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REVIEW

The Novel Compounds with Biological Activity Derived from Soil Fungi in the Past Decade

Danyu Zhang[1], Shoujie Li[1], Mohan Fan[2], Changqi Zhao[1]

[1]Gene Engineering and Biotechnology Beijing Key Laboratory, College of Life Science, Beijing Normal University, Beijing, People's Republic of China; [2]Dongzhimen Hospital, Beijing University of Chinese Medicine, Beijing, People's Republic of China

Correspondence: Changqi Zhao, Tel +86-5880-5046, Email 04020@bnu.edu.cn

Abstract: The secondary metabolites isolated from soil fungi have received more and more attention, especially new compounds that exhibited good biological activities. In this review, a total of 546 new compounds are included in the relevant literature since 2011. The new compounds are isolated from soil fungi, We divided these compounds into seven categories, including alkaloids, terpenoids, steroids, ketones, phenylpropanoids, quinones, esters, lactones, etc. In addition, the biological activities and structure–activity relationships of these compounds have also been fully discussed. The activities of these compounds are roughly divided into eight categories, including anticancer activity, antimicrobial activity, anti-inflammatory activity, antioxidant activity, antiviral activity, antimalarial activity, immunosuppressive activity and other activities. Since natural products are an important source of new drugs, this review may have a positive guiding effect on drug screening.

Keywords: soil fungi, new compounds, chemical structure, biological activity

Introduction

During the period of 1981 to 2019, almost 60% of the clinically approved drugs were derived directly or indirectly from natural products.[1] Nature can breed many species, including prokaryotes and eukaryotes. Among them, fungi play an important role in the ecosystems of plants, animals and humans.[2] Soil is an excellent natural habitat for microorganisms and has a large number of microorganisms.[3] Soil represents a very heterogeneous environment for its microbiota. Among the soil inhabitants, bacteria and fungi are important organisms as they are involved in key biogeochemical cycling processes.[4] Terrestrial microorganisms have long been regarded as profile producers of specialised metabolites with unique structures or new modes of action, and particularly in recent years, the discovery of new active natural products from soil-derived microorganisms has increased rapidly, contributing significantly to drug development.[5] Since Alexander Fleming discovered penicillin in 1928, fungi have become a considerable resource for novel compounds and new drugs.[6] The secondary metabolites of fungi are a rich source of small molecule compound libraries, and some metabolites have significant biological activities,[7] such as the antibacterial agent penicillins, immunosuppressive drug cyclosporin A, antifungal drug echinocandin B, and cholesterol-lowering agent lovastatin.[8] Fungi are an ideal source for obtaining novel skeletons through large-scale culture: compared with plants, fungi can proliferate rapidly from small amounts of spores to a mass of branching hyphaes, which are more environmentally friendly than collecting plant materials; compared with bacteria, fungi can be cultured in a solid medium for a longer time.[9] Therefore, soil-derived fungi are receiving continuous attention as the source of biologically active secondary metabolites. Since 2011, a large number of new compounds have been obtained from soil-derived fungi, but few people have summarized and analyzed these compounds. This review summarizes the compounds derived from soil fungi from 2011 to 2022, and classifies their structures and activities. Importantly, we made statistical analysis of these new compounds, readers can clearly understand which genus of soil fungi has great potential to produce new compounds. In addition, through the analysis of activity data, readers can clearly understand which kind of structural compounds account for the majority of compounds with certain activities, which kind of structural compounds account for the majority of compounds with certain activity. By summarizing the structure and activity of the new compound, a total of 546 compounds were isolated

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from the metabolites of soil fungi during the decade of 2011–2022, mainly including alkaloids, terpenes, steroids, ketones, phenylpropanoids, quinones, esters and lactones, of which ketones (31.9%), terpenoids and steroids (22.2%) are the main structural types. Among the 546 compounds, 279 compounds (approximately 51%) have good biological activities, including anticancer, antimicrobial, anti-inflammatory, antioxidant, antiviral, antimalaria, and immunosuppressive activities. Among them, anticancer and antimicrobial activities accounted for the highest proportion (Figure 1).

In the author's personal view, this review can provide a positive guidance for the screening of new drugs. This is also the significance of writing this review. In addition, we also analyzed the habitat sources of these soil fungi, which provides some directions for researchers who want to obtain new compounds from soil fungi from special habitats.

Structure Types of New Compounds Derived from Soil Fungi

Alkaloids

Indole alkaloids

A quinazolinone-containing indole derivative, named pseudofischerine **1** (Figure 2A), was isolated from the fungus *Neosartorya pseudofischeri* S.W. Peterson.[10] Two new compounds, named peneciraistins E **2** and F **3** (Figure 2A), were isolated from saline soil-derived fungus *Penicillium raistrickii*. Compounds **2** and **3** are the first naturally occurring 3-indoleformic acid derivatives.[11] A new indole alkaloid named exopisiod **4** (Figure 2A) was obtained from the fermentation products of *Exophiala pisciphila* PHF-9.[12] Waikialoid A **5** (Figure 2A) was isolated from *Aspergillus* sp.[13] Effusin A **6** and dihydrocryptoechinulin D **7** (Figure 2A), two new spiropolyketide-diketopiperazines were isolated from the fungus *Aspergillus effuses* H1-1. Effusin A **6** possessed an unprecedented 3′,3a′,5′,6′-tetrahydrospiro[piperazine-2,2′-pyrano [2,3,4-de]chromene] skeleton.[14] One new prenylated indole diketopiperazine alkaloid, named dihydroneochinulin B **8** (Figure 2A), was isolated from the mangrove rhizosphere soil-derived fungus, Aspergillus effuses H1-1.[15] A new aszonalenin analogue **9c** (Figure 2A) was isolated from the culture of the soil fungus *Neosartorya fischeri* (KUFC 6344).[16] Six new indole-diterpenoids **10**–**15** (Figure 2A and B) were isolated from the fermentation broth of an aciduric fungal strain *Penicillium camemberti* OUCMDZ-1492 grown at pH 5.0.[17] Asperdiazapinones A-F **16**–**21** (Figure 2B) were isolated from the mycelial extract of the soil fungus *Aspergillus* sp. PSU-RSPG185.[18] Mangrovamides A-C **22**–**24** (Figure 2B), featured a bicyclo [2.2.2] diazaoctane core and possessed a novel γ-methyl proline and isoprene derived dimethyl γ-pyrone functionalities hitherto unknown among the family of paraherquamides, were isolated from the fungus *Penicillium* sp. SYFz-1.[19] Rubrumazines A-C **25**–**27** (Figure 2B) were isolated and identified from a culture extract of *Eurotium rubrum* MA-150, a fungus obtained from mangrove-derived rhizospheric soil collected from the Andaman Sea

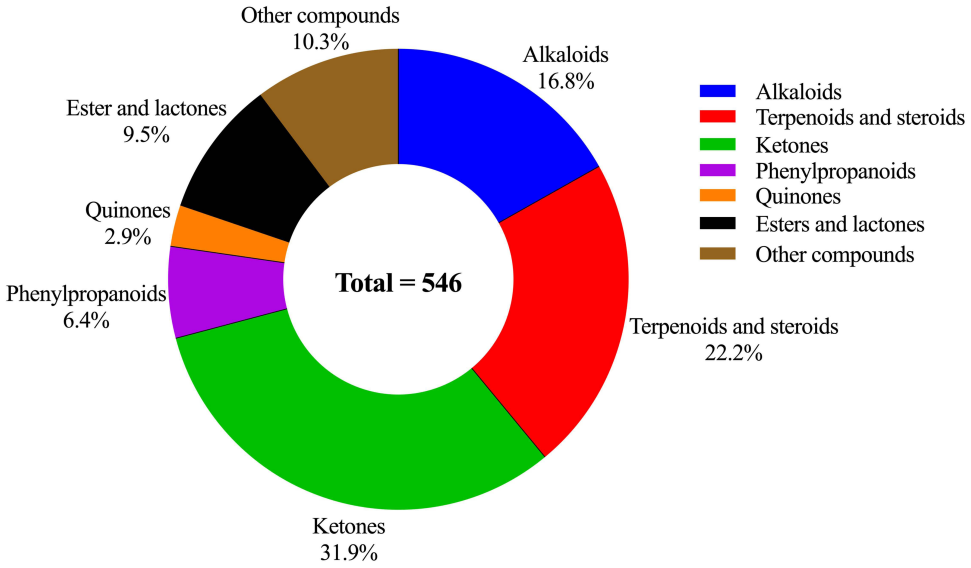
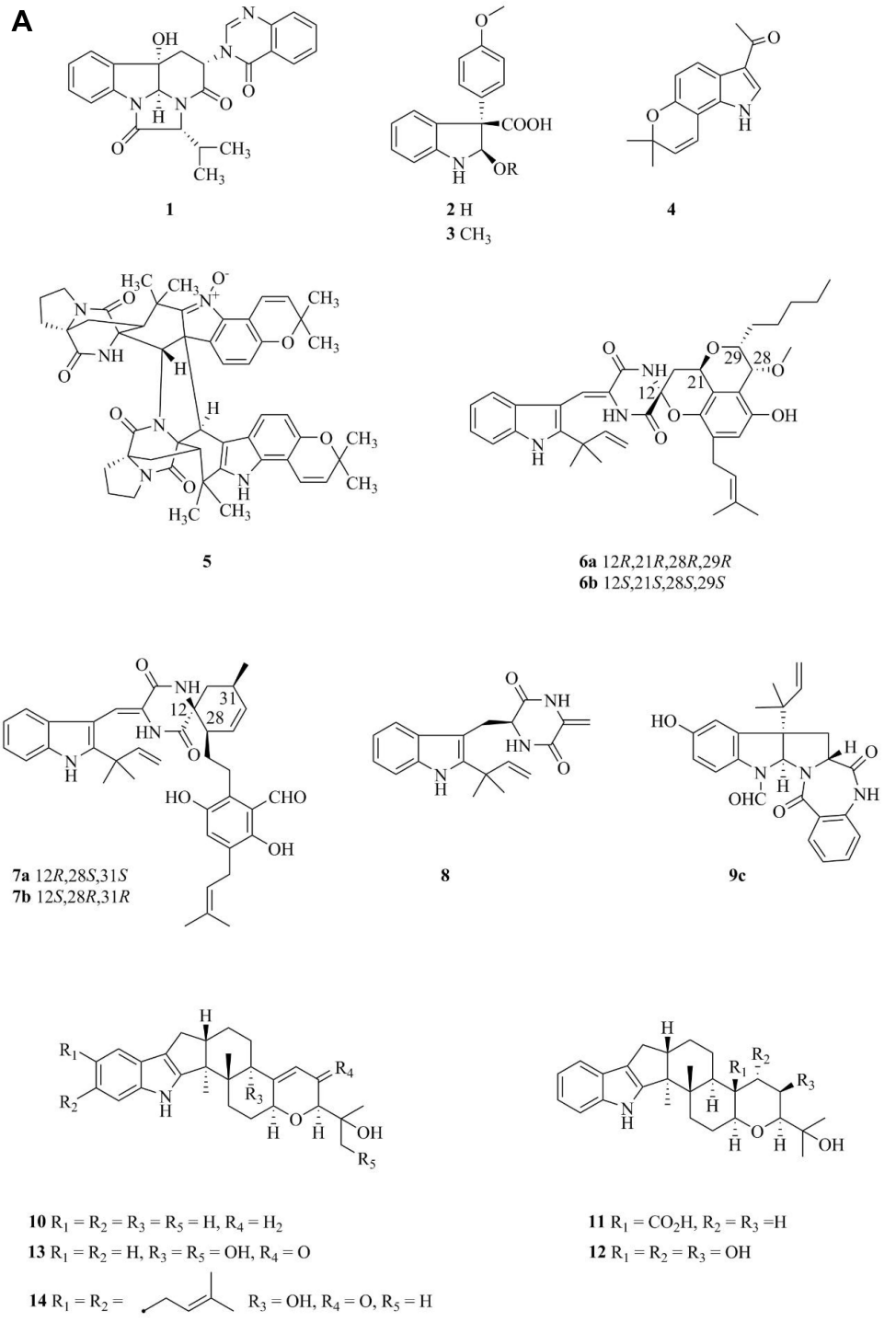


Figure 1 The percentage of various compounds.



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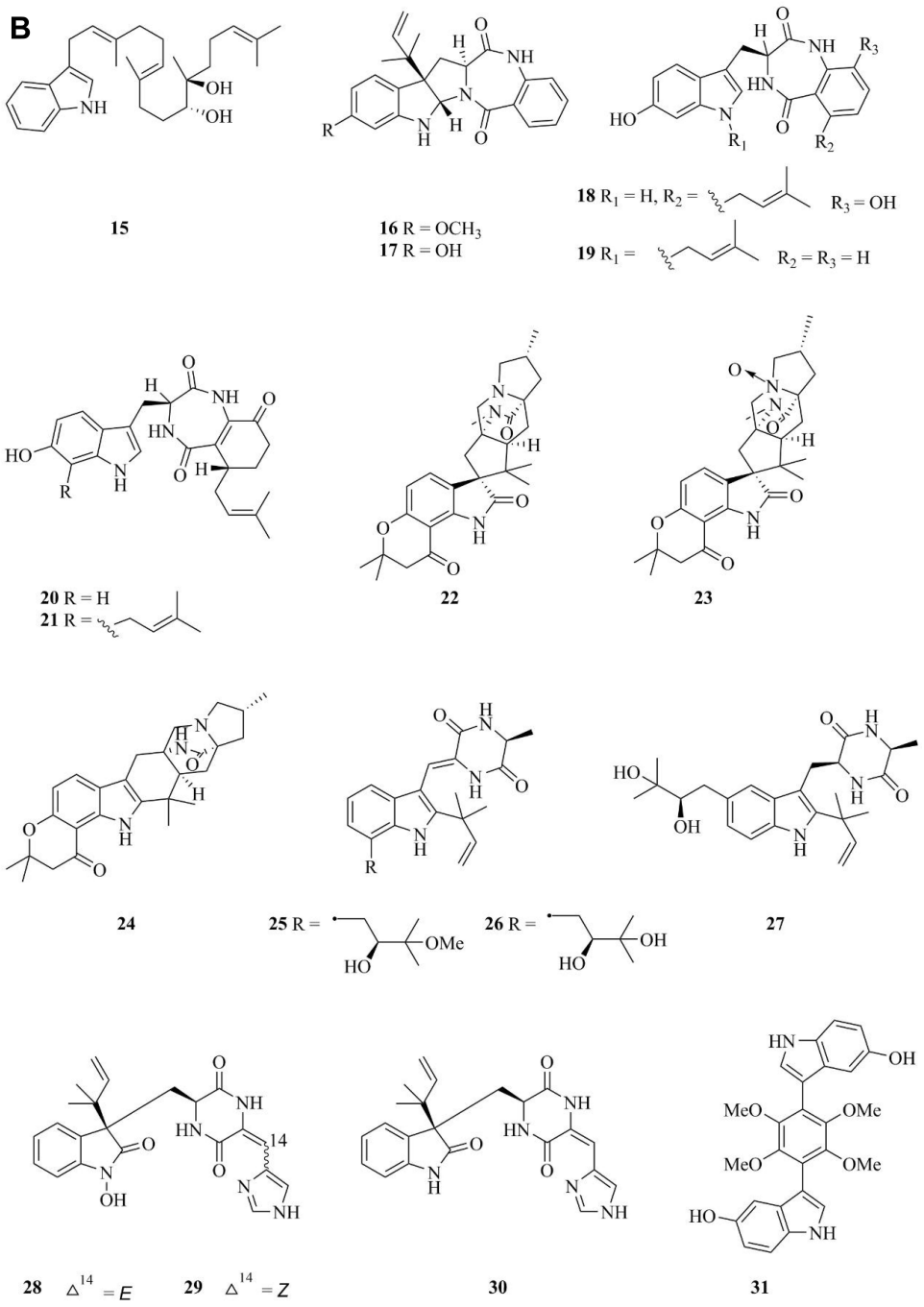
coastline, Thailand.[20] Three new indolyl diketopiperazine derivatives, penillines A **28** and B **30** (Figure 2B), isopenilline A **29** (Figure 2B), were isolated from the Antarctic soil-derived fungus *Penicillium* sp. SCSIO 05705.[21] Cultivation and fractionation of secondary metabolites from *Aspergillus kumbius* revealed a unique chemotype comprising three new bis-indolyl benzenoids, kumbicins A-C **31**–**33** (Figure 2B and C).[22] Two new bisindolylbenzenoid alkaloids asterriquinols E **34** and F **35** (Figure 2C) were isolated from the fermentation products of the fungus *Aspergillus* sp. CBS-P-2.[23] Cyclopiamines C **36** and D **37** (Figure 2C) were obtained from *Penicillium* sp. CML 3020, a fungus sourced from an



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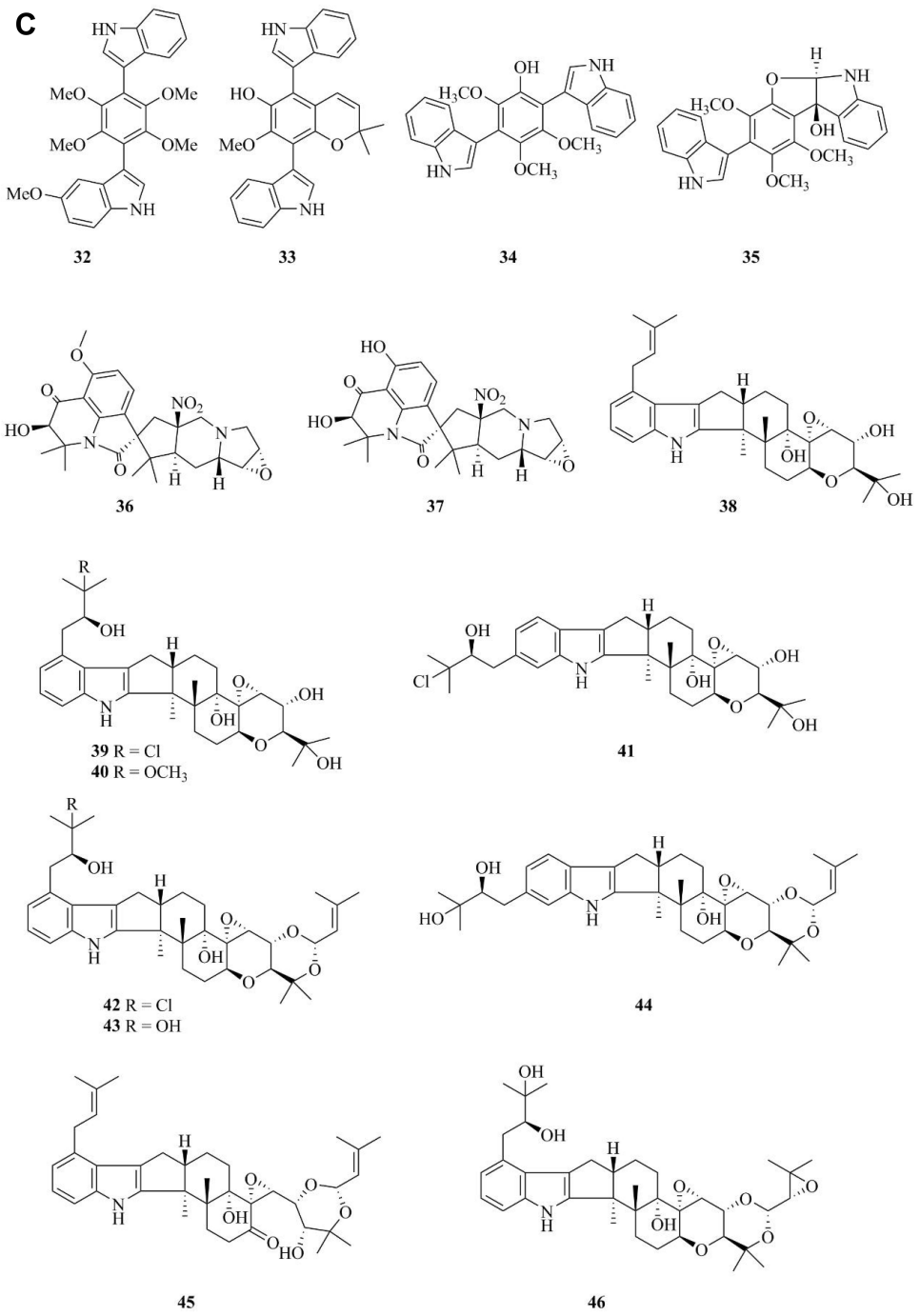
Atlantic Forest soil sample.[24] Tolypocladins A-J **38**–**47** (Figure 2C and D) have been isolated from a culture of a mine-soil-derived fungus, *Tolypocladium* sp. XL115.[25] Two novel cytochalasan alkaloids, chaetomadrasins A **48** and B **49** (Figure 2D), were isolated from the solid-state fermented culture of desert soil-derived *Chaetomium madrasense* 375.[26] Paraherquamide J **50** (Figure 2D) was isolated from the fermentation product of the fungus *Penicillium janthinellum* HK1-6.[27] Two new compounds tryptoquivalines W **51** and X **52** (Figure 2D) were isolated from a Hawaiian soil fungal strain *Aspergillus terreus* FS107.[28] Three new cytochalasins Z_{24}, Z_{25}, Z_{26} (**53**–**55**, resp.) (Figure 2D) were isolated from the fungus *Eutypella* sp. D-1 which was isolated from the soil of high latitude of the Arctic.[29] Purification of an extract from the broth of the soil fungus *Aspergillus* sp. PSU-RSPG185 resulted in the isolation of one new cytochalasin,



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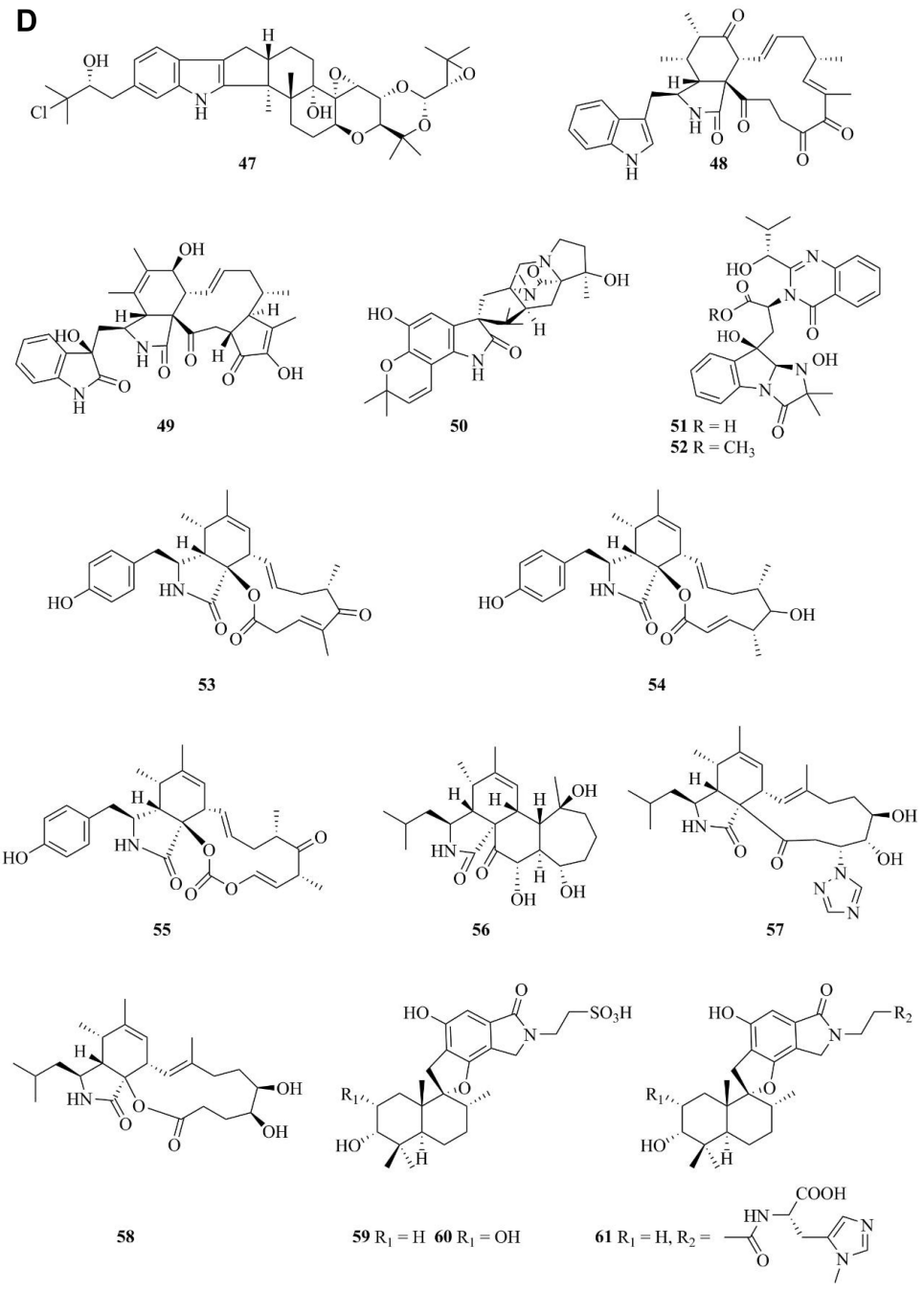
aspergilluchalasin **56** (Figure 2D).[30] Two new alkaloids, iizukines C **57** and D **58** (Figure 2D), were isolated from the culture of *Aspergillus iizukae*.[31] Chemical screening of culture medium from the soil fungus *Stachybotrys* sp. resulted in the isolation of the three new phenylspirodrimanes MBJ-0030 **59** (Figure 2D), MBJ-0031 **60** and MBJ-0032 **61** (Figure 2D).[32] Pycnidiophorones A-D **62**–**65** (Figure 2E) were isolated from cultures of the wetland-soil-derived fungus Pycnidiophora dispersa.[33] Clonorosins A **66** and B **67** (Figure 2E), two novel indole alkaloids featuring unprecedented 6/5/6/6/5 and 6/5/5 cores, were isolated from the soil-derived fungus *Clonostachys rosea* YRS-06.[34]



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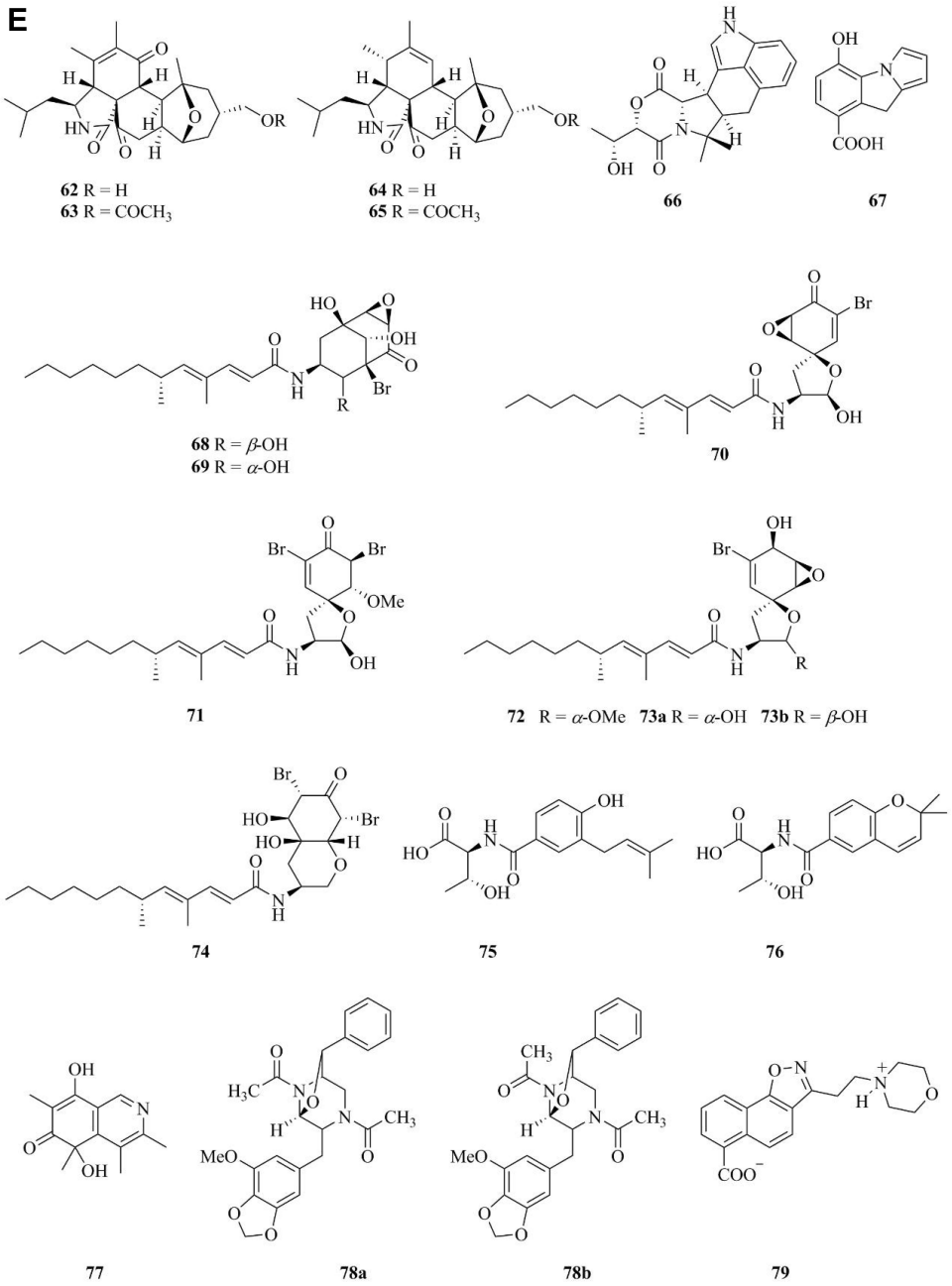
Other Alkaloids

Gymnastatins T-Y **68**–**73** (Figure 2E) and dankastatin D **74** (Figure 2E), were isolated from the soil fungus *Gymnascella dankaliensis* through fermentation on solid rice medium following addition of NaBr.[35] Two new threonine-containing metabolites, *N*-[4-hydroxy-3-prenyl-benzoyl]-L-threonine **75** (Figure 2E) and *N*-[2,2-dimethyl-2*H*-chromene- 6-carbonyl]-L-threonine **76** (Figure 2E), were isolated from the fermentation broth of the soil fungus *Curvularia inaequalis* strain HS-FG-257.[36] A new isoquinolinone alkaloid, (5*S*)-3,4,5,7-tetramethyl-5,8-dihydroxyl-6(5*H*)- isoquinolinone **77** (Figure 2E) was isolated from *Penicillium* sp. H9318.[37] Compound **78** (Figure 2E), named 3,8-Diacetyl-4-(3-methoxy-4,5-methylenedioxy)benzyl-7-phenyl-6-oxa-3,8-diazabicyclo[3.2.1]octane, was isolated from the fungus *Neosartorya*



