Baimantuoluolines D – F, Three New Withanolides from the Flower of *Datura metel* L.

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Three new withanolide compounds, named baimantuoluolines D – F, along with three known withanolides and a lignan were isolated from the flower of *Datura metel* L., the parts effective against psoriasis. The structures of the new compounds were elucidated as (5*α*,6*β*,12*β*,20*R*,22*R*,24*R*,25*S*)-21,24-epoxy-5,6,12-trihydroxy-27-methoxy-1-oxowith-2-enolide (**1**), (5*α*,6*β*,12*β*,20*R*,22*R*,24*R*,25*S*)-21,24-epoxy-5,6,12,27-tetrahydroxy-1-oxowith-2-enolide (**2**), and (5*α*,6*β*,12*β*,22*R*)-5,6,12,21-tetrahydroxy-1-oxo-with-24-enolide(**3**) on the basis of physicochemical evidence.

Introduction. – Flos Daturae, the dry flower of *D. metel* L. (Solanaceae) widely distributed in the Jiangsu, Zhejiang, Fujian, Guangdong, and Sichuan provinces of China, has been used as a traditional Chinese medicine for the treatment of cough, asthma, convulsion, *etc.* due to its strong and wide biological activities [1].

Withanolides are a group of naturally occurring oxygenated ergostane-type steroids generally having an *α*,*β*-unsaturated *δ*-lactone ring formed in the side chain. Biogenetic transformations, however, can produce highly modified compounds, both at the steroid nucleus and within the side chain. They were first isolated from *Withania somnifera*, from which they derive their name. Most withanolide compounds are produced by Solanaceae plants belonging to the genera *Withania*, *Physalis*, *Datura*, *Dunalia*, *Jaborosa*, *Lycium*, *Hyoscyamus* and *Solanum* [2]. The biological activities of withanolides have been studied extensively in the past. Many of the withanolides exhibit interesting biological activities including insecticide, antifeedant, anticonvulsive, antibacterial, anti-inflammatory, immunosuppressive, and antioxidant properties [2][3].

Flos Daturae has an obvious effect during the treatment of psoriasis and is clinically used in China. However, its active constituents and pharmacological effects related to the treatment of psoriasis were not fully illuminated. In continuation of our search for active substances of *D. metel* L. for psoriasis, we investigated a 50% EtOH eluate fraction of the flower of *D. metel* L., which resulted in the discovery of three new withanolides, three known withanolides and a lignan (*Fig. 1*). This article deals with the structural elucidation of these compounds.

Results and Discussion. – Compound **1**, named baimantuoluoline D, was obtained as a white amorphous powder with a m.p. of 205 – 208°. The positive ESI-MS showed an $[M+Na]^+$ ion peak at 541. The molecular formula was determined by positive HR-

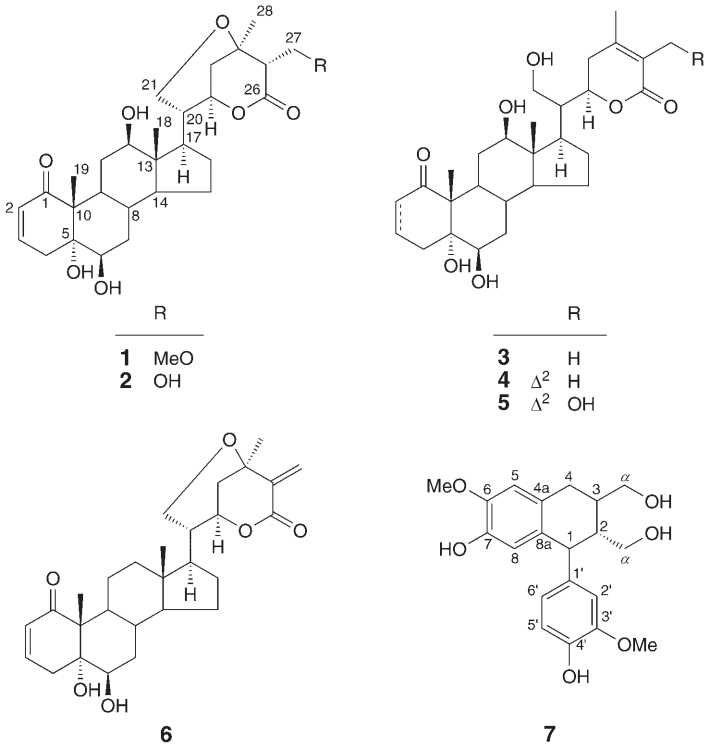

Fig. 1. *Structures of* **1**–**7**

ESI-MS as $C_{29}H_{42}O_8$ from the $[M+Na]^+$ and $[M+K]^+$ signals at *m/z* 541.2784 (calc. for $C_{29}H_{42}NaO_8^+$, $[M+Na]^+$; 541.2778) and 557.2518 (calc. for $C_{29}H_{42}KO_8^+$, $[M+K]^+$; 557.2517).

