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RESEARCH NOTE

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Consoramides A–C, New Zwitterionic Alkaloids from the Fungus *Irpex consors*

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ABSTRACT

In our ongoing search for new secondary metabolites from fungi, a basidiomycete fungus *Irpex consors* was selected for mycochemical investigation, and three new zwitterionic alkaloids (**1**-**3**) and five known compounds (**4**-**8**) were isolated from the culture broth (16 l) of *I. consors*. The culture filtrate was fractionated by a series of column chromatography including Diaion HP-20, silica gel, and Sephadex LH-20, Sep-Pak C_{18} cartridge, medium pressure liquid chromatography (MPLC), and high pressure liquid chromatography (HPLC) to yield eight compounds (**1**-**8**). The structures of the isolated compounds were elucidated by the interpretation of nuclear magnetic resonance (NMR) spectra and high-resolution mass spectrometry (HR-MS). Their antioxidant and antibacterial activities were examined. The zwitterionic structures of three new sesquiterpene alkaloids (**1**-**3**) were determined together with five known compounds identified as stereumamide E (**4**), stereumamide G (**5**), stereumamide H (**6**), stereumamide D (**7**), and sterostrein H (**8**). This is the first report of the zwitterionic alkaloids in the culture broth of *I. consors*. Three new zwitterionic alkaloids were named as consoramides A–C (**1**-**3**).

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Mushrooms are a good source of functional foods and traditional therapeutic agents [1]. They produce a wide range of biologically active compounds with unique chemical structures [2–4]. The mushroom *Irpex consors*, belonging to the family Meruliacease, is distributed in India and East Asian countries such as Korea and Japan [5]. Previous investigations of *I. consors* have reported that it possesses tricyclic sesquiterpene derivatives with anti-bacterial and anti-tumor activities [6–8]. In our ongoing search for new secondary metabolites from fungal strains, three new zwitterionic alkaloids (**1**-**3**) together with five known compounds (**4**-**8**) were isolated from the culture broth of the fungus *I. consors*. Herein, we describe the isolation and structure determination of these compounds (Figure 1).

Fungal strain *Irpex consors* was obtained from Rural Development Administration, Korea. The fungal strain *I. consors* was cultured on potato dextrose agar at 27 °C for two weeks. Small pieces of fresh mycelium were inoculated into 40 1-l flasks containing 400 ml of potato dextrose broth and cultured on a rotary shaker of 120 rpm at 27 °C for four weeks. The culture broth (about 16 l) was filtered to remove mycelia. The culture filtrate was fractionated by Diaion HP-20 column chromatography eluted with a mixture of methanol-water (30:70–100:0, v/v, stepwise), followed by silica gel column chromatography with stepwise chloroform-methanol (30:1–0:100, v/v) to afford four fractions (Fractions A-D). Fraction A was subjected to Sephadex LH-20 column chromatography, followed by medium pressure liquid chromatography (MPLC) to give two fractions A1 and A2. Fraction A1 was purified by Sep-Pak C_{18} cartridge eluted with 20% aqueous methanol to obtain two compounds **1** (4.3 mg) and **2** (12.9 mg). Fraction A2 was further separated by a Sep-Pak C_{18} cartridge eluted with 15% aqueous methanol to obtain compound **7** (4.5 mg). Fraction B was fractionated by Sephadex LH-20 column chromatography, followed by preparative reversed-phase high pressure liquid chromatography (HPLC) eluted with 18% aqueous methanol to yield two compounds **4** (9.3 mg) and **6** (9.5 mg). Fraction C was subjected to MPLC, followed by preparative reversed-phase HPLC eluted with 18% aqueous methanol to

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Supplemental data for this article can be accessed here.

