

Chapter 7

Nematode-Toxic Fungi and their Nematicidal Metabolites

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Abstract This chapter summarizes more than 200 compounds from fungi that have been shown to possess nematicidal activities. These compounds belong to diverse chemical groups including alkaloid, quinone, isoeoxydon, pyran, furan, peptide, macrolide, terpenoid, fatty acid, diketopiperazine, aphythalene and simple aromatics. They have mainly been isolated from a variety of ascomycetous and basidiomycetous fungal taxa. Their nematicidal activities are described and their potential roles in the biocontrol of nematodes are discussed.

Keywords Fungi • Nematode • Nematicidal compounds • Biocontrol

Introduction

Nematodes can attack, infect and consume a wide variety of organisms, including animals, microorganisms and plants. In recent years, the use of synthetic chemical compounds has been the most common strategy for controlling parasitic nematodes (Haydock et al. 2006). While these have been effective in certain circumstances, the widespread use of man-made chemical nematicides has caused significant problems to both the environment and human health. Consequently, their use for pest control in agriculture and forestry has been reduced significantly. The reduced use of synthetic chemical nematicides has generated significant demands for environmentally friendly alternative strategies (Meira et al. 2006). Biological control is a potentially effective alternative for the management of nematode pests. Biological agents include both live organisms as well as their metabolic products (Willis and Thomas 1998). Fungi are known to possess a huge diversity of metabolic pathways and they have provided several large classes of commercial compounds, including many antibiotics used in medicine (Harvey 2000). Therefore, secondary metabolites in fungi could have much potential in their novel structures and nematicidal activities.

Many nematicidal compounds had been discovered from nematode-toxic fungi, a group of nematophagous fungi. The aim of this chapter is to review the nematode-toxic fungi, the different types, their structure and the nematicidal activity of compounds isolated from nematode-toxic fungi.

Nematode-Toxic Fungi and Their Nematicidal Metabolites

About 280 fungal species in 150 genera of Ascomycota and Basidiomycota have been reported to possess nematicidal activity as they produce toxic compounds which are active against nematodes. More than 200 of these compounds with nematicidal activities are summarized in this chapter.

Nematode-Toxic Ascomycetes and Their Nematicidal Metabolites

About 80 genera comprising more than 120 species have been reported to produce nematicidal active components. *Lachnum papyraceum* (*Hyaloscyphaceae*) is one of the most prolific producers of nematicidal secondary metabolites and a number of nematicidal metabolites have been isolated from this taxa, culturing under different conditions. The structures of 30 compounds isolated from *L. papyraceum* have been elucidated to be isoeoxydon, isocoumarin, mycorrhizin and furan, and

24 compounds including 15 new isolates having nematicidal activities (Stadler and Anke 1993a, b; Stadler et al. 1995a, b, c, d, e; Shan et al. 1996).

The production of nematicidal compounds by three species of *Nematocytus* have been demonstrated by Giurma and Cooke (1971) and Giurma et al. (1973), and these compounds were termed nematoxins. The result indicated that *Nematocytus* species quickly retard and kill their nematode hosts by the production of toxin, but the toxin had not been identified. *Nematocytus robustus* was shown to have nematode-immobilizing activity in culture filtrate (Kennedy and Tampion 1978). The nematicidal effect of filtrates from 15 asexual ascomycetes were tested against *Meloidogyne incognita*, and *Acremonium strictum*, *Alternaria alternata*, *Curvularia pallescens*, *Nigrospora sphaerica*, *Paecilomyces lilacinus*, *Penicillium spinulosu*, *Trichoderma harzianum*, were most effective hatch inhibitors of root-knot nematodes and the nematicidal action of culture filtrates against nematode might be attributed to the production of certain toxic metabolites (Khan and Kgan 1992).

Besides producing special structures that trap nematodes, some trapping fungi can produce nematicidal compounds at the same time as the process of trapping nematodes. The nematicidal compound linoleic acid was isolated from the nematophagous *Arthrobotrys brochopaga*, *A. conoides*, *A. dactyloides*, *A. oligospora*, and oligosporon, with 4',5'-dihydro-oligosporon and arthrobotrisin A being obtained from *A. oligospora* (Stadler et al. 1993; Anke et al. 1995; Anderson et al. 1995; Wei et al. 2011). These compounds have nematicidal activity and thus the process by which these fungi overcome and capture the nematode is complex.

Beauveria bassiana is an important insect pathogenic fungus which produces the bioactive substance beauvericin which has nematicidal activity against *Meloidogyne incognita* (Hamill et al. 1969; Mayer 1995), *Caenorhabditis elegans* and *Bursaphelenchus xylophilus* (Shimada et al. 2010). The compound is also produced by *Fusarium* sp. (Mayer 1995) and *Paecilomyces fumoso-roseus* (Bernardini et al. 1975).

Isolates of 130 freshwater fungal taxa have been assayed for nematicidal activity against *B. xylophilus* and 22 filtrates and 13 water-soluble extracts of broken fungal mycelia were found to be active against the nematode. The mobility of over 90% of nematodes were inhibited by filtrates from *Annulatasacus* sp., *Caryospora callicarpa*, *Massarina thalassioidea*, *Ophioceras commune*, *Pseudohalonestria adversaria*, *Pseudohalonestria lignicola*, and mycelia extracts from *Helicomyces roseus*, *Phomatospora berkeleyi* and *P. lignicola* (Dong et al. 2003). Several new nematicidal compounds were obtained from these freshwater fungi (Dong et al. 2007, 2008, 2010). A novel class of potent nematicidal thermolides was isolated from a thermophilic fungus *Talaromyces thermophilus*. Thermolides A and B showed the strongest activities against nematodes with similar activity of avermectins (Guo et al. 2012). These and other nematode-toxic ascomycetes (and anamorphs), and their nematicidal compounds are listed in Table 7.1.

Table 7.1 Nematode-toxic ascomycetes and their nematicidal compounds

Species	Test nematodes	Nematicidal compounds	References
<i>Acremonium</i> sp.	<i>Meloidogyne incognita</i>	–	Yan et al. (2010)
<i>Acremonium</i> sp.	<i>B. xylophilus</i>	–	Meng et al. (2012)
<i>A. strictum</i>	<i>Tylenchulus</i> <i>Semipenetrans</i>	–	Verdejo-Lucas et al. (2009)
<i>A. strictum</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Acrophialophora</i> <i>funisporae</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Alternaria alternata</i>	<i>H. contortus</i> <i>M. incognita</i>	Helmidol	Khan and Kgan (1992); Kind et al. (1996)
<i>A. carthami</i>	<i>A. aceti</i>	Brefeldin A	Bačková et al. (1965); Vurro et al. (1998)
<i>A. zinnia</i>	<i>A. aceti</i>	Brefeldin A	Bačková et al. (1965); Vurro et al. (1998)
<i>Aniptodera</i> sp.	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Annulatuscus</i> sp.	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>A. triseptata</i>	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Apiocrea chrysosepma</i>	Nematicidal agent	Chrysosepmins A, B, C, and D	Metzger et al. (1994); Dombberger et al. (1995)
<i>Arthrobotrys brochopaga</i>	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
	<i>M. incognita</i>		
<i>A. conoides</i>	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
	<i>M. incognita</i>		
<i>A. dactyloides</i>	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
	<i>M. incognita</i>		
<i>A. oligospora</i>	<i>H. contortus</i>	Oligosporon, Linoleic acid, 4',5'-dihydro-oligosporon, Arthrobotrisin A	Stadler et al. (1993); Anke et al. (1995); Anderson et al. (1995); Wei et al. (2011)
	<i>C. elegans</i>		
	<i>M. incognita</i>		
	<i>P. redivivus</i>		
<i>Ascochyta imperfecta</i>	<i>A. aceti</i>	Brefeldin A	Bačková et al. (1965); Suzuki et al. (1970)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Aspergillus clavatus</i>	<i>A. aceti</i>	Brefeldin A	Bačková et al. (1965); Wang et al. (2002)
<i>A. flavus</i>	<i>M. incognita</i>	—	Khan and Kgan (1992)
<i>A. fumigatus</i>	<i>A. aceti</i>	Fumagillin, Gliotoxin, Fumiquinones A and B, Spinulysin, LL-S490, Pseurotin A	Tarbell et al. (1960); Bačková et al. (1965); Beecham et al. (1966); Hayashi et al. (2007)
	<i>P. penetrans</i>	—	
	<i>B. xylophilus</i>	—	
<i>A. glaucus</i>	<i>M. incognita</i>	Emodin	Anke et al. (1980a); Anke et al. (1980b); Mayer (1995)
<i>A. melles</i>	<i>P. penetrans</i>	Aspyrone	Kimura et al. (1996)
<i>A. niger</i>	<i>A. suum</i>	Nafuredin, Nafuredin- γ	Uji et al. (2001); Omura et al. (2001); Shiomi et al. (2005)
	<i>H. cortortus</i>	—	
<i>A. niger</i>	<i>M. incognita</i>	—	
<i>Aspergillus</i> sp.	<i>B. xylophilus</i>	5-hydroxymethyl-2-furoic acid	Khan and Kgan (1992)
	<i>C. elegans</i>	—	Kimura et al. (2007)
<i>Aspergillus</i> sp.	<i>H. glycines</i>	—	
<i>Aspergillus</i> sp.	<i>M. incognita</i>	Patulin, Penicillic acid	Meyer et al. (2004)
	<i>A. aceti</i>	—	Bačková et al. (1965); Mayer (1995)
<i>Aspergillus</i> sp.	<i>P. penetrans</i>	$\beta\gamma$ -dehydrocurvularin, $\alpha\beta$ -dehydrocurvularin, 7-oxo-curvularin, 8- β -hydroxy-7-oxo-curvularin	Kusano et al. (2003)
<i>Aspergillus</i> sp.	<i>T. colubriformis</i>	Aspergillimide, 16-keto aspergillimide, VM54159, SB203105, SB200437	Banks et al. (1997)
	<i>H. contortus</i>	—	
<i>A. ustus</i>	<i>C. elegans</i>	Ophiobolin K, 6-epiophiobolin K	Singh et al. (1991)
<i>Beauveria bassiana</i>	<i>M. incognita</i>	Beauvericin	Hamill et al. (1969); Mayer (1995); Shimada et al. (2010)
	<i>C. elegans</i>	—	
<i>Bulgaria inquinans</i>	<i>C. elegans</i>	Bulgarialactone A, B	Stadler et al. (1995)
<i>Byssoschlamys nivea</i>	<i>C. elegans</i>	—	Park et al. (2001)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Caryospora callicarpa</i>	<i>B. xylophilus</i>	Caryosporin A, B and C, 4,8-dihydroxy-3,4-dihydronaphthalen-1(2H)-one, 4,6-dihydroxy-3,4-dihydronaphthalen-1(2H)-one, 4,6,8-trihydroxy-3,4-dihydronaphthalen-1(2H)-one, 3,4,6,8-tetrahydroxy-3,4-dihydronaphthalen-1(2H)-one (<i>cis</i> -4-hydroxyxycitalone)	Dong et al. (2007); Zhu et al. (2008)
<i>Chaetomium globosum</i>	<i>M. incognita</i> <i>H. glycines</i>	Flavipin	Nitao et al. (2002)
<i>C. robustum</i>	<i>T. semipenetrans</i>	–	Verdejo-Lucas et al. (2009)
<i>Chaetomium</i> sp.	<i>M. incognita</i>	–	Yan et al. (2010)
<i>Chlorosplenium</i> sp.	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
<i>Cladobotryum</i>	<i>M. incognita</i>	Cladobotrim I	Wagner et al. (1998)
<i>rubrobrunnescens</i>			
<i>Cladosporium</i> sp.	<i>B. xylophilus</i>	–	Zhao et al. (2004)
<i>Clonostachys</i>	<i>H. cortortus</i>	Clonostachdiol	Grabley et al. (1993); Rao et al. (1995)
<i>cylindrospora</i>			
<i>Cochliobolus</i>	<i>C. elegans</i>	Ophiobolin M, 6-epiophiobolin M, Ophiobolin C, 6-epiophiobolin C	Tsipouras et al. (1996)
<i>heterostrophus</i>			
<i>C. miyabeanus</i>	<i>C. elegans</i>	Cochliquinone A	Barrow and Murphy (1972); Schaeffer et al. (1990)
<i>Coelomyces</i> sp.	<i>P. penetrans</i>		
<i>B. xylophilus</i>	Preussomerins C, D, E, (4RS)4,8-dihydroxy-3,4-dihydronaphthalen-1(2H)-one, 4,6,8-trihydroxy-3,4-dihydronaphthalen-1(2H)-one	Zhou et al. (2009)	

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Cordyceps ophioglossoides</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Coronophora gregaria</i>	<i>C. elegans</i>	MK 7924	Kumazawa et al. (2003)
<i>Curvularia pallenscens</i>	<i>M. incognita</i>	–	Khan and Khan (1992)
<i>Cylindrocarpon olidum</i>	<i>Heterorhabditis nematode</i>	Cannabiorchromenic acid, 8-chloro-cannabiorchromenic acid	Quaghebeur et al. (1994)
<i>Dactylella candida</i>	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
<i>Daldinia concentrica</i>	<i>M. incognita</i>	–	–
	<i>C. elegans</i>	1-methoxy-8-hydroxynaphthalene, 1,8-dimethoxynaphthalene	Dasenbrock (1994); Anke et al. (1995)
<i>Diaporthe</i> sp.	<i>M. incognita</i>	–	Dong et al. (2003)
<i>Emericella rugulosa</i>	<i>B. xylophilus</i>	–	Verdejo-Lucas et al. (2009)
<i>Emericellopsis poonensis</i>	<i>T. semipenetrans</i>	Antiamoebin I	Thirumalachur (1968); Pandey et al. (1977)
<i>E. symmematicola</i>	Against helminths	Antiamoebin I	Thirumalachur (1968); Pandey et al. (1977)
<i>Epicoccum nigrum</i>	Against helminths	Favipin	Burge et al. (1976); Nitao et al. (2002)
	<i>M. incognita</i>	–	–
	<i>H. glycines</i>	–	–
<i>E. purpurascens</i>	<i>M. incognita</i>	Favipin	Brown et al. (1987); Nitao et al. (2002)
	<i>H. glycines</i>	–	–
<i>Fusarium bulbicola</i>	<i>M. incognita</i>	Beauvericin	Mayer (1995); Shimada et al. (2010)
	<i>M. incognita</i>	–	–
<i>F. compactum</i>	<i>C. elegans</i>	–	Meyer et al. (2004)
	<i>B. xylophilus</i>	–	–
	<i>H. glycines</i>	–	–
<i>F. equiseti</i>	<i>M. incognita</i>	–	Meyer et al. (2004)
<i>F. oxysporum</i>	<i>M. incognita</i>	–	Meyer et al. (2004)
	<i>M. incognita</i>	–	–
	<i>Radopholus similis</i>	–	–
	<i>Pratylenchus goodeyi</i>	–	–
	<i>Helicotylenchus multicinctus</i>	–	–
		–	Khan and Kgan (1992); Van Dessel et al. (2011)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>F. redolens</i>	<i>M. incognita</i> <i>C. elegans</i> <i>B. xylophilus</i> <i>A. aceti</i>	Beauvericin	Mayer (1995); Xu et al. (2010); Shimada et al. (2010)
<i>F. roseum</i>		Trichothecolone	Freeman et al. (1959); Bačlková et al. (1965)
<i>Fusarium</i> sp.	<i>M. incognita</i>	Enniatin A, Enniatin B	Mayer (1995); Tomoda et al. (1992)
<i>Fusarium</i> sp.	<i>M. incognita</i> <i>C. elegans</i>	Beauvericin	Mayer (1995); Bernardini et al. (1975); Shimada et al. (2010)
<i>Fusarium</i> sp.	<i>B. xylophilus</i>	—	
<i>Fusarium</i> sp.	<i>M. incognita</i>	—	Ruanpanun et al. (2010)
<i>Geotrichum</i> sp.	<i>P. redivivus</i> , <i>B. xylophilus</i>	1-((2 <i>R</i> *,4 <i>S</i> *,5 <i>S</i> *)-2-chloro-4-methyl-1,3-oxazinan-5-yl)ethanone, 1-((2 <i>R</i> *,4 <i>S</i> *,5 <i>R</i> *)-2-chloro-4-methyl-1,3-oxazinan-5-yl)ethanone, 2',4'-dihydroxyacetophenone	Li et al. (2007)
<i>Gliocladium deliquescens</i>	<i>M. javanica</i>	—	Sankaranarayanan et al. (1997)
<i>G. fimbriatum</i>	<i>M. incognita</i> <i>A. aceti</i>	Gliotoxin	Bačlková et al. (1965); Beecham et al. (1966)
<i>G. roseum</i>	<i>C. elegans</i> <i>P. redivivus</i>	Gliocladiol A, B, C, D and F, verticillin A, 11'-deoxyverticillin A, Sch52900, Sch52901, Gliocladiolase	Dong et al. (2005); Dong et al. (2006)
<i>G. virens</i>	<i>B. xylophilus</i>	Viridin	Bačlková et al. (1965); Blight et al. (1968)
<i>Gymnoascus reesii</i>	<i>A. aceti</i> <i>M. incognita</i>	(3 <i>E</i> ,5 <i>E</i>)-2,5-dihydroxy-2,7-dihydrooxepine-3-carboxylic anhydride	Liu et al. (2011)
<i>Helicomyces roseus</i>	<i>B. xylophilus</i>	—	Dong et al. (2003)
<i>Helminthosporium leersii</i>	<i>C. elegans</i>	Cochloquinone A	Barrow and Murphy (1972); Schaeffer et al. (1990)
<i>H. sativum</i>	<i>C. elegans</i>	Cochloquinone A	Barrow and Murphy (1972); Schaeffer et al. (1990)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Hemicarpensteles paradoxus</i>	<i>A. aceti</i>	Brefeldin A	Bačliková et al. (1965); Anke et al. (1995)
<i>Hirsutiella thompsonii</i> var. <i>symmetatosa</i>	<i>M. incognita</i>	Phomalactone	Krasnoff and Gupta (1994); Khambay et al. (2000)
<i>Hymenoscyphus</i> sp.	<i>C. elegans</i>	–	Anke et al. (1995)
<i>Hypomyces</i> sp.	<i>B. xylophilus</i>	Hypocrellin A, Elsinochrome A	Dong et al. (2001)
Imperfect fungus, D1084	<i>B. xylophilus</i>	Bursaphelocides A, B	Kawazu et al. (1993)
Imperfect fungus, PF1022	<i>A. galli</i>	Cyclodepsipeptide PF1022A	Sasaki et al. (1992); Samson-Himmelstjerna et al. (2005)
<i>Isaria citridae</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Lachnum papyraceum</i>	<i>C. elegans</i>	Lachnum, Lachnumon A, Lachnumon B1, Lachnumon B2, Mycorrhizin A, Chloromycorrhizin A, (1'-E)-dechloromycorrhizin A, 6-hydroxymellein, 4-chloro-6-hydroxymellein, 4-bromo-6-hydroxymellein, 6-methoxymellein, 4-chloro-6-methoxymellein, 4-chloro-6,7-dihydroxymellein, (1'-Z)-dechloromycorrhizin, Papyracon A, Papyracon B, Papyracon C, Mycorrhizin B1, Mycorrhizin B2, Papyracon, 6-O-methylpapyracon B, 6-O-methylpapyracon C, Lachnumfuran A, Lachnumlactone A	Stadler and Anke (1993a, b); Stadler et al. (1995a, b, c, d, e); Shan et al. (1996)
<i>Leptosphaeria</i> sp.	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Massarina bipolaris</i>	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>M. thalassioidea</i>	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Melanconium betulinum</i>	<i>M. incognita</i>	3-hydroxypropionic acid	Schwarz et al. (2004)
	<i>C. elegans</i>	–	
<i>Mollisia</i> sp.	<i>C. elegans</i>	–	Anke et al. (1995)
<i>Monacrosporium doedycoides</i>	<i>C. elegans</i>	Linoleic acid	Anke et al. (1995)
	<i>M. incognita</i>	–	