The ^{1}H-NMR spectrum of **1** showed several features which are characteristic for a withanolide steroid. Three *singlet*s at δ(H) 0.71, 1.30 and 1.28 were attributed to Me(18), Me(19), and Me(28), respectively. The signal at δ(H) 3.34 (*s*, 3 H) was unambiguously assigned to a MeO group. δ(H) 5.78 (*dd*, $J = 10.0, 2.4$ Hz, 1 H) and 6.65 (*ddd*, $J = 10.0, 5.2, 2.0$ Hz, 1 H) were attributed to H–C(2) and H–C(3), of a steroidal Δ^2-1-one system, respectively. The multiplicities of the H–C(2) and H–C(3) signals indicated that C(4) was unsubstituted. The double *doublet* at δ(H) 3.55 ($J = 11.2$, 4.4 Hz, 1 H) was characteristic for a 12β-hydroxywithanolide. A Me(21) signal was missing, it was replaced by a *doublet* and a double *doublet* at δ(H) 4.60 ($J = 13.6$ Hz, 1 H) and 3.38 ($J = 13.6$, 3.2 Hz, 1 H). The H–C(22) signal of withametelin G (**6**) appeared as a broad *singlet* at δ(H) 4.69 ($w_{1/2}$ *ca.* 5.0 Hz), while the signals for H–C(22) of baimantuoluolines A–C [4] were double *triplet*s (*dt*, 1 H). Namely, when C(20) is linked to C(24) to form a ring *via* $-CH_2(21)-O-$, the H–C(22) signal appears as a broad *singlet* ($w_{1/2}$ *ca.* 5.0 Hz), while in the absence of ring-closure (usual withanolide-type), the H–C(22) signal appears as a double *triplet* (*dt*, 1 H). These facts suggested that due to a broad *singlet* at 4.72 ($w_{1/2}$ *ca.* 5.0 Hz) for H–C(22) in **1** C(20) is connected

to C(24) *via* a $-CH_2(21)-O-$ bridge, which is consistent with the Me(28) signal appearing at δ(H) 1.28 (*s.*, 3 H). Furthermore, the signals of CH_2(27) (δ(H) 3.92 (*dd*, $J = 10.0$, 3.0 Hz, 1 H) and 3.76 (*dd*, $J = 10.0$, 5.6 Hz, 1 H)) showed an *ABX* type coupling pattern, which strongly suggested that C(25) should be a methine C-atom.

The ^{13}C-NMR (DEPT) spectrum showed the presence of 29 C-atoms, including three Me and a MeO, eight CH_2, and eleven CH groups, and six quaternary C-atoms, which indicated that **1** was a withanolide compound with 28 skeletal C-atoms. A notable feature of ^{13}C-NMR spectra was the appearance of four downfield quaternary C-atom signals at δ(C) 207.2, 174.8, 144.0 and 128.9 which were due to two CO groups and two olefinic C-atoms, respectively. The typical signals at δ(C) 78.2, 78.2, 78.1, 75.1, 71.9, and 62.8 were assigned to the oxygenated C-atoms at C(5), C(22), C(12), C(6), C(24), and C(21), respectively.

Assignments of all functional groups were achieved by DEPT, ^{1}H,^{1}H-COSY, HSQC and HMBC spectra. Key HMBC correlations (*Fig. 2*) were observed between the Me(18) and C(12), C(13), C(14), and C(17), between Me(19) and C(1), C(5), C(9), and C(10), between Me(28) and C(23), C(24), and C(25), between CH_2(21) and C(22) and C(24), and between MeO and CH_2(27).

Daturametelin D and daturametelin G-Ac were isolated from the methanolic extract of the aerial parts of *D. metel* L. and their stereochemistry at C(20), C(22), C(24) and C(25) showed several common features which are characteristic of (20*R*,22*R*,24*R*,25*S*) [5]. For **1**, the absolute configuration at C(20), C(22), C(24), and C(25) was finally elucidated as (*R*), (*R*), (*R*), and (*S*), respectively, by comparison with ^{1}H- and ^{13}C-NMR shifts with those of withanolide compounds, having the same configuration at C(20), C(22), and C(24) [5b][6]. From these data, in combination with an HMBC experiment (*Fig. 2*), the structure of **1** was identified as (5α,6β,12β,20*R*,22*R*,24*R*,25*S*)-21,24-epoxy-5,6,12-trihydroxy-27-methoxy-1-oxowith-2-enolide.

