Cytotoxic and Antimicrobial Secondary Metabolites from *Penicillium hetheringtonii* IMBC-NMTP04

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Received 15 March 2022  Revised 27 April 2023  Accepted 07 August 2023

**Abstract:** Chemical investigation of the sesame-associated fungal strain *Penicillium hetheringtonii* IMBC-NMTP04 resulted in isolation of five compounds, penicitrinone A (1), dihydrocitrinin (2), janthinone (3), coniochaetone B (4), and 9-oxo-10(E),12(E)-octadecadienoic acid (5). Their chemical structures were elucidated by spectroscopic methods, including 1D and 2D NMR and mass spectra in comparison with the literature data. Compound 1 showed modest cytotoxicity toward LNCaP, HepG2, MCF-7, KB, SK-Mel-2, and HL-60 human cancer cell lines, with IC₅₀ values ranging from 60.1 to 84.2 μM while 5 was cytotoxic toward only HL-60 cell line (IC₅₀ = 71.6 μM). All the compounds significantly inhibited *E. faecalis*, *S. enterica*, and *C. albicans* growth, with MIC values ranging from 12.5 to 50.0 μM. Compounds 2, 4, and 5 suppressed the growth of *B. cereus*, while both 1 and 2 showed antimicrobial effect against *E. coli*, with the same MIC value of 200 μM. This is the first time to report the chemical constituents of *Penicillium hetheringtonii* and the antimicrobial effect of 2–4.

**Keywords:** *Penicillium hetheringtonii*, secondary metabolites, cytotoxic; antimicrobial.

1. **Introduction**

*Penicillium* is a diverse fungal genus that comprises more than 300 species. The *Penicillium* species are found in various types of substrates, such as soil, food, and in different processes from necrotrophic pathogenicity to endophytic mutualism. Among the *Penicillium* species, *Penicillium hetheringtonii* is a relative new fungal species as it was first isolated from beach soil in 2010 [1]. This fungus is considered to have a close relationship with
P. citrinum, with several slight differences in morphology, such as having slightly broader stipes, metulae in verticils of four or more [1]. Chemical profile of P. hetheringtonii remains little known so far, except that citrinin, quinolactacin, and PR1-x have been reported as its extrolites by using a combination of partial β-tubulin, calmodulin and ITS sequence data, metabolite patterns, and phenotypic characters [1]. In the present study, we report isolation and structural elucidation of five compounds from a fermentation culture of P. hetheringtonii IMBC-NMTP-04. Furthermore, cytotoxic and antimicrobial effects of the isolates were also evaluated.

2. Methodology

2.1. Fungal Material

The fungal strain IMBC-NMTP04 was isolated from mouldy sesame collected from a market in Hanoi, Vietnam in 2019. The fungus was taxonomically identified based on the DNA amplification and analysis of the ITS region of the rDNA sequence. By searching the ITS rDNA sequence in Genbank (website: https://www.ncbi.nlm.nih.gov/genbank/), the fungal strain IMBC-NMTP04 was identified as Penicillium hetheringtonii (Genbank accession number: OR288524).

2.2. General Experimental Procedures

Optical rotations were determined using a Jasco P-2000 digital polarimeter. The NMR spectra were recorded on Bruker AVANCE III HD 500 FT-NMR spectrometer. HRESIMS data were obtained using an ESI Q-TOF MS/MS system (AB SCIEX Triple). TLC was performed on Kieselgel 60 F254 (Merck) or RP-18 F254s (Merck) plates. Column chromatography was performed on silica gel (Kieselgel 60, 70-230 mesh and 230-400 mesh, Merck) and YMC RP-18 resins. Preparative high-performance liquid chromatography (HPLC) was performed on an Agilent 1200 Preparative HPLC System.

2.3. Fermentation and Extraction

The fungus Penicillium hetheringtonii IMBC-NMTP04 was grown on PDA medium in 100 replicate 2L-Erlenmeyer flasks at the room temperature under static condition for 30 days. The fungal mass growth was then extracted exhaustively with EtOAc under ultrasonic condition to provide an organic phase which was subsequently concentrated under reduced pressure to give a residue (10.56 g).

