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Volatile Glycosides from the Leaves of Morus alba with a Potential Contribution to the Complex Anti-diabetic Activity

Attila Hunyadi, Ibolya Herke, Katalin Veres, Anna Erdei, András Simon and Gábor Tóth Keywords: Morus alba, Mulberry leaves, Megastigmane glycoside, Phenyl-propane, GC-MS, Type 2 diabetes, NIDDM, Anti-diabetic.

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Abstract (104KB)

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Abstract (100KB)

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Steroidal Aglycones from Stems of Marsdenia tenacissima that Inhibited the Hedgehog Signaling Pathway

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Chemical Constituents, and their Cytotoxicity, of the Rare Wood Decaying Fungus Xylaria humosa

Sirirath Sodngam, Sasiphimol Sawadsitang, Nuttika Suwannasai and Wiyada Mongkolthanaruk Keywords: Xylaria humosa, Xylariaceae, Naturai products, Cytotoxicity, Tryptoquivaline, Triterpenoid, Quinazolinone.

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Kimberly Chinea, Willian Vera and Ajoy K. Banerjee

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Anthraquinone and Naphthoquinone Derivatives from the Roots of Coptosapelta flavescens

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Methicillin-resistant Staphylococcus aureus, Vancomycin-resistant Enterococcus faecalis and Enterococcus faecium active Dimeric Isobutyrylphloroglucinol from Ivesia gordonii

Marwa H. Ahmed, Mohamed All Ibrahim, Jin Zhang, Farouk R. Melek, Seham S. El-Hawary, Melissa R. Jacob and Ilias Muhammad

Keywords: Ivesia gordonii, 1,5-Dihydroxy-2-(2'-methylpropionyl)-3-methoxy-6-methylbenzene, Diacetylphloroglucinol, Antimicrobial, Methicillin-resistant Staphylococcus aureus, Vancomycinresistant Enterococcus faecium, Enterococcus faecalis.

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Biological Studies of Turmeric Oil, Part 3: Anti-Inflammatory and Analgesic Properties of Turmeric Oil and Fish Oil in Comparison with Aspirin

James N. Jacob and Dinesh K. Badyal

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- Abstract (64KB)

Cyclic Dipeptides Produced by Marine Sponge-Associated Bacteria as **Quorum Sensing Signals**

Gennaro Roberto Abbamondi, Salvatore De Rosa, Carmine Iodice and Giuseppina Tommonaro Keywords: Quorum sensing, Diketopiperazines, Plate "T" streak bioassay, Inter-kingdom cross talking.

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The Co-identity of Lipiarmycin A3 and Tiacumicin B

Angelo Bedeschi, Piera Fonte, Giovanni Fronza, Claudio Fuganti and Stefano Serra

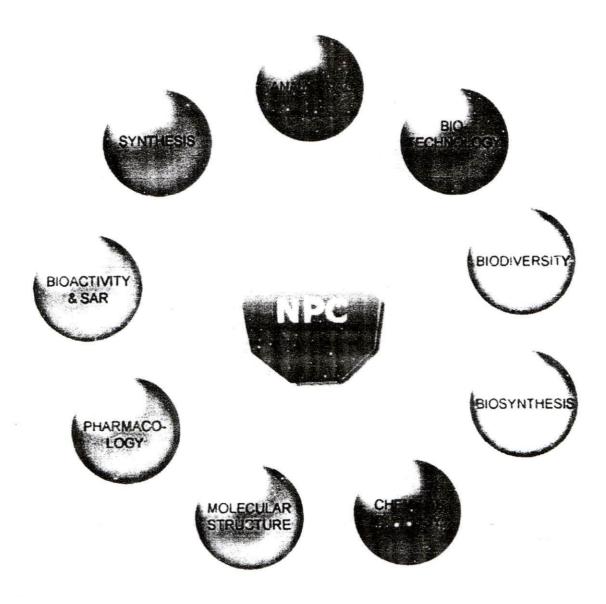
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Isolation of the Tetrapeptide Apicidins G, H and I from the Fungus Fusarium semitectum

Suciatiab and Mary J. Garsona"

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This study reports the isolation and characterization of three new tetrapeptides, apicidins G (1), H (2) and I (3), along with the known apicidin (4), apicidin A (5), apicidin C (6), diketopiperazine 7, equisetin (8) and 7-hydroxy-2-(2-hydroxypropyl)-5-methylchromone (9). The structures of the new compounds were deduced by 2D NMR spectroscopic and MS data.