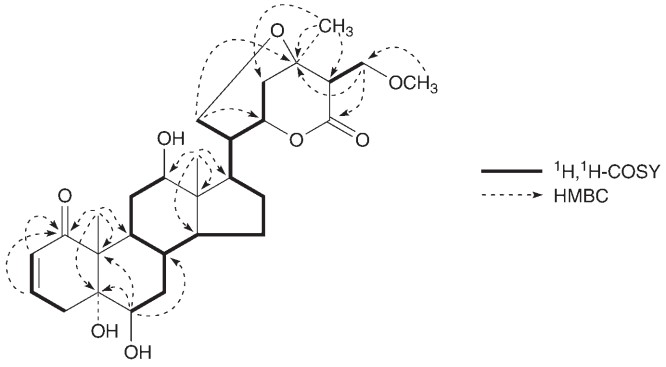

Fig. 2. *Key ^{1}H,^{1}H-COSY and HMBC correlations of* **1**

Compound **2**, named baimantuoluoline E, was obtained as a white amorphous powder, with a melting point of 217–220°. The ESI-MS showed an $[M + Na]^+$ ion peak at 527. The molecular formula was determined by positive HR-ESI-MS as $C_{28}H_{40}O_8$

from the $[M+Na]^+$ and $[M+K]^+$ signals at *m/z* 527.2632 (calc. for $C_{28}H_{40}NaO_8^+$, $[M+Na]^+$; 527.2621) and 543.2373 (calc.for $C_{28}H_{40}KO_8^+$, $[M+K]^+$; 543.2360).

The ^{13}C-NMR (DEPT) spectra of **2** showed resonances for all 28 C-atoms including three Me, eight CH_2, and eleven CH groups, and six quaternary C-atoms. Compared to the ^{13}C-NMR data of **1**, it showed a striking resemblance of the chemical shifts, and the only observed difference was observed for the CH_2(27) group. The signal for C(27) was shifted highfield ($\Delta\delta$(C) 10.5), which indicated that the additional MeO group of **1** was absent in this position. From the above data, the structure of **2** was identified as (5α,6β,12β,20*R*,22*R*,24*R*,25*S*)-21,24-epoxy-5,6,12,27-tetrahydroxy-1-oxowith-2-enolide.

Compound **3**, named baimantuoluoline F, was obtained as a white amorphous powder, with a melting point of 247–249°. The molecular formula was determined as $C_{28}H_{42}O_7$ by analysis of HR-ESI-MS, indicating 8 degrees of unsaturation. The positive HR-ESI-MS displayed characteristic peaks at *m/z* 513.2821 (calc. for $C_{28}H_{42}NaO_7^+$, $[M+Na]^+$; 513.2828) and 529.2562 (calc. for $C_{28}H_{42}KO_7^+$, $[M+K]^+$; 529.2568).

The ^{1}H-NMR spectrum of **3** did not show any olefinic signal, and consequently the most common α,β-unsaturated C=O system in ring *A* of withanolides was absent [7]. The ^{1}H-NMR spectrum showed four Me *singlet*s assignable to two tertiary Me groups (δ(H) 0.80, 1.39), and two vinylic Me groups (δ(H) 1.85, 1.97). A Me(21) signal was missing, but appearance of a pair double *doublet*s at δ(H) 3.90 (J = 11.6, 3.6 Hz, 1 H) and 3.83 (J = 11.6, 3.2 Hz, 1 H) was observed, which strongly suggested that C(21) was present as a HO–CH_2– group. The secondary OH group was assigned to C(6) in β-configuration because of a *triplet* with a small coupling constant at δ(H) 3.50 (J = 2.8 Hz, 1 H) for H–C(6). One of the tertiary OH groups was assigned to C(5) in α-configuration, as the chemical shifts of the H-atoms of rings *A*/*B* were in complete agreement with those of withanolides with a 5α,6β-dihydroxy-1-oxo moiety [4]. The double *doublet* at δ(H) 3.56 (J = 11.0, 4.0 Hz, 1 H) was characteristic for a 12β-hydroxywithanolide.

With the aid of a DEPT experiment, the ^{13}C-NMR spectra of **3** (*Table*) showed four Me, nine CH_2, and eight CH groups, and seven quaternary C-atom signals. The notable feature of the ^{13}C-NMR spectra was the appearance of a downfield aquaternary C-atom signal at δ(C) 216.8 that was due to a ketone CO group. The three aquaternary C-atom signals at δ(C) 153.3, 122.0, 169.4 were due to two alkene C-atoms and an ester CO group, respectively. Comparison of the ^{13}C-NMR spectrum of **3** with withatatulin D (**4**), showed that the chemical shifts were of striking resemblance from C(5) to C(28) and the only observed differences were the chemical shifts from C(1) to C(4) in ring *A*.

