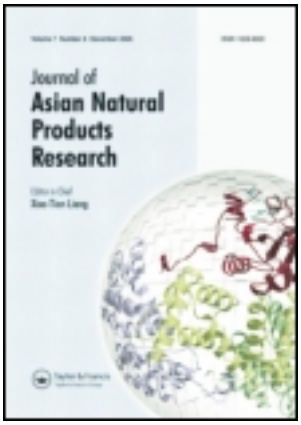

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Three new glycosides from *Hylocereus undatus*

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Three new glycosides, undatusides A–C (**1**–**3**), and 11 known compounds (**4**–**14**) were isolated from the flowers of *Hylocereus undatus*. Their structures were elucidated on the basis of spectroscopic data and chemical method.

Keywords: *Hylocereus undatus*; Cactaceae; undatusides A–C

1. Introduction

The plant *Hylocereus undatus* (Cactaceae) is widely distributed in the tropical areas of Africa, south America, and south Asia. The fruits of *Hylocereus* species, known as pitaya or dragon fruit, can be consumed freshly or processed as ingredient in juice, jams, or ice cream. In the southern China, the flowers of *H. undatus* have been used as food and folk medicine for the treatment of hyperactivity, cough, tuberculosis, mumps, bronchitis, and cervical lymph node tuberculosis for a long time. Previous phytochemical studies on this plant had resulted in the isolation of two triterpenes with microvascular protective activity [1]. As a part of the program to assess the chemical and biological diversity of the medicinal plants in the southern China, we carried out the chemical investigation of the flowers of *H. undatus*, which led to the isolation of three new glycosides, undatusides A–C (**1**–**3**), as well as 11 known compounds (**4**–**14**) (Figure 1). Herein, we report the isolation and structural elucidation of the three new compounds.

2. Results and discussion

The molecular formula of **1** was established as $C_{19}H_{26}O_{10}$ by the pseudo-molecular ion in its HR-ESI-MS at *m/z* 437.1423 $[M + Na]^+$. The UV spectrum of **1** showed the absorption maxima at 208 and 251 nm. The IR spectrum implied the presence of hydroxyl (3325 cm^{-1}), carbonyl (1723 cm^{-1}), and aromatic ring (1637 and 1455 cm^{-1}). The ^1H NMR spectrum of **1** indicated the presence of five aromatic protons [δ_H 7.39 − 7.25 (5H, m)], three methylenes [δ_H 4.85 (1H, d, $J = 12.0$ Hz), 4.62 (1H, d, $J = 12.0$ Hz), 2.77 (1H, d, $J = 15.6$ Hz), 2.72 (1H, d, $J = 15.6$ Hz), and 2.67 (2H, s)], and a methyl [δ_H 1.38 (3H, s)]. Furthermore, the ^1H NMR spectrum displayed the signals due to an anomeric proton [δ_H 4.36 (1H, d, $J = 7.5$ Hz)] and a

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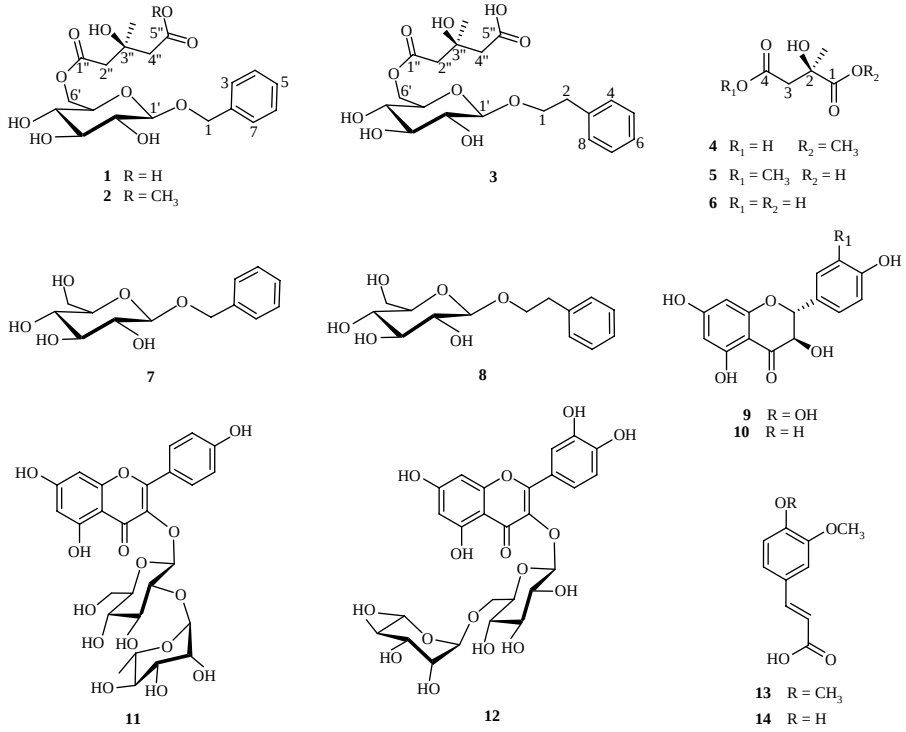