Keywords: Tetrapeptides, Apicidins, Fungus, Fusarium.

Fusarium semitectum (Syn. Fusarium pallidoroseum) is a fast growing fungus which was first described in 1875 from the petioles of banana leaves [1]. In common with other Fusarium species, F. semitectum has the ability to produce mycotoxins, such as nivalenol and (-)-zearalenone [2,3]. Other metabolites isolated include the antibiotic equisetin and a-pyrones, for example fusapyrone and deoxyfusapyrone [4,5]. In 1996, Singh et al. reported the isolation of the cyclic tetrapeptides apicidin and apicidin A from Fusarium pallidoroseum [6a]. Subsequent investigation of the same F. pallidoroseum sample by Singh et al. yielded apicidins B, C, D1, D2 and D₃ [6b-6c]. The unusual structural motif in apicidins is the presence of the amino acid 2-amino-8-oxo-decanoic acid (Aoda). Substitution of the Aoda residues has been reported for apicidins D1-D3 [6c]. All apicidins contain a (D)-pipecolic acid (Pip) unit, except for apicidin B, which has a (D)-proline (Pro) residue. Apicidin C has a (L)-valine residue instead of (L)-isoleucine (Ile). An N-methoxy-(L)-tryptophan is present in both apicidin and its congeners, except for apicidin A. This series of compounds has shown antiprotozoal activity by reversible blocking of histone deacetylase (HDAC) inhibitors [6d]. Apicidins are structurally related to trapoxin A, HC-toxin, WF-3161, Cyl-2 and chlamydocin [7-11]. The long chain amino acid with a terminal epoxy group in each of these cyclic tetrapeptides has been suggested to be responsible for their antiproliferative activity [12]. Jin et al. have identified the gene cluster responsible for apicidin biosynthesis in F. semitectum, and isolated apicidin E containing a 2-aminodecanoic acid unit [13]. Apicidin F, with L-phenylaianine (Phe) instead of Ile and L-2-aminooctanedioic acid instead of Aoda, has recently been identified from F. fujikuroi [14]. In this report, we describe the isolation and structure elucidation of three new tetrapeptides, apicidins G, H and I (1-3), together with six known compounds from F. semitectum (Figure 1). The stereochemistry of the new apicidins was proposed by comparison with the known apicidins and from biosynthetic considerations.

F. semitectum was isolated from a dead cicada skin collected from the Tawangmangu Botanic Garden in Central Java, Indonesia. The fungus was cultured in rice media, extracted with MeOH, then with EtOAc, to obtain a dark purple extract. This was chromatographed on silica gel and RP-HPLC to yield three new apicidins (1-3), together with the known (-)-apicidin (4), apicidins A (5) and C (6),

Figure 1: Structures of metabolites isolated from F. semitectum

(-)-cyclo-(D-pipecolinyl-L-isoleucine) (7) [15], (-)-equisetin (8) [6], and (+)-7-hydroxy-2-(2-hydroxypropyl)-5-methylchromone (9) [16].

Apicidin G (1) was isolated together with apicidin C (6) as a 1:1 mixture using RP-HPLC (MeOH/H₂O). The HRESIMS data of the fraction containing 1 suggested a nitrogenous compound from an adduct ion at m/z 577.3360 [M+Na]⁺, corresponding to the molecular formula $C_{31}H_{46}N_4O_5$. The ¹H NMR spectrum of 1 (Table 1) showed signals for four α -protons (δ_H 5.06, 4.72, 4.16 and 3.80), three NH signals (δ_H 7.25, 6.46 and 6.43), five aromatic protons [δ_H 7.27 (2H), 7.19 (2H) and 7.22 (1H)] and three methyl groups

Table 1 NMR spectroscopic data for apicidins G, H and I.