The HMBC correlations of the four Me signals on rings *A*–*E* (Me(18), Me(19), Me(27), and Me(28)) firmly established the linkage of these partial structural units. In the HMBC spectrum (*Fig. 3*), long-range correlations were observed between the Me(18) and C(12), C(13), C(14), and C(17), between Me(19) and C(1), C(5), C(9), and C(10), between Me(27) and C(24), C(25), and C(26), and between Me(28) and C(23), C(24), and C(25). Furthermore, the ^{1}H,^{1}H-COSY spectrum of **3** established the H-atom sequences from rings *A* to *E*. The absolute configuration at C(22) was finally elucidated as (*R*) by a positive *Cotton* effect at 251 nm in the CD spectrum [4][8][9]. On the basis of the above data, **3** was elucidated as (5α,6β,12β,22*R*)-5,6,12,21-tetrahydroxy-1-oxowith-24-enolide.

Table. *[1]H- and [13]C-NMR Data of* **1**, **2**, *and* **3**. At 400/100 MHz, resp. in CD_3OD; δ in ppm, J in Hz.

Position	**1**		**2**		**3**	
	δ(H)	δ(C)	δ(H)	δ(C)	δ(H)	δ(C)
C(1)	–	207.2	–	207.2	–	216.8
H–C(2) or CH_2(2)	5.78 (*dd*, *J* = 10.0, 2.4)	128.9	5.77 (*dd*, *J* = 10.0, 2.4)	128.9	2.72–2.81 (*m*), 1.96–2.04 (*m*)	38.1
H–C(3) or CH_2(3)	6.65 (*ddd*, *J* = 10.0, 5.2, 2.0)	144.0	6.65 (*ddd*, *J* = 10.0, 5.2, 2.0)	144.0	1.96–2.04 (*m*), 1.86–1.94 (*m*)	21.8
CH_2(4)	3.25 (*dt*, *J* = 20.0, 2.4), 2.05 (*dd*, *J* = 20.0, 5.2)	36.5	3.25 (*dt*, *J* = 20.0, 2.4), 2.05 (*dd*, *J* = 20.0, 5.2)	36.5	2.61–2.69 (*m*), 1.27–1.36 (*m*)	31.3
C(5)	–	78.2	–	78.2	–	79.3
H–C(6)	3.52 (*t*, *J* = 2.0)	75.1	3.52 (*t*, *J* = 2.0)	75.2	3.50 (*t*, *J* = 2.8)	76.4
CH_2(7)	1.62–1.71 (*m*), 1.49–1.59 (*m*)	33.7	1.61–1.71 (*m*), 1.48–1.58 (*m*)	33.7	1.62–1.75 (*m*), 1.49–1.58 (*m*)	34.2
H–C(8)	1.62–1.71 (*m*)	30.7	1.61–1.71 (*m*)	30.7	1.62–1.75 (*m*)	30.1
H–C(9)	1.83–1.93 (*m*)	40.8	1.82–1.91 (*m*)	40.8	1.94–2.03 (*m*)	40.5
C(10)	–	52.8	–	52.8	–	55.3
CH_2(11)	2.43 (*dt*, *J* = 12.4, 3.8), 1.26–1.39 (*m*)	34.8	2.42 (*dt*, *J* = 12.8, 3.8), 1.28–1.39 (*m*)	34.8	2.03 (*dt*, *J* = 12.8, 4.0), 1.27–1.36 (*m*)	33.1
H–C(12)	3.55 (*dd*, *J* = 11.2, 4.4)	78.1	3.54 (*dd*, *J* = 11.2, 4.4)	78.1	3.56 (*dd*, *J* = 11.0, 4.0)	79.9
C(13)	–	49.0	–	49.0	–	49.6
H–C(14)	1.15–1.26 (*m*)	54.7	1.15–1.28 (*m*)	54.7	1.16–1.24 (*m*)	55.3
CH_2(15)	1.74–1.78 (*m*), 1.29–1.34 (*m*)	24.4	1.73–1.78 (*m*), 1.28–1.35 (*m*)	24.4	1.62–1.75 (*m*), 1.27–1.36 (*m*)	24.8
CH_2(16)	1.74–1.78 (*m*), 1.48–1.54 (*m*)	26.1	1.73–1.78 (*m*), 1.46–1.56 (*m*)	26.1	1.82–1.90 (*m*), 1.49–1.58 (*m*)	28.8
H–C(17)	1.83–1.93 (*m*)	51.0	1.81–1.92 (*m*)	51.0	1.78–1.86 (*m*)	49.3
Me(18)	0.71 (*s*)	8.0	0.71 (*s*)	8.0	0.80 (*s*)	8.3
Me(19)	1.30 (*s*)	16.2	1.30 (*s*)	16.2	1.39 (*s*)	17.4
H–C(20)	1.74–1.82 (*m*)	38.8	1.73–1.78 (*m*)	38.9	1.86–1.94 (*m*)	47.4
CH_2(21)	4.60 (*d*, *J* = 13.6), 3.38 (*dd*, *J* = 13.6, 3.2)	62.8	4.59 (*d*, *J* = 13.6), 3.47 (*dd*, *J* = 13.6, 3.2)	62.9	3.90 (*dd*, *J* = 11.6, 3.6), 3.83 (*dd*, *J* = 11.6, 3.2)	60.6
H–C(22)	4.72 (br. *s*)	78.2	4.73 (br. *s*)	78.2	4.52 (*dt*, *J* = 13.6, 3.6)	79.6
CH_2(23)	1.92–1.99 (*m*)	34.3	1.91–1.98 (*m*)	34.4	2.73 (*dd*, *J* = 18.0, 12.8), 2.27 (*dd*, *J* = 18.0, 2.4)	33.3
C(24)	–	71.9	–	71.9	–	153.3
C(25) or H–C(25)	2.66 (*dd*, *J* = 5.6, 3.0)	50.8	2.55 (*t*, *J* = 4.6)	52.8	–	122.0
C(26)	–	174.8	–	175.7	–	169.4
Me(27) or CH_2(27)	3.92 (*dd*, *J* = 10.0, 3.0), 3.76 (*dd*, *J* = 10.0, 5.6)	70.3	4.07 (*dd*, *J* = 11.6, 4.4), 3.92 (*dd*, *J* = 11.6, 4.8)	59.8	1.85 (*s*)	12.4
Me(28)	1.28 (*s*)	27.1	1.32 (*s*)	27.0	1.97 (*s*)	20.4
*Me*O-C(27)	3.34 (*s*)	58.8	–	–	–	–