2.4. Isolation and Identification

The EtOAc extract of P. hetheringtonii IMBC-NMTP04 was subjected to a fractionation by reversed phase (RP) C18 flash column chromatography (CC), eluting with increasing ratio of MeOH in H2O to yield six fractions (V1–V6). V2 was subjected to Sephadex LH-20, eluting with MeOH-H2O (3:1, v/v) to give subfractions V2.1–V2.4. V2.2 was further purified by RP C18 prep. HPLC, using an isocratic elution of ACN-H2O (30:70, v/v) to obtain 2 (7 mg). V3 was fractionated over silica gel, using n-hexane-EtOAc (2:1, v/v) as mobile phase to provide three subfractions (V3.1–V3.3). V3.2 was separated by RP C18 prep. HPLC, using 30% ACN in H2O as eluent to furnish 4 (2 mg). V4 was subjected to fractionation using Sephadex LH-20 CC, eluting with MeOH-H2O (3:1, v/v) to give three subfractions (V4.1–V4.3). V4.1 was separated by silica gel CC, eluting with n-hexane-EtOAc (1:1, v/v) and then purified by RP C18 prep. HPLC, using 60% ACN in H2O as eluent to afford 1 (6 mg). V4.2 was separated by RP C18 CC, utilizing MeOH-H2O (5:1, v/v) to provide subfractions V4.2.1 and V4.2.2. V4.2.1 was introduced to silica gel CC, eluting with n-hexane-EtOAc (2:1, v/v), and further purified by RP C18 prep. HPLC, using ACN-H2O (55:45, v/v) as mobile phase to give 3 (2.8 mg). Using the similar method, compound 5 (2.1 mg) was isolated from V4.2.2 utilizing RP C18 prep. HPLC and ACN-H2O (60:40, v/v) as mobile phase.

2.5. Cytotoxic Assay

Cytotoxic effects of compounds 1–5 on five human cancer cell lines, including LNCaP,
HepG2, MCF7, KB, SK-Mel-2, and HL-60 were evaluated by SRB assay [2, 3].

2.6. Antimicrobial Assay

Antimicrobial effects of compounds 1–5 toward the Gram-positive bacterial strains E. faecalis (ATCC13124), S. aureus (ATCC25923), and B. cereus (ATCC12545), Gram-negative bacterial strains E. coli (ATCC25922), P. aeruginosa (ATCC27853), and S. enterica (ATCC12228), and a yeast strain C. albicans (ATCC1023) were tested using a micro broth dilution method in 96-well microplates [4].

3. Results and Discussion

3.1. Spectroscopic Data of Compounds 1–5

Penicitrinone A (1): white, amorphous powder; C_{23}H_{28}O_5; ESIMS: m/z 381 [M+H]^+; \textsuperscript{1}H (CD\_3OD, 600 MHz): δ\textsubscript{H} 5.22 (q, J = 6.0 Hz, H-3), 3.33 (m, H-4), 6.30 (s, H-7), 1.44 (d, J = 6.6 Hz, H-1), 1.36 (d, J = 6.6 Hz, H-2), 2.13 (s, H-3\textprime{}), 4.65 (m, H-2\textprime{}), 3.28 (m, H-3\textprime{}), 1.41 (d, J = 6.6 Hz, H-3\textprime{}), 0.97 (t, J = 7.2 Hz, H-4\textprime{}), 2.25 (s, H-10\textprime{}); \textsuperscript{13}C NMR data (CD\_3OD, 150 MHz): δ\textsubscript{C} 161.3 (C-1), 84.4 (C-3), 36.0 (C-4), 134.8 (C-6a), 131.5 (C-5), 185.7 (C-6), 102.8 (C-7), 160.4 (C-8), 100.7 (C-8a), 18.7 (C-9), 19.3 (C-10), 10.8 (C-11), 89.3 (C-2\textprime{}), 45.9 (C-3\textprime{}), 142.3 (C-3a\textprime{}), 118.8 (C-4\textprime{}), 149.5 (C-5\textprime{}), 103.8 (C-6\textprime{}), 137.4 (C-7\textprime{}), 139.0 (C-7a\textprime{}), 21.1 (C-8\prime{}), 19.4 (C-9\prime{}), 11.8 (C-10\prime{}).