	1					2		3	
Residue	Position	óc*	δ _s mult (J in Hz) ^h	Residue	Position	δc	δ _H mult (J in Hz) ^b	δc*	δ _H mult (J in Hz) ³
Pipecolic acid	1	171,6	-	Pipecolic acid	1	170.3	•	172.8	•
i specone acia	2	50.8	5.06 br d (6.0)		2	51.0	3.49 br s	58.3	4.12 br d (10.0)
	3	24.5	a 2.01 m		3	24.3	a 2.04 m	26.7	a 2.13 br d (13.5)
	-		b 1.57 m				b 1.59 m		b 1.84 m
	4	19.2	a 2.14 m		4	19.3	a 2.20 m	21.8	a 1.89 m
	-	17.0	b 1.58 m				b 1.62 m		b 1.57 m
	5	25.4	a 1.80 m		5	25.1	a 1.87 m	22.1	1.80 m
	-		b 1.40 m				b 1.41 m		
	6	44.1	a 4.04 m		6	44.0	a 3.83 br d (12.8)	44.4	a 3.47 br d (12.0)
	•		b 3.04 br t (12.9)				b 3.53 td (12.8, 2.0)		b 2.92 td (12.0; 3.5)
			0 3,51 01 1 (12.07)		OMe		100 (100 (100 (100 (100 (100 (100 (100	52.2	3.56 s
Isoleucine	1	174.4	_	Isoleucine	1	171.2	-	172.7	-
rsorodonic	2	54.4	4.72 (10.5)		2	54.5	4.65 br ((9.3)	56.8	4,37 dd (8.0, 5.5)
	3	34.5	2.08 m		3	34.4	1.97 m	37.6	1.84 m
	4	24.7	a 1.59 m		4	24.7	a 1.71 m	25.3	1.36 ddd (13.5, 7.2, 4.6)
	-	24.7	b 1.19 m				b 1.20 m		
	5	10.7	0.94 t (7.4)		5	10.6	0.91 ((7.5)	11.4	0.86 ((7.5)
	6	15.7	0.87 d (6.6)		6	15.6	0.90 d (6.5)	15.5	0.83 d (7.0)
	NH	13.1	7.25 d (10.0)		NH	-	7.12 m ^d		7.14 br d (7.5)
Phenylalanine	1	174.7	7.25 a (10.0)	Tryptophan-N-OMe	1	171.3	•	172.2	-
Paenyialanine	2	62.7	3.80 m	(epoxy)	2	65.6	4.73 br d (9.9)	54.6	4.71 td (8.5, 6.5)
	3	35.3	a 3.72 dd (13.5, 11.2)	(char),	3	42.5	a 2.57 d (14.6)	27.6	a 3.30 dd (15.0, 9.0)
	,	32.3	b 3.25 dd (13.5, 5.8)			-	b 2.41 br d (14.6)		b 3.22 dd (15.0, 6.5)
	4	137.1	0 3.23 04 (13.3, 3.6)		4	84.2	-	106.8	
	5/9	129.1	7.19 m		5	129.6		123,9	•
	6/8	128.8	7.27 m		6	121.8	7.31 d (8.5)	119.3	7.67 d (8.0)
	7	127.3	7.22 m		7	124.3	7.09 td (7.8, 0.5)	122.5	7.19 td (8.0, 1.0)
91 Casi	NH	127.5	6.43 d (6.8)		8	130.6	7.34 td (7.6, 0.5)	119.8	7.08 td (8.0, 1.0)
	NH	•	0.43 4 (0.6)		9	114.9	7.04 d (7.9)	108.1	7.34 d (8.0)
					10	148.9	-	132.4	-
					11	97.0	5.99 s	122.4	7.31 s
					12	64.1	3.85 a	65.8	4.02 s
					NH	04.1	7.12 m ^e	-	8.29 br d (7.5)
	2			Aoda	1	173.1	7.12 111	172.4	
Aoda	1	175.8	ī.,	AGGA	2	53.7	4.32 dd (9.5, 4.2)	55.3	4.18 br q (7.5)
	2	53.5	4.16 m		3	32.9	4. 2.03 m	31.4	a 1.62 m
	3	29.0	a 1.75 m		3	34.9	b 1.96 m	21.4	b 1.55 m
			b 1.52 m		4	25.6	1.32 m	25.3	1.07 m
	4	25.2	1.19 m			29.2	1.32 m	28.4	1.10 m
	5	28.6	1.24 m		5	23.8	1.53 m	23.4	1.40 m
	6	23.4	1.52 m		7	42.3		42.1	2.29 t (7.0)
	7 -	42.1	2.34 t (7.4)		8	211.8	2.36 t (7.5)	212.1	2.271(7.0)
	8	211.8				36.0	2.38 q (7.4)	36.0	2.32 g (7.5)
	9	35.9	2.40 q (7.4)		9			7.8	1.03 (7.0)
	10	7.7	1.94 (7.4)		10 NH/NH₂*	7.9	1.01 t (7.3) 6.19 br d (7.6)	7.8	8.35 br d (6.5)