Compounds **4**, **5**, **6**, and **7** were identified as withatatulin D ((5α,6β,12β,22*R*)-5,6,12,21-tetrahydroxy-1-oxowitha-2,24-dienolide) [10][11], withafastuosin F ((5α,6β,12β,22*R*)-5,6,12,21,27-pentahydroxy-1-oxowitha-2,24-dienolide) [10], withametelin G ((5α,6β)-21,24-epoxy-5,6-dihydroxy-1-oxowitha-2,25(27)-dienolide) [12],

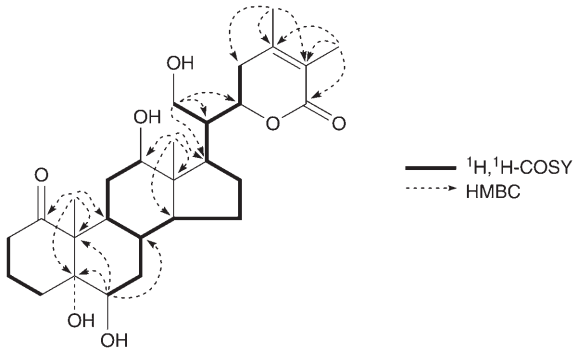

Fig. 3. *Key ^{1}H,^{1}H-COSY and HMBC correlations of* **3**

and isolariciresinol (4,4′,9,9′-tetrahydroxy-3,3′-dimethoxytetrahydrocycloligan)[1]), respectively, [13] with the help of different spectroscopic techniques, respectively. Their ^{1}H-NMR and ^{13}C-NMR data were in agreement with those of reference.

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Experimental Part

General. Column chromatography (CC): Macroporous absorption resin (*AB-8* Crosslinked Polystyrene, Nankai University, Tianjin, China); silica gel (SiO_2) (200–300 mesh, *Yinhai*, Qingdao, China); *ODS-A 120A* (50 μm; *YMC Co*). Prep. HPLC: *Waters Delta-600* (*Waters 2487* dual λ absorbance detector); *Hypersil-ODS II* (10 μm, 20 × 300 mm, *Yilite*, Dalian, China). M.p.: *Kofler* micrometing point apparatus; uncorrected. Optical rotations: *Perkin Elmer 341* polarimeter. UV spectra: *SHIMADZU UV-1601*; λ_{max} (log ε) in nm. CD Spectra: *Jasco J-715* spectrometer; $\lambda(\Delta\varepsilon)$ in nm. NMR Spectra: *Bruker DPX-400* spectrometer; at 400 MHz for (^{1}H) and 100 MHz (^{13}C); chemical shifts δ in ppm rel. to Me_4Si as internal standard, coupling constants *J* in Hz. HR-ESI-MS and ESI-MS: *IonSpec Ultima 7.0 T FTICR* and *Finnigan MAT LCQ* mass spectrometer, resp.; in *m/z*.

Plant Material. The dry flowers of *D. metel* L. were collected from Jiangsu Province of China in 2002. The voucher specimen (2002035) was deposited at Heilongjiang University of Traditional Chinese Medicine, Harbin, China.