Dihydrocrotinin (2): white, amorphous powder; C_{15}H_{11}O_5; ESIMS: m/z 253 [M+H]^+; \textsuperscript{1}H (DMSO-d_{6}, 600 MHz): δ\textsubscript{H} 4.47 (d, J = 15.0 Hz, H-2\textprime{}), 4.41 (d, J = 15.0 Hz, H-3\textprime{}), 3.77 (m, H-3), 2.53 (m, H-4), 1.13 (each d, J = 6.6 Hz, H-5 and H-6), 1.93 (s, H-1); \textsuperscript{13}C NMR data (CD\_3OD, 150 MHz): δ\textsubscript{C} 58.7 (C-1), 73.4 (C-2), 34.7 (C-4), 139.3 (C-3a), 109.4 (C-5), 158.2 (C-6), 101.4 (C-7), 155.2 (C-8), 108.3 (C-8a), 20.2 (C-9), 17.9 (C-10), 9.7 (C-11), 175.6 (7-COOH).

Janthinone (3): white, amorphous powder; C_{16}H_{21}O_5; ESIMS: m/z 285 [M+H]^+; \textsuperscript{1}H (DMSO-d_{6}, 600 MHz): δ\textsubscript{H} 6.72 (s, H-2), 6.96 (s, H-4), 7.78 (d, J = 8.5 Hz, H-5), 7.95 (t, J = 8.5 Hz, H-6), 7.47 (d, J = 8.5 Hz, H-7), 2.43 (s, 3-CH\textsubscript{3}), 3.91 (s, 8-CH\textsubscript{3}); \textsuperscript{13}C NMR data (DMSO-d_{6}, 150 MHz): δ\textsubscript{C} 160.4 (C-1), 111.3 (C-2), 149.7 (C-3), 107.6 (C-4), 155.3 (C-4a), 119.6 (C-5), 136.0 (C-6), 122.8 (C-7), 168.1 (C-8), 116.5 (C-8a), 180.0 (C-9), 106.4 (C-9a), 155.5 (C-10), 22.0 (s, 3-CH\textsubscript{3}), 52.7 (s, 8-CH\textsubscript{3}).

Coniochaetone B (4): white, amorphous powder; C_{13}H_{12}O_4; ESIMS: m/z 233 [M+H]^+; \textsuperscript{1}H (CD\_3OD, 600 MHz): δ\textsubscript{H} 5.31 (d, J = 6.6 Hz, H-1), 3.18 (m, H-2), 2.86 (m, H-3), 2.49 (m, H-4), 1.99 (m, H-5), 6.85 (s, H-7), 6.65 (s, H-8), 2.42 (s, 8-CH\textsubscript{3}); \textsuperscript{13}C NMR data (CD\_3OD, 150 MHz): δ\textsubscript{C} 71.5 (C-1), 30.6 (C-2), 31.5 (C-3), 175.0 (C-4), 159.1 (C-6), 108.9 (C-7), 148.5 (C-8), 113.3 (C-9), 162.1 (C-10), 110.0 (C-11), 182.4 (C-12), 122.2 (C-13), 22.2 (8-CH\textsubscript{3}).

9-oxo-10(E),12(E)-octadecadienonic acid (5): white, amorphous powder; C_{18}H_{20}O_4; ESIMS: m/z 295 [M+H]^+; \textsuperscript{1}H (CD\_3OD, 600 MHz): δ\textsubscript{H} 2.29 (br s, H-2), 1.63 (m, H-3), 1.34 (m, H-4–H-6, H-16, H-17), 2.61 (t, J = 7.8 Hz, H-8), 6.15 (d, J = 15.6 Hz, H-10), 7.26 (dd, J = 9.6, 15.6 Hz, H-11), 6.29 (m, H-12), 6.28 (m, H-13), 2.23 (q, J = 6.6 Hz, H-14), 1.49 (m, H-15), 0.93 (t, J = 7.2 Hz, H-18); \textsuperscript{13}C NMR (CD\_3OD, 150 MHz): δ\textsubscript{C} 178.0 (C-1), 35.3 (C-2), 26.1 (C-3), 30.1 (C-4), 30.2 (C-5 and C-6), 25.6 (C-7), 41.0 (C-8), 204.0 (C-9), 128.8 (C-10), 145.3 (C-11), 130.3 (C-12), 147.4 (C-13), 34.1 (C-14), 29.5 (C-15), 32.5 (C-16), 23.5 (C-17), 14.3 (C-18).