"Chemical shifts (ppm) taken from 2D NMR spectra referenced to CDCl₃ ($\delta_{\rm c}$ 77.16), data recorded at S00 MHz, Chemical shifts (ppm) referenced to CHCl₃ ($\delta_{\rm c}$ 7.26), data recorded at S00 MHz.

'Assignments may be interchangeable; 'Overlapping signals, assigned by 2D-TOCSY; 'NH for 2, NH₂ for 3.

N H HN O OCH3

Pigure 2: TOCSY and selected HMBC correlations for apicidins G (1), H (2) and I (3).

 $(\delta_H~1.04,~0.94,~0.87)$. The 13 C NMR spectrum contained amide signals at δ_C 175.8, 174.7, 174.4 and 171.6 and a ketone signal at δ_C 211.8. The side chain signals of individual amino acids were determined by DQFCOSY and 2D-TOCSY data, and were consistent with the presence of Ile, Phe, Pip and Aoda residues. The signal at δ_H 5.06 (br d, 6.0 Hz) was assigned as the α-proton of Pip since it was linked to four methylene groups (including two downfield methylene protons at δ_H 4.04 and 3.04) by 2D-TOCSY (Figure 2). For Ile, the α-proton signal at δ_H 4.72 was a triplet with 10.0 Hz couplings to both NH (δ_H 7.25) and methine (δ_H 2.08)

signals. The TOCSY data revealed cross peaks from this α -proton to the methyl groups at δ_H 0.94 (t, 7.4 Hz) and 0.87 (d, 6.6 Hz). The presence of Phe was established from an α -proton signal at δ_H 3.80, which showed couplings to methylene signals at δ_H 3.72 and 3.25 by TOCSY, and by HMBC correlations from the methylene protons to an aromatic carbon at δ_C 129.1. The amino acid 2-amino-8-oxodecanoic acid (Aoda) was apparent from signals for five methylene groups [δ_H 2.34 (2H, t, 7.4), 1.75 (1H, m), 1.52 (3H, m), 1.24 (2H, m), 1.19 (2H, m)], an ethyl group [δ_H 1.04 (3H, t, 7.4 Hz), 2.40 (2H, q, 7.4 Hz)], and by HMBC correlations from the methyl group at δ_H 1.04 and the methylene protons at δ_H 1.52 and at δ_H 2.40 to the ketone signal at δ_C 211.8.

The amide carbons of Aoda, Fhe, and Pip were assigned to the signals at $\delta_{\rm C}$ 175.8, 174.7, and 171.6, respectively, by the $^3J_{\rm CH}$ correlations from their β protons; the remaining amide signal at $\delta_{\rm C}$ 174.4 therefore belonged to Ile. $^2J_{\rm CH}$ correlations from the respective α -protons fully supported these assignments. The sequence of the amino acid residues in apicidin G was determined from HMBC correlations, in particular from the α -proton of Pip to the carbonyl group ($\delta_{\rm C}$ 174.4) of Ile, from the α -proton of Ile to the carbonyl group ($\delta_{\rm C}$ 174.7) of Phe, and from the α -proton of the Aoda residue to the carbonyl group ($\delta_{\rm C}$ 171.6) of Pip. The sequence was identical to that in apicidin (4) [6a] except for the Trp-N-OMe moiety, which was replaced by Phe in apicidin G (1).

The configuration of 1 was determined by analysis of proton NMR coupling constants compared with those in other apicidins [6]. The

α-proton of Phe was coupled to the adjacent NH proton with a J value of 6.8 Hz, and indicated a syn-relationship. In contrast, the 10.4 and 10.0 Hz coupling between the α-protons of the Aoda and Ile residues and the corresponding NH protons suggested an anti-relationship, as reported for apicidin (4). In the pipecolic acid unit the 6.0 Hz coupling of the α-proton matched the 5.5 Hz coupling for the corresponding signal in apicidin [6a]. In view of the co-isolation of (-)-apicidin (4), the absolute configurations of the shared amino acid constituents were inferred to be (R)-Pip, (S)-Ile, and (S)-Aoda. An (S)-Phe residue was inferred from the $J_{NH/H-2}$ value [6a,6b], and by analogy with trapoxin-A [7]. Specific rotation measurements and verification of the amino acid configurations were not undertaken owing to the inseparable mixture of 1 and 6.

Apicidin H (2) was obtained as a colorless oil by RP-HPLC using MeOH/H2O. The HRESIMS data of 2 indicated a molecular formula of C34H49N5O7 from a sodiated adduct ion at m/z 662.3545, and established the presence of one additional oxygen in 2 with respect to apicidin (4). The 1H NMR data suggested that 2 was structurally related to 4 from the characteristic signals corresponding to Pip [δ_H 3.49, 3.83 and 3.53], Ile [δ_H 4.65, 0.91 (3H), 0.90 (3H)] and Aoda residues [δ_H 4.32, 2.38 (2H), 2.36 (2H) and 1.01 (3H)]. The signal at δ_H 4.73 (d, 9.9) linked to a signal at δ_C 65.6 by HSQC was assigned as the α-proton of the remaining amino acid unit, and showed 2D-TOCSY correlations to a methylene group at δ_H 2.57 and 2.41, and to an NH proton (δ_H 7.12). A methine signal at δ_H 5.99 (H-11) was linked to a signal at δ_C 97.0 by HSOC. These chemical shifts, together with HMBC correlations from this methine proton to a methylene carbon (δ_C 42.5, C-3) and to a quaternary carbon (δ_C 84.2, C-4), were all consistent with an epoxy-derivatized Trp-N-OMe moiety. An amide signal at δ_C 171.3 was assigned to the epoxy-Trp-N-OMe moiety by 3JCH correlations from the \$\beta\$ protons; HMBC correlations were seen from the NH proton (δ_H 6.19) of the Aoda residue to signals at δ_C 173.1 and 170.3, therefore the remaining amide signal at δ_C 171.2 could be assigned to Ile. This assignment is valid providing the sequence of amino acid constituents is unchanged from those in other apicidins. The signals at δ_C 173.1 and 170.3 were provisionally assigned to Aoda and Pip, respectively, with the δ_{H} 6.19/ δ_{C} 170.3 correlation representing an inter-unit correlation. Intra-unit correlations from the α -proton of epoxy-Trp-N-OMe to the carbonyl at δ_C 171.3 and from the α -proton of Ile to the carbonyl at δ_C 171.2 were observed.

The relative configuration of the epoxy ring was not determined. The specific rotation of 2 was -42, and when compared to literature values reported for apicidin $\{[\alpha]_D -80.4\}$ [6a], apicidin D_1 ($[\alpha]_D -72.6\}$), apicidin D_2 ($[\alpha]_D -68.5$), and apicidin D_3 ($[\alpha]_D -60.4$) [6c], the three amino acid constituents shared between these various metabolites were suggested to be (R)-Pip, (S)-Ile, and (S)-Aoda. The structural similarity of apicidin H with other apicidin metabolites implies that the configuration of the epoxy-Trp-N-OMe residue should be S.

Apicidin I (3) was the final apicidin metabolite isolated from F. semitectum. The HRESIMS data of 3 exhibited an adduct ion at m/2 656.4037 [M+H]⁺, corresponding to a molecular formula $C_{38}H_{53}N_5O_7$, which was 32 mass units larger than that of 4. The ¹H and ¹³C NMR spectra of 3 (Table 1) closely resembled those of 4, revealing the presence of four α -protons (δ_H 4.71, 4.37, 4.18, and 4.12), five aromatic signals (δ_H 7.67, 7.34, 7.31, 7.19 and 7.08), two methyl triplets (δ_H 1.03, 0.86) and one methyl doublet (δ_H 0.83). The NMR spectra of 3 also indicated the presence of two amide protons (2 x NH, δ_H 8.29, 7.14), one amino group (NH₂, δ_H 8.35) and one additional methoxy group (δ_H 3.56, δ_C 52.2). Assignments of the amino acid residues were undertaken by HMBC, DQFCOSY,

and 2D-TOCSY experiments, and by comparison with the data reported for apicidins [6a-6c]. TOCSY data revealed correlations from the NH₂ protons to the α -proton (δ_H 4.18) and to the five methylene groups of the Aoda residue. The methoxy group at δ_H 3.56 showed a HMBC correlation to the carbonyl group (8c 172.8) of the Pip unit. This information, together with the MS data, suggested a linear tetrapeptide as opposed to the cyclic tetrapeptide core of apicidin and its congeners. HMBC correlations were observed from the three a-protons at δ_H 4.37 (Ile), 4.71 (Trp-N-OMe) and 4.18 (Aoda) to the carbonyl groups at δ_C 172.7, 172.2 and 172.4, respectively. No inter-amino acid correlations were apparent in the HMBC spectrum, but the presence of Pip-OMe and Aoda-NH2 implies that apicidin I is an artefact from methanolysis of apicidin at the Pip residue. The same absolute configuration is therefore proposed. Apicidin I gave the same negative sign of specific rotation [a]p -17.3 (c 0.16, MeOH) as previous apicidins.

Apicidin was screened against a panel of bacterial (Gram-positive and -negative) and fungal strains, but was without activity. There was insufficient quantity of the new apicidins for biological screening. In conclusion, three new tetrapeptides, apicidins G (1), H (2) and I (3) were isolated together with six known compounds from Fusarium semitectum. The results from our study have shown modification at the Trp-N-OMe unit with an epoxy group in apicidin H. The absolute configurations of the apicidin metabolites were proposed by comparison of J values, specific rotation values, and from the biosynthetic similarities between the various metabolites. Tetrapeptides such as apicidin and its congeners may be chemotaxonomic markers for this fungal species.

Experimental

General: NMR data of 1-3 were measured on a Bruker Avance 500 MHz spectrometer (5 mm inverse probe, gradient selection) in CDCl₃ at 298K. For HSQC and HMBC spectra, data were acquired using a $^1J_{\rm C-H}$ of 135 Hz, while HMBC spectra were acquired using $^nJ_{\rm C-H}$ of 8 Hz. TOCSY data (mixing time 60 msec) were determined in phase sensitive mode. Positive ion electrospray mass spectra were determined using either a Bruker Esquire HCT instrument (LRESIMS) or a MicroTof Q instrument (HRESIMS) with MeOH as solvent. Reverse phase HPLC was carried out on an Agilent 1100 series instrument fitted with either a Phenomenex Gemini C₁₈ (250 x 10 mm i.d., 5 μ) column or a C₁₈ analytical column with UV detection at 254 nm. Silica gel 60 G and silica TLC plates F₂₅₄ were purchased from Merck. All solvents were either distilled or were of HPLC grade.

Fungal material: A white fungus isolated from a dead cicada skin was collected at the Tawangmangu Botanic Garden, Indonesia, and identified as Fusarium semitectum based on morphological comparison with F. semitectum. [2,4]. A voucher specimen (SC-131208-1, AQIS IP09011654) is held in the School of Biology, UQ.

Culture conditions: The fungus was grown on Petri dishes containing PDA media at room temperature for 7 days. Rice media for fermentation was prepared by soaking 50 g of long grain rice in 50 mL of distilled water in 250 mL Erlenmeyer flasks. After 6 h, the rice media was autoclaved for 15 min. Thirty Erlenmeyer flasks containing rice media were inoculated with a small plug of agar containing the mycelia of F. semitectum, and the cultures were kept in the dark at room temperature for 21 days.

Extraction and isolation of metabolites: Mycelia and media were homogenized by stirring, then extracted with MeOH (3 x 700 mL) using ultrasonic vibration for 30 min. The extract was filtered, then concentrated in vacuo to an aqueous residue, which was partitioned

with EtOAc (3 x 300 mL) to give a dark purple oil (3.6 g). The extract was subjected to vacuum liquid chromatography using stepwise gradient elution (100% hexanes to 100% EtOAc) to obtain 11 fractions. Fraction 5 (225 mg) was subjected to NP-flash column chromatography using a stepwise elution of DCM/MeOH to give equisetin (8) (59.3 mg). Combined fractions 6 and 7 (570 mg) were chromatographed on silica using a stepwise elution of DCM/EtOAc/MeOH to give 11 fractions coded 6n7-1 to 6n7-11. Combined fractions 6n7-1 to 7-3 (17.4 mg) were purified by RP-HPLC (65-100% MeOH/H2O) to yield (-)-apicidin (4) (3.7 mg) then (-)-equisetin (8) (1.8 mg). Fraction 6n7-5 (150 mg) was subjected to RP flash column chromatography with MeOH/H2O to give apicidin (4) (16.2 mg), a mixture of apicidin (4) and equisetin (8) (41.1 mg) and fraction 6n7-5-1 (9.5 mg), which was further purified by RP-HPLC (70-100% MeOH/H₂O) to yield apicidin I (3) (2.4 mg). Fraction 6n7-6 (99 mg) was purified by RP-HPLC (80-100% MeOH/H2O) and gave 7 fractions. (-)-Cyclo-(D-pipecolinyl-Lisoleucine) [15] (7) (0.9 mg) was in fraction 6n7-6-2. Fraction 6n7-6-5 contained a 1:1 mixture of apicidins G (1) and C (6) (5.4 mg). Apicidin (4) (36.4 mg) was in fraction 6n7-6-6. Fraction 6n7-6-4 (3.2 mg) was purified by RP-HPLC (75% MeOH/H2O) affording apicidin H (2) (0.5 mg) and apicidin A (5) (1.3 mg). Combined fractions 6n7-7 and 7-8 (43.5 mg) were chromatographed using a RP Sep-pak™ (20-100% McOH/H₂O) to give (+)-7-hydroxy-2-(2hydroxypropyl)-5-methylchromone (9) [16] (2.2 mg), apicidin (4) (16.2 mg), and a mixture of apicidin (4) and equisetin (8) (5.5 mg).

Apicidin G 1

Colorless film

H NMR and 13C NMR (CDCl3): Table 1.

HRESIMS: m/z [M+Na] calcd for C31H46N4NaO5: 577.3360; found:

577.3360.

Apicidin H 2 Colorless film

 $[\alpha]^{24}_{D}$: -42 (c 0.03, MeOH) $^{1}_{H}$ NMR and 13 C NMR (CDCl₃): Table 1.

HRESIMS: m/z [M+Na] calcd for C34H49N5NaO7: 662.3524; found:

662.3545.

Apicidin 1 3

Colorless film

[α]²⁴_D: -17 (c 0.16, MeOH)

¹H NMR and ¹³C NMR (CDCl₃): Table 1.

HRESIMS: m/z [M+H] calcd for C35H54N5O7: 656.4018; found:

656.4037.

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