Extraction and Isolation. The dried flowers (30 kg) of *Datura metel* L. were extracted with 70% EtOH under reflux (2 × 100 l) for 2.5 h, and the combined soln. was filtered and concentrated under vacuum to a syrup, followed by suspension in H_2O. The suspension was acidified with 0.1% HCl, and then filtered and exchanged over *Styrene-DVB* (001 × 7).The exchanged soln. was passed through *AB-8* Crosslinked Polystyrene, and sequentially eluted with H_2O, 50% EtOH, and 95% EtOH, resp. The 50% EtOH-elutate was concentrated under vacuum to yield a syrup (52.0 g), and this crude residue was subjected to CC (SiO_2), and eluted successively with $CHCl_3$/MeOH (10:1 → 1:1) gradient to give 10 fractions (*Fr. 1–10*). *Fr. 6* (4.2 g) was subjected to CC (SiO_2, $CHCl_3$/MeOH, 8:1 → 5:1; then *ODS*, MeOH/H_2O, 1:1) to yield seven substances. Each was obtained as a yellow powder, which was then purified by preparative HPLC on a *Hypersil-ODS II* column (10 μm, 20 × 300 mm, flow rate 8 ml/min) with MeOH/H_2O (65:35) to afford **1** (13 mg, t_R = 15.0 min), **2** (12 mg, t_R = 15.9 min), **3** (30 mg, t_R =

[1]) For the systematic name of **7**, see *Exper. Part*.

13.8 min), **4** (28 mg, t_R = 20.6 min), **5** (31 mg, t_R = 19.3 min), **6** (35 mg, t_R = 23.0 min), and **7** (45 mg, t_R = 13.0 min).

Baimantuoluoline D (= *(5α,6β,12β,20*R,*22*R,*24*R,*25*S*)-21,24-Epoxy-5,6,12-trihydroxy-27-methoxy-1-oxoergost-2-en-26,21-olide*; **1**). White amorphous powder. M.p. 205–208°. $[\alpha]_D^{20} = +9.3$ (c = 0.08, MeOH). CD (MeOH): 251 (+0.26, pos. max). ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS (pos.): 541 ($[M+Na]^+$). HR-ESI-MS (pos.): 541.2784 ($[M+Na]^+$, $C_{29}H_{42}NaO_8^+$; calc. 541.2778), 557.2518 ($[M+K]^+$, $C_{29}H_{42}KO_8^+$; calc. 557.2517).

Baimantuoluoline E (= *(5α,6β,12β,20*R,*22*R,*24*R,*25*S*)-21,24-Epoxy-5,6,12,27-tetrahydroxy-1-oxoergost-2-en-26,21-olide*; **2**). White amorphous powder. M.p. 217–220°. $[\alpha]_D^{20} = +22.8$ (c = 0.15, MeOH). CD(MeOH): 252 (+0.83, pos. max). ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS (pos.): 527 ($[M+Na]^+$). HR-ESI-MS (pos.): 527.2632 ($[M+Na]^+$, $C_{28}H_{40}NaO_8^+$; calc. 527.2621), 543.2373 ($[M+K]^+$, $C_{28}H_{40}KO_8^+$; calc. 543.2360).

Baimantuoluoline F (= *(5α,6β,12β,22*R*)-5,6,12,21-Tetrahydroxy-1-oxoergost-24-en-26,21-olide*; **3**). White amorphous powder. M.p. 247–249°. $[\alpha]_D^{20} = +12.4$ (c = 0.10, MeOH). UV (MeOH): 221 (1.5). CD (MeOH): 251 (+0.75, pos. max). ^{1}H- and ^{13}C-NMR: *Table*. ESI-MS (pos.): 1003 ($[2\,M+Na]^+$). HR-ESI-MS (pos.): 513.2821 ($[M+Na]^+$, $C_{28}H_{42}NaO_7^+$; calc. 513.2828), 529. 2562 ($[M+K]^+$, $C_{28}H_{42}KO_7^+$; calc. 529.2568).