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Muscodor albus</i>	<i>M. chitwoodi</i> <i>M. hapla</i> <i>P. allius</i> <i>P. penetrans</i>	—	Ekaterini et al. (2008)
<i>Mycosphaerella lethalis</i>	<i>C. elegans</i>	Lethaloxin	Stadler (1993); Arnone et al. (1993)
<i>Myrothecium verrucaria</i>	<i>T. semipenetrans</i>	—	Verdejo-Lucas et al. (2009)
<i>Nectria radicola</i>	soil nematode	Radicol, Radicol B, Radicol C	Mirrington et al. (1964); Stadler (1993)
<i>Nectria</i> sp.	<i>B. xylophilus</i>	—	Anke et al. (1995); Dong et al. (2003)
<i>Nematotomus concurrens</i>	<i>C. elegans</i>	—	
	<i>P. redivivus</i>	—	Giama and Cooke (1971); Giama et al. (1973)
<i>N. haptocladus</i>	<i>P. redivivus</i>	—	Giama and Cooke (1971); Giama et al. (1973)
<i>N. robustus</i>	<i>P. redivivus</i>	—	Kennedy and Tampion (1978)
<i>N. tripolitanus</i>	<i>P. redivivus</i>	—	Giama and Cooke (1971); Giama et al. (1973)
<i>Neobulgaria pura</i>	<i>C. elegans</i>	14-epicochloroquinone B	Lorenzen et al. (1994); Anke et al. (1995)
<i>Nigrospora sphaerica</i>	<i>M. incognita</i>	Phomalactone	Khambay et al. (2000); Kim et al. (2001)
<i>Oidiodendron</i> sp.	<i>P. penetrans</i>	4-hydroxyphenylacetic acid (4-HPA)	Ohtani et al. (2011)
	<i>B. xylophilus</i>	Oidiolactone D	
<i>Ophioceras commune</i>	<i>B. xylophilus</i>	—	Dong et al. (2003)
<i>O. dolichostomum</i>	<i>B. xylophilus</i>	Isoamericanoic acid A, Caffeic acid	Dong et al. (2010)
<i>Paecilomyces cateniamulatus</i>	<i>P. redivivus</i>	—	Yao et al. (2006)
<i>P. fumoso-roseus</i>	<i>M. incognita</i>	Beauvericin	Bernardini et al. (1975); Mayer (1995); Shimada et al. (2010)
	<i>C. elegans</i>		
	<i>B. xylophilus</i>		

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>P. litacinus</i>	<i>C. elegans</i> <i>M. incognita</i> <i>M. javanica</i> <i>T. semipenetrans</i>	Acetic acid	Djian et al. (1991); Park et al. (2004) Verdejo-Lucas et al. (2009)
<i>Paecilomyces</i> sp.	<i>R. pseudoelongata</i>	Paeciloxazine	Kanai et al. (2004)
<i>Paecilomyces</i> sp.	<i>B. xylophilus</i>	Cerebroside A and B	Zhang et al. (2010)
<i>Paecilomyces</i> sp.	<i>M. incognita</i>	4-(4'-carboxy-2'-ethyl-hydroxy)pentyl-5,6-dihydro-6-methyl-cyclobutylpyridine-3,6-dicarboxylic acid	Liu et al. (2009)
<i>Paecilomyces</i> sp.	<i>B. xylophilus</i>	Brefeldin A	Bačlková et al. (1965); Wang et al. (2002)
<i>Paecilomyces</i> sp.	<i>A. aceti</i>	—	Ruanpanun et al. (2010)
<i>Paecilomyces</i> sp.	<i>M. incognita</i>	—	Khan and Kgan (1992)
<i>P. varioti</i>	<i>M. incognita</i>	—	Dong (2005)
<i>Paraniesslia</i> sp.	<i>B. xylophilus</i>	3,5-dicarboxyaldehyde-4-hydroxy-acetophenone	Dong et al. (2005)
<i>Paraniesslia</i> sp.	<i>B. xylophilus</i>	(2 <i>S</i> ,2' <i>R</i> ,3 <i>R</i> ,3' <i>E</i> ,4 <i>E</i> ,8 <i>E</i>)-1-O-(β-D-glucopyranosyl)-3-hydroxy-1-2-[N-2'-hydroxyl-3'-eicosadecenoyl]amino-9-methyl-4,8-octadecadiene, (2 <i>S</i> ,2' <i>R</i> -3 <i>R</i> ,3' <i>E</i> ,4 <i>E</i> ,8 <i>E</i>)-1-O-(β-D-glucopyranosyl)-3-hydroxy-1-2-[N-2'-hydroxyl-3'-octadecenoyl]amino-9-methyl-4,8-octadecadiene	
<i>Penicillium bilaiae</i>	<i>P. penetrans</i>	Penitratynolene, 6-methoxy-carbonylpicolinic acid, 2,6-pyridimedicarboxylic acid	Alfaro et al. (2003); Kimura et al. (1981); Mori et al. (1982); Nakahara et al. (2004)
<i>P. brefeldianum</i>	<i>A. aceti</i>	Brefeldin A	Bačlková et al. (1965); Kim and Kochevar (1995)
<i>P. camemberti</i>	<i>A. aceti</i>	Brefeldin A	Bačlková et al. (1965); Abraham and Arfmann (1992)
<i>P. charlesii</i>	<i>C. elegans</i> <i>T. columbriformis</i>	Paraherquamide, Paraherquamides B, C, D, E, F and G	Ondeyka et al. (1990); Liesch and Wichmann (1990); Blanchflower et al. (1991)
<i>P. decumbens</i>	<i>H. contortus</i> <i>A. aceti</i>	Brefeldin A	Singleton et al. (1958); Bačlková et al. (1965)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>P. nigricans</i>	<i>A. aceti</i>	Fumagillin	Tarbell et al. (1960)
<i>P. paraherquei</i>	<i>C. elegans</i> <i>T. columbriformis</i> <i>H. contortus</i>	Paraherquamide	Yamazaki et al. (1981); Blanchflower et al. (1991)
<i>P. roqueforti</i>	plant parasitic nematode	Marcfortine A, B, and C	Polondky et al. (1980); Prangé et al. (1981)
<i>P. simplicissimum</i>	<i>P. penetrans</i> <i>C. elegans</i>	Peniprequinolone, Penigequinolones A and B, 3-methoxy-4,6-dihydroxy-4-(4'-methoxyphenyl)quinolinone	Kusano et al. (2000)
<i>Penicillium</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Penicillium</i> sp.	<i>T. columbriformis</i>	Paraherquamide, VM55594, VM54158, VM54159, VM55595, VM55596, VM55597, VM55599	Blanchflower et al. (1991); Blanchflower et al. (1993)
<i>Penicillium</i> sp.	<i>H. contortus</i> <i>M. incognita</i> <i>A. aceti</i>	Patulin, Penicillic acid	Bačliková et al. (1965); Mayer (1995)
<i>Penicillium</i> sp.	<i>A. aceti</i>	Gliotoxin	Bačliková et al. (1965); Beecham et al. (1966)
<i>Penicillium</i> sp.	<i>M. incognita</i>	–	Ruanpanun et al. (2010)
<i>P. spinulosum</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Rhizopus stolonifer</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Phoma multistrostrata</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Phoma</i> sp.	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Phomatospora berkeleyi</i>	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Phomopsis phaseoli</i>	<i>M. incognita</i> <i>C. elegans</i>	3-hydroxypropionic acid	Schwarz et al. (2004)
<i>Phyllosticta</i> sp.	<i>M. incognita</i>	–	Yan et al. (2010)
<i>Pochonia chlamydosporia</i>	<i>P. redivivus</i>	Aurovertins F and D	Niu et al. (2010)
<i>Pseudohalonectria adversaria</i>	<i>B. xylophilus</i>	Pseudohalonectrin A and B	Dong et al. (2006)

Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>P. lignicola</i>	<i>B. xylophilus</i>	–	Dong et al. (2003)
<i>Selenosporaella</i> sp.	<i>M. incognita</i>	–	Reyes-Estebanez et al. (2011)
<i>Syncephalastrum racemosum</i>	<i>B. xylophilus</i>	–	Sun (1997); Zhang (2004); Sun et al. (2008)
<i>Talaromyces cyanescens</i>	<i>Tylenchulus semipenetrans</i>	–	Verdejo-Lucas et al. (2009)
<i>T. thermophilus</i>	<i>B. xylophilus</i> <i>M. incognita</i> <i>P. redivivus</i>	Thermolides A, B, C and D	Guo et al. (2012)
<i>Theilavia terricola</i>	<i>M. incognita</i>	–	Khan and Kgan (1992)
<i>Trichoderma album</i>	<i>M. incognita</i>	–	Radwan et al. (2012)
<i>Trichoderma compactus</i>	<i>P. redivivus</i>	–	Yang (2008)
<i>T. harzianum</i>	<i>M. javanica</i> <i>M. incognita</i>	–	Khan and Khan (1992); Sankaranarayanan et al. (1997); Khan and Haque (2011); Radwan et al. (2012)
<i>T. koningi</i>	<i>M. javanica</i> <i>M. incognita</i> <i>R. reniformis</i>	–	Robertson et al. (2002); Fardos (2009)
<i>T. longibrachiatum</i>	<i>C. elegans</i>	Acetic acid	Djian et al. (1991)
<i>T. pituliferum</i>	<i>C. elegans</i>	–	Yang (2008)
<i>T. pseudokoningii</i>	<i>M. javanica</i> <i>M. incognita</i>	–	Sun (1997)
<i>T. reesei</i>	<i>P. redivivus</i> , <i>C. elegans</i>	Trichodermin	Yang et al. (2010); Watts et al. (1988)
<i>Trichoderma</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Trichoderma</i> sp.	<i>B. xylophilus</i> , <i>P. redivivus</i> , <i>C. elegans</i>	6-pentyl-2H-pyran-2-one	Yang et al. (2012)
<i>Trichoderma</i> sp.	<i>P. redivivus</i> , <i>C. elegans</i>	Trichodermin	Yang et al. (2010)

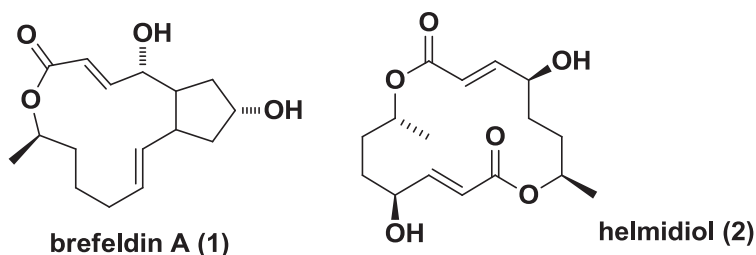
Table 7.1 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>T. viride</i>	<i>M. javanica</i> <i>M. incognita</i>	–	Sun (1997)
<i>Trichotheicum roseum</i>	<i>A. aceti</i>	Trichotheicolone	Freeman et al. (1959); Bačková et al. (1965); Konishi et al. (2003)
unidentified ascomycete of <i>Dermateaceae</i>	<i>C. elegans</i> <i>A. besseyi</i>	5-pentyl-2-furaldehyde	Anke et al. (1995)
unidentified freshwater fungus YMF 1.01029	<i>M. incognita</i> <i>B. xylophilus</i>	Ymf 1029 A, B, C, D and E, Preus-somerin C and D, (4 <i>RS</i>)-4,8-dihydroxy-3,4-dihydronaphthalen-1(2 <i>H</i>)-one, 4,6,8-trihydroxy-3,4-dihydronaphthalen-1(2 <i>H</i>)-one	Dong et al. (2008)
unidentified ascomycete A111-95	<i>C. elegans</i> <i>M. incognita</i>	5-(2 <i>E</i>)-2-buten-1-ylidene-3-(1 <i>E</i>)-1-propen-1-yl-2(5 <i>H</i>)-furanone, Pregallielactone, 5(<i>R</i>)-(1 <i>E</i>)-1,3-butadien-1-yl-3-(1 <i>E</i>)-1-propen-1-yl-2(5 <i>H</i>)-furanone, 5(<i>R</i>)-(3-buten-1-yl)dihydro-3-vinylidihy-2(3 <i>H</i>)-furanone	Köpcke et al. (2002)
<i>Verticillium chlamydosporium</i>	<i>M. incognita</i>	Phomalactone	Khambay et al. (2000)
<i>V. leptobactrum</i>	<i>M. incognita</i>	–	Regateg et al. (2010)
<i>Verticillium</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Xylaria</i> sp.	<i>C. elegans</i> <i>B. xylophilus</i>	–	Anke et al. (1995); Yuan et al. (2010)

No nematicidal compounds were reported from the taxon

Nematicidal Metabolites from Alternaria, Ascochyta, Aspergillus, Hemicarpenteles, Paecilomyces and Penicillium Species

Brefeldin A (**1**) is identical to two known chemicals ascotoxin and decumbin. It was first obtained from *Penicillium decumbens* (Singleton et al. 1958), and subsequently isolated from several other fungal species including *P. brefeldianis* (Kima and Kochevar 1995), *P. camemberti* (Abraham and Arfmann 1992), *Hemicarpenteles paradoxus* (Anke et al. 1995), *Alternaria carthami*, *A. zinniae* (Vurro et al. 1998), *Paecilomyces* sp., *Aspergillus clavatus* (Wang et al. 2002) and *Ascochyta imperfecta* (Suzuki et al. 1970). Screening against the nematode *A. aceti* with brefeldin A (**1**) resulted in significant nematicidal activity (BačÍkovÁ et al. 1965). A symmetric 16-membered macrodiolide helmidiol (**2**) was produced by *Alternaria alternata* (Kind et al. 1996). The compound had activity against *Haemunchus cortortus* (Kind et al. 1996) and *Meloidogyne incognita* (Khan and Kgan 1992).



Nematicidal Metabolites from Apiocrea Chrysosperma

Four linear lipophilic peptides chrysospermins A (**3**), B (**4**), C (**5**) and D (**6**) were isolated from the mycelium of *Apiocrea chrysosperma* Ap101 (Dornberger et al. 1995). These compounds have been patented as nematicidal and anthelmintic agents (Metzger et al. 1994). Each of these four peptides contains 19 amino acids and possesses a C-terminal Trp_{ol} and one labile Aib-Pro bond (Table 7.2, Bodo et al. 1985).

