PERGAMON

Phytochemistry 60 (2002) 431–435

PHYTOCHEMISTRY

www.elsevier.com/locate/phytochem

Hericenols A–D and a chromanone from submerged cultures of a *Stereum* species

Josiah Ouma Omolo[a], Heidrun Anke[a,b,*], Olov Sterner[c,*]

[a]*LB Biotechnology, University of Kaiserslautern, Paul-Ehrlich-Str. 23, D-67663 Kaiserslautern, Germany*
[b]*Institute for Biotechnology and Drug Research, IBWF, Erwin-Schroedinger-Str. 56, D-67663, Kaiserslautern, Germany*
[c]*Department of Organic and Bioorganic Chemistry, Lund University, PO Box 124, SE-221 00 Lund, Sweden*

Received 18 September 2001; received in revised form 11 February 2002

Abstract

Extracts of submerged cultures of a *Stereum* species afforded four new pentasubstituted phenolic compounds, named hericenols A, B, C, and D (**1**–**4**), 6-hydroxymethyl-2,2-dimethylchroman-4-one (**5**) and the known erinapyrone C. Hericenol A (**1**) showed weak antimicrobial activity while hericenol C (**3**) was weakly cytotoxic. The structures of the metabolites were determined by spectroscopic techniques.

Keywords: Stereum species; Basidiomycete; Hericenols A–D; 6-Hydroxymethyl-2,2-dimethylchroman-4-one; Erinapyrone C

1. Introduction

Members of stipitate steroid fungi belonging to the Stereaceae family have predominantly tropical or subtropical distribution and are often found associated with woody debris, rotting trunks and sometimes on buried dead wood (Reid, 1965). Not many tropical basidiomycetes have been investigated for the production of secondary metabolites. During our continuing search for biologically active secondary fungal metabolites, we found that extracts from submerged cultures of a *Stereum* sp. (strain 99123 collected in Kenya) exhibited antimicrobial and cytotoxic activities. The isolation of the active compounds led to five new metabolites. Four of them were named hericenols A (**1**), B, (**2**), C (**3**), and D (**4**), as they share the carbon skeleton and the oxidation pattern with the hericenones reported both from submerged cultures (Lorenzen and Anke, 1998) and from fruiting bodies (Kawagishi et al., 1990, 1991, 1993) of the edible mushroom *Hericium erinaceum*. In addition, 6-hydroxymethyl-2,2-dimethylchromanone (**5**), a new benzopyranone, and the already known erinapyrone C (**6**) (Arnone et al., 1994) were isolated. This paper describes the isolation, structure elucidation and biological activities of the new metabolites **1–5**.

2. Results and discussion

The antimicrobial activity of the extracts of the culture broth of *Stereum* sp., 99123, grown in YMG medium, reached a maximum after 6 days of fermentation, and the metabolites were isolated as described in the experimental section. The amounts isolated were rather small, around or below 1 mg of each compound per l culture filtrate (see the experimental section for details).

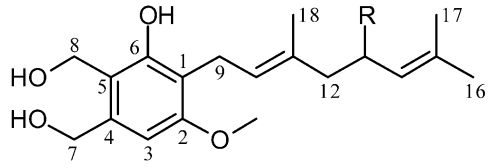
The structures of the compounds (see Fig. 1) were determined by NMR spectroscopy and mass spectrometry. Erinapyrone C was identified by comparing the data with those published (Arnone et al., 1994). Both NMR and MS data for the new compounds were consistent with the molecular formulae; $C_{19}H_{28}O_4$ for hericenol A (**1**), $C_{19}H_{28}O_5$ for hericenol B (**2**), $C_{20}H_{30}O_5$ for hericenol C (**3**) $C_{21}H_{32}O_5$ for hericenol D (**4**) and $C_{12}H_{14}O_3$ for 6-hydroxymethyl-2,2-dimethyl-chromanone (**5**), all having 6 degrees of unsaturation.