Withatatulin D (= *(5α,6β,12β,22*R*)-5,6,12,21-Tetrahydroxy-1-oxoergosta-2,24-dien-26,21-olide*; **4**). ^{1}H-NMR (400 MHz, CD_3OD): 0.82 (*s*, Me(18)); 1.18–1.25 (*m*, H–C(14)); 1.26–1.34 (*m*, 1 H of CH_2(15)); 1.31 (*s*, Me(19)); 1.35–1.44 (*m*, 1 H of CH_2(11)); 1.49–1.56 (*m*, 1 H of CH_2(16)); 1.55–1.70 (*m*, CH_2(7)); 1.67–1.74 (*m*, H–C(8), 1 H of CH_2(15)); 1.78–1.84 (*m*, H–C(17)); 1.82–1.88 (*m*, 1 H of CH_2(16)); 1.85 (*s*, Me(27)); 1.88–1.96 (*m*, H–C(9), H–C(20)); 1.98 (*s*, Me(28)); 2.07 (*dd*, *J* = 20.0, 5.2, 1 H of CH_2(4)); 2.28 (*dd*, *J* = 18.0, 2.4, 1 H of CH_2(23)); 2.45 (*dt*, *J* = 12.8, 4.0, 1 H of CH_2(11)); 2.73 (*dd*, *J* = 18.0, 13.2, 1 H of CH_2(23)); 3.23 (*dt*, *J* = 20.0, 2.5, 1 H of CH_2(4)); 3.53 (*t*, *J* = 2.0, H–C(6)); 3.58 (*dd*, *J* = 11.2, 4.4, H–C(12)); 3.84 (*dd*, *J* = 11.8, 3.2, 1 H of CH_2(21)); 3.91 (*dd*, *J* = 11.8, 4.0, 1 H of CH_2(21)); 4.55 (*dt*, *J* = 13.2, 3.6, H–C(22)); 5.77 (*dd*, *J* = 10.0, 2.5, H–C(2)); 6.66 (*ddd*, *J* = 10.0, 5.2, 2.0, H–C(3)). ^{13}C-NMR (100 MHz, CD_3OD): 8.3 (C(18)); 12.4 (C(27)); 16.1 (C(19)); 20.4 (C(28)); 24.9 (C(15)); 28.8 (C(16)); 30.5 (C(8)); 33.3 (C(23)); 33.6 (C(11)); 33.9 (C(7)); 36.5 (C(4)); 40.9 (C(9)); 47.5 (C(20)); 49.3 (C(17)); 49.7 (C(13)); 52.8 (C(10)); 55.3 (C(14)); 60.5 (C(21)); 75.2 (C(6)); 78.2 (C(5)); 79.6 (C(22)); 80.0 (C(12)); 122.0 (C(25)); 128.9 (C(2)); 144.0 (C(3)); 153.3 (C(24)); 169.5 (C(26)); 207.3 (C(1)).

Withafastuosin F (= *(5α,6β,12β,22*R*)-5,6,12,21,27-Pentahydroxy-1-oxoergosta-2,24-dien-26,21-olide*; **5**). ^{1}H-NMR (400 MHz, CD_3OD): 0.82 (*s*, Me(18)); 1.18–1.24 (*m*, H–C(14)); 1.26–1.34 (*m*, 1 H of CH_2(15)); 1.31 (*s*, Me(19)); 1.34–1.43 (*m*, 1 H of CH_2(11)); 1.48–1.56 (*m*, 1 H of CH_2(16)); 1.56–1.70 (*m*, CH_2(7)); 1.68–1.74 (*m*, H–C(8), 1 H of CH_2(15)); 1.82–1.88 (*m*, 1 H of CH_2(16), H–C(17)); 1.88–1.95 (*m*, H–C(9), H–C(20)); 2.06 (*dd*, *J* = 20.0, 5.2, 1 H of CH_2(4)); 2.08 (*s*, Me(28)); 2.36 (*dd*, *J* = 18.4, 3.2, 1 H of CH_2(23)); 2.45 (*dt*, *J* = 12.4, 3.6, 1 H of CH_2(11)); 2.81 (*dd*, *J* = 18.4, 13.2, 1 H of CH_2(23)); 3.26 (*dt*, *J* = 20.0, 2.4, 1 H of CH_2(4)); 3.53 (*t*, *J* = 2.0, H–C(6)); 3.58 (*dd*, *J* = 11.2, 4.0, H–C(12)); 3.85 (*dd*, *J* = 11.6, 4.0, 1 H of CH_2(21)); 3.91 (*dd*, *J* = 11.6, 3.2, 1 H of CH_2(21)); 4.31 (*d*, *J* = 11.6, 1 H of CH_2(27)); 4.38 (*d*, *J* = 11.6, 1 H of CH_2(27)); 4.56 (*dt*, *J* = 13.2, 3.6, H–C(22)); 5.78 (*dd*, *J* = 10.0, 2.4, H–C(2)), 6.66 (*ddd*, *J* = 10.0, 5.2, 2.0, H–C(3)). ^{13}C-NMR (100 MHz, CD_3OD): 8.3 (C(18)); 16.1 (C(19)); 20.2 (C(28)); 24.9 (C(15)); 28.8 (C(16)); 30.4 (C(8)); 33.6 (C(11)); 33.6 (C(23)); 33.9 (C(7)); 36.5 (C(4)); 41.0 (C(9)); 47.5 (C(20)); 49.3 (C(17)); 49.6 (C(13)); 52.8 (C(10)); 55.4 (C(14)); 56.4 (C(27)); 60.6 (C(21)); 75.2 (C(6)); 78.2 (C(5)); 79.5 (C(22)); 80.0 (C(12)); 126.3 (C(25)); 128.9 (C(2)); 144.0 (C(3)); 153.8 (C(24)); 168.5 (C(26)); 207.2 (C(1)).