3.2. Structural Elucidation of Compounds 1–5

Compound 1 was isolated as a white, amorphous powder. The \textsuperscript{1}H NMR spectrum exhibited signals for one olefinic proton at 6.30 (s, H-7), two tertiary methyls at 2.13 and 2.25 (each s, H-11 and H-10\textprime{}) and four secondary methyls at δ\textsubscript{H} 1.44, 1.36, and 1.41 (each d, J = 6.6 Hz, H-9, H-10, H-8\textprime{}), and 1.37 (d, J = 7.2 Hz, H-9\textprime{}). Analysis of the \textsuperscript{13}C NMR and HSQC spectra revealed the occurrence of 23 carbon signals, including one carbonyl carbon at δ\textsubscript{C}
nonprotonated carbons \([\text{of which five are oxygenated at } \delta_{C} \text{ 161.3 (C-1), 160.4 (C-8), 149.5 (C-5'), 137.4 (C-7'), and 139.0 (C-7'a)}\])], two oxymethines at \(\delta_{C} \text{ 84.4 (C-3) and 89.3 (C-2')}\), two methines at \(\delta_{C} \text{ 36.0 (C-4) and 45.9 (C-3')}\), and six methyl carbons. Comparison of the \(^1\text{H}\) and \(^{13}\text{C}\) NMR data of 1 with those of the reported citrinin derivative, penicitrinone A revealed the good agreement, suggesting that both structures are identical \([5]\). In the HMBC spectrum, correlations from \(\text{H}_7-9\) to C-3 and C-4, \(\text{H}_2-10\) to C-3, C-4, and C-4a, from \(\text{H}_7-11\) to C-4a, C-5, and C-6, and from \(\text{H}-7\) to C-5, C-6, C-8, and C-8a, from \(\text{H}_7-10'\) to C-3'a, C-4', and C-5', confirmed the presence of a 3,4,5-trimethyl-3,4-dihydro-6\(\text{H}\)-isochromen-6-one structural moiety of 1 (Figure 2). The remaining structure part, 2,3,4-trimethyl-2,3-dihydrobenzofuran-5,7-diol was recognized by HMBC cross-peaks from \(\text{H}_7-10'\) to C-3'a, C-4', and C-5', from \(\text{H}_2-8'\) to C-2' and C-3', and from \(\text{H}_7-9'\) to C-2', C-3', and C-3'a. On the basis of the spectroscopic evidence, compound 1 was identified as penicitrinone A, a metabolite was first isolated from \textit{Penicillium citrinum} \([5]\).

Compound 2 was afforded as a white, amorphous powder. The \(^1\text{H}\) NMR spectrum contained signals for one oxymethylene \([\delta_{H} \text{ 4.47 and 4.41 (each d, } J = 15.0 \text{ Hz, H-1 and H-2})\]), one oxymethine at \(\delta_{H} \text{ 3.77 (m, H-3), two secondary methyls } \delta_{H} \text{ 1.13 (each d, } J = 6.6 \text{ Hz, H-9 and H-10})\] and one tertiary methyl at \(\delta_{H} \text{ 1.93 (s, H-11)}\). The \(^{13}\text{C}\) NMR and HSQC spectra revealed 13 carbon signals, including one carbonyl carbon at \(\delta_{C} \text{ 175.6 (7-OCOOH), six aromatic nonprotonated carbons } \delta_{C} \text{ 139.3 (C-4a), 109.4 (C-5), 158.2 (C-6), 101.4 (C-7), 155.2 (C-8), 108.3 (C-8a)}, \) one oxymethylene at \(\delta_{C} \text{ 58.7 (C-1), one oxymethine at } \delta_{C} \text{ 73.4 (C-3'), one methine at } \delta_{C} \text{ 34.7 (C-4), and three methyls. This data suggested that 2 belongs to the isochromane skeleton type, which was further supported by an agreement on comparing the } \text{ \(^1\text{H}\) and } \text{ \(^{13}\text{C}\) NMR data of 2 with those of the reported isochromane} \([6]\). Finally, the structure of 2 was confirmed by HMBC correlations as shown in Figure 2. Thus, 2 was assigned as dihydrocitrinin.