^{1}H NMR and ^{13}C NMR data for hericenol A (**1**) and B (**2**) (see Tables 1 and 2) are similar, and the major difference is that a non-substituted methylene group in **1**

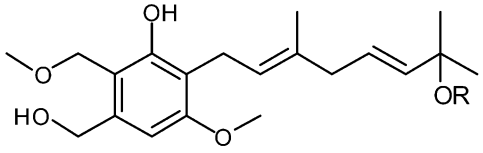
* Corresponding authors. Tel:. +49-631-205-2615; fax: +40-631-205-2999 (H. Anke), tel.: +46-46-222-8213; fax +46-46-222-8209 (O. Sterner).

E-mail addresses: anke@ibwf.de (H. Anke), olov.sterner@orgk2.lth.se (O. Sterner).

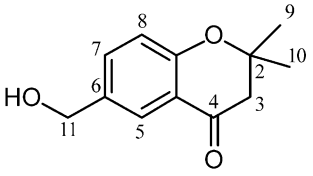
0031-9422/02/$ - see front matter
PII: S0031-9422(02)00070-5



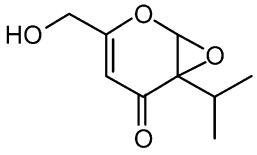
1 R = H
2 R = OH



3 R = H
4 R = CH_3



5



6

Fig. 1. Structures of secondary metabolites investigated. **1**, 5-(*E*)-but-2-enylidene-3-propyl-5*H*-furan-2-one; **2**, 5-(*E*)-but-2-enylidene-3-(*E*)-propenyl-5*H*-furan-2-one; **3**, 5-(*E*)-buta-1,3-dienyl-3(*E*)-propenyl-5*H*-furan-2-one; **4**, 5-(*E*)-but-3-enyl-3-(*E*)-propenyl-dihydrofuran-2-one; **5**, (-)-pregaliellalactone; **6**, (+)-deoxygaliellalactone; **7**, (-)-galiellalactone; **8**, 6-pentyl-4-methoxy-6-pyran-2-one; **9**, 6-(1-hydroxypentyl)-4-methoxy-6-pyran-2-one.

appears to be hydroxylated in **2**. The data are consistent with a pentasubstituted aromatic system, with one hydroxyl group, two hydroxymethyls, one methoxy group and a carbon chain containing no (hericenol A) or one (hericenol B) oxygen and starting with a methylene group (C-9). The complete structure of the two compounds was determined based on the long-range ^{1}H–^{13}C correlations observed in HMBC experiments. The methylene protons 9-H_2 correlate to C-1, C-2 and C-6, the methoxy group is situated on C-2 according to the HMBC correlation between the –OCH_3 protons (a singlet integrating for three protons at 3.82 ppm in the ^{1}H NMR spectrum of **1** and 3.80 ppm in the ^{1}H NMR spectrum of **2** and correlating (in the HMQC spectrum) with a signal at 55.7 ppm in the ^{13}C NMR spectra of both compounds) and C-2, and the two hydroxymethyl groups correlate to C-3, C-4 as well as C-5, and C-4, C-5 as well as C-6, respectively. These correlations determine the pattern of the aromatic substituents, and this was confirmed by the NOESY correlations between 3-H and 2-OCH_3 as well as 7-H_2 and the HMBC correlations between 3-H and C-1, C-2, C-5 and C-7. The ^{1}H–^{1}H coupling between 9-H_2 and 10-H attach the trisubstituted C-10/C-11 double bond to C-9 and HMBC correlations from the C-18 methyl protons to C-10, C-11 and C-12 show that the chain continues with an additional methylene group. The *E* configuration of the double bond was determined by the NOESY correlation between 10-H and 12-H_2. In hericenol A (**1**), the spin system 12-H_2, 13-H_2 and 14-H demonstrates that the final double bond is between C-14 and C-15, and puts the two remaining methyls on C-15. Both 16-H_3 and 17-H_3 give HMBC correlations to C-14 as well as C-15, in

Table 1
^{1}H (500 MHz) NMR data for hericenol A–D (**1–4**) in $CDCl_3$. The chemical shifts are given in ppm relative to the solvent signal (7.26 ppm), and the coupling constants (*J*) in Hz