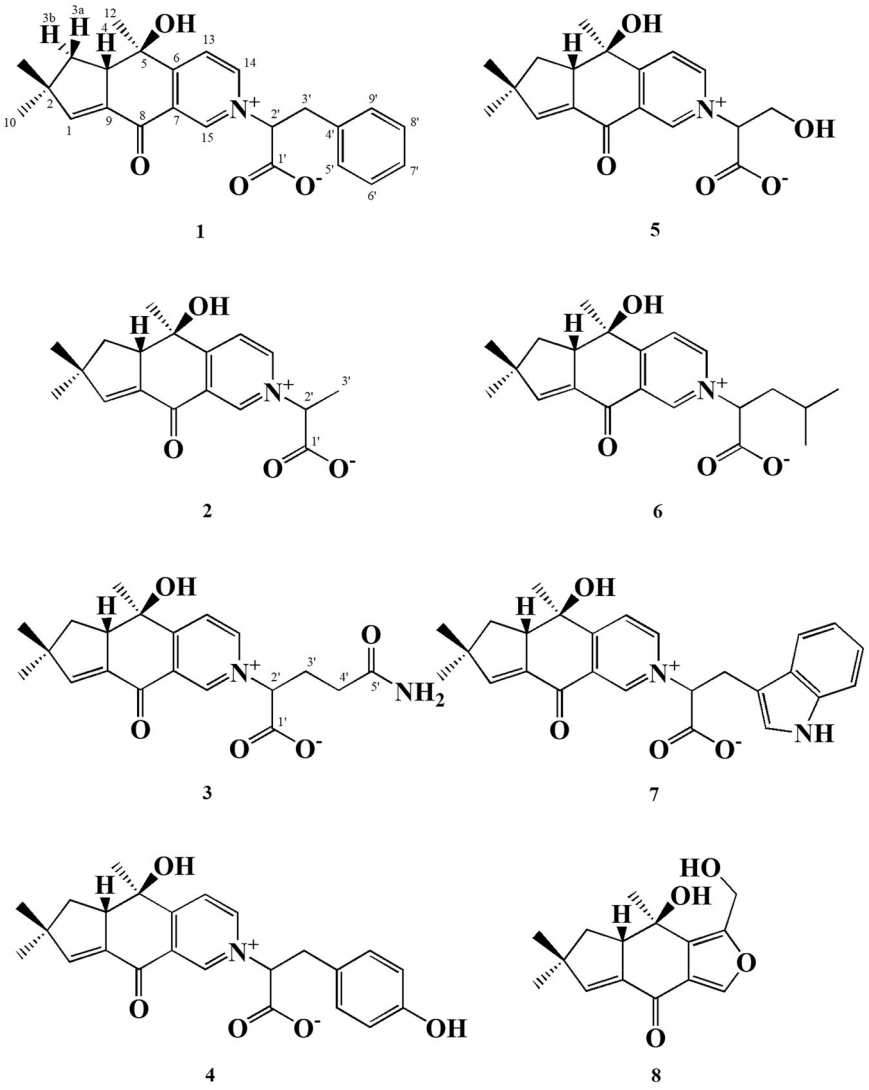

Figure 1. Structures of compounds **1-8**.

provide two compounds **5** (12.0 mg) and **8** (9.0 mg). Fraction D was separated by MPLC eluted with a gradient of increasing methanol (20–100%) in water, followed by preparative reversed-phase HPLC eluted with 27% aqueous methanol to obtain a compound **3** (4.8 mg).