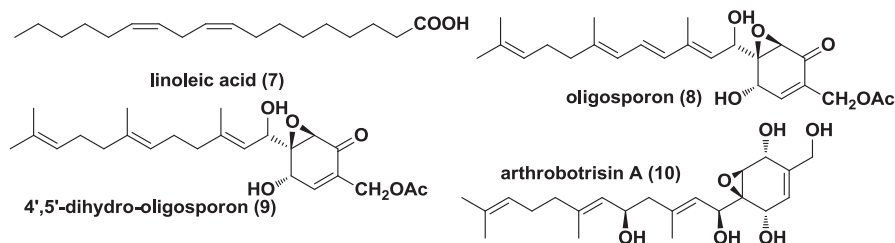
Nematicidal Metabolites from Nematode-Trapping Fungi Arthrobotrys, Chlorosplenium, Dactylella and Monacrosporium

An aliphatic compound linoleic acid (**7**) was detected in the mycelial extracts of the nematode-trapping fungi *Arthrobotrys conoides*, *A. brochopaga*, *A. dactyloides*, *A. oligospora*, *Dactylella candida* and *Monacrosporium doedycoides*. The LD₅₀ of the compound towards *Caenorhabditis elegans* was 10 µg mL⁻¹ and the LD₃₀ to *Meloidogyne incognita* was 100 µg mL⁻¹ (Stadler et al. 1994c; Anke et al. 1995). Besides linoleic acid (**7**), two isoeopoxydon compounds oligosporon (**8**) and its dihydro-derivative 4',5'-dihydro-oligosporon (**9**) were isolated from *Arthrobotrys oligospora*. These two compounds were active against *Haemunchus cortortus* with LD₅₀ values of 25 and 50–100 µg mL⁻¹. However, they were inactive against the nematode

Table 7.2 The structures of chrysoespermins A, B, C and D

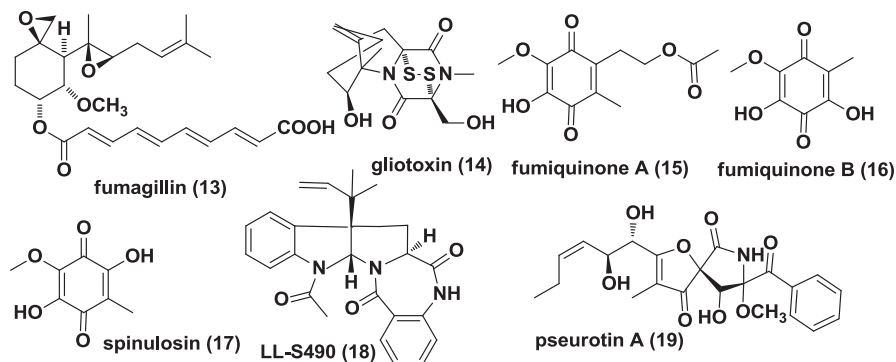
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19
A	AcPhe-	Aib-	Ser-	Aib-	Aib-	Leu-	Gln-	Gly-	Aib-	Aib-	Ala-	Aib-	Pro-	Aib-	Aib-	Aib-	Gln-	Trp
B	AcPhe-	Aib-	Ser-	Aib-	Aib-	Leu-	Gln-	Gly-	Aib-	Aib-	Ala-	Aib-	Pro-	Iva-	Aib-	Aib-	Gln-	Trp
C	AcPhe-	Aib-	Ser-	Aib-	Iva-	Leu-	Gln-	Gly-	Aib-	Aib-	Ala-	Aib-	Pro-	Aib-	Aib-	Aib-	Gln-	Trp
D	AcPhe-	Aib-	Ser-	Aib-	Iva-	Leu-	Gln-	Gly-	Aib-	Aib-	Ala-	Aib-	Pro-	Iva-	Aib-	Aib-	Gln-	Trp

Caenorhabditis elegans at concentrations up to $100 \mu\text{g mL}^{-1}$ (Anderson et al. 1995; Stadler et al. 1993). Recently, three novel oligosporons, named arthrobotrisins A-C (10–12) were isolated from *A. oligospora*, but only arthrobotrisin A (10) had nematocidal activity against *Panagrellus redivivus* (Wei et al. 2011). Linoleic acid (7) was also found in *Chlorosplenium* sp. (Anke et al. 1995), and the basidiomycete *Hericium coralloides* (Xiang and Feng 2001) and *Pleurotus pulmonarius* (Stadler et al. 1994c).



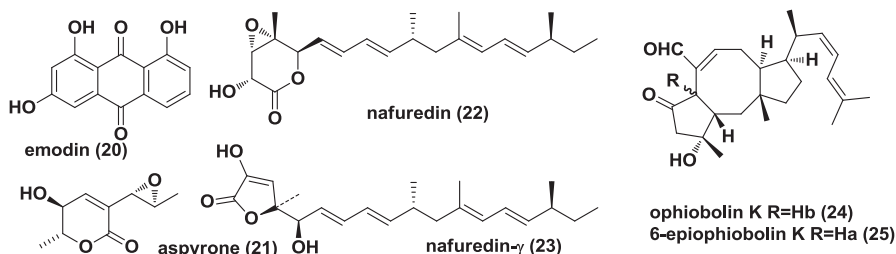
Nematicidal Metabolites from Aspergillus Fumigatus, Penicillium Nigricans, Gliocladium Fimbriatum and Penicillium Sp.

A terpenoid, fumagillin (13), isolated from both *Aspergillus fumigatus* and *Penicillium nigricans*, was reported to be moderately active against nematode *Anguillula aceti* (Tarbell et al. 1960; Bačková et al. 1965; Beecham et al. 1966). Gliotoxin (14), a known antibiotic, was also weakly active against *A. aceti* (Bačková et al. 1965). Gliotoxin (14) had been isolated from *Gliocladium fimbriatum*, *Aspergillus fumigatus*, *Penicillium* sp. and other fungi (Tarbell et al. 1960; Beecham et al. 1966). Besides the two compounds, five compounds including two new active fumiquinones A (15), B (16) and three known spinulosin (17), LL-S490 (18) and pseurotin A (19) were also isolated from *A. fumigatus*. Fumiquinone A (15) showed effective nematocidal activities against *Pratylenchus penetrans* and *Bursaphelenchus xylophilus*, but fumiquinone B (16) and the three known compounds only showed activity against *B. xylophilus*. All of these five compounds had no nematocidal activities against *Caenorhabditis elegans* (Hayashi et al. 2007).



Nematicidal Metabolites from Aspergillus Glaucus, A. Melleus and A. Niger

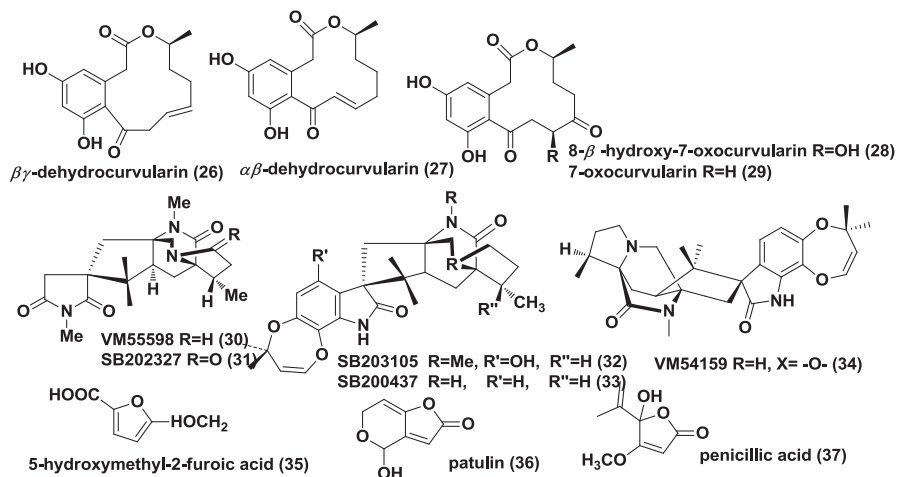
A widely distributed anthraquinone in plants, emodin (**20**) was also obtained from *Aspergillus glaucus* (Anke et al. 1980a, b). Emodin (**20**) has shown activity against *Meloidogyne incognita* (Mayer 1995). Aspyrone (**21**) was isolated from *Aspergillus melleus* and showed a nematicidal activity against *Pratylenchus penetrans* with killing rates of 39% and 80.8% at concentrations of 100 mg L⁻¹ and 300 mg L⁻¹, respectively (Kimura et al. 1996). Nafuredin (**22**) was isolated as an inhibitor of an anaerobic electron transporter from the culture broth of *Aspergillus niger* FT-0554 (Ui et al. 2001; Ōmura et al. 2001). *In vivo* trials with sheep indicated that nafuredin (**22**) had significant nematicidal activity against *Haemunchus cortortus*. Nafuredin (**22**) could be easily converted to nafuredin- γ (**23**) by weak alkaline treatment. The latter also showed an inhibitory activity similar to nafuredin (**22**) (Shiomi et al. 2005). The IC₅₀ values of nafuredin (**22**) and nafuredin- γ (**23**) were 9.7 nM and 6.4 nM respectively in their inhibition against NADH-fumarate reductase (NFRD) of *Ascaris suum* (Shiomi et al. 2005). Two new nematicidal ophiobolins, ophiobolin K (**24**) and 6-epiophiobolin K (**25**) were obtained from *Aspergillus ustus* (Singh et al. 1991). The two compounds were also isolated from *Cochliobolus heterostrophus* (Rosegay et al. 1996).



Nematicidal Metabolites from Aspergillus Spp.

Four macrolides including a new compound $\beta\beta,\gamma$ -dehydrocurvularin (**26**) and three known ones $\alpha\beta$ -dehydrocurvularin (**27**), 8- β -hydroxy-7-oxocurvularin (**28**) and 7-oxocurvularin (**29**) were obtained from *Aspergillus* sp. These four macrolides have shown nematicidal activities against the root-lesion nematode *Pratylenchus penetrans* (Kusano et al. 2003). However, none of the four compounds had any observable effects on *Caenorhabditis elegans* at the tested concentrations (1–1000 mg L⁻¹). The three known compounds are produced by many species in the genera *Alternaria*, *Cochliobolus*, *Curvularia* and *Penicillium* (Munro et al. 1967; Hyeon et al. 1976; Robeson and Strobel 1981, 1985; Kobayashi et al. 1988; Arai et al. 1989; Lai et al. 1989, 1990; Ghisalberti and Rowland 1997). Two members of a new class of anthelmintics, aspergillimide (VM55598) (**30**) and 16-keto aspergil-

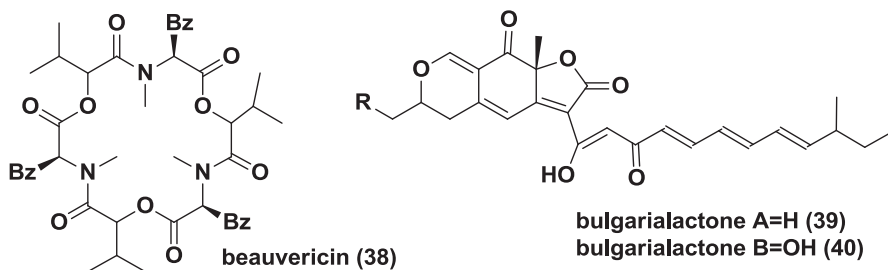
limide (SB202327) (**31**), were isolated from *Aspergillus* sp. IMI 337664 (Banks et al. 1997). In addition, three new paraherquamides SB203105 (**32**), SB200437 (**33**) and VM54159 (**34**) were also isolated from this strain. This study was the first to report paraherquamides from an organism outside the fungal genus *Penicillium*. These compounds had activity against *Trichostrongylus columbriformis*. Tests showed that the 16-keto analogue of aspergillimide (**31**) was active against *Haemunchus contortus* L₃ larvae *in vitro* but not *in vivo* (Banks et al. 1997). A new nematicide 5-hydroxymethyl-2-furoic acid (**35**) was obtained from the cultures of an *Aspergillus* sp. The compound showed effective nematicidal activities against *Bursaphelenchus xylophilus* and *Caenorhabditis elegans* (Kimura et al. 2007). A pyran compound patulin (**36**) was proven to be active against *Meloidogyne incognita* with the LD₃₀ dose at 100 µg mL⁻¹ and a oxygen heterocycle penicillic acid (**37**) was found to possess weak activities against *Anguillula aceti* (Bačkov et al. 1965; Mayer 1995). Patulin (**36**) was found in several fungi including *Aspergillus* spp. (Lopez-Diaz and Flannigan 1997), *Penicillium* spp. (Adams et al. 1976; Alfaro et al. 2003; Dombink-Kurtzman and Blackburn 2005), and *Byssosclamyces* spp. (Moul and Hately 1977). Penicillic acid (**37**) has been isolated from several fungal species and strains belonging to *Aspergillus* (He et al. 2004; Kang and Kim 2004), *Penicillium* (Wirth et al. 1956; Reimerdes et al. 1975), and *Malbranchea aurantiaca* (Martnez-Luis et al. 2005).



Nematicidal Metabolites from Beauveria Bassiana, Bulgaria Inquinans and Paecilomyces Fumoso-Roseus

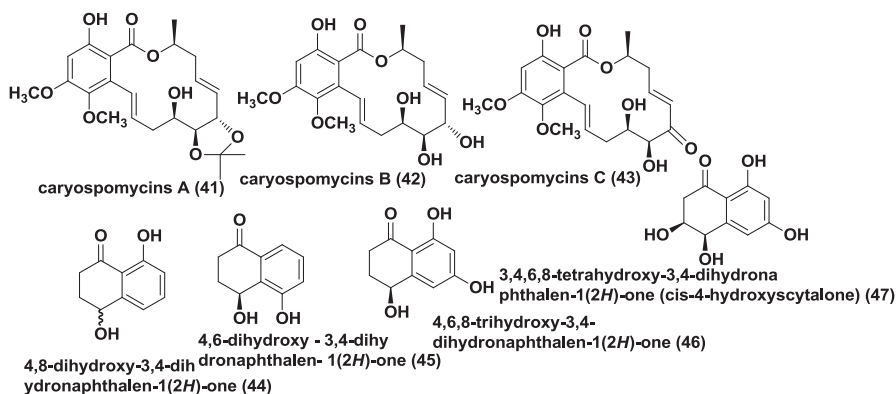
The cyclic depsipeptide beauvericin (**38**) was weakly active against *Meloidogyne incognita* (Mayer 1995), and then was proved to be active against *Caenorhabdi-*

tis elegans and *Bursaphelenchus xylophilus* (Shimada et al. 2010). This peptide was isolated from *Beauveria bassiana* (Hamill et al. 1969), *Paecilomyces fumosoroseus* (Bernardini et al. 1975), *Fusarium* spp. (Bernardini et al. 1975), *Beauveria* sp. FKI-1366 (Fukuda et al. 2004), *Fusarium bulbicola* (Shimada et al. 2010) and *F. redolens* (Xu et al. 2010), and the basidiomycete *Polyporus sulphureus* (Deol et al. 1978). Two new azaphilones, bulgarialactone A (39) and B (40) were isolated from both the mycelia and fruit bodies of the *Bulgaria inquinans*. The LD₅₀ value of bulgarialactone A (39) and B (40) against the nematode *Caenorhabditis elegans* was 5 µg mL⁻¹ and 10–25 µg mL⁻¹ respectively (Stadler et al. 1995).



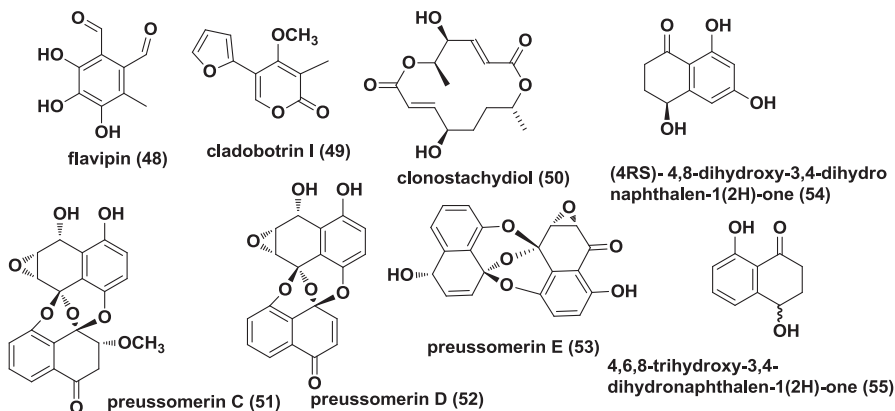
Nematicidal Metabolites from Caryospora Callicarpa

Three new macrolide caryospomycins A (41), B (42) and C (43), and four known compounds (44–47) were isolated from the mycelium and fermentation broth of freshwater taxon *C. callicarpa* YMF1.01026 (Dong et al. 2007; Zhu et al. 2008). These compounds were active against *Bursaphelenchus xylophilus* (Dong et al. 2007; Zhu et al. 2008).