H	**1** (*δ*; *J*)	**2** (*δ*; *J*)	**3** (*δ*; *J*)	**4** (*δ*; *J*)
3	6.48; *s*	6.43; *s*	6.46; *s*	6.46; *s*
7	4.66; *s*	4.58; *s*	4.60; *s*	4.60; *s*
8	4.86; *s*	4.82; *s*	4.72; *s*	4.75; *s*
9	3.42; *d*; 7.1	3.41; *d*; 7.1	3.39; *d*; 7.1	3.39; *d*; 7.1
10	5.22; *t*; 7	5.30; *d*; 7.1	5.24; *d*; 7.1	5.26; *d*; 7.1
12	2.03; *t*; 7	2.15; *dd*; 4, 13 2.09; *dd*; 9, 13	2.68; *d*; 6.2	2.70; *d*; 6.8
13	2.10; *dt*;7, 7	4.43; *ddd*;4, 8, 9	5.56; *dd*; 15.7, 6.2	5.50; *dt*;15.7, 6.8
14	5.06; *t*; 7	5.11; *d*; 8.1	5.61; *d*; 15.7	5.41; *d*; 15.7
16	1.67; *s*	1.70; *s*	1.30; *s*	1.24; *s*
17	1.59; *s*	1.68; *s*	1.30; *s*	1.24; *s*
18	1.81; *s*	1.82; *s*	1.76; *s*	1.76; *s*
2-OCH_3	3.82; *s*	3.80; *s*	3.81; *s*	3.81; *s*
6-OH	not obs.	not obs.	7.32; *s*	7.35; *s*
8-OCH_3	–	–	3.44; *s*	3.44; *s*
15-OCH_3	–	–	–	3.13; *s*

Table 2
^{13}C (125 MHz) NMR data for hericenol A-D (**1**–**4**) in $CDCl_3$. The chemical shifts are given in ppm relative to the solvent signal (77.0 ppm)

C^n	**1** (δ)	**2** (δ)	**3** (δ)	**4** (δ)
1	115.9; *s*	116.5; *s*	116.3; *s*	116.3; *s*
2	157.4; *s*	157.4; *s*	157.6; *s*	157.6; *s*
3	103.9; *d*	103.7; *d*	103.6; *d*	103.5; *d*
4	138.0; *s*	137.1; *s*	137.7; *s*	137.6; *s*
5	117.9; *s*	117.5; *s*	114.1; *s*	114.1; *s*
6	155.3; *s*	155.4; *s*	155.5; *s*	155.5; *s*
7	64.3; *t*	64.0; *t*	64.2; *t*	64.2; *t*
8	58.0; *t*	58.6; *t*	68.5; *t*	68.5; *t*
9	22.3; *t*	22.3; *t*	22.2; *t*	22.3; *t*
10	121.8; *d*	126.8; *d*	123.1; *d*	123.2; *d*
11	138.0; *s*	132.6; *s*	135.0; *s*	134.9; *s*
12	39.7; *t*	48.0; *t*	42.4; *t*	42.8; *t*
13	26.5; *t*	65.7; *d*	125.2; *d*	128.4; *d*
14	124.0; *d*	127.3; *d*	139.3; *d*	136.6; *d*
15	131.8; *s*	135.0; *s*	70.7; *s*	74.8; *s*
16	25.7; *q*	25.7; *q*	29.7; *q*	25.8; *q*
17	17.7; *q*	18.1; *q*	29.7; *q*	25.8; *q*
18	16.1; *q*	16.2; *q*	16.1; *q*	16.6; *q*
2-OCH_3	55.7; *q*	55.7; *q*	55.6; *q*	55.6; *q*
8-OCH_3	–	–	58.0; *q*	58.0; *q*
15-OCH_3	–	–	–	50.2; *q*

The multiplicity was determined indirectly from HMQC spectra.

addition to themselves. In both **1** and **2** the chemical shifts for C-16 and C-17 were determined by a combination of NMR methods: NOESY correlations between 14-H and 16-H_3 as well as between 13-H_2 (in **1**) or 13-H (in **2**) and 17-H_3 demonstrated that C-13 and C-16 (as well as 14-H and C-17) are *trans* in both compounds, and HMQC correlations between 16-H_3/17-H_3 and C-16/C-17 determined the chemical shifts. In hericenol B (**2**), C-13 has only one proton and the chemical shifts for 13-H and C-13 show that it is hydroxylated. C-13 in **2** is consequently chiral, and hericenol B (**2**) is optically active. However, with the data presented here it is not possible to determine the absolute configuration of the compound.

The NMR data of hericenol C (**3**) and hericenol D (**4**) are almost identical, indicating that the two compounds are closely related. The only difference is that a hydroxyl group in **3** has been exchanged for a methoxy group in **4**. As with hericenols A and B (vide supra), the structure of the pentasubstituted aromatic system could be established based on HMBC correlations, this was even more facile with **3** and **4** as the signals for the phenolic protons were visible and gave HMBC correlations to C-1, C-5 and C-6. In both **3** and **4** the 8-OH is methylated, as shown by the HMBC correlation between 8-OCH_3 (a singlet integrating for three protons at 3.44 ppm in the ^1H NMR spectrum and correlating (in the HMQC spectrum) with a signal at 58.0 ppm in the ^{13}C NMR spectrum), and C-8. The C-1 substituent is identical to that in hericenol B (**2**) up till C-12, but the final double bond has shifted to C-13/C-14 and is only disubstituted in **3** and **4**. The *E* configuration was determined by the ^1H–^1H coupling constant between 13-H and 14-H. Instead it is C-15 that is hydroxylated (in **3**), and 16-H_3 as well as 17-H_3 give HMBC correlations to this carbon as well as to C-14. In hericenol D (**4**) 15-OH is methylated, as shown by the HMBC correlation between the methoxy protons (a singlet integrating for three protons at 3.13 ppm in the ^1H NMR spectrum and correlating (in the HMQC spectrum) with a signal at 50.2 ppm in the ^{13}C NMR spectrum) to C-15.

6-Hydroxymethyl-2,2-dimethylchromanone (**5**) is structurally related to chromans reported from fruiting bodies of *Hericium erinaceum* (Kawagishi et al., 1993), from submerged cultures of *Lentinus crinitus* (Abraham and Abate, 1995) and even from some plants (Le-Van and Pham, 1981; Lourenco et al., 1981; Roussis et al., 1990). **5** Obviously contains a 1,3,4-trisubstituted benzene, judged from the coupling constants of the three aromatic protons (see Table 2). One of the substituents is a hydroxymethyl group, and the HMBC correlations from its methylene protons to C-6, C-7 and C-8 determine its position. 6-H gives HMBC correlations to the two aromatic carbons C-8 and C-10 (which according to its chemical shift could be substituted with oxygen), as well as to C-11 and C-4. The latter, a ketone, is therefore attached to C-5. On the other side of the keto function is a methylene group, which protons (3-H_2) correlate to C-2, a quaternary oxygenated carbon according to its chemical shift and the HMQC data, to C-4 and to C-5. The protons of the two remaining methyl groups, with identical chemical shifts, correlate to C-2 and C-3, as well as to themselves, and in order to keep within the elemental composition suggested by the MS data an ether link between C-2 and C-10 must be present. The NOESY correlations between 12-H_3 as well as 13-H_3 and 9-H confirm this.

The minimal inhibitory concentrations (MICs) towards bacteria and fungi of the hericenols were determined, but are not presented in detail as none of the compounds can be regarded as potent. Hericenol A (**1**) is the most active, with MICs of 5 μg/ml towards the fungi *Absidia glauca* (+) CBS 101.08, *Mucor miehei* TÜ 284 and *Zygorhynchus moelleri* CBS 111.10, and the Gram positive bacterium *Arthrobacter citreus* ATCC 11624. The cytotoxicity towards different mammalian cells lines was found to be weak, although hericenol C (**3**) is more active than the others with IC_{50} values of 5 μg/ml against COS-7 and Colon 320 cells.