Figure 1. Chemical structures of compounds **1**–**14**.

hydroxymethyl group [δ_H 4.48 (1H, dd, $J = 11.8$, 2.0 Hz) and 4.23 (1H, dd, $J = 11.8$, 5.7 Hz)], as well as proton signals in the region δ_H 3.46 − 3.24 (4H, overlapped), suggesting the presence of a sugar moiety. Acid hydrolysis of **1** afforded D-glucose, which was identified by gas chromatography (GC) analysis using an authentic sample as reference. The β-configuration of D-glucose was determined based on the $^3J_{H1,H2}$ coupling constant ($J = 7.5$ Hz) of the anomeric proton. The ^{13}C NMR and DEPT spectra of **1** revealed the presence of 19 carbon signals, including two carbonyl groups, a monosubstituted benzene ring, as well as a β-D-glucopyranosyl unit. With the aid of ^{1}H–^{1}H COSY, HSQC, and HMBC experiments, all the ^{1}H and ^{13}C NMR signals of **1** were assigned as shown in Table 1.

The ^{1}H and ^{13}C NMR signals of **1** assigned to **1a** were very similar to those of 3-hydroxy-3-methylglutaryl (HMG) moiety [2], indicating that **1** possessed the same substructure, which was further supported by the HMBC correlations between H_2-2″ [δ_H 2.77 (1H, d, $J = 15.6$ Hz) and 2.72 (1H, d, $J = 15.6$ Hz)] and C-4″ (δ_C 45.9)/3″-CH_3 (δ_C 27.7), between H-4″ [δ_H 2.67 (2H, s)] and C-2″ (δ_C 46.3)/3″-CH_3 (δ_C 27.7), as well as between 3″-CH_3 [δ_H 1.38 (3H, s)] and C-2″ (δ_C 46.3)/C-4″ (δ_C 45.9) (Figure 2). *S*-configuration for the C-3″ of the HMG moiety was assumed because naturally occurring HMG esters are formed via the acylation of the hydroxyl group with (*S*)-HMG-CoA [3,4]. Comparison of the NMR spectral data assigned to **1b** with those of benzyl-β-D-glucopyranoside (**7**) suggested that they were very similar, except for the obvious downfield shift of C-6′ and upfield shift of C-5′, suggesting that the HMG moiety (**1a**) was esterified with the hydroxyl group at C-6′ of the glucose moiety. Moreover, the HMBC correlations between H-6′ (δ_H 4.48 and 4.23) and C-1″ (δ_C 172.4)

Table 1. ^{1}H and ^{13}C NMR spectral data of compounds **1**–**3** (CD_3OD, J in Hz)[a,b].