Compound 3 was isolated as a white, amorphous powder. The \(^1\text{H}\) NMR spectrum showed typical aromatic signals for AX \([\delta_{H} \text{ 6.72 and 6.96 (each s, H-2 and H-4)}\] and ABC \([\delta_{H} \text{ 7.47 and 7.78 (each d, } J = 8.5, \text{ H-5 and H-7) and 7.95 (t, } J = 8.5, \text{ H-6})\] spin patterns, one tertiary methyl at \(\delta_{H} \text{ 2.43 (s, 3-CH}_{3}\text{)}, and one methoxy group at \(\delta_{H} \text{ 3.91 (s, 8-OCH}_{3}\text{)}. Analysis of \(^{13}\text{C}\) NMR and HSQC spectra indicated 16 carbon signals, including two carbonyl carbons at \(\delta_{C} \text{ 180.0 (C-9) and 155.5 (C-10)}, along with 12 sp\(^3\) carbons of which three oxygen-bearing nonprotonated carbons \(\delta_{C} \text{ 160.4 (C-1), 155.3 (C-4a), and 168.1 (C-8)}\] and four nonprotonated carbons \(\delta_{C} \text{ 149.7 (C-3), 132.9 (C-5a), 116.5 (C-8a), and 106.4 (C-9a)}\] were recognized. The shielded chemical shift of the carbonyl carbon resonated at \(\delta_{C} \text{ 155.5}\) suggested the presence of a lactone functional group. The above spectroscopic evidence suggested that 3 has the dibenzoepindione structural type \([7]\). Accordingly, the \(^1\text{H}\) and \(^{13}\text{C}\) NMR data of 3 were shown to be in a good match with those of the reported dibenzoepindione, janthinone, suggesting that both compounds have the identical structures \([7]\). This was corroborated by HMBC spectrum. As depicted in Figure 2, correlations observed from \(\delta_{H} \text{ 2.43 to C-2, C-3, and C-4 and from } \delta_{H} \text{ 3.91 to C-7, C-8, and C-8a}\] approved the locations of a methyl at C-3 and a methoxy at C-8, respectively. Based on the spectroscopic analysis, 3 was determined to be janthinone.

Compound 4 was obtained as a white, amorphous powder. In the \(^1\text{H}\) NMR spectrum, signals of aromatic protons for an AX spin system were observed at \(\delta_{H} \text{ 6.65 and 6.85 (each s, H-7 and H-9)}\) were observed, suggesting the presence of a 1,3,5,6-tetrasubstituted benzene ring. In addition, proton signals for one oxymethine group at \(\delta_{H} \text{ 5.31 (d, } J = 6.6 \text{ Hz, H-1)}\) and one methyl group at \(\delta_{H} \text{ 2.42 (s, 8-CH}_{3}\text{)}\] were also recognized in the \(^1\text{H}\) NMR spectrum. The \(^{13}\text{C}\) NMR spectrum displayed 13
carbon signals, of which one carbonyl carbon at $\delta_{C} 182.4$ (C-12), eight sp$^2$ carbons (of those four were oxygenated [C-175.0 (C-4), 159.1 (C-6) and 162.1 (C-10)]), and four sp$^3$ carbons [including one oxymethine at $\delta_{C} 71.5$ (C-1), two methylenes at $\delta_{C} 30.6$ (C-2) and 31.5 (C-3), and one methyl at $\delta_{C} 22.2$ (8-CH$_3$)] were identified using the HSQC experiment. This spectroscopic data suggested that the structure of 4 composes of a benzopyranone in conjugation with a cyclopentane ring [8].

Accordingly, the $^1$H and $^{13}$C NMR data of 4 were in a good agreement with those of the reported benzopyranone, coniochaetone B, suggesting the similar structures of both compounds. By detailed analysis of the HMBC spectrum, which showed correlations from 8-CH$_3$ to C-7, C-8, and C-9, from H-7 to C-6 and C-12, and from H$_2$-2 to C-1, C-3, C-4, and C-12, the planar structure of 4 was established (Figure 2). Based on the aforementioned analysis, together with comparison of the specific optical rotations between 4 ($[\alpha]_D^{28} = +38.6$ (c = 0.08, MeOH)) and both enantiomers [(+)-coniochaetone B: $[\alpha]_D^{20} = +84.70$ (c = 0.058, MeOH); (−)-isoconiochaetone B: $[\alpha]_D^{20} = −86.96$ (c = 0.056, MeOH), compound 4 was elucidated as coniochaetone B [9].