Compound **1** was obtained as a brown powder with a specific rotation value of −92.8° ($c = 0.1$, 24.5 °C, methanol). Its molecular formula was established as $C_{24}H_{25}NO_4$ by a high-resolution fast atom bombardment (FAB)-mass measurement (*m/z* 392.1849 $[M+H]^+$, Δ −1.2 mmu). The ^{1}H NMR spectrum of **1** revealed the presence of a substituted benzene moiety at δ 7.18 (× 2), 7.14, and 7.09 (× 2), a 3,4-disubstituted pyridine moiety at δ 9.05, 8.99, and 8.27, a olefinic methine at δ 6.93, two methines at δ 5.59 and 3.69, two methylenes at δ 3.88/3.47 and 2.10/1.97, and three methyls at δ 1.28, 1.24, and 1.19 (Table 1). In the ^{13}C NMR spectrum, twenty-four carbons including one ketone carbon at δ 181.1, one carbonyl carbon at δ 171.0, nine sp^2 methine carbons at δ 155.7, 148.6, 145.7, 130.1 (× 2), 129.9 (× 2), 128.6, and 125.0, four sp^2 quaternary carbons at δ 171.4, 137.4, 137.3, and 131.6, one oxygenated quaternary carbon at δ 74.1, two methine carbons at δ 78.8 and 53.8, one quaternary carbon at δ 47.0, two methylene carbons at δ 40.7 and 40.6, and three methyl carbons at δ 28.6, 27.6, and 25.2 were evident (Table 1). In the ^{1}H-^{1}H correlated spectroscopy (COSY) spectrum, correlations between H-3 and H-4 and between H-13 and H-14 were observed, and the long-range correlations from H-1 to C-8 and C-9, from H-3 to C-5 and C-9, from H-10 and H-11 to C-1, C-2, and C-3, from H-12 to C-4, C-5, and C-6, from H-13 to C-5 and C-7, from H-14 to C-6 and C-15, and from H-15 to C-6 and C-8 established the presence of sterostrein Q moiety. The long-range correlations from H-2′ to C-1′, C-3′ and C-4′, from H-8′ to C-4′, and from H-9′ to C-3′ and C-7′ as well as ^{1}H-^{1}H COSY correlations of H-5′/H-6′/H-7′/H-8′/H-9′ and H-2′/H-3′ revealed the presence of a phenylalanine moiety. Finally, the long-range correlations from H-14 and H-15 to C-2′ and from H-2′ to C-14 and C-15 indicated that the phenylalanine moiety was connected to sterostrein Q *via* carbon-nitrogen bond

Table 1. ^{1}H and ^{13}C NMR data of compounds **1-3** in methanol-d_4.

	1[a]		**2**[a]		**3**[a]	
No.	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)	δ_C	δ_H (mult, *J* in Hz)
1	155.7	6.93 (d, 2.7)	155.6	6.98 (d, 2.5)	155.8	6.99 (d, 2.3)
2	47.0		47.0		47.1	
3a	40.6	2.10 (dd, 13.0, 8.2)	40.6	2.14 (dd, 13.0, 8.3)	40.6	2.15 (dd, 13.5, 7.9)
3 b		1.97 (dd, 13.0, 8.2)		2.05 (dd, 13.0, 8.3)		2.05 (dd, 13.5, 7.9)
4	53.8	3.69 (td, 8.2, 2.7)	53.9	3.77 (td, 8.3, 2.5)	53.9	3.78 (td, 8.2, 2.3)
5	74.1		74.2		74.3	
6	171.4		171.1		172.3	
7	131.6		132.0		132.2	
8	181.2		181.6		181.3	
9	137.4		137.6		137.5	
10	28.6	1.28 (s)	28.6	1.31 (s)	28.6	1.31 (s)
11	27.6	1.19 (s)	27.7	1.22 (s)	27.6	1.22 (s)
12	25.2	1.24 (s)	25.2	1.34 (s)	25.2	1.36 (s)
13	125.0	8.27 (d, 6.4)	125.2	8.38 (d, 6.1)	125.6	8.43 (d, 6.1)
14	148.6	8.99 (dd, 6.4, 1.3)	147.9	9.08 (d, 6.1)	148.6	9.13 (d, 6.1)
15	145.7	9.05 (d, 1.3)	145.3	9.25 (s)	146.2	9.32 (s)
1′	171.0		172.6		170.5	
2′	78.8	5.59 (dd, 11.0, 4.8)	73.0	5.41 (q, 7.5)	75.0	5.63 (m)
3a′	40.7	3.88 (m)	19.3	1.94 (d, 7.5)	29.6	2.80 (m)
3 b′		3.47 (m)				2.60 (m)
4′	137.3				32.5	2.38 (t, 6.8)
5′	129.9	7.09 (d, 6.8)			176.3	
6′	130.1	7.18 (d, 7.5)				
7′	128.6	7.14 (t, 7.5)				
8′	130.1	7.18 (d, 7.5)				
9′	129.9	7.09 (d, 6.8)				

[a]Measured at 600 MHz for ^{1}H and 150 MHz for ^{13}C.