	1		**2**		**3**	
Position	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H
1	71.8	4.85 (d, 12.0) 4.62 (d, 12.0)	71.8	4.85 (d, 12.0) 4.62 (d, 12.0)	71.8	4.01 (dt, 9.6, 7.3) 3.74 (dt, 9.6, 7.3)
2	138.8		138.9		37.1	2.90 (2H, t, 7.3)
3	129.1	7.39	129.1	7.39	139.9	
4	129.2	7.32	129.2	7.32	129.9	7.24
5	128.7	7.25	128.7	7.25	129.3	7.24
6	129.2	7.32	129.2	7.32	127.1	7.16
7	129.1	7.39	129.1	7.39	129.3	7.24
8					129.9	7.24
1′	103.2	4.36 (d, 7.5)	103.3	4.36 (d, 7.5)	104.3	4.30 (d, 7.5)
2′	74.9	3.24	75.0	3.25	74.9	3.19
3′	77.7	3.36	77.8	3.36	77.7	3.36
4′	71.5	3.34	71.6	3.34	71.5	3.28
5′	75.9	3.46	75.2	3.44	75.1	3.45
6′	64.6	4.48 (dd, 11.8, 2.0) 4.23 (dd, 11.8, 5.7)	64.6	4.48 (dd, 11.8, 2.0) 4.22 (dd, 11.8, 5.7)	64.6	4.44 (dd, 11.8, 1.6) 4.20 (dd, 11.8, 5.8)
1″	172.4		172.4		172.4	
2″	46.3	2.77 (d, 15.6) 2.72 (d, 15.6)	46.4	2.76 (d, 14.4) 2.70 (d, 14.4)	46.4	2.72 (d, 14.6) 2.67 (d, 14.6)
3″	70.7		70.8		70.7	
4″	45.9	2.67 (2H, s)	45.9	2.70 (2H, s)	45.9	2.63 (2H, s)
5″	172.4		173.1		172.4	
3″-CH_3	27.7	1.38 (3H, s)	27.8	1.38 (3H, s)	27.7	1.38 (3H, s)
5″-COOCH_3			51.9	3.63 (3H, s)		

Notes: [a]Assignments were established by interpretation of the ^{1}H–^{1}H COSY, HSQC, and HMBC spectra.
[b] Overlapped signals are reported without designating multiplicity.

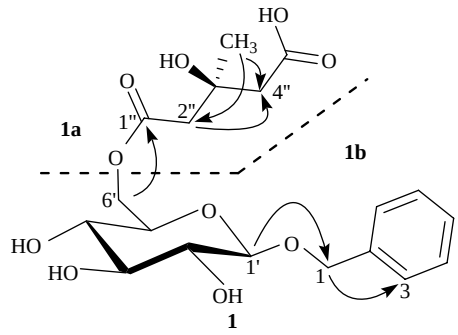

Figure 2. Key HMBC correlations of **1**.

confirmed the above deducement. Therefore, the structure of **1** was elucidated as benzyl-1-*O*-[6′-*O*-(*S*)-3″-hydroxy-3″-methylglutaryl]-β-D-glucopyranoside and named as undatuside A.

The molecular formula of **2** was established as $C_{20}H_{28}O_{10}$ by the pseudo-molecular ion in its HR-ESI-MS at *m/z* 451.1584 $[M + Na]^+$. The UV spectrum of **2** showed the absorption maxima at 211 and 258 nm. The IR spectrum implied the presence of hydroxyl (3377 cm^{-1}), carbonyl (1729 cm^{-1}), and aromatic ring (1687 and 1452 cm^{-1}). Acid hydrolysis of **2** also afforded D-glucose. The ^1H and ^{13}C NMR spectral data of **2** were very similar to those of **1** except for the presence of methyl ester [δ_H 3.63 (3H, s); δ_C 173.1 and 51.9] instead of the aliphatic acid group. Thus, the structure of **2** was assigned as benzyl-1-*O*-[6′-*O*-(*S*)-3″-hydroxy-3″-methyl-5″-methoxyglutaryl]-β-D-glucopyranoside and named as undatuside B.