Withametelin G (= *(5α,6β,22*R*)-5,6-Dihydroxy-21,24-epoxy-1-oxoergosta-2,25(27)-dien-26,21-olide*; **6**). ^{1}H-NMR (400 MHz, CD_3OD): 0.75 (*s*, Me(18)); 1.19–1.23 (*m*, 1 H of CH_2(15)); 1.24–1.30 (*m*, H–C(14)); 1.29 (*s*, Me(19)); 1.34–1.38 (*m*, 1 H of CH_2(11)); 1.40–1.45 (*m*, 1 H of CH_2(16)); 1.44 (*s*, Me(28)); 1.45–1.51 (*m*, 1 H of CH_2(12)); 1.52–1.57 (*m*, 1 H of CH_2(7)); 1.68–1.72 (*m*, 1 H of CH_2(15)); 1.70–1.74 (*m*, 1 H of CH_2(7)); 1.75–1.82 (*m*, H–C(8)); 1.79–1.84 (*m*, H–C(9), 1 H of CH_2(16), H–C(17), H–C(20)); 1.90–1.96 (*m*, 1 H of CH_2(12)); 1.95 (*dd*, *J* = 14.0, 4.2, 1 H of CH_2(23)); 2.04 (*dd*, *J* = 19.8, 5.2, 1 H of CH_2(4)); 2.14 (*dd*, *J* = 14.0, 0.8, 1 H of CH_2(23)); 2.20–2.25 (*m*, 1 H of CH_2(11)); 3.25 (*dt*, *J* = 19.8, 2.5, of CH_2(4)); 3.52 (*t*, *J* = 2.6, H–C(6)); 3.68 (br. *d*, *J* = 13.2, 1 H of CH_2(21)); 3.92

(br. *d*, *J* = 13.2, 1 H of CH_2(21)); 4.69 (br. *s*, H–C(22)); 5.76 (*dd*, *J* = 10.0, 2.5, H–C(2)); 6.08 (br. *s*, 1 H of CH_2(27)); 6.64 (*ddd*, *J* = 10.0, 5.2, 2.0, H–C(3)); 6.66 (br. *s*, 1 H of CH_2(27)). ^{13}C-NMR (100 MHz, CD_3OD): 13.4 (C(18)); 16.3 (C(19)); 24.5 (C(11)); 25.1 (C(15)); 25.7 (C(28)); 27.4 (C(16)); 31.4 (C(8)); 33.9 (C(23)); 34.0 (C(7)); 36.6 (C(4)); 41.3 (C(12)); 41.5 (C(20)); 42.5 (C(9)); 44.2 (C(13)); 49.1 (C(17)); 53.0 (C(10)); 56.9 (C(14)); 61.6 (C(21)); 70.8 (C(24)); 75.2 (C(6)); 77.4 (C(22)); 78.3 (C(5)); 129.0 (C(2)); 130.5 (C(27)); 140.9 (C(25)); 143.9 (C(3)); 167.5 (C(26)); 207.5 (C(1)).

Isolariciresinol (=*(2*R*)-1,2,3,4-Tetrahydro-7-hydroxy-1-(4-hydroxy-3-methoxyphenyl)-6-methoxy-2,3-naphthalenedimethanol*; **7**). ^{1}H-NMR (400 MHz, CD_3OD): 1.72–1.76 (*m*, 1 H); 1.96–2.02 (*m*, 1 H); 2.76 (*d*, *J* = 7.6, 2 H); 3.39 (*dd*, *J* = 11.2, 4.0, 1 H); 3.65–3.73 (*m*, 1 H); 3.77 (*s*, 3 H); 3.79 (*d*, *J* = 5.2, 1 H); 3.80 (*s*, 3 H); 6.17 (*s*, 1 H); 6.60 (*dd*, *J* = 7.6, 1.6, 1 H); 6.66 (*s*, 1 H); 6.66 (*d*, *J* = 1.6, 1 H); 6.73 (*d*, *J* = 7.6, 1 H). ^{13}C-NMR (100 MHz, CD_3OD): 33.6 (C(4)); 39.9 (C(3)); 47.9 (C(2)); 48.0 (C(1)); 56.3 (2 MeO); 62.1 (C(α)); 65.9 (C(α)); 112.3 (C(5)); 113.7 (C(2′)); 115.9 (C(5′)); 117.3 (C(8)); 123.1 (C(6′)); 128.9 (C(4a)); 134.1 (C(1′)); 138.6 (C(8a)); 145.2 (C(4′)); 145.9 (C(7)); 147.2 (C(6)); 149.0 (C(3′)).

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