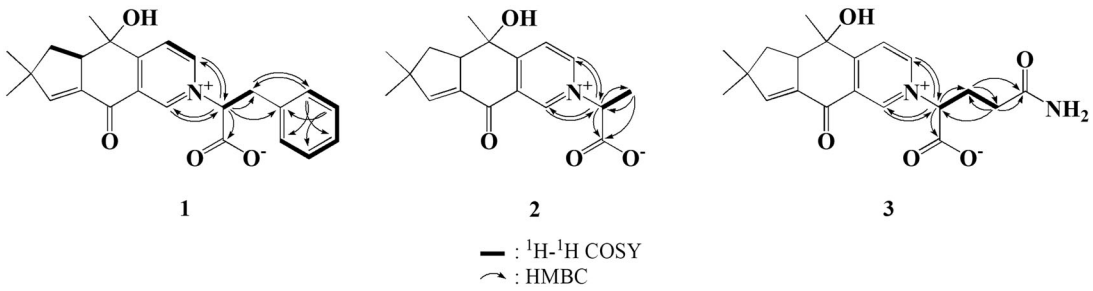

Figure 2. ^{1}H-^{1}H COSY and HMBC correlations of compounds **1-3**.

(Figure 2). The partial relative stereochemistry of **1** was established by the NOESY correlations. The cross peaks of H-4/H-3a and H-4/H-11 indicated the same face, while those of H-10/3b and H-3b/H-12 confirmed the other face. Therefore, the structure of **1** was determined as a new zwitterionic alkaloid and named consoramide A.

Compound **2** was purified as a yellow oil with specific rotation of −107.2° (*c* = 1.0, 25.0 °C, methanol) and exhibited UV maxima (log ε) at 203 (3.34) and 238 (3.61) nm. Its molecular formula was determined to be $C_{18}H_{21}NO_4$ by the high-resolution FAB-mass measurement (*m/z* 316.1531 $[M+H]^+$, Δ −1.8 mmu). The 1 D NMR spectra of **2** revealed that the hydroxymethyl group in **5** was replaced by a methyl group (Table 1). The long-range correlations from H-3′ to C-1′ and C-2′ as well as ^{1}H-^{1}H COSY correlations between H-2′and H-3′ supported the presence of an alanine moiety in **2** (Figure 2). Therefore, compound **2** was determined to be a new zwitterionic alkaloid and named consoramide B.

Compound **3** was obtained as a yellow powder with the specific rotation of −89.2° (*c* = 1.0, 25.0 °C, methanol) and showed UV maxima (log ε) at 202.0 (3.37) nm. Its molecular formula was established as $C_{20}H_{24}N_2O_5$ by the high-resolution FAB-mass measurement (*m/z* 373.1745 $[M+H]^+$, Δ −1.9 mmu). The NMR spectra revealed that **3** was consisted of sterostrein Q and glutamine (Table 1). The glutamine moiety was determined by the ^{1}H-^{1}H COSY correlations and the long-range correlations from H-2′ to C-1′ and C-3′ and from H-3′ and H-4′ to C-5′ (Figure 2). Thus, compound **3** was determined to be a new zwitterionic alkaloid and named consoramide C. The configuration of all amino acid moieties in **1-3** was tentatively deduced as L-form, because the L-amino acids are abundant in nature literature [9,11].

Compounds **4-8** were identified as stereumamide E (**4**), stereumamide G (**5**), stereumamide H (**6**),

stereumamide D (**7**), and sterostrein H (**8**), respectively, by the comparison of their spectroscopic data with the literatures previously reported [9–11].

The antioxidant activities of these compounds (**1**-**8**) were evaluated by the ABTS (2,2′-azinobis [3-ethylbenzothiazoline-6-sulonate]) and DPPH (1,1-diphenyl-2-picrylhydrazyl) radical-scavenging assays [12]. All compounds (**1**-**8**) displayed no radical scavenging activity up to 200 μM. In the present study, all compounds exhibited no antibacterial activity up to 50 μg/disk against *Bacillus subtilis*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Propionibacterium acnes,* and *Escherichia coli*.

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Disclosure statement

No potential conflict of interest was reported by the author(s).

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Supplementary information

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