119) T. harzianum R5 - [9] | 7-hydroxy-2-(2′S-hydroxypropyl)-5-methylchromone (320) Trichoderma sp. SCSIO41004 - [66] |
| 5,6-dihydro-4-methyl-2H-pyran-2-one (125) T. harzianum R5-1 | - [21] 7-hydroxy-2-(2′S-hydroxypropyl)-5-methylchromone (320) Trichoderma sp. SCSIO41004 - [66] |
| demethylincisterol A3 (126) T. harzianum R5-1 T. viridis Y13-3 | cyclonerotriol (321) Trichoderma sp. SCSIO41004 - [66] |
| palmitic acid (127) T. harzianum T-4 T. koningii T-8 | - [22] [38] adenosine (322) Trichoderma sp. SCSIO41004 - [66] |
| 1,8-dihydroxy-3-methylantraquinone (128) T. harzianum T-4 T. harzianum T22 T. harzianum T39 | - [22] [23] microsphaeropsin B (323) Trichoderma sp. SCSIO41004 - [66] |
| 6-pentyl-2H-pyran-2-one (129) T. harzianum T-4 T. viridicercis TS0404 Trichoderma sp | Antifungal Growth inhibiting [22] [61] | microsphaeropsin C (324) Trichoderma sp. SCSIO41004 - [66] |
| 2(5H)-furanone (130) T. harzianum T-4 | - [22] (3R,7R)-7-hydroxy-de-o-methylasiodiplodin (325) Trichoderma sp. SCSIO41004 - [66] |
| stigmasteral (131) T. harzianum T-4 T. koningii T-11 | - [22] [38] (3R)-5-exo-de-o-methylasiodiplodin (326) Trichoderma sp. SCSIO41004 - Enzyme inhibiting [66] |
| 1-hydroxy-3-methylantraquinone (132) T. harzianum T-4 T. harzianum T22 T. harzianum T39 | - [22] [23] (3R)-7-exo-de-o-methylasiodiplodin (327) Trichoderma sp. SCSIO41004 - [66] |
| δ-decanolactone (133) T. harzianum T-4 T. koningii T-8 | - [22] [38] microsphaeropsin (328) Trichoderma sp. SCSIO41004 - [66] |
| ergosterol (134) T. harzianum T-4 T. longibrachiatum Trichoderma sp. YM31505 Trichoderma sp. Xy24 | - [22] [33] [75] [77] | (3R)-5-exolasiadiplodin (329) Trichoderma sp. SCSIO41004 - [66] |
| Metabolites | Species            | Activity       | Refs.      | Metabolites                      | Species                  | Activity       | Refs. |
|-------------|--------------------|----------------|------------|----------------------------------|--------------------------|----------------|-------|
| harzianopyridone (135) | T. harzianum T-4 | Antifungal     | [22]       | (35)-6-oxo-de-o-methylasiodiplodin (330) | Trichoderma sp. 307 | -              | [64]  |
| 6-methyl-1,3,8-trihydroxyanthraquinone (136) | T. harzianum T-4 | -              | [22]       | (3R)-de-o-methylasiodiplodin (331) | Trichoderma sp. 307 | -              | [64]  |
| T22azaphilone (137) | T. harzianum T22 | Antifungal     | [23]       | (3R,4R)-4-hydroxy-de-o-methylasiodiplodin (332) | Trichoderma sp. 307 | -              | [64]  |
| T39buteinolide (138) | T. harzianum T22 | Antifungal     | [23]       | (3R,5R)-5-hydroxy-de-o-methylasiodiplodin (333) | Trichoderma sp. 307 | -              | [64]  |
| (22E,24R)-5α,8β-epidioxyergosta-6,22-dien-3β-ol (139) | T. harzianum dl-36 | -              | [24]       | (3R,6R)-6-hydroxy-de-o-methylasiodiplodin (334) | Trichoderma sp. 307 | -              | [64]  |
| ergosta-7,22-dien-3β,5α,6β-triol (140) | T. harzianum dl-36 | -              | [24]       | (3R)-lasiodiplodin (335) | Trichoderma sp. 307 | -              | [64]  |
| harzianic acid (141) | T. harzianum Trichoderma sp | Antibiotic Growth enhancing | [27]       | (35)-ozoroalide (336) | Trichoderma sp. 307 | -              | [64]  |
| 15-hydroxyacorenone (142) | T. harzianum | -              | [28]       | (35,5R)-5-hydroxyasiodiplodin (337) | Trichoderma sp. 307 | -              | [64]  |
| 2460A (143) | T. harzianum | Anti-tumor      | [29]       | (E)-9-etheno-lasiodiplodin (338) | Trichoderma sp. 307 | -              | [64]  |
| trichokindin I (144) | T. harzianum Bioinducer |          | [30]       | 2,5-cyclohexadiene-1,4-diene-2,6-bis(1,1-dimethylethyl) (340) | Trichoderma sp. T-33 | Antifungal |       |
| trichokindin II (145) | T. harzianum Bioinducer |          | [30]       | (E)-3-acetylbenzylbut-2-enoate (341) | Trichoderma sp. KK19L1 | -              | [69]  |
| trichokindin III (146) | T. harzianum Bioinducer |          | [30]       | 1-hydroxy-6-methyl-9,10-anthraquinone (342) | Trichoderma sp. KK19L1 | -              | [69]  |
| trichokindin IV (147) | T. harzianum Bioinducer |          | [30]       | methyl hexadecanoate (343) | Trichoderma sp. 09 | -              | [70]  |
| trichokindin V (148) | T. harzianum Bioinducer |          | [30]       | N-[2′-hydroxy-3′E-octadecenoyl]-1′-o-β-D-glucopyranosyl-9-methyl-4E,8E-sphingadiene (344) | Trichoderma sp. 09 | Antifungal   | [70]  |
| trichokindin VI (149) | T. harzianum Bioinducer |          | [30]       | (4E,8E)-1′-o-[β-D-glucopyranosyl]-2′-2′′-hydroxy-(E)-3′-heptadecenoylamide)-3-hydroxy-9-methyl-4,8-nonadecadiene (345) | Trichoderma sp. 09 | Antifungal   | [70]  |
| trichokindin VII (150) | T. harzianum Bioinducer |          | [30]       | Octaketide keto diol (155) | T. harzianum | -              | [32]  |
| trichorozin I (151) | T. harzianum | -              | [31]       | ergosta-7,24(28)-diene-3β-ol (346) | Trichoderma sp. 09 | -              | [70]  |
| trichorozin II (152) | T. harzianum | -              | [31]       | cholest-4-ene-3-ol (347) | Trichoderma sp. 09 | -              | [70]  |
| trichorozin III (153) | T. harzianum | -              | [31]       | methyl decanoate (348) | Trichoderma sp. 09 | -              | [70]  |
| trichorozin IV (154) | T. harzianum | -              | [31]       | trichodin A (349) | Trichoderma sp. MF106 | Antibiotic |       |
| octaketide keto diol (155) | T. harzianum | -              | [32]       | trichodin B (350) | Trichoderma sp. MF106 | -              | [71]  |
| Metabolites       | Species                  | Activity                          | Refs. | Metabolites       | Species                  | Activity                          | Refs. |
|-------------------|--------------------------|-----------------------------------|-------|-------------------|--------------------------|-----------------------------------|-------|
| oxidized analog   | T. harzianum             | -                                 | [1]   | pyridoxatin       | Trichoderma sp. MF106    | Antibiotic                        | [71]  |
| T. harzianum      | -                        | [33]                              |       | trichodermon B    | Trichoderma sp. YLF-3    | -                                 | [73]  |
| tyrosol           | T. harzianum             | Anti-tumor                        | [33]  | demethylsorbicillin | Trichoderma sp. USF-2690 | -                                 | [74]  |
| 6-n-pentyl- •-pyrone | T. harzianum             | Antifungal                        | [34]  | alternariol       | Trichoderma sp. Jing-8   | Growth inhibiting                 | [75]  |
| cyclo-(R-Pro-Gly) | T. harzianum             | -                                 | [34]  | alternariol 1'-hydroxy-9-methyl ether | Trichoderma sp. Jing-8 | -                                 | [75]  |
| cyclo-(S-Pro-R-Ala) | T. harzianum             | -                                 | [34]  | alternariol 1'-hydroxy-9-methyl ether | Trichoderma sp. Jing-8 | -                                 | [75]  |
| m-hydroxylphenylethanol | T. harzianum | -                                 | [34]  | α-acetylorcinol   | Trichoderma sp. Jing-8   | Growth inhibiting                 | [75]  |
| 3-dimethylaminos-5-hydroxy-9-vinyl-2-cyclopenten-5-one | T. koningii | -                                 | [36]  | α-palmitoyl-β-linoeyl-o′-linoeyl glycerol | Trichoderma sp. Jing-8 | -                                 | [75]  |
| Trichodermaketone A | T. koningii              | Antifungal                        | [36]  | 1,2-benzene dicarboxylic acid bis(25-methyl heptyl ester) | Trichoderma sp. Jing-8 | -                                 | [75]  |
| Trichodermaketone B | T. koningii              | -                                 | [36]  | pachybasin        | Trichoderma sp. TA26-28  | -                                 | [76]  |
| Trichodermaketone C | T. koningii              | -                                 | [36]  | chrysophanol       | Trichoderma sp. TA26-28  | -                                 | [76]  |
| Trichodermaketone D | T. koningii              | -                                 | [36]  | 5α,6α-epoxyergosta-8(14),22-diene-3β,7α-diol | Trichoderma sp. YM311505 | -                                 | [77]  |
| Trichodermaketone E | T. koningii              | -                                 | [36]  | campesterol       | Trichoderma sp. YM311505 | -                                 | [77]  |
| Trichodermaketone F | T. koningii              | -                                 | [36]  | 7-hydroxy-4,6-dimethyl phthalide | Trichoderma sp. YM311505 | -                                 | [77]  |
| Metabolites                                  | Species          | Activity     | Refs.   | Metabolites                                  | Species          | Activity    | Refs.   |
|---------------------------------------------|------------------|--------------|---------|---------------------------------------------|------------------|-------------|---------|
| 6-pentyl-α-pyranone (180)                   | T. koningii T-8  | Antifungal   | [38]    | daidzein (375)                              | Trichoderma sp. YM311505 | Antibacterial | [77]    |
| 2H-pyran-2-one (181)                        | T. koningii T-8  | Antifungal   | [38]    | cinnamic acid (376)                         | Trichoderma sp. YM311505 | -           | [77]    |
| tricho-acorenol (182)                       | T. koningii -    | -            | [39]    | trichoacorenol (377)                        | Trichoderma sp. Xy24 | -           | [79]    |
| methyl benzoate (183)                       | T. koningii -    | -            | [40]    | trichoacorenol B (378)                      | Trichoderma sp. Xy24 | -           | [79]    |
| cyclo-(L-Pro-L-Leu) (184)                   | T. koningii -    | -            | [40]    | 1α-isopropyl-4α,8-dimethylspiro[4.5]-dec8-ene-2β,7α-di-ol (379) | Trichoderma sp. Xy24 | -           | [79]    |
| 4-hydroxyphenethylalcohol (185)             | T. koningii -    | -            | [40]    | 1α-isopropyl-4α,8-dimethylspiro[4.5]dec-8-ene-3β,7α-diol (380) | Trichoderma sp. Xy24 | -           | [79]    |
| ceramide (186)                              | T. koningii -    | -            | [40]    | 10,11-dihydroxy-cyclonerodiol (381)         | Trichoderma sp. Xy24 | -           | [79]    |
| trichokonin-V (187)                         | T. koningii -    | -            | [40]    | 14-hydroxy-trichoacorenol (382)             | Trichoderma sp. Xy24 | -           | [79]    |
| trichokonin-VI (188)                        | T. koningii -    | -            | [40]    | harzianone (383)                            | Trichoderma sp. Xy24 | -           | [79]    |
| trichokonin-II (189)                        | T. koningii -    | -            | [40]    | (9R,10R)-dihydro-harzianone (384)           | Trichoderma sp. Xy24 | Cytotoxic   | [79]    |
| trichokonin-III (190)                       | T. koningii -    | -            | [40]    | ergokonin B (385)                           | Trichoderma sp. Xy24 | -           | [79]    |
| trichokonin-Ia (191)                        | T. koningii -    | -            | [40]    | methyl stearate (386)                       | Trichoderma sp. Xy24 | -           | [79]    |
| trichokonin-Ib (192)                        | T. koningii -    | -            | [40]    | harzianelactone (387)                       | Trichoderma sp. Xy24 | -           | [80]    |
| trichokonin-IX (193)                        | T. koningii -    | -            | [40]    | trichoacorenol B (388)                      | Trichoderma sp. Xy24 | -           | [80]    |
| trikoningin KAY (194)                       | T. koningiopsis -| -            | [1]     | trichoacorenol C (389)                      | Trichoderma sp. Xy24 | -           | [80]    |
| 11-residue lipopeptidols (195)               | T. koningiopsis -| -            | [1]     | cyclonerodiol B (390)                       | Trichoderma sp. Xy24 | Anti-inflammatory | [80]    |
3. Conclusions

*Trichoderma* species are known for their diverse bioactivity owing to the production of abundant secondary metabolites. Hundreds of metabolites produced by *Trichoderma* have been isolated and characterized. In this review, 390 non-volatile compounds from 20 known species and various *Trichoderma* spp. were summarized. These compounds included peptaibols, terpenes, diketopiperazines, steroids, amides, lactones, polyketides, tetronic acid derivatives, peptides, pyranone derivatives, pyridines, and cyclopentenones. These compounds exhibited numerous biological activities, including cytotoxic, anti-tumor, antifungal, antibacterial, antiviral, antibiotic, anti-inflammatory, antimicroalgal, plant-growth-enhancing/inhibiting, bioinducer, hyperplasia inhibitory, siderophoric, antagonism, nematicidal, plant resistance, DPPH radical scavenging, and enzyme inhibitory effects.

Some metabolites were found in different species of *Trichoderma*. The antifungal and nematicidal compound trichodermin (70) was found in *T. brevicompactum*, *T. harzianum*, and *Trichoderma* sp. YMF1.02647. The bioactive metabolite 6-pentyl-α-pyrone (67) was distributed both in *T. atroviride* and *T. harzianum*. Cyclonerodiol (92) was found in *T. citrinoviride*, *T. harzianum*, *T. koningii*, *T. reesei*, and *Trichoderma* sp. Lignoren (64) was obtained from three species (*T. atroviride*, *T. citrinoviride*, and *T. lignorum*) and showed antimicrobial activity. Numerous strains from different species of *Trichoderma* had the same bioactivity, perhaps due to their identical metabolites.

Although *Trichoderma* spp. have been widely studied, more metabolites will likely be identified in the future.

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