3. Experimental

3.1. General experimental procedures

Preparative HPLC was carried out using JASCO MD910 equipped with diode array detector. UV and IR

were recorded with Perkin Elmer λ16 and Bruker IFS48 spectrometers, respectively. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) were recorded at room temperature with a Bruker ARX500 spectrometer with an inverse multinuclear 5 mm probehead equipped with a shielded gradient coil. The spectra were recorded in $CDCl_3$, and the solvent signals (7.26 and 77.0 ppm, respectively) were used as reference. The chemical shifts (δ) are given in ppm, and the coupling constants (J) in Hz. COSY, HMQC and HMBC experiments were recorded with gradient enhancements using sine shaped gradient pulses. For the 2D heteronuclear correlation spectroscopy the refocusing delays were optimised for $^1J_{CH} = 145$ Hz and $^nJ_{CH} = 10$ Hz. The raw data were transformed and the spectra were evaluated with the standard Bruker XWIN-NMR software (rev. 010101). Mass spectra were recorded with a LC–MS (HP 1100; APCI, negative mode) and a Jeol SX102 (HRFAB, positive mode) spectrometer.

3.2. Producing strain and fermentation

The resupinate fruiting body was collected near Rongo in Kenya on a dead stump of a *Eucalyptus* sp. tree. Mycelial cultures of the fungus, strain 99123, were obtained from basidiospores. The spores were globose to subglobose in shape measuring 2.5–3×5–6 μm. The fruiting body had distinct septate cystidia which were numerous and close to one another. The basidia (5–6×12–15 μm) were 4-spored and were smaller than the cystidia. The hyphae had round encrustation. These observations are in agreement with the description given by Reid (1965) for *Stereum* species. The mycelial culture is deposited in the culture collection of the Department of Biotechnology, University of Kaiserslautern. The fungus was cultured in an YMG medium consisting of glucose (0.4%) yeast extract (0.4%) and malt extract (1.0%) for 6 days. Fermentation was done on a 100 l-scale in a fermenter type U100, Braun, Melsungen. The fungus was grown at 24 °C with stirring (120 rpm) and an aeration rate of 15 l/min.

3.3. Isolation of the metabolites

At the end of fermentation, the culture filtrate (90 l) was separated from the mycelium by filtration. The metabolites were adsorbed on a resin, Mitsubushi HP21, and the resin washed with distilled H_2O. The compounds were eluted stepwise with 50% aq. Me_2CO (2 l) and 100% Me_2CO (2 l). The combined eluents were concentrated under reduced pressure and the remaining aq. phase was extracted four times with an equal volume of EtOAc and concentrated. The final oily extract (10 g) was then subjected to repeated silica gel column chromatography (Silica gel 60, Merck, Darmstadt) followed by preparative HPLC (Nucloesil RP18: 7 μm; 250 × 21 mm, Macherey Nagel) to afford the compounds. The compounds were eluted using a linear gradient of H_2O–MeOH. The compounds were obtained at the following MeOH concentrations: **6**: 20–30%, **5**: 52–60%, **2:** 72–76%, **3:** 76–80%, **1:** 85–89% and **4** directly afterwards. This yielded 25 mg of **1** (0.27 mg/l), 20 mg of **2** (0.22 mg/l), 12 mg of **3** (0.13 mg/l), 40 mg of **4** (0.44 mg/l), 45 mg of **5** (0.50 mg/l) and 150 mg of **6** (1.6 mg/l).

Hericenol A (**1**) (1-hydroxy-5,6-bis(hydroxymethyl)-3-methoxy-2-(3,7-dimethylocta-2,6-dienyl)-benzene) was obtained as a colourless oil. UV (MeOH) λ_{max} (ε): 277 nm (2,100). IR (KBr): 3420, 2925, 1615, 1585, 1455, 1425, 1380, 1320, 1220, 1165, 1115, 1005 and 830 cm^{-1}. See Tables 1 and 2 for ^{1}H and ^{13}C NMR data. CI–MS gave the molecular ion only, m/z 319.15 (M–H$^+$, 100%). HRFAB-MS 321.2070 (M + H$^+$, $C_{19}H_{29}O_4$ requires 321.2066).