Compound 5 was given as a white, amorphous powder. The $^1$H NMR spectrum had signals of four olefinic protons at $\delta_{H}$ 6.15 (d, $J$ = 15.6 Hz, H-10), 7.26 (dd, $J$ = 9.6, 15.6 Hz, H-11), 6.29 and 6.28 (overlapped, H-12 and H-13), implying the presence of two disubstituted double bonds. In addition, a triplet signal of a primary methyl was also observed at $\delta_{H}$ 0.93 (t, $J$ = 7.2 Hz, H$_3$-18). The $^{13}$C NMR
spectroscopic data, 5 was suggested to be an octadecadienoic acid containing two double bonds and one ketone. By comparison of the $^1$H and $^{13}$C NMR data of 5 with a previously reported octadecadienoic acid [10], its structure, 9-oxo-10(E),12(E)-octadecadienoic acid was established. This was confirmed by HMBC correlations observed from H$_2$-2 to C-1, C-3, and C-4, from H$_3$-18 to C-17 and C-16, from H-10 to C-8, C-9, C-12, from H-11 to C-9, C-12, C-13, from H-12 to C-13, C-14, and from H-13 to C-12, C-11, C-14 (Figure 2).

Table 1. Cytotoxic effects of compounds 1–5 at concentration of 100 µM

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(*): positive control at concentration of 2 µg/mL.

Table 2. Antimicrobial effects of compounds 1–5

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EF: Enterococcus faecalis ATCC299212; SA: Staphylococcus aureus ATCC25923; BC: Bacillus cereus ATCC13245; EC: Escherichia coli ATCC25922; PA: Pseudomonas aeruginosa ATCC27853; SE: Salmonella enterica ATCC13076; CA: Candida albicans ATCC10231; (-): inactive; (*) positive control.

3.3. Cytotoxic Effect of Compounds 1–5

Cytotoxicity of compounds 1–5 was evaluated using LNCaP, HepG2, MCF-7, KB, and SK-Mel-2 human cancer cell lines using the sulforhodamine B (SRB) assay at the concentration of 100 µM [2, 3]. The result showed that only penicitrinone A (1) displays cytotoxicity toward all the cancer cell lines, with the induction of 60.4–72.1% cell death, whereas 5 induced 74.49% HL-60 cell death (Table 1). Compounds 3 and 5 were cytotoxic against only KB cell line, with induction of 47.6 and 42.5% cell death, respectively while other compounds were considered to be noncytotoxic toward all the cell lines. Based on the preliminary screening results, 1 and 5 were further examined their cytotoxicity at different concentrations. As the result, 1 showed cytotoxicity toward LNCaP, HepG2, MCF-7, KB, SK-Mel-2, and HL-60 cell lines, with IC$_{50}$ values of 77.1 ± 4.1, 84.2 ± 4.7, 74.8 ± 3.9, 71.1 ± 7.5, 60.1 ± 3.9, and 64.0 ± 3.2 µM, respectively, while
5 was cytotoxic toward HL-60 cell line, with an IC₅₀ value of 71.63 ± 3.76 µM.

3.4. Antimicrobial Effect of Compounds 1–5

Effect of 1–5 on the growth of Gram-positive (Enterococcus faecalis ATCC299212, Staphylococcus aureus ATCC25923, and Bacillus cereus ATCC13245) and Gram-negative bacteria (Escherichia coli ATCC 25922, Pseudomonas aeruginosa ATCC 9027, and Salmonella enterica ATCC13076), and a yeast Candida albicans ATCC 24433 were also examined [4]. As the result, all the compounds significantly inhibited E. faecalis, S. enterica and C. albicans growth, with MIC values ranging from 12.5 to 50.0 µM (Table 2). In addition, compounds 2, 4, and 5 suppressed the growth of B. cereus, with MIC values of 200, 200, and 100 µM, respectively, while both compounds 1 and 2 showed antimicrobial effect against E. coli, with MIC values of 200 µM.

4. Conclusion

Five compounds, penicitrinone A (1), dihydrocitrinin (2), janthinone (3), coniochaetone B (4), and 9-oxo-10(E),12(E)-octadecadienoic acid (5) were isolated from a culture fermentation of the sesame-associated fungal strain P. hetheringtonii IMBC-NMTP04. Compound 1 showed modest cytotoxicity toward LNCaP, HepG2, MCF-7, KB, SK-Mel-2, and HL-60 human cancer cell lines while 5 was cytotoxic toward only HL-60 cell line. It is noted that this is the first isolation of 9-oxo-10(E),12(E)-octadecadienoic acid from the genus Penicillium and all compounds from the fungus P. hetheringtonii. Furthermore, this is also the first case to communicate the antimicrobial effects of 2–4.

Acknowledgements

This work was financially supported by Vietnam Academy of Science and Technology under grant number TDNDTP.06/19-21.

References


