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Review

The Genus *Cladosporium*: A Rich Source of Diverse and Bioactive Natural Compounds

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Abstract: Fungi are renowned as one of the most fruitful sources of chemodiversity and for their ubiquitous occurrence. Among the many taxonomic groupings considered for the implications deriving from their biosynthetic aptitudes, the genus *Cladosporium* stands out as one of the most common in indoor environments. A better understanding of the impact of these fungi on human health and activities is clearly based on the improvement of our knowledge of the structural aspects and biological properties of their secondary metabolites, which are reviewed in the present paper.

Keywords: natural products; bioactive secondary metabolites; fungal species; fungal extrolites

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1. Introduction

Results of recent research in the mycological field have further disclosed the pervasive diffusion of fungi in the genus *Cladosporium* (Dothideomycetes, Cladosporiaceae). Basically saprophytic, these Ascomycetes are spread in every kind of terrestrial and marine environment, where they establish various symbiotic relationships with plants and animals [1]; moreover, they are among the most frequent fungi detected in indoor spaces [2,3]. This latter connotation implies obvious opportunities for interactions with people, which can sometimes evolve into undesirable effects in terms of allergic or even pathogenic reactions [4–8].

Over the past two decades, investigations into the occurrence of *Cladosporium* spp. have been boosted by their tremendous ecological adaptability, as well as their frequent implication in human activities and medical aspects. Fundamental support from the molecular tools for species identification has enabled mycologists to disclose an exceptional taxonomic variation, with as many as 218 accepted species considered in the most recent update [3] and more new species added to the list in the last three years [9–11]. Considering the importance of secondary metabolites as mediators of biological interactions, this versatility has also generated notable research activity concerning the metabolome of these fungi and its biological properties, which are revised in the present paper.

2. Fifty Years of Metabolomic Studies in *Cladosporium*

A set of 68 *Cladosporium* strains have been examined so far, about 2/3 of which have been formally classified at the species level and ascribed to 12 taxa (Table 1). In this respect, the most frequent species are represented by the progenitors of the three main species complexes of the genus [1,3]. This may imply that in some cases the taxonomic identification has been approximate, as it only relied on morphological characters or ITS sequences. Concerning the origin, the examined strains are almost equally distributed

between terrestrial and marine sources, with a prevalence of those recovered as endophytes or from sediments (Figure 1).

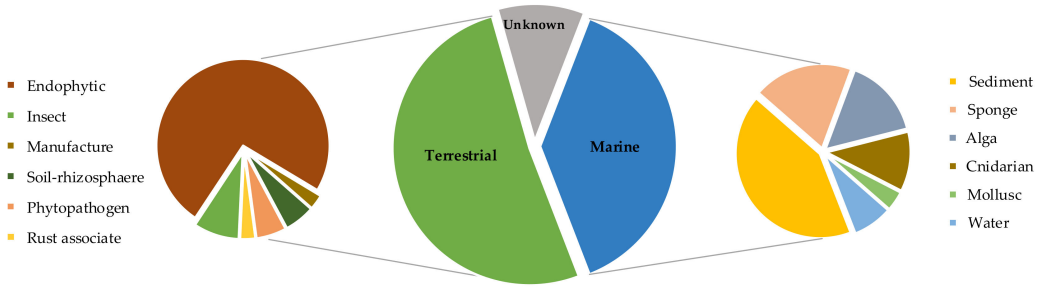


Figure 1. Pie charts of the origin of the strains examined in the present review.

Despite the low number of strains, a long list of products has been reported from *Cladosporium*, starting with the finding of cladosporin in 1971 [12]. In fact, from analysis of the available literature, a total of 244 chemically defined compounds can be extracted, belonging to different classes of secondary metabolites, such as azaphilones, benzofluoranthenones, coumarins and isocumarins, lactones, naphthalenones, macrolides, perylenequinones, sterols and others (Table 2). Of course, this list includes both known metabolites and compounds, which have been first characterized from these fungi, with the latter representing a remarkable share (147, corresponding to about 60%). In our survey, we avoided considering some products that are known intermediates in biosynthetic processes, clearly represent possible contaminants of the fungal cultures, or were just tentatively identified [13–21].

Table 1. *Cladosporium* species/strains reported for production of secondary metabolites.

Species/Strain	Substrate	Location	Refs.
C. cladosporioides	-	-	[12]
C. cladosporioides	sediment of hypersaline lake	El Hamra, Egypt	[22]
C. cladosporioides	sponge (*Cliona* sp.)	Los Molles, Chile	[23]
C. cladosporioides	aphid (*Aphis craccivora*)	Egypt	[17,18]
C. cladosporioides	endophytic in *Zygophyllum mandavillei*	Al-Ahsa, Saudi Arabia	[24]
C. cladosporioides	endophytic in unspecified plant	Tifton, United States	[25]
C. cladosporioides	-	Japan	[26]
C. cladosporioides/CBUK20700	dead insect	Thailand	[27,28]
C. cladosporioides/FERMBP-1285	block fence	Osaka, Japan	[29,30]
C. cladosporioides/IPV-F167	-	Italy	[31]
C. cladosporioides/LWL5	endophytic in *Helianthus annuus*	Daegu, South Korea	[16]
C. cladosporioides/MA-299	endophytic in *Bruguiera gymnorrhiza*	Hainan, China	[32–34]
C. cladosporioides/MCCC3A00182	deep sea sediment	Pacific Ocean	[35]
C. cladosporioides/MUPGBIOCHEM-CC-07-2015	brown alga (*Sargassum wightii*)	Tamil Nadu, India	[21]
C. cladosporioides/NRRL5507	-	-	[36,37]
C. cladosporioides/CL-1	rhizosphere of red pepper	South Korea	[38]
C. cladosporioides/EN-399	red alga (*Laurencia okamurai*)	Qingdao, China	[39]
C. cladosporioides/HDN14-342	deep sea sediment	Indian Ocean	[40]
C. colocasiae/A801	endophytic in *Callistemon viminalis*	Guangzhou, China	[41]
C. delicatulum/EF33	endophytic in *Terminalia pallida*	Andhra Pradesh, India	[42]
C. halotolerans/GXIMD 02502	coral (*Porites lutea*)	Weizhou islands, China	[43]
C. herbarum	sponge (*Callyspongia aerizusa*)	Bali, Indonesia	[44,45]

Table 1. *Cont.*

Species/Strain	Substrate	Location	Refs.
C. herbarum/FC27P	endophytic in *Beta vulgaris*	Dublin, United States	[46]
C. herbarum/IFB-E002	endophytic in *Cynodon dactylon*	Yancheng reserve, China	[47]
C. oxysporum	endophytic in *Aglaia odorata*	Java, Indonesia	[14]
C. oxysporum	endophytic in *Alyxia reinwardtii*	Java, Indonesia	[48]
C. oxysporum/DH14	locust (*Oxya chinensis*)	Jinhua, China	[49]
C. oxysporum/HDN13-314	endophytic in *Avicennia marina*	Hainan, China	[50]
C. oxysporum/RM1	endophytic in *Moringa oleifera*	Tamil Nadu, India	[51]
C. perangustum/FS62	deep sea sediment	South China Sea	[52]
C. phlei/C-273 w	pathogenic on *Phleum pratense*	Hokkaido, Japan	[53]
C. phlei/CBS 358.69	pathogenic on *Phleum pratense*	Germany	[54]
C. sphaerospermum/2005-01-E3	deep sea sludge	Pacific Ocean	[55,56]
C. sphaerospermum/DK-1-1	endophytic in *Glycine max*	South Korea	[57]
C. sphaerospermum/EIODSF 008	deep sea sediment	Indian Ocean	[58]
C. sphaerospermum/L3P3	deep sea sediment	Mariana Trench	[59]
C. sphaerospermum/SW67	hydroid (*Hydractinia echinata*)	South Korea	[60–62]
C. sphaerospermum/WBS017	endophytic in *Fritillaria unibracteata* var. *wabuensis*	China	[63]
C. tenuissimum	soil	Karo-cho, Japan	[64]
C. tenuissimum/DMG 3	endophytic in *Swietenia mahagoni*	Sumatra, Indonesia	[65]
C. tenuissimum/ITT21	pine rust (*Cronartium flaccidum*)	Tuscany, Italy	[66]
C. tenuissimum/LR463	endophytic in *Maytenus hookeri*	Yunnan, China	[67]
C. tenuissimum/P1S11	endophytic in *Pinus wallichiana*	Kashmir, India	[68]
C. uredinicola	endophytic in *Psidium guajava*	São Carlos, Brazil	[69]
C. velox/TN-9S	endophytic in *Tinospora cordifolia*	Amritsar, India	[70]
Cladosporium sp.	sponge (*Niphates rowi*)	Gulf of Aqaba, Israel	[71]
Cladosporium sp./486	intertidal sediment	San Antonio Oeste, Argentina	[19]
Cladosporium sp./501-7w	-	Japan	[72–74]
Cladosporium sp./F14	sea water	Sai Kung, China	[13,75]
Cladosporium sp./HDN17-58	deep sea sediment	Pacific Ocean	[76]
Cladosporium sp./I(R)9-2	endophytic in *Quercus variabilis*	Nanjing, China	[77]
Cladosporium sp./IFB3lp-2	endophytic in *Rhizophora stylosa*	Hainan, China	[78]
Cladosporium sp./IFM 49189	-	Japan	[79,80]
Cladosporium sp./JJM22	endophytic in *Ceriops tagal*	Hainan, China	[81–83]
Cladosporium sp./JNU17DTH12-9-0	unknown	China	[84]
Cladosporium sp./JS1-2	endophytic in *Ceriops tagal*	Hainan, China	[85]
Cladosporium sp./KcFL6′	endophytic in *Kandelia candel*	Daya Bay, China	[86]
Cladosporium sp./KFD33	blood cockle	Hainan, China	[87]
Cladosporium sp./L037	brown alga (*Actinotrichia fragilis*)	Okinawa, Japan	[88]
Cladosporium sp./N5	red alga (*Porphyra yezoensis*)	Lianyungang, China	[15]
Cladosporium sp./OUCMDZ-1635	sponge	Xisha Islands, China	[89]
Cladosporium sp./RSBE-3	endophytic in *Rauwolfia serpentina*	Bangladesh	[90]
Cladosporium sp./SCNU-F0001	endophytic in unspecified mangrove	Zhuhai, China	[91]
Cladosporium sp./SCSIO z01	deep sea sediment	East China Sea	[92]
Cladosporium sp./TPU1507	unidentified sponge	Manado, Indonesia	[93]
Cladosporium sp./TZP-29	unidentified soft coral	Guangzhou, China	[94]
Cladosporium sp./KF501	water sample	Wadden Sea, Germany	[95]
Cladosporium sp./SCSIO z0025	deep sea sediment	Okinawa, Japan	[96]

Some errors and overlapping in the compound names attribution have arisen during the accurate examination of the available literature on this topic. In particular, we can consider two recurring issues, which are "more names, one chemical structure" and "one name, more chemical structures". For instance, cladosporin certainly belongs to the first case because its chemical structure is also known by the name asperentin [97]. For this reason, in Table 2, we added in brackets eventual additional names for compounds that fall under this case.

On the other hand, due to the intense research activity concerning this fungal genus, it has happened that some authors conducted their research parallel to the finding of closely related compounds. The temporal proximity in publishing has sometimes caused the attribution of the same name to different chemical structures (e.g., cladosporiumin I). In the case of cladosporol G, this issue was rather a consequence of author inaccuracy, since the elapsed time of about one year between the consecutive reports would have afforded an accurate preliminary check. In all cases of homonymy in Table 2, we have added the Latin suffix "*bis*" to the compounds that have been characterized later, as inferred from the date of submission to the journal.

Additional nomenclatural issues are represented by the absence of a proposed name, or authors' choice to follow IUPAC rules instead of introducing trivial names derived from closely related compounds. Indeed, the use of trivial names represents a very common and useful guideline in natural product research because systematic names can be so convoluted and difficult to parse.

Table 2. List of secondary metabolites produced by *Cladosporium* species. The Latin suffix "*bis*" is added when the same name has been previously introduced for another compound. The names of novel compounds are underlined.

Code	Name	Formula	Nominal Mass (U)	Refs.
	Alkaloids			
1	Aspernigrin A	$C_{13}H_{12}N_2O_2$	228	[47]
2	Aspidospermidin-20-ol, 1-acetyl-17-methoxy	$C_{22}H_{30}N_2O_3$	370	[24]
3	Cladosin E	$C_{13}H_{17}NO_4$	251	[55]
4	Cladosporine A	$C_{28}H_{39}NO_2$	421	[84]
5	Cytochalasin D	$C_{30}H_{37}NO_6$	507	[85]
6	2-Methylacetate-3,5,6-trimethylpyrazine	$C_{10}H_{14}N_2O_2$	194	[85]
7	Nonanal oxime	$C_9H_{19}NO$	157	[17]
8	2-Piperidinone methyl	$C_6H_{11}NO$	113	[17]
	Azaphilones			
9	Bicyclic diol	$C_{11}H_{14}O_4$	210	[52]
10	Lunatoic acid A	$C_{21}H_{24}O_7$	388	[49]
11	Perangustol A	$C_{11}H_{14}O_4$	210	[52]
12	Perangustol B	$C_{11}H_{14}O_4$	210	[52]
	Benzofluoranthenones			
13	(6b*S*,7*R*,8*S*)-4,9-Dihydroxy-7,8-dimethoxy-1,6b,7,8-tetrahydro-2*H*-benzo[J]fluoranthen-3-one	$C_{23}H_{22}O_4$	362	[27]
14	(6b*S*,7*R*)-4,9-Dihydroxy-7-methoxy-1,2,6b,7-tetrahydrobenzo[J]fluoranthen-3,8-dione	$C_{22}H_{18}O_4$	346	[27]
15	(6b*R*,7*R*,8*S*)-7-Methoxy-4,8,9-trihydroxy-1,6b,7,8-tetrahydro-2*H*-benzo[J]fluoranthen-3-one	$C_{22}H_{20}O_4$	348	[27]
16	(6b*S*,7*R*,8*S*)-7-Methoxy-4,8,9-trihydroxy-1,6b,7,8-tetrahydro-2*H*-benzo[J]fluoranthen-3-one	$C_{22}H_{20}O_4$	348	[27,28]
	Benzopyranones			
17	Coniochaetone A	$C_{13}H_{10}O_4$	230	[43]
18	Coniochaetone B	$C_{13}H_{12}O_4$	232	[43]
19	Coniochaetone K	$C_{13}H_{10}O_6$	262	[43]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
	Binaphthopyrones			
20	Cladosporinone	$C_{33}H_{30}O_{14}$	650	[22]
21	Viriditoxin	$C_{34}H_{30}O_{14}$	662	[22]
22	Viriditoxin SC-28763	$C_{34}H_{30}O_{13}$	646	[22]
23	Viriditoxin SC-30532	$C_{34}H_{30}O_{12}$	630	[22]
	Butenolides and butanolides			
24	Cladospolide F	$C_{12}H_{22}O_4$	230	[94]
25	Cladospolide G	$C_{14}H_{24}O_5$	272	[32]
26	Cladospolide H	$C_{12}H_{18}O_3$	210	[32]
27	ent-Cladospolide F	$C_{12}H_{22}O_4$	230	[32]
28	11-Hydroxy-γ-dodecalactone	$C_{12}H_{20}O_3$	212	[94]
29	iso-Cladospolide B	$C_{12}H_{20}O_4$	228	[32,44,50,67,71,94]
	Cinnamic acid derivatives			
30	Chlorogenic acid	$C_{16}H_{18}O_9$	354	[70]
31	Caffeic acid	$C_9H_8O_4$	180	[70]
32	Coumaric acid	$C_9H_8O_3$	164	[70]
	Citrinin derivatives			
33	Citrinin H1	$C_{25}H_{30}O_7$	442	[85]
34	Cladosporin A	$C_{13}H_{15}NO_3$	233	[92]
35	Cladosporin B	$C_{13}H_{15}NO_3$	233	[92]
36	Cladosporin C	$C_{14}H_{16}O_4$	248	[92]
37	Cladosporin D	$C_{12}H_{16}O_4$	224	[92]
	Coumarins and Isocoumarins			
38	Asperentin-8-methyl ether (= cladosporin-8-methyl ether)	$C_{17}H_{22}O_6$	322	[25]
39	Cladosporin (= asperentin)	$C_{16}H_{20}O_5$	292	[12,24,25,36,37]
40	5′-Hydroxyasperentin	$C_{16}H_{20}O_6$	308	[24,25]
41	7-Hydroxy-4-methoxy-5-methylcoumarin	$C_{11}H_{10}O_4$	206	[47]
42	Isocladosporin	$C_{16}H_{20}O_5$	292	[24,25,37]
43	Kotanin	$C_{24}H_{22}O_8$	438	[47]
44	Orlandin	$C_{22}H_{18}O_8$	410	[47]
45	Phomasatin	$C_{10}H_8O_5$	208	[35]
46	Umbelliferone	$C_9H_6O_3$	162	[70]
	Cyclohexene derivatives			
47	Cladoscyclitol A	$C_{12}H_{20}O_5$	244	[82]
48	Cladoscyclitol B	$C_{13}H_{22}O_7$	290	[82]
49	Cladoscyclitol C	$C_{12}H_{22}O_4$	230	[82]
50	Cladoscyclitol D	$C_{12}H_{22}O_5$	246	[82]
	Despsides			
51	3-Hydroxy-2,4,5-trimethylphenyl 2,4-dihydroxy-3,6-dimethylbenzoate	$C_{18}H_{20}O_5$	316	[69,98]
52	3-Hydroxy-2,4,5-trimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate	$C_{27}H_{28}O_8$	480	[69,98]
53	3-Hydroxy-2,5-dimethylphenyl 2,4-dihydroxy-3,6-dimethylbenzoate	$C_{17}H_{18}O_5$	302	[69,98]
54	3-Hydroxy-2,5-dimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate	$C_{26}H_{26}O_8$	466	[69,98]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
	Diketopiperazines			
55	(3*R*,8a*R*)-*Cyclo*(leucylprolyl)	$C_{11}H_{18}N_2O_2$	210	[17]
56	(3*S*,8a*S*)-*Cyclo*(leucylprolyl)	$C_{11}H_{18}N_2O_2$	210	[17]
57	(3*R*,8a*R*)-*Cyclo*(phenylalanylprolyl)	$C_{14}H_{16}N_2O_2$	244	[17]
58	(3*S*,8a*S*)-*Cyclo*(phenylalanylprolyl)	$C_{14}H_{16}N_2O_2$	244	[17]
	Flavonoids			
59	(2*S*)-7,4′-Dihydroxy-5-methoxy-8-(γ,γ-dimethylallyl)-flavanone	$C_{21}H_{22}O_5$	354	[93]
60	Catechin	$C_{15}H_{14}O_6$	290	[70]
61	Epicatechin	$C_{15}H_{14}O_6$	290	[70]
	Gibberelines			
62	GA3	$C_{19}H_{22}O_6$	346	[57]
63	GA4	$C_{19}H_{24}O_5$	332	[57]
64	GA5	$C_{19}H_{22}O_5$	330	[57]
65	GA7	$C_{19}H_{22}O_5$	330	[57]
66	GA15	$C_{20}H_{26}O_4$	330	[57]
67	GA19	$C_{20}H_{26}O_6$	362	[57]
68	GA24	$C_{20}H_{26}O_5$	346	[57]
	Fusicoccane diterpene glycosides			
69	Cotylenin A	$C_{33}H_{50}O_{11}$	622	[72–74]
70	Cotylenin B	$C_{33}H_{51}ClO_{11}$	659	[73,74]
71	Cotylenin C	$C_{33}H_{52}O_{11}$	624	[73]
72	Cotylenin D	$C_{33}H_{52}O_{12}$	640	[73]
73	Cotylenin E	$C_{28}H_{46}O_9$	526	[73]
	Lactones			
74	Cladosporactone A	$C_{10}H_{12}O_4$	196	[35]
75	Cladosporamide A	$C_{14}H_{11}NO_5$	273	[93]
76	5-Decanolide	$C_{10}H_{18}O_2$	170	[17]
77	Herbaric acid	$C_{10}H_8O_6$	224	[45]
78	Isochracinic acid	$C_{10}H_8O_5$	208	[35]
	Macrolides			
79	Brefeldin A	$C_{16}H_{24}O_4$	280	[77]
80	Cladocladosin A	$C_{13}H_{18}O_3$	222	[34]
81	Cladospamide A	$C_{13}H_{20}N_2O_4$	268	[91]
82	Cladospolide A	$C_{12}H_{20}O_4$	228	[41,64,67,78,91]
83	Cladospolide B	$C_{12}H_{20}O_4$	228	[44,64,67,78]
84	Cladospolide C	$C_{12}H_{20}O_4$	228	[64]
85	4,5-Dihydroxy-12-methyloxacyclododecan-2-one	$C_{12}H_{22}O_4$	230	[67]
86	(6*R*,12*S*)-6-Hydroxy-12-methyl-oxacyclodoecane-2,5-dione	$C_{12}H_{20}O_4$	228	[67]
87	(10*S*,12*S*)-10-Hydroxy-12-methyloxacyclododecane-2,5-dione	$C_{12}H_{20}O_4$	228	[67]
88	4-Hydroxy-12-methyloxacyclododecane-2,5,6-trione	$C_{12}H_{18}O_5$	242	[41]
89	(*E*)-(3*R*,6*S*)-6-Hydroxy-12-methyl-2,5-dioxooxacyclododecan-3-yl 4,11-dihydroxydodec-2-enoate	$C_{24}H_{40}O_8$	456	[78]
90	5*R*-Hydroxyrecifeiolide	$C_{12}H_{20}O_3$	212	[32]
91	5*S*-Hydroxyrecifeiolide	$C_{12}H_{20}O_3$	212	[32]
92	12-Methyloxacyclododecane-2,5,6-trione	$C_{12}H_{18}O_4$	226	[41]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
93	Methyl 2-(((4*R*,6*S*,12*R*)-6-hydroxy-12-methyl-2,5-dioxooxacyclododecan-4-yl)thio)acetate	$C_{15}H_{24}O_6S$	332	[78]
94	5Z-7-Oxozeaenol	$C_{19}H_{22}O_7$	362	[49]
95	Pandangolide 1	$C_{12}H_{20}O_5$	244	[32,41,48,71,78]
96	Pandangolide 1a	$C_{12}H_{20}O_5$	244	[71,78]
97	Pandangolide 2	$C_{14}H_{22}O_6S$	318	[44,78]
98	Pandangolide 3	$C_{16}H_{26}O_7S$	362	[33,44,50,78]
99	Pandangolide 4	$C_{24}H_{38}O_8S$	486	[44]
100	Patulolide B	$C_{13}H_{20}O_3$	224	[41]
101	Sporiolide A	$C_{19}H_{24}O_6$	348	[88]
102	Sporiolide B	$C_{14}H_{24}O_4$	256	[88]
103	Thiocladospolide A	$C_{16}H_{26}O_6S$	346	[33,50]
104	Thiocladospolide B	$C_{16}H_{24}O_7S$	360	[33]
105	Thiocladospolide C	$C_{15}H_{22}O_6S$	330	[33]
106	Thiocladospolide D	$C_{16}H_{28}O_7S$	364	[33]
107	Thiocladospolide E	$C_{14}H_{26}O_5S$	306	[91]
108	Thiocladospolide F	$C_{16}H_{28}O_5S$	332	[34]
109	Thiocladospolide F *bis*	$C_{24}H_{38}O_8S$	486	[50]
110	Thiocladospolide G	$C_{16}H_{28}O_6S$	348	[34]
111	Thiocladospolide G *bis*	$C_{15}H_{24}O_7S$	348	[50]
112	Thiocladospolide H	$C_{15}H_{24}O_6S$	332	[50]
113	Thiocladospolide I	$C_{27}H_{44}O_{10}S$	560	[50]
114	Thiocladospolide J	$C_{27}H_{42}O_{10}S$	558	[50]
115	Zeaenol	$C_{19}H_{24}O_7$	364	[49]
	Naphthalene derivatives			
116	Cladonaphchrom A	$C_{22}H_{22}O_4$	350	[83]
117	Cladonaphchrom B	$C_{22}H_{22}O_4$	350	[83]
118	1,8-Dimethoxynaphthalene	$C_{12}H_{12}O_2$	188	[81,83]
119	8-Methoxynaphthalen-1-ol	$C_{11}H_{10}O_2$	174	[83]
	Naphtalenones			
120	Altertoxin XII	$C_{20}H_{18}O_4$	322	[87]
121	Cladosporol A	$C_{20}H_{16}O_6$	352	[26,66,86]
122	Cladosporol B	$C_{20}H_{14}O_6$	350	[66]
123	Cladosporol C	$C_{20}H_{18}O_5$	338	[35,39,40,66,85,86]
124	Cladosporol D	$C_{20}H_{18}O_6$	354	[66,86]
125	Cladosporol E	$C_{20}H_{18}O_7$	370	[40,66,85]
126	Cladosporol F	$C_{21}H_{20}O_5$	352	[39,40]
127	Cladosporol G	$C_{20}H_{17}ClO_6$	388	[40]
128	Cladosporol G *bis*	$C_{21}H_{20}O_5$	352	[39]
129	Cladosporol H	$C_{20}H_{16}O_5$	336	[39]
130	Cladosporol I	$C_{20}H_{18}O_5$	338	[39,92]
131	Cladosporol J	$C_{20}H_{18}O_5$	338	[39]
132	Cladosporone A	$C_{20}H_{16}O_6$	352	[86]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
133	Clindanone A	$C_{22}H_{18}O_7$	394	[40]
134	Clindanone B	$C_{22}H_{18}O_7$	394	[40]
135	(3*R*,4*R*)-3,4-Dihydro-3,4,8-trihydroxy-1(2*H*)-napthalenone	$C_{10}H_{10}O_4$	194	[81]
136	4,8-Dihydroxy-1-tetralone	$C_{10}H_{10}O_3$	178	[52]
137	(3*S*)-3,8-Dihydroxy-6,7-dimethyl-α-tetralone	$C_{12}H_{14}O_3$	206	[81]
138	Isosclerone	$C_{10}H_{10}O_3$	178	[40]
139	Scytalone	$C_{10}H_{10}O_4$	194	[68]
140	(−)-(4*R*)-Regiolone	$C_{10}H_{10}O_3$	178	[81]
141	(−)-*trans*-(3*R*,4*R*)-3,4,8-Trihydroxy-6,7-dimethyl-3,4-dihydronaphtha- len-1(2*H*)-one	$C_{12}H_{14}O_4$	222	[81]
	Naphthoquinones and anthraquinones			
142	Anhydrofusarubin	$C_{15}H_{12}O_6$	288	[90]
143	Methyl ether of fusarubin	$C_{16}H_{16}O_7$	320	[90]
144	Plumbagin	$C_{11}H_8O_3$	188	[42]
	Perylenequinones			
145	Altertoxin VIII	$C_{20}H_{16}O_3$	304	[87]
146	Altertoxin IX	$C_{20}H_{18}O_2$	290	[87]
147	Aterotoxin X	$C_{20}H_{18}O_2$	290	[87]
148	Altertoxin XI	$C_{21}H_{20}O_2$	304	[87]
149	Calphostin A (= UCN-1028A)	$C_{44}H_{38}O_{12}$	758	[29,30]
150	Calphostin B	$C_{37}H_{34}O_{11}$	654	[30]
151	Calphostin C (= Cladochrome E)	$C_{44}H_{38}O_{14}$	790	[30,31]
152	Calphostin D (= ent-isophleinchrome)	$C_{30}H_{30}O_{10}$	550	[30,46]
153	Calphostin I (= Cladochrome D)	$C_{44}H_{38}O_{15}$	806	[30,31]
154	Phleichrome	$C_{30}H_{30}O_{10}$	550	[53,54,99]
	Pyrones			
155	Citreoviridin A	$C_{23}H_{30}O_6$	402	[45]
156	Herbarin A	$C_{12}H_{12}O_5$	236	[45]
157	Herbarin B	$C_{10}H_{10}O_5$	210	[45]
158	5-Hydroxy-2-oxo-2*H*-piran-4-yl) methyl acetate	$C_8H_8O_5$	184	[65]
	Seco acids			
159	Cladospolide E	$C_{12}H_{20}O_4$	228	[94]
160	11-Hydroxy-4,5-dioxododecanoic acid	$C_{12}H_{20}O_5$	244	[78]
161	seco-Patulolide A	$C_{12}H_{20}O_4$	228	[94]
162	seco-Patulolide C	$C_{12}H_{22}O_4$	230	[33,41,50,94]
163	(3*S*,5*S*, 11*S*)-Trihydroxydodecanoic acid	$C_{12}H_{24}O_5$	248	[68]
	Sterols			
164	Cladosporide A	$C_{25}H_{40}O_3$	388	[79]
165	Cladosporide B	$C_{25}H_{38}O_3$	386	[80]
166	Cladosporide C	$C_{25}H_{40}O_3$	388	[80]
167	Cladosporide D	$C_{25}H_{38}O_3$	386	[80]
168	Cladosporisteroid B	$C_{21}H_{30}O_3$	330	[35]
169	(22*E*,24*R*)-3β,5α-Dihydroxyergosta-7,22-dien-6-one	$C_{28}H_{44}O_3$	428	[35]
170	Ergosterol	$C_{28}H_{44}O$	396	[79]
171	3α-Hydroxy-pregn-7-ene-6,20-dione	$C_{21}H_{30}O_3$	330	[62]
172	23,24,25,26,27-Pentanorlanost-8-ene-3β,22-diol	$C_{28}H_{42}O_5$	458	[79]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
173	Peroxyergosterol (= (22*E*)-5α,8α-epidioxyergosta-6,22-dien-3β-ol)	$C_{28}H_{44}O_3$	428	[23,35,79]
174	3β,5α,6β-Trihydroxyergosta-7,22-diene	$C_{29}H_{48}O_3$	444	[47]
175	3β,5α,9α-Trihydroxy-(22*E*,24*R*)-ergosta-6-one	$C_{28}H_{44}O_4$	444	[35]
	Tetramic acids			
176	Cladodionen	$C_{13}H_{15}NO_3$	233	[58,63,89,96]
177	Cladosin A	$C_{13}H_{20}N_2O_4$	268	[55]
178	Cladosin B	$C_{12}H_{18}N_2O_4$	254	[55,60,63]
179	Cladosin C	$C_{12}H_{16}N_2O_3$	236	[55,60,63]
180	Cladosin D	$C_{13}H_{18}N_2O_3$	250	[55]
181	Cladosin F	$C_{12}H_{18}N_2O_4$	254	[56,60,63]
182	Cladosin G	$C_{13}H_{20}N_2O_4$	268	[56]
183	Cladosin H	$C_{20}H_{26}N_2O_4$	358	[89]
184	Cladosin I	$C_{20}H_{26}N_2O_4$	358	[89]
185	Cladosin J	$C_{25}H_{29}N_3O_3$	419	[89]
186	Cladosin K	$C_{25}H_{29}N_3O_3$	419	[89]
187	Cladosin L	$C_{13}H_{22}N_2O_4$	270	[60]
188	Cladosin L *bis*	$C_{14}H_{13}NO_3$	243	[63]
189	Cladosin M	$C_{13}H_{17}NO_4$	251	[63]
190	Cladosin N	$C_{13}H_{17}NO_4$	251	[63]
191	Cladosin O	$C_9H_{12}N_2O$	164	[63]
192	Cladosporicin A	$C_{21}H_{27}N_3O_5$	401	[61]
193	Cladosporiumin A	$C_{19}H_{27}NO_5$	349	[59]
194	Cladosporiumin B	$C_{19}H_{27}NO_5$	349	[59]
195	Cladosporiumin C	$C_{19}H_{27}NO_5$	349	[59]
196	Cladosporiumin D	$C_{14}H_{21}NO_3$	251	[59]
197	Cladosporiumin E	$C_{13}H_{17}NO_4$	251	[58,59]
198	Cladosporiumin F	$C_{13}H_{19}NO_5$	269	[59]
199	Cladosporiumin G	$C_{13}H_{19}NO_4$	253	[58,59]
200	Cladosporiumin H	$C_{14}H_{23}NO_5$	285	[59]
201	Cladosporiumin I	$C_{13}H_{19}NO_3$	237	[58]
202	Cladosporiumin I *bis*	$C_{19}H_{27}NO_5$	**349**	[61]
203	Cladosporiumin J	$C_{13}H_{17}NO_4$	251	[58]
204	Cladosporiumin J *bis*	$C_{19}H_{27}NO_5$	349	[61]
205	Cladosporiumin K	$C_{13}H_{17}NO_4$	**251**	[58]
206	Cladosporiumin L	$(C_{13}H_{20}NO_5)_3Mg_2$	889	[58]
207	Cladosporiumin M	$C_{13}H_{15}NO_3$	233	[58]
208	Cladosporiumin N	$C_{13}H_{19}NO_4$	253	[58]
209	Cladosporiumin O	$C_{13}H_{17}NO_4$	251	[58]
	Tropolones			
210	Malettinin A	$C_{16}H_{16}O_5$	288	[95]
211	Malettinin B	$C_{16}H_{20}O_5$	292	[95]
212	Malettinin C	$C_{16}H_{20}O_5$	292	[95]
213	Malettinin E	$C_{16}H_{20}O_5$	292	[95]

Table 2. *Cont.*

Code	Name	Formula	Nominal Mass (U)	Refs.
	Volatile terpenes			
214	(−)-*trans*-Caryophyllene	$C_{15}H_{24}$	204	[38]
215	Dehydro aromdendrene	$C_{15}H_{22}$	202	[38]
216	α-Pinene	$C_{10}H_{16}$	136	[38]
217	(+)-Sativene	$C_{15}H_{24}$	204	[38]
	Xanthones			
218	Conioxanthone A	$C_{16}H_{12}O_7$	316	[43]
219	3,8-Dihydroxy-6-methyl-9-oxo-9*H*-xanthene-1-carboxylate	$C_{16}H_{12}O_6$	300	[43]
220	α-Diversonolic ester	$C_{16}H_{16}O_7$	320	[43]
221	β-Diversonolic ester	$C_{16}H_{16}O_7$	320	[43]
222	8-Hydroxy-6-methylxanthone-1-carboxylic acid	$C_{15}H_{12}O_5$	272	[43]
223	Methyl 8-hydroxy-6-(hydroxymethyl)-9-oxo-9*H*-xanthene-1-carboxylate	$C_{16}H_{12}O_6$	300	[43]
224	Methyl 8-hydroxy-6-methyl-9-oxo-9*H*-xanthene-1- carboxylate	$C_{16}H_{12}O_5$	284	[43]
225	8-(Methoxycarbonyl)-1-hydroxy-9-oxo-9*H*-xanthene-3-carboxylic acid	$C_{16}H_{10}O_7$	314	[43]
226	Secalonic acid D	$C_{32}H_{30}O_{14}$	638	[85]
227	Vertixanthone	$C_{15}H_{10}O_5$	270	[43]
	Miscellaneous			
228	α-Acetylorcinol	$C_9H_{10}O_3$	166	[52]
229	Acetyl Sumiki's acid	$C_9H_{10}O_4$	182	[44]
230	Cladosacid	$C_{15}H_{22}O_3$	250	[96]
231	(2*R**,4*R**)-3,4-dihydro-5-methoxy-2-methyl-1(2*H*)-benzopyran-4-ol	$C_{10}H_{12}O_2$	164	[81]
232	1-(3,5-Dihydroxy-4-methylphenyl)propan-2-one	$C_{10}H_{12}O_3$	180	[52]
233	1,1′-Dioxine-2,2′-dipropionic acid	$C_{10}H_{12}O_6$	228	[85]
234	Ellagic acid	$C_{14}H_6O_8$	302	[70]
235	Fonsecinone A	$C_{32}H_{26}O_{10}$	570	[47]
236	5-Hydroxy-2-methyl-4*H*-chromen-4-one	$C_{10}H_8O_3$	176	[83]
237	(2*S*)-5-Hydroxy-2-methyl-chroman-4-one	$C_{10}H_{10}O_2$	162	[81,83]
238	4-*O*-α-D-Ribofuranose-2-pentyl-3-phemethylol	$C_{17}H_{26}O_6$	326	[82]
239	4-*O*-α-D-Ribofuranose-3-hydroxymethyl-2-pentylphenol	$C_{17}H_{26}O_7$	342	[81]
240	Rubrofusarin B	$C_{16}H_{14}O_5$	286	[47]
241	Sumiki's acid	$C_6H_6O_4$	142	[44]
242	Taxol	$C_{47}H_{51}NO_{14}$	853	[51]
243	tert-Butylhydroquinone	$C_{10}H_{14}O_2$	166	[70]
244	Vermistatin	$C_{18}H_{16}O_6$	328	[85]

2.1. Alkaloids

Aspernigrin A (**1**) was originally characterized from the culture of a sponge-derived *Aspergillus niger* strain with its structure assigned mainly from its NMR and MS data [100], but it was structurally revised after reisolating from an endophytic strain of *Cladosporium herbarum* [47].

Cladosporine A (**4**) is the first indole diterpenoid alkaloid reported as a product of a *Cladosporium* strain [84]. In the class of alkaloids (Figure 2), cladosin E (**3**) and 2-methylacetate-3,5,6-trimethylpyrazine (**6**) are other new natural products from strains of *Cladosporium sphaerospermum* [60] and an endophytic *Cladosporium* sp. [85].

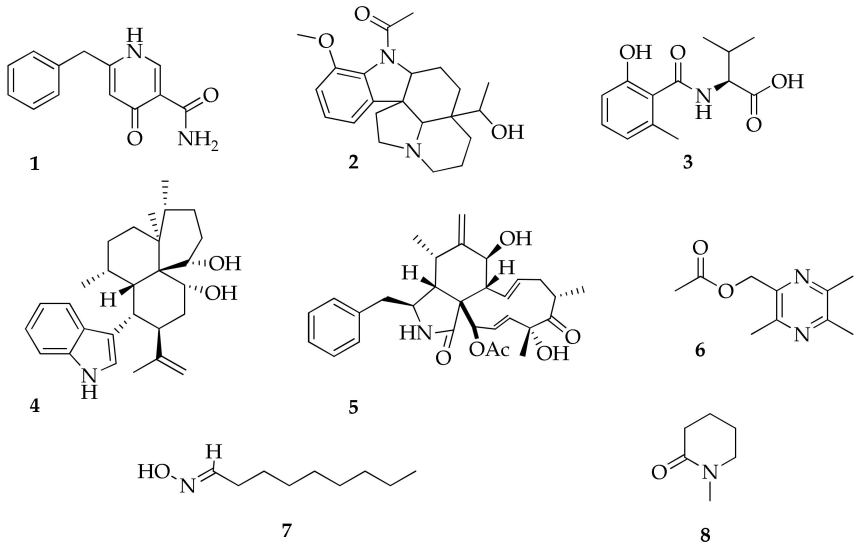


Figure 2. Structures of alkaloids.

2.2. Azaphilones

Azaphilones are a structurally variable family of fungal polyketide metabolites possessing a highly oxygentated pyranoquinone bicyclic core and a quaternary carbon center. Well-known from genera such as *Aspergillus*, *Penicillium* and *Talaromyces* [101,102], these compounds have also been reported from the *Cladosporium* species (Figure 3) [49,52]. In particular, two new azaphilones, named perangustols A and B (**11**,**12**), were isolated from a marine-derived isolate of *Cladosporium perangustum* together with the new natural product, bicyclic diol (**9**) [52].

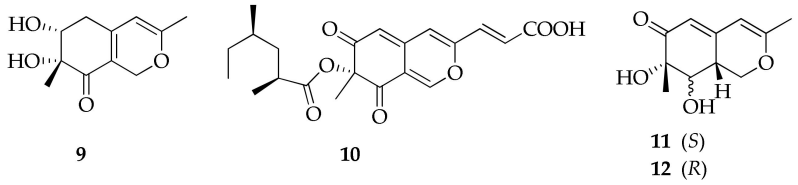
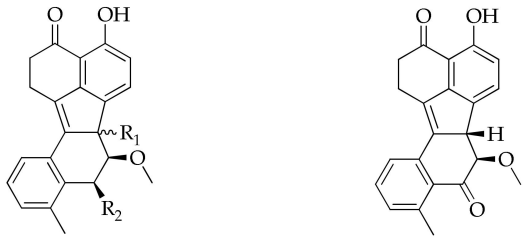


Figure 3. Structures of azaphilones.

2.3. Benzofluorantheneones

During a screening of microbial extracts, a series of novel reduced benzofluorantheneones (**13**–**16**) was identified in the fermentation broth of a strain of *Cladosporium cladosporioides* recovered from a dead insect (Figure 4) [27,28].



13 R_1=H (*S*) R_2=OMe

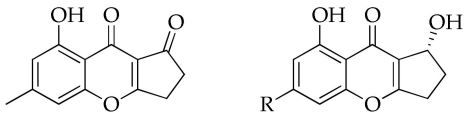
15 R_1=H (*R*) R_2=OH

16 R_1=H (*S*) R_2=OH

Figure 4. Structures of benzofluoranthenones.

2.4. Benzopyrones

A member of the benzopyrenes family named coniochaetone K (**19**) was isolated for the first time as a product of a coral symbiotic strain of *Cladosporium halotolerans* (Figure 5) [43]. This compound is particularly interesting because it has an uncommon carboxylic group in the backbone at position C-8′. It was identified together with the already known coniochaetones A-B (**17**,**18**) and several compounds belonging to the xanthones group. However, it must be underlined that a compound with the same name was previously characterized from a strain of *Penicillium oxalicum*, which differs in the absence of a carboxylic group and the presence of an additional hydroxyl group in the cyclopentane ring [103].



17 **18** R=Me
19 R=COOH

Figure 5. Structures of benozopyranones.

2.5. Binaphtopyrones

So far, members of the family of binaphthopyrones (Figure 6) were isolated only from an extremophilic strain of *C. cladosporioides* collected from a hypersaline lake in Egypt. In particular, cladosporinone (**20**), together with some viriditoxin derivatives (**21**–**23**), was isolated for the first time from this strain grown in a fermentation broth fortified with 3.5% sea salt [22]. The finding of compounds with original structures from fungi in extreme habitats is not unusual, considering that these microorganisms require special survival strategies for growing and reproducing, and adaptation to such conditions requires the modification of gene regulation and metabolic pathways [104].

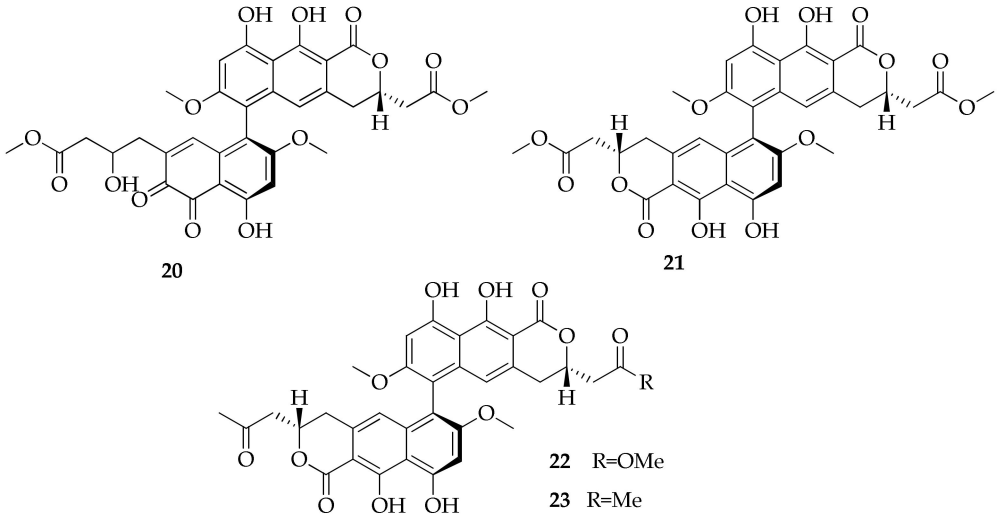


Figure 6. Structures of binaphthopyrones.

2.6. Butanolides and Butenolides

Some metabolites from the cladospolide series are members of the family of butanolides and butenolides (Figure 7), a subgroup of lactones with a four-carbon ring structure. Many of them were isolated from several species of *Cladosporium* along with other cladospolides that are members of the series of macrolides [32,44,67,71,94].

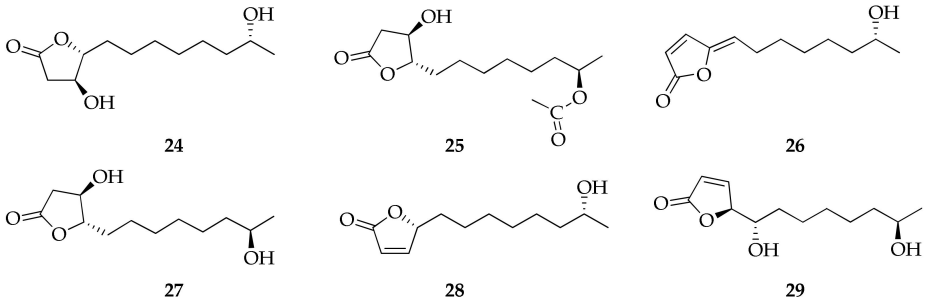


Figure 7. Structures of butanolides and butenolides.

2.7. Cinnamic acid Derivatives

Phenylalanine and tyrosine are precursors for a wide range of natural products. Commonly in plants and fungi, a frequent step is the elimination of ammonia from the side chain to generate cinnamic acids and related compounds. Caffeic and coumaric acids are among the most common naturally occurring cinnamic acids, which can also be found in a range of esterified forms, such as quinic acid forming chlorogenic acid [105]. Caffeic, chlorogenic and coumaric acids (**30**–**32**, Figure 8) were detected in the culture extract of an endophytic strain of *Cladosporium velox* isolated from stem of *Tinospora cordifolia*. Comparative analysis of the metabolite profiles of this strain showed similar composition with stem and leaf extracts of the host plant [70].

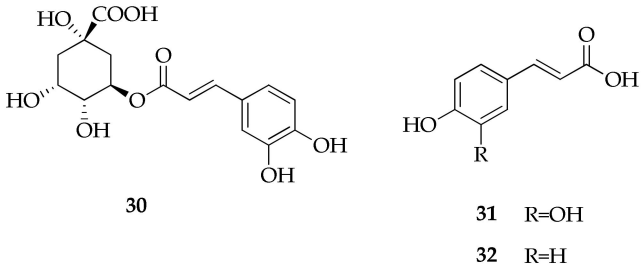


Figure 8. Structures of cinnamic acid derivatives.

2.8. Citrinin Derivatives

Four new compounds from a marine-derived strain of *Cladosporium* sp. were reported as citrinin derivatives (**34**–**37**, Figure 9) [92]. Citrinin is a polyketide mycotoxin first isolated from *Penicillium citrinum* [106]. Considering the existence of the name cladosporin for the product (**39**) since 1971 [12] and cladosporine A (**4**) [84], the use of the same name for this new series is questionable. Furthermore, a known citrinin dimeric derivative named citrinin H1 (**33**) was isolated from a strain of *Cladosporium* sp. [85].

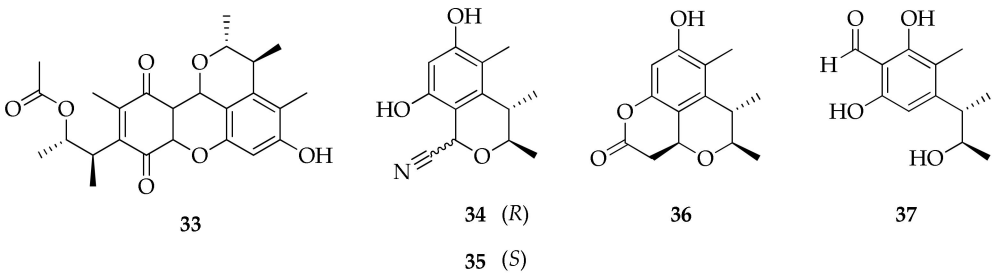


Figure 9. Structures of citrinin derivatives.

2.9. Coumarins and Isocoumarins

Cladosporin (**39**) is a member of 3,4-dihydroisocoumarins, a subgroup of isocoumarins that are commonly produced by fungi, along with coumarins [107]. Coumarins and iso-

coumarins are structural isomers, and their general moieties are respectively characterized by a chromen-2-one and 1*H*-isochromen-1-one [108]. Cladosporin was reported for the first time from mycelium of *C. cladosporioides* [12], but its absolute stereochemistry was elucidated only 17 years later using ^{2}H decoupled ^{2}H, ^{13}C NMR shift correlation [36]. Cladosporin has also been isolated from the culture filtrate of another strain of *C. cladosporioides* together with its epimer in C-6′ named isocladosporin (**42**, Figure 10) [24,37]. It must be noted that **39** was later found from *Aspergillus flavus* [97] and an unidentified *Aspergillus* strain [109], but it was wrongly reported as a new compound with the name asperentin. As a consequence, some of its analogues were characterized as asperentin-8-methyl ether (**38**) and 5′-hydroxyasperentin (**40**) [25].

Kotanin (**43**) and orlandin (**44**) are two closely related dimeric coumarins produced by an endophytic strain of *C. herbarum* isolated from the leaves of *Cynodon dactylon* [47], which were previously reported as products of plant-associated *Aspergillus* strains [110,111].

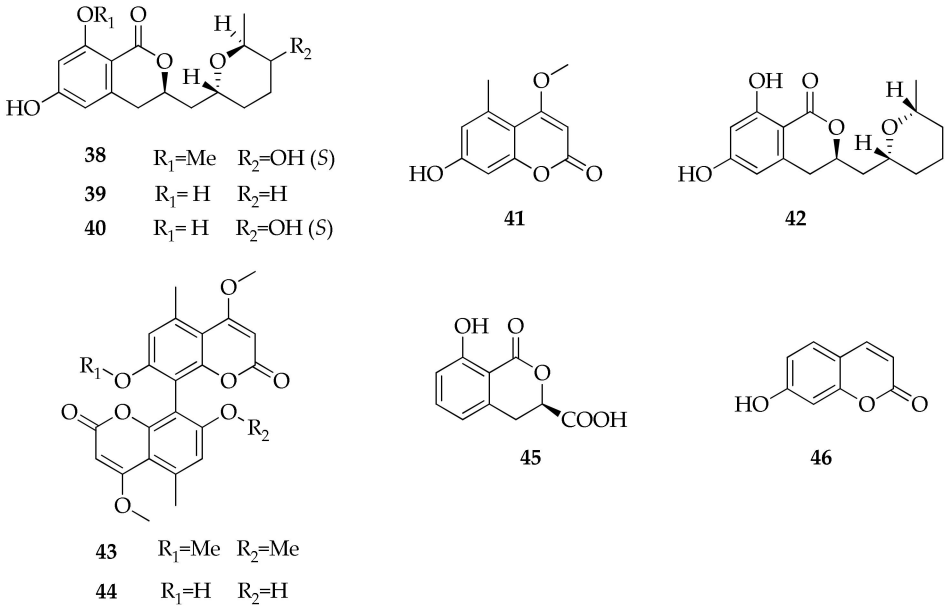


Figure 10. Structures of coumarins and isocoumarins.

2.10. Cyclohexene Derivatives

Four new cyclohexene derivatives named cladoscyclitols A–D (**47**–**50**) were obtained from the culture broth of a mangrove endophytic fungus *Cladosporium* sp. (Figure 11) [82].

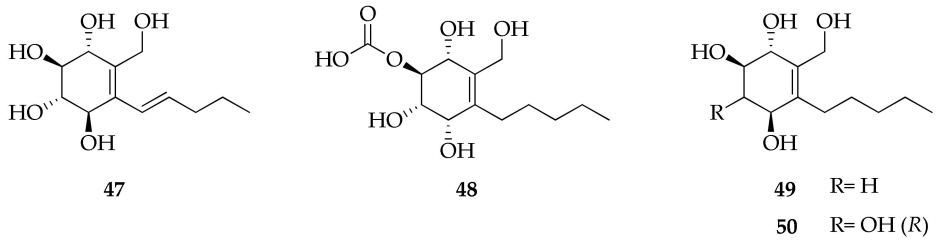
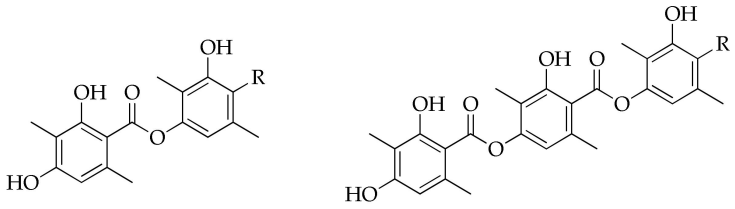


Figure 11. Structures of cyclohexene derivatives.

2.11. Depsides

Four new despsides (**51**–**54**) were isolated from an endophytic strain of *Cladosporium uredinicola* (Figure 12) [69]. The authors later revised the structures of 3-hydroxy-2,4,5-trimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate (**52**) and 3-hydroxy-2,5-dimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate (**54**) [98].

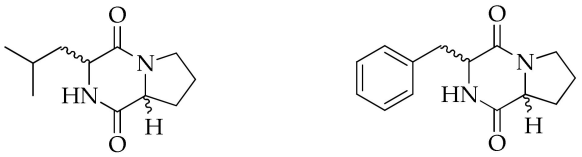


51 R=Me
53 R=H
52 R=Me
54 R=H

Figure 12. Structures of depsides.

2.12. Diketopiperazines

The diketopiperazines (**55**–**58**) reported in Figure 13 were identified via GC-MS in the crude extract of the culture filtrate of a strain of *C. cladosporioides* along with several volatile metabolites [17]. The structure of compounds in this class is based on a cyclic scaffold deriving from the condensation of two α-amino acids.



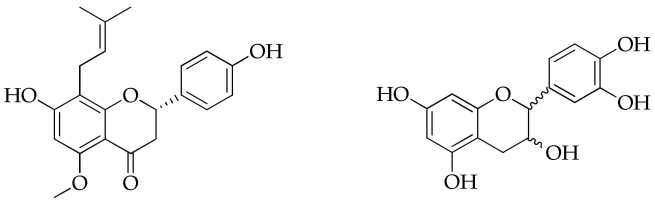
55 (3*R*, 8*R*)
56 (3*S*, 8*S*)
57 (3*R*, 8*R*)
58 (3*S*, 8*S*)

Figure 13. Structures of diketopiperazines.

2.13. Flavonoids

The investigation of compounds produced by a previously mentioned endophytic strain of *C. velox* isolated from *Tinospora cordifolia* led to the identification, via RP-HPLC, of the known flavonenes called catechin (**60**) and epicatechin (**61**) by comparison of their retention times with those of commercially available standard compounds (Figure 14) [70].

The known (2*S*)-7,4′-dihydroxy-5-methoxy-8-(γ,γ-dimethylallyl)-flavanone (**59**) is a prenylated flavanone in which prenylation is represented by 3,3-dimethylallyl substituent at position 8′ [93].



59
60 (*R*,*S*)
61 (*S*, *S*)

Figure 14. Structures of flavonoids.

2.14. Gibberellins

A strain of *C. sphaerospermum* from salt-stressed soybean plants was able to induce maximum plant growth in both soybean and Waito-C rice. Interestingly, high amounts of gibberellins (**62**–**68**) were detected in its culture filtrate (Figure 15) [57]. Gibberellins are diterpenoid hormones involved in many aspects of plant growth and development, hence playing a role in the mutualistic plant-endophyte interactions [112].

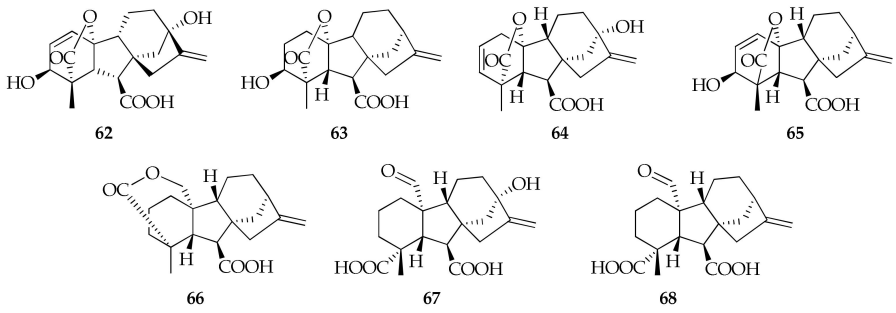


Figure 15. Structures of gibberellins.

2.15. Fusicoccane Diterpene Glycosides

Cotylenin A (**69**) is the major and most structurally complex metabolite of fusicoccane diterpene glycosides isolated from the *Cladosporium* species (Figure 16). Cotylenins A–D (**69**–**72**) are characterized by the presence of a common aglycone named cotylenol and an unusual sugar moiety consisting in a 6-*O*-methyl-α-D-glucosyl derivative with an oxygenated C5-isoprene unit [72–74].

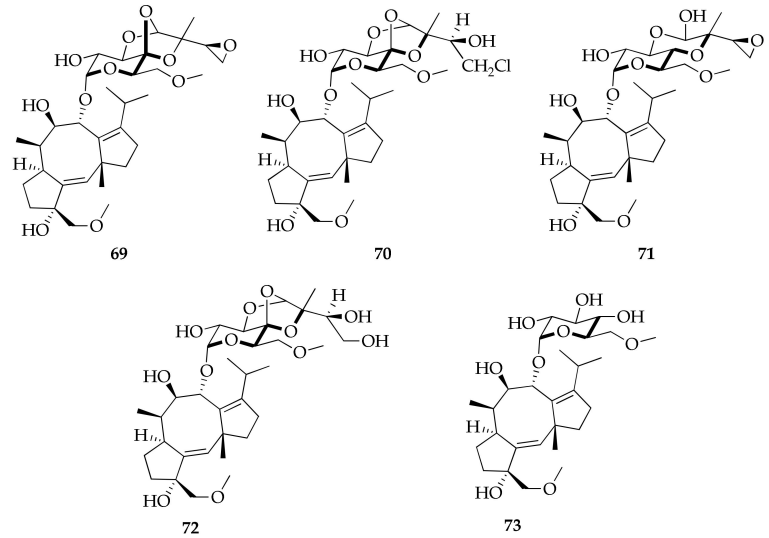


Figure 16. Structures of fusicoccane diterpene glycosides.

2.16. Lactones

This class includes structurally diverse compounds with a 1-oxacycloalkan-2-one structure in common. Cladosporactone A (**74**), cladosporimide A (**75**) and herbaric acid (**76**) are lactones isolated for the first time from a marine-derived strain of *Cladosporium* sp. (Figure 17) [35,45,93].

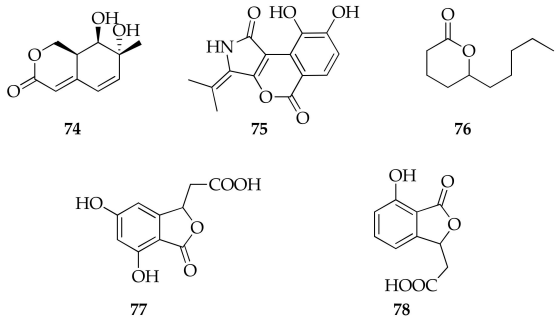


Figure 17. Structures of lactones.

2.17. Macrolides

Macrolides are a large family of compounds characterized by a macrocyclic lactone ring. Rings are commonly 12, 14, or 16 membered [105].

Macrolides with a different number of members were also isolated from cultures of *Cladosporium* spp. (Figures 18 and 19), many of them reported for the first time. In fact, several 12-membered macrolides were reported from marine-derived strains of the *Cladosporium* species, such as recifeiolide analogues, namely 5*R* and 5*S*-hydroxyrecifeiolides (**90**–**91**) [32] and sporiolides A and B (**101**–**102**) [88].

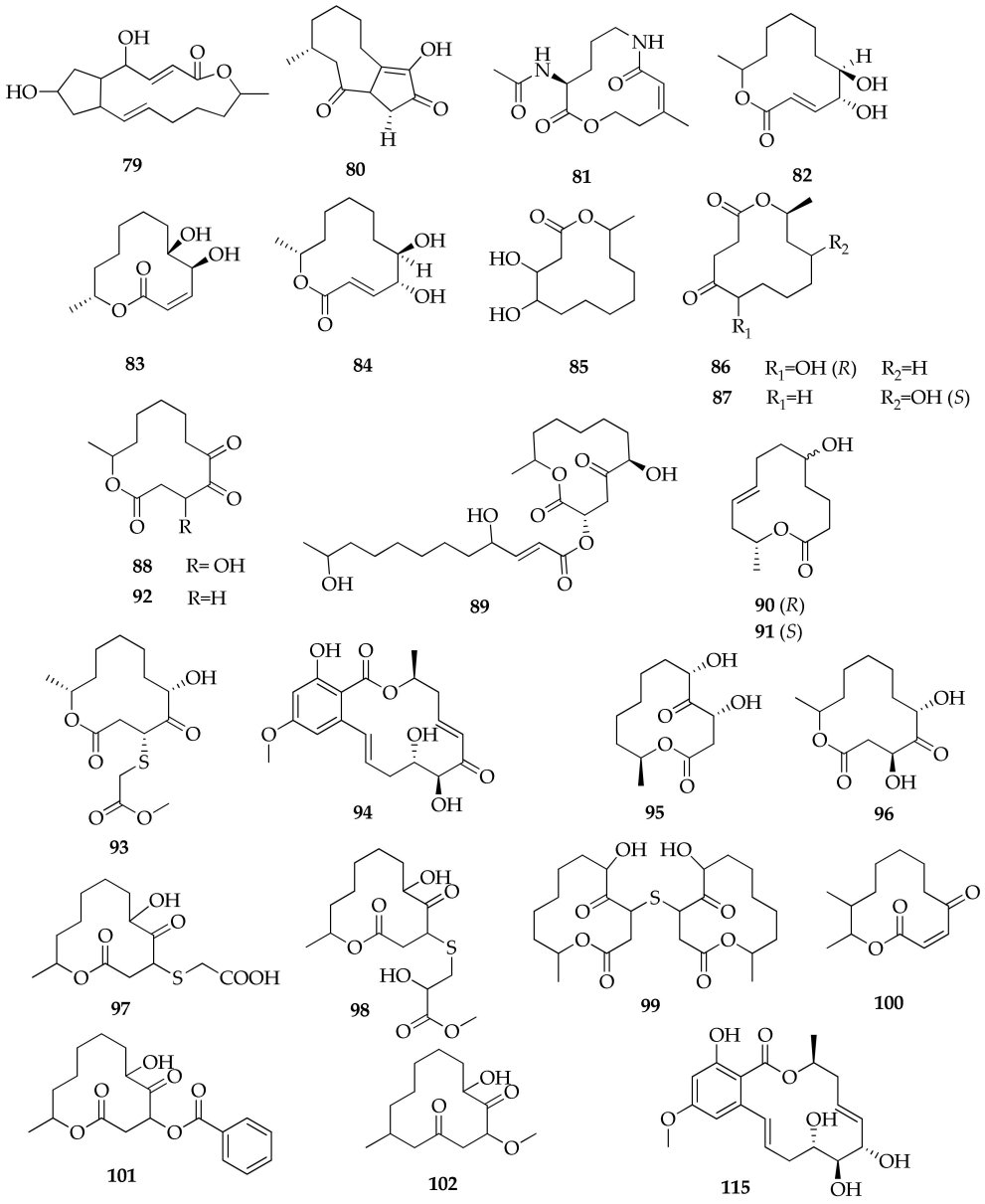


Figure 18. Structures of macrodiolides.

The list of macrolides from the *Cladosporium* species includes pandangolide 1a and pandangolides 1–4 (**95**–**99**). Pandangolide 1 and 2 were already known as products of an unidentified fungal species obtained from a marine sponge [113], while pandangolides 3 and 4 were identified for the first time from *C. herbarum* [44]. Pandangolide 1a was isolated, together with its known diastereomer **95**, from a sponge-associated *Cladosporium* sp. [71].

The investigation of metabolites produced by the mangrove endophytic *Cladosporium* sp. led to the isolation of new compounds called thiocladospolides A–E (**103**–**107**, Figure 19)

and the macrodiolide lactam derived from ornithine, called cladospamide A (**81**), together with the known cladospolide B (**83**) [33,91]. This latter compound was previously isolated and identified during a screening for new plant growth regulators produced by *C. cladosporioides*, along with its isomer cladospolide A (**82**) [114–116]. The cladospolide series also includes the diastereomer of **82**, named cladospolide C (**84**), which was isolated from *Cladosporium tenuissimum* [64].

Two new macrolides (i.e., 4-hydroxy-12-methyloxacyclododecane-2,5,6-trione (**88**) and 12-methyloxacyclododecane-2,5,6-trione (**92**)), were isolated from an endophytic strain of *C. colocasiae*, together with known compounds identified as cladospolide A (**82**), (6*R*,12*S*)-6-hydroxy-12-methyl-1-oxacyclododecane-2,5-dione (**86**), pandangolide 1 (**95**), patulolide B (**100**) and seco-patulolide C (162) [41].

An unusual macrolide with a bicyclo 5–9 ring system, named cladocladosin A (**80**), was isolated from the mangrove-derived endophytic fungus *C. cladosporioides*, along with two new sulfur-containing macrodiolides, namely thiocladospolides F and G (**108**,**110**) [34]. Moreover, five new thiocladospolides were identified together with some known compounds from a strain of *Cladosporium oxysporum* (Figure 19) [50]. These new compounds were named thiocladospolides F-J, even if thiocladospolides F and G (**109**,**111**) had been previously reported with different structures, representing another example of the issue "one name, more structures". For this reason, these compounds are reported in Table 2 as thiocladospolides F *bis* and G *bis*.

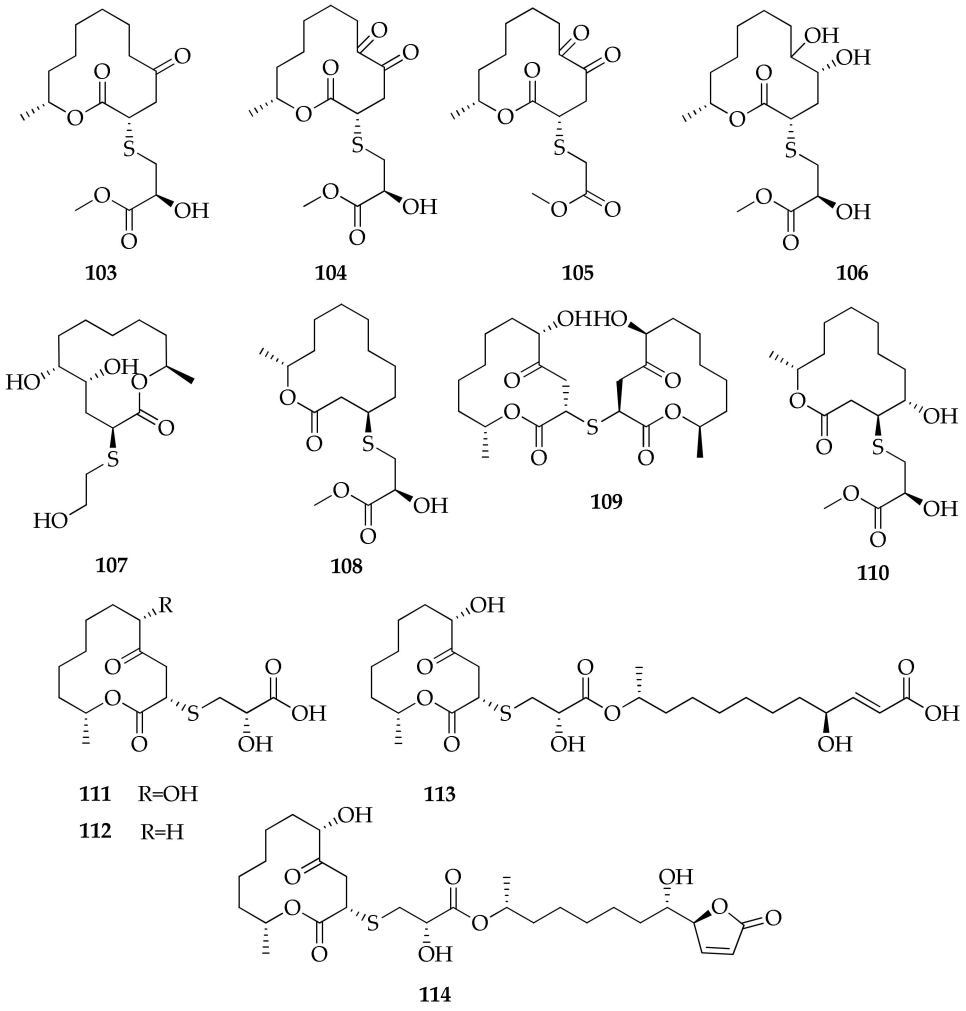
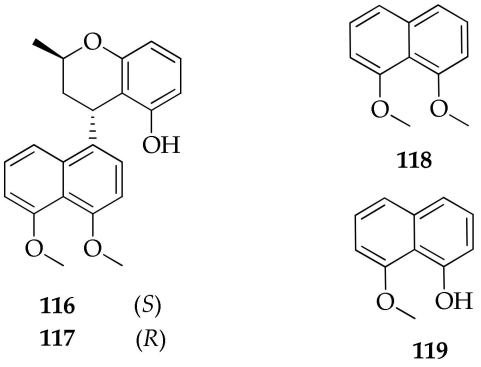


Figure 19. Structures of thiocladospolides.

2.18. Naphthalene Derivatives

Two new dimeric naphthalene derivatives, named cladonaphchroms A and B (**116**, **117**), were obtained from a mangrove-derived strain of *Cladosporium* sp. (Figure 20). These compounds were detected in the fungal culture extract along with some known metabolites, such as 5-hydroxy-2-methyl-4*H*-chromen-4-one (**236**), (*R*)-5-hydroxy-2-methyl-chroman-4-one (**237**), 1,8-dimethoxynaphthalene (**118**) and 8-methoxynaphthalen-1-ol (**119**) [83]. Additionally, **118** was also obtained as product of a mangrove-derived strain of *Cladosporium* sp. [81].



116 (*S*)
117 (*R*)

118

119

Figure 20. Structures of naphthalene derivatives.

2.19. Naphthalenones

(−)-*trans*-(3*R*,4*R*)-3,4,8-Trihydroxy-6,7-dimethyl-3,4-dihydronaphthalen-1(2*H*)-one (**141**) is a new compound isolated from a mangrove-derived *Cladosporium* sp. (Figure 21), produced along with six known compounds (i.e., **118**,**135**,**137**,**140**) [81]. Scytalone (**139**) is another compound from this class, isolated from an endophytic strain of *C. tenuissimum* from *Pinus wallichiana* [68]. It is a polyketide known as an intermediate in melanin biosynthesis produced by many fungi associated with plants [117,118].

Dimeric tetralones are a subclass of naphthalenones made from two monomers of bicyclic aromatic hydrocarbon and a ketone. A marine-derived strain of *Cladosporium* sp. also produces new dimeric tetralones: the newly isolated altertoxin XII (**120**) and the known cladosporol I (**130**) [87].

Among the compounds in this family, cladosporol A (**121**) was isolated for the first time from *C. cladosporioides* [26] and later on from *C. tenuissimum* together with some analogues, cladosporol B–E (**122**–**125**) [66]. Their absolute configurations were revised some years later from (4′*R*) to (4′*S*) when five new dimeric tetralones (i.e., cladosporols F–J) and the known cladosporol C (**123**) were isolated from an algal endophytic strain of *C. cladosporioides* [39]. Four new dimeric tetralones, namely clindanones A and B (**133**,**134**) and cladosporols F and G (**126**,**127**), were identified by a deep-sea derived strain of *C. cladosporioides* along with the known isosclerone (**138**), which is the only monomeric tetralone isolated from the *Cladosporium* species so far [40]. Clindanones (**133**,**134**) possess new dimeric forms of the skeleton composed by the coupling of indanone and 1-tetralone units. As introduced in chapter 2, cladosporol G (**128**) produced by the algal strain [39] is different from the compound (**127**) with the same name previously discovered as a product of the deep-sea derived strain.

Some cladosporols (i.e., **121**, **123** and **124**) were also isolated from a strain of *Cladosporium* sp. derived from the mangrove plant *Kandelia candel*, along with the new dimeric tetralone named cladosporone A (**132**) [86].

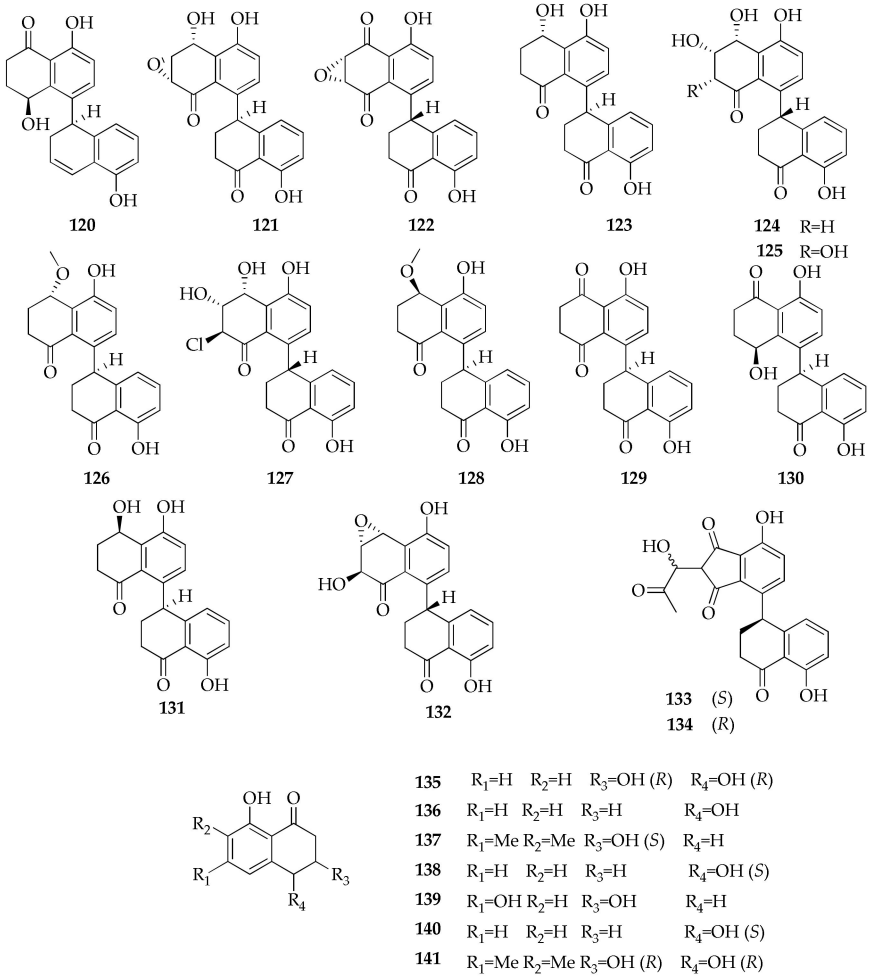


Figure 21. Structures of naphthalenones.

2.20. Naphtoquinones and Anthraquinones

Naphthoquinones and anthraquinones have been widely identified as metabolites from various plants, microbes and marine organisms [102,119,120]. Two anthraquinones, namely anhydrofusarubin (**142**) and methyl ether of fusarubin (**143**), were isolated from *Cladosporium* sp. from the bark of the plant *Rauwolfia serpentina* [90]. The only naphthoquinone known from *Cladosporium*, plumbagin (**144**), was isolated from a strain of *Cladosporium delicatulum*, which resulted as the most potent producer of this valuable drug after a dedicated screening of endophytic fungi carried out to find strains able to synthesize this valuable drug (Figure 22) [42].

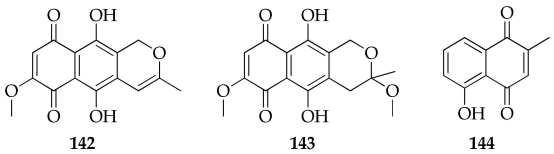


Figure 22. Structures of naphthoquinones and anthraquinones.

2.21. Perylenquinones

The first member of the family of perylenquinones (Figure 23), named phleichrome (**154**), was reported as a new phytotoxic compound produced by *Cladosporium phlei* [53,99]. The stereochemistry of phleichrome was investigated in detail in a subsequent study, which reports the conversion of **154** in isophleichrome, highlighting the similarity in behavior and physical data with another couple of fungal perylenquinones, cercosporin and isocercosporin [54]. In fact, perylenquinones show intriguing stereochemical features, such as axial chirality due to the helical shape of the constrained pentacyclic ring, combined

with asymmetric carbons in the side chains. Even if it was indicated that phleichrome can be thermally converted in its unnatural diastereoisomer named isophleichrome [54], the production by *C. cladosporioides* of ent-isophleichrome (**152**) was reported [46]. Moreover, several esters of **152**, belonging to the series of calphostins, were isolated from a strain of *Cladosporium* sp. Calphostin C and I (**151**,**153**) [30,121] have also been incorrectly reported as new products with the names cladochromes E and D [31]. In fact, these compounds had been previously isolated, and their physico-chemical properties investigated in the course of screening the potential inhibitors of protein kinase C (PKC) from a strain of *C. cladosporioides*, along with several other calphostins (**149**–**153**) [29,30]. Moreover, four new perylenquinones, altertoxins VIII-XI (**145**–**148**), were isolated from the fermentation broth of a marine-derived strain of *Cladosporium* sp. [87]. These new metabolites partially share structures with a series of metabolites originally isolated from the *Alternaria* species [122].

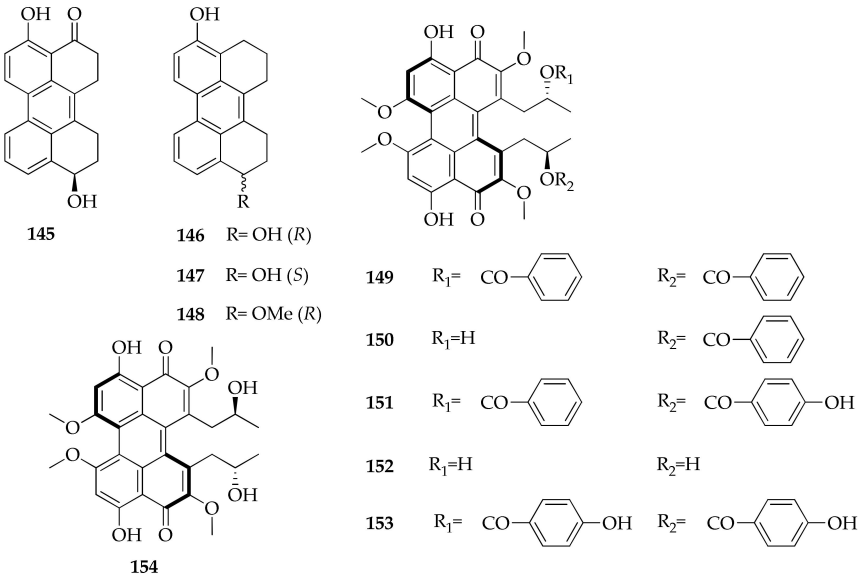


Figure 23. Structures of perylenequinones.

2.22. Pyrones

Pyrones represent a family of six-membered unsaturated cyclic compounds containing oxygen that naturally occurs in two isomeric forms, either as 2-pyrone or 4-pyrone. 2-pyrone is extremely prevalent in numerous natural products isolated from plants, animals, marine organisms, bacteria, fungi, and insects [123,124]. Two new 2-pyrones (i.e., herbarins A and B (**156**,**157**)) were obtained from a spongiculous strain of *C. herbarum* isolated (Figure 24) [45].

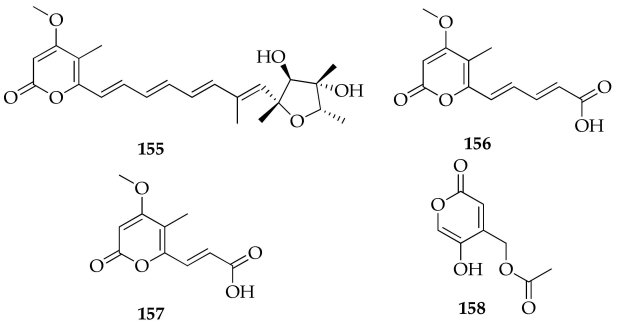


Figure 24. Structures of pyrones.

2.23. Seco Acids

The 12 membered seco acids reported in Figure 25 were found to be produced by strains of *C. cladosporioides* and *C. tenuissimum*, along with members of the families of

lactones or macrolides [33,67,68,94]. It can be speculated that these compounds are intermediates in the biosynthesis of cyclic compounds because seco acids are the starting material for the production of lactones [125].

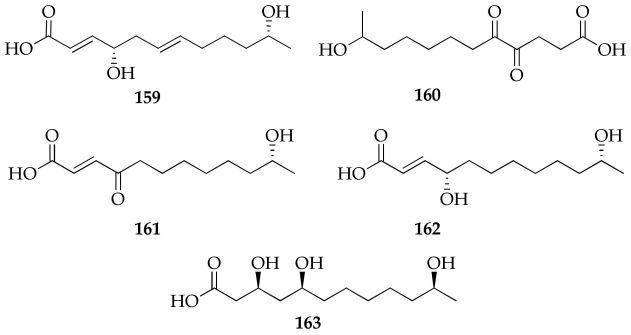


Figure 25. Structures of seco acids.

2.24. Sterols

Sterols are a class of lipids involved in several metabolic reactions since they are components of the membrane of eukaryotic organisms playing a crucial role in permeability and fluidity [126]. They are modified triterpenoids containing the tetracyclic ring system of lanosterol but lacking the three methyl groups at C-4 and C14. The predominant sterol found in fungi is ergosterol, which has frequently been investigated in human pathogenic fungal strains [127]. Ergosterol (**170**) was also identified as product of a strain of *Cladosporium* sp., along with 23,24,25,26,27-pentanorlanost-8-ene-3β,22-diol (**172**), peroxyergosterol (**173**) and four new pentanorlanostane derivatives named cladosporides A–D (**164**–**167**) (Figure 26) [79,80].

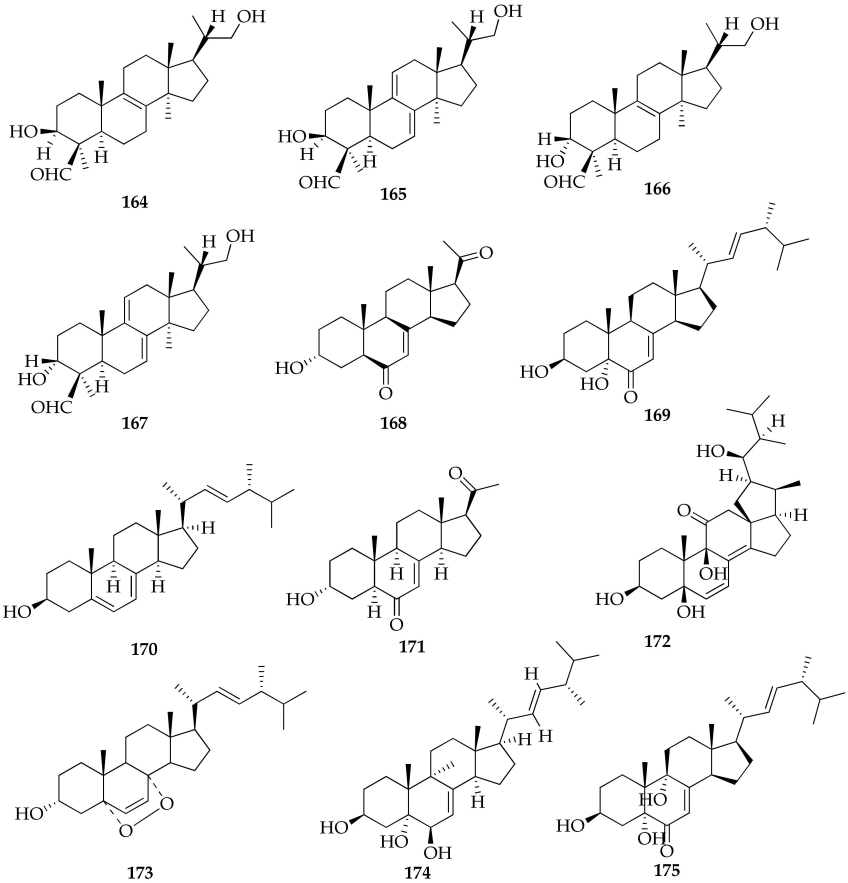


Figure 26. Structures of sterols.

2.25. Tetramic Acids

Tetramic acids are compounds containing 2,4-pyrrolidinedione backbone obtained by the fusion of an amino acid with polyketide units. The series of cladosporimins and cladosins belong to this class, with the latter reported exclusively from *C. sphaerospermum* (Figures 27 and 28). In fact, six novel cladosins, the structures of which are constituted by a tetramic acid core and 6(3)-enamino-8,10-dihydroxy or 6(3)-enamino-7(8)-en-10-ol side chains, named cladosins A–D (**177**–**180**) and F–G (**181**,**182**), were reported from a strain of *C. sphaerospermum* from sediments collected in the Pacific Ocean [55,56]. Each compound exists as two tautomeric forms differing in configuration of the enamine. Moreover, investigation into the fermentation extracts of another isolate of *C. sphaerospermum* from marine sediments led to the discovery of cladosins H–K (**183**–**186**) [89]. Finally, cladosins L–O (187, 189–191), together with another tetramic acid named cladodionen (176), were isolated from a strain of this species obtained from healthy bulbs of *Fritillaria unibracteata* var. *wabuensis* [63].

Two structurally different compounds were reported as cladosin L (**187**,**188**) in two papers published almost at the same time [60,63]. In fact, a second product labeled with this name (**188**) was identified from a *Hydractinia*-associated strain of *C. sphaerospermum*.

Even in the cladosporiumin series (Figure 28) there are some compounds that were given the same name because of the contemporaneous publication of work dealing with the structural identification of novel tetramic acids. In fact, Liang et al. [58] and Risher et al. [61] identified two tetramic acids continuing the series of cladosporiumins (**192**–**209**), and both research teams named their new compounds cladosporiumins I and J (**201**,**203**). Furthermore, cladosporiumin L (**206**), reported by Liang et al. [58], is a metal complex of tetramic acid. In fact, considering that the formation of metal complexes of tetramic acid derivatives (e.g., harzianic acid [128,129]) affect the chemical shifts of H-5 an N-methyl proton or NH, the authors can speculate that the structure of cladosporiumin L is a Mg_2 complex. The authors also reported the structure of cladosporiumins F (**198**) and H (**200**) as their Na complexes.

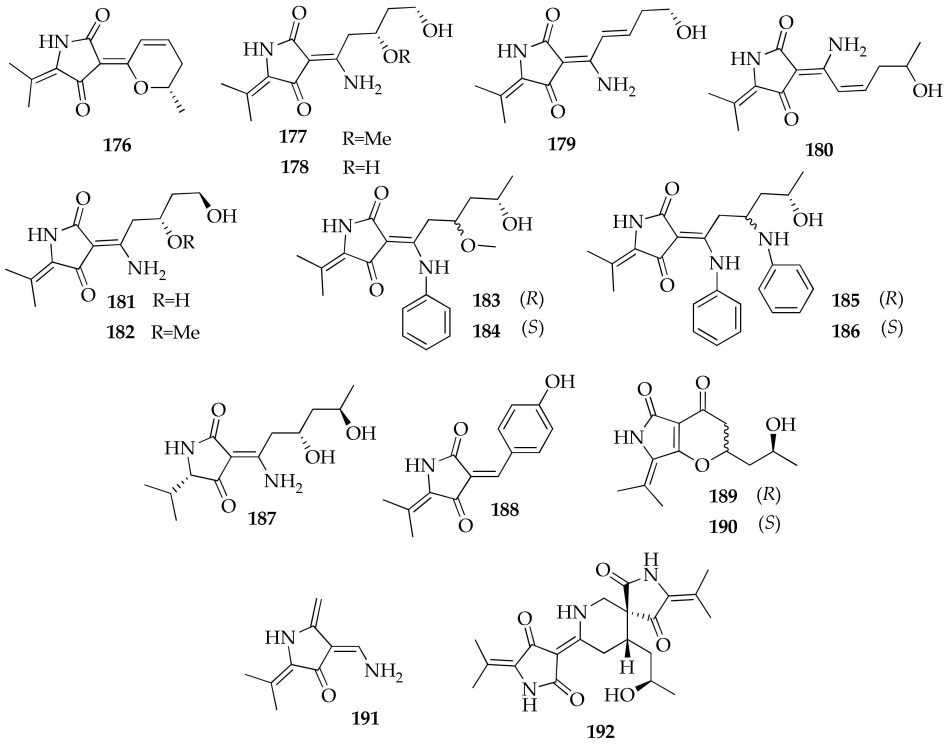


Figure 27. Structures of tetramic acids.

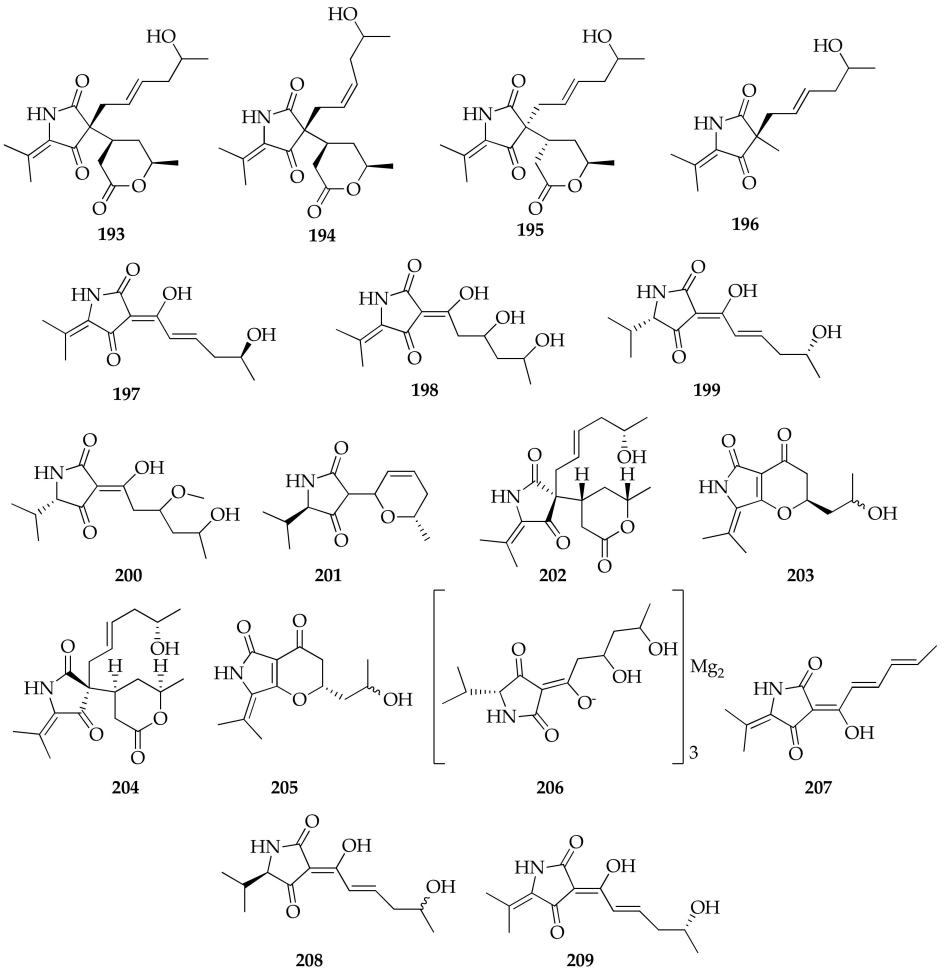


Figure 28. Structures of cladosporiumins.

2.26. Tropolones

Malettinins A–C (**210–212**) were isolated and structurally elucidated from a marine strain of *Cladosporium* sp., along with the new malettinin E (**213**) (Figure 29) [95]. This represents the first isolation of tropolones from a fungus belonging to the genus *Cladosporium*. In fact, malettinins A–C were originally isolated from an unidentified fungus, which additionally produced a fourth metabolite, named malettinin D. This latter compound was not identified in the culture extracts of *Cladosporium* sp.; instead, its new 13-epimer was detected (**213**).

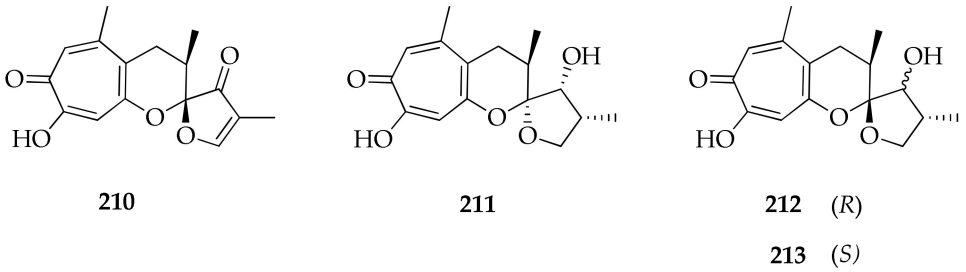


Figure 29. Structures of tropolones.

2.27. Volatile Terpenes

An isolate of *C. cladosporioides* obtained from the rhizosphere of red pepper has been investigated for the production of volatile terpenes using solid phase microextraction (SPME) coupled to GC-MS (Figure 30) [38]. Identification of volatiles revealed mainly

(−)-trans-caryophyllene, dehydroaromadendrene, α-pinene and (+)-sativene (**214**–**217**). In previous research on Plant Growth Promoting Rhizobacteria (PGPR) and Plant Growth Promoting Fungi (PGPF), it was reported that volatile terpenes play important chemo-ecological roles in the interactions between plants and their environments [130]. In fact, this strain seems to be able to improve the growth of tobacco seedlings and their root development through the production of volatile terpenes [38].

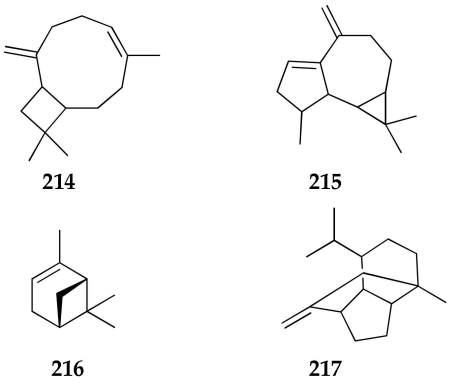
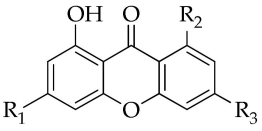


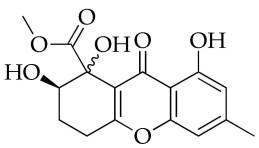
Figure 30. Structures of volatile terpenes.

2.28. Xanthones

The class of xanthones includes compounds with a backbone designated as dibenzo-7-pyrone. A huge number of xanthones have been isolated from natural sources of higher plants, fungi, ferns, and lichens [131]. A strain of *C. halotolerans* symbiotic with the coral *Porites lutea* produces nine metabolites (**218**–**225**,**227**) belonging to this class (Figure 31) [43]. Furthermore, a dimeric tetrahydroxanthone (**226**), where two tetrahydroxanthone monomers are connected through a 2,2′-biphenol linkage, was also isolated from an endophytic strain of *Cladosporium* sp. [85].

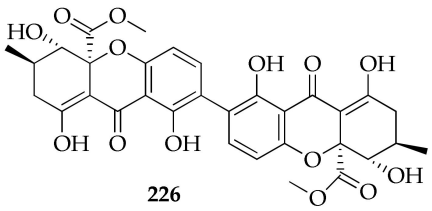


218	R_1=CH_2OH	R_2=COOMe	R_3=OH
219	R_1=Me	R_2=COOMe	R_3=OH
222	R_1=COOH	R_2=COOMe	R_3=H
223	R_1=CH_2OH	R_2=COOMe	R_3=H
224	R_1=Me	R_2=COOMe	R_3=H
225	R_1=COOH	R_2=COOMe	R_3=H
227	R_1=H	R_2=COOMe	R_3=H



220 (*R*)

221 (*S*)



226

Figure 31. Structures of xanthones.

2.29. Miscellaneous

Finally, a number of products of *Cladosporium* are placed in a miscellaneous class because they have no structural affinity with previous groups (Figure 32). This is the case for a new abscisic acid analogue named cladosacid (**230**) [96], sumiki's acids (**229**,**241**) [44], the new pentenoic acid derivative named 1,1′-dioxine-2,2′-dipropionic acid (**233**) [85] and two new ribofuranose phenol derivatives named 4-*O*-α-D-ribofuranose-3-hydroxymethyl-2-pentylphenol (**239**) and 4-*O*-α-D-ribofuranose-2-pentyl-3-phemethylol (**238**) [81,82].

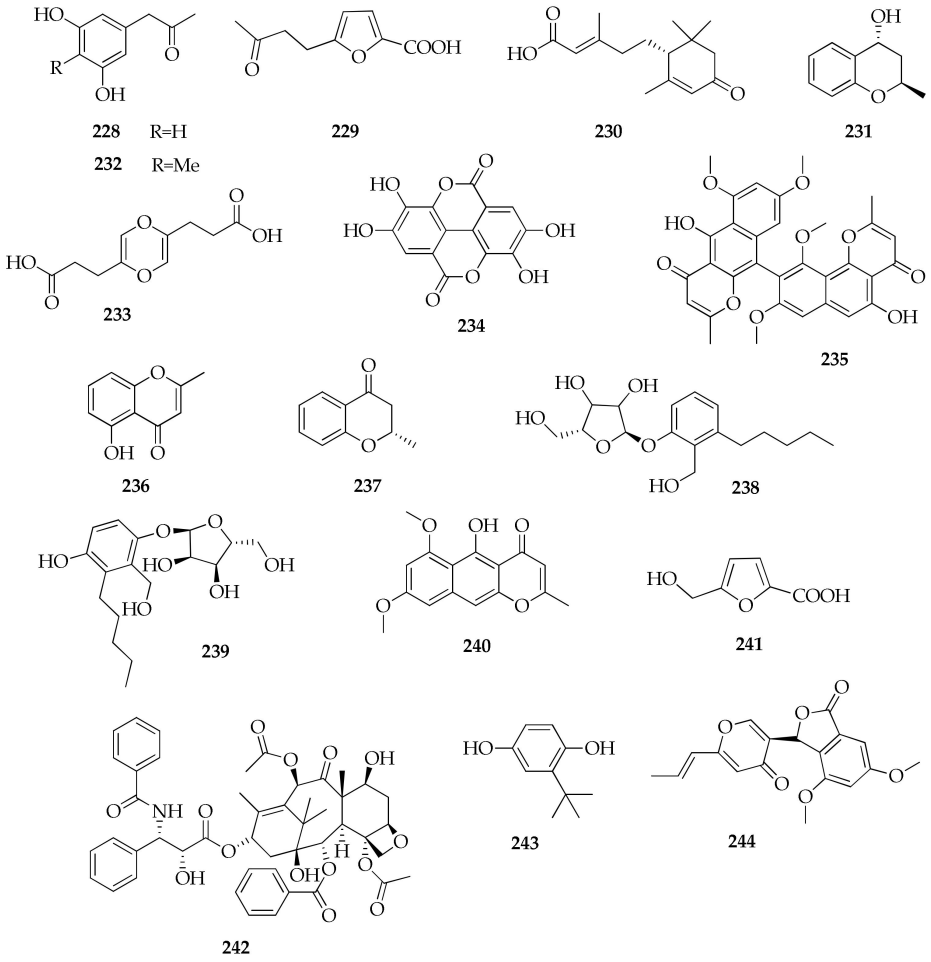


Figure 32. Structures of compounds from the group "miscellaneous".

3. Biological Activities of Secondary Metabolites

Most secondary metabolites reported in Table 3 have been investigated for biological properties, including antifungal, antibacterial cytotoxic and phytotoxic activities, which are summarized in Table 3. For some well-known compounds (e.g., the tetracyclic diterpenoid taxol and the funicone compound vermistatin), which have been extensively investigated and have been the subject of dedicated reviews [132], this table only considers data resulting from reports concerning the isolation of these compounds from *Cladosporium* strains.

Particularly valuable in the study of the bioactivities of natural products is the structure–activity relationship (SAR), but this aspect has only been taken into account in few research papers on *Cladosporium* compounds. An interesting evaluation of the relationships between structures and bioactivity was reported for cladosporin analogues by Wang et al. [25], who considered the presence of several essential positions in the chemical structures of these compounds that might be responsible for their antifungal activity. As a consequence, the antifungal activity of the parent compound seems to be influenced by the R configuration of C-6′. This configuration greatly decreased the antifungal activity of isocladosporin against the *Colletotrichum* species but slightly increased the antifungal activity against the *Phomopsis* species. Comparing the structures of cladosporin and 5′-hydroxyasperentin, the hydroxylation of the C-5′ position causes the loss of the antifungal activity against the *Colletotrichum* species and decreases the selectivity against the *Phomopsis* species. Comparison of 5′-hydroxyasperentin and the synthesized 6,5′-diacetyl derivative revealed that the replacement of the hydrogen in the hydroxyl group at C-6 and the hydrogen at C-5′ in the acetyl groups greatly increased selectivity toward the two *Phomopsis* species. Furthermore, the C-8 position also seems to be responsible for antifungal activity, demonstrated by the inactivity of asperentin-8-methyl ether against all the tested fungi [25].

Table 3. Bioactivities of secondary metabolites produced by the *Cladosporium* species.

Name (Code)	Biological Activity	Concentration	Results	Ref.
Alkaloids				
Aspidospermidin-20-ol, 1-acetyl-17-methoxy (**2**)	Antimicrobial	125 μg mL^{-1}; 62.50 μg mL^{-1}; 320.5 μg mL^{-1}	*Xanthomonas oryzae* (MIC); *Pseudomonas syringae* (MIC); *Aspergillus flavus* (MIC)	[24]
Cladosporine A (**4**)	Antimicrobial	4 μg mL^{-1}; 16 μg mL^{-1}	*Staphylococcus aureus* (MIC); *Candida albicans* (MIC)	[84]
Cytochalasin D (**5**)	Antibacterial	25 μg mL^{-1}	*S. aureus* (MIC)	[85]
2-Methylacetate-3,5,6-trimethylpyrazine (**6**)	Antibacterial	12.5 μg mL^{-1}	*S. aureus* (MIC)	[85]
Azaphilones				
Lunatoic acid A (**10**)	Phytotoxic	100 μg mL^{-1}	*Brassica rapa*; *Sorghum durra*; *Brassica campestris*; *Capsicum annuum*; *Raphanus sativus*	[49]
Benzofluoranthenones				
(6b*S*,7*R*,8*S*)-4,9-Dihydroxy-7,8-dimethoxy-1,6b,7,8-tetra-hydro-2*H*-benzo[J]fluoranthen-3-one (**13**)	Inhibition of anti-CD28-induced IL2	2.4 μM	IC_{50}	[27]
(6b*R*,7*R*,8*S*)-7-Methoxy-4,8,9-trihydroxy-1,6b,7,8-tetrahydro-2*H*-benzo[J]fluoranthen-3-one (**15**)	Inhibition of anti-CD28-induced IL2	2.5 μM	IC_{50}	[27]
	Abl tyrosine kinase	0.76 μM	IC_{50}	
(6b*S*,7*R*,8*S*)-7-Methoxy-4,8,9-trihydroxy-1,6b,7,8-tetrahydro-2*H*-benzo[J]fluoranthen-3-one (**16**)	Inhibition of anti-CD28-induced IL2	0.4 μM	IC_{50}	[27]
	Abl tyrosine kinase	0.06 μM	IC_{50}	
Benzopyranones				
Coniochaetone A (**17**)	Cytotoxic	10 μM	22RV1 (67.4%), C4-2B (13.87%), RWPE-1 (17.3%)	[43]
Coniochaetone B (**18**)	Cytotoxic	10 μM	22RV1 (32.7%), C4-2B (2.9%), RWPE-1 (19.7%)	[43]
Coniochaetone K (**19**)	Cytotoxic	10 μM	22RV1 (64.6%), C4-2B (7.2%), RWPE-1 (11.7%)	[43]
Binaphthopyrones				
Cladosporinone (**20**)	Cytotoxic	53.7 μM	L5178Y (IC_{50})	[22]
	Antibacterial	64 μg mL^{-1}	*S. aureus* (MIC)	
Viriditoxin (**21**)	Cytotoxic	0.1 μM	L5178Y (IC_{50})	[22]
	Antibacterial	0.015 μg mL^{-1}	*S. aureus* (MIC)	
Viriditoxin SC-28763 (**22**)	Cytotoxic	0.25 μM	L5178Y (IC_{50})	[22]
	Antibacterial	2 μg mL^{-1}	*S. aureus* (MIC)	
Viriditoxin SC-30532 (**23**)	Antibacterial	16 μg mL^{-1}	*S. aureus* (MIC)	[22]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Butenolides and butanolides				
Cladospolide F (**24**)	Lipid accumulation	10 μM	Oleic acid	[94]
Cladospolide G (**25**)	Antimicrobial	32 μg mL^{-1}; 1 μg mL^{-1}; 32 μg mL^{-1}; 1 μg mL^{-1}	*E. coli* (MIC); *Glomerella cingulata* (MIC); *Bipolaris sorokiniana* (MIC); *Fusarium oxysporum* f. sp. *cucumerinum* (MIC)	[32]
ent-Cladospolide F (**27**)	Antibacterial	8 μg mL^{-1}; 16 μg mL^{-1}; 64 μg mL^{-1}	*S. aureus* (MIC); *Edwardsiella ictarda* (MIC); *P. aeruginosa* (MIC)	[32]
	Acetylcholinesterase	40.46 μM	IC_{50}	
11-Hydroxy-γ-dodecalactone (**28**)	Lipid accumulation	10 μM	Oleic acid	[94]
iso-Cladospolide B (**29**)	Antimicrobial	32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}; 64 μg mL^{-1}	*E. coli* (MIC); *Edwardsiella tarda* (MIC); *E. ictarda* (MIC); *G. cingulata* (MIC)	[32]
	Antimicrobial	16 μg mL^{-1}; 8 μg mL^{-1}; 8 μg mL^{-1}; 16 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *Clematis mandshurica Miura* (MIC); *Colletotrichum gloeosporioides* (MIC); *B. sorokiniana* (MIC); *F. oxysporum* f. sp. *cucumerinum* (MIC)	[50]
Citrinin dervatives				
Citrinin H1 (**33**)	Antibacterial	6.25 μg mL^{-1}; 12.5 μg mL^{-1}; 12.5 μg mL^{-1}	*S. aureus* (MIC); *E. coli* (MIC); *B. cereus* (MIC)	[85]
Cladosporin A (**34**)	Toxic	72.0 μM	brine shrine nauplii (IC_{50})	[92]
Cladosporin B (**35**)	Toxic	81.7 μM	brine shrine nauplii (IC_{50})	[92]
Cladosporin C (**36**)	Toxic	49.9 μM	brine shrine nauplii (IC_{50})	[92]
Cladosporin D (**37**)	Antioxidant	16.4 μM	DPPH radicals (IC_{50})	[92]
	Toxic	81.4 μM	brine shrine nauplii (IC_{50})	

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Coumarins and isocoumarins				
Cladosporin (**39**)	Antimicrobial	75 μg mL^{-1}; 40 μg mL^{-1}	dermatophytes (100%); spore germination of *Penicillium* sp. (100%) and *Aspergillus* sp. (100%)	[12]
		30 μM	*Colletotrichum acutatum* (92.7%), *Colletotrichum fragariae* (90.1%), *C. gloeosporioides* (95.4%), *Plasmopara viticola* (79.9%)	[25]
		500 μg mL^{-1}; 62.50 μg mL^{-1}	*X. oryzae* (MIC), *A. flavus* (MIC); *Fusarium solani* (MIC)	[24]
	Phytotoxic	10^{-3} M	etiolated wheat (81%)	[37]
5′-Hydroxyasperentin (**40**)	Antimicrobial	15.62 μg mL^{-1}; 62.50 μg mL^{-1}; 15.62 μg mL^{-1}; 7.81 μg mL^{-1}	*X. oryzae* (MIC); *P. syringae* (MIC); *A. flavus* (MIC); *F. solani* (MIC)	[24]
		30 μM	*P. viticola* (53.9%), *Phomopsis obscurans* (25.6%)	[25]
Isocladosporin (**41**)	Antimicrobial	30 μM	*C. fragariae* (50.4%), *C. gloeosporioides* (60.2%), *P. viticola* (83.0%)	[25]
		15.62 μg mL^{-1}; 125 μg mL^{-1}; 62.50 μg mL^{-1}	*X. oryzae* (MIC), *P. syringae* (MIC); *A. flavus* (MIC); *F. solani* (MIC)	[24]
	Phytotoxic	10^{-3} M	etiolated wheat (100%)	[37]
Cyclohexene derivatives				
Cladoscyclitol B (**48**)	Inhibition of α-glucosidase	2.95 μM	IC_{50}	[82]
Depsides				
3-Hydroxy-2,4,5-trimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate (**51**)	Antimicrobial	25 μg mL^{-1}; 25 μg mL^{-1}; 250 μg mL^{-1}; 250 μg mL^{-1}	*B. subtilis* (bacteriostatic); *P. aeruginosa* (bacteriostatic); *E. coli* (bacteriostatic); *S. aureus* (bacteriostatic)	[69,98]
3-Hydroxy-2,5-dimethylphenyl 2,4-dihydroxy-3,6-dimethylbenzoate (**53**)	Antimicrobial	25 μg mL^{-1}; 25 μg mL^{-1}; 250 μg mL^{-1}; 250 μg mL^{-1};	*B. subtilis* (MIC); *P. aeruginosa* (MIC); *E. coli* (MIC); *S. aureus* (MIC)	[69,98]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
3-Hydroxy-2,5-dimethylphenyl 4-[(2,4-dihydroxy-3,6-dimethylbenzoyl)oxy]-2-hydroxy-3,6-dimethylbenzoate (**54**)	Antimicrobial	250 μg mL^{-1}; 250 μg mL^{-1}; 250 μg mL^{-1}; 250 μg mL^{-1}	*B. subtilis* (bacteriostatic); *P. aeruginosa* (bacteriostatic); *E. coli* (bacteriostatic); *S. aureus* (bacteriostatic)	[69,98]
Flavonoids				
(2S)-7,4′-Dihydroxy-5-methoxy-8-(γ,γ-dimethylallyl)- flavanone (**59**)	Enzymatic inhibitory	11 μM; 27 μM	PTP1B (IC_{50}); TCPTP (IC_{50})	[93]
Lactones				
Cladosporamide A (**75**)	Enzymatic inhibitory	48 μM; 54 μM	PTP1B (IC_{50}); TCPTP (IC_{50})	[93]
Macrolides				
Cladocladosin A (**80**)	Antimicrobial	16 μg mL^{-1}; 1 μg mL^{-1}; 4 μg mL^{-1}; 2 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}; 8 μg mL^{-1}	*E. coli* (MIC); *E. tarda* (MIC); *P. aeruginosa* (MIC); *Vibrio anguillarum* (MIC); *F. oxysporium f. sp. momordicae* (MIC); *Penicillium digitatum* (MIC); *Harpophora maydis* (MIC)	[34]
Cladospolide B (**83**)	Phytotoxic	1 μg $plant^{-1}$	*Oryza sativa* (37.8%)	[64]
5*R*-Hydroxyrecifeiolide (**90**)	Antimicrobial	32 μg mL^{-1}; 32 μg mL^{-1}	*E. ictarda* (MIC); *P. aeruginosa* (MIC)	[32]
5*S*-Hydroxyrecifeiolide (**91**)	Antimicrobial	16 μg mL^{-1}	*G. cingulata* (MIC)	[32]
5*Z*-7-Oxozeaenol (**94**)	Phytotoxic	4.8 μg mL^{-1}	*Amaranthus retroflexus* (IC_{50})	[49]
Pandangolide 1 (**95**)	Antimicrobial	32 μg mL^{-1}; 4 μg mL^{-1}; 1 μg mL^{-1}; 32 μg mL^{-1}	*S. aureus* (MIC); *E. ictarda* (MIC); *G. cingulata* (MIC); *P. aeruginosa* (MIC)	[32]
Pandangolide 3 (**98**)	Antimicrobial	2 μg mL^{-1}; 8 μg mL^{-1}	*C. gloeosporioides* (MIC); *B. sorokiniana* (MIC)	[33]
		32 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. gloeosporioides* (MIC); *F. oxysporum* f. sp. *cucumerinum* (MIC)	[50]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Sporiolide A (**101**)	Antimicrobial	16.7 μg mL^{-1}; 16.7 μg mL^{-1}; 8.4 μg mL^{-1}; 16.7 μg mL^{-1}; 8.4 μg mL^{-1}	*Micrococcus luteus* (MIC); *C. albicans* (MIC); *Cryptococcus neoformans* (MIC); *Aspergillus niger* (MIC); *Neurospora crassa* (MIC)	[88]
	Cytotoxic	0.13 μg mL^{-1}	L1210 (IC_{50})	
Sporiolide B (**102**)	Antimicrobial	16.7 μg mL^{-1}	*M. luteus* (MIC)	[88]
	Cytotoxic	0.81 μg mL^{-1}	L1210 (IC_{50})	
Thiocladospolide A (**103**)	Antimicrobial	1 μg mL^{-1}; 8 μg mL^{-1}; 2 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. glecosporioides* (MIC)	[33]
		32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. gloeosporioides* (MIC)	[50]
Thiocladospolide B (**104**)	Antimicrobial	2 μg mL^{-1}; 32 μg mL^{-1}; 1 μg mL^{-1}ù	*C. gloeosporioides* (MIC); *Physalospora piricola* (MIC); *F. oxysporum* (MIC)	[33]
Thiocladospolide C (**105**)	Antimicrobial	1 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}	*C. gloeosporioides* (MIC); *P. piricola* (MIC); *F. oxysporum* (MIC)	[33]
Thiocladospolide D (**106**)	Antimicrobial	1 μg mL^{-1}; 1 μg mL^{-1}; 32 μg mL^{-1}; 1 μg mL^{-1}	*E. ictarda* (MIC); *C. gloeosporioides* (MIC); *P. piricola* (MIC); *F. oxysporum* (MIC)	[33]
Thiocladospolide F (**108**)	Antimicrobial	16 μg mL^{-1}; 2 μg mL^{-1}; 2 μg mL^{-1}; 16 μg mL^{-1}; 16 μg mL^{-1}; 4 μg mL^{-1}	*E. coli* (MIC); *E. tarda* (MIC); *V. anguillarum* (MIC); *F. oxysporium f. sp. momordicae* (MIC); *P. digitatum* (MIC); *H. maydis* (MIC)	[34]
Thiocladospolide F *bis* (**109**)	Antimicrobial	32 μg mL^{-1}; 16 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *B. sorokiniana* (MIC)	[50]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Thiocladospolide G (**110**)	Antimicrobial	2 μg mL^{-1}; 2 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}; 8 μg mL^{-1}	*E. tarda* (MIC); *V. anguillarum* (MIC); *F. oxysporium f. sp. momordicae* (MIC); *P. digitatum* (MIC); *H. maydis* (MIC)	[34]
Thiocladospolide G *bis* (**111**)	Antimicrobial	4 μg mL^{-1}; 32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}; 32 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. mandshurica Miura* (MIC); *C. gloeosporioides* (MIC); *F. oxysporum* f. sp. *cucumerinum* (MIC)	[50]
Thiocladospolide H (**112**)	Antimicrobial	16 μg mL^{-1}; 8 μg mL^{-1}; 16 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. gloeosporioides* (MIC); *B. sorokiniana* (MIC)	[50]
Thiocladospolide I (**113**)	Antimicrobial	32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *F. oxysporum* f. sp. *cucumerinum* (MIC)	[50]
Thiocladospolide J (**114**)	Antimicrobial	16 μg mL^{-1}; 16 μg mL^{-1}; 16 μg mL^{-1}; 16 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. mandshurica Miura* (MIC); *C. gloeosporioides* (MIC); *B. sorokiniana* (MIC); *F. oxysporum* f. sp. *cucumerinum* (MIC)	[50]
Zeaenol (**115**)	Phytotoxic	8.16 μg mL^{-1}	*A. retroflexus* (IC_{50})	[49]
	Naphthalene derivatives			
Cladonaphchrom A (**116**)	Antimicrobial	1.25 μg mL^{-1}; 2.5 μg mL^{-1}; 10 μg mL^{-1}; 5 μg mL^{-1}; 10 μg mL^{-1}; 50 μg mL^{-1}; 50 μg mL^{-1}; 25 μg mL^{-1}; 100 μg mL^{-1}; 50 μg mL^{-1}; 50 μg mL^{-1}	*Scaphirhynchus albus* (MIC); *E. coli* (MIC); *B. subtilis* (MIC); *Micrococcus tetragenus* (MIC); *M. luteus* (MIC); *Alternaria brassicicola* (MIC); *Phytophthora parasitica var. nicotianae* (MIC); *Colletotrichum capsici* (MIC); *B. oryzae* (MIC); *Diaporthe medusaea* (MIC); *Cyanophora paradoxa* (MIC)	[83]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Cladonaphchrom B (**117**)	Antibacterial	2.5 μg mL^{-1}; 2.5 μg mL^{-1}; 5 μg mL^{-1}; 5 μg mL^{-1}; 10 μg mL^{-1}; 25 μg mL^{-1}; 50 μg mL^{-1}; 25 μg mL^{-1}; 100 μg mL^{-1}; 50 μg mL^{-1}	*S. albus* (MIC); *E. coli* (MIC); *B. subtilis* (MIC); *M. tetragenus* (MIC); *M. luteus* (MIC); *A. brassicicola* (MIC); *P. parasitica var. nicotianae* (MIC); *C. capsici* (MIC); *D. medusaea* (MIC); *C. paradoxa* (MIC)	[83]
Naphtalenones				
Altertoxin XII (**120**)	Quorum sensing inhibitory	20 μg $well^{-1}$	*Chromobacterium violaceum* (MIC)	[87]
Cladosporol A (**121**)	Antifungal	100 ppm	*Uromyces appendiculatus* (84.2%)	[66]
	B-1,3-glucan biosynthesis inhibitor	10 μg ml	IC_{50}	[26]
Cladosporol B (**122**)	Antifungal	100 ppm	*U. appendiculatus* (100%)	[66]
Cladosporol C (**123**)	Antifungal	100 ppm	*U. appendiculatus* (77.6%)	[66]
	Antibacterial	8 μg mL^{-1}; 64 μg mL^{-1}; 16 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *Vibrio harveyi* (MIC)	[39]
	Cytotoxic	33.9 μM; 45.6 μM; 72.5 μM; 11.4 μM	*A549 (100%);* H1975 (100%); HL60 (100%); MOLT-4 (100%)	[86]
		14 μM; 4 μM	A549 (IC_{50}); H446 (IC_{50})	[39]
Cladosporol D (**124**)	Antifungal	100 ppm	*U. appendiculatus* (69.4%)	[66]
	Anti-COX-2	60.2 μM	IC_{50}	[86]
Cladosporol E (**125**)	Antifungal	100 ppm	*U. appendiculatus* (74.8%)	[66,85]
Cladosporol F (**126**)	Antibacterial	32 μg mL^{-1}; 64 μg mL^{-1}; 32 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *V. harveyi* (MIC)	[39]
	Cytotoxic	15 μM; 10 μM; 23 μM; 23 μM	A549 (IC_{50}); HeLa (IC_{50}); K562 (IC_{50}); HCT-116 (IC_{50})	[39,40]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Cladosporol G (**127**)	Cytotoxic	3.9 μM; 8.8 μM; 19.5 μM	HeLa (IC_{50}); K562 (IC_{50}); HCT-116 (IC_{50})	[40]
Cladosporol G *bis* (**128**)	Antibacterial	64 μg mL^{-1}; 128 μg mL^{-1}; 64 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *V. harveyi* (MIC)	[39]
	Cytotoxic	13 μM; 11 μM; 10 μM; 11 μM; 14 μM; 15 μM	A549 (IC_{50}); HeLa (IC_{50}); Huh7 (IC_{50}); L02 (IC_{50}); LM3 (IC_{50}); SW1990 (IC_{50})	
Cladosporol H (**129**)	Antibacterial	32 μg mL^{-1}; 64 μg mL^{-1}; 4 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *V. harveyi* (MIC)	[39]
	Cytotoxic	5 μM; 10 μM; 1 μM; 4.1 μM; 10 μM; 14 μM	A549 (IC_{50}); H446 (IC_{50}); Huh7 (IC_{50}); LM3 (IC_{50}); MCF-7 (IC_{50}); SW1990 (IC_{50})	
Cladosporol I (**130**)	Quorum sensing inhibitory	30 μg $well^{-1}$	*C. violaceum* (MIC)	[87]
	Antibacterial	64 μg mL^{-1}; 64 μg mL^{-1}; 16 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *V. harveyi* (MIC)	[39]
	Cytotoxic	10.8 μM	HeLa (IC_{50})	
Cladosporol J (**131**)	Antibacterial	16 μg mL^{-1}; 64 μg mL^{-1}; 32 μg mL^{-1}	*E. coli* (MIC); *M. luteus* (MIC); *V. harveyi* (MIC)	[39]
	Cytotoxic	15 μM; 4 μM; 4.9 μM; 6.2 μM; 13 μM; 9.1 μM; 1.8 μM; 2.2 μM	*A549 (IC_{50});* H446 (IC_{50}); HeLa (IC_{50}); Huh7 (IC_{50}); L02 (IC_{50}); LM3 (IC_{50}); MCF-7 (IC_{50}); SW1990 (IC_{50})	

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Cladosporone A (**132**)	Cytotoxic	14.3 μM; 15.7 μM; 29.9 μM; 40.6 μM; 21.3 μM; 10.5 μM; 17.0 μM; 10.1 μM; 53.7 μM; 14.6 μM	K562 (100%); A549 (100%); Huh-7 (100%); H1975 (100%); MCF-7 (100%): U937 (100%); BGC823 (100%); HL60 (100%); HeLa (100%) MOLT-4 (100%)	[86]
	Anti-COX-2	49.1 μM	IC_{50}	
(3*S*)-3,8-Dihydroxy-6,7-dimethyl-α- tetralone (**137**)	Antibacterial	20 μM	*S. aureus*, *B. cereus*, *E. coli*, *Vibrio alginolyticus*, *Vibrio parahemolyticus*, methicillin-resistant *S. aureus*	[81]
Scytalone (**139**)	Antibacterial	63.6 μg mL^{-1}; 95.5 μg mL^{-1}	*Bacillus cereus* (IC_{50}); *E. coli* (IC_{50})	[68]
Naphtoquinones and anthraquinones				
Anhydrofusarubin (**142**)	Cytotoxic	3.97 μg mL^{-1}	K-562 (IC_{50})	[90]
Methyl ether of fusarubin (**143**)	Cytotoxic	3.58 μg mL^{-1}	K-562 (IC_{50})	[90]
	Antibacterial	40 μg $disc^{-1}$	*S. aureus* (27 mm), *Bacillus megaterium* (22 mm), *E coli* (25 mm), *P. aeruginosa* (24 mm)	
	Toxic	81.4 μM	brine shrine naupalii (IC_{50})	
Perylenequinones				
Altertoxin VIII (**145**)	Quorum sensing inhibitory	30 μg $well^{-1}$	*C. violaceum* (MIC)	[87]
Altertoxin IX (**146**)	Quorum sensing inhibitory	30 μg $well^{-1}$	*C. violaceum* (MIC)	[87]
Aterotoxin X (**147**)	Quorum sensing inhibitory	20 μg $well^{-1}$	*C. violaceum* (MIC)	[87]
Altertoxin XI (**148**)	Quorum sensing inhibitory	30 μg $well^{-1}$	*C. violaceum* (MIC)	[87]
Calphostin A (=UCN-1028A) (**149**)	PK inhibition	0.19 μg mL^{-1}; 40 μg mL^{-1}	PKC (IC_{50}); PKA (IC_{50})	[29,30]
	Cytotoxic	0.29 μg mL^{-1}; 0.21 μg mL^{-1}	HeLa S3 (IC_{50}); MCF-7 (IC_{50})	
Calphostin B (**150**)	PK inhibition	1.04 μg mL^{-1}; 22.9 μg mL^{-1}	PKC (IC_{50}); PKA (IC_{50})	[7]
	Cytotoxic	2.56 μg mL^{-1}; 1.61 μg mL^{-1}	HeLa S3 (IC_{50}); MCF-7 (IC_{50})	

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Calphostin C (=cladochrome E) (**151**)	PK inhibition	0.05 μg mL^{-1}	PKC (IC_{50})	[30]
	Cytotoxic	0.23 μg mL^{-1}; 0.18 μg mL^{-1}	HeLa S3 (IC_{50}); MCF-7 (IC_{50})	
Calphostin D (= ent-isophleinchrome) (**152**)	PK inhibition	6.36 μg mL^{-1}; 12.7 μg mL^{-1}	PKC (IC_{50}); PKA (IC_{50})	[30]
	Cytotoxic	8.45 μg mL^{-1}; 2.69 μg mL^{-1}	HeLa S3 (IC_{50}); MCF-7 (IC_{50})	
	Phytotoxic	5 μg L^{-1}	Sugar beet cells (100% inhibition in the light, 37–64% inhibition in the dark)	[46]
		33 μg L^{-1}	Necrosis on sugar beet leaves	
Calphostin I (= Cladochrome D) (**153**)	PK inhibition	6.36 μg mL^{-1}; 12.7 μg mL^{-1}	PKC (IC_{50}); PKA (IC_{50})	[30]
	Cytotoxic	0.24 μg mL^{-1}; 0.16 μg mL^{-1}	HeLa S3 (IC_{50}); MCF-7 (IC_{50})	
Phleichrome (**154**)	Invertase I inhibition	0.5 mM	62%	[99]
	Seco acids			
Cladospolide E (**159**)	Lipid accumulation	10 μM	Oleic acid; Triglycerides (~170 μg mg^{-1} protein); Total cholesterol (~3 μg mg^{-1} protein)	[94]
Seco-patulolide A (**161**)	Lipid accumulation	10 μM	Oleic acid; Triglycerides (~150 μg mg^{-1} protein); Total cholesterol (~3 μg mg^{-1} protein)	[94]
Seco-patulolide C (**162**)	Lipid accumulation	10 μM	Oleic acid; Triglycerides (~150 μg mg^{-1} protein); Total cholesterol (~3 μg mg^{-1} protein)	[94]
	Antimicrobial	32 μg mL^{-1}; 32 μg mL^{-1}; 16 μg mL^{-1}	*E. tarda* (MIC); *E. ictarda* (MIC); *C. gloeosporioides* (MIC)	[50]
(3*S*,5*S*,11*S*)-Trihydroxydodecanoic acid (**163**)	Antibacterial	63.6 μg mL^{-1}	*B. cereus* (MIC)	[68]
	Cytotoxic	42 μM; 82 μM	MCF-7; T47D	
	Antibacterial	40 μg $disc^{-1}$	*S. aureus* (27 mm), *B. megaterium* (22 mm), *E coli* (25 mm), *P. aeruginosa* (24 mm)	
	Toxic	81.4 μM	brine shrine naupalii (IC_{50})	

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Sterols				
Cladosporide A (**164**)	Antifungal	0.5 μg mL^{-1}	*Aspergillus fumigatus* (IC_{50})	[79]
Cladosporide B (**165**)	Antifungal	3 μg $disc^{-1}$	*A. fumigatus* (11 mm)	[80]
Cladosporide C (**166**)	Antifungal	1.5 μg $disc^{-1}$	*A. fumigatus* (11 mm)	[80]
3α-Hydroxy-pregn-7-ene-6,20-dione (**171**)	Anti-adipogenic	1.25 – 10 μM	3T3-L1	[62]
Tetramic acids				
Cladodionen (**176**)	Cytotoxic	28.6 μM	HL-60 (IC_{50})	[58]
		4.5 μM; 6.6 μM; 12 μM; 11 μM; 15 μM; 22 μM	K562 (IC_{50}); HL-60 (IC_{50}); HCT-116 (IC_{50}); PC-3 (IC_{50}); SH-SYSY (IC_{50}); MGC-803 (IC_{50})	[89]
		18.7 μM; 19.1 μM; 17.9 μM; 9.1 μM	MCF-7 (IC_{50}); HeLa (IC_{50}); HCT-116 (IC_{50}); HL-60 (IC_{50})	[96]
		3.7 μM	L5178 (IC_{50})	
	Antifungal	100 mg/plate; 100 mg/plate	*Ustilago maydis* (0.97 cm); *Saccharomyces cerevisiae* (3.27 cm)	[63]
Cladosin B (**178**)	Renoprotective effects against cisplatin-induced kidney cell damage	25 μM; 50 μM; 100 μM	LLC-PK1 (dose-dependent)	[60]
Cladosin C (**179**)	Antiviral	276 μM	H1N1 (IC_{50})	[55]
Cladosin F (**181**)	Renoprotective effects against cisplatin-induced kidney cell damage	25 μM; 50 μM; 100 μM	LLC-PK1 (dose-dependent)	[60]
Cladosin I (**184**)	Cytotoxic	4.1 μM; 2.8 μM; 11 μM; 13 μM; 12 μM; 19 μM	K562 (IC_{50}); HL-60 (IC_{50}); HCT-116 (IC_{50}); PC-3 (IC_{50}); SH-SYSY (IC_{50}); MGC-803 (IC_{50})	[89]
Cladosin J (**185**)	Cytotoxic	6.8 μM; 7.8 μM	K562 (IC_{50}); HL-60 (IC_{50})	[89]
Cladosin K (**186**)	Cytotoxic	5.9 μM; 7.5 μM; 14 μM; 18 μM	K562 (IC_{50}); HL-60 (IC_{50}); HCT-116 (IC_{50}); PC-3 (IC_{50})	[89]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Cladosin L (**187**)	Renoprotective effects against cisplatin-induced kidney cell damage	25 μM; 50 μM; 100 μM	LLC-PK1 (dose-indipendent)	[60]
Cladosin L *bis* (**188**)	Antibacterial	25 μM; 50 μM	*S. aureus* ATCC 700699 (IC_{50}); *S. aureus* ATCC 29213 (IC_{50})	[63]
Cladosporicin A (**192**)	Cytotoxic	70.88 μM; 74.48 μM; 75.54 μM; 79.36 μM	Bt549 (IC_{50}); HCC70 (IC_{50}); MDA-MB-231 (IC_{50}); MDA-MB-468 (IC_{50})	[61]
Cladosporiumin I *bis* (**202**)	Cytotoxic	76.18 μM; 85.29 μM; 82.37 μM; 81.44 μM	Bt549 (IC_{50}); HCC70 (IC_{50}); MDA-MB-231 (IC_{50}); MDA-MB-468 (IC_{50})	[61]
Cladosporiumin J *bis* (**204**)	Cytotoxic	78.96 μM; 76.41 μM; 79.27 μM; 74.64 μM	Bt549 (IC_{50}); HCC70 (IC_{50}); MDA-MB-231 (IC_{50}); MDA-MB-468 (IC_{50})	[61]
Tropolones				
Malettinin A (**210**)	Antimicrobial	33.1 μM; 100 μM	*Trichophyton rubrum* (IC_{50}); *C. albicans* (81%)	[95]
Malettinin B (**211**)	Antimicrobial	28.3 μM; 60.6 μM; 100 μM; 100 μM; 100 μM	*Xanthomonas campestris* (IC_{50}); *T. rubrum* (IC_{50}); *Staphylococcus epidermidis* (<80%); *B. subtilis* (<80%); *C. albicans* (<80%)	[95]
Malettinin C (**212**)	Antimicrobial	37.9 μM; 83.2 μM; 100 μM; 100 μM; 100 μM	*X. campestris* (IC_{50}); *T. rubrum* (IC_{50}); *S. epidermidis* (<80%); *B. subtilis* (<80%); *C. albicans* (<80%)	[95]
Malettinin E (**213**)	Antimicrobial	28.7 μM; 30.7 μM;	*X. campestris* (IC_{50}); *T. rubrum* (IC_{50})	[95]
Xanthones				
Conioxanthone A (**218**)	Cytotoxic	10 μM	22RV1 (36.8%), C4-2B (3.3%), RWPE-1 (20.3%)	[43]
3,8-Dihydroxy-6-methyl-9-oxo-9*H*-xanthene-1-carboxylate (**219**)	Cytotoxic	10 μM	22RV1 (82.1%), C4-2B (77.7%), RWPE-1 (11.5%)	[43]
α-Diversonolic ester (**220**)	Cytotoxic	10 μM	22RV1 (28.8%), C4-2B (12.9%), RWPE-1 (24.3%)	[43]
β-Diversonolic ester (**221**)	Cytotoxic	10 μM	22RV1 (40.2%), C4-2B (2.8%), RWPE-1 (10.3%)	[43]
8-Hydroxy-6-methylxanthone-1-carboxylic acid (**222**)	Cytotoxic	10 μM	22RV1 (71.3%), C4-2B (60.7%), RWPE-1 (19.7%)	[43]
Methyl 8-hydroxy-6-(hydroxymethyl)- 9-oxo-9*H*-xanthene-1-carboxylate (**223**)	Cytotoxic	10 μM	22RV1 (68.1%), C4-2B (20.2%), RWPE-1 (19.0%)	[43]

Table 3. *Cont.*

Name (Code)	Biological Activity	Concentration	Results	Refs.
Methyl 8-hydroxy-6-methyl-9-oxo-9*H*-xanthene-1-carboxylate (**224**)	Cytotoxic	10 μM	22RV1 (55.8%), C4-2B (8.1%), RWPE-1 (5.3%)	[43]
8-(Methoxycarbonyl)-1-hydroxy-9-oxo-9*H*-xanthene-3-carboxylic acid (**225**)	Cytotoxic	10 μM	22RV1 (63.9%), C4-2B (12.2%), RWPE-1 (27.0%)	[43]
Vertixanthone (**227**)	Cytotoxic	10 μM	22RV1 (27.1%), RWPE-1 (25.0%)	[43]
		Miscellaneous		
Acetyl Sumiki's acid (**229**)	Antibacterial	5 μg disc^{-1}	*B. subtilis* (7 mm), *S. aureus* (7 mm)	[44]
1,1′-Dioxine-2,2′-dipropionic acid (**233**)	Antibacterial	25 μg mL^{-1}; 25 μg mL^{-1}; 12.5 μg mL^{-1}	*S. aureus* (MIC); *E. coli* (MIC); *B. cereus* (MIC)	[85]
4-*O*-α-D-Ribofuranose-2-pentyl-3-phemethylol (**238**)	Inhibition of α-glucosidase	2.50 μM	IC_{50}	[82]
Sumiki's acid (**241**)	Antibacterial	5 μg disc^{-1}	*B. subtilis* (7 mm), *S. aureus* (7 mm)	[44]
Taxol (**242**)	Cytotoxic	3.5 μM	HCT 15 (IC_{50})	[51]
	Antibacterial	30 μL disc^{-1}; 20 μL disc^{-1}; 30 μL disc^{-1}; 20 μL disc^{-1}; 40 μL disc^{-1}	*Pseudomonas aeruginosa* (2 mm); *Escherichia coli* (3 mm); *Klebsiella pneumoniae* (2 mm); *Acetobacter* sp. (2 mm); *Bacillus subtilis* (1 mm)	
Vermistatin (**244**)	Antibacterial	25 μg mL^{-1};	*S. aureus* (MIC);	[85]
		25 μg mL^{-1}	*B. cereus* (MIC)	

Another interesting correlation between chemical structure and bioactivity arises from the investigation on the inhibitory activity of cladosporol towards β-l,3-glucan synthetase. In fact, the epoxy-alcohol moiety in cladosporol is very similar to another β-l,3-glucan biosynthesis inhibitor, (+)-isoepoxydon; hence, the epoxy-alcohol structure seems to play an important role in the inhibitory activity of β-l,3-glucan synthetase [26].

4. Conclusions

As resulting from the available information examined in this review, data concerning secondary metabolite production and properties in *Cladosporium* are notable in quantitative terms. Indeed, the biosynthetic aptitudes of these fungi are quite original, with several series of products for which they represent the only source known so far. At the same time, at least some strains have resulted in the sharing of genetic bases for producing bioactive compounds previously reported from other fungal genera, such as cytochalasin D, brefeldin A, vermistatin, zeaenol, the coniochaetones, the malettinins and the viridotoxins, or even from plants, such as the gibberellins, plumbagin and taxol, which represent a direction for their possible biotechnological exploitation.

Besides implications deriving from the bioactive properties of some valuable products, metabolomics has been also used as a tool for species description and discrimination in several fungal genera, such as *Penicillium, Talaromyces*, *Aspergillus* [133], *Alternaria* [134] and *Trichoderma* [135]. The great diversity of secondary metabolites reported from *Cladosporium* spp. could represent a notable base material for verifying if a similar approach can be consistent for this genus as well. So far, the number of isolates that have been examined in this respect is too small, with as many as 23 of them not having been ascribed to any definite species, and the only consistent aspect resulting from the analysis of the available literature is represented by the production of tetramic acids by *C. sphaerospermum*. However, it is to be expected that the likely accumulation of new reports based on accurate molecular identification referring to the most recent taxonomic schemes may pave the way to a chemotaxonomic perspective for *Cladosporium* too.

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