The molecular formula of **3** was determined to be $C_{20}H_{28}O_{10}$ by the pseudo-molecular ion in its HR-ESI-MS at *m/z* 451.1584 $[M + Na]^+$. Similar to **1** and **2**, the IR spectrum of **3** showed the presence of hydroxyl (3331 cm^{-1}), carbonyl (1723 cm^{-1}), and aromatic ring (1637, 1455 cm^{-1}). Acid hydrolysis of **3** also afforded D-glucose. The ^1H and ^{13}C NMR spectral data of **3** were closely similar to those of **1** except for the presence of an additional methylene [δ_H 2.90 (2H, d, $J = 7.3$ Hz); δ_C 37.1], indicating the presence of phenethyl unit in **3** instead of benzyl moiety. With the aid of ^1H–^1H COSY, HSQC, and HMBC experiments, all the ^1H and ^{13}C NMR signals of **3** were assigned as shown in Table 1. Furthermore, the HMBC correlations between H-1′ (δ_H 4.30) and C-1 (δ_C 71.8), as well as between H_2-6′ (δ_H 4.44 and 4.20) and C-1″ (δ_C 172.4), suggested that the phenethyl and HMG units were connected to the C-1′ and C-6′ positions of glucose, respectively. Based on the above results, the structure of **3** was established as phenethyl-1-*O*-[6′-*O*-(*S*)-3″-hydroxy-3″-methylglutaryl]-β-D-glucopyranoside and named as undatuside C.

In addition, the 11 known compounds were elucidated as (*R*)-(−)-citramalic acid 1-methyl ester (**4**) [5], (*R*)-(−)-citramalic acid 4-methyl ester (**5**) [6], (*R*)-(−)-citramalic acid (**6**) [7], benzyl-β-D-glucopyranoside (**7**) [8,9], phenethyl-β-D-glucopyranoside (**8**) [10], dihydroquercetin (**9**) [11], dihydrokaempferol (**10**) [12], kaempferol 3-neohesperidoside (**11**) [13], quercetin 3-*O*-β-D-rutinoside (**12**) [14], *trans*-3,4-dimethoxycinnamic acid (**13**) [15], and *trans*-ferulic acid (**14**) [16], respectively, by comparison of their physical and spectroscopic data with those reported in the literature.

3. Experimental

3.1 General experimental procedures

Optical rotation values were measured on a JASCO P-1020 digital polarimeter at room temperature. UV spectra were recorded on a JASCO V-550 UV/VIS spectrophotometer. IR spectra were measured on a JASCO FT/IR-480 plus Fourier transform infrared spectrometer with KBr pellets. 1D and 2D NMR spectra were recorded on Bruker AV-300 spectrometer. HR-ESI-MS data were acquired using an Agilent 6210 LC/MSD TOF mass spectrometer. ESI-MS data were determined on a Finnigan LCQ Advantage spectrometer. Column chromatographies (CC) were carried out

using silica gel (200–300 mesh, Qingdao Haiyang Chemical Group Corporation, Qingdao, China) and Sephadex LH-20 (Pharmacia Biotech AB, Uppsala, Sweden). TLC analysis was performed on precoated silica gel GF254 plates (Yantai Chemical Industrial Institute, Yantai, China). Analytical high-performance liquid chromatography (HPLC) was carried out on a Dionex chromatography equipped with a P680 pump, a PDA-100 photodiode array detector, and a Cosmosil 5C18-MS-II reversed-phase column (4.6 mm × 250 mm, 5.0 μm, Nacalai Tesque, Kyoto, Japan). Preparative HPLC was carried out on a Varian instrument equipped with a Prostar 215 pump, a Prostar 325 UV/VIS detector, and a Cosmosil 5C18-MS-II reversed-phase column (20 mm × 250 mm, 5.0 μm, Nacalai Tesque, Kyoto, Japan).

3.2 Plant material

The flowers of *H. undatus* were collected in Zhaoqing city, Guangdong Province of China, in February 2010, and authenticated by Prof. Guang-Xiong Zhou (Institute of Traditional Chinese Medicine & Natural Products, Jinan University). A voucher specimen (No. 20100215) has been deposited in the Institute of Traditional Chinese Medicine & Natural Products, Jinan University, Guangzhou, China.

3.3 Extraction and isolation

The air-dried flowers of *H. undatus* (15 kg) were powdered and extracted with 95% (V/V) EtOH at room temperature, and the solution was evaporated under vacuum to yield a residue (5700 g). The crude EtOH extract was subsequently suspended in distilled water and partitioned successively with petroleum ether, ethyl acetate, and *n*-butanol, respectively. After removing the solