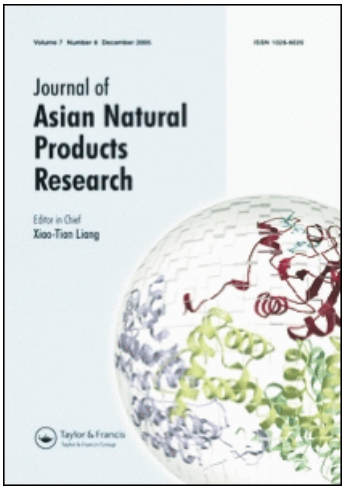

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Hederyne A, a new antimicrobial polyacetylene from galls of *Hedera rhombea* Bean

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A new C_{17}-polyacetylene, named hederyne A (**1**), has been isolated from the MeOH extract of galls of *Hedera rhombea* Bean (Araliaceae), together with two known polyacetylenes, falcarindiol (**2**) and 11,12-dehydrofalcarinol (**3**). The structure elucidation of **1** was achieved by NMR, MS, IR, and UV spectroscopy. Hederyne A (**1**) was a new C_{17}-diacetylene containing 1,3-propanediol and exhibited selective antimicrobial activity against *Micrococus luteus*.

Keywords: *Hedera rhombea* Bean; Polyacetylenes; Gall; Hederyne A; Antimicrobial activity

1. Introduction

Hedera rhombea Bean (Kizuta in Japanese) is an evergreen viny plant of the family Araliaceae, which is widely distributed in Japan, Korea and China. The extract of the leaves of *H. rhombea* has been used as a therapeutic agent for various diseases. Although the constituents of normal tissue of this plant have been investigated, those of galled tissue, which was induced by infection of ivy flower bud gall midge *Asphondylia* sp. (Cecidomyiidae), have not been studied [1–4]. Since it is known that gall formation leads to changes in plant metabolism, study on constituents of galled tissue of *H. rhombea* will be expected to result in the isolation of new bioactive compounds [5]. The analysis of the MeOH extract allowed to characterise a new C_{17}-polyacetylene, named hederyne A (**1**), together with two known polyacetylenes, falcarindiol (**2**) and 11,12-dehydrofalcarinol (**3**) [6,7]. In this paper we describe the isolation, structure elucidation, and antimicrobial activity of hederyne A (**1**).

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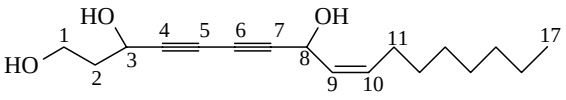
2. Results and discussion

The MeOH extract of galls of *Hedera rhombea* Bean was partitioned between H_2O and EtOAc, and H_2O-soluble fraction was further partitioned with BuOH to give EtOAc, BuOH, and H_2O layer. EtOAc-soluble materials were purified by silica gel column chromatography, ODS high-performance liquid chromatography (HPLC), and preparative thin-layer chromatography (PTLC) to afford hederyne A (**1**, 0.0007% wet wt) and falcarindiol (**2**). BuOH-soluble materials were separated by ODS column chromatography, and reversed-phase HPLC to obtain 11,12-dehydrofalcarinol (**3**).

Hederyne A (**1**) showed a pseudomolecular ion peak at *m/z* 301 $[M + Na]^+$ in the FAB-MS spectrum. HRFAB-MS analysis revealed the molecular formula to be $C_{17}H_{26}O_3$ (at *m/z* 301.1779 $[M + Na]^+$). It showed very similar UV absorption (242, 248, and 260 nm) to those of falcarindiol (**2**) (233, 245, and 259 nm) [8], suggesting the presence of a conjugated diyne in **1**. This was also supported by the IR absorptions (2362 and 2260 cm^{-1}) [8]. Its ^1H NMR spectrum indicated the presence of two olefinic protons (δ 5.62 and 5.54), two oxymethine protons (δ 5.20 and 4.72), four nonequivalent methylene protons (δ 4.02, 3.88, 2.04, and 1.95), ten methylene protons (δ 1.28, 1.37, and 2.11), and a methyl (δ 0.88). The ^{13}C NMR spectrum of **1** showed signals due to two olefinic carbons, four acetylenic carbons, two oxymethines, an oxymethylene, seven methylenes, and a methyl group. From consideration of $^1H-^1H$ COSY and HMQC spectra of **1**, the partial structures of C-1—C-3 and C-8—C-17 could be deduced (figure 1). The conjunction between the two substructures (C-1—C-3 and C-8—C-17) was necessarily possible throughout the triple bond (C-4—C-7). This was also supported by the $^1H-^1H$ COSY long-range correlation between H-3 and H-8 and HMBC correlations between H-8 and C-4 (δ 79.5), C-5 (δ 68.7), C-6 (δ 69.4), and C-7 (δ 79.9). The *Z*-geometry of the double bond (C-9, 10) was deduced on the basis of the $^1H-^1H$ coupling constant ($J_{9,10} = 10.6$ Hz) between H-9 and H-10. Thus, the structure of hederyne A (**1**) is elucidated to be (*Z*)-heptadeca-9-en-4,6-diyne-1,3,8-triol, which was a rare C_{17}-diacetylene containing 1,3-propanediol.



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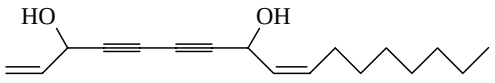

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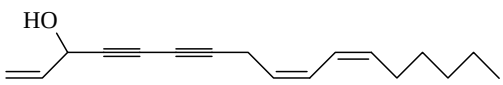

3

Figure 1. The structures of compounds **1**–**3**.

Since it has been reported that falcarindiol (**2**) exhibits antimicrobial activity [9], structurally related compounds **1** and **3**, together with **2** were evaluated for antimicrobial activities against the Gram-positive bacteria *Bacillus subtilis*, *Micrococcus luteus*, and *Stapylococcus aureus*, and the Gram-negative bacterium *Escherichia coli*. They were also tested against three fungal strains *Cryptococcus neoformans*, *Candida albicans*, and *Aspergillus niger*. The results are shown in table 1. Among these polyacetylenes (**1**–**3**), the highest active compound appeared to be compound **2**, followed by compound **1** and compound **3**. Compound **1** showed growth inhibitory activity against some Gram-positive bacteria and fungi, and compound **1** exhibited selective antimicrobial activity against *M. luteus*.

3. Experimental

3.1 General experimental procedures

Optical rotations were measured with a JASCO DIP-370 polarimeter. IR spectra were recorded on a JASCO FT/IR-300 spectrometer. ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were measured and recorded in $CDCl_3$ on a Bruker Avance 500 spectrometer. Chemical shift values (δ) were reported in parts per million (ppm) relative to NMR solvent $CDCl_3$ (δ_H 7.26, δ_C 77.0). FAB-MS spectra were recorded in the positive-ion mode, on a JEOL IMS-SX102 mass spectrometer.

3.2 Plant material

Galls of *Hedera rhombea* induced by infection of *Asphondylia* sp. were collected at Tsuchiura city, Japan. A voucher specimen has been deposited at the Graduate School of Life and Environmental Sciences, University of Tsukuba, Japan.

3.3 Extraction and isolation

Galls of *H. rhombea* (110 g) were homogenised by a blender, and extracted with MeOH (420 ml) and concentrated *in vacuo*. The MeOH extracts (9.37 g) were partitioned between EtOAc (500 ml × 3) and H_2O (500 ml) and the H_2O-layer was further partitioned with BuOH (500 ml × 3). EtOAc-soluble portion (1.24 g) was chromatographed on a silica gel

Table 1. Antimicrobial activities of hederyne A (**1**), falcarindiol (**2**), and 11,12-dehydrofalcarinol (**3**).

	MIC (μg/ml)		
	1	***2***	***3***
Bacillus subtilis	83	5.2	>166
Micrococcus luteus	5.2	2.6	>166
Stapylococcus aureus	166	10.4	>166
Escherichia coli	>166	>166	>166
Cryptococcus neoformans	83	5.2	83
Candida albicans	>166	41.5	>166
Aspergillus niger	83	20.8	166

using hexane-EtOAc (19:1 → 0:1) as the eluting solvents and separated into 12 fractions (EA-1 to EA-12). Fraction EA-6 (75.0 mg) was purified by reversed-phase HPLC (TSK-GEL ODS-80Ts, Tosoh Co. Ltd, 7.8 mm × 30.0 cm, flow rate 2.0 ml/min, MeOH/H_2O, 85:15) to give **2** (55.9 mg, t_R 11 min). Fraction EA-11 (36.5 mg) was separated by silica gel PTLC ($CHCl_3$/MeOH, 12:1), followed by reversed-phase HPLC (TSK-GEL ODS-80Ts, 7.8 mm × 30.0 cm, flow rate 2.0 ml/min, CH_3CN/H_2O, 60:40) to give **1** (0.8 mg, t_R 22 min). BuOH-soluble portion (2.34 g) was subjected to an ODS column (Cosmosil 75 C_{18}-PREP. Nacalai tesque, 22 mm × 30.0 cm) using MeOH/H_2O (3:2 → 1:0) to give 19 fractions (BU-1 to BU-19). Fraction BU-11 (12.6 mg) was separated by reversed-phase HPLC (TSK-GEL ODS-80Ts, 7.8 mm × 30.0 cm, flow rate 2.0 ml/min, MeOH/H_2O, 85:15) to give **3** (2.4 mg, t_R 18 min).

Hederyne A (1): Colourless oil; $[\alpha]_D^{22}$ + 20 ($CHCl_3$; *c* 0.5); UV $\lambda_{max}^{Et_2O}$ nm (log ε): 206 (3.9), 243 (3.3), 248 (3.3), 254 (3.3), and 260 (3.2); IR (KBr) ν_{max}: 3334, 2923, 2362, 2260, 1714, and 1261 cm^{-1}; ^1H NMR ($CDCl_3$): δ 5.62 (1H, dt, J = 10.6 and 7.5 Hz, H-10), 5.54 (1H, dd, J = 10.6 and 8.4 Hz, H-9), 5.20 (1H, d, J = 8.4 Hz, H-8), 4.72 (1H, dd, J = 6.3 and 4.8 Hz, H-3), 4.02 (1H, ddd, J = 10.8, 7.9, and 3.7 Hz, H-1a), 3.88 (1H, ddd, J = 10.8, 6.3, and 4.3 Hz, H-1b), 2.11 (2H, q, J = 7.5 Hz, H-11), 2.04 (1H, m, H-2a), 1.95 (1H, m, H-2b), 1.37 (2H, t-like, J = 7.5 Hz, H-12), 1.28 (8H, m, H-13-H-16), and 0.88 (3H, t, J = 6.8 Hz, H-17), ^{13}C NMR ($CDCl_3$) δ 134.7 (C-10), 127.7 (C-9), 79.9 (C-7), 79.5 (C-4), 69.4 (C-6), 68.7 (C-5), 62.1 (C-3), 60.4 (C-1), 58.6 (C-8), 38.4 (C-2), 31.8 (C-15), 29.3 (C-12), 29.1 (C-13), 29.0 (C-14), 27.7 (C-11), 22.6 (C-16), and 14.1 (C-17); FAB-MS *m/z* 301 $[M + Na]^+$, HRFAB-MS *m/z* 301.1779 $[M + Na]^+$ (calcd for $C_{17}H_{26}O_3Na$, 301.1752).

Physicochemical and spectral data (MS, $[\alpha]_D$, IR, ^1H NMR, and ^{13}C NMR) of compounds **2** and **3** were consistent with published values [6,7].

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References

[1] B.M. Kwon, S.H. Lee, K.S. Kim, I.R. Lee, U.C. Lee, S.H. Hong, S.H. Bok. *Bioorg. Med. Chem.*, **7**, 971 (1997).
[2] M. Shimizu, M. Arisawa, N. Morita, H. Kizu, T. Tomimori. *Chem. Pharm. Bull.*, **26**, 655 (1978).
[3] H. Kizu, M. Koshijima, T. Tomimori. *Chem. Pharm. Bull.*, **33**, 3176 (1985).
[4] H. Kizu, M. Koshijima, M. Hayashi, T. Tomimori. *Chem. Pharm. Bull.*, **33**, 1400 (1985).
[5] C. Kraus, G. Spiteller. *Phytochemistry*, **44**, 59 (1997).
[6] S. Tanaka, Y. Ikeshiro, M. Tabata, M. Konoshima. *Arzneimittelforschung*, **27**, 2039 (1977).
[7] F. Gafner, E. Rodriguez. *Rev. Latinoamer. Quim.*, **20**, 30 (1989).
[8] K.E. Schule, B. Potter. *Arch. Pharm.*, **310**, 945 (1977).
[9] A. Satoh, Y. Narita, N. Endo, H. Nishiyama. *Biosci. Biotech. Biochem.*, **60**, 152 (1996).