Hericenol B (**2**) (1-hydroxy-5,6-bis(hydroxymethyl)-3-methoxy-2-(5-hydroxy-3,7-dimethylocta-2,6-dienyl)-benzene) was obtained as a colourless oil, $[\alpha]_D$ −25 (c 0.5 in $CHCl_3$). UV (MeOH) λ_{max} (ε): 277 nm (1800). IR (KBr): 3400, 2930, 1615, 1585, 1430, 1385, 1320, 1220, 1165, 1115, 1050, 1010 and 830 cm^{-1}. See Tables 1 and 2 for ^{1}H and ^{13}C NMR data. CI–MS gave the molecular ion only, m/z 335.15 (M–H$^+$, 100%). HRFAB–MS 337.2019 (M + H$^+$, $C_{19}H_{29}O_5$ requires 337.2015).

Hericenol C (**3**) (1-hydroxy-5-hydroxymethyl-6-methoxymethyl-3-methoxy-2-(7-hydroxy-3,7-dimethylocta-2,6-dienyl)-benzene) was obtained as a colourless oil. UV (MeOH) λ_{max} (ε): 278 (1800). IR (KBr): 3410, 2930, 1620, 1585, 1455, 1425, 1385, 1320, 1220, 1160, 1115, 1080 and 830 cm^{-1}. See Tables 1 and 2 for ^{1}H and ^{13}C NMR data. CI–MS gave the molecular ion only, m/z 349.25 (M–H$^+$, 100%). HRFAB–MS 351.2167 (M + H$^+$, $C_{20}H_{31}O_5$ requires 351.2171).

Hericenol D (**4**) (1-hydroxy-5-hydroxymethyl-6-methoxymethyl-3-methoxy-2-(7-methoxy-3,7-dimethylocta-2,6-dienyl)-benzene) was obtained as a colourless oil. UV (MeOH) λ_{max} (ε): 278 (1,900). IR (KBr): 3420, 2930, 1620, 1585, 1455, 1425, 1385, 1320, 1220, 1175, 1115, 1080 and 830 cm^{-1}. See Tables 1 and 2 for ^{1}H and ^{13}C NMR data. CI–MS gave the molecular ion only, m/z 363.25 (M–H$^+$, 100%). HRFAB–MS 365.2322 (M + H$^+$, $C_{21}H_{33}O_5$ requires 365.2328).

6-Hydroxymethyl-2,2-dimethylchromanone (**5**) was obtained as a colourless oil. UV (MeOH) λ_{max} (ε): 253 nm (8111) and 329 nm (3,220). IR (KBr): 3420, 2980, 2730, 1690, 1620 and 1490 cm^{-1}. ^{1}H NMR (500 MHz) δ: 7.78, (*d*, $J = 2.3$ Hz, 5-H); 7.48, (*dd*, $J = 2.3$ and 8.5 Hz, 7-H); 6.90, (*d*, $J = 8.5$ Hz, 8-H); 4.59, (*s*, 11-H$_2$); 2.79, (*s*, 3-H$_2$); 1.42, (*s*, 9-H$_3$ and 10-H$_3$). ^{13}C NMR (125 MHz) δ: 192.9 (*s*, C-4), 159.5 (*s*, C-8a), 135.5 (*d*, C-7), 133.4 (*s*, C-6), 124.8 (*d*, C-5), 119.7 (*s*, C-4a), 118.6 (*d*, C-8), 79.2 (*s*, C-2), 64.1 (*t*, C-11), 48.7 (*t*, C-3), 26.5 (*q* and *q*, C-9 and C-10). CI–MS gave the molecular

ion only, m/z 205.05 ($M–H^+$, 100%). HRFAB–MS 207.1022 ($M+H^+$, $C_{12}H_{15}O_3$ requires 207.1021).