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pseudofischeri S.W. Peterson.[10] In search for antibiotics from soil and endophytic fungi, the secondary metabolites of *Fusarium avenaceum* SF-1502. An alkaloid, fusaravenin **79** (Figure 2E), representing a new naphthoisoxazole formic acid connected with a morpholino carbon frame, the first example of a natural naphthoisoxazole type zwitter-ionic alkaloid, was characterized.[38] (–) Benzomalvins E **80** (Figure 2F) was isolated from solid cultures of a interrhizospheric fungus *Penicillium* sp. SYPF 8411.[39] A new tryptoquivaline analog, tryptoquivaline V **81** (Figure 2F) and a new brasiliamide analog, brasiliamide G **82** (Figure 2F), were isolated from the fungus *Neosartorya pseudofischeri*.[40] A new compound, talarodone A **83** (Figure 2F) in co-culture of *Talaromyces pinophilus* and *Paraphaeosphaeria* sp. isolated from soil collected in Miyazaki Prefecture, Japan.[41] One new pyrrolidine derivative, asperidine A **84** (Figure 2F), and two new piperidine derivatives, asperidines B **85** and C **86** (Figure 2F), were isolated from the soil-derived fungus *Aspergillus sclerotiorum* PSU-RSPG178. Compound **86** possessed an unprecedented 7-oxa-1-azabicyclo[3.2.1]octane

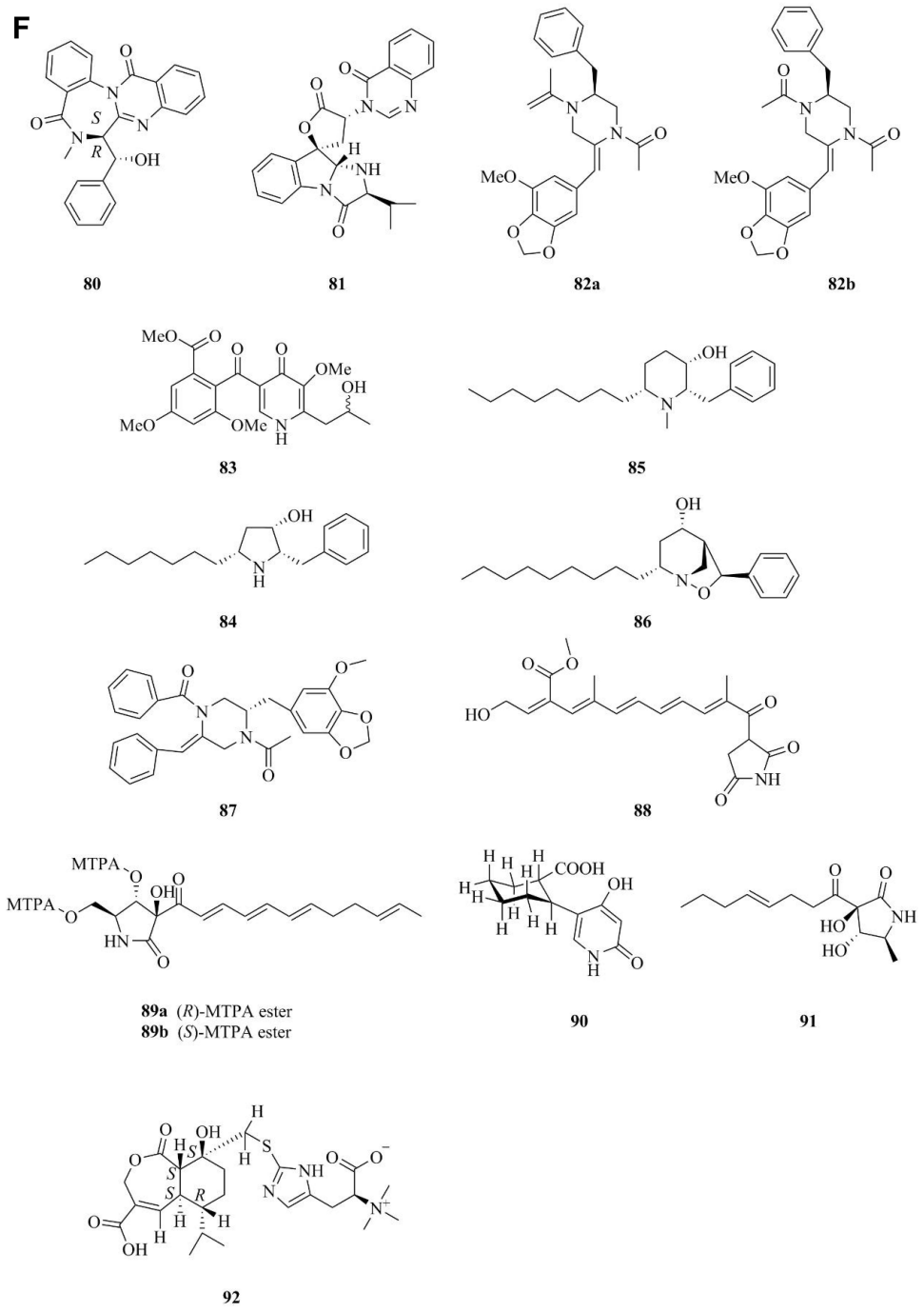


Figure 2 Alkaloids **1–92**. (**A**) Alkaloids **1–14**. (**B**) Alkaloids **15–31**. (**C**) Alkaloids **32–46**. (**D**) Alkaloids **47–61**. (**E**) Alkaloids **62–79**. (**F**) Alkaloids **80–92**.

skeleton with four chiral centers.[42] A new alkaloid, named iizukine E **87** (Figure 2F) was isolated from the culture of *Aspergillus iizukae*.[31] In order to investigate bioactive metabolites from aciduric fungi, *Aspergillus* sp. OUCMDZ-1914 was isolated from the mangrove soil in Wenchang Hainan, China. The strain was fermented under low pH and the products were extracted and the extract was purified by column chromatography over silica gel, Sephadex LH-20 and semi-preparative HPLC. The structures were identified by means of NMR, MS, UV, IR and X-ray single crystal diffraction. As a result, a new compound, methyl (2*Z*,3*E*,5*E*,7*E*,9*E*)-4,10-dimethyl-11-(2,5-dioxopyrrolidin-3-yl)-2-(2-hydroxyethylidene)-11-oxoundeca-3,5,7,9-tetraenoate **88** (Figure 2F) was obtained.[43] A new γ-lactam, virgaricin B **89** (Figure 2F), was isolated from a fermentation broth of the fungus *Virgaria boninensis* FKI-4958.[44] From this active

Paecilomyces lilacinus extract, a novel pyridone alkaloid, named Paecilomide **90** (Figure 2F), was isolated and its structure was elucidated by modern nuclear magnetic resonance techniques and mass spectrometric analyses.[45] The soil-derived fungus *Clonostachys rosea*. Fermentation of the fungus on white beans instead of rice afforded a new γ-lactam **91** (Figure 2F), named Clonostalactam.[46] A new nitrogen-containing compound, trichothioneic acid **92** (Figure 2F), was discovered from the metabolites of fungal strain *Trichoderma virens* FKI-7573.[47]

Terpenoids and Steroids

Terpenoids

Sesquiterpene

Two new drimane sesquiterpenoids, fudecadiones A **93** and B **94** (Figure 3A), were isolated from the soil fungus *Penicillium* sp. BCC 17468.[48] Two new trichothecenes, named 8*α*-hydroxyroridin H **95** and myrothecin A **96** (Figure 3A), were isolated from the fermentation broth of a halotolerant fungus *Myrothecium* sp. GS-17, which was separated from the soil sample of a salina. Among them, compound **96** represents a class of rare trichothecenes with the linkage from C-13 to C-10, missing the epoxide group normally observed at C-12, C-13.[49] Penicibilaenes A **97** and B **98** (Figure 3A) were characterized from *Penicillium bilaiae* MA-267, a fungus obtained from the rhizospheric soil of the mangrove plant *Lumnitzera racemosa*.[50] Two eremophilane sesquiterpenes, penicilleremophilanes A **99** and B **100** (Figure 3A) were isolated from the soil fungus *Penicillium copticola* PSURSPG138.[51] A new sesquiterpenoid derivative, named aspergiketone **101** (Figure 3A), was isolated from the coastal saline soil fungus *Aspergillus fumigatus*.[52] Ochraceopones A-E **102–106** (Figure 3A) were isolated from an Antarctic soil-derived fungus, *Aspergillus ochraceopetaliformis* SCSIO 05702. Ochraceopones A-D **102–105** are the first examples of *α*-pyrone merosesquiterpenoids possessing a linear tetracyclic carbon skeleton.[53] Four new 12.8-Eudesmanolides **107–110** (Figure 3A) were isolated from a mangrove rhizosphere-derived fungus *Eutypella* sp. 1–15.[54] A new acorane sesquiterpene, 3*β*-hydroxy-*β*-acorenol **111** (Figure 3A), has been discovered from the green Chinese onion-derived fungus *F.proliferatum* AF-04. and a sesquiterpenoid **112** (Figure 3A), cyclonerotriol B, was isolated from the extracts of the soil fungus *F. avenaceum* SF-1502.[38] Three new sesquiterpenes Trichodermapenes A-C **113–115** (Figure 3A) were isolated from the soil-derived fungus *Trichoderma reesei* PSU-SPSF013.[55] Chemical investigation of the *Dictyosporium digitatum* fungus resulted in the identification of three undescribed compounds **116–118** (Figure 3A). which were named Dictyosporin A **116**, Dictyosporin B **117**, Dictyosporin C **118** respectively.[56] Two new sesquiterpenes, trichocitrinovirenes A **119** and B **120** (Figure 3A), were isolated from the soil-derived fungus *Trichoderma citrinoviride* PSU-SPSF346.[57] Five new sesquiterpenoids (**121–125**) (Figure 3B), one new ophiobolin sesterterpenoid (**126**) (Figure 3B), and one new 3.5-dimethylorsellinic acid (DMOA)-based meroterpenoid (**127**) (Figure 3B), were isolated and characterized from fungus *Aspergillus calidoustus*, which was separated from the wetland soil collected at Dianchi Lake, Yunnan Province.[58]

Diterpene

A new meroditerpene sartorypyrone A **128** (Figure 3B) was isolated from the culture of the soil fungus *Neosartorya fischeri* (KUFC 6344). Interestingly, sartorypyrone A **128**, which possesses a monocyclic diterpene core.[16] Libertellenones G **129** and H **130** (Figure 3B) were isolated from the fungus *Eutypella* sp. D-1 isolated from the soil of high latitude of Arctic.[59] Compounds **131** and **132** (Figure 3B) were isolated from the fermentation broth and the mycelia of the soil fungus *Penicillium* sp. CM-7.[60] Libertellenones O-S **133–137** (Figure 3B and C), eutypellenones A **138** and B **139**, libertellenones M **140** and N **141** (Figure 3C), were isolated from the culture of *Eutypella* sp. D-1 obtained from high-latitude soil of the Arctic. Structurally, compounds **133–137** possess a cyclopropyl-fused pimarane diterpene moiety, whereas compounds **138** and **139** share an unusual cyclobutyl-fused pimarane diterpene skeleton.[61,62] Five new diterpenoid glycosides, dongtingnoids A-E **142–146** (Figure 3C), two new diterpenoid aglycones, dongtingnoids F **147** and G **148** (Figure 3C), were isolated from the fungus *Penicillium* sp. DT10, which was derived from wetland soil from Dongting Lake.[63] Tolypocladins K **149** and L **150** (Figure 3C), were isolated from the solid fermentation culture of a mine soil-derived fungus *Tolypocladium* sp. XL115.[64]

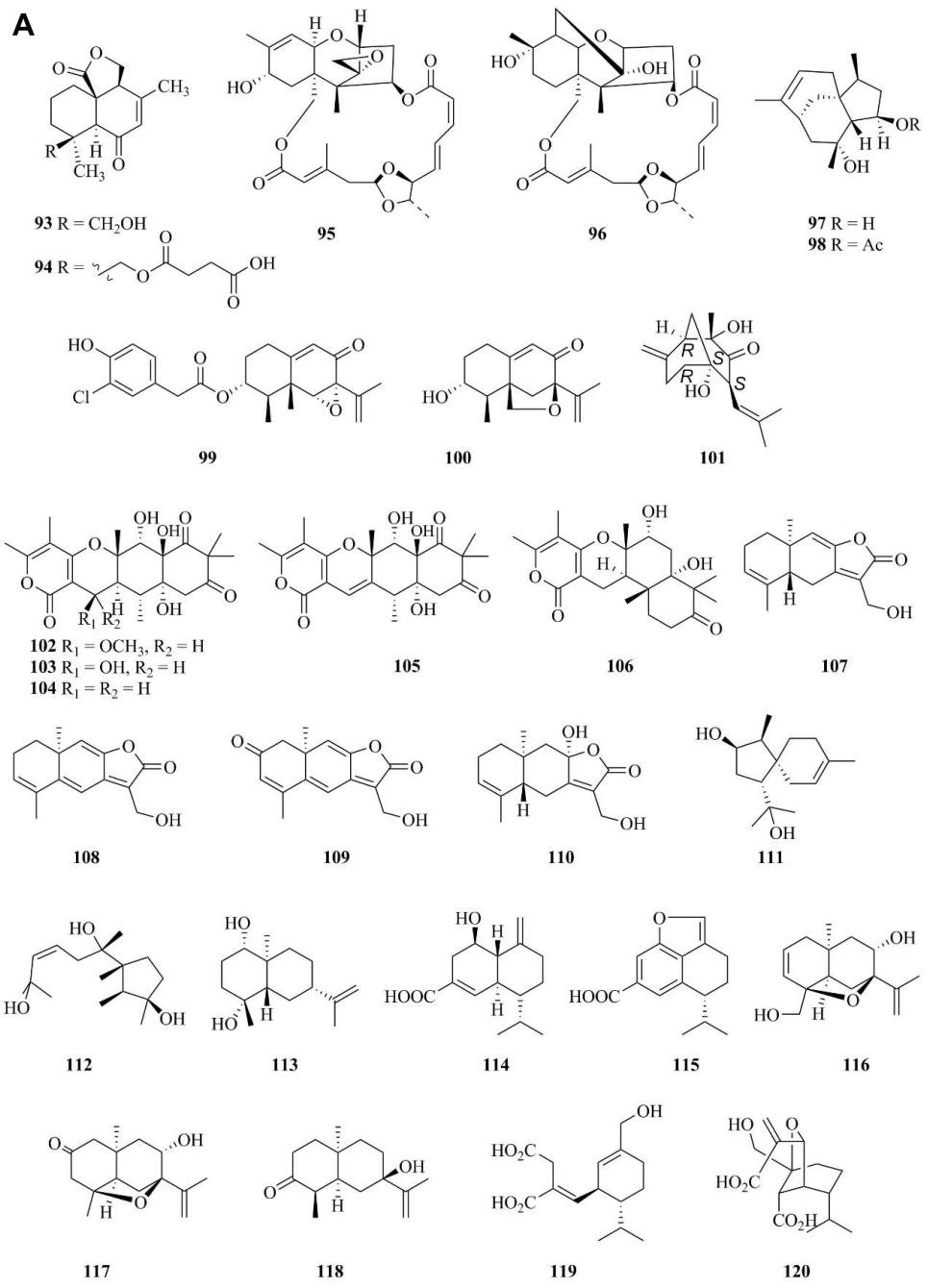
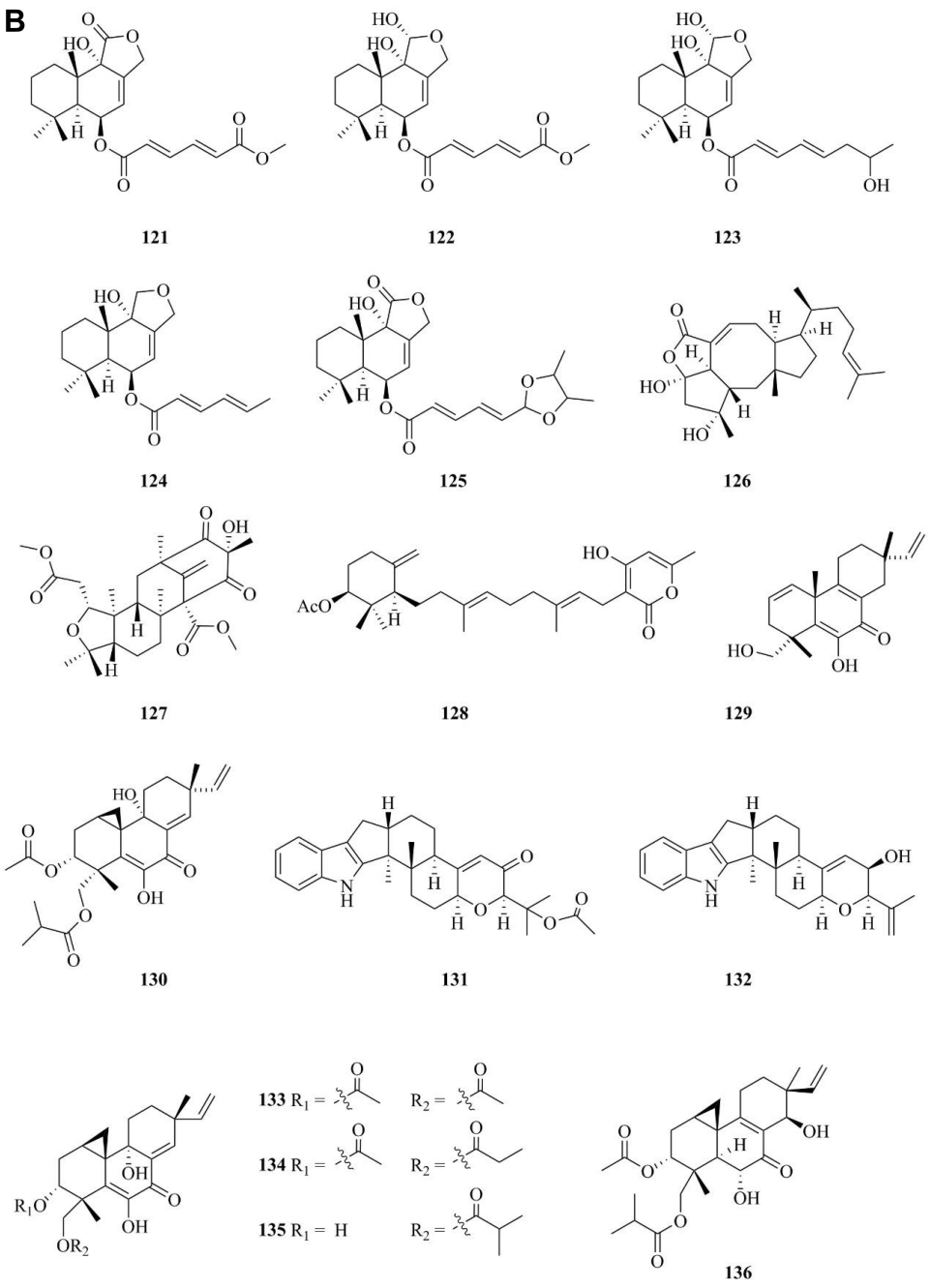


Figure 3 Continued.

Other Terpenoids

One new monoterpene named Trichodermanene **151** (Figure 3C) was isolated from the soil-derived fungus *Trichoderma reesei* PSU-SPSF013.[55] Three new meroterpenoid derivatives, 4.25-dehydrominiolutelide B **152** (Figure 3C), 4,25-dehydro-22- deoxyminiolutelide B **153** and isominiolutelide A **154** (Figure 3C), were isolated from the shaken culture of the fungus *Penicillium* sp. MA-37.[65] Purpurogenolides A-E **155–159** (Figure 3C and D), were isolated from the solid substrate fermentation cultures of the fungus *Penicillium purpurogenum* MHz 111.[66] A search for cytotoxic agents from cultures of the *Penicillium* sp., isolated from the rhizosphere soil of *Penicillium* sp., led to the isolation of four new hybrid polyketide-terpenoid metabolites **160–163** (Figure 3D).[67] Terretonin M **164** (Figure 3D), a new highly oxygenated tetracyclic meroterpenoid, was isolated from the thermophilic fungus *Aspergillus terreus* TM8.[68] Nine novel polyketide



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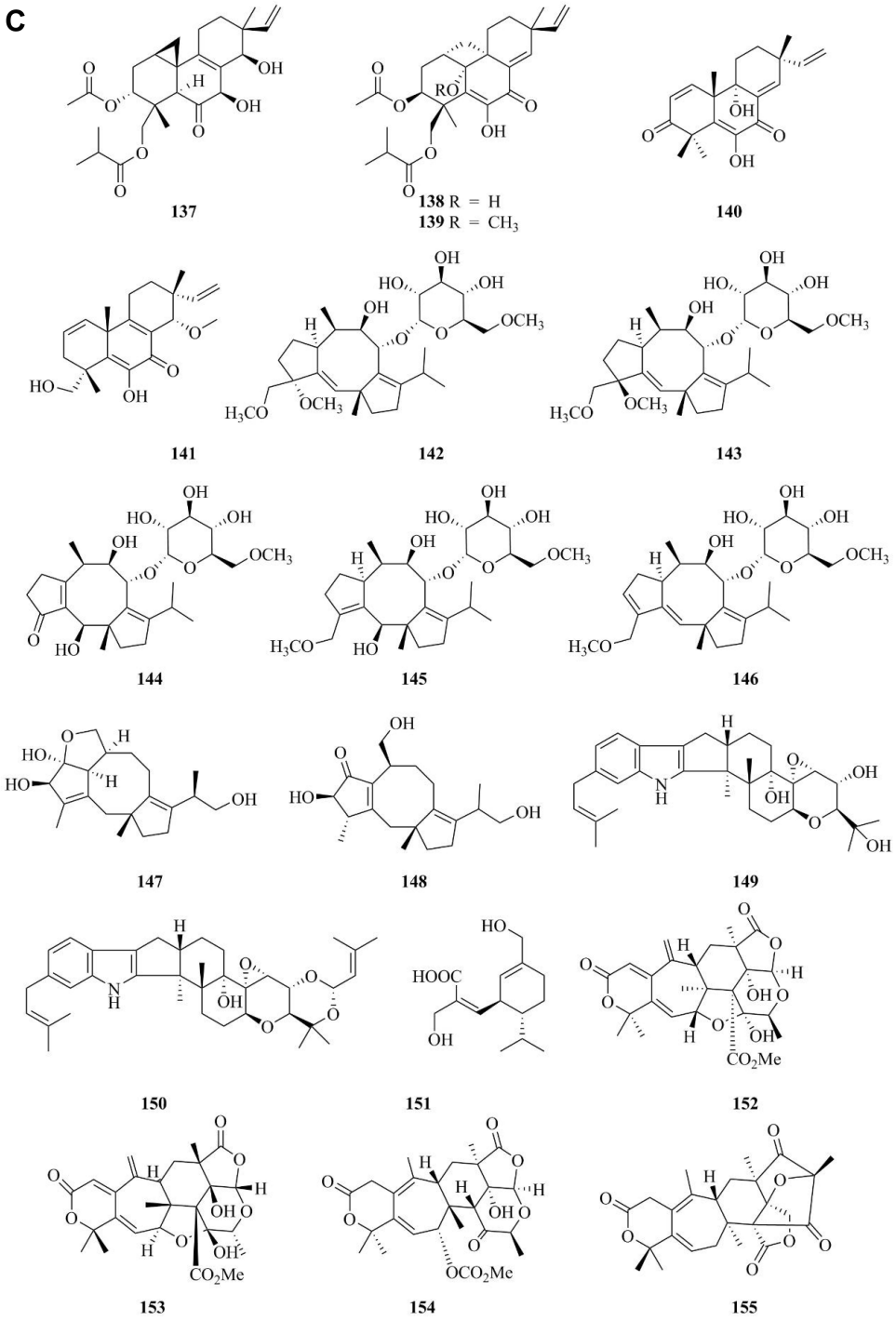
−terpenoid hybrids **165**–**173** (Figure 3D), characterized by a 1-alkylated-3,5-dihydroxyphenyl derivative coupled with a modified farnesyl pyrophosphate (FPP) unit, were isolated from a soil-derived fungus *Bipolaris zeicola*. Compound **173** represents the first example of meroterpenoid having an unusual thiazol-2(3*H*)-one moiety.[69] Four dimeric acremines, bisacremines A-D **175**–**178** (Figure 3D), with a novel carbon skeleton and a new monomer, acremine T **174** (Figure 3D), were obtained from cultures of the soil-derived fungus *Acremonium persicinum* SC0105.[5] Three dimeric acremines, bisacremines E-G **179**–**181** (Figure 3D and E), with an unusual carbon skeleton were isolated from cultures of the soil-derived fungus *Acremonium persicinum* SC0105.[70] By employing a large-scale culture approach, five undescribed compounds, namely asperanstinoids A–E **182**–**186** (Figure 3E), were obtained from fungus *Aspergillus calidoustus*, which was isolated from the wetland soil collected at Dianchi Lake, Yunnan Province.[71] Ten new meroterpenoids,



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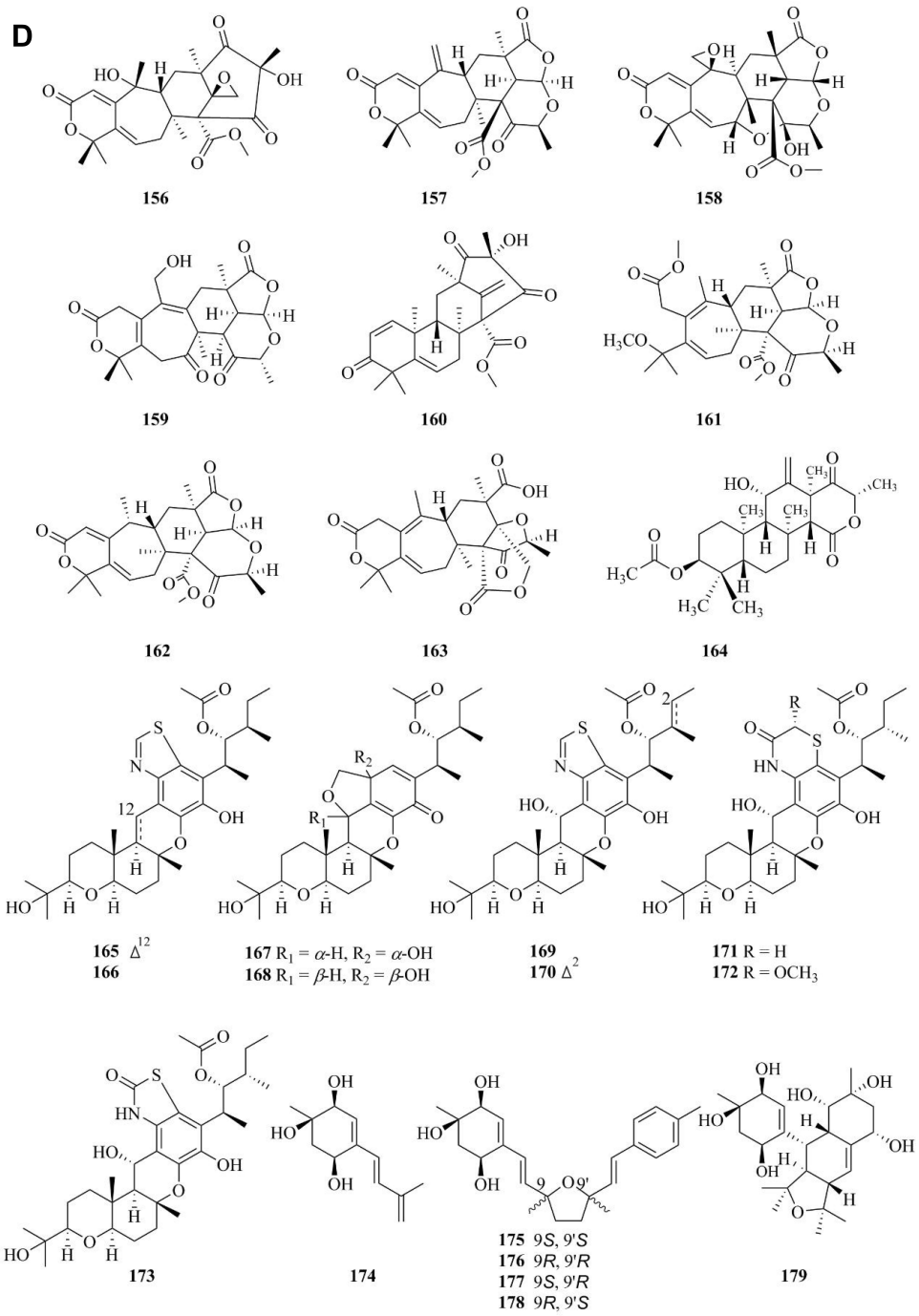
bipolaquinones A−J **187**–**196** (Figure 3E), were isolated and identified from the fermented rice cultures of a soil-derived fungus, *Bipolaris zeicola*.[72] Six new meroterpenoids, bipolarinoids A—F **197**–**202** (Figure 3E and F), were isolated from a soil-derived fungus *Bipolaris zeicola*.[73] Three nortriterpenoids aspergorakhins B–D **203**–**205** (Figure 3F) were obtained from *Aspergillus gorakhpurensis* F07ZB1707, which was fermented by a salt-containing medium.[6] Encindolenes D-H **206**–**210** (Figure 3F), were isolated from the fungus *Penicillium* sp. HFF16 from the rhizosphere soil of *Cynanchum bungei* Decne.[74]



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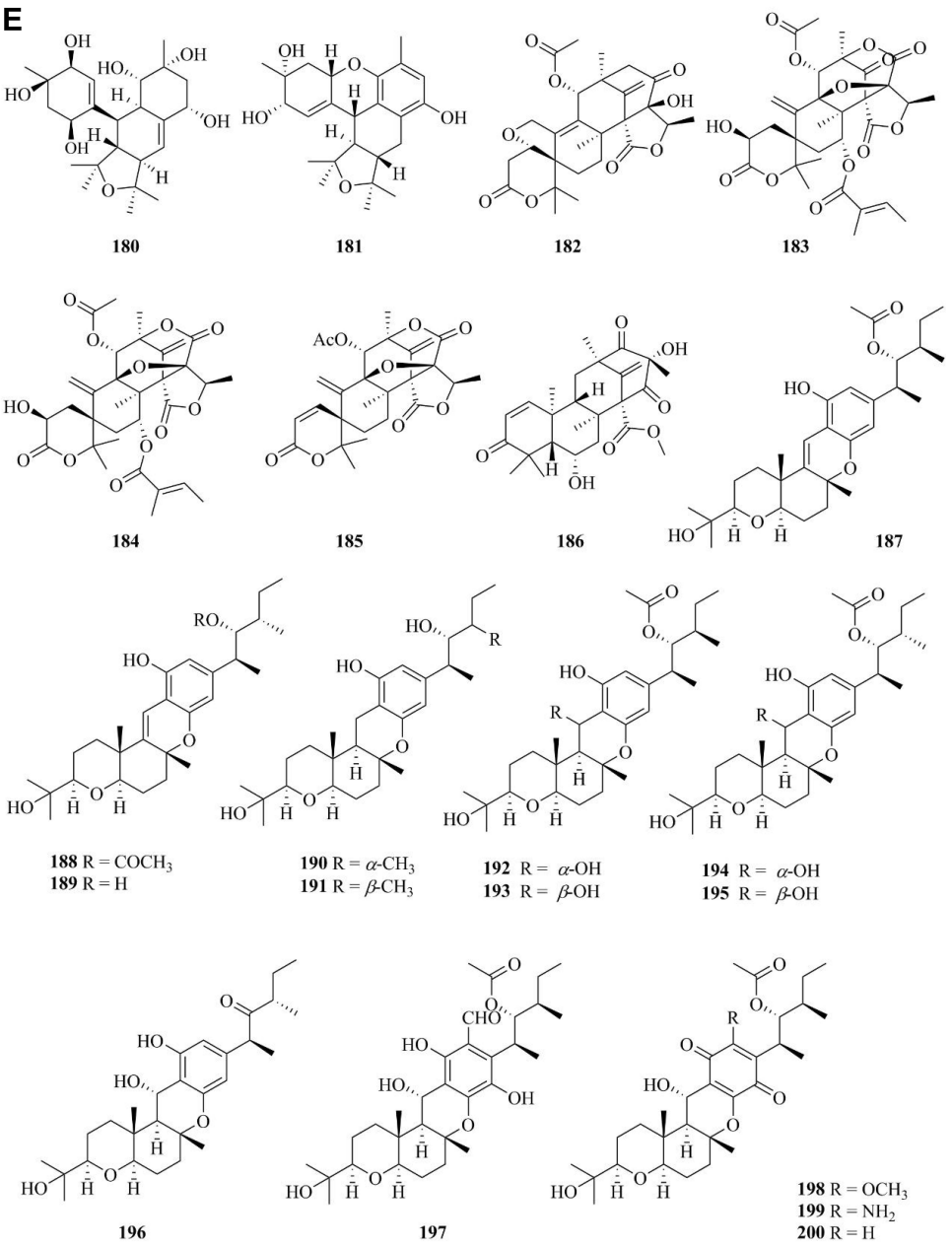
Steroids

Compound **211** (Figure 3F) was isolated from a soil fungus *Curvularia borreriae* (Pleosporaceae) strain HS-FG-237.[75] One new steroid **212** (Figure 3F) was discovered in the extract of a soil-derived fungus *Aspergillus flavus* JDW-1.[76] Aspergorakhin A **213** (Figure 3F) was obtained from the extract of soil-derived fungus *Aspergillus gorakhpurensis* F07ZB1707.[6]



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Ketones

Polyketides

A new polyketide compound **214** (Figure 4A) was characterized from the ethyl acetate extract of a soil-derived fungal strain, *Exophiala pisciphila* PHF-9.[77] Pyrenocine J **215** and pyrenochaetic acid D **216** (Figure 4A) were obtained from the fermentation broth of *Curvularia affinis* strain HS-FG-196.[78] Phytochemical investigation of the soil microfungus *Eupenicillium parvum* led to the isolation of two new compounds: a chromone derivative euparvione **217** and a new mycophenolic derivative euparvilactone **218** (Figure 4A).[79] A new polyketide penicillither **219** (Figure 4A), was isolated from the soil fungus *Penicillium* sp. PSU-RSPG9.[80] Tanzawaic acids I-L **220**–**223** (Figure 4A), were isolated from the culture filtrates of the fungal strain *Penicillium* sp. IBWF104-06 isolated from a soil sample.[81] Four new pyrenochaetic acid derivatives pyrenochaetic acids E-H **227**–**230** (Figure 4A), three new secalonic acid analogues Blennolides H-J **224**–**226** (Figure 4A) were purified from an *Alternaria* sp. isolate obtained from a Hawaiian soil sample.[82] Three new

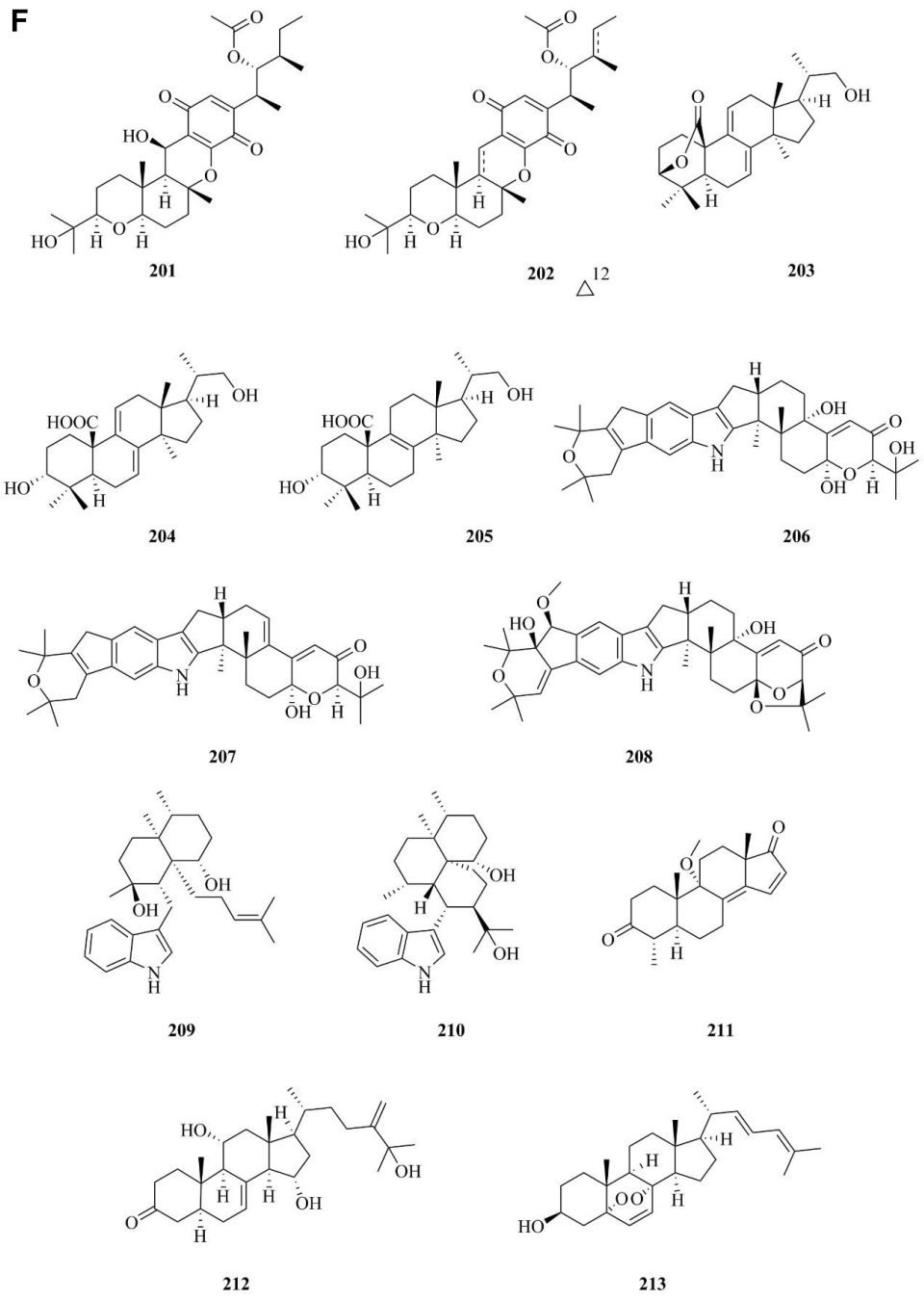
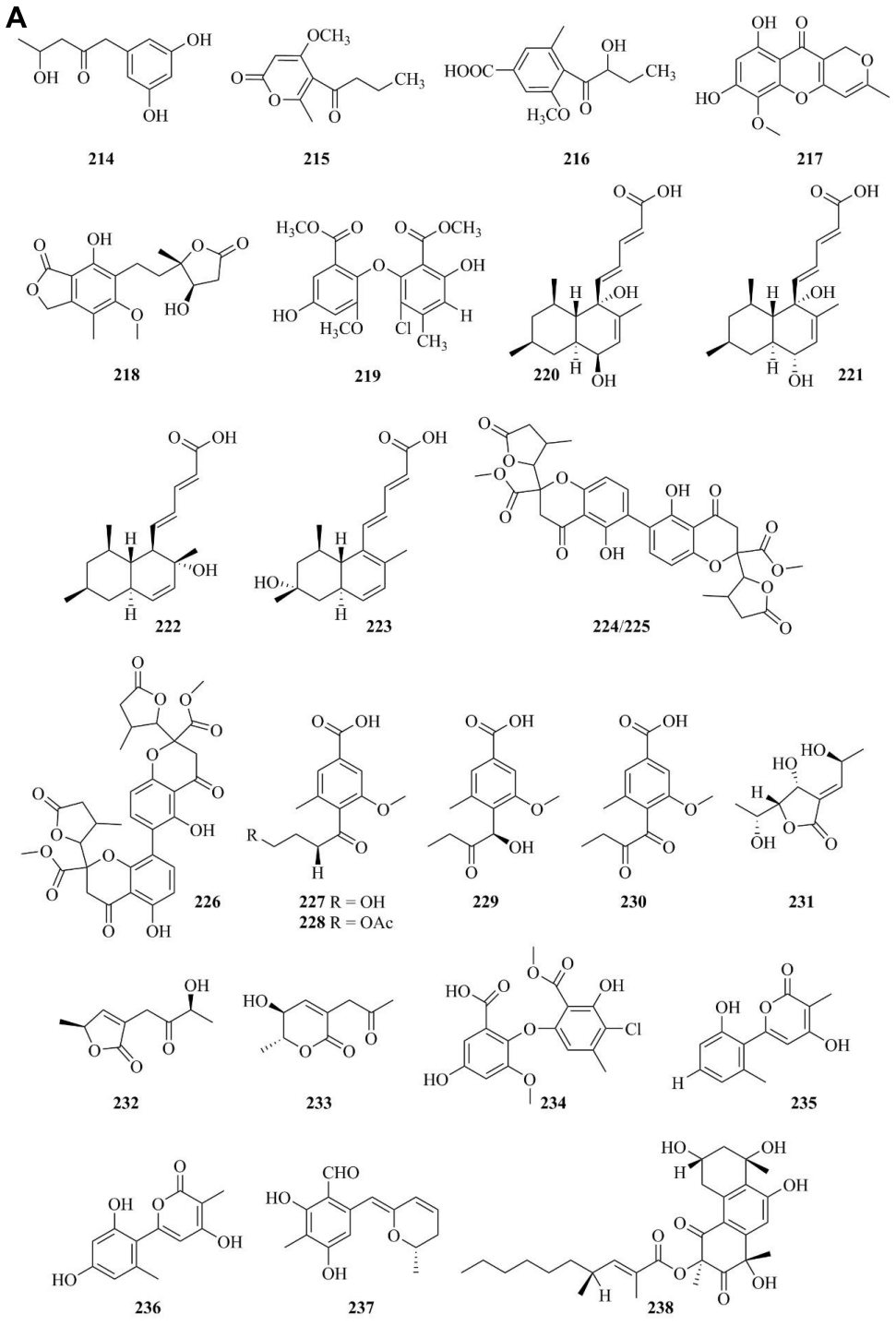


Figure 3 Terpenoids and steroids **93–213**. (**A**) Terpenoids **93–120**. (**B**) Terpenoids **121–136**. (**C**) Terpenoids **137–155**. (**D**) Terpenoids **156–179**. (**E**) Terpenoids **180–200**. (**F**) Terpenoids and steroids **201–213**.

polyketides, namely, asperochrins A-C **231**–**233** (Figure 4A), were isolated from *Aspergillus ochraceus* MA-15, a fungus obtained from the rhizospheric soil of marine mangrove plant *Bruguiera gymnorrhiza*.[83] A new diphenyl derivative, named iizukine A **234** (Figure 4A) was isolated from coastal saline soil-derived fungus *Aspergillus iizukae*.[84] Three new pyran rings containing polyketides, penicipyrans A-B **235**–**236** (Figure 4A), and penicipyran E **237** (Figure 4A) were isolated from the saline soil-derived *Penicillium raistrickii*.[85] Cultivation of the mangrove rhizosphere soil-derived fungus *Penicillium janthinellum* HK1-6 with NaBr led to the isolation of two new tricyclic polyketides, penijanthinones A **238** (Figure 4A) and B **239** (Figure 4B).[86] Two novel oxaphenalenone dimers, talaroketals A **240** and B **241** (Figure 4B), were isolated from the soil fungus *Talaromyces stipitatus*. Compound **240** features a rare benzannulated



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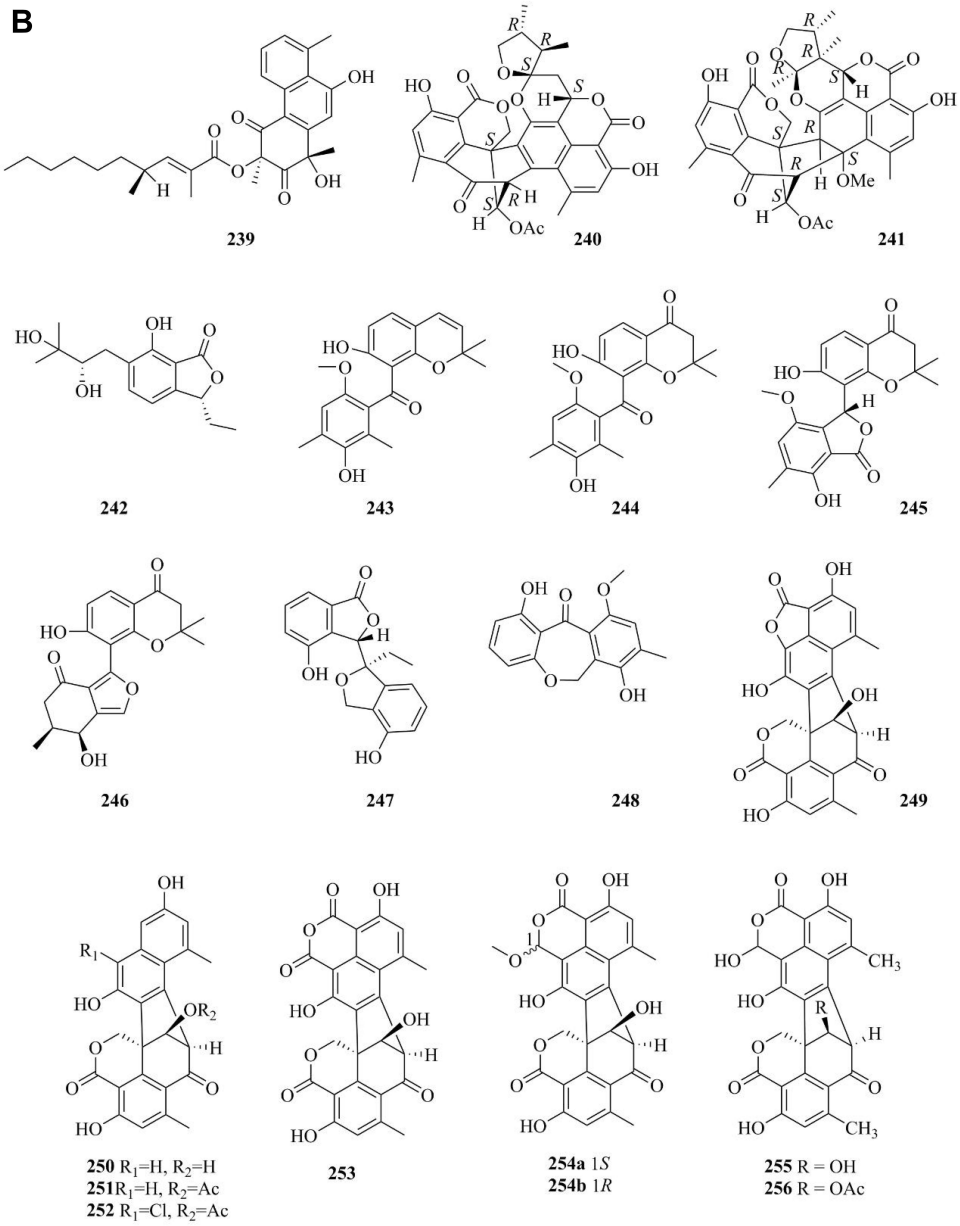
5.6-spiroketal ring system within the dimeric bis(oxaphenalenone) skeleton, while the parent compound **241** harbors a fused bicyclic furano-pyran moiety.[87] Aspergorakhins E–J, L (**242–247, 248**) (Figure 4B) were obtained from the extract of soil-derived fungus *Aspergillus gorakhpurensis* F07ZB1707.[6] Six new polyketide-derived oxaphenalenone dimers, talaromycesone C **249** and macrosporusones A-E **250–254** (Figure 4B), were isolated from the mycelium of the fungus *Talaromyces macrosporus* KKU-1NK8.[88] Four new oxaphenalenone dimers (bacillisporins I **255** and J **256** (Figure 4B), duclauxamides B **257** and C **258** (Figure 4C)) were isolated from the soil fungus *Talaromyces bacillisporus* BCC17645.



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Duclauxamides B and C were the rare *N*-containing oxaphenalenone dimers isolated from this fungus.[89] New polyketide-derived oligophenalenone dimers, 9a-*epi*-bacillisporin E **259** and bacillisporins F-H **260**–**263** (Figure 4C), were isolated from the fungus *Talaromyces stipitatus*.[90] A new chromanone derivative Aspergone **264** (Figure 4C) was isolated from *Aspergillus* sp. SCSIO41002.[91] A novel compound 7-methoxy-2,2-dimethyl-4-octa-4′,6′-dienyl-2*H*-napthalene-1-one **265** (Figure 4C) was isolated from *Penicillium* sp.[92] Aspereusins C-E **266**–**268** (Figure 4C) were obtained from the fermentation product of *Aspergillus terreus* YIM PH30711.[93]

Flavones

One new xanthone, penicillixanthone **269** (Figure 4C), was isolated from the soil fungus *Penicillium* sp. PSU-RSPG9.[80] Castochrin **270** (Figure 4C), a new dimer of sulochrin linked by thioether bonds and a new secalonic acid analogues (–)-Blennolide G **271** (Figure 4C) were purified from an *Alternaria* sp. isolate obtained from a Hawaiian soil sample.[82] One new xanthone, penicillone C **272** (Figure 4C), is isolated from the soil fungus *Penicillium citrinum* PSU-RSPG95.[94]

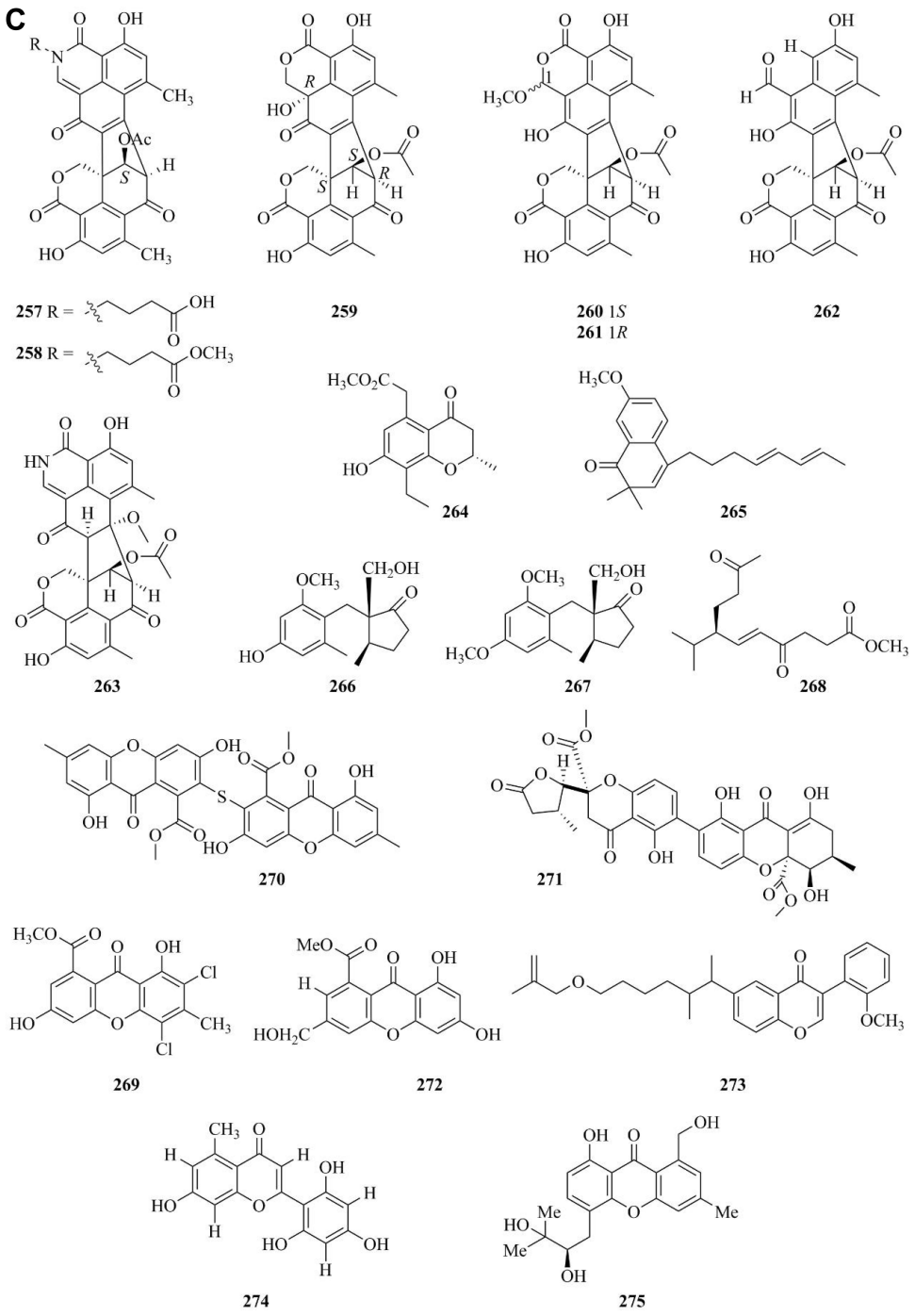
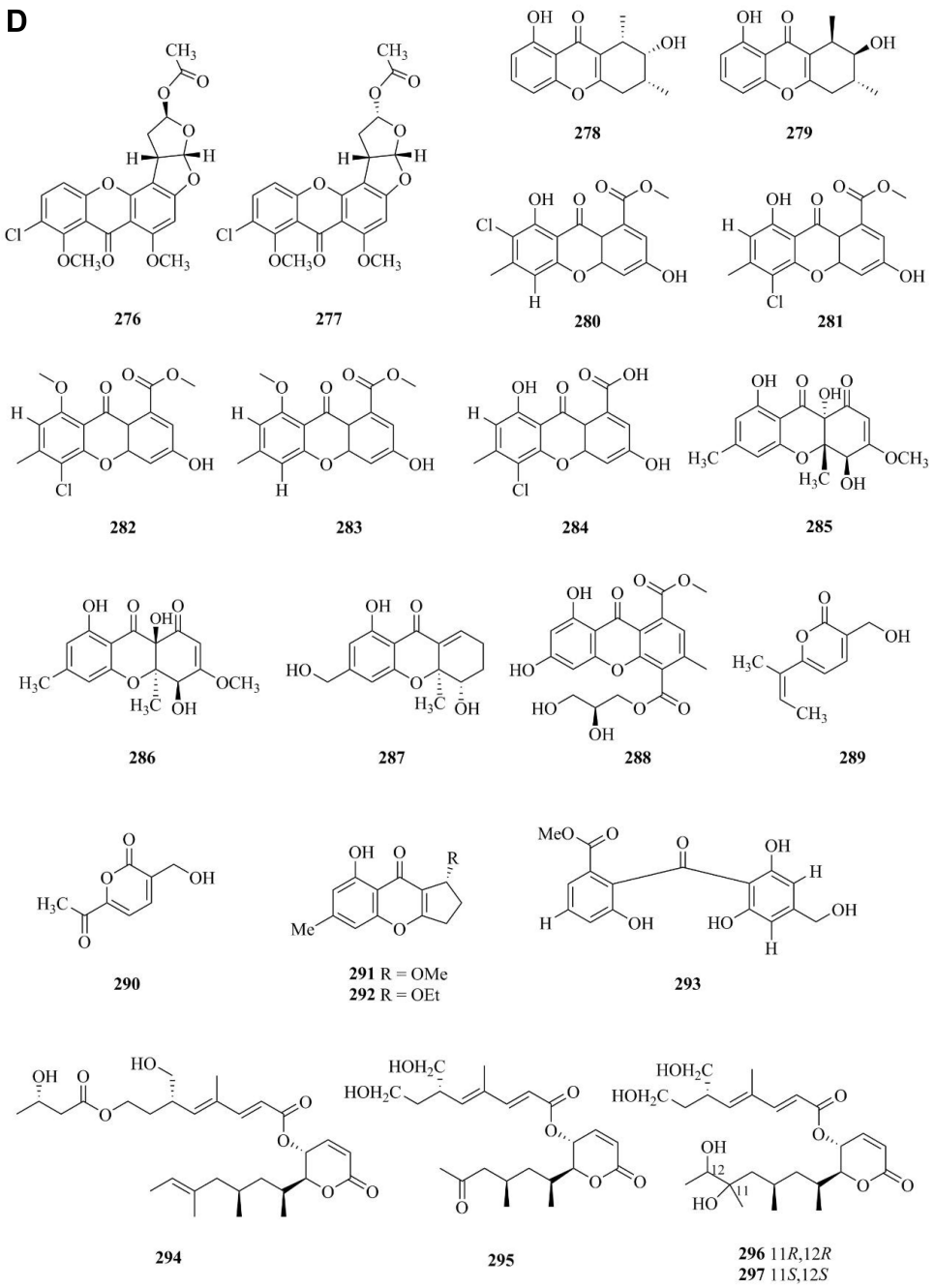


Figure 4 Continued.

Compound **273** (Figure 4C) was found from the fermentation product of *Penicillium* sp., HT-28 by various spectroscopic techniques.[95] In order to investigate new bioactive compounds, a piece of fungi *Aspergillus aculeatus* was obtained from the Jinyun mountain soil in Chongqing, China. A new compound 2-(2',4',6'-Trihydroxyphenyl)-(7-hydroxy-5-methyl) chromone **274** (Figure 4C) was obtained.[96] A new xanthone (penicillanthone, **275**) (Figure 4C) was isolated from the soil-derived fungus *Penicillium aculeatum* PSU-RSPG105.[97] Two new sterigmatocystin derivatives, oxisterigmatocystins E **276** and F **277** (Figure 4D), were isolated from the fungus *Botryotrichum piluliferum*.[98] Penixanthones A **278** and B **279** (Figure 4D), were isolated from the ethyl acetate extract of a culture of the fungus *Penicillium* sp. SYFz-1.[99] Five



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new **280**–**284** (Figure 4D) xanthones were isolated from the coastal saline soil-derived *Aspergillus iizukae* by application of an OSMAC (one strain many compounds) approach.[100] Three new blennolide derivatives, blennolides L-N **285**–**287** (Figure 4D), were isolated from the soil-derived fungus *Trichoderma asperellum* PSU-PSF14.[101] A new metabolite, wentixanthone A **288** (Figure 4D), was obtained from the fungus *Aspergillus wentii*, isolated from soil of the hypersaline lake El Hamra in Wadi El-Natrun, Egypt.[102]

Other ketones

Fusarpyrones A **289** and B **290** (Figure 4D), two new pyrone derivatives, were isolated from the soil fungus *Fusarium solani* PSU-RSPG37.[103] Two new benzopyranones, named coniochaetones E **291** and F **292** (Figure 4D), and one new

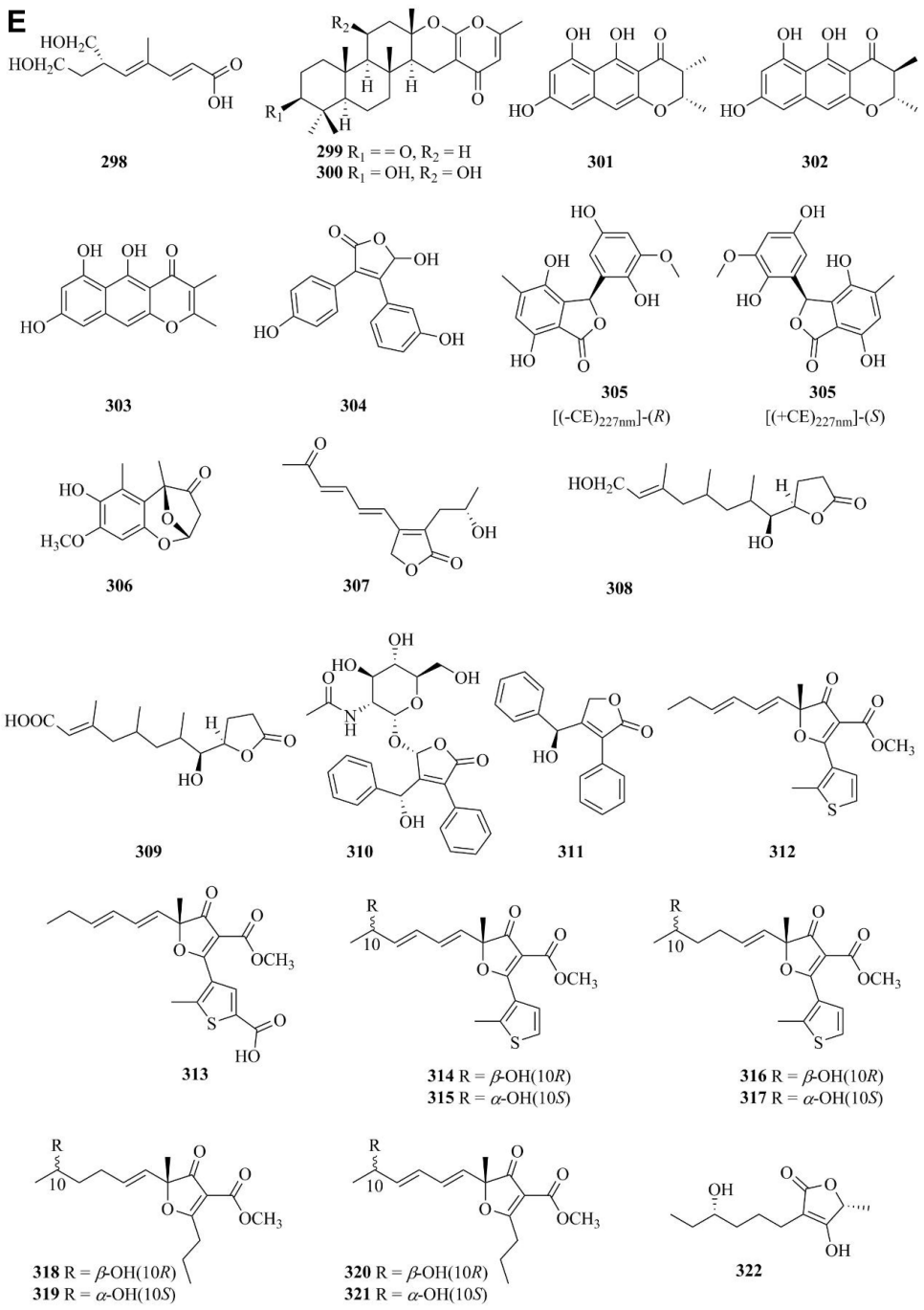
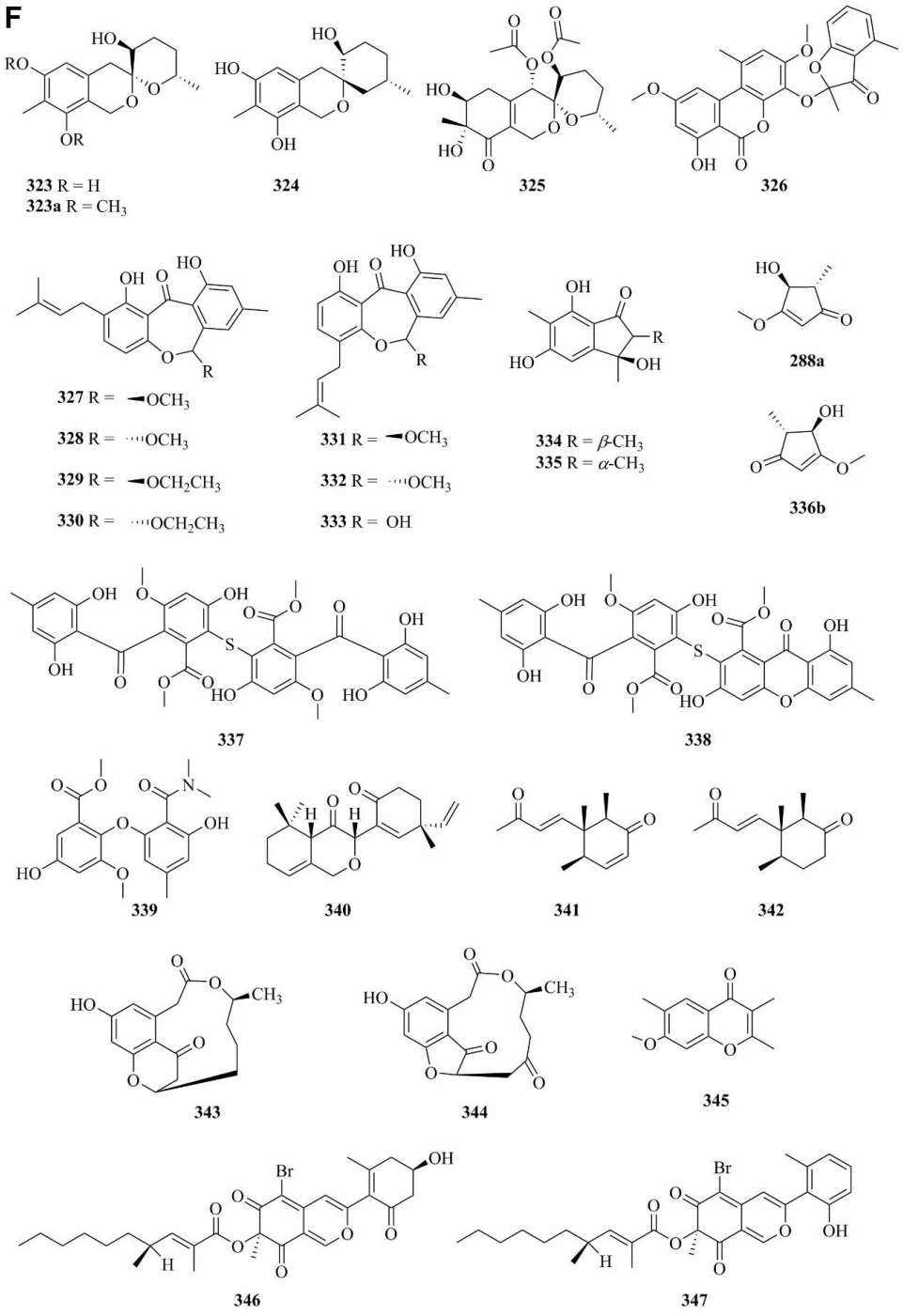


Figure 4 Continued.

benzophenone, penicillanone **293** (Figure 4D), are isolated from the soil fungus *Penicillium citrinum* PSU-RSPG95.[94] Five new secondary metabolites **294**–**297** (Figure 4D) and **298** (Figure 4E) of *Cephalotrichum microsporum* were isolated, which were described, respectively, as 8′-*O*-(3*R*-Hydroxy-butyryl)-rasfonin **294**, Cemironin A **295**, Cemironin B **296**, Cemironin C **297**, 4-Methyl-8,10-dihydroxy-caprylic acid **298**.[104] Two new meroditerpene pyrones, chevalone F **299** and 11-hydroxychevalone E **300** (Figure 4E), were isolated from the fungus *Neosartorya pseudofischeri*.[40] Peninaphones A-C **301**–**303** (Figure 4E), were isolated from mangrove rhizosphere soil-derived fungus *Penicillium* sp. HK1-22.[105] The fungus, *Aspergillus nidulans* BF0142, was isolated from hot spring-derived soil collected at Hell Valley in Noboribetsu, Hokkaido, Japan. A new furanone compound designated helvafuranone **304** (Figure 4E) was isolated from a culture broth of *A. nidulans*



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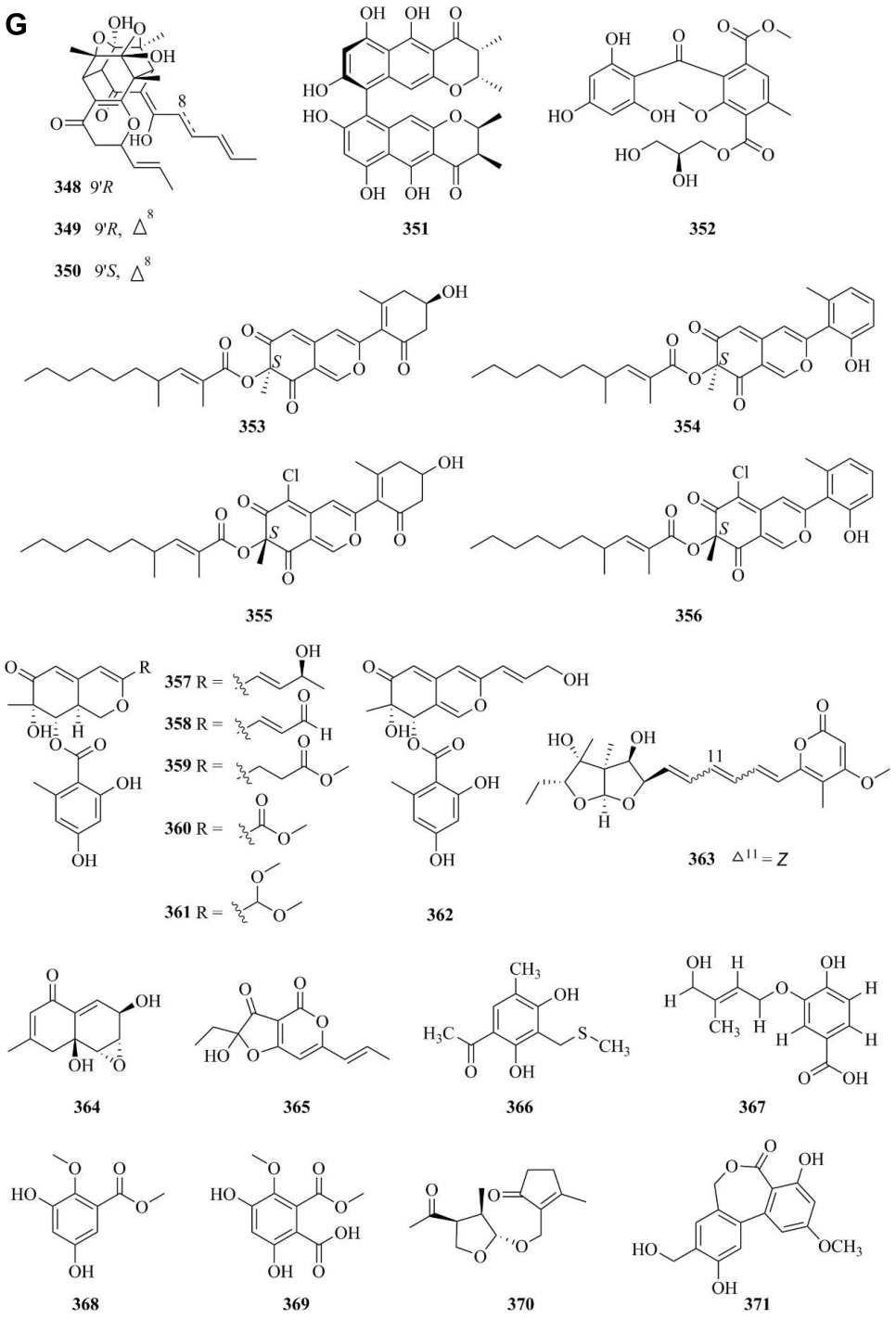
BF0142.[106] Enantiomers of a 2-benzofuran-1(3*H*)-one derivative [(–)-1 and (+)-1] described as (±)-europhenol A **305** (Figure 4E), was isolated and identified from the culture extract of *Eurotium rubrum* MA–150, a fungus obtained from the mangrove-derived rhizospheric soil.[107] Chromatographic separation of the broth extract of the soil-derived fungus *Aspergillus sclerotiorum* PSURSPG178 resulted in isolation of a furanone derivative, aspersclerotiorone E **306** (Figure 4E).[108] Three new secondary metabolites identified as harzianone **307** (Figure 4E), harzianol **308** (Figure 4E), harzianol acid **309** (Figure 4E) were isolated from a culture of *Cephalotrichum microsporum*.[109] Two new aromatic butenolides, gotjawaside **310** and gotjawalide **311** (Figure 4E), possessing the 4-benzyl-3-phenylbutenolide motif, were isolated from a soil ascomycete



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Auxarthron sp. KCB15F070.[110] Ten novel furancarboxylic acids including four pairs of epimers (**314, 315; 316, 317; 318, 319; 320, 321**) (Figure 4E), were isolated from the fermentation of the soil-derived fungus *Penicillium* sp. sb62. Compounds **312**–**317** represent the first class of natural furancarboxylic acids featuring a thiophene moiety.[111] We present a new furanone derivative from a white, woolly and fast-growing soil fungus, *Penicillium* sp. FG9RK, isolated from a soil sample collected from Agulu in Anambra state, Nigeria. The compound was identified as a new natural product, *R*-hexitronic acid **322** (Figure 4E).[112] Three new compounds, named peneciraistins A-C **323**–**325** (Figure 4F), were isolated from saline soil-derived

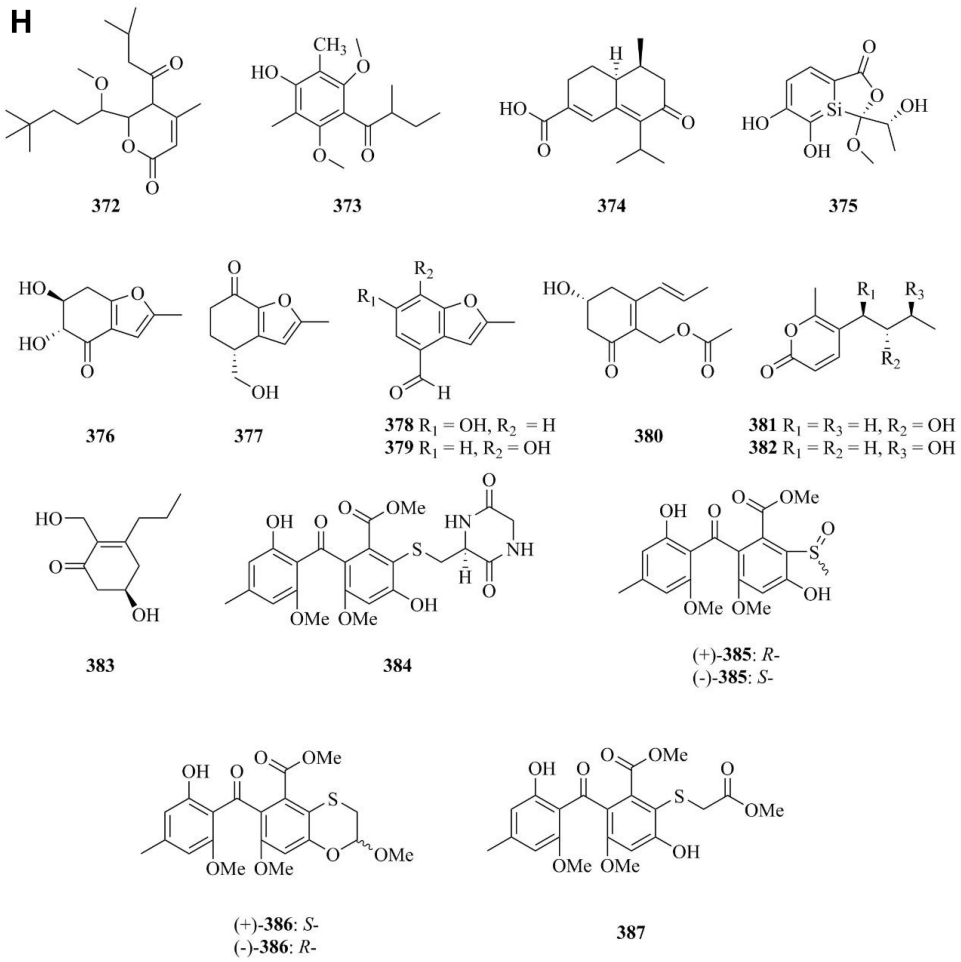


Figure 4 Ketones **214–387**. (**A**) Ketones **214–238**. (**B**) Ketones **239–256**. (**C**) Ketones **257–275**. (**D**) Ketones **276–297**. (**E**) Ketones **298–322**. (**F**) Ketones **323–347**. (**G**) Ketones **348–371**. (**H**) Ketones **372–387**.

fungus *Penicillium raistrickii*. Among them, compounds **323** and **324** are rare benzannulate 6.6-spitoketals.[11] Sporulosol **326** (Figure 4F), a new ketal, has been isolated from the liquid fermentation cultures of a wetland-soil-derived fungus, *Paraconiothyrium sporulosum*.[113] Three pairs of new isopentenyl dibenzo[b, e]oxepinone enantiomers, (+)-(5*S*)-arugosin K **327**, (-)-(5*R*)-arugosin K **328**, (+)-(5*S*)-arugosin L **329**, (-)-(5*R*)-arugosin L **330**, (+)-(5*S*)-arugosin M **331**, (-)-(5*R*)-arugosin M **332**, and a new isopentenyl dibenzo[*b, e*]oxepinone, arugosin N **333** (Figure 4F), were isolated from a wetland soil-derived fungus *Talaromyces flavus*.[114] Two new indanones, asperunguisones A **334** and B **335** (Figure 4F), were isolated from the soil-derived fungus *Aspergillus unguis* PSU-RSPG204.[115] A pair of enantiomeric cyclopentenones (**336a** new and **336b** new natural) were isolated from *Aspergillus sclerotiorum*.[116] Polluxochrin **337** and dioschrin **338** (Figure 4F), two new dimers of sulochrin linked by thioether bonds, and an additional new asterric acid analogue Dimethylamide asterrate **339** (Figure 4F), were purified from an *Alternaria* sp. isolate obtained from a Hawaiian soil sample.[82] Two new cyclohexanone derivatives, nectriatones A **340** and B **341** (Figure 4F), and one new natural product, nectriatone C **342** (Figure 4F), were isolated from the culture of *Nectria* sp. B-13 obtained from high-latitude soil of the Arctic.[117] Two new curvularin derivatives, curvulopyran **343** and *ent*-curvulone A **344** (Figure 4F), were isolated from a culture broth of the soil-derived fungus *Aspergillus polyporicola* PSU-RSPG187.[118] 7-methoxy-2,3,6-trimethylchromone **345** was obtained from the ethyl acetate extract of a soil-derived fungal strain, *Exophiala pisciphila* PHF-9.[77] Cultivation of the mangrove rhizosphere soil-derived fungus *Penicillium janthinellum* HK1-6 with NaBr led to the isolation of two new brominated azaphilones, penicilones G **346** and H **347** (Figure 4F).[86] As part of the ongoing search for antibiotics from fungi obtained from soil samples, the secondary metabolites of *Clonostachys rosea* YRS-06 were investigated. Through efficient bioassay-guided isolation, three new bisorbicillinoids

possessing open-ended cage structures, tetrahydrotrichodimer ether **348** (Figure 4G) and dihydrotrichodimer ether A **349** and B **350** (Figure 4G), were obtained. Compounds **348–350** are rare bisorbicillinoids with a γ-pyrone moiety.[119] Isochaetomium A_2 **351** (Figure 4G), a new bis(naphthodihydropyran-4-one), was isolated from the solid-state fermented rice culture of *Chaetomium microcephalum*.[120] Wentiphenone A **352** (Figure 4G), was obtained from the fungus *Aspergillus wentii*.[102] Four new azaphilones, penicilones A-D **353–356** (Figure 4G), were isolated from the mangrove rhizosphere soil-derived fungus *Penicillium janthinellum* HK1-6.[121] Six new azaphilone derivatives, talaraculones A-F **357–362** (Figure 4G), were obtained from the saline soil-derived fungus *Talaromyces aculeatus*.[122] One new double bond isomer of asteltoxin, isoasteltoxin **363** (Figure 4G), were isolated from an Antarctic soil-derived fungus, *Aspergillus ochraceopetaliformis* SCSIO 05702.[53] Pang et al found curvularone A **364** and 4-hydroxyradianthin **365** (Figure 4G) from *Curvularia inaequalis* strain HS-FG-257.[123] A new compound 1-(2′,4′-dihydroxy-5′-methyl-3′-methylsulfanylmethylphenyl)-ethanone **366** (Figure 4G) was isolated from the ethyl acetate extract of the fermentation broth of the fungus *Penicillium crustosum* YN-HT-15 isolated from the red soil in Yunnan Province, China.[124] A new compound (*E*)-4-hydroxy-3-[(4-hydroxy-3-methylbut-2-en-1-yl)oxy] benzoic acid **367** (Figure 4G) was obtained from *Aspergillus aculeatus*.[96] Two new metabolites, talaflavuols B **368** and C **369** (Figure 4G) were isolated from the wetland soil-derived fungus *Talaromyces flavus* BYD07-13.[125] Aspereusin B **370** (Figure 4G) was isolated from the culture of *Aspergillus terreus* YIM PH30711.[93] Compounds Pyrenochaetayu **371** and compound Galinsogisoliyu **372** (Figure 4G and H) were successfully separated from the fermentation broth of *Seltsamia galinsogisoli* sp. nov.[126] A novel compound 1-(4-hydroxy-2,6-dimethoxy-3,5-dimethylphenyl)-2-methyl-1-butanone **373** (Figure 4H) was obtained from the soil-derived fungus *Aspergillus* sp. isolated from the rhizospheric soil of *Phoenix dactylifera* (Date palm tree).[127] Chemical investigation of the *Dictyosporium digitatum* fungus resulted in the identification of nine undescribed compounds **374–382** (Figure 4H): Dictyosporin D **374**, Dictyophthalide A **375**, Dictyofuran A **376**, Dictyofuran B **377**, Dictyofuran C **378**, Dictyofuran D **379**, Dictyosporone A **380**, Xylariolide E **381**, Xylariolide F **382**.[56] One cyclohexanone derivative aspergorakhin K **383** (Figure 4H) was obtained from *Aspergillus gorakhpurensis* F07ZB1707.[6] Yanchao Xu et al fermented *Aspergillus fumigatus* GZWMJZ-152 in a rice solid medium and isolated four new sulfur-containing benzophenones, sulfurasperines A−D **384–387** (Figure 4H).[128]

Phenylpropanoids

Eight new polyphenols namely spiromastols A-F **388–393** and spiromastols J-K **394–395** (Figure 5A) were obtained from the fermentation broth of *Spiromastix* sp. MCCC 3A00308.[129] Three new tetralol analogs, myrochromanols A-C **396–398** (Figure 5A), were isolated from a soil fungus *Myrothecium verrucaria* HL-P-1.[130] Peneciraistin D **399** (Figure 5A), which belong isocoumarin, was isolated from saline soil-derived fungus *Penicillium raistrickii*.[11] Talacoumarins A **400** and B **401** (Figure 5A), were isolated from the ethyl acetate extract of the wetland soil-derived fungus *Talaromyces flavus* BYD07-13.[131] Compounds **402–404** (Figure 5A) were isolated from the fermentation broth of a deep sea-derived fungus *Spiromastix* sp. MCCC 3A00308.[129] Eight new isocoumarin glycosides **405–412** (Figure 5A) were obtained from the solid culture of the wetland soil-derived fungus *Metarhizium anisopliae* (No. DTH12-10).[132] Two new isocoumarin derivatives, talaisocoumarins A **413** and B **414** (Figure 5A), and one new related metabolite, talaflavuol A **415** (Figure 5A) were isolated from the wetland soil-derived fungus *Talaromyces flavus* BYD07-13.[125] Penicipyrans C **416** and D **417** (Figure 5A), were isolated from *Penicillium raistrickii*.[85] In research on novel secondary metabolites from microorganisms, two new **418–419** (Figure 5B) were derived from soil fungus *Hypoxylon* sp. The two new compounds are assigned as (3*R*, 4*R*)-4,8-Dihydroxy-5-(hydroxymethyl)-3-methylisochroman-1-one **418** and (3*R*, 4*S*)-4,8-dihydroxy-5-(hydroxymethyl)-3-methylisochroman-1-one **419**.[133] Two new epimeric dihalogenated diaporthins, (9*R**)-8-methyl-9,11-dichlorodiaporthin **420** and (9*S**)-8-methyl-9,11-dichlorodiaporthin **421** (Figure 5B), have been isolated from the soil fungus Hamigera fusca NRRL 35721.[134] Chemical characterization of ethyl acetate extract of *Exophiala* sp. has afforded the isolation of three compounds including a new isocoumarin named exophiarin **422** (Figure 5B).[135]

Quinones

Two new benzoquinones, citriquinones A **423** and B **424** (Figure 6), were isolated from *Penicillium citrinum*.[136] Penicilliquinone **425** (Figure 6) was isolated from the fermentation product of *Penicillium* sp. PSU-RSPG9.[80] Tansakul et al investigated secondary metabolites produced by *Penicillium herquei* PSU-RSPG93 isolated from soil

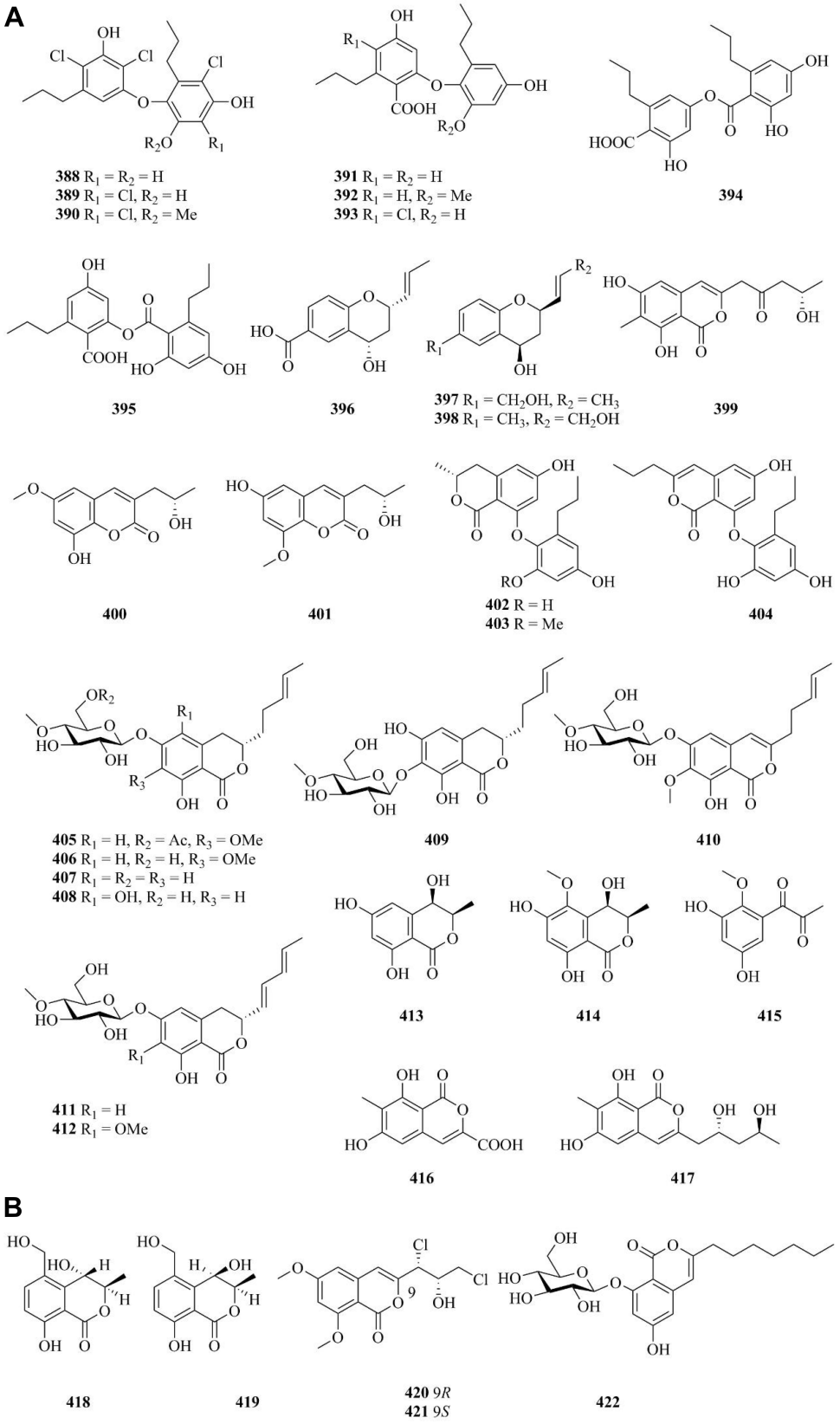


Figure 5 Phenylpropanoids **388–422**. (**A**) Phenylpropanoids **388–417**. (**B**) Phenylpropanoids **418–422**.

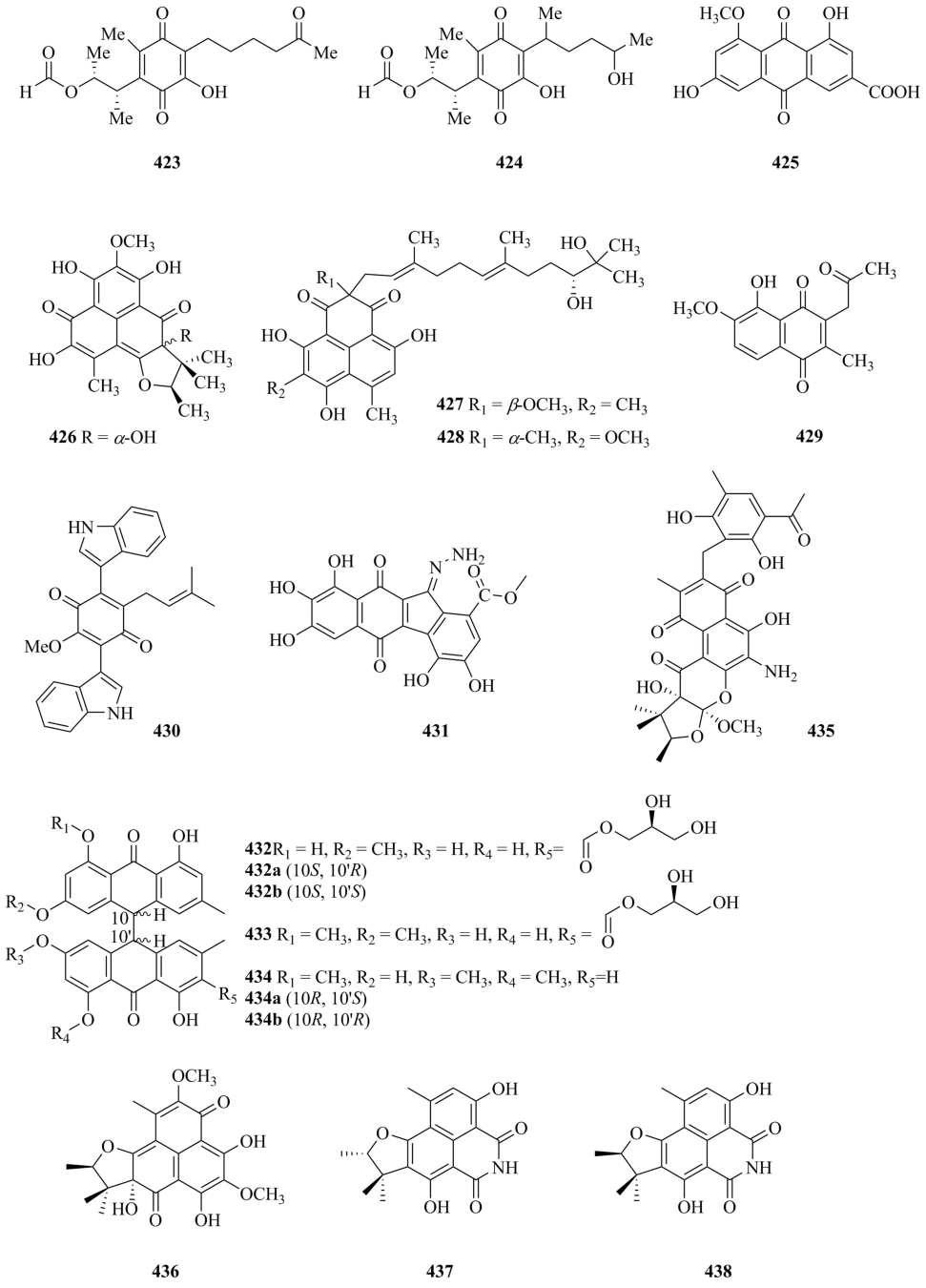


Figure 6 Quinones **423–438**.

collected from the Plant Genetic Conservation Project under the Royal Initiation of Her Royal Highness Princess Maha Chakri Sirindhorn at Ratchaprapa Dam in Suratthani province, Thailand. They obtained one new phenalenone derivative, peniciherqueinone **426** (Figure 6).[137] Two new phenalenones, aspergillussanones A **427** and B **428** (Figure 6) were obtained from the mycelial extract of the soil fungus *Aspergillus* sp. PSU-RSPG185.[30] A new naphthoquinone, solaninaphthoquione **429** (Figure 6), was isolated from the soil fungus *Fusarium solani* PSU-RSPG227.[138] Cultivation and fractionation of secondary metabolites from *Aspergillus kumbius* revealed a new bis-indolyl benzoquinone, kumbicin D **430** (Figure 6).[22] Membrane active compound PA3-d10 **431** (Figure 6) produced by *Aspergillus flavus* strain demonstrated antimicrobial activities against bacteria and yeast strains.[139] The diastereomeric mixtures of the bianthrones wentibianthrone A (**432a, b**) (Figure 6) and wentibianthrone B (**433a, b**) (Figure 6), as well as (10*R*,10′*S*)-

wentibianthrone C (**434a**) and (10*R*,10′*R*)-wentibianthrone C (**434b**) (Figure 6) were obtained from the fungus *Aspergillus wentii*.[102] The study of a Hawaiian volcanic soil-associated fungal strain Penicillium herquei FT729 led to the isolation of one unprecedented benzoquinone-chromanone, herqueilenone A **435** (Figure 6) Herqueilenone A **435** contains a chroman-4-one core flanked by a tetrahydrofuran and a benzoquinone with an acetophenone moiety.[140] Three unreported phenalenone derivatives **436–438** (Figure 6), named *ent*-12-methoxyisoherqueinone (**436**) (Figure 6), (−)-scleroamide (**437**) (Figure 6), and (+)-scleroamide (**438**) (Figure 6) were isolated from the Hawaiian soil fungus *Penicillium herquei* FT729, collected on the Big Island, Hawaii.[141]

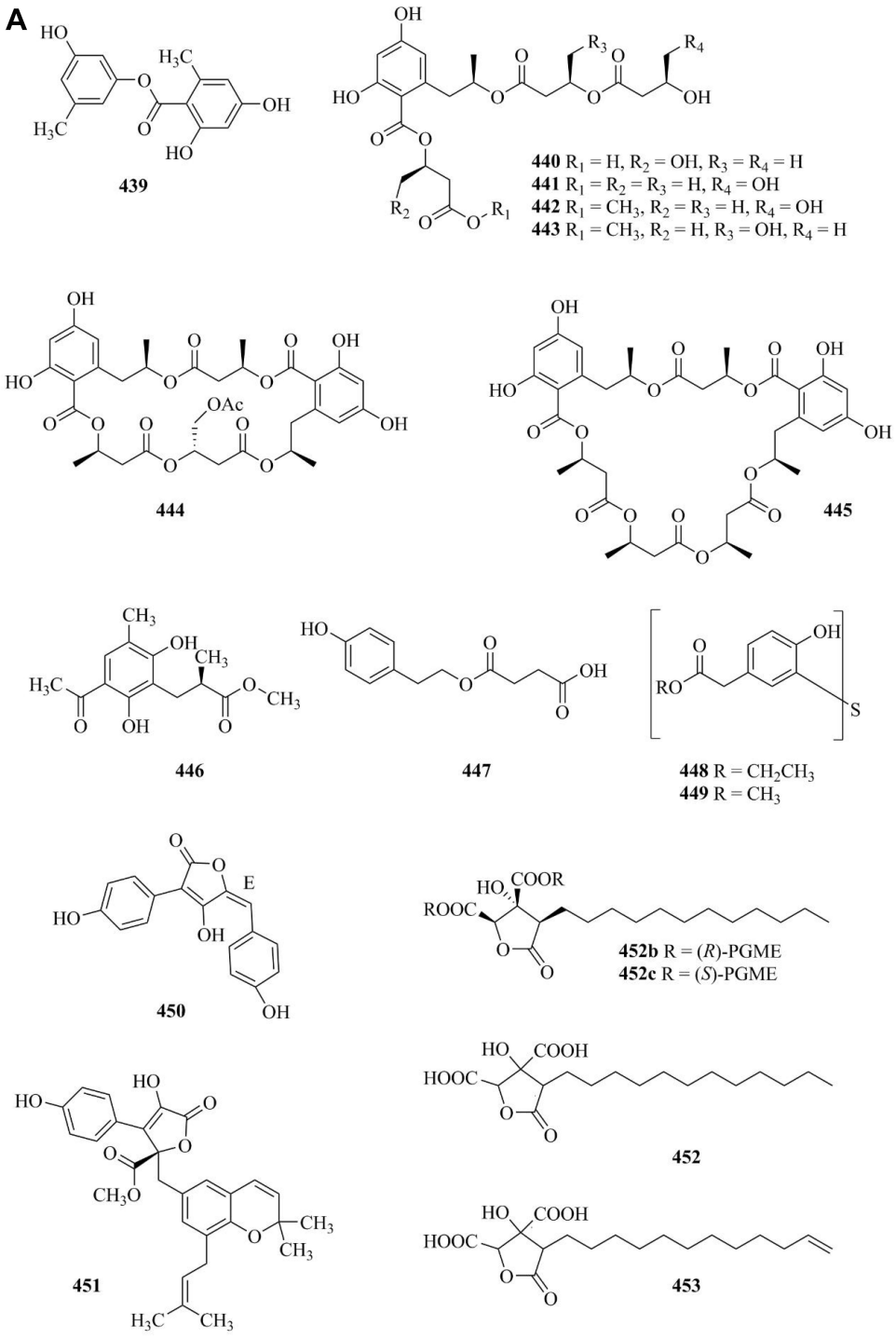
Esters and Lactones

Esters

A new ester of 2.4-dihydroxy-6-methylbenzoic acid **439** (Figure 7A) named 3-Hydroxy-5-methylphenyl 2.4-dihydroxy-6-methylbenzoate was isolated from the fungus *Neosartorya pseudofischeri* S.W. Peterson.[10] Six new polyesters, talapolyesters A-F **440–445** (Figure 7A), were isolated from the wetland soil-derived fungus *Talaromyces flavus* BYD07-13. All the polyesters are composed of (*R*)-2,4-dihydroxy-6-(2-hydroxypropyl)benzoic acid and (*R*)-3-hydroxybutyric acid/(*S*)-3,4-dihydroxybutyric acid residues.[142] Liu et al obtained a new compound *R*-3-(3′-acetyl-2′,6′-dihydroxy-5′-methylphenyl)-2-methylpropionic acid methyl ester **446** (Figure 7A) isolated from the ethyl acetate extract of the fermentation broth of the fungus *Penicillium crustosum* YN-HT-15.[124] Compound 4-(4- hydroxyphenethoxy)-4-oxobutanoic acid **447** (Figure 7A), was isolated from the soil fungus *Fusarium solani* PSU-RSPG227.[138] Penicillithiophenols A **448** and B **449** (Figure 7A) were isolated from *Penicillium copticola* PSURSPG138.[51]

Lactones

In search for anti-influenza virus inhibitors from marine-derived fungi, a strain identified as *Aspergillus terreus* Gwq-48, was isolated from a mangrove rhizosphere soil sample collected in the coast of Fujian province. The study of its chemical components led to the isolation of one new aspulvinone, isoaspulvinone E **450** (Figure 7A).[143] One new γ-butyrolactone, aspergillulactone **451** (Figure 7A) was isolated from the mycelial extract of the soil fungus *Aspergillus* sp. PSU-RSPG185.[30] Two new hydroxycitric acid lactone derivatives named cinatrins D **452** and E **453** (Figure 7A), were obtained from the fungus *Virgaria boninensis* FKI-4958.[44] One phthalide (asperlide, **454**) and one depsidone (aspersidone, **455**) (Figure 7B) were obtained from the fungus *Aspergillus unguis* PSURSPG199.[144] Penicimenolides A-E **456–460** (Figure 7B) and penicimenolide F **461** (Figure 7B) were isolated from the culture broth of a strain of *Penicillium* sp. (NO. SYP-F-7919).[145] Chromatographic separation of the broth extract of the soil-derived fungus *Aspergillus sclerotiorum* PSURSPG178 resulted in isolation of four γ-butenolide-furanone dimers, aspersclerotiorones A-D **462–465** (Figure 7B), and two γ-butenolide derivatives, aspersclerotiorones F **466** and G **467** (Figure 7B).[108] Zhou et al isolated and identified a new sesquiterpene lactone named *eut*-Guaiane sesquiterpene **468** (Figure 7B) from the fungus *Eutypella* sp. derived from the soil of high latitude of Arctic.[146] New natural products, designated pochoniolides A and B **469–470** (Figure 7B), were isolated from the cultured broth of fungal strain FKI-7537 using a physicochemical screening methodology.[147] Three new γ -hydroxyl butenolides named aspersclerolides A-C **471–473** (Figure 7B), a pair of new enantiomeric spiro-butenolides named (±)-aspersclerolide D **474** (Figure 7B), were isolated from *Aspergillus sclerotiorum*.[116] Investigation of the soil-derived fungus *Lasiodiplodia theobromae* NSTRU-PN1.4 resulted in the isolation of two new dimeric c-lactones botryosphaerilactones D **475** and E **476** (Figure 7B).[148] One new metabolite, therlanubutanolide A **477** (Figure 7C), was isolated from the YGP culture broth of *Thermomyces lanuginosus*.[149] During screening for microbial regulators of bone metabolism, a new compound, 6-ethoxy-5,6-dihydropenillic acid **478** (Figure 7B), was isolated from the culture broth of the soil-derived fungus *Penicillium* sp. BF-0343.[150] Twelve new resorcylic acid lactones (RALs) including three new 16-membered RALs **479–481** (Figure 7C), eight new 14-membered RALs **482−489** (Figure 7C), and one new 12-membered RAL **490** (Figure 7C), were identified from the fermentation of the soil-derived fungus Ilyonectria sp. sb65. These new compounds are assigned, respectively, as Ilyoresorcy A **479**, Atrop-ilyoresorcy A **480** Ilyoresorcy B **481**, Ilyoresorcy C **482**, Ilyoresorcy D **483**, Ilyoresorcy E **484**, Ilyoresorcy F **485**, Ilyoresorcy G **486**, Ilyoresorcy H **487**, Ilyoresorcy I **488**, Ilyoresorcy J **489** and Ilyoresorcy K **490**.[151]



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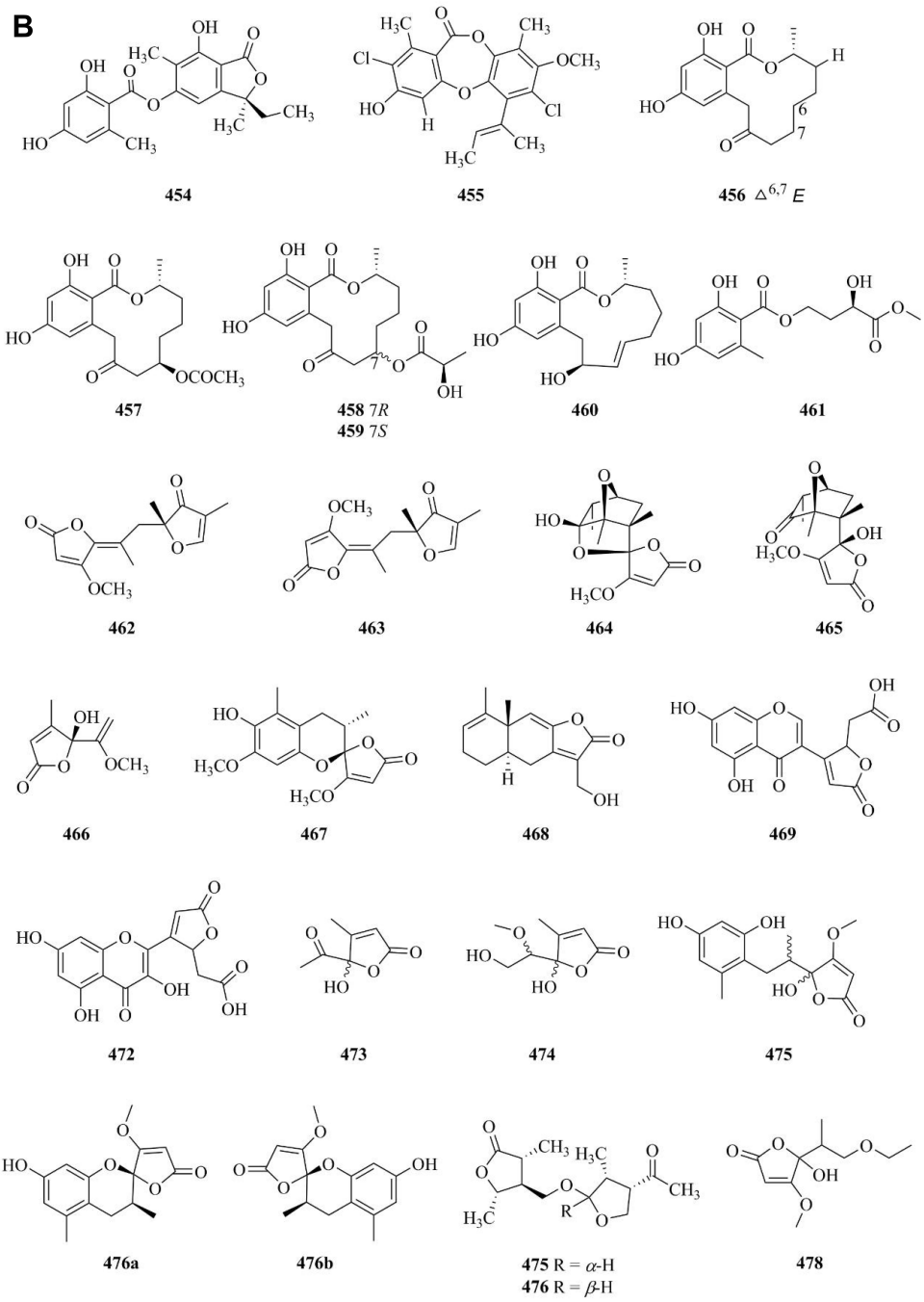
Other Compounds

Prenylterphenyllins A-C **491**–**493** (Figure 8A) and prenylcandidusins A-C **495**–**497** (Figure 8A), and one new polyhydroxy-pterphenyl named 4″-dehydro-3-hydroxyterphenyllin **494** (Figure 8A), were obtained from *Aspergillus taichungensis* ZHN-7-07, a root soil fungus isolated from the mangrove plant *Acrostichum aureum*.[152] A new benzoic acid derivative 4-hydroxy-3-(3-methyoxy-3-methylbutyl)-benzoic acid **498** (Figure 8A) was isolated from *Curvularia inaequalis* strain HS-FG-257.[153] Eight new 2-pentenedioic acid derivatives **499**–**506** (Figure 8A) were isolated from a soil-



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derived fungus *Gongronella butleri* collected in Cameroon. The isolated compounds feature a 2-pentenedioic acid core structure substituted by a 2-alkyl chain that has even number of carbon atoms (C_6, C_8, and C_{10}) with or without an oxygenated substituent.[154] Peniciketals A-C **507**–**509** (Figure 8A), three new spiroketals with a benzo-fused 2.8-dioxabicyclo[3.3.1]nonane moiety, were isolated from the saline soil-derived fungus *Penicillium raistrichii*.[155] Masaphy et al report on the purification and characterization of a novel anticandidal echinocandin – MIG0310 **510** (Figure 8A) from *Fusarium brachygibbosum* strain MS-R1 and the elucidation of its molecular structure.[156] Two new cyclic carbonate derivatives, aspergillusols A **511** and B **512** (Figure 8A) which contain an unusual cyclic carbonate functionality, and one new eutypinic acid derivative, aspergillusic acid **513** (Figure 8A) were found from *Aspergillus* sp.

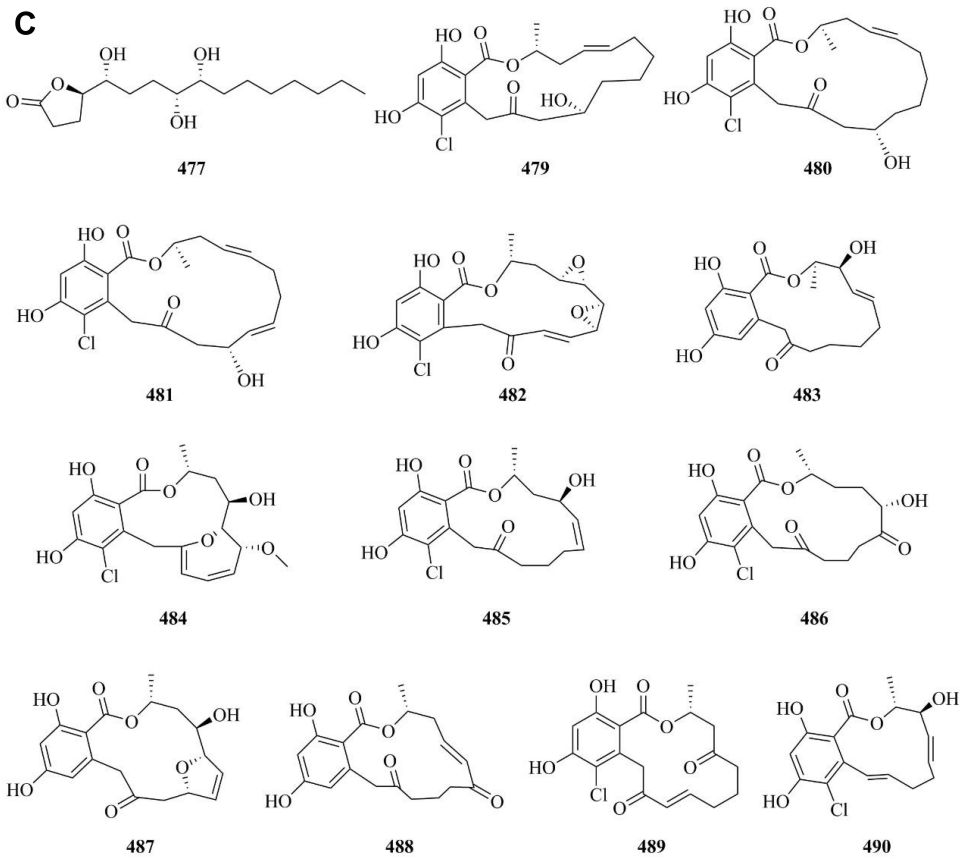
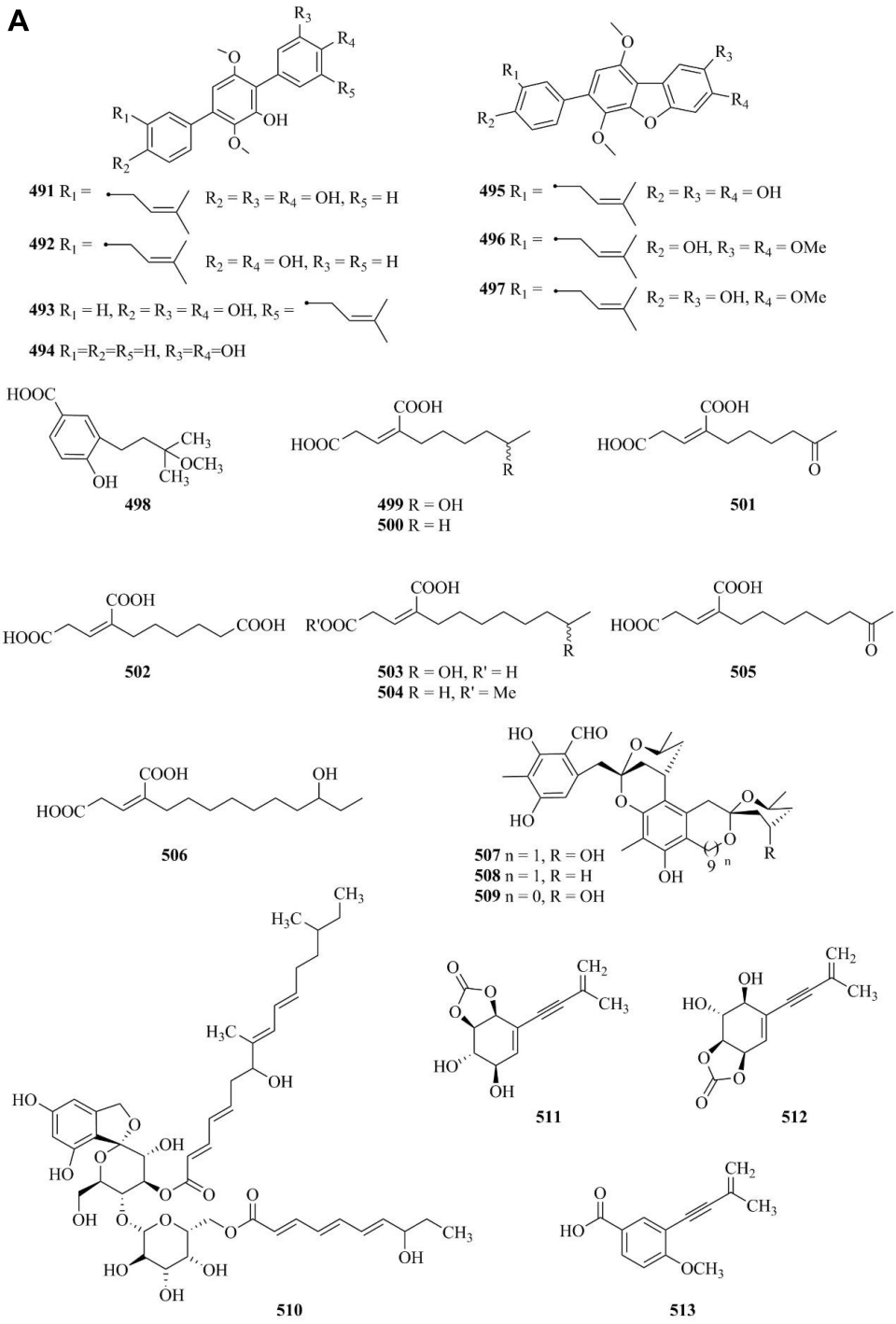


Figure 7 Esters and lactones **439–490**. (**A**) Esters and lactones **439–453**. (**B**) Esters and lactones **454–478**. (**C**) Lactones **479–490**.

PSU-RSPG185.[30] The soil fungus *Gymnascella dankaliensis* was collected in the vicinity of the Giza pyramids, Egypt. When grown on solid rice medium the fungus yielded four new compounds including 11′-carboxygymnastatin N **514**, gymnastatin S **515**, dankamide **516**, and aranorosin-2-methylether **517** (Figure 8B).[157] A new diphenyl derivative, named iizukine B **518** (Figure 8B), was isolated from coastal saline soil-derived fungus *Aspergillus iizukae*.[84] A new compound namely (13-(3,3-dihydroxypropyl)-1,6-dihydroxy-3,4-dihydro-1H-isochromen-8(5H)-one **519** (Figure 8B) was isolated from an ethyl acetate extract of the borne fungi *Sclerotium rolfsii*. The new compound is also known as Sclerotium.[158] A new lovastatin analogue versicorin **520** (Figure 8B), was isolated from mycelial solid cultures of *Aspergillus versicolor* SC0156. The new compound versicorin **520** possesses a hexahydro-2*H*-naphtho[1,8-*bc*]furan moiety, which is a rare type of the lovastatin-analogous compounds.[159] Three new lovastatin analogues **521–523** (Figure 8B) were isolated from the soil-derived fungus *Aspergillus sclerotiorum* PSU-RSPG178.[160] Four previously undescribed metabolites including two lovastatin analogues, asterreusin A **524** and one unnamed compound **525** (Figure 8B), additionally aspereusin A **526** and epiaspereusin A **527** (Figure 8B) were isolated from the culture of *Aspergillus terreus* YIM PH30711.[93] Three new diphenyl ether derivatives (penicillidic acids A-C, **528**–**530**) (Figure 8B) were isolated from the soil-derived fungus *Penicillium aculeatum* PSU-RSPG105.[97] Three new diphenyl ethers, aspergillusethers B-D **531**–**533** (Figure 8B), were isolated from the soil-derived fungus *Aspergillus unguis* PSU-RSPG204.[115] Two new aspinotriol derivatives **534**–**535** (Figure 8B and C) determined as melleusin A **534**, B **535** were isolated from a soil-borne fungus *Aspergillus melleus*.[161] A new diphenyl ether 3-methylpentyl-2, 4-dichloroasterrate **536** (Figure 8C), was isolated from the metabolites of a wetland fungus *Aspergillus flavipes*. PJ03-11.[162] Two new unsaturated fatty acids, 6*R*,8*R*-dihydroxy-9*Z*,12*Z*-octadeca-dienoic acid **537** (Figure 8C) and methyl-6*R*,8*R*-dihydroxy-9*Z*,12*Z*-octadecadienoate **538** (Figure 8C), were isolated from the mangrove rhizosphere soil-derived fungus *Penicillium javanicum* HK1-22.[163] A new azo compound, penoxalin **539** (Figure 8C), a new isochroman carboxylic acid, penisochroman B **541** (Figure 8C), two new natural products,



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penisochroman A **540** (Figure 8C) and 2,6-dihydroxy-4-[(2*R*)-2-hydroxyheptyl] benzoic acid **542** (Figure 8C), were isolated from wetland soil fungus *Penicillium oxalicum* GY1.[164] Fan et al report a new pentacyclic decalinoylspirotetramic acid derivative, pyrenosetin D **543** (Figure 8C), from an endophytic strain *Pyrenochaetopsis* FVE-087.[165] One new benzofuranoid **544** (Figure 8C), was isolated and characterized from fungus *Aspergillus calidoustus*.[58] Two new benzothiazoles (**545** and **546**) (Figure 8C) were isolated from the cave soil-derived fungus *Aspergillus fumigatus* GZWMJZ-152.[128]

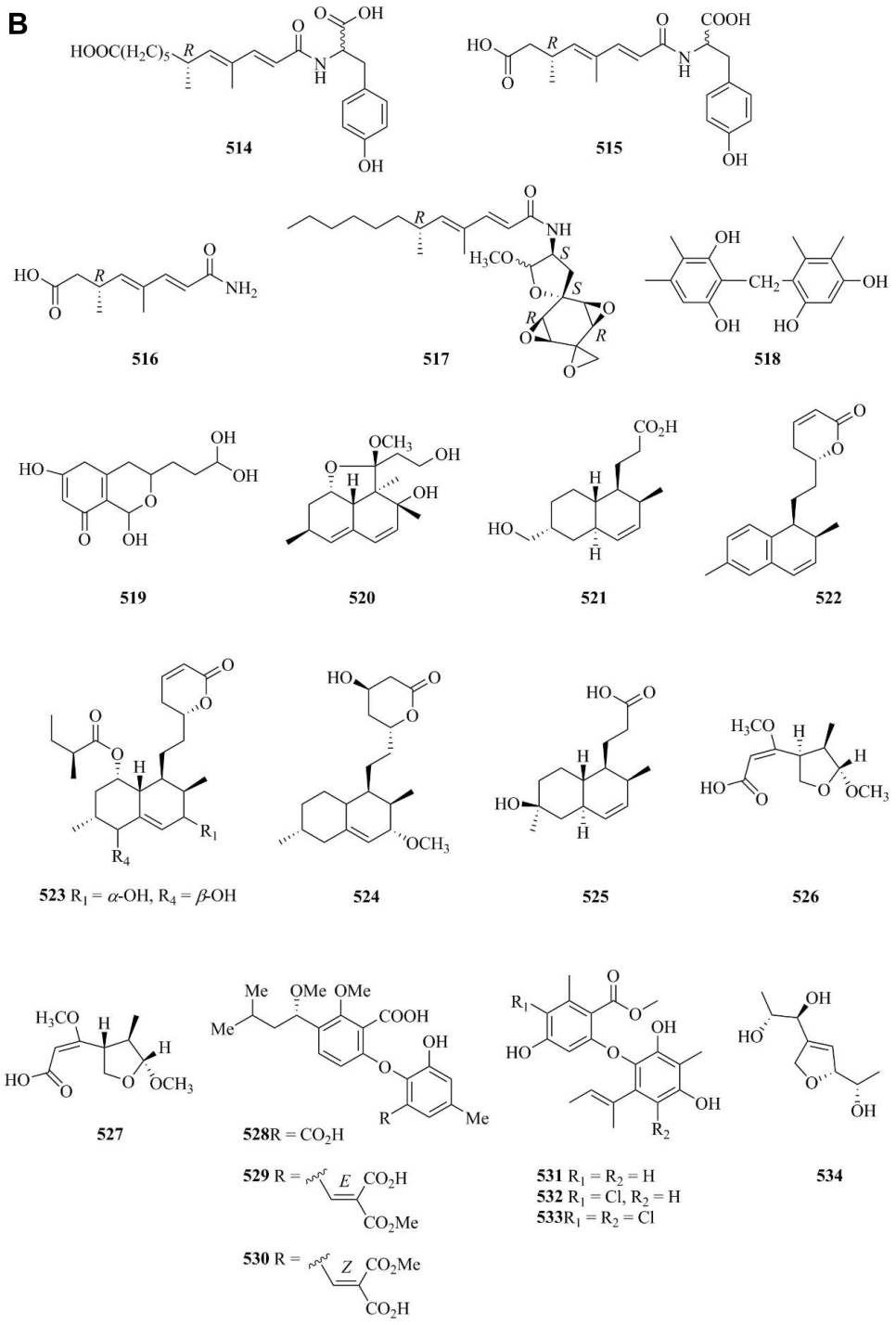

Figure 8 Continued.

Biological Activity of New Compounds Derived from Soil Fungi

Anticancer Activities

The cytotoxicity of compounds **491, 494** and **496** was evaluated on HL-60, A-549, and P-388 cell lines using the SRB and MTT methods with adriamycin (ADM) as positive control Compound **491** exhibited moderate activities against all three cell lines (IC_{50} 1.53–10.89 μM), whereas compounds **494** and **496** displayed moderate activities only against the P-388 cell line (IC_{50} of 2.70 and 1.57 μM, respectively).[152] Compound **93** exhibited anticancer activity against MCF-7,

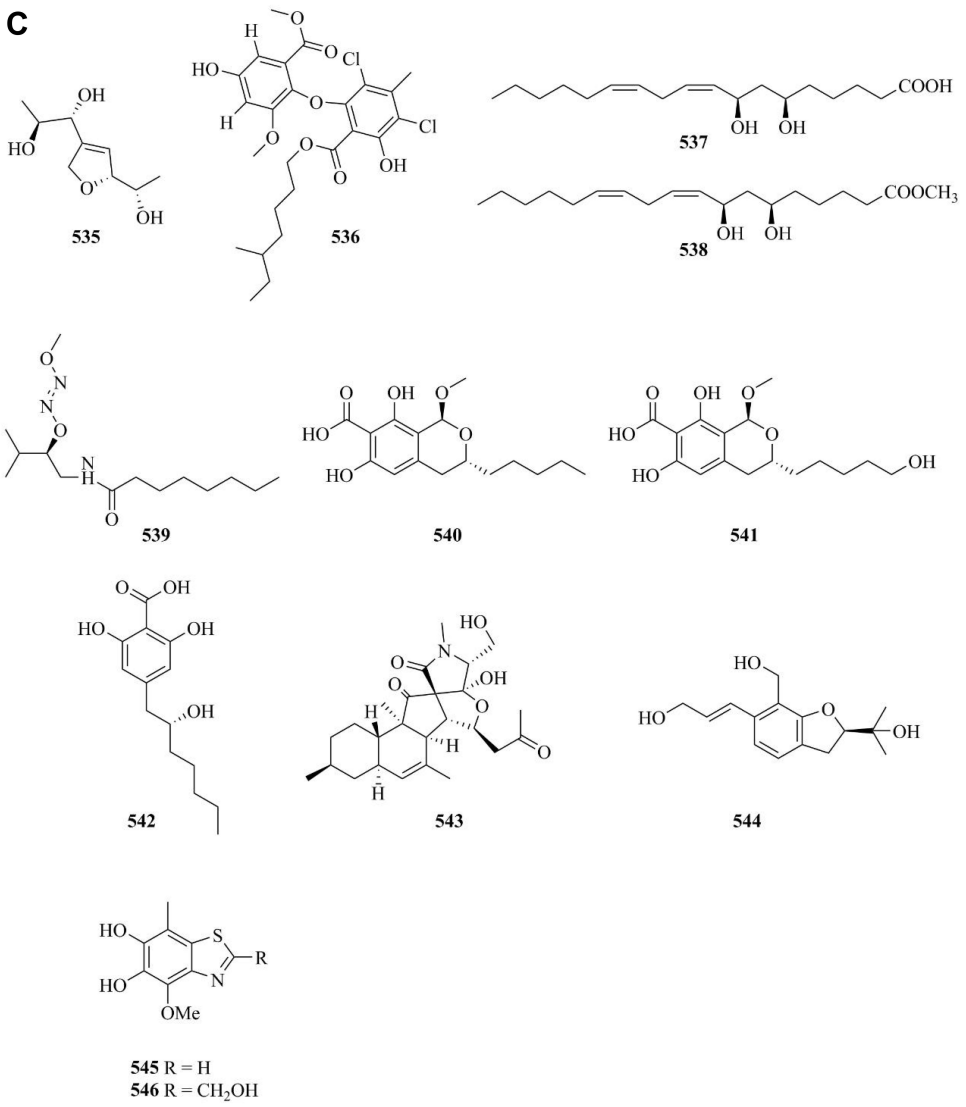

Figure 8 Other compounds **491–546**. (**A**) Other compounds **491–513**. (**B**) Other compounds **514–534**. (**C**) Other compounds **535–546**.

KB, and NCI-H187, with IC_{50} values in the range of 12.56–24.91 μg/mL.[48] Compound **214** exhibited moderate growth inhibition against A-549, Hela, PANC-28 and BEL-7402 cell lines with the IC_{50} values of 16.4, 23.4, 20.3, and 30.1 μg/mL, respectively. 10-hydroxycamptothecin was used as the positive control with the IC_{50} values of 0.5, 5.9, 10.6, and 4.6 μg/mL, respectively.[77] The cytotoxic effects of compound peneciraistin C **325** were preliminarily evaluated against human lung adenocarcinoma (A549) and human breast adenocarcinoma (MCF-7) cell lines by the MTT method. Compound **325** showed comparatively significant cytotoxicities against A549 and MCF-7-60 cell lines with IC_{50} values of 3.2 and 7.6 μM, respectively.[11] Pan et al report the anticancer mechanisms of Pe-C in a variety of lung cancer cells. The results showed that Pe-C induced caspase-independent autophagic cell death and elevated mitochondrial-derived reactive oxygen species levels, which indicated that Pe-C could be a potential drug candidate for therapy of lung cancer.[166] Compound pyrenocine J **215** showed cytotoxic activity against the human hepatic cancer cell line HepG2 with an IC_{50} value of 28.5 μg/mL.[78] Compound **4** showed cytotoxic activity against A-549, Hela, PANC-28 and BEL-7402 cell lines with IC_{50} values of 76.3, 77.2, 107.5 and 89.5 $\mu mol \cdot L^{-1}$, respectively.[12] Compound **7** showed remarkable activities with IC_{50} values of 1.83 and 4.80 μM on P388 and HL-60 cells, respectively. The target of racemic **7** was also investigated and the (12*R*,28*S*,31*S*)-**7** enantiomer showed selectivity against topoisomerase I.[14] Compound **8** showed weak activity with IC_{50} values of 55.1 and 30.5 μM on BEL-7402 and A-549 cells, respectively.[15] Compound **364**

exhibited cytotoxic activity against the ACHN and HepG2 cell lines with IC_{50} values of 4.78 and 13.11 μg mL^{-1}, respectively. The values of **365** were 54.18 and 52.07 μg mL^{-1}.[123] Sartorypyrone A **128** was evaluated for its capacity to inhibit the in vitro growth of MCF-7 (breast adenocarcinoma), NCI-H460 (nonsmall cell lung cancer) and A375-C5 (melanoma) cell lines, using the protein binding dye SRB method. Interestingly, sartorypyrone A **128**, which possesses a monocyclic diterpene core, was more selective, exhibiting similar inhibitory activity to sartorypyrone B against A375-C5 (GI_{50}=21.5±1.9 μM), but less active against MCF-7 (GI_{50}=46.3±7.6 μM) and NCI-H460 (GI_{50}=37.3±4.0 μM) cell lines.[16] Citriquinone A **423** was assayed for cell migration inhibitory activity using human cancer cell line HEp 2. After growing cells in vitro in 96 well plates a scratch was made on wells with cells at the confluence stage. Citriquinone A **423** at a concentration of 0.5 mg/mL (dissolved in growth medium containing 1% DMSO) was introduced into wells and incubated for 24 h. Development of new cells to reduce the width of the scratch from its initial stage was determined qualitatively by comparing the width of the scratch after incubation in each well in the presence of test sample and control (1% DMSO in the growth medium) using microscopic images. It was revealed that **423** had a moderate inhibitory effect on the growth/migration of the HEp2 cells when compared with the control.[136] Compounds **444** and **445** were evaluated by MTT method for their cytotoxic activities against five tumor cell lines, HL-60, SMMC-7721, A-549, MCF-7, and SW480, with cisplatin and paclitaxel as the positive controls. They exhibited cytotoxicity against the tested tumor cell lines. The IC_{50} values of compound **444** are 14.81,18.39,17.66,14.59 and 26.62 μM respectively. The IC_{50} values of compound **445** are 13.62,15.74,11.09,15.96 and 15.54 μM, respectively.[142] Peniciketals A-C **507**–**509** showed selective activities against HL-60 cells with IC_{50} values of 3.2, 6.7, and 4.5 μM, respectively (doxorubicin as a positive control (IC_{50}s: 0.31, 0.085, and 0.23 μM, respectively)), while were not active on other cells (IC_{50} > 10 μM).[155] Libertellenone H **130** showed cytotoxicity against seven human tumor cell lines: U251, SW-1990, SG7901, MCF-7, Huh-7, Hela and H460 cell lines at a range between 3.31 and 44.1 μM.[59] Compound cytochalasin Z_{24} **53** exhibited moderate cytotoxicity toward human breast cancer MCF-7 cell line with IC_{50} of 9.33 μM.[29] Compound aspergillussanone A **427** exhibited weak activity toward KB and Vero cells with IC_{50} values of 48.4 and 34.2 μM, respectively.[30] Compounds Polluxochrin **337**, dioschrin **338** and Castochrin **270** showed weak mammalian cell cytotoxicity effects against pancreatic cancer cells (MIA PaCa-2) with IC_{50} values of 50.8, 30.3, and 29.3 μM, respectively.[82] Bisacremines A-B **175**–**176** exhibited weak cytotoxicity against HeLa cells with IC_{50} values of 10.7±1.0 and 9.3±1.7 μM respectively. And **176** also showed modest activity against A549 and HepG2 cells with IC_{50} values of 41.3±4.1 and 31.1±2.1 μM respectively.[5] Compound aranorosin-2-methylether **517** showed potent cytotoxicity against the murine lymphoma cell line L5178Y with IC_{50} values of 0.44 μM.[157] Compound solaninaphthoquione **429** showed significant cytotoxic activity against breast cancer (MCF-7) cells and mild cytotoxic activity against oral human carcinoma (KB) cells (IC_{50} values of 21.3 and 22.6 μM, respectively) compared to standard compound.[138] Iizukines A **234** and B **518** were tested their cytotoxicities against HL-60 (human promyelocytic leukemia), BEL-7402 (human hepatoma) and A-549 (human lung carcinoma) were tested by the MTT assay in vitro with 5-fluorouracil (5-FU) as positive control. The two compounds showed weak cytotoxic activities. IC_{50} values of compound **234** were 26.5, 32.7 and 18.2 μM respectively, and IC_{50} values of compound **518** were 48.7, 56.6 and 32.3 μM.[84] Penicilleremophilane A **99** was obtained from *Penicillium copticola* PSURSPG138. It showed much weaker cytotoxic activity.[51] Cytotoxicity studies of the compound **265** on cancer cell lines showed a valuable cytotoxic potential against all tested human cancer cell lines. Further, the compound induces apoptosis in lung cancer (A549) cells revealed by increase the distribution of nuclear DNA in Sub-G1 phase as observed in flow cytometry.[92] For compound **519**, in the present study rhodamine-123 exclusion screening test on human mdr1 gene transfected mouse gene transfected L5178 and L5178Y mouse T-cell lymphoma which showed excellent MDR reversing effect in a dose-dependent manner against mouse T-lymphoma cell line. Moreover, molecular docking studies of compound **519** also showed better results as compared with the standard.[158] Kumbicin C **33** was found to inhibit the growth of mouse myeloma cells (IC_{50} 0.74 μg mL^{-1}).[22] Penicimenolides B-D **457**–**459** exhibited potent cytotoxicity against the U937 and MCF-7 tumour cell lines and showed moderate cytotoxic activity against the SH-SY5Y and SW480 tumour cell lines. There is experimental evidence that compound **457** may act as a potential MEK/ERK inhibitor, it is still need further study in the future.[145] Penicipyran E **237** showed cytotoxicity effects on HL-60 and K562 cell lines with IC_{50} values of 4.4 and 8.5 μM, respectively.[85] Compounds **68**–**74** showed potent to moderate cytotoxicity against the L5178Y mouse lymphoma cell line with IC_{50} values ranging from 0.99 to 14.1 μM.[35] Asterriquinol E **34** was bioassayed

for its inhibitory effects on NO production induced by LPS in microglia cells with N^G-monomethyl-$_L$-arginine ($_L$-NMMA) as a positive control (IC_{50} 4.8 μM). The results showed that compound **34** showed moderate activity with IC_{50} 49.7 μM. Cell viability was determined at the same time by the MTT method and only compound 1 exhibited cytotoxicity with an IC_{50} 9.7 μM.[23] Bacillisporin H **263** exhibited modest cytotoxicity against HeLa cells.[90] Compound Aspergiketone **101** was cytotoxic towards HL-60 and A549 cell lines with IC_{50} values of 12.4 and 22.1 μM, respectively.[52] Oxisterigmatocystins E and F (**276** and **277**, respectively) exhibited cytotoxicity against KB, MCF-7, and NCI-H187 cell lines (IC_{50} = 7.7–78.6 μM). However, compounds **276**–**277** showed cytotoxic effects against the Vero cell line (IC_{50} = 4.3–9.7 μM).[98] Compound **107** displayed growth inhibitory effect against human Mantle cell lymphoma JEKO-1 and human hepatoma carcinoma HepG2 with IC_{50} values of 8.4 and 28.5 μM, respectively.[54] Compound penixanthone A **278** had weak cytotoxicity against the tested cancer cell lines, H1975, MCF-7, K562, HL7702 at concentration of 30 μM.[99] Compound **211** exhibited poor cytotoxicity toward HCT-116 cells (20.5% inhibition at the dose of 100 μM, IC_{50} >100 μM), while the IC_{50} value of the positive control (doxorubicin) was 0.365±0.023 μM.[75] Compound **468** exhibited in vitro a little cytotoxicity towards SGC7901 cell line with IC_{50} value of 39.8 μM.[146] Compound **160** showed potent cytotoxic capability against HL-60, THP-1 and Caco 2 cell with IC_{50} values of 3.4 μM, 4.3 μM, 10.5 μM, and compound **161** showed significant inhibiting activities against HL-60 cell line and THP-1 cell line (IC_{50} =7.9 μM, 11.3 μM, respectively), using 5-fluorouracil as the positive drug with IC_{50} values of 6.4 μM, 4.4 μM, 56.6 μM for HL-60, THP-1 and Caco 2 cells, respectively.[67] The cytotoxic effects of 3-methylpentyl-2, 4-dichloroastterrate **536** was evaluated using the MTT method on HL-60, HCT116, PC-3, and HT-29 cancer cell lines. The results showed that its IC_{50} values were larger than 5-fluorouracil, smaller than 80 μM.[162] Libertellenones O-S **133**–**137** and eutypellenones A and B (**138** and **139**) exhibited cytotoxicities against HeLa, MCF-7, HCT-116, PANC-1, and SW1990 cells, with IC_{50} values in the range of 0.8 to 29.4 μM. Compounds **138** and **139** could dose-dependently inhibit the activity of NF-κB and exhibited significantly inhibitory effects on nitric oxide production induced by lipopolysaccharide.[61] (9*R**)-8-methyl-9,11-dichlorodiaporthin **420** and (9*S**)-8-methyl-9,11-dichlorodiaporthin **421**, were evaluated the cytotoxicity against seven cancer cell lines: human-derived cell lines CCD25sk (human fibroblasts), SHSY5 (neuroblastoma), MiaPaca-2 (epithelial pancreas carcinoma), MCF-7 (breast adenocarcinoma), HepG2 (hepatocellular carcinoma), A2058 (epithelial melanoma), and A549 (lung carcinoma), exhibiting moderate activity against two of them. While both dichlorinated compounds **420**–**421** were active against neuroblastoma (SHSY5y cells: **420** CC_{50} = 39.2 μM, and **421** CC_{50} = 36.2 μM). These results correlate well with the cytotoxicity against HeLa cells recently reported for dichlorodiaporthin (CC_{50} = 9 μg/mL = 28 μM), a compound considered as a mycotoxin.[134] Sporulosol **326** showed modest cytotoxicity toward the human tumor cell line T24, with an IC_{50} value of 18.2 μM.[113] Libertellenone M **140** and libertellenone N **141** were tested for cytotoxic activities against HeLa, MCF-7, HCT-116, K562, and SW1990 cell lines. Compound **141** displayed potent cytotoxicity against K562 cells with IC_{50} value of 7.67 μM and moderate cytotoxicity against HeLa, MCF-7, and SW1990 cell lines with IC_{50} values of 30.06, 18.52, and 24.36 μM, respectively, and compound **140** showed weaker cytotoxic activity against these five tumor cell lines with IC_{50} values of 34.78, 32.20, 26.67, 40.85 and 24.36 μM, respectively.[62] Compound iizukine C **57** exhibited cytotoxic effect towards HL-60 and A549 cell lines with IC_{50} values of 3.8 and 7.2 μM, respectively.[31] Compounds **471** and **473** showed selective cytotoxicity against HL60 (IC_{50}: 6.5 and 12.1 μM, respectively), A549 (IC_{50}: 8.9 and 16.7 μM, respectively), and HL-7702 (IC_{50}: 17.6 and 22.8 μM, respectively) cell lines.[116] The cytotoxicities of Compound **212** was evaluated against A-549, Hela, HCT-116, MGC-803, and HO-8910 cell lines. Compound **212** exhibited various activities with the IC_{50} values 5.0 to 22.4 μM, respectively.[76] Tolypocladin A **38** displayed weak cytotoxicity against A549, Huh7, LN229, MGC and MHCC97H, LOVO and MDA231 cell lines with IC_{50} values from 16.32 to 37.80 μM (positive control camptothecin: 0.32–31.8 nM) and suppressed the growth and viability of the HCC cells T1224 in the patient-derived organoids (PDOs) model.[25] 8′-*O*-(3*R*-Hydroxy-butyryl)-rasfonin **294** and Cemironin A **295** displayed significant cytotoxicity on five human cancer cell lines: 786-O, A549, HeLa and MCF-7 cell lines, with the IC_{50} values <20 μM, which are more effective than positive control 5-fluorouracil and could be considered to be potential as antitumor agents, in which they could significantly inhibit the cancer cells growth in a dose-dependent manner.[104] Nectriatone A **340** showed cytotoxicities against SW1990, HCT-116, MCF-7, and K562 cells, with IC_{50} values in the range of 26.37–42.64 μM.[117] Compound **251** also showed cytotoxicity against NCI-H187 cells with an IC_{50} value of 16.73 μM. Moreover, macrosporusones A-B **250**–**251** and

macrosporusone D **253** exhibited cytotoxicity against Vero cells with IC_{50} values in the range of 13.74–69.77 μM.[88] Compounds **48** and **49** showed moderate cytotoxicity against HepG2 human hepatocellular carcinoma cells with an IC_{50} of 8.7 and 19.4 μM, respectively. The IC_{50} value of the positive control (cis-platin) was 3.14 μM.[26] Compound **542** displayed significant cytotoxicity against human esophageal carcinoma cells OE19 with an IC_{50} value of 5.50 μM.[164] Compounds **255–258** had low cytotoxicity against both cancerous (MCF-7 and NCIeH187) and non-cancerous (Vero) cells.[89] Compounds **62–6**5 showed moderate cytotoxicity against five tested human tumor cell lines: HeLa, PC-3, A549, HepG-2 and HL-60.[33] Pyrenosetin D **543** showed toxicity towards both A-375 and HaCaT cells with IC_{50} values of 77.5 and 39.3 μM, respectively.[165] Compounds **165,166**, and **168** exhibited moderate cytotoxic activities with IC50 values ranging from 18.4 to 29.4 μM.[69] The cytotoxicity assay revealed that asperanstinoid D **185**, dehydroaustinol, and austin displayed considerable cytotoxicity against the HL-60 and SU-DHL-4 tumor cell lines with IC_{50} values ranging from 15.7 to 27.8 μM.[71] Protein tyrosine phosphatases (PTPs) are signaling enzymes that regulate tyrosine phosphorylation. The disorder of PTPs could induce human diseases such as tumor, diabetes, autoimmune diabetes, and infectious diseases. Compounds **213, 203**, and **383** showed inhibitory effect against PTPs including PTP1B, SHP1, and TCPTP in vitro. Among them, compound **213** might exhibit selective activities against PTP1B and SHP1 over TCPTP with IC_{50} values 0.57, 1.19, and 22.97 μM, respectively. Compounds **213** and **203** exhibited modest cytotoxicity against tumor cell lines A549, HeLa, Bel-7402, and SMMC-7721 with IC_{50} values in the range of 6.75–83.4 μM.[6] The inhibitory activity of the isolated compounds (**436–438**) against indoleamine 2.3-dioxygenase 1 (IDO1) was assessed. Compounds **436** inhibited IDO1, with the IC_{50} value of 32.59 μM.[141]

Antimicrobial Activities

Compounds **95** and **96** were tested for antifungal activities. **95** and **96** were active against plant pathogenic fungi *Rhizoctonia solani* and *Fusarium oxysporum* using standard agar diffusion tests at 20 μg/disk.[49] Compound **5** was tested for its abilities to inhibit both cell viability and biofilm formation of *Candida albicans*. It demonstrated dose-dependent activity in the biofilm inhibition assay with an IC_{50} value of 1.4 ± 0.2 μM.[13] Citriquinone A **423** was evaluated for antibacterial activity against *Bacillus* sp. At a dose of 250 μg/disc using the Kirby-Bauer Disc Diffusion method. Amoxicillin 25 μg and a disc soaked with MeOH and dried completely served as positive and negative control, respectively. It was found that **423** had moderate antibacterial activity compared with amoxicillin.[136] Compounds **97** and **98** exhibited selective activity against *Colletotrichum gloeosporioides* with MIC values of 1.0 and 0.125 μg/mL, respectively, the latter of which is better than that of the positive control, zeocin (MIC 0.25 μg/mL). This result indicated that compounds **97** and **98** are responsible for the activity against *C. gloeosporioides* during the preliminary assay of the crude extract, and acetylation of 4-OH likely enhanced the activity.[50] Libertellenone G **129** exhibited antibacterial activity against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus*.[59] Novel echinocandin compound MIG0310 **510** exhibiting anticandidal activity, MIG0310 showed activity against two ATCC strains and 10 clinical isolates of *Candida albicans*. It also showed activity against a clinical isolate of *C. tropicalis*, showing a potential inhibition of this particular *Candida* species as well. The anticandidal agent had MFC values (killing activity) similar to the MIC for *C. albicans*, reminiscent of other echinocandins used as drugs, which showed also kill at growth-inhibiting concentrations for most of Candida species isolates (Moore et al 2001).[156] Isochaetomium A_2 **351** possessed significant antimicrobial activity against *Escherichia coli* 1.044, *Staphylococcus aureus* 1.252, and *Bacillus subtilis* 1.079.[120] Minimum inhibitory concentration (MIC) of the active compound **273** ranged from 0.5 to 15 μg/mL. Viable cell count studies of the active compound **273** showed *Staphylococcus aureus, Escherichia coli, Staphylococcus epidermidis*, and *Salmonella typhimurium* 1 to be the most sensitive.[95] Compounds Polluxochrin **337**, dioschrin **338** and Castochrin **270** exhibited anti-MRSA activity, with MIC values of 4.1, 4.9, and 3.2 μM (2.9, 3.2, and 2.0 μg/mL), respectively, whereas the MIC for chloramphenicol was 5 μM (1.6 μg/mL).[82] Compounds **388–390** exhibited potent antibacterial activities against all tested strains of bacteria, including *Xanthomanes vesicatoria* ATCC 11633, *Pseudomonas lachrymans* ATCC11921, *Agrobacterium tumefaciens* ATCC11158, *Ralstonia solanacearum* ATCC11696, *Bacillus thuringiensis* ATCC 10792, *Staphylococcus aureus* ATCC 25923 and *Bacillus subtilis* CMCC 63501, with minimal inhibitory concentration (MIC) values ranging from 0.25 to 4 μg/mL, while compounds **394–395** and **404** showed moderate inhibition with MIC values in the range of 8–64 μg/mL.[129] The antibacterial activity of asperochrin A **231** was evaluated. Compound **231** showed inhibitory activity against aquatic pathogenic bacterial *Aeromonas hydrophil*a, *Vibrio anguillarum*, and *Vibrio harveyi*. However, compound **231** displayed

selective antibacterial activity against *A. hydrophilia, V. anguillarum*, and *V. harveyi*, with IC_{50} values ranging from 8.0 to 16.0 μg/mL.[83] Compounds **452** and **453** were shown to be weakly active against the bacteria *Bacillus subtilis* KB 211 (ATCC 6633) with inhibition zones of 7.3 and 7.2 mm, respectively, as well as against *E. coli* KB 213 (NIHJ), with inhibition zones of 10.9 and 14.7 mm, respectively, at 100 μg per 6 mm disc. Compound **89** displayed only weak antibacterial activity against *E. coli* KB 213 (NIHJ) with an inhibition zone of 7.8 mm at 30 μg per 6 mm disc.[44] Penicilleremophilane A **99** was approximately half as active against *Plasmodium falciparum* with the IC_{50} value of 3.45 μM.[51] MIC of the compound **265** ranged from 0.5 to 15 μg/mL, which was found to be comparable with the standard antibiotics.[92] Compound **349** (MIC 25 μg/mL) exhibited stronger antibacterial activity against *E. coli* than erythromycin, streptomycin, and ampicillin. Compound **350** (MIC 50 μg/mL) exhibited more prominent activity than streptomycin against *Bacillus subtilis*. Compound **350** (MIC 50 μg/mL) also displayed similar activity against *Escherichia coli* compared to erythromycin and ampicillin, and greater than streptomycin.[119] Kumbicin C **33** was found to inhibit the growth of Gram-positive bacterium *Bacillus subtilis* (MIC 1.6 μg mL^{-1}).[22] Compound **405** showed antibacterial activity comparable with (*Z*)-4-bromo- 5-(bromomethylene)-2(5*H*)-furanone (BF), which may block the QS system of *Pseudomonas aeruginosa* with the mechanism of reducing biofilm formation and virulence factor secretion.[132] Talaroketals A **240** and B **241** display modest antimicrobial activity against *Staphylococcus aureus* with an IC_{50} value around 50 μg mL^{-1} but no activity against the other bacterial strains:*Staphylococcus haemolyticus, Escherichia coli* and *E. faecalis*.[87] The antimicrobial activity of bacillisporin H **263** was evaluated against a panel of human pathogenic bacteria: *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Staphylococcus hemolyticus* (MNHN26), and *Enterococcus faecalis* (CIP 103014). Also of note is the effect of compound **263** against *Staphylococcus aureus* with a MIC value of 5.0 μM.[90] Compound **533** exhibited moderate antifungal activity against *Candida albicans* (NCPF3153), flucytosine-resistant *Cryptococcus neoformans* (ATCC90113) and *Penicillium marnefeii* with the MIC values of 16, 8 and 16 μg/mL, respectively.[115] Compound **107** exhibited inhibitory efficacy to *Bacillus subtilis* CMCC63501 and *Bacillus pumilus* CMCC63202 with IC_{50} value of 18.1 and 23.8 μM, respectively[54] The antibacterial activities of Penicilones B-D **354–356** were evaluated with Gram-positive *S. aureus* (ATCC 43300), *S. aureus* (ATCC 33591), *S. aureus* (ATCC 29213), *S. aureus* (ATCC 25923), *Enterococcus faecalis* (ATCC 51299), *E. faecium* (ATCC 35667), and Gram-negative *Escherichia coli* (ATCC 25922). The results indicated that **354–356** showed significant antibacterial activities against the tested Gram-positive bacteria including both antibiotic-resistant and -susceptible strains with MIC values ranging from 3.13 to 12.5 μg/mL, while none of the tested compounds exhibited activity against *E. coli*.[121] The antibacterial activities of talaraculone B **358** against three Gram-positive bacteria and three Gram-negative bacteria were tested. It showed selective activities against the pathogenic bacteria *Vibrio anguillarum*, with the same MIC values of 0.26 μg/mL, stronger than the positive control ciprofloxacin (MIC = 0.52 μg/mL).[122] When the compound was 50 μg on the antibacterial paper (Ø 6 mm), compound **468** showed strong antibacterial activities against *Escherichia coli, Bacillus subtilis* and *Staphylococcus aureus* such as the positive control ampicillin.[146] Compound **160** showed antibacterial activity toward *Bacillus cereus* (IC_{50}=49 μg/mL, IC_{90} =111 μg/mL) and *Bacillus subtilis* (IC_{50}=10 μg/mL, IC_{90}=85 μg/mL) [191]. Libertellenone M **140** exhibited antibacterial activity against *Escherichia coli* (ATCC 25922), *Staphylococcus aureus* (ATCC 27217), and *Vibrio vulnificus* (ATCC 27562) with MIC values of 32, 32, and 16 μg/mL, respectively.[62] Compound **285** displayed antifungal activity against *Cryptococcus neoformans* ATCC90112 and ATCC90113 flucytosine-resistant with the MIC values of 128 and 64 μg/mL, respectively.[101] 11-Hydroxychevalone E **300** showed weak antibacterial activity against *Escherichia coli* and *Salmonella enterica* serovar *Typhimurium*., both with MIC 128 μg/mL.[40] Membrane active compound PA3-d10 **431** produced by *Aspergillus flavus* strain demonstrated antimicrobial activities against bacteria and yeast strains.[139] Compounds **346** and **347** showed moderate to strong inhibitory activity against the tested Gram-positive bacteria. It is worth noting that **347** and **238** displayed potent antibacterial activities against methicillin-resistant *Staphylococcus aureus* ATCC 33591 with the same MIC value of 3.13 μg/mL, which was close to the positive control vancomycin (MIC 1.56 μg/mL).[86] Compounds **372** and **371** both displayed antimicrobial activities against *Staphylococcus aureus* with MIC values of 25 and 75μg/mL, respectively. Moreover, morphological observation showed the coccoid cells of *S. aureus* to be swollen to a volume of 1.4 and 1.7-fold after treatment with compounds **371** and **372**, respectively. Microbial filamentous temperature-sensitive protein Z (FtsZ) is a novel target for drug discovery, which plays a key role in cell division. The inhibitors of FtsZ prevent the cellular fusion of bacteria, which lead to apoptosis of bacteria. Molecular docking was carried out to investigate interactions of filamentous temperature-sensitive protein Z (FtsZ) with compounds **371** and **372**. The results indicated that compounds **372** might form lower potential energies

and more stable binding sites with the target protein FtsZ compared to compound **371** which validated the observed antimicrobial activities.[126] MIC values of 200 μg/mL were obtained for compounds **472**–**473** towards *Staphylococcus aureus* and *Escherichia coli* using the micro-broth dilution method.[116] Peninaphones A-C (**301**–**303**) showed antibacterial activity against *Staphylococcus aureus*. Compound **303** exhibited significant activity against the rice sheath blight pathogen *Rhizoctonia solani*.[105] Compounds **308** and **309** displayed moderate inhibitory effects on *Staphylococcus aureus* and *Bacillus cereus* with an inhibition rate of more than 50%. Additionally, compounds **307**–**309** showed weak antibacterial effects on MR *Staphylococcus aureus*.[109] Compounds **38** and **45** displayed significant antimicrobial activities. Compound **38** showed obvious inhibitory activities against seven pathogenic fungi (*Alteranira f ragariae, Corynespora cassiicola, Alternaria alternata, Botrytis cinereal Pers., Cercospora personata, Verticillium dahliae Kleb, Sclerotinia sclerotiorum*) with MIC values of 6.25–25 μg/mL (ketoconazole: 0.78–1.56 μg/mL), and compounds **38**–**47** except for **45** were active against *A. fragariae* with MIC values of 6.25–50 μg/mL (ketoconazole: 0.78 μg/mL). Compounds **38**–**47** were also evaluated for their antibacterial activity toward Gram-positive and Gram-negative human pathogenic bacterial strains. The results indicated that compound **45** was active against all tested bacteria and compound **38** was active against *Bacillus cereus* and methicillin-resistant *Staphylococcus aureus*. Moreover, compound **39** exhibited weak activity against methicillin-resistant *S. aureus*.[25] Compound **373** exhibited potent antimicrobial activities against *Staphylococcus aureus* with MIC values of 2.3 μg mL^{-1} and significant growth inhibitions of 82.3 ± 3.3 against *Candida albicans* and of 79.2 ± 2.6 against *Candida parapsilosis*. Compound **373** further showed strong activity against the pathogenic bacteria *Escherichia fergusonii* with MIC of 3.1 μg mL^{-1}.[127] Compounds **115** and **151** displayed interesting antifungal activity against *Cryptococcus neoformans* ATCC90113 with the respective MIC values of 8 and 4 μg/mL. Moreover, only **115** was active against *C. neoformans* ATCC90112 with the MIC value of 32 μg/mL.[55] Compounds **295**–**297** also displayed moderate inhibitory effects on MR *Staphylococcus aureus, Staphylococcus aureus* and *Bacillus subtilis*, which could be the major anti-bacterial constituents of *Cephalotrichum microsporum*.[104] Tolypocladin K **149** displayed moderate antifungal activity against *Sclerotinia sclerotiorun, Helminthosporium maydis, Botrytis* cinereal Pers. and *Colletotrichum acutatum* Simmonds with an MIC value of 50 μg/mL.[64] Duclauxamide B **257** showed *anti-Mycobacterium tuberculosis* activity with MIC value of 12.5 μg/mL and also had *anti-Bacillus cereus* and *anti-Staphylococcus aureus* with equal MIC values of 12.5 μg/mL.[89] Compounds **312**–**321** showed antimicrobial inhibitory activities against *Escherichia coli, Staphylococcus aureus*, and *Candida albicans* with MIC values ranging from 0.9 to 7.0 μg/mL, from 1.7 to 3.5 μg/mL, and from 3.3 to 7.0 μg/mL, respectively.[111] Compound **66** was active against *Fusarium oxysporum* with an MIC value of 50 μg/mL.[34]

Anti-Inflammatory Activities

In the in vitro anti-inflammation assay, bisacremine G **181** exhibited dose-dependent inhibitory effects on the production of TNF-α, IL-6, and nitric oxide (NO) in LPS-stimulated RAW 264.7 macrophages. At 50 μM, it inhibited TNF-α, IL-6, and NO production by 80.1%, 89.4%, and 55.7%, respectively. The inhibition was comparable to that of dexamethasone (inhibition rates at 50 μM: 78.0%, 92.6%, and 62.6%, respectively).[70] Compounds **156**–**158** showed inhibitory activity against NO production in BV-2 microglial cells using the Griess assay with IC_{50} values of 30.0 ± 1.5, 15.5 ± 0.5 and 8.8 ± 0.1μM, respectively. Indomethacin was used as a positive control (IC_{50} = 34.5 ± 1.2 μM).[66] Compounds **457**–**459** exhibited a significant inhibitory effect on the production of nitric oxide (NO) in murine macrophages (RAW 264.7) activated by lipopolysaccharide (LPS).[145] Asterriquinol E **34** and asterriquinol F **35** have inhibitory effects on NO production induced by LPS in microglia cells with N^G-monomethyl-$_L$-arginine ($_L$-NMMA) as a positive control (IC_{50} 4.8 μM) with IC_{50} values of 11.3 μM and 49.7 μM respectively.[23] Compared with dimethyl fumarate (DMF), a potent inflammation inhibitor, compound **211** exhibited weak anti-inflammatory activity in an ANA-1 murine macrophages model.[75] There is experimental evidence that **138** and **139** could dose-dependently inhibit the activity of NF-κB and exhibited significantly inhibitory effects on nitric oxide (NO) production induced by lipopolysaccharide (LPS) in the murine RAW 264.7 macrophage cells.[61] Myrochromanols A **396** and C **398** inhibited lipopolysaccharide (LPS)-induced NO production in BV2 cells with IC_{50} values of 26.04 and 25.80 μM, respectively.[130]

Antioxidant Activities

Compounds **323, 324** and **399** showed radical scavenging activity against DPPH with IC_{50} values of 38.9, 42.7, and 87.5 μM, respectively.[11]

(*E*)-4-hydroxy-3-[(4-hydroxy-3-methylbut-2-en-1-yl)oxy] benzoic acid **367** showed radical scavenging activity against DPPH with IC_{50} value of 0.51 mg/mL.[96] Compound **305** exhibited potent DPPH radical scavenging activities with IC_{50} value of 1.23μg/mL.[107] Pochoniolides A **469** and B **470** showed hydroxyl radical-scavenging and singlet oxygen-quenching activities. Quercetin, pochoniolides A **469** and B **470** all showed scavenging activity against ·OH as well as a quenching effect on O_2. The detected values of ·OH and O_2 were suppressed by 6.7% and 4.3% in quercetin, 7.9% and 3.1% in pochoniolide A, and 1.2% and 0.5% in pochoniolide B, with being assumed that 100% generation represented a negative control.[147] Trichothioneic acid **92** exhibited hydroxyl radical-scavenging and singlet oxygen-quenching activities.[47] Compounds **545**–**546** displayed radical-scavenging activity against 2,2-diphenyl-1-picrylhydrazyl free radicals with the IC_{50} values of 3.45 ± 0.02, 23.73 ± 0.08 μM, respectively. Compounds (±)-**385, 387** exhibited potent antioxidant capacity with oxygen radical absorbance capacity values of 1.73 ± 0.13, 1.65 ± 0.03 μmol TE/μmol, respectively. Compounds (±)-**385** and (±)-**386** also exhibited protective effects on oxidative injury of PC12 cells induced by H_2O_2.[128]

Antiviral Activities

Isoaspulvinone E **450** showed significant anti-influenza A H1N1 virus activities, with IC_{50} value of 32.3 μg/mL.[143] When compared with ribavirin (IC_{50} 113.1 μM), compounds **10**–**12** and **14**–**15** exhibited significant protection against H1N1 virus-induced cytopathogenicity in MDCK cells with IC_{50} values of 28.3, 38.9, 32.2, 73.3, 34.1 μM, respectively.[17] Ochraceopone A **102** and isoasteltoxin **363** exhibited antiviral activities against the H1N1 and H3N2 influenza viruses with IC_{50} values of >20.0/12.2 ± 4.10 and 0.23 ± 0.05/0.66 ± 0.09 μM, respectively. It was noteworthy that the selectivity indexes (SI) of anti-H1N1 activity of **363** was 2.35.[53] Compounds **280** and **281** exhibited anti-H1N1 activity with IC_{50} values of 133.4, 44.6, respectively (ribavirin was used as the positive control, IC_{50} 101.4 μM). They also showed a strong anti-HSV-1 activity with IC_{50} values of 55.5and 21.4 μM, respectively, compared with the positive control (acyclovir, IC_{50} 150.2 μM). Compound **281** also possessed a strong anti-HSV-2 effect with IC_{50} value of 76.7 μM (acyclovir as the positive control, IC_{50} 128.6 μM), respectively.[100]

Antimalarial Activities

Compound **17** was tested for antimalarial activity against the parasite *Plasmodium falciparum* (K1, multidrug resistant strain), and it showed weak antimalarial activity with an IC_{50} value of 16.7 μM.[18] Solaninaphthoquione **429** displayed weak antimalarial activity (IC_{50} of 26.1 μM).[138] Penicilleremophilane A **99** was approximately half as active against *Plasmodium falciparum* with the IC_{50} value of 3.45 μM.[51] Oxisterigmatocystin E **276** showed antimalarial activity against *Plasmodium falciparum* with IC_{50} value of 7.9 μM.[98] Macrosporusone B **251** exhibited antimalarial activity against *Plasmodium falciparum* with IC_{50} values of 10.28 μM.[88]

Immunosuppressive Activities

Isochaetomium A_2 **351**, compound **351** showed obvious inhibitory effects on mouse spleen cell proliferation with successive IC_{50} values of 0.52 μM.[120] Compounds **481** and **482** exhibited significant inhibition of ConA-induced T-cell proliferation, with IC_{50} values of 4.1 and 1.9 μM, and LPS-induced B-cell proliferation with IC_{50} values of 9.8 and 1.1 μM, respectively. Compounds **484, 485**, and **488** exhibited selective immunosuppressive effects toward the LPS-induced B-cell proliferation with IC_{50} values ranging from 5.5 to 21.9 μM.[151] The bioactivity assays revealed that compounds **165, 166, 169, 170**, and **173** exhibited a significant immunosuppressive effect against concanavalin A (ConA)-induced T lymphocyte proliferation with IC_{50} values ranging from 5.6 to 8.8 μM.[69] The immunosuppressive activity assay revealed that compounds **188, 189**, and **193**−**196** showed significant inhibitory activity against concanavalin A (ConA)-induced T lymphocyte proliferation with IC_{50} values ranging from 4.1 to 9.4 μM.[72] In the immunosuppressive activity assay, compounds **201**–**202** showed potent inhibitory activity against concanavalin A (ConA)-induced T

lymphocyte proliferation with IC_{50} values of 78.3, 81.1 nmol/L, respectively, which provided promising leads for designing and developing new immunosuppressive agents to treat auto-immunological diseases.[73]

Other Activities

Paecilomide **90** was evaluated for acetylcholinesterase inhibition, presenting 57.5±5.50% of acetylcholinesterase inhibition.[45] Compound **217** was evaluated using in vitro binding assays of opioid receptors (subtypes δ, κ, and μ) and cannabinoid receptors (CB1 and CB2). Compound **217** selectively inhibited 42% of the specific binding of [3H]-DAMGO to CHO-K1 cell membranes expressing human μ-opioid receptors at 10 μM.[79] For antiacetylcholinesterase activity, Mangrovamide C **24** showed moderate acetylcholinesterase inhibitory effect with an IC_{50} value of 58.0 μM.[19] Compounds **222** and **223** were found to inhibit the conidial germination in the rice blast fungus *Magnaporthe oryzae* at concentrations of 25 μg/mL, 50 μg/mL, respectively.[81] Talacoumarins A **400** and B **401** had moderate anti-$A\beta_{42}$ aggregation activity, with relative inhibitory rates of (49.33 ± 3.16)% and (44.99 ± 3.64)% [the positive control EGCG had a relative inhibitory rate of (67.23 ± 2.51)%] at the concentration of 100 μM, and this is the first report on the $A\beta_{42}$ inhibitory aggregation activity of coumarins.[131] In the brine shrimp lethality assay, rubrumazine B **26** exhibited potent activity, with LD_{50} value of 2.43 μM, Compounds **25, 27** displayed modest activities, with LD_{50} values of 29.8 and 16.5 μM.[20] Compound **523** exhibited the most potent activity against HMG-CoA reductase, with an IC_{50} value of 387 μM. In addition, the present study indicated the direct interaction of compound **523** with HMG-CoA reductase.[160] Talaraculones A and B (**357** and **358**) exhibited stronger inhibitory activity against α-glucosidase than the positive control acarbose (IC_{50} = 101.5 μM), with IC_{50} values of 78.6 and 22.9 μM, respectively.[122] Aspereusin A **526** was active against acetylcholinesterase (AchE) with a ratio of 62% at the concentration of 50 μM.[93] (–) Benzomalvins E **80** enhanced the cytotoxic capability of 5-fluorouracil against A549 on a different level.[39] Compounds **142, 145**, and **146** showed comparable seed-germination-promoting activities to that previously reported for the growth regulator cotylenin E.[63] Exophiarin **422** has been evaluated by glucose uptake assay (GUA) using L6 skeletal muscle cells (myotubes), which takes up glucose for its metabolic activities through the glucose transporter protein, GLUT4. And exophiarin **422** with TPI-2 and TPI-5 have displayed moderate improvement in glucose uptake activity when tested in rat skeletal muscle cell line L6.[135] Compound **478** dose-dependently inhibited bone morphogenetic protein–induced alkaline phosphatase activity in myoblasts with half-maximal inhibitory concentration values of 19.8 μM.[150] Compounds **206–210** could inhibit the hepatic glucose production with EC_{50} values of 17.6, 30.1, 21.3, 9.6, and 9.9 μM, respectively, and decrease the cAMP contents in glucagon-induced HepG2 cells.[74]

Concluding Remarks and Discussion

Based on the above literature, as mentioned above, we analyzed the classification of these new compounds and the proportion of different types of these new compounds. From the analysis data, 279 of the 546 new compounds are active. In these activity categories, anticancer and antimicrobial active compounds accounted for a large proportion, 36.2% and 30.8%, respectively (Figure 9). From the strain sources of these new compounds, *Aspergillus, Penicillium* and *Talaromyces* accounted for the majority, accounting for about 56%. We also classified and analyzed the compounds from different strains, as illustrated in Figure 10. In addition, we also analyzed the habitats of these source strains. Compared with special habitats, such as alpinc, polar regions, oceans, etc., most of the strains are from non-extreme living environments (66.9%) and rhizosphere soil (21.8%) (Figure 11). We also made an interesting analysis to analyze the proportion of different compounds in the same activity, for example, among the 86 compounds with antimicrobial activity, there are 44 ketone compounds, accounting for about 51%. Among the compounds with immunosuppressive activity, terpenes and steroids accounted for about 68% (Figure 12).

In this review, we summarized 546 new compounds derived from soil fungi, classified them according to their structures, and classified their activities, including anticancer, antimicrobial, anti-inflammatory, antioxidant, antiviral, antimalaria, and immunosuppressive activities. From the 546 new compounds from soil fungi and their activities summarized in this review since 2011, it is noteworthy that among these active compounds, anticancer and antimicrobial activities account for almost 51%. In order to facilitate readers' understanding, we have made a table In this table, readers can more clearly and simply understand the microbial sources, biological activities, habitats of microbial sources, and

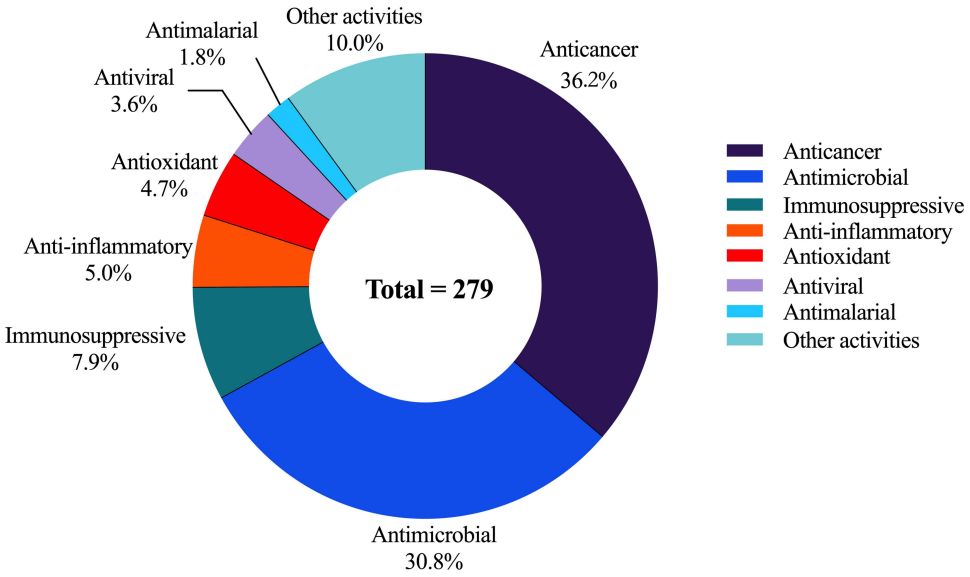

Figure 9 The percentage of compounds with various activities.

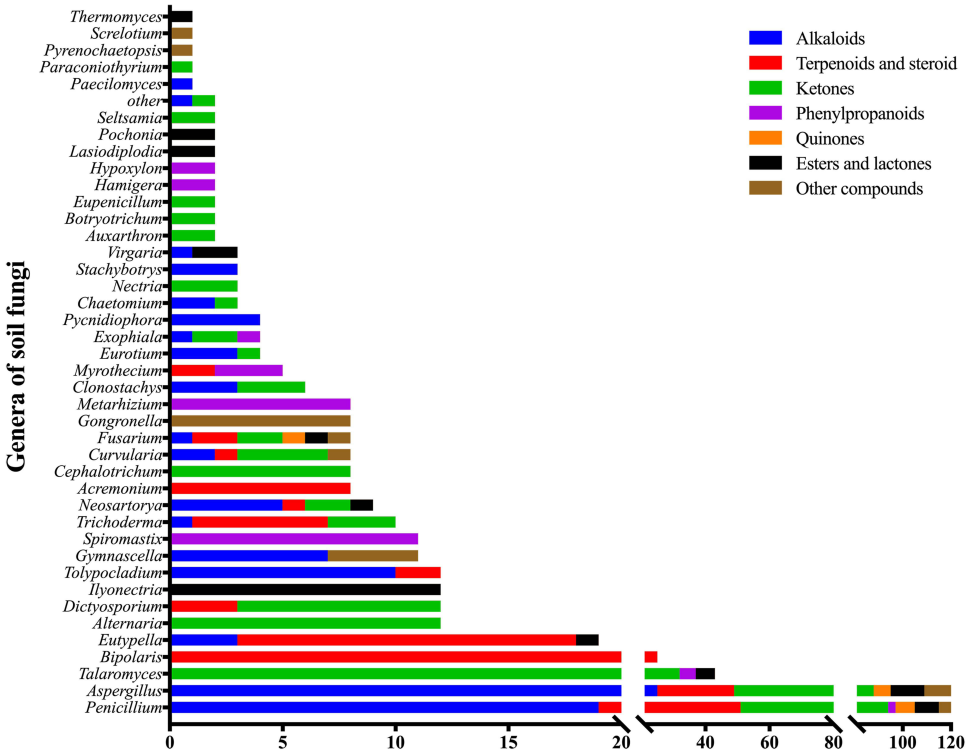

Figure 10 The number of various compounds from each genus.

relevant references of these new compounds. All information about the new compounds are briefly summarized in Table 1. It may provide a lot of help for future drug research and development. Microorganisms have provided abundant sources of natural products, which have been developed as commercial products for human medicine, animal health, and plant crop protection.[167] Fungi are an ideal source for obtaining novel skeletons through large-scale culture: compared with plants, fungi can proliferate rapidly from small amounts of spores to a mass of branching hyphaes, which are more environmentally friendly than collecting plant materials; compared with bacteria, fungi can be cultured in a solid medium

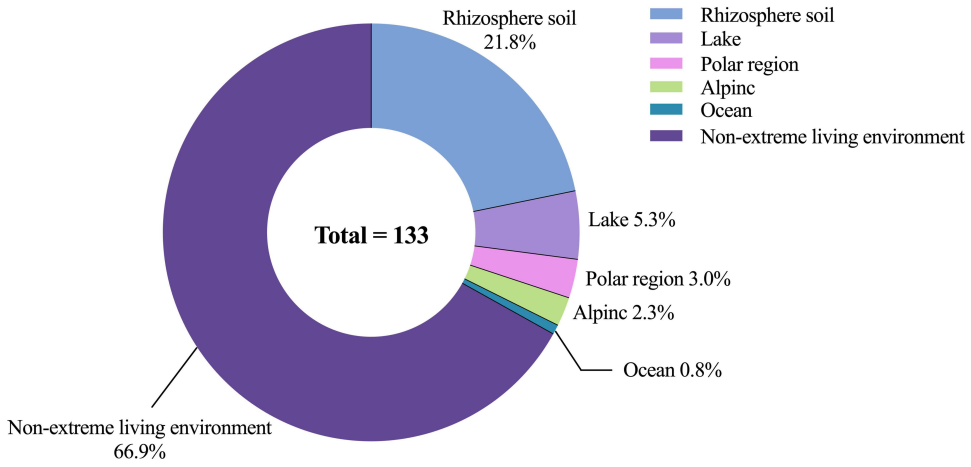

Figure 11 Proportion of strains in different living environments.

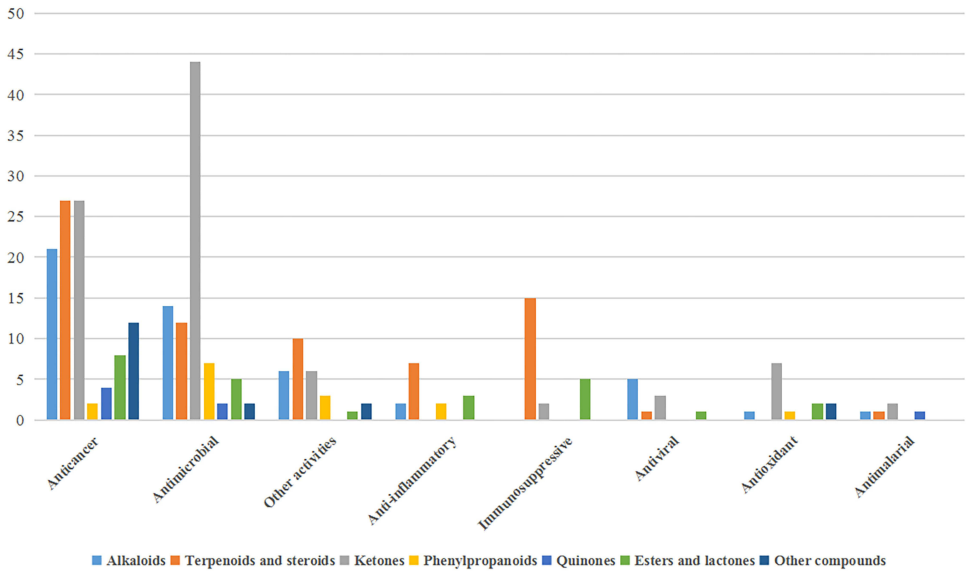

Figure 12 Number of different compounds with different activities.

for a longer time. Specifically, a large-scale culture can produce unexpected rearrangements and combinatorial chemistry, which serve as "dark tunnels" to novel scaffolds.[9] Artifacts are formed during isolation/purification of natural products. Factors such as pH, temperature, light, oxygen, humidity, and metal ions can lead to structural changes. Specific examples have been discussed in detail in a recent review on the formation of natural-product artifacts.[168] Artifacts are often intentionally or unintentionally overlooked, but in large-scale culture it is an issue that cannot be ignored. Extensive separation of large-scale extracts exposes natural products to longer expose to solvents, heat, air, light, and pH variations during extraction, partitioning, chromatography and drying.[9] The change of these external factors will inevitably affect the metabolism of microorganisms and the change of compound structure. Therefore, one problem arising from the use of large-scale cultivation of fungi is how to obtain stable access to those minor metabolites with novel skeletons. This may need to be solved in combination with chemical synthesis. Another problem is the habitat source of the strains. In this review, we analyzed the habitats of the strains involved. Although most of the strains come from non-extreme habitats, we still expect to obtain fungal strains from some extreme habitats. The extremobiosphere encompasses a broad range of biomes that include hyperarid deserts, deep-sea sediments and permafrost soils, as well as acid and high-temperature environments. Such extreme habitats are characterized by combinations of environmental

Table 1 Brief Summary of New Compounds

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
Alkaloids					
1	Pseudofischerine	*Neosartorya pseudofischeri*	Angthong Province, Thailand	–	[10]
2–3	Peneciraistins E-F	*Penicillium raistrickii*	Shandong Province, China	-	[11]
4*	Exopisiod	*Exophiala pisciphila* strain PHF-9	Yunnan Province, China	Induction of apoptosis	[12]
5*	Waikialoid A	*Aspergillus* sp.	Honolulu, Hawaii	Suppresses Hyphal Morphogenesis and Inhibits Biofilm Development in Pathogenic *Candida albicans*	[13]
6	Effusin A	*Aspergillus effuses* H1-1	Fujian Province, China	Antitumor activity	[14]
7*	Dihydrocryptoechinulin D				
8*	Dihydroneochinulin B	*Aspergillus effuses* H1-1	Fujian Province, China	Cytotoxic activity	[15]
9	Unnamed	*Neosartorya fischeri* KUFC 6344	Thailand	-	[16]
10*	3-deoxo-4b-deoxypaxilline	*Penicillium camemberti* OUCMDZ-1492	Hainan Province, China	Antiviral activity against the H1N1 virus	[17]
11*	4a-demethylpaspaline-4a-carboxylic acid				
12*	4a-demethylpaspaline-3,4,4a-triol				
13	2'-hydroxypaxilline				
14*	9,10-diisopentenylpaxilline				
15*	(6*S*,7*R*,10*E*,14*E*)-16-(1*H*-Indol-3-yl)-2,6,10,14-tetramethylhexadeca-2,10,14-triene-6,7-diol				
16, 17*, 18–21	Asperdiazapinones A-F	*Aspergillus* sp. PSU-RSPG185	Suratthani Province, Thailand	Antimalarial activity	[18]
22–23, 24*	Mangrovamides A-C	*Penicillium* sp. SYFz-1	Hainan Province, China	Moderate acetylcholinesterase inhibitory activity	[19]
25*, 26*, 27*	Rubrumazines A-C	*Eurotium rubrum* MA-150	Andaman Sea coastline, Thailand	Brine shrimp lethality	[20]
28	Penilline A	*Penicillium* sp. SCSIO 05705	Chinese Antarctic station	-	[21]
29	Isopenilline A				
30	Penilline B				
31–32, 33*	Kumbicins A-C	*Aspergillus kumbius* FRR6049	Southern Queensland, Australia	Antitumour activity; Antimicrobial activity	[22]
34*, 35*	Asterriquinols E-F	*Aspergillus* sp.CBS-P-2	Jilin Province, China	Inhibitory activities against LPS-induced NO production in microglia BV-2 cells (34*, 35*); Cytotoxicity (34*)	[23]
36–37	Cyclopiamines C-D	*Penicillium* sp. CML 3020	Atlantic Forest, Brazil	-	[24]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
38*, 39*, 40*, 41*, 42*, 43*, 44*, 45*, 46*, 47*	Tolypocladins A-J	*Tolypocladium* sp. XL115	Hunan Province, China	Cytotoxic activity (38*); Antibacterial activity (38*, 39*, 45*); Antifungal activity (38*, 40*, 41*, 42*, 43*, 44*, 46*, 47*)	[25]
48*, 49*	Chaetomadrasins A-B	*Chaetomium madrasense* 375	Sinkiang Province, China	Cytotoxicity	[26]
50	Paraherquamide J	*Penicillium janthinellum* HK1-6	Hainan Province, China	-	[27]
51–52	Tryptoquivalines W-X	*Aspergillus terreus* FS107	Top of Mauna Kea, Hawaii	-	[28]
53*, 54–55	Cytochalasins Z_{24-26}	*Eutypella* sp. D-1	London Island of Kongsfjorden, Arctic	Cytotoxicity	[29]
56	Aspergilluchalasin	*Aspergillus* sp. PSU-RSPG185	Surat Thani Province, Thailand	-	[30]
57*, 58	Iizukines C-D	*Aspergillus iizukae*	Shandong Province, China	Cytotoxicity	[31]
59	MBJ-0030	*Stachybotrys* sp. f23793	Shizuoka prefecture, Japan	-	[32]
60	MBJ-0031				
61	MBJ-0032				
62*, 63*, 64*, 65*	Pycnidiophorones A-D	*Pycnidiophora dispersa*	Hebei Province, China	Cytotoxicity	[33]
66*	Clonorosin A	*Clonostachys rosea*	Bank of the Yellow River in Lanzhou, Gansu, China	Active (66*) against Fusarium oxysporum	[34]
67	Clonorosin B		Bank of the Yellow River in Lanzhou, Gansu, China		
68*, 69*, 70*, 71*, 72*, 73*	Gymnastatins T-Y	*Gymnascella dankaliensis*	Giza pyramids, Egypt	Cytotoxicity	[35]
74*	Dankastatin D				
75	*N*-[4-hydroxy-3-prenyl-benzoyl]-L-threonine	*Curvularia inaequalis strain* HS-FG-257	Heilongjiang Province, China	-	[36]
76	*N*-[2,2-dimethyl-2*H*-chromene-6-carbonyl]-L-threonine				
77	(5*S*)-3,4,5,7-tetramethyl-5,8-dihydroxyl-6(5*H*)-isoquinolinone	*Penicillium* sp. H9318	Malaysia	-	[37]
78	3,8-Diacetyl-4-(3-methoxy-4,5-methylenedioxy)benzyl-7-phenyl-6-oxa-3,8-diazabicyclo[3.2.1]octane	*Neosartorya pseudofischeri*	Angthong Province, Thailand	-	[10]
79	Fusaravenin	*Fusarium avenaceum* SF-1502	Gansu Province, China	-	[38]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
80*	(-) Benzomalvins E	*Penicillium* sp. SYPF 8411	Xinjiang Uygur Autonomous Region, China	Indoleamine 2.3-dioxygenase (IDO) inhibitor	[39]
81	Tryptoquivaline V	*Neosartorya pseudofischeri*	Chiang Mai forest, Thailand	-	[40]
82	Brasiliamide G				
83	Talarodone A	Co-culture of *Talaromyces pinophilus* and *Paraphaeosphaeria* sp.	Miyazaki Prefecture, Japan	-	[41]
84–86	Asperidines A-C	*Aspergillus sclerotiorum* PSU-RSPG178	Surat Thani Province, Thailand	-	[42]
87	Iizukine E	*Aspergillus iizukae*	Shandong Province, China	-	[31]
88	Methyl (2*Z*,3*E*,5*E*,7*E*,9*E*)-4,10-dimethyl-11-(2,5-dioxopyrrolidin-3-yl)-2-(2-hydroxyethylidene)-11-oxoundeca-3,5,7,9-tetraenoate	*Aspergillus sp.* OUCMDZ-1914	Hainan Province, China	-	[43]
89*	Virgaricin B	*Virgaria boninensis* FKI-4958	The Bonin Islands, Tokyo, Japan	Antibacterial activity	[44]
90*	Paecilomide	*Paecilomyces lilacinus*	UFMG, MG, Brazil	Acetylcholinesterase inhibitory activity	[45]
91	Clonostalactam	*Clonostachys rosea*	Banyumas, Indonesia	-	[46]
92*	Trichothioneic acid	*Trichoderma virens* FKI-7573	Obihiro, Hokkaido, Japan	Hydroxyl radical-scavenging; Singlet oxygen-quenching activity	[47]
Terpenoids and steroids					
93*, 94	Fudecadiones A-B	*Penicillium* sp. BCC 17468	Khao Yai National Park, Nakhon Ratchasima, Thailand	Anticancer activity	[48]
95*	8α-Hydroxyroridin H	*Myrothecium* sp. GS-17	Gansu Province, China	Antifungal Activity	[49]
96*	Myrothecin A				
97*, 98*	Penicibilaenes A-B	*Penicillium bilaiae* MA-267	Hainan Province, China	Antifungal activity	[50]
99*, 100	Penicilleremophilanes A-B	*Penicillium copticola* PSU-RSPG138	Surat Thani Province, Thailand	Cytotoxic activity; Antimycobacterial activity; Antimalarial activity	[51]
101*	Aspergiketone	*Aspergillus fumigatus*	Shandong Province, China	Cytotoxicity	[52]
102*, 103–106	Ochraceopones A-E	*Aspergillus ochraceopetaliformis* SCSIO 05702	Chinese Antarctic station	Antiviral activity	[53]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
107*	13-Hydroxy-3,8,7(11)-eudesmatrien-12,8-olide	*Eutypella* sp. 1–15	Fujian Province, China	Antibacterial activity; Anticancer activity	[54]
108	13-Hydroxy-3,5,8,7(11)-eudesmatetraen-12,8-olide				
109	2-One-13-hydroxy-3,5,8,7(11)-eudesmatetraen-12,8-olide				
110	8,13-Dihydroxy-3,7(11)-eudesmadien-12,8-olide				
111	3β-hydroxy-β-acorenol	*Fusarium proliferatum* AF-04	Green Chinese onion	-	[38]
112	Cyclonerotriol B	*Fusarium avenaceum* SF-1502	-		
113–114, 115*	Trichodermapenes A-C	*Trichoderma reesei* PSU-SPSF013	Narathiwat Province, Thailand	Antifungal activity	[55]
116–118	Dictyosporins A-C	*Dictyosporium digitatum*	Herod, Illinois, USA	-	[56]
119	Trichocitrinovirene A	*Trichoderma citrinoviride* PSU-SPSF346	Sirindhorn Peat Swamp Forest, Narathiwat Province, Thailand.	-	[57]
120	Trichocitrinovirene B				
121	Unnamed	*Aspergillus calidoustus*	Dianchi Lake, Yunnan Province.China	-	[58]
122	Unnamed				
123	Unnamed				
124	Unnamed				
125	Unnamed				
126	Unnamed				
127	Unnamed				
128*	Sartorypyrone A	*Neosartorya fischeri* KUFC 6344	Thailand	Anticancer activity	[16]
129*, 130*	Libertellenones G-H	*Eutypella* sp. D-1	London Island of Kongsfjorden, Arctic	Antibacterial activity (129*); Anticancer activity (130*)	[59]
131	4b-deoxy-1'-*O*-acetylpaxilline	*Penicillium* sp. CM-7	Yunnan Province, China	-	[60]
132	4b-deoxypenijanthine A				
133*, 134*, 135*, 136*, 137*	Libertellenones O-S	*Eutypella* sp. D-1	London Island of Kongsfjorden, Arctic	Cytotoxic activity (133*-139*); Inhibit the activity of NF-κB inhibitory effects on nitric oxide production induced by lipopolysaccharide (138*, 139*)	[61]
138*, 139*	Eutypellenones A-B				
140*, 141*	Libertellenones M-N	*Eutypella* sp. D-1	London Island of Kongsfjorden, Arctic	Cytotoxicity (140*, 141*); Antibacterial activity (140*)	[62]
142*, 143, 144, 145*, 146*, 147, 148	Dongtingnoids A-G	*Penicillium* sp. DT10	Hunan Province, China	Seed-germination-promoting activity	[63]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
149*, 150	Tolypocladins K-L	*Tolypocladium* sp. XL115	Hunan Province, China	Antifungal activity (149*)	[64]
151*	Trichodermanene	*Trichoderma reesei* PSU-SPSF013	Narathiwat Province, Thailand	Antifungal activity	[55]
152	4,25-dehydrominiolutelide B	*Penicillium* sp. MA-37	Hainan Province, China	-	[65]
153	4,25-dehydro-22-deoxyminiolutelide B				
154	Isominiolutelide A				
155, 156*, 157*, 158*, 159	Purpurogenolides A-E	*Penicillium purpurogenum* MHz 111	Heilongjiang Province, China	Inhibition of nitric oxide production	[66]
160*, 161*, 162–163	Unnamed	*Penicillium* sp.	Liaoning Province, China	Cytotoxic activity (160*, 161*); Antibacterial activity (160*)	[67]
164	Terretonin M	*Aspergillus terreus* TM8	A hot (~50 °C) desert place, South Egypt	-	[68]
165*	Δ^{12}-19-dehydroxyarthripenoid A	*Bipolaris zeicola*	Hubei Province, China	Significant inhibitory effect against concanavalin A (ConA)-induced T lymphocyte proliferation (165*, 166*, 169*, 170*, 173*); Cytotoxic activity (165*, 166*, 168*)	[69]
166*	12,19-didehydroxy-arthripenoid A				
167	Tetrahydrofuran-3-*epi*-cochlioquinone A				
168*	Isotetrahydrofuran-3-*epi*-cochlioquinone A				
169*	19-dehydroxy-arthripenoid A				
170*	Δ^{2}-19-dehydroxy-arthripenoid A				
171	4-acetoxy-isocochlioquinone D				
172	4-acetoxy-31α-methoxy-isocochlioquinone D				
173*	19-dehydroxyl-31-keto-3-*epi*-arthripenoid A				
174	Acremine T	*Acremonium persicinum* SC0105	Guangdong Province, China	Cytotoxicity	[5]
175*, 176*,177–178	Bisacremines A-D				
179–180,181*	Bisacremines E-G	*Acremonium persicinum* SC0105	Guangdong Province, China	Anti-inflammatory activity	[70]
182	Asperanstinoid A	*Aspergillus calidoustus*	Dianchi Lake, Yunnan Province.China	Cytotoxicity (185*) against the HL- 60 and SU-DHL-4 tumor cell lines.	[71]
183	Asperanstinoid B				
184	Asperanstinoid C				
185*	Asperanstinoid D				
186	Asperanstinoid E				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
187	Bipolaquinone A	*Bipolaris zeicola*	Mo Mountain of East Lake, Wuhan City of Hubei Province, China,	Inhibitory activity (188*, 189*, 193*, 194*, 195*, 196*) against concanavalin A (ConA)-induced T lymphocyte proliferation	[72]
188*	Bipolaquinone B				
189*	Bipolaquinone C				
190	Bipolaquinone D				
191	Bipolaquinone E				
192	Bipolaquinone F				
193*	Bipolaquinone G				
194*	Bipolaquinone H				
195*	Bipolaquinone I				
196*	Bipolaquinone J				
197	Bipolarinoid A	*Bipolaris zeicola*	Mo Mountain of East Lake, Wuhan City of Hubei Province, China	Inhibitory activity (201*, 202*) against concanavalin A (ConA)-induced T lymphocyte proliferation	[73]
198	Bipolarinoid B				
199	Bipolarinoid C				
200	Bipolarinoid D				
201*	Bipolarinoid E				
202*	Bipolarinoid F				
203*	Aspergorakhin B	*Aspergillus gorakhpurensis* F07ZB1707	Mountainous region of shennongjia Forestry District, Hubei Province of China	Inhibitory effect (203*) against Protein tyrosine phosphatases including PTP1B, SHP1, and TCPTP in vitro.	[6]
204	Aspergorakhin C				
205	Aspergorakhin D				
206*	Encindolene D	*Penicillium sp.* HFF16	Rhizosphere soil of *Cynanchum bungei* Decne., in Mount Tai, China	Inhibit the hepatic glucose production(206*, 207*, 208*, 209*, 210*)	[74]
207*	Encindolene E				
208*	Encindolene F				
209*	Encindolene G				
210*	Encindolene H				
211*	4α-methyl-9α-methoxyandrosta-8,15-diene-3,17-dione	*Curvularia borreriae* strain HS-FG-237	-	Cytotoxicity; anti-inflammatory activity	[75]
212*	Unnamed	*Aspergillus flavus* JDW-1	-	Cytotoxicity	[76]
213*	Aspergorakhin A	*Aspergillus gorakhpurensis* F07ZB1707	Mountainous region of Shennongjia Forestry District, Hubei Province of China	Inhibitory effect against Protein tyrosine phosphatases including PTP1B, SHP1, and TCPTP in vitro.	[6]
Ketones					
214*	1-(3,5-dihydroxyphenyl)-4-hydroxypentan-2-one	*Exophiala pisciphila* PHF-9	Yunnan Province, China,	Cytotoxicity	[77]
215*	Pyrenocine J	*Curvularia affifinis* strain HS-FG-196	Jilin Province, China	Cytotoxicity	[78]
216	Pyrenochaetic acid D				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
217*	Euparvione	*Eupenicillium parvum*	Cuba	Binding human μ–opioid receptors	[79]
218	Euparvilactone				
219	Penicillither	*Penicillium* sp. PSU-RSPG99	Surat Thani Province, Thailand	-	[80]
220–221, 222*, 223*	Tanzawaic acids I-L	*Penicillium sp.* IBWF104-06	Kaiserslautern, Germany	Inhibited the conidial germination in Magnaporthe oryzae	[81]
224–226	Blennolides H-J	*Alternaria sp.*	Vicinity of Wailua Falls, Hawaii	-	[82]
227–230	Pyrenochaetic acids E-H				
231*, 232,233	Asperochrins A-C	*Aspergillus ochraceus* MA-15	Hainan Province, China	Antibacterial activity	[83]
234*	Iizukine A	*Aspergillus iizukae*	Shandong Province, China	Cytotoxicity against cancer cell	[84]
235–236	Penicipyrans A-B	*Penicillium raistrickii*	Shandong Province, China	Cytotoxicity	[85]
237*	Penicipyran E				
238*, 239	Penijanthinones A-B	*Penicillium janthinellum* HK1-6	Hainan Province, China	Displayed potent antibacterial activity	[86]
240*, 241*	Talaroketals A-B	*Talaromyces stipitatus* ATCC 10500	-	Antibacterial activity	[87]
242	Aspergorakhin E	*Aspergillus gorakhpurensis* F07ZB1707	Mountainous region of Shennongjia Forestry District, Hubei Province of China	-	[6]
243	Aspergorakhin F				
244	Aspergorakhin G				
245	Aspergorakhin H				
246	Aspergorakhin I				
247	Aspergorakhin J				
248	Aspergorakhin L				
249	Talaromycesone C	*Talaromyces macrosporus* KKU-1NK8	Khon Kaen Province, Thailand	Antimalarial activity (251*); Cytotoxicity (250*, 251*, 253*)	[88]
250*, 251*, 252, 253*, 254	Macrosporusones A-E				
255*, 256*	Bacillisporins I-J	*Talaromyces bacillisporus* BCC17645	Khao Yai National Park, Nakhon Ratchasima Province, Thailand	Cytotoxicity (255*-258*); Antibacterial activity (257*)	[89]
257*, 258*	Duclauxamides B-C				
259	9a-*epi*-Bacillisporin E	*Talaromyces stipitatus*	-	Antimicrobial activity; Cytotoxicity	[90]
260	Bacillisporin F				
261	1-*epi*-bacillisporin F				
262, 263*	Bacillisporins G-H				
264	Aspergone	*Aspergillus* sp. SCSIO41002	Hainan Province, China	-	[91]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
265*	7-methoxy-2,2-dimethyl-4-octa-4',6'-dienyl-2H-napthalene-1-one	*Penicillium* sp	Punjab, India	Antimicrobial activity; Cytotoxicity	[92]
266–268	Aspereusins C-E	*Aspergillus terreus* YIM PH30711	New Delhi, India	-	[93]
269	Penicillixanthone	*Penicillium* sp. PSU-RSPG99	Surat Thani Province, Thailand		[80]
270*	Castochrin	*Alternaria sp.*	Vicinity of Wailua Falls, Hawaii	Antibacterial activity; Cytotoxic activity	[82]
271	Blennolide G				
272	Penicillone C	*Penicillium citrinum* PSU-RSPG95	Surat Thani Province, Thailand.	-	[94]
273*	6-[1,2-dimethyl-6-(2-methyl-allyloxy)-hexyl]-3-(2-methoxy-phenyl)-chromen-4-one	*Penicillium* sp. HT-28	Punjab, India	Antibacterial activity	[95]
274	2-(2',4',6'-Trihydroxyphenyl)-(7-hydroxy-5-methyl) chromone	*Aspergillus aculeatus*	Chongqing, China	-	[96]
275	Penicillanthone	*Penicillium aculeatum* PSU-RSPG105	Surat Thani Province, Thailand	-	[97]
276*, 277*	Oxisterigmatocystins E-F	*Botryotrichum piluliferum*	Sangkhla Buri, Kanchanaburi Province, Thailand	Antimalarial activity (276*); Cytotoxicity(276*, 277*)	[98]
278*, 279	Penixanthones A-B	*Penicillium* sp. SYFz-1	Hainan Province, China	Cytotoxicity	[99]
280*	Methyl-(2-chloro-l,6-dihydroxy-3-methylxanthone)-8-carboxylate	*Aspergillus iizukae*	Shandong Province, China	Antiviral activity	[100]
281*	Methyl-(4-chloro-l,6-dihydroxy-3-methylxanthone)-8-carboxylate				
282	Methyl-(4-chloro-6-hydroxy-1-methoxy-3-methylxanthone)-8-carboxylate				
283	Methyl-(6-hydroxy-1-methoxy-3-methylxanthone)-8-carboxylate				
284	4-chloro-1,6-dihydroxy-3-methylxanthone-8-carboxylic acid				
285*,286–287	Blennolides L-N	*Trichoderma asperellum* PSU-PSF14	Narathiwat Province, Thailand	Antifungal activity	[101]
288	Wentixanthone A	*Aspergillus wentii*	Hypersaline lake El Hamra in Wadi El-Natrun, Egypt	-	[102]
289–290	Fusarpyrones A-B	*Fusarium solani* PSU-RSPG37	Suratthani Province, Thailand	-	[103]
291–292	Coniochaetones E-F	*Penicillium citrinum* PSU-RSPG95	Surat Thani Province, Thailand	-	[94]
293	Penicillanone				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
294*	8'-*O*-(3*R*-Hydroxy-butyryl)-rasfonin	*Cephalotrichum microsporum* (SYP-F 7763)	Yunnan Province, China	Antibacterial (295*-297*) activity; Anti-tumor activity (294*, 295*)	[104]
295*-297*	Cemironins A-C				
298	4-Methyl-8,10-dihydroxy-caprylic acid				
299	Chevalone F	*Neosartorya pseudofischeri*	Chiang Mai forest, Thailand	Antibacterial activity	[40]
300*	11-hydroxychevalone E				
301*, 302*, 303*	Peninaphones A-C	*Penicillium* sp. HK1-22	Hainan Province, China	Antibacterial activity (301*, 302*); Antimicrobial activity (303*)	[105]
304	Helvafuranone	*Aspergillus nidulans* BF0142	Hokkaido, Japan	-	[106]
305*	(±)-europhenol A	*Eurotium rubrum* MA-150	Andaman Sea coastline, Thailand	DPPH radical scavenging activities	[107]
306	Aspersclerotiorone E	*Aspergillus sclerotiorum* PSU-RSPG178	Surat Thani Province, Thailand	-	[108]
307*	Harzianone	*Cephalotrichum microsporum*	Yunnan Province, China	Antibacterial activity	[109]
308*	Harzianol				
309*	Harzianol acid				
310	Gotjawaside	*Auxarthron* sp. KCB15F070	Volcanic island Jeju, Korea	-	[110]
311	Gotjawalide				
312*, 313*	Thiocarboxylics A-B	*Penicillium* sp. sb62	Hunan Province, China	Antibacterial activity	[111]
314*, 315*	Thiocarboxylics C_{1-2}				
316*, 317*	Thiocarboxylics D_{1-2}				
318*, 319*	GregatinsF_{1-2}				
320*, 321*	Gregatins G_{1-2}				
322	*R*-Hexitronic acid	*Penicillium* sp. FG9RK	Agulu in Anambra state, Nigeria	-	[112]
323*, 324*, 325*	Peneciraistins A-C	*Penicillium raistrickii*	Shandong Province, China	Radical scavenging activity against DPPH (323*, 324*); Induces caspase-independent autophagic cell death through mitochondrial-derived reactive oxygen species production in lung cancer cells (325*)	[11,166]
326*	Sporulosol	*Paraconiothyrium sporulosum*	Jiangxi Province, China	Cytotoxicity	[113]
327	(+)-(5*S*)-arugosin K	*Talaromyces flavus*	Sinkiang Province, China	-	[114]
328	(-)-(5*R*)-arugosin K				
329	(+)-(5*S*)-arugosin L				
330	(-)-(5*R*)-arugosin L				
331	(+)-(5*S*)-arugosin M				
332	(-)-(5*R*)-arugosin M				
333	Arugosin N				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
334–335	Asperunguisones A-B	*Aspergillus unguis* PSU-RSPG204	Surat Thani Province, Thailand	-	[115]
336	(±)-4-hydroxy-3-methoxy-5-methyl-2-cyclopentenone	*Aspergillus Sclerotiorum*	Shandong Province, China	-	[116]
337*	Polluxochrin	*Alternaria* sp.	Vicinity of Wailua Falls, Hawaii	Antibacterial activity; Cytotoxic activity	[82]
338*	Dioschrin				
339	Dimethylamide asterrate				
340*, 341–342	Nectriatones A-C	*Nectria* sp. B-13	Arctic island of Spitzbergen, Svalbard	Cytotoxicity	[117]
343	Curvulopyran	*Aspergillus polyporicola* PSU-RSPG187	Surat Thani Province, Thailand	-	[118]
344	*ent*-curvulone A				
345	7-methoxy-2,3,6-trimethylchromone	*Exophiala pisciphila* PHF-9	Yunnan Province, China	-	[77]
346*, 347*	Penicilones G-H	*Penicillium janthinellum* HK1-6	Hainan Province, China	Show moderate inhibitory activity against Gram-positive bacteria (346*); Antibacterial activity (347*)	[86]
348	Tetrahydrotrichodimer ether	*Clonostachys rosea* YRS-06	Gansu Province, China	Antibacterial activity	[119]
349*, 350*	Dihydrotrichodimer ethers A-B				
351*	Isochaetomium A_2	*Chaetomium microcephalum*	Sichuan Province, China	Antibacterial activity; Inhibitory effects on mouse spleen cell proliferation	[120]
352	Wentiphenone A	*Aspergillus wentii*	Hypersaline lake El Hamra in Wadi El-Natrun, Egypt	-	[102]
353, 354*, 355*, 356*	Penicilones A-D	*Penicillium janthinellum* HK1-6	Hainan Province, China	Antibacterial activity	[121]
357*, 358*, 359–362	Talaraculones A-F	*Talaromyces aculeatus*	Shandong Province, China	Inhibitory activity against α-glucosidase (357*, 358*); Antibacterial activity (358*)	[122]
363*	Isoasteltoxin	*Aspergillus ochraceopetaliformis* SCSIO 05702	Chinese Antarctic station	Antiviral activity	[53]
364*	Curvularone A	*Curvularia inaequalis* strain HS-FG-257	Heilongjiang Province, China	Antitumor activity	[123]
365*	4-hydroxyradianthin				
366	1-(2',4'-dihydroxy-5'-methyl-3'-methylsulfanylmethylphenyl)-ethanone	*Penicillium crustosum* YN-HT-15	Yunnan Province, China	-	[124]
367*	(*E*)-4-Hydroxy-3-[(4-hydroxy-3-methylbut-2-en-1-yl)oxy] benzoic acid	*Aspergillus aculeatus*	Chongqing, China	Antagonism to DPPH	[96]
368–369	Talaflavuols B-C	*Talaromyces flavus* BYD07-13	Guangzhou Province, China	-	[125]
370	Aspereusin B	*Aspergillus terreus* YIM PH30711	New Delhi, India	-	[93]
371*	Seltsamiayu	*Seltsamia galinsogisoli* sp. nov.	Liaoning Province, China	Antibacterial activity	[126]
372*	Galinsogisoliyu				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
373*	1-(4-hydroxy-2,6-dimethoxy-3,5-dimethylphenyl)-2-methyl-1-butanone	*Aspergillus* sp.	Riyadh, Saudi Arabia	Antimicrobial activity	[127]
374	Dictyosporin D	*Dictyosporium digitatum*	Herod, Illinois, USA	-	[56]
375	Dictyophthalide A				
376–379	Dictyofurans A-D				
380	Dictyosporone A				
381–382	Xylariolides E-F				
383*	Aspergorakhin K	*Aspergillus gorakhpurensis* F07ZB1707	Mountainous region of Shennongjia Forestry District, Hubei Province of China	inhibitory effect against Protein tyrosine phosphatases including PTP1B, SHP1, and TCPTP in vitro.	[6]
384	Sulfurasperine A	*Aspergillus fumigatus* GZWMJZ-152	Caves in Guizhou province of China	Antioxidant capacity (385*, 387*);protective effects (385*, 386*) on oxidative injury of PC12 cells induced by H2O2	[128]
385*	Sulfurasperine B ((±)-2)				
386*	Sulfurasperine C ((±)-3)				
387*	Sulfurasperine D				
Phenylpropanoids					
388*, 389*, 390*, 391–393	Spiromastols A-F	*Spiromastix* sp. MCCC 3A00308	South Atlantic Ocean	Antibacterial activity	[129]
394*, 395*	Spiromastols J-K				
396*, 397*, 398*	Myrochromanols A-C	*Myrothecium verrucaria* HL-P-1	Heilongjiang Province, China	Inhibited lipopolysaccharide (LPS)-induced NO production in BV2 cells	[130]
399*	Peneciraistin D	*Penicillium raistrickii*	Shandong Province, China	Radical scavenging activity against DPPH	[11]
400*, 401*	Talacoumarins A-B	*Talaromyces flavus* BYD07-13	Hebei Province, China	Anti-Aβ_{42} aggregation activity	[131]]
402–403, 404*	Spiromastols G-I	*Spiromastix* sp. MCCC 3A00308	South Atlantic Ocean	Antibacterial activity	[129]
405*	(3*S*)-6-*O*-(4'-*O*-methyl-6'-acetyl-*β*-D-glucopyranoside)-7-*O*-methyl-8-hydroxyl-3-[(3*E*)-penta-3-enyl]-3,4-dihydroisocoumarin	*Metarhizium anisopliae* DTH12-10	-	Antibacterial activity	[132]
406	(3*S*)-7-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-6,8-dihydroxyl-3-[(3*E*)-pent-3-enyl]-3,4-dihydroisocoumarin				
407	(3*S*)-6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-7-*O*-methyl-8-hydroxyl-3-[(3*E*)-pent-3-enyl]-3,4-dihydroisocoumarin				
408	(3*S*)-6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-8-hydroxyl-3-[(3*E*)-pent-3-enyl]-3,4-dihydroisocoumarin				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
409	(3*S*)-6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-5,8-dihydroxyl-3-[(3*E*)-pent-3-enyl]-3,4-dihydroisocoumarin				
410	6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-7-*O*-methyl-8-hydroxyl-3-[(3*E*)-penta-3-enyl]-isocoumarin				
411	(3*R*)-6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-8-hydroxyl-3-[(1*E*,3*E*)-penta-1,3-dienyl]-dihydroisocoumarin				
412	(3*R*)-6-*O*-(4'-*O*-methyl-*β*-D-glucopyranoside)-7-*O*-methyl-8-hydroxyl-3-[(1*E*,3*E*)-penta-1,3-dienyl]-dihydroisocoumarin				
413–414	Talaisocoumarins A-B	*Talaromyces flavus* BYD07-13	Guangzhou Province, China	-	[125]
415	Talaflavuol A				
416–417	Penicipyrans C-D	*Penicillium raistrickii*	Shandong Province, China	-	[85]
418	(3*R*,4*R*)-4,8-Dihydroxy-5-(hydroxymethyl)-3-methylisochroman-1-one	*Hypoxylon* sp.	Heilongjiang Province, China	-	[133]
419	(3*R*,4*S*)-4,8-Dihydroxy-5-(hydroxymethyl)-3-methylisochroman-1-one				
420*	(9*R**)-8-methyl-9,11-dichlorodiaporthin	*Hamigera fusca* NRRL 35721	Maoueni, Grande Comore Island	Cytotoxic activity against cancer cell lines	[134]
421*	(9*S**)-8-methyl-9,11-dichlorodiaporthin				
422*	Exophiarin	*Exophiala* sp.	Kaziranga National Park, Assam	Improvement in glucose uptake activity when tested in rat skeletal muscle cell line L6	[135]
Quinones					
423*, 424	Citriquinones A-B	*Penicillium citrinum*	University of SriJayewardenepura, Sri Lanka	Antibacterial activity; Cell migration inhibitory activity	[136]
425	Penicilliquinone	*Penicillium* sp. PSU-RSPG99	Surat Thani Province, Thailand	-	[80]
426	Peniciherqueinone	*Penicillium herquei* PSU-RSPG93	Surat Thani Province, Thailand	-	[137]
427*, 428	Aspergillussanones A-B	*Aspergillus* sp. PSU-RSPG185	Surat Thani Province, Thailand	Cytotoxicity	[30]
429*	Solaninaphthoquione	*Fusarium solani* PSU-RSPG227	Surat Thani Province, Thailand	Cytotoxic; Antimalarial activity	[138]
430	Kumbicin D	*Aspergillus kumbius* FRR6049	Queensland, Australia	-	[22]
431*	PA3-d10	*Aspergillus flavus*	Iran	Antimicrobial activity	[139]

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
432–433	Wentibianthrones A-B	*Aspergillus wentii*	Hypersaline lake El Hamra in Wadi El-Natrun, Egypt	-	[102]
434	Wentibianthrone C (cis/trans)				
435	Herqueilenone A	*Penicillium herquei* FT729	Active volcano, Hawaii	-	[140]
436*	*ent*-12-methoxyisoherqueinone	*Penicillium herquei* FT729	Big Island, Hawaii.	Inhibitory activity (436*) against indoleamine 2.3-dioxygenase 1 (IDO1)	[141]
437	(−)-scleroamide				
438	(+)-scleroamide				
Esters and lactones					
439	3-Hydroxy-5-methylphenyl 2.4-dihydroxy-6-methylbenzoate	*Neosartorya pseudofischeri*	Angthong Province, Thailand	-	[10]
440–443, 444*, 445*	Talapolyesters A-F	*Talaromyces flavus* BYD07-13	Hebei Province, China	Cytotoxic activity	[142]
446	*R*-3-(3'-acetyl-2',6'-dihydroxy-5'-methylphenyl)-2-methyl-propionic acid methyl ester	*Penicillium crustosum* YN-HT-15	Yunnan Province, China	-	[124]
447	4-(4-Hydroxyphenethoxy)-4-oxobutanoic acid	*Fusarium solani* PSU-RSPG227	Surat Thani Province, Thailand	-	[138]
448–449	Penicillithiophenols A-B	*Penicillium copticola* PSU-RSPG138	Surat Thani Province, Thailand	-	[51]
450*	Isoaspulvinone E	*Aspergillus terreus* Gwq-48	Fujian Province, China	Anti-influenza A viral (H1N1)	[143]
451	Aspergillulactone	*Aspergillus* sp. PSU-RSPG185	Surat Thani Province, Thailand	-	[30]
452*, 453*	Cinatrins D-E	*Virgaria boninensis* FKI-4958	Bonin Islands, Tokyo, Japan	Antibacterial activity	[44]
454	Asperlide	*Aspergillus unguis* PSU-RSPG199	Surat Thani Province, Thailand	-	[144]
455	Aspersidone				
456, 457*, 458*, 459*, 460, 461	Penicimenolides A-F	*Penicillium* sp. SYP-F-7919	Yunnan Province, China	Cytotoxicity; Inhibitory effect on NO production	[145]
462–465	Aspersclerotiorones A-D	*Aspergillus sclerotiorum* PSU-RSPG178	Surat Thani Province, Thailand	-	[108]
466–467	Aspersclerotiorones F-G				
468*	*eut*-Guaiane sesquiterpene	*Eutypella* sp. D-1	London Island of Kongsfjorden, Arctic	Antibacterial activity; Cytotoxicity	[146]
469*, 470*	Pochoniolides A-B	*Pochonia chlamydosporia* var. *spinulospora* FKI-7537	Niijima, Tokyo, Japan	Antioxidant activity	[147]
471*, 472*, 473*	Aspersclerolides A-C	*Aspergillus Sclerotiorum*	Shangdong Province, China	Cytotoxic activity (471*, 473*); Antibacterial activity (472*, 473*)	[116]
474	(±)-Aspersclerolide D				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
475–476	Botryosphaerilactones D-E	*Lasiodiplodia theobromae* NSTRU-PN1.4	Nakhon Si Thammarat Province, Thailand	-	[148]
477	Therlanubutanolide A	*Thermomyces lanuginosus*	Yunnan Province, China	-	[149]
478*	6-ethoxy-5,6-dihydropenillic acid	*Penicillium* sp. BF-0343	Fuji Cemetery, Shizuoka, Japan	Inhibited BMP-induced ALP activity	[150]
479	Ilyoresorcy A	*Ilyonectria* sp. sb65	Hunan Province, China	Inhibition of ConA-induced T-cell proliferation (481*, 482*); Immunosuppressive effects toward the LPS-induced B-cell proliferation (484*, 485*, 488*)	[151]
480*	Atrop-ilyoresorcy A				
481*, 482, 483*, 484*, 485, 486, 487*, 488–490	Ilyoresorcys B-K				
Other compounds					
491*, 492–493	Prenylterphenyllins A-C	*Aspergillus taichungensis* ZHN-7-07	-	Cytotoxicity	[152]
494*	4''-dehydro-3-hydroxyterphenyllin				
495, 496*, 497	Prenylcandidusins A-C				
498	4-hydroxy-3-(3-methyoxy-3-methylbutyl)-benzoic acid	*Curvularia inaequalis* strain.HS-FG-257	Heilongjiang Province, China	-	[153]
499	(Z)-2-(5-hydroxyhexyl)pent-2-enedioic acid	*Gongronella butleri*	Forest at Koukoue, Cameroon	-	[154]
500	(Z)-2-hexylpent-2-enedioic acid				
501	(Z)-2-(5-oxohexyl)pent-2-enedioic acid				
502	(Z)-oct-2-ene-1,3,8-tricarboxylic acid				
503	(Z)-2-(7-hydroxyoctyl)pent-2-enedioic acid				
504	(Z)-2-(3-methoxy-3-oxopropylidene) decanoic acid				
505	(Z)-2-(7-oxooctyl)-pent-2-enedioic acid				
506	(Z)-2-(8-hydroxydecyl)pent-2-enedioic acid				
507*, 508*, 509*	Peniciketals A-C	*Penicillium raistrichii*	Shangdong Province, China	Cytotoxic activity	[155]
510*	MIG0310	*Fusarium brachygibbosum* strain MS-R1	Mediterranean forest, Israel	Antimicrobial activity	[156]
511–512	Aspergillusols A-B	*Aspergillus* sp. PSU-RSPG185	Surat Thani Province, Thailand	-	[30]
513	Aspergillusic acid				

(*Continued*)

Table 1 (Continued).

NO	Compounds	Fungal Strain	Place	Biological activity	Ref.
514	11'-carboxygymnastatin N	*Gymnascella dankaliensis*	Giza pyramids, Egypt	Cytotoxicity	[157]
515	Gymnastatin S				
516	Dankamide				
517*	Aranorosin-2-methylether				
518*	Iizukine B	*Aspergillus iizukae*	Shandong Province, China	Cytotoxicity against cancer cell	[84]
519*	Screlotiumol	*Sclerotium rolfsii*	District Malakand, Khyber Pakhtunkhwa Pakistan	Effective multidrug resistant (MDR) mediated by P-glycoprotein (P-gp) modulator	[158]
520	Versicorin	*Aspergillus versicolor* SC0156	Guangdong Province, China	-	[159]
521–522, 523*	Unnamed	*Aspergillus sclerotiorum* PSU-RSPG178	Surat Thani Province, Thailand	Activity against HMG-CoA reductase	[160]
524	Asterreusin A	*Aspergillus terreus* YIM PH30711	New Delhi, India	Inhibitive activities against acetylcholinesterase (AChE)	[93]
525	Unnamed				
526*	Aspereusin A				
527	Epiaspereusin A				
528–530	Penicillidic acids A-C	*Penicillium aculeatum* PSU-RSPG105	Surat Thani Province, Thailand	-	[97]
531–532, 533*	Aspergillusethers B-D	*Aspergillus unguis* PSU-RSPG204	Surat Thani Province, Thailand	Antifungal activity	[115]
534–535	Melleusins A-B	*Aspergillus melleus*YIM PHI001	New Delhi, India	-	[161]
536*	3-methylpentyl-2,4-dichloroasterrate	*Aspergillus flavipes* PJ03-11	Liaoning Province, China	Cytotoxic activity	[162]
537	6*R*,8*R*-dihydroxy-9*Z*,12*Z*-octadecadienoic acid	*Penicillium javanicum* HK1-22	Hainan Province, China.	-	[163]
538	Methyl-6*R*,8*R*-dihydroxy-9*Z*,12*Z*-octadecadienoate				
539	Penoxalin	*Penicillium oxalicum* GY1	Shanghai, China	Cytotoxic activity	[164]
540–541	Penisochromans A-B				
542*	2,6-dihydroxy-4-[(2*R*)-2-hydroxyheptyl] benzoic acid				
543*	Pyrenosetin D	*Pyrenochaetopsis* sp. FVE-087	Falckenstein Beach, Kiel Fjord, Baltic Sea, Germany	Cytotoxic activity	[165]
544	Unnamed	*Aspergillus calidoustus*	Dianchi Lake, Yunnan Province.China		[58]
545*	4-Methoxy-7-methylbenzo[d]thiazole-5,6-diol	*Aspergillus fumigatus* GZWMJZ-152	Caves in Guizhou province of China	Radical-scavenging activity (545*, 546*) against 2.2-diphenyl-1-picrylhydrazyl free radicals	[128]
546*	2-Hydroxymethyl-4-methoxy-7-methylbenzo[d]thiazole-5,6-diol				

Note: *Bioactive compounds.

variables, such as anoxia, aridity, extreme temperatures, low concentrations of organic matter, high salinity and intense irradiation. The search for new bioactive compounds from the extremobiosphere rests on the premise that harsh abiotic conditions select for novel microorganisms that express new chemistry.[169] In order to adapt to extreme habitats, the strains are bound to adjust their metabolism, and new secondary metabolites will increase in this process, we may get some compounds with good biological activity.

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Disclosure

The authors report no conflicts of interest in this work.

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