Nematicidal Metabolites from Chaetomium Globosum, Cladobotryum Rubrobrunnescens, Clonostachys Cylindrospora, Coelomyces Sp., Epicoccum Nigrum and E. Purpurascens

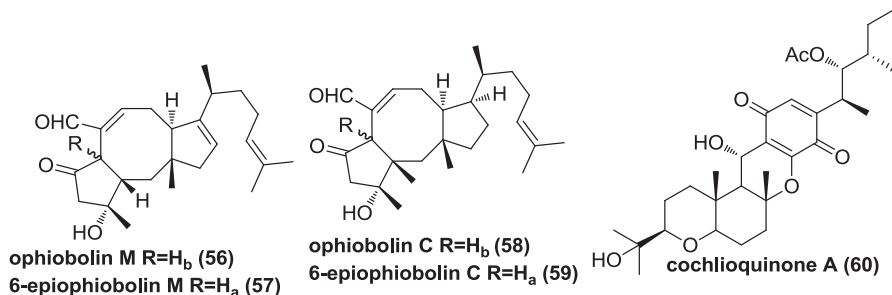
A simple aromatic flavipin (**48**), produced by *Chaetomium globosum*, could inhibit *in vitro* egg hatch and juvenile mobility of *Meloidogyne incognita*, and could also inhibit the hatch of *Heterodera glycines* (Nitao et al. 2002). Flavipin (**48**) was also found in *Epicoccum nigrum* (Burge et al. 1976) and *E. purpurascens* (Brown et al. 1987). Cladobotrin I (**49**) exhibited nematocidal activity towards *Meloidogyne incognita* with an LD₅₀ at 100 µg mL⁻¹, and it was isolated from *Cladobotryum rubrobrunnescens* (Wagner et al. 1998). A 14-membered macrodiolide clonostachydiol (**50**) was isolated from the *Clonostachys cylindrospora* (Grabley et al. 1993). Its synthesis *in vitro* has been achieved (Rao et al. 1995). A dose of 2.5 mg kg⁻¹ subcutaneously administered to sheep artificially infected with the nematode *Haemonchus cortortus* caused 80 to 90% reduction of nematode (Grabley et al. 1993). Five nematocidal compounds preussomerin C (**51**), preussomerin D (**52**), preussomerin E (**53**), (4RS)-4,8-dihydroxy-3,4-dihydronaphthalen-1(2H)-one (**54**) and 4,6,8-trihydroxy-3,4-dihydronaphthalen-1(2H)-one (**55**) were isolated from an aquatic fungus *Coelomyces* sp. YMF 1.01029 (Zhou et al. 2009).



Nematicidal Metabolites from Cochliobolus Heterostrophus, C. Miyabeanus, Helminthosporium Leersii and H. Sativum

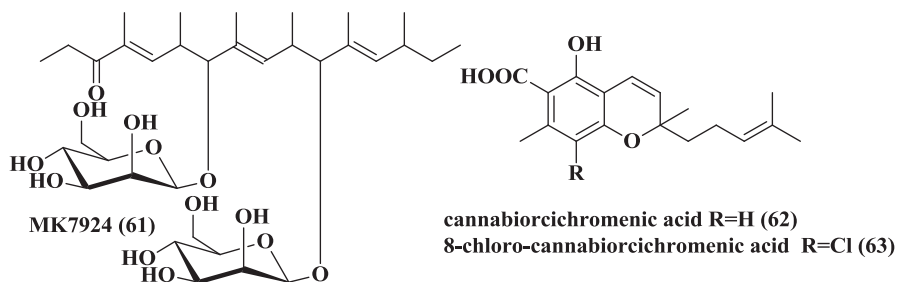
Four ophiobolane-type sesterterpenes including ophiobolin M (**56**), 6-epiophiobolin M (**57**), ophiobolin C (**58**) and 6-epiophiobolin C (**59**) have been isolated from *Cochliobolus heterostrophus* (Tsipouras et al. 1996). Ophiobolin C (**58**) was first obtained from *Helminthosporium* species (Cutler et al. 1984) and it was the most active compound among these compounds with an LD₅₀ value of 5 µM against *Caenorhabditis*

elegans. These compounds are non-competitive inhibitors of ivermectin binding to membranes prepared from *C. elegans* (Tsipouras et al. 1996). A quinone cochlioquinone A (60) has been isolated from *Cochliobolus miyabeanus*, *Helminthosporium leersii* and *H. sativum* (Barrow and Murphy 1972; Schaeffer et al. 1990). The ED_{50} of cochlioquinone A (60) against *Caenorhabditis elegans* was 135 μM (Snook et al. 1998). Cochlioquinone A (60) may have a similar mode of action as that of the widely used avermectin because the compound is a competitive inhibitor of [^3H] ivermectin and both can bind to the cell membrane of *Caenorhabditis elegans*.



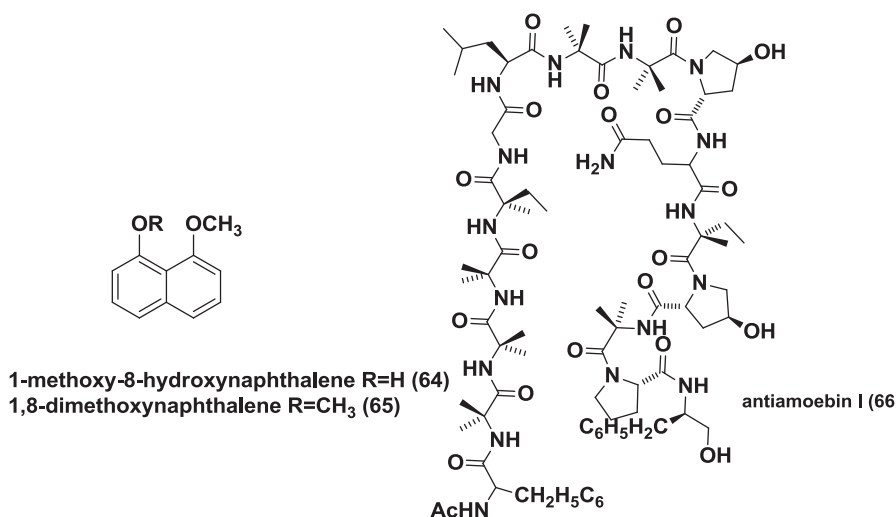
Nematicidal Metabolites from *Coronophora Gregaria* and *Cylindrocarpon Olidum*

A highly methylated polyketide MK7924 (61) was isolated from the culture broth of *Coronophora gregaria* L2495 and the compound exhibited significant nematicidal activity against *Caenorhabditis elegans* at 100 $\mu\text{g mL}^{-1}$ (Kumazawa et al. 2003). There were significant structural differences between MK7924 (61) and other known anthelmintic agents. Therefore, MK7924 (61) could be developed as a promising new type of anthelmintic. Two nematicidal compounds cannabioreichromenic acid (62) and its 8-chloro derivative (63) were isolated from *Cylindrocarpon olidum* (Quaghebeur et al. 1994). The mixture of these two compounds could kill 50% of *Heterorhabditis* nematodes at 20 $\mu\text{g mL}^{-1}$ (Quaghebeur et al. 1994).



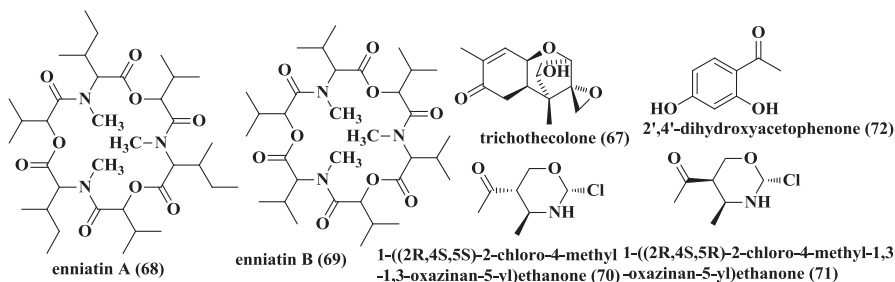
Nematicidal Metabolites from Daldinia Concentrica, Emericellopsis Poonensis and E. Synnematicola

Two naphthalenes 1-methoxy-8-hydroxynaphthalene (**64**) and 1,8-dimethoxynaphthalene (**65**) were isolated from *Daldinia concentrica* (Dasenbrock 1994) and both were active against *C. elegans* with LD₅₀ values at 10 µg mL⁻¹ and 25 µg mL⁻¹ respectively. However, these two compounds were only weakly active against *Meloidogyne incognita* (Anke et al. 1995). The N-terminally acetylated lipophilic linear polypeptide anti amoebin I (**66**) had been obtained from fungal species *Emericellopsis poonensis* and *E. synnematicola*, which showed activity against helminthes (Thirumalachur 1968; Pandey et al. 1977). The structure of anti amoebin I (**66**) was determined by several spectral methods including X-ray crystallography (Brückner et al. 1980; Snook et al. 1998).



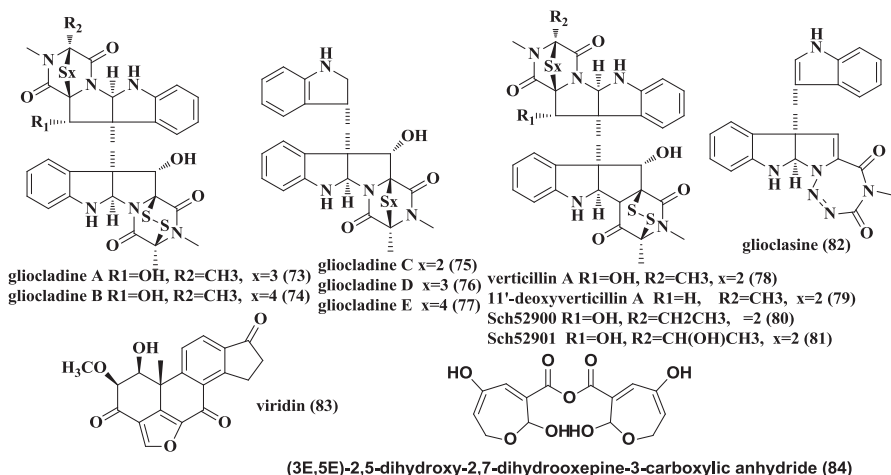
Nematicidal Metabolites from Fusarium Roseum, Trichothecium Roseum, Fusarium Sp. and Geotrichum Sp.

Trichothecolone (**67**) was obtained from *Fusarium roseum* and *Trichothecium roseum*, which had weakly activity against the nematode *Anguillula aceti* (Freeman et al. 1959; Bačlková et al. 1965; Konishi et al. 2003). Two cyclodepsipeptides, enniatin A (**68**) and enniatin B (**69**), were isolated from the culture broth of *Fusarium* spp. (Tomoda et al. 1992), and both were weakly active against *Meloidogyne incognita* (Mayer 1995). An endophytic fungus *Geotrichum* sp. AL4 was isolated from the leaf of *Azadirachta indica*. Two new metabolites, 1-((2*R*,4*S*,5*S*)-2-chloro-4-methyl-1,3-oxazinan-5-yl) ethanone (**70**) and 1-((2*R*,4*S*,5*R*)-2-chloro-4-methyl-1,3-oxazinan-5-yl)ethanone (**71**) as well as one known compound 2',4'-dihydroxyacetophenone (**72**) were isolated from this strain. The three compounds exhibited nematicidal activity against nematodes *Bursaphelenchus xylophilus* and *Panagrellus redivivus* (Li et al. 2007).



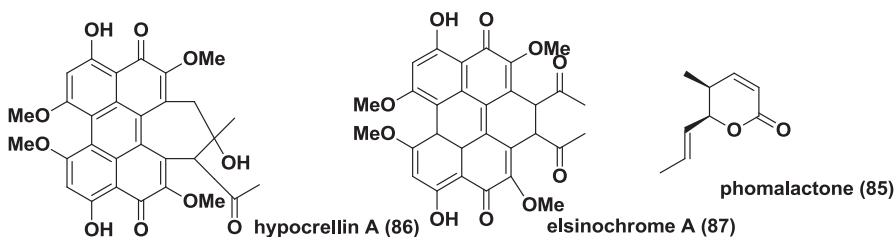
Nematicidal Metabolites from *Gliocladium Roseum*, *G. Virens* and *Gymnoascus Reesii*

A series of diketopiperazine compounds were isolated from the solid-substrate fermentation cultures of *Gliocladium roseum* (Dong et al. 2005, 2006). These compounds include gliocladine A (73), B (74), C (75), D (76), E (77), verticillin A (78), 11'-deoxyverticillin A (79), Sch52900 (80), Sch52901 (81) and glioclasine (82). The compounds showed nematicidal activities against *Caenorhabditis elegans* and *Panagrellus redivivus*. However, they showed little activity against *Bursaphelenchus xylophilus*. Compared to the other compounds in this group, glioclasine (82) showed the strongest activities against *Bursaphelenchus xylophilus*, *Caenorhabditis elegans* and *Panagrellus redivivus* with LD₅₀ values at 15, 50 and 200 µg mL⁻¹, respectively (Dong et al. 2005). A sterol, viridian (83) was obtained from *Gliocladium virens* and some strains of *Trichoderma* (Blight et al. 1968), and it has been found to possess weak activity against *Anguillula aceti* (Bačĭková et al. 1965). A nematicidal metabolite (3E,5E)-2,5-dihydroxy-2,7-dihydrooxepine-3-carboxylic anhydride (84) was isolated based on bioassay-guided fractionation from the extracts of the fungus *Gymnoascus reesii*, which showed activity against *M. incoginta* (Liu et al. 2011).



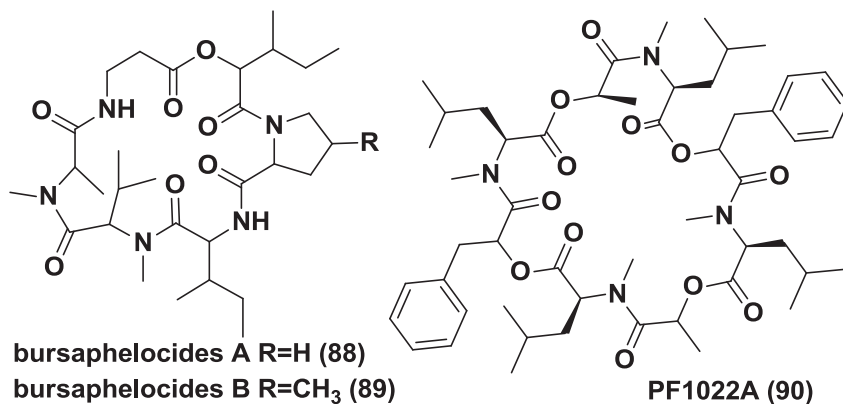
Nematicidal Metabolites from *Hirsutella Thompsonii* Var. *Synnematosa*, *Nigrospora Sphaerica*, *Verticillium Chlamydosporium* and *Hypomyces Sp.*

A nematicidal compound phomalactone (**85**) was obtained by bioassay-directed fractionation from *Verticillium chlamydosporium* (Khambay et al. 2000). The mortality of *Meloidogyne incognita* reached 84% in 96 h when the concentration of phomalactone (**85**) was 500 mg L⁻¹ (Khambay et al. 2000). This compound has been found in other fungi, e.g. the entomopathogenic fungi *Hirsutella thompsonii* var. *synnematoso* (Krasnoff and Gupta 1994) and *Nigrospora sphaerica* (Kim et al. 2001). Two photosensitive compounds hypocrellin A (**86**) and elsinochrome A (**87**) were isolated from *Hypomyces* sp. (Dong et al. 2001). These two compounds were able to kill 50% of the nematode *Bursaphelenchus xylophilus* within 18 h at concentrations of 50 µg mL⁻¹ for hypocrellin A (**86**), and 15 µg mL⁻¹ for elsinochrome A (**87**) (Dong et al. 2001).



Nematicidal Metabolites from Anamorphic Fungi Strains D1084 and PF1022

Two novel depsipeptides bursaphelocides A (**88**) and B (**89**) were isolated from an unidentified anamorph strain, D1084. These two compounds were active against *B. xylophilus* at a dose of 100 µg per ball using the “cotton ball on the fungal mat method” (Kawazu et al. 1993). Another unidentified anamorph strain PF1022 produced a novel cyclodepsipeptide PF1022A (**90**) showed potent anthelmintic activity against *Ascaridia galli* (Sasaki et al. 1992). Importantly, no toxic effect was observed to the host animals. The efficacy of compound PF1022A (**90**) against anthelmintic-resistant nematodes in sheep and cattle was investigated and the result confirmed that PF1022A (**90**) was fully effective against these parasite nematode populations (Samson-Himmelstjerna et al. 2005).

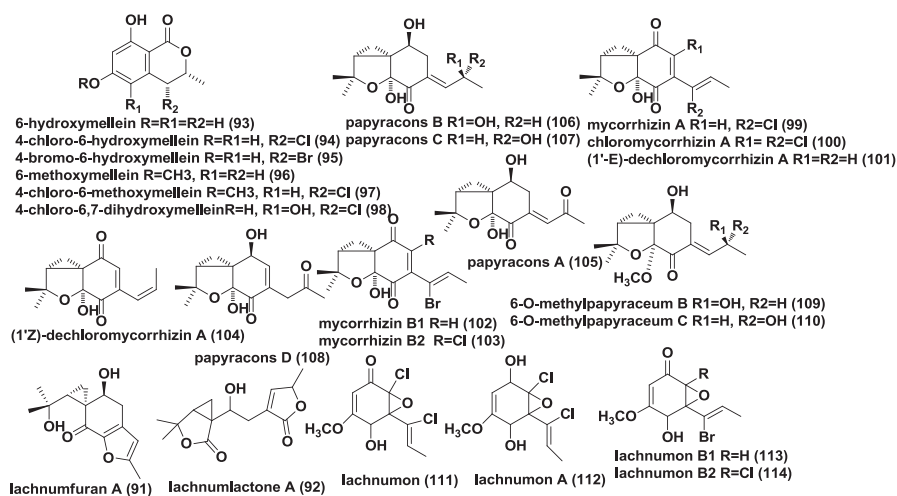


Nematicidal Metabolites from Lachnum Papyraceum

Two new compounds lachnumfuran A (91) and lachnumlactone A (92) were obtained from *Lachnum papyraceum* (Shan et al. 1996). The two compounds had relatively weak activities against *Caenorhabditis elegans* with ND₉₀ dosages at 100 and 50 µg mL⁻¹ respectively (Shan et al. 1996). During the investigations of the influences of CaBr₂ on the biosynthesis of chlorinated secondary metabolites in *Lachnum papyraceum*, six isocoumarin derivatives, 6-hydroxymellein (93), 4-chloro-6-hydroxymellein (94), 4-bromo-6-hydroxymellein (95), 6-methoxymellein (96), 4-chloro-6-methoxymellein (97) and 4-chloro-6,7-dihydroxymellein (98) were obtained. Among them, compounds 4-chloro-6-hydroxymellein (94), 4-bromo-6-hydroxymellein (95), 6-methoxymellein (96) and 4-chloro-6,7-dihydroxymellein (98) were isolated for the first time from a natural source (Stadler et al. 1995a, b). These isocoumarin derivatives showed only weak nematicidal effects and the ND₉₀ values of these compounds against *Caenorhabditis elegans* were all within the region of 100 µg mL⁻¹ (Stadler et al. 1995a).

In addition, a series of mycorrhizins, mycorrhizin A (99), chloromycorrhizin A (100) and (1'-E)-dechloromycorrhizin A (101) were commonly found in normal fermentations of the fungus (Stadler and Anke 1993a). However, in fermentations in media containing a large amount of CaBr₂, additional mycorrhizins could be found. These included two brominated derivatives mycorrhizin B1 (102) and mycorrhizin B2 (103) as well as (1'Z)-dechloromycorrhizin A (104) (Stadler et al. 1995c, d, e; Shan et al. 1996). These mycorrhizins were all toxic towards *Caenorhabditis elegans* but were only weakly active against *Meloidogyne incognita*. Among these mycorrhizins, mycorrhizin A (99) showed the highest activity against *Caenorhabditis elegans* with an LD_{50 at} 1 µg mL⁻¹. Based on structural and functional comparisons, it was suggested that chlorine substitutions in the side chains could increase their biological activities, whereas chlorine substitutions within the ring systems seem to weaken their activities (Stadler et al. 1995a). The brominated mycorrhizins showed weaker activities than their chlorinated analogues. However, these differences were

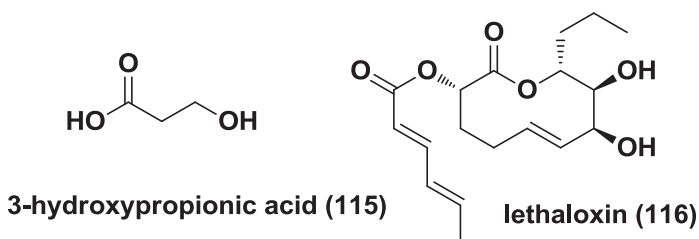
not statistically significant (Stadler et al. 1995c). Several minor metabolites, papyracons A (105), B (106), C (107) and D (108), 6-*O*-methylpapyraceum B (109) and 6-*O*-methylpapyraceum C (110) have also been isolated from *Lachnum papyraceum* and they are all weakly active against *Caenorhabditis elegans* (Stadler et al. 1995c, d, e; Shan et al. 1996). In addition, four isoeopoxydon compounds were isolated from *Lachnum papyraceum* (Stadler and Anke 1993a, b; Stadler et al. 1995c, e). These compounds were lachnumon (111), lachnumon A (112), lachnumon B1 (113) and lachnumon B2 (114). Lachnumon (111) and lachnumon A (112) had similar activities against *Caenorhabditis elegans* with an LD₅₀ at 25 µg mL⁻¹. Their activities against *Meloidogyne incognita* were weak, with an LD₅₀ exceeding 100 µg mL⁻¹ for both (Stadler and Anke 1993a, b). The LD₉₀ values of lachnumon B1 (113) and lachnumon B2 (114) against *Caenorhabditis elegans* were 25 µg mL⁻¹ and 50 µg mL⁻¹, respectively. Their activities against *Meloidogyne incognita* were similar to those of compounds lachnumon (111) and lachnumon A (112) (Stadler et al. 1995c, e). 6-hydroxymellein (93) has also obtained from other taxa including *Discula* spp. (Venkatasubbaiah and Chilton 1991) and *Myxotrichum stipitatum* (Kimura et al. 2002). In addition, mycorrhizin A (99) and chloromycorrhizin A (100) have been isolated from a mycorrhizal fungus *Monotropia hypopitys* (Trofast and Wickberg 1977; Trofast 1978).



Nematicidal Metabolites from Melanconium Betulinum, Mycosphaerella Lethalis and Phomopsis Phaseoli

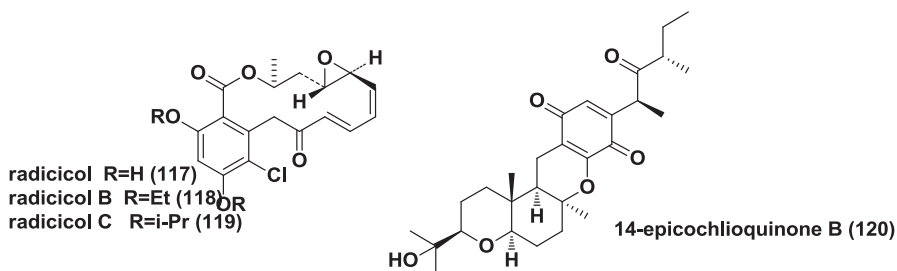
3-hydroxypropionic acid (3-HPA) (115) was isolated as the main nematocide from the submerged culture of fungus *Phomopsis phaseoli* originally found on a tropical tree. This compound has also been found from *Melanconium betuli-*

mum associated with *Betula pendula* and *B. pubescens* (Schwarz et al. 2004). The compound showed selective nematicidal activity against *Meloidogyne incognita* with an LD₅₀ value of 12.5–15 µg mL⁻¹, and against *Caenorhabditis elegans* with an LD₅₀ value about five times lower (Schwarz et al. 2004). A 9-lactide decane compound lethaloxin (**116**) isolated from *Mycosphaerella lethalis* (Arnone et al. 1993), which was proven capable of killing *C. elegans* with an LD_{50 at} 25 µg mL⁻¹ (Stadler 1993).



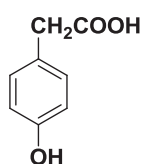
Nematicidal Metabolites from Nectria Radicola and Neobulgaria Pura

A macrolide radicicol (**117**) produced by *Nectria radicola* was a highly cytotoxic antiprotozoal and antineoplastic agent (Mirrington et al. 1964). This compound has also been isolated from other fungal species such as *Monosporium bonorden*, *Penicillium luteo-aurantium* (Nozawa and Nakajima 1979) and *Chaetomium chiversii* (Kithsiri Wijeratne et al. 2006). Its two dialkoxy derivatives radicicol B (**118**) and radicicol C (**119**) also possessed nematicidal activities against an unidentified soil nematode with an LD₅₀ value at 200 µg mL⁻¹ (Stadler 1993). Compound 14-epicochlioquinone B (**120**) was isolated as a platelet aggregation inhibitor from the ascomycete *Neobulgaria pura* (Lorenzen et al. 1994). This compound had a strong nematicidal activity against *C. elegans* with LD₅₀ value at 10 µg mL⁻¹ (Anke et al. 1995). However, it was approximately 10 times less active against *Meloidogyne incognita* (Anke et al. 1995).

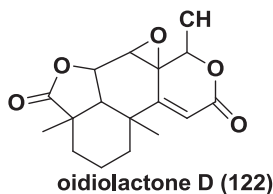


Nematicidal Metabolites from Oidiodendron Sp. and Ophioceras Dolichostomum

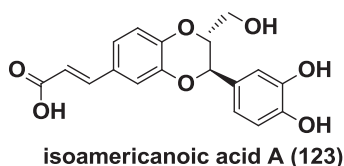
Two compounds including 4-hydroxyphenylacetic acid (4-HPA) (**121**) and oidiolactone D (**122**), were isolated from cultures of *Oidiodendron* sp.. The two compounds showed nematicidal activities against *Pratylenchus penetrans* and *Bursaphelenchus xylophilus* (Ohtani et al. 2011). Isoamericanoic acid A (**123**) and caffeic acid (**124**) were isolated from the freshwater taxon *Ophioceras dolichostomum* YMF1.00988. The LD₅₀ values of the two compounds against *Bursaphelenchus xylophilus* were 133.7 and 46.8 µg mL⁻¹ respectively (Dong et al. 2010).



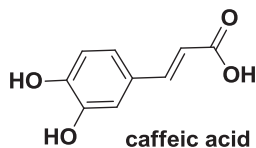
4-hydroxyphenylacetic acid (**121**)



oidiolactone D (**122**)



isoamericanoic acid A (**123**)



caffeic acid (**124**)



acetic acid (**125**)

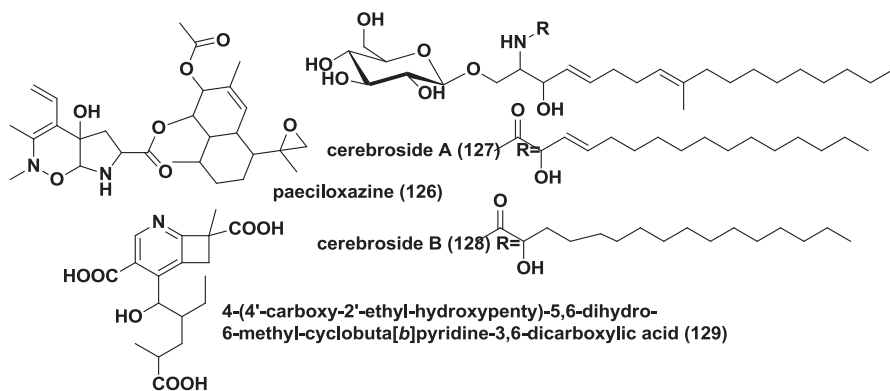
Nematicidal Metabolites from Paecilomyces Lilacinus and Trichoderma Longibrachiatum

The common acetic acid (**125**) has been isolated from culture filtrates of *Paecilomyces lilacinus* and *Trichoderma longibrachiatum* (Djjan et al. 1991; Park et al. 2004). Acetic acid (**125**) has been shown to have selective nematicidal activities against certain nematodes (Djjan et al. 1991). *P. lilacinus* showed effective treatment on against root-knot nematode on tomato plants under greenhouse conditions (El-Din et al. 2012).

Nematicidal Metabolites from Paecilomyces Spp.

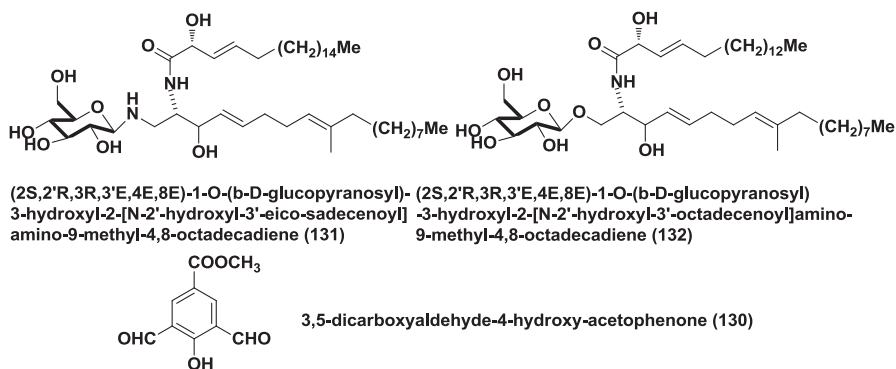
A new macrocyclic lactone derivative paeciloxazine (**126**) with the pyrrolobenzoxazine skeleton was isolated from the culture broth of *Paecilomyces* sp. BAUA3058 (Kanai et al. 2004). Biological assay showed that the compound was active against *Rhabditis pseudoelongata* at 50 µg mL⁻¹. Nematicidal compounds cerebroside A (**127**) and B (**128**) were isolated from another strain of *Paecilomyces* (Zhang et al. 2010). A new nematicidal compound 4-(4'-carboxy-2'-ethyl-

hydroxypentyl)-5,6-dihydro-6-methyl-cyclobuta[*b*]pyridine-3,6-dicarboxylic acid (**129**) was identified from *Paecilomyces* sp. YMF1.01761. The LD₅₀ value of the compound within 48 h against *Panagrellus redivivus* was 50.86 mg L⁻¹, *Meloidogyne incognita* was 47.1 mg L⁻¹, and *Bursaphelenchus xylophilus* was 167.7 mg L⁻¹ (Liu et al. 2009).



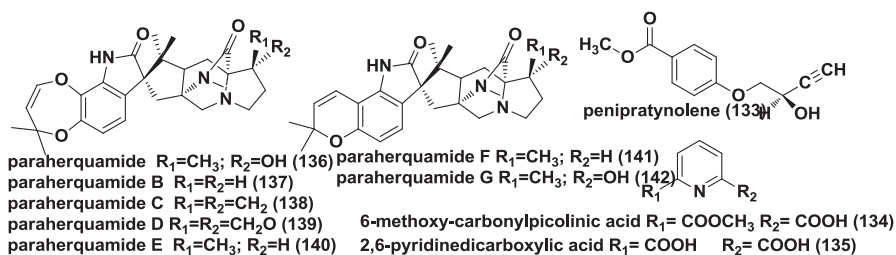
Nematicidal Metabolites from *Paraniesslia* Spp.

A new compound 3,5-dicarboxyaldehyde-4-hydroxy-acetophenone (**130**) was obtained from the freshwater fungus *Paraniesslia* sp. 83. This compound had a nematicidal activity against *Bursaphelenchus xylophilus* with an LD₅₀ value at 200 ppm in 24 h (Dong 2005). Two sphingolipids including a new (2*S*,2'*R*,3*R*,3'*E*,4*E*,8*E*)-1-*O*-(β-D-glucopyranosyl)-3-hydroxyl-2-[*N*-2'-hydroxyl-3'-eicosadecenoyl]amino-9-methyl-4,8-octadecadiene (**131**) and a known (2*S*,2'*R*,3*R*,3'*E*,4*E*,8*E*)-1-*O*-(β-D-glucopyranosyl)-3-hydroxyl-2-[*N*-2'-hydroxyl-3'-octadecenoyl]amino-9-methyl-4,8-octadecadiene (**132**) were isolated from another strain of *Paraniesslia* sp. YMF1.01400. Both compounds showed moderately nematicidal activities against *Bursaphelenchus xylophilus* (Dong et al. 2005).



Nematicidal Metabolites from *Penicillium Bilaiae*, *P. Charlesii* and *P. Paraherquei*

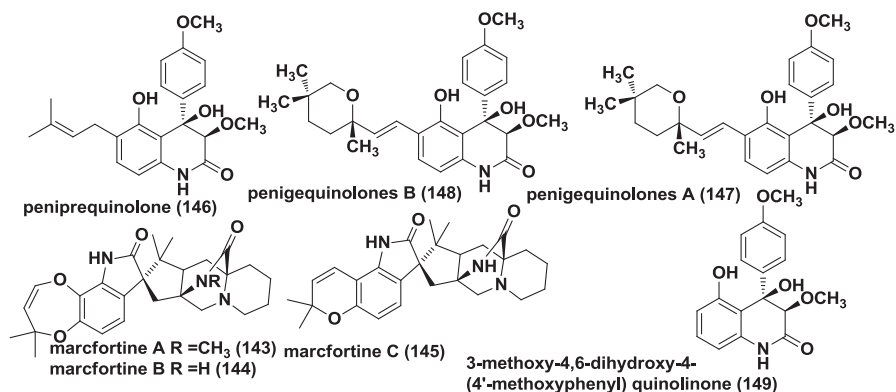
A new acetylenic nematicidal compound penipratynolene (**133**) was obtained from the culture filtrate of the fungus *Penicillium bilaiae* (Nakahara et al. 2004). The compound showed nematicidal activity against the root-lesion nematode *Pratylenchus penetrans*, capable of killing 77% of the nematode at a concentration of 300 mg L⁻¹ (Alfaro et al. 2003). It was suggested that the alkyne carbons are likely to play an important role in the nematicidal activities of this group of compounds (Kimura et al. 1981; Mori et al. 1982). Two known compounds, 6-methoxy-carboxylpicolinic acid (**134**) and 2,6-pyridinedicarboxylic acid (**135**), were also obtained from the culture filtrate of the strain (Nakahara et al. 2004). By a bioassay at 300 mg L⁻¹, both the two compounds showed nematicidal activities with a mortality of 52% and 98% respectively against *Pratylenchus penetrans* (Nakahara et al. 2004). Nakahara et al. (2004) suggested that the carboxy groups in the compounds are likely to play important roles in their nematicidal activities. The oxindole alkaloid paraherquamide (**136**) was originally isolated from *Penicillium paraherquei* and its structure was determined by X-ray diffraction analysis (Yamazaki et al. 1981). Subsequently, paraherquamide (**136**) and its novel analogs paraherquamides B (**137**), C (**138**), D (**139**), E (**140**), F (**141**), G (**142**) were obtained from another species of *Penicillium charlesii* (ATCC 20841) (Ondeyka et al. 1990; Liesch and Wichmann 1990). All seven metabolites possessed nematicidal activities against *Caenorhabditis elegans* with LD₅₀ values in the range of 2.5–160 µg mL⁻¹. Among them, paraherquamide (**136**) was the most potent with an LD₅₀ value of 2.5 µg mL⁻¹ (Ondeyka et al. 1990; Blanchflower et al. 1991).



Nematicidal Metabolites from *Penicillium Roqueforti* and *P. Simplicissimum*

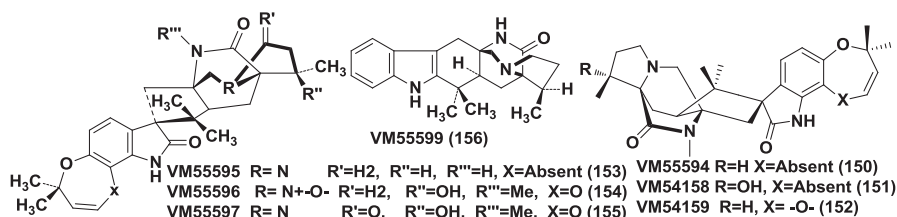
Three new alkaloids marcfortine A (**143**), B (**144**), and C (**145**) were obtained from the mycelium of *Penicillium roqueforti* (Polondky et al. 1980; Prangé et al. 1981). The chemical structures of marcfortine A (**143**) and C (**145**) were established by X-ray analysis. These three compounds possessed potent anthelmithic properties against plant-parasitic and animal-endoparasitic nematodes. A new alkaloid, peni-

prequinolone (**146**), together with the known compounds penigequinolones A (**147**), B (**148**) and 3-methoxy-4,6-dihydroxy-4-(4'-methoxyphenyl) quinolinone (**149**) were isolated from the liquid culture of *Penicillium* cf. *simplicissimum* (Kusano et al. 2000). The three known compounds were first isolated from other species of the genus *Penicillium* (Kimura et al. 1996; Hayashi et al. 1997). These compounds were active against the nematode *Pratylenchus penetrans* at the killing rates of 82.4%, 69.2% and 57.7% respectively at the concentration of 1000 mg L⁻¹. These results indicated that either a phenolic hydroxyl group at C-5 or a tetrahydropyran ring in these compounds might be responsible for their nematicidal activities against *Pratylenchus penetrans* (Kusano et al. 2000).



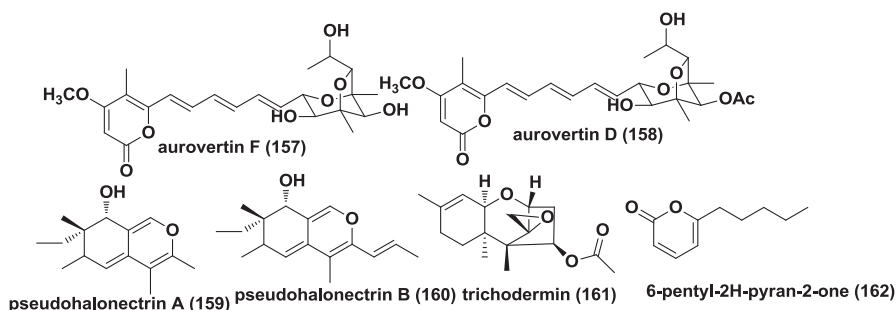
Nematicidal Metabolites from Penicillium Sp.

Paraherquamide (**136**) and its seven novel analogues VM55594 (**150**), VM54158 (**151**), VM54159 (**152**), VM55595 (**153**), VM55596 (**154**), VM55597 (**155**) and VM55599 (**156**) were isolated from a strain of *Penicillium*, IMI 332995 (Blanchflower et al. 1991, 1993). The nematicidal activities of compounds paraherquamide (**136**), VM55594 (**150**), VM54158 (**151**), VM54159 (**152**) were assayed against both *Haemunchus contortus* larvae and *Trichjostrongylus colubriformis* adults *in vitro*. Paraherquamide (**136**) and VM54159 (**152**) were more active than compounds VM55594 (**150**) and VM54158 (**151**), with MIC₅₀ values of 31.2 and 25.6 µg mL⁻¹ against *Haemunchus contortus* for paraherquamide (**136**) and VM54159 (**152**) respectively. In addition, paraherquamide (**136**) and VM54159 (**152**) could cause 99.5% and 100% reductions in faecal egg counts of the nematode *Trichjostrongylus colubriformis* at 4 mg kg⁻¹. The group of 14-de-hydroxy in paraherquamide (**136**) and VM54159 (**152**) was more potent than their corresponding the group of 14-hydroxy in analogues VM55594 (**150**) and VM54158 (**151**) (Blanchflower et al. 1991). Compound VM55596 (**154**) was the first *N*-oxide member in the paraherquamide family and it was found capable of eliminating 94% faecal eggs of *Trichjostrongylus colubriformis* when dosed at 2 mg kg⁻¹ (Blanchflower et al. 1993).



Nematicidal Metabolites from *Pochonia Chlamydosporia*

Two nematicidal aurovertin compounds aurovertins F (**157**) and D (**158**) were isolated from *Pochonia chlamydosporia*. The LD₅₀ value of the two compounds against *Panagrellus redivivus* was 88.6 and 41.7 μg mL⁻¹ respectively (Niu et al. 2010). Two new azaphilone metabolites pseudohalonectrin A (**159**) and B (**160**) were produced by the aquatic fungus *P. adversaria* YMF 1.01019 (Dong et al. 2006). These two compounds possessed nematicidal activities against the pine wood nematode *Bursaphelenchus xylophilus* (Dong et al. 2006).

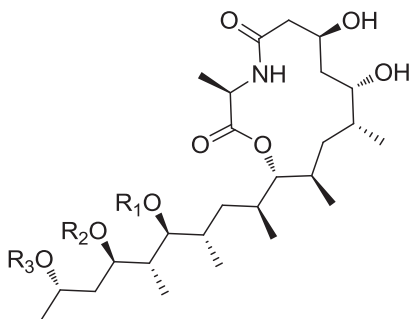


Nematicidal Metabolites from *Trichoderma* Spp.

A nematicidal sesquiterpene trichodermin (**161**) was isolated from ethyl acetate extract of *Trichoderma* sp. YMF1.02647. The compound could kill more than 95% both *Panagrellus redivivus* and *Caenorhabditis elegans* in 72 h at 0.4 g L⁻¹ (Yang et al. 2010). Trichodermin (**161**) had been isolated from several species of *Trichoderma* including *T. viride*, *T. harzianum*, *T. longibrachiatum* and *T. reesei*, and other taxa such as *Stachybotrys cylindrospora* and *Memnoniella echinata* (Godtfredsen and Vangedal 1964; Watts et al. 1988; Nielsen et al. 1998; Reino et al. 2008). The volatile organic compound 6-pentyl-2H-pyran-2-one (**162**) was isolated from *Trichoderma* sp. YMF 1.00416. Nematicidal activity assays showed that the compound could kill >85% of *Panagrellus redivivus*, *Caenorhabditis elegans*, and *Bursaphelenchus xylophilus* in 48 h at 200 mg L⁻¹ in a 2 mL vial (Yang et al. 2012).

Nematicidal Metabolites from Talaromyces Thermophiles

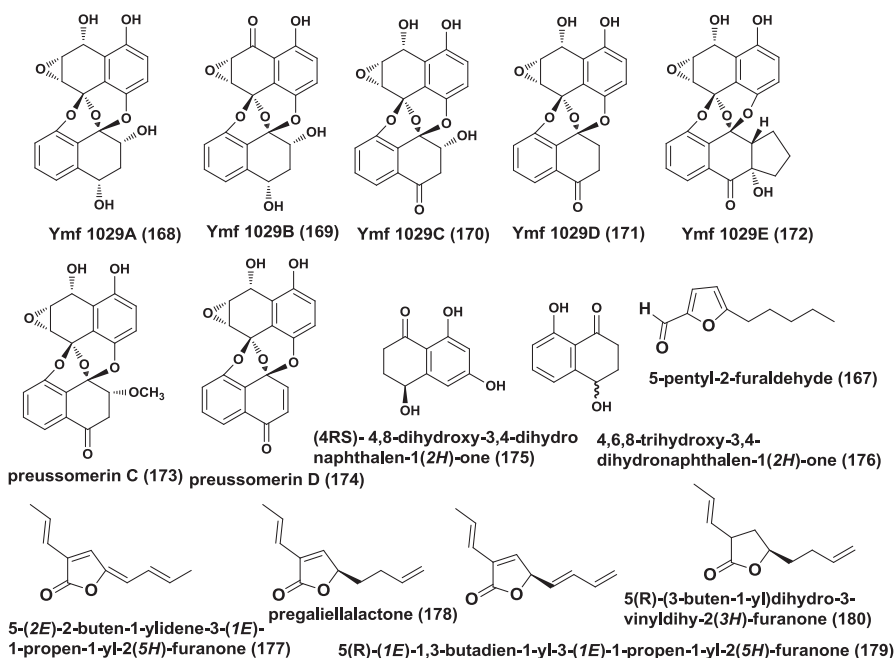
A novel class of potent nematocidal thermolides A-D was isolated from a thermophilic fungus *T. thermophilus*. Thermolides A (**163**) and B (**164**) showed the strongest activities against *Meloidogyne incognita*, *Bursaphelenchus xylophilus* and *Panagrellus redivivus* with LC_{50} values ranging from 0.5–1.0 $\mu\text{g/mL}$, similar to those of avermectins. Thermolide C (**165**) displayed moderate activity, and weak inhibitory effect on the worms was observed for thermolide D (**166**) (Guo et al. 2012).



thermolide A R₁=R₃=H, R₂=Ac (**163**)
thermolide B R₁=R₂=H, R₃=Ac (**164**)
thermolide C R₂=R₃=H, R₁=Ac (**165**)
thermolide D R₁=R₂=R₃=H (**166**)

Nematicidal Metabolites from Unidentified Ascomycete

5-pentyl-2-furaldehyde (**167**) was isolated as the principal nematocide from an unidentified ascomycete belonging to the *Dermateaceae* (Anke et al. 1995). In addition, it has been found in other taxa such as a basidiomycete *Irpex lacteus* (Hayashi et al. 1981) and an unidentified fungal strain Kyu-W63 (Koitabashi et al. 2004). 5-pentyl-2-furaldehyde (**167**) was one of the few metabolites with nematocidal activity found in both ascomycetes and basidiomycetes. This compound was active against *Caenorhabditis elegans* with $LD_{50 \text{ at } 75} \mu\text{g mL}^{-1}$, against *Meloidogyne incognita* with $LD_{50 \text{ at } 60} \mu\text{g mL}^{-1}$ and against *Aphelenchoides besseyi* with $LD_{90 \text{ at } 200} \mu\text{g mL}^{-1}$ (Anke et al. 1995; Hayashi et al. 1981). Compounds ymf 1029 A (**168**), B (**169**), C (**170**), D (**171**), E (**172**), preussomerin C (**173**), D (**174**), (4*RS*)-4,8-dihydroxy-3,4-dihydronaphthalen-1(2*H*)-one (**175**) and 4,6,8-trihydroxy-3,4-dihydronaphthalen-1(2*H*)-one (**176**) were isolated from an unidentified freshwater fungus YMF 1.01029. These compounds had various nematocidal activities against *Bursaphelenchus xylophilus* (Dong et al. 2008). From the cultures of the ascomycete A111-95, four compounds 5-(2*E*)-2-buten-1-ylidene-3-(1*E*)-1-propen-1-yl-2(5*H*)-furanone (**177**), pregaliellalactone (**178**), and the mixture of 5(*R*)-(1*E*)-1,3-butadien-1-yl-3-(1*E*)-1-propen-1-yl-2(5*H*)-furanone (**179**) and 5(*R*)-(3-buten-1-yl)dihydro-3-vinyldihy-2(3*H*)-furanone (**180**) with nematocidal activity towards *Caenorhabditis elegans* and *Meloidogyne incognita* were obtained (Köpcke et al. 2002). Compound 5-(2*E*)-2-buten-1-ylidene-3-(1*E*)-1-propen-1-yl-2(5*H*)-furanone (**177**) was also obtained from the basidiomycete *Galiella rufa* (Hautzel and Anke 1990).



Nematode-Toxic Basidiomycetes and Their Nematicidal Metabolites

Thorn and Barron (1984) reported that ten species of gilled fungi could attack and consume nematodes and considered that five species of *Pleurotus* could release a potent toxin which completely inactivated nematodes prior to penetration. Later, Barron and Thorn (1987) reported the details of *Pleurotus* used to attack its nematode victims and figured *Pleurotus ostreatus* produced tiny droplets of toxin from minute spatulate secretory areas and the toxin trans-2-decenedioic acid was isolated from *P. ostreatus* (Kwok et al. 1992) which inhibited 95% *Panagrellus redivivus* at 300 ppm in 1 hour and was postulated to be identical with ostreatin. Subsequently, six nematicidal compounds were isolated from *Pleurotus pulmonarius*, and one of them was a new compound (Stadler et al. 1994c). Up to now, 23 species of *Pleurotus* have been reported to have nematicidal activity. Nematicidal activity had been considered as one of characters of the genus *Pleurotus* (Hibbett and Thorn 1994). It is interesting that some edible mushrooms have such nematicidal activity. In addition, *Poria cocos*, a traditional Chinese medicine, had been also shown to possess nematicidal activity (Li et al. 2005).

Omphalotin A and its derivatives with potent and selective nematicidal activity were produced by the basidiomycete *Omphalotus olearius* (Mayer et al. 1997; Stener et al. 1997; Büchel et al. 1998). Omphalotin A and its derivatives had similar nematicidal activity with commercially available nematicide ivermectin.

Conversion of secondary metabolites as a response to injury in fruit bodies in basidiomycetes formed extracts with high nematicidal activity (Table 7.3) (Stadler and Sterner 1998). *Tricholoma terreum* and in all tested *Lepista* species, the nematicidal activity increased in response to injury, and *Tricholoma terreum* produced linoleic acid and S-coriolic acid while *Lepista* spp. produced free linoleic acid, along with unidentified metabolites (Stadler and Sterner 1998). *Melanoleuca cognate*, *M. melaleuca*, *Laccaria amethystine* and *Marasmius wynnei* produced fatty acids upon fruit body injury (Stadler and Sterner 1998). These findings reflect the presence of chemical defence systems in mushrooms, which is mediated by enzymatic conversions activated by physical injury.

Up to now, about 77 genera of basidiomycetes containing more than 160 species have been reported to possess nematicidal activity by producing active components. The nematode-toxic basidiomycete and their nematicidal compounds are listed in Table 7.3.

Nematicidal Metabolites from Calocybe Gambosa, Cheimonophyllum Candidissimum and Pycnoporus Sanguineus

The alkaloid phenoxazone (**181**) was isolated from the mycelial cultures of *Calocybe gambosa* and fruiting bodies of *Pycnoporus sanguineus* (Schlunegger et al. 1976; Gill 1994). This compound showed nematicidal activity against *Meloidogyne incognita* (LD_{50} : $50 \mu\text{g mL}^{-1}$) (Mayer 1995). Six new bisabolane sesquiterpenes cheimonophyllons A (**182**), B (**183**), C (**184**), D (**185**), E (**186**) and cheimonophyllal (**187**) were obtained from the submerged cultures of *Cheimonophyllum candidissimum* TA 8644. These compounds were active against *Caenorhabditis elegans* with LD_{50} between 10 and $100 \mu\text{g mL}^{-1}$ (Stadler et al. 1994a, b). In a further study, compound 1,2-dihydroxymintlactone (**188**) was isolated from the same fungus (Stadler et al. 1995). 1,2-Dihydroxymintlactone (**188**) was a new menithol monoterpene and possessed nematicidal activity. The LD_{50} of 1,2-dihydroxymintlactone (**188**) against *Caenorhabditis elegans* was $25 \mu\text{g mL}^{-1}$. This was the first compound in the *p*-menthane group reported from a basidiomycete (Stadler et al. 1995).

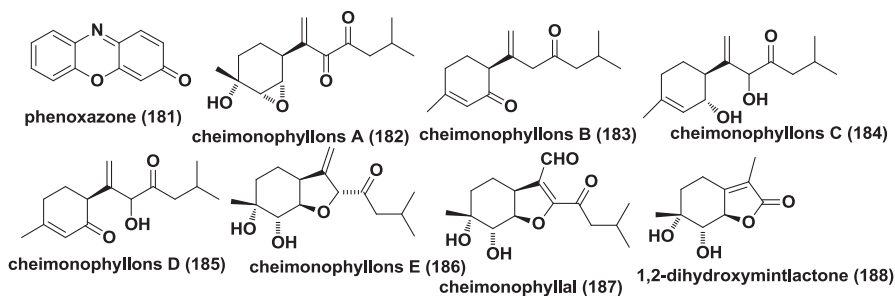


Table 7.3 Nematode-toxic basidiomycete and their nematocidal compounds

Species	Test nematodes	Nematicidal compounds	References
<i>Agaricus arvensis</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Amanita excelsa</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>A. fulva</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>A. japonica</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>A. rubescens</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>A. virosa</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Amauroderma brunneopitius</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Auricularia auricular</i>	<i>B. xylophilus</i>	–	Zhang and Zhao (2003)
<i>Boletus albus</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>B. fratremus</i>	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Boletus</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Calocera viscosa</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>C. excipuliformis</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Calocybe gambosa</i>	<i>M. incognita</i>	Phenoxazone	Schlunegger et al. (1976); Mayer (1995)
<i>C. tubaeformis</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Cheimonophyllum candidissimum</i>	<i>C. elegans</i>	Cheimonophyllal, Cheimonophyllons A, B, C, D and E, 1,2-dihydroxymintlactone	Stadler et al. (1994a, b); Stadler et al. (1995)
<i>Chroogomphus rutilus</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Clavulinopsis corniculata</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Clitocybe</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Clitocybe odora</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Clitocybula oculatus</i>	<i>Aphelenchoides</i> sp.	–	William et al. (1998)
<i>Collybia acervata</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>C. confluenta</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>C. dryophila</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Coltricia</i> sp.	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Coprinus elastophyllus</i>	<i>P. redivivus</i>	—	Liu (2005)
<i>C. comatus</i>	<i>P. redivivus</i> , <i>M. arenaria</i> <i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-</i> <i>ditis</i> sp., <i>A. basseyi</i>	4,6-dimethoxyisobenzofuran-1(3 <i>H</i>)-one, 5-methylfuran-3-carboxylic acid, 5-hydroxy-3,5-dimethylfuran-2(5 <i>H</i>)- one, 4,6-dihydroxybenzofuran-3(2 <i>H</i>)- one, 3-formyl-2,5-dihydroxybenzyl acetate, 5-hydroxy-3-(hydroxymethyl)- 5-methylfuran-2(5 <i>H</i>)-one, 4,6-dihydroxyisobenzofuran-1,3-dione	Luo et al. (2007); Chen et al. (2010)
<i>C. disseminatus</i>	<i>P. redivivus</i>	—	Liu (2005)
<i>C. erythrocephalus</i>	<i>P. redivivus</i>	—	Liu (2005)
<i>C. micaceus</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-</i> <i>ditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>C. plicatilis</i>	<i>P. redivivus</i>	—	Liu (2005)
<i>Coprinus</i> sp.	<i>P. redivivus</i>	—	Liu (2005)
<i>C. verticillatus</i>	<i>P. redivivus</i>	—	Liu (2005)
<i>C. xanthotrix</i>	<i>P. redivivus</i>	Xanthothone, 7,8,11-drimanetriol, 2-(1 <i>H</i> -pyrrol-1-yl) ethanol	Liu et al. (2008)
<i>Cyathus intermedius</i>	<i>M. arenaria</i>	—	Zhao (2004)
<i>C. pallidus</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Cyathus</i> sp.	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Daedalea biennis</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-</i> <i>ditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>Dichomitus squalen</i>	<i>B. xylophilus</i>	2 β , 13-dihydroxyledol	Huang et al. (2004)
<i>Fomitopsis pinicola</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-</i> <i>ditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Ganoderma</i> sp.	<i>P. redivivus</i>	—	Li (2005)
<i>Gastroboletus</i> sp.	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Galiella rufa</i>	<i>C. elegans</i>	5-(2 <i>E</i>)-2-buten-1-ylidene-3-(1 <i>E</i>)-1-pro-pen-1-yl-2-(5 <i>FF</i>)-furanone	Hautzel and Anke (1990); Köpcke et al. (2002)
<i>Gloeophyllum trabeum</i>	<i>M. incognita</i>	—	Zhang and Zhao (2003)
<i>Hericium coralloides</i>	<i>B. xylophilus</i>	—	Xiang and Feng (2001)
<i>Hexagonia tenuis</i>	<i>C. elegans</i>	Linoleic acid, Oleic acid, Palmitic acid	Chen et al. (2010)
<i>Hohenbuehelia grisea</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-ditis</i> sp., <i>A. basseyi</i>	—	Stadler and Sterner (1998)
<i>Hydnum rufescens</i> (injured)	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>Hygrophorus mesotephrus</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>H. albicans</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. amoenum</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. appendiculatum</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhab-ditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>H. heterocystidium</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. mediotuburiensis</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. mutatum</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. obtusiforame</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. pallidum</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. piceae</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>H. populneum</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. pustulatus</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>H. radula</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. setigerum</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>H. typhicola</i>	<i>Aphelenchooides</i> sp.	—	Tzean and Liou (1993)
<i>Irpex lacteus</i>	<i>C. elegans</i>	5-pentyl-2-furaldehyd, 5-(4-pentenyl)-2-furaldehyd, Methyl	Hayashi et al. (1981)
	<i>A. basseyi</i>	3- <i>p</i> -anisoxypropionate	
	<i>M. incognita</i>	—	

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Laccaria amethystine</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Lachnella</i> sp. 541	<i>M. incognita</i>	Marasmic acid	Kupka et al. (1983); Mayer (1995)
<i>L. villosa</i>	<i>M. incognita</i>	Marasmic acid	Sterner et al. (1985); Mayer (1995)
<i>Lactarius deliciosus</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>L. deterrimus</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. helvus</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. mitissimus</i>	<i>C. elegans</i>	Lactarorufin A and B, Furantriol	Daniewski et al. (1990); Stadler and Sterner (1998)
<i>L. porrninsis</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. rufus</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. torminosus</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. trivialis</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. vellereus</i>	<i>C. elegans</i>	Isovelleral	Sterner et al. (1985); Mayer (1995); Hansson et al. (1995)
<i>Lampteromyces japonicus</i>	<i>M. incognita</i>	–	Mo et al. (2000); Dong et al. (2000)
<i>L. unuunescens</i>	<i>P. redivivus</i>	–	Mo et al. (2000)
<i>Leatiporus sulphureus</i>	<i>P. redivivus</i>	–	Zhao (2004)
<i>Lentinus edodes</i>	<i>B. xylophilus</i>	–	Zhang and Zhao (2003)
<i>L. lepideus</i>	<i>B. xylophilus</i>	–	Zhang and Zhao (2003)
<i>L. similis</i>	<i>B. xylophilus</i>	–	Chen et al. (2010)
<i>Lenzites trabea</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Zhang and Zhao (2003)
<i>Lepista gifu</i> (injured)	<i>B. xylophilus</i>	–	Stadler and Sterner (1998)
<i>L. inversa</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. irina</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. nebularis</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. nuda</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>L. personata</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Leucopaxillus albissimus</i> var. <i>paradoxus</i> form <i>albiformis</i>	<i>N. braziliensis</i>	2-aminoquinoline	Pfister (1988)
<i>Limacella illinita</i>	<i>C. elegans</i>	Illinitone A	Gruhn et al. (2007)
<i>Lycopodon pyriforme</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>L. pusillus</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Marasmius alliaceus</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>M. conigenus</i>	<i>M. incognita</i>	Marasmic acid	Kavanagh et al. (1949); Mayer (1995)
<i>M. wynnei</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Melanoleuca cognate</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>M. melaleuca</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Meripilus giganteus</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Mutinus caninus</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Mycena pura</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>M. septia</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Mycena</i> sp.	<i>C. elegans</i>	Mycenon	Hautzel et al. (1990); Stadler (1993)
<i>Nidularia</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Omphalotus olearius</i>	<i>M. incognita</i> , <i>C. elegans</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	Omphalotin A, B, C and D	Mayer et al. (1997); Stener et al. (1997); Büchel et al. (1998); Anke et al. (1999)
<i>Oudemansiella longipes</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>O. platyphylla</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Pentophora laeta</i>	<i>M. incognita</i>	Marasmic acid	Kupka et al. (1983); Mayer (1995)
<i>Phanocollyleio</i> sp.	<i>B. xylophilus</i>	–	Zhao (2004)
<i>Plerotus cericautus</i>	<i>P. redivivus</i>	–	Li et al. (2001)
<i>P. citrinopileatus</i>	<i>P. redivivus</i>	–	Li et al. (2001)
<i>P. colombinus</i>	<i>P. redivivus</i>	–	Li et al. (2001)

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>P. cornuopitae</i>	<i>P. redivivus</i>	—	Thorn and Barron (1984)
<i>P. corticatus</i>	<i>P. redivivus</i>	—	Chen et al. (2010)
<i>P. cystidiosus</i>	<i>P. redivivus</i>	—	Dong et al. (2010)
<i>P. dryinus</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. eryngii</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. euosmus</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. ferulae</i>	<i>P. redivivus</i>	Cheimonophyllon E, 5-hydroxymethyl-furancarbaldehyde	Li et al. (2001, 2007)
<i>P. florrida</i>	<i>B. xylophilus</i>	—	Li et al. (2001)
<i>P. levis</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. memberancens</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. ostreatus</i>	<i>P. redivivus</i>	<i>Trans</i> -2-decenedioic acid	Thorn and Barron (1984); Barron and Thorn (1987); Kwok et al. (1992); Stadler et al. (1994a)
<i>P. pulmonarius</i>	<i>B. xylophilus</i>	—	Stadler et al. (1994c)
	<i>C. elegans</i>	S-cortiolic acid, Linoleic acid, <i>p</i> -anisaldehyde, <i>p</i> -anisyl alcohol, 1-(4-methoxyphenyl)-1,2-propanediol, 2-hydroxy-(4'-methoxy)-propiophenone	Sharma (1994); Li et al. (2001)
<i>P. sajorcaju</i>	<i>P. redivivus</i>	—	Li et al. (2001)
	<i>A. campositicola</i>	—	Li et al. (2001)
<i>P. salmonseostraminus</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. sapidis</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. shodophyllus</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. spodoleucus</i>	<i>P. redivivus</i>	—	Li et al. (2001)
<i>P. strigosus</i>	<i>P. redivivus</i>	—	Thorn and Barron (1984)
<i>P. subareolatus</i>	<i>P. redivivus</i>	—	Thorn and Barron (1984)
<i>P. tuberregium</i>	<i>P. redivivus</i>	—	Hibbett and Thorn (1994)
<i>Pluteus fulve</i>	<i>B. xylophilus</i>	—	Zhao (2004)

Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>Polyporus sulphureus</i>	<i>M. incognita</i> <i>C. elegans</i> <i>B. xylophilus</i> <i>B. xylophilus</i> <i>P. redivivus</i> <i>M. arenaria</i>	Beauvericin – 2,4,6-triacetylenic octane diacid	Deol et al. (1978); Maye (1995); Shimada et al. (2010) Zhang and Zhao (2003) Li et al. (2005)
<i>Porphyrellus pseudoscaber</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Psathyrella velutina</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Pseudocolus fusiformis</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Pterula multifida</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>Pycnoporus cinnabarinus</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>P. sanguineus</i>	<i>M. incognita</i>	Phenoxazone	Gill (1994); Mayer (1995)
<i>Russula albonigra</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>R. alutacea</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>Russula cuprea</i>	<i>C. elegans</i> <i>M. incognita</i>	Isovelleral	Mayer (1995); Clerkyzio and Sterner (1997)
<i>R. decolorans</i>	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>R. depalens</i>	<i>B. xylophilus</i>	–	Kavanagh et al. (1949)
<i>R. emetica</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>R. feltea</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>R. nigricans</i> (injured)	<i>C. elegans</i>	–	Stadler and Sterner (1998)
<i>R. ochroleuca</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)
<i>R. sanguinea</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	–	Chen et al. (2010)

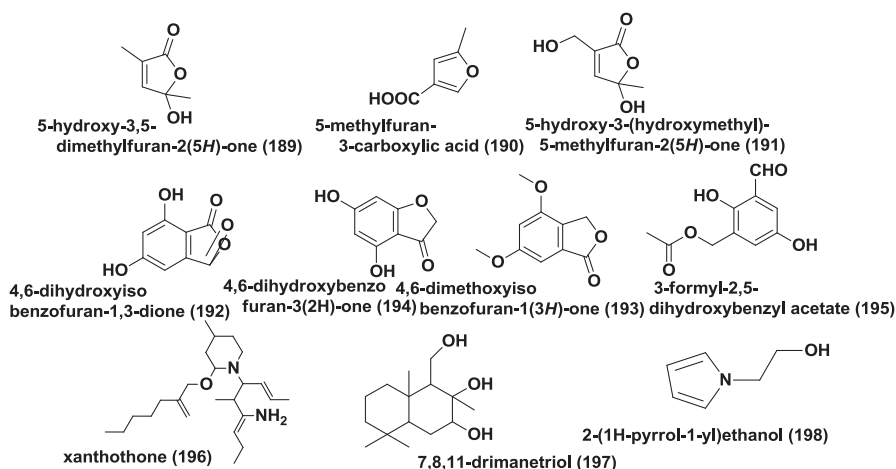
Table 7.3 (continued)

Species	Test nematodes	Nematicidal compounds	References
<i>R. virescens</i>	<i>B. xylophilus</i> , <i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	—	Zhao (2004); Chen et al. (2010)
<i>Schizophyllum commune</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>Sinotermitomyces carnosus</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Sparassis crispa</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>Spongipellis spumeus</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>Stereum</i> sp. 8954	<i>P. redivivus</i>	3,5-dihydroxy-4-(3-methyl-but-2-enyl)-benzene-1,2-dicarbaldehyde, Butyl 2,4-dihydroxy-6-methylbenzoate	Li et al. (2006)
<i>Stereum</i> sp. CCTCC AF 207024	<i>P. redivivus</i>	Stereumins A, B, C, D and E	Li et al. (2008)
<i>Stropharia aeruginosa</i> (injured)	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>Thelephora gambajun</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Trametes cinnabarina</i>	<i>M. incognita</i> , <i>H. glycines</i> , <i>Caenorhabditis</i> sp., <i>A. basseyi</i>	—	Chen et al. (2010)
<i>Trametes</i> sp.	<i>P. redivivus</i>	—	Li (2005)
<i>Tremella</i> sp.	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Trichaptium</i> sp.	<i>P. redivivus</i>	—	Li (2005)
<i>Tricholoma columbetta</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>T. flavovirens</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>T. fuva</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>T. terreum</i> (injured)	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>T. ustale</i>	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>Tricholomopsis</i> sp.	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Tylophilus scabrissus</i>	<i>B. xylophilus</i>	—	Zhao (2004)
<i>Xerocomus chrysenteron</i> (injured)	<i>C. elegans</i>	—	Stadler and Sterner (1998)
<i>X. rubellus</i> (injured)	<i>C. elegans</i>	—	Stadler and Sterner (1998)

No nematicidal compounds were reported from the fungus

Nematicidal Metabolites from *Coprinus Comatus* and *C. Xanthothrix*

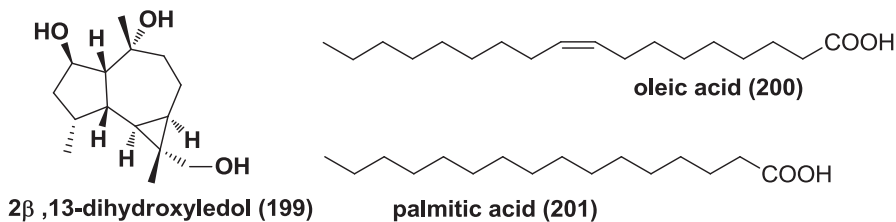
Coprinus comatus has been proven to be active against several nematodes (Luo et al. 2007; Chen et al. 2010). A new furan 5-hydroxy-3-(hydroxymethyl)-5-methylfuran-2(5H)-one (**189**), two known furan compounds 5-methylfuran-3-carboxylic acid (**190**) and 5-hydroxy-3,5-dimethylfuran-2(5H)-one (**191**), as well as three benzofurans including a new 4,6-dihydroxyisobenzofuran-1,3-dione (**192**) and known 4,6-dimethoxyisobenzofuran-1(3H)-one (**193**), and 4,6-dihydroxybenzofuran-3(2H)-one (**194**), together with 3-formyl-2,5-dihydroxybenzyl acetate (**195**) were all obtained from *Coprinus comatus* (Luo et al. 2007). All compounds had nematicidal activities against *Panagrellus redivivus* and *Meloidogyne arenaria* at 400 ppm. The LD₅₀ values of 5-methylfuran-3-carboxylic acid (**190**) and 5-hydroxy-3,5-dimethylfuran-2(5H)-one (**191**) were 100 ppm at 12 h (Luo et al. 2007). *Coprinus xanthothrix* produced three nematicidal compounds including a new compound xanthothone (**196**) and two known compounds 7,8,11-drimanetriol (**197**) and 2-(1H-pyrrol-1-yl) ethanol (**198**) (Liu et al. 2008). The LD₅₀ of these compounds against *Panagrellus redivivus* and *Meloidogyne arenaria* was 125–250 ppm (Liu et al. 2008).



Nematicidal Metabolites from *Dichomitus Squalens* and *Hericium Coralloides*

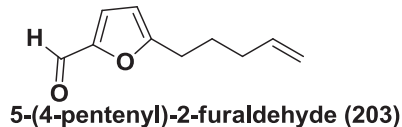
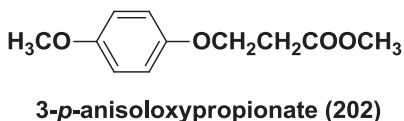
A new aromadendrane, 2 β ,13-dihydroxyledol (**199**) was isolated from the solid mycelial cultures of *Dichomitus squalens* and this compound exhibited potent activity against *Bursaphelenchus xylophilus* with LC_{50 at} 35.6 $\mu\text{g mL}^{-1}$ (Huang et al. 2004). A nematicidal fatty acid mixture containing linoleic acid (**7**), oleic acid (**200**), and palmitic acid (**201**) were obtained from the culture of *Hericium coralloides*. This

mixture showed a nematicidal activity against *Caenorhabditis elegans* (Xiang and Feng 2001). These fatty acids have also obtained from several other taxa.



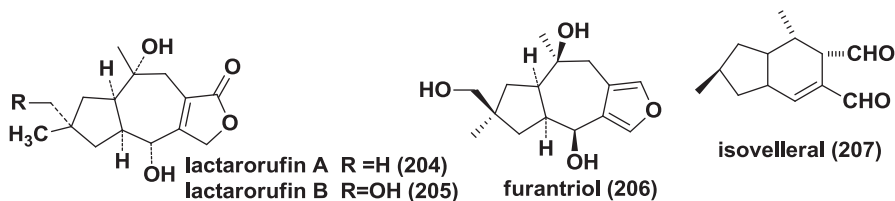
Nematicidal Metabolites from Irpex Lacteus

A new aromatic compound methyl 3-*p*-anisloxypropionate (202) and a new furan compound 5-(4-pentenyl)-2-furaldehyde (203) were isolated from *Irpex lacteus*. The LD₅₀ value of the two compounds against *A. besseyi* was 25 μg mL⁻¹ and 50 μg mL⁻¹ respectively (Hayashi et al. 1981). In addition, 5-pentyl-2-furaldehyde (167) was also isolated from *Irpex lacteus* (Hayashi et al. 1981). The compound was obtained from an unidentified ascomycete (Anke et al. 1995) and an unidentified fungal strain Kyu-W63 (Koitabashi et al. 2004).



Nematicidal Metabolites from Lactarius Mitissimus, L. Vellereus and Russula Cuprea

Three furan sesquiterpenoids lactarorufin A (204), lactarorufin B (205) and furantriol (206) were isolated from *Lactarius mitissimus* and the all three compounds showed nematicidal activities against *Caenorhabditis elegans* with LD₅₀ values at around 100 μg mL⁻¹ (Daniewski et al. 1990; Stadler and Sterner 1998). Marasmane sesquiterpene isovelleral (207) could be found in injured fruiting bodies of the mushroom *Lactarius vellereus*. This compound was considered a key component of the chemical defense system against nematodes in this mushroom species (Sterner et al. 1985; Hansson et al. 1995). Isovelleral (207) showed nematicidal activity against *Meloidogyne incognita* with LD₃₀ at 100 μg mL⁻¹ and against *Caenorhabditis elegans* with LD₅₀ at 50 μg mL⁻¹ (Mayer 1995). Isovelleral (207) has also been found in injured fruiting bodies of other mushrooms such as *Russula cuprea* (Clerkyjzio and Sterner 1997).

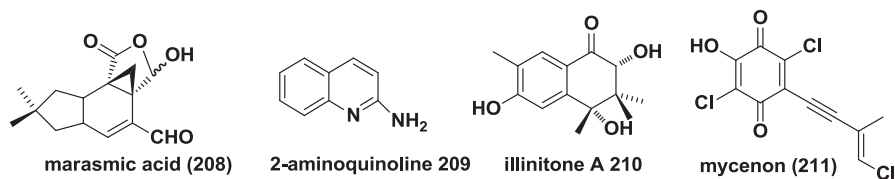


Nematicidal Metabolites from Lachnella Villosa, Marasmius Conigenus and Peniophora Laeta

Sesquiterpene marasmic acid (**208**) was reported to have a weak activity against *M. incognita* by Mayer (1995). Marasmic acid (**208**) was originally isolated from *Marasmius conigenus* (Kavanagh et al. 1949). Subsequently, marasmic acid (**208**) was obtained from several other basidiomycetes including *Lachnella villosa*, *Lachnella* sp. and *Peniophora laeta* (Kupka et al. 1983; Sterner et al. 1985).

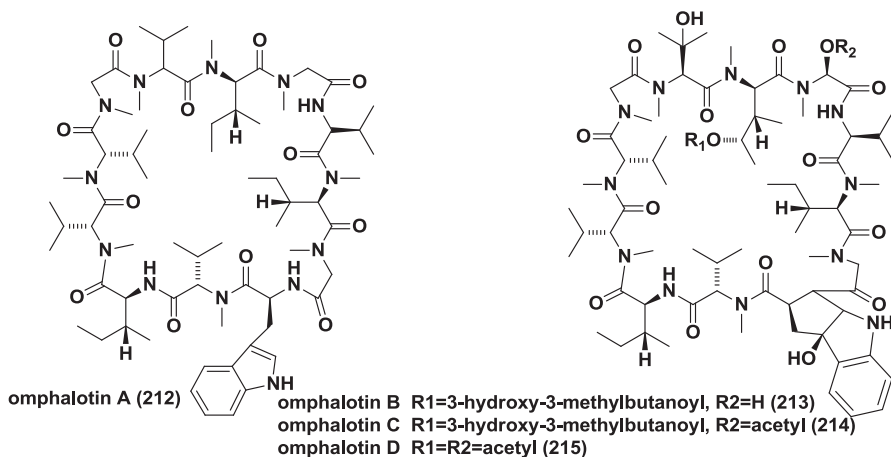
Nematicidal Metabolites from Leucopaxillus Albissimus Var. Paradoxus form Albiformis, Limacella Illinita and Mycena Sp.

A novel alkaloid 2-aminoquinoline (**209**) was isolated from the fruiting bodies of *Leucopaxillus albissimus* var. *paradoxus* form *albiformis* (Pfister 1988). At a concentration of 50 $\mu\text{g mL}^{-1}$, 2-aminoquinoline (**209**) caused 50% motility, 74% viability, and 52% cast formation reductions in the nematode *Nippostrongylus braziliensis* (Pfister 1988). A new compound illinitone A (**210**) was obtained from fermentations of *Limacella illinita*, which exhibited nematicidal activity on *C. elegans* with $\text{IC}_{50\text{at}}$ 25 $\mu\text{g mL}^{-1}$ (Gruhn et al. 2007). Mycenon (**211**) is a chlorinated benzoquinone derivative isolated from the culture broth of a basidiomycete, *Mycena* sp. TA 87202 (Hautzel et al. 1990). It was shown to be active against *Caenorhabditis elegans*, with an $\text{LD}_{50\text{at}}$ 50 $\mu\text{g mL}^{-1}$ (Stadler 1993).



Nematicidal Metabolites from Omphalotus Olearius

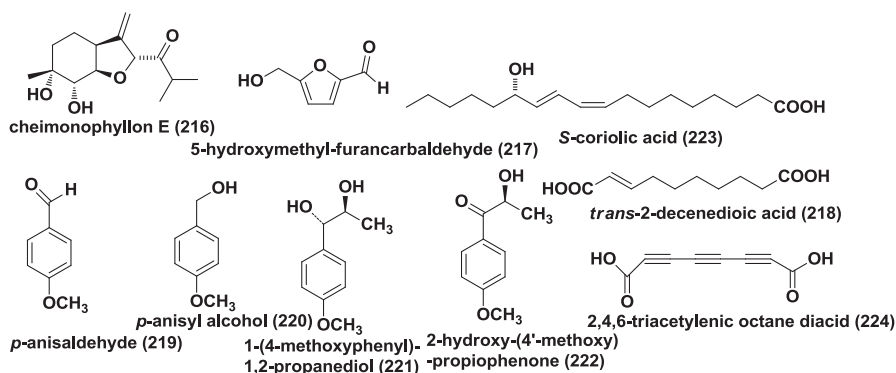
Peptidal compounds omphalotin A (**212**) and its derivatives omphalotin B (**213**), C (**214**) and D (**215**) were obtained from *Omphalotus olearius*. All compounds possessed strong nematicidal activities against nematodes (Mayer et al. 1997; Stener et al. 1997; Büchel et al. 1998; Anke et al. 1999). Omphalotin A (**212**), a cyclic dodecapeptide, was highly toxic (LD_{90} : 0.76 μ M) towards *Meloidogyne incognita*. However, it was approximately 50 times less active against *Caenorhabditis elegans* (LD_{90} : 38 μ M) (Stener et al. 1997; Büchel et al. 1998). The corresponding LD_{90} values for the commercially available nematicide ivermectin were 4.6 μ M and 0.46 μ M respectively against *Meloidogyne incognita* and *Caenorhabditis elegans*. Omphalotin A (**212**) lacks any antimicrobial and phytotoxic activities, and contains only weak cytotoxic activity, making it a potentially useful nematicide. The three derivatives omphalotin B (**213**), C (**214**) and D (**215**) all possessed nematicidal activities similar to that of omphalotin A (Anke et al. 1999). Although the yield of these active compounds is low, the strong nematicidal activity showed it is possible to find new natural nematicidals from products of fungi.



Nematicidal Metabolites from Pleurotus Ferulae, P. Ostreatus and P. Pulmonarius

Pleurotus ferulae was shown to be active against *Bursaphelenchus xylophilus* and *Panagrellus redivivus* (Li et al. 2001, 2007) and two nematicidal compounds cheimonophyllon E (**216**) and 5-hydroxymethyl-furancarbaldehyde (**217**) were isolated from the taxon. *Pleurotus ostreatus* was also reported to be active against nematodes (Thorn and Barron 1984, 1987; Kwok et al. 1992; Stadler et al. 1994a). *Trans*-2-decenedioic acid (**218**) was isolated from *P. ostreatus* as the principal nematicide

(Kwok et al. 1992). The compound could immobilize 95% of the nematode *Panagrellus redivivus* at a concentration of 300 ppm (Kwok et al. 1992). Four aromatics *p*-anisaldehyde (**219**), *p*-anisyl alcohol (**220**), 1-(4-methoxyphenyl)-1,2-propanediol (**221**) and 2-hydroxy-(4'-methoxy)-propiophenone (**222**) were isolated from *Pleurotus pulmonarius* (Stadler et al. 1994a). The LD₅₀ values of these compounds against *Caenorhabditis elegans* were all similar, at about 100 ppm (Stadler et al. 1994a). Extracts of the mushroom *Pleurotus pulmonarius* contained a nematocidal fatty acid *S*-coriolic acid (**223**). This fatty acid could kill the nematode *Caenorhabditis elegans* with an LD₅₀ value at 10 ppm (Koitabashi et al. 2004). In addition, linoleic acid (**7**) was also found from the fungus (Stadler et al. 1994).



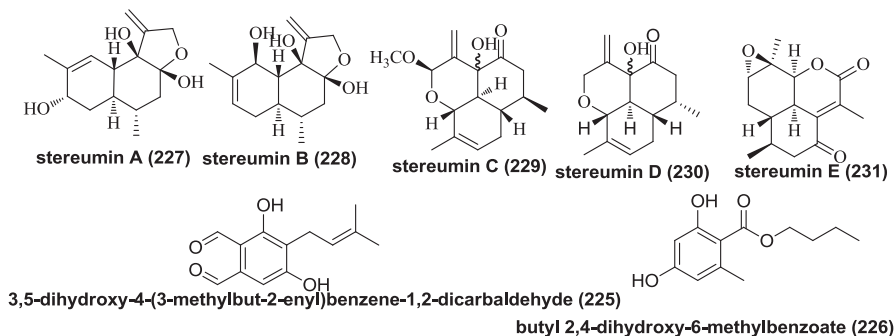
Nematicidal Metabolites from *Polyporus Sulphureus* and *Poria Cocos*

The cyclic depsipeptide beauvericin (**38**) was active against *Meloidogyne incognita*, *Caenorhabditis elegans* and *Bursaphelenchus xylophilus*. This peptide beauvericin (**39**) has also been isolated from several ascomycetes, but also was isolated from the basidiomycete *Polyporus sulphureus* (Deol et al. 1978). *Polyporus cocos* is a widely used traditional medicinal fungus, and produces a novel alkyne 2,4,6-triacetylenic octane diacid (**224**) found capable of killing 83.9% of *Meloidogyne arenaria* and 73.4% of *Panagrellus redivivus* at 500 ppm within 12 h (Li et al. 2005).

Nematicidal metabolites from *Stereum* spp.

Stereum sp. 8954 produced two new aromatics, 3,5-dihydroxy-4-(3-methyl-but-2-enyl)-benzene-1,2-dicarbaldehyde (**225**) and butyl 2,4-dihydroxy-6-methylbenzoate (**226**). 3,5-Dihydroxy-4-(3-methyl-but-2-enyl)-benzene-1,2-dicarbaldehyde (**225**) could kill about 90% of *Panagrellus redivivus* at 100 ppm in 12 h, while butyl 2,4-dihydroxy-6-methylbenzoate (**226**) was less active, capable of killing about 50% of the same nematode at 200 ppm in 24 h (Li et al. 2006). Five cadinane sesquiterpenoids, named stereumin A (**227**), B (**228**), C (**229**), D (**230**) and E (**231**) were isolated from the culture broth of the fungal strain *Stereum* sp. CCTCC AF

207024. The five compounds showed nematicidal activities against the nematode *P. redivivus* at 400 mg L⁻¹. Stereumin C (**229**) and stereumin D (**230**) killed 84.4% and 94.9% of *P. redivivus* respectively in 48 h (Li et al. 2008).



Conclusions

More than 200 nematicidal compounds have been obtained from fungi, and their diversified structures mainly belong to alkaloids, quinones, isoeoxydons, pyrans, furans, peptides, macrolides, terpenoids, fatty acids, diketopiperazines, phthalenes, simple aromatics and other kinds of compounds. Among these nematicidal compounds, about 60% are new natural isolates, which implies that searching for new compounds by screening with different models is an efficient method. Secondary metabolites in fungi are abundant, e.g., 24 compounds including 15 new isolates with nematicidal activities have been isolated from the cultures of *Lachnum papyraceum* and elucidated to be isoeoxydon, isocoumarin, mycorrhizin and furan compounds (Stadler and Anke 1993a, b; Stadler et al. 1995a, b, c, d, e; Shan et al. 1996), and six new sesquiterpenes and a novel monoterpene possessing nematicidal activity are fungal metabolites isolated from cultures of the basidiomycete *Cheimonophyllum candidissimum* (Stadler et al. 1995). Fungi are therefore a major source of biologically active natural products.

Many attempts have been made to find potent nematicidal substances. Ivermectin isolated from actinomycete is a commercially available nematicide up to now, but no major commercial product based on nematode-toxic fungi and the compounds isolated from fungi have been developed at present. Sharma (1994) reported that broth cultures of *Pleurotus sajor-caju* can immobilize the mushroom nematode in *Agaricus bisporus*. Xiang et al (2000) reported on the effects of *Pleurotus ostreatus* on the peanut root-knot nematode *Meloidogyne arenaria* in a greenhouse. The experiment showed that *Pleurotus ostreatus* could markedly lower *Meloidogyne arenaria* infection numbers and peanut root knot disease was also reduced by 87–94%. The key factor affecting control effectiveness was the application time of *Pleurotus ostreatus* in the soil (Xiang and Feng 2000). The potential of oyster mushrooms to

attack and kill *Heterodera schachtii* was studied, and the result showed some mushrooms could significantly control the nematode (Palizi et al. 2009). Omphalotin A, B, C and D isolated from *Omphalotus olearius* had similar nematocidal activity to the commercially available nematicide ivermectin (Mayer et al. 1997; Stener et al. 1997; Büchel et al. 1998; Anke et al. 1999). It is necessary to search for nematode-toxic fungi and their active compounds to exploit novel nematicides.

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