3.4. Biological assays

Antimicrobial activities of the new compounds were determined in the serial dilution assay according to Anke et al. (1989), against the following organisms: Fungi: *Absidia glauca* (+) CBS 101.08, *Mucor miehei* TÜ 284, *Nematospora coryli* ATCC 10647, *Paecilomyces variotii* ETH 114646, *Penicillium notatum,* and *Zygorhynchus moelleri* CBS 111.10. Gram positive bacteria: *Arthrobacter citreus* ATCC 11624, *Bacillus brevis* ATCC 9999, *B. licheniformis* ATCC 21415, *B. subtilis* ATCC 6633, *Corynebacterium insidiosum* ATCC 19253, *Micrococcus luteus* ATCC 381, *Mycobacterium phlei* and *Streptomyces* ATCC 23836. Gram negative bacteria: *Acinetobacter calcoaceticus* DSM 30006 and *Salmonella typhimurium* TA98. Cytotoxic activities towards L1210 cells (ATCC CCL 219), COS-7 cells (ATCC CRL 1651) and Colon 320 cells (DSMZ ACC 144) were assayed as described by Zapf et al. (1995). After suitable intervals the cells were examined under a microscope and finally stained according to the method described by Mirabelli et al. (1985).

Acknowledgements

We wish to thank the DAAD Bonn, and the Swedish National Research Council for financial support. We thank A. Meffert for expert technical assistance with the LC–MS.

References

Abraham, W.R., Abate, D., 1995. Chromanones from *Lentinus crinitus* (basidiomycetes). Z. Naturforsch. 50C, 748–750.

Anke, H., Bergendorff, O., Sterner, O., 1989. Assays of the biological activities of guaiane sesquiterpenoids isolated from the fruit bodies of edible *Lactarius* species. Food. Chem. Toxicol. 27, 393–397.

Arnone, A., Cardillo, R., Nasini, G., Pava, O.V., 1994. Secondary mold metabolites: Part 46. Hericenes A-C and erinapyrone C, new metabolites produced by the fungus *Hericium erinaceus*. J. Nat. Prod. 57, 602–606.

Kawagishi, H., Ando, M., Mizuno, T., 1990. Hericenone A and B as cytotoxic principles from the mushroom *Hericium erinaceum*. Tetrahedron Lett. 31, 373–376.

Kawagishi, H., Ando, M., Sakamoto, H., Yoshida, S., Ojima, F., Ishiguro, Y., Ukai, N., Furukawa, S., 1991. Hericenones C, D and E, stimulators of nerve growth factor (NGF)-synthesis from the mushroom *Hericium erinaceum*. Tetrahedron Lett. 32, 4561–4564.

Kawagishi, H., Ando, M., Sakamoto, H., Yoshida, S., Ojima, F., Ishiguro, Y., Ukai, N., Furukawa, S., 1993. Chromans, hericenones F, G and H from the mushroom *Hericeum erinaceum*. Phytochemistry 32, 175–178.

Le-Van, N., Pham, T.V.C., 1981. An unusual *m*-hydroxyectophenone and three new chromanone derivatives from *Chrysothamnus viscidiflorus*. Phytochemistry 20, 485–487.

Lorenzen, K., Anke, T., 1998. Basidiomycetes as a source for new bioactive natural products. Current Organic Chemistry 2, 329–364.

Lourenco, T.O., Akisue, G., Roque, N.F., 1981. Reduced acetophenone derivatives from *Calea cuneifolia*. Phytochemistry 20, 773–776.

Mirabelli, C.K., Bartus, H., Bartus, J.O.L., Johnson, R., Mong, S.M., Sung, C.P., Crooke, S.T., 1985. Application of tissue culture microtiter test for the detection of cytotoxic agents from natural products. J. Antibiotics 38, 758–766.

Reid, D.A., 1965. A Monograph of the Stipitate Steroid Fungi. J. Cramer Press, Weinheim.

Roussis, V., Ampofo, S.A., Wiemer, D.F., 1990. A prenylated benzoic acid derivative from the leaves of *Piper taboganum*. Phytochemistry 29, 1787–1788.

Zapf, S., Hossfeld, M., Anke, H., Velten, R., Steglich, W., 1995. Darlucins A and B, new isocyanide antibiotics from *Sphaerellopsis filum* (*Darluca filum*). J. Antibiotics 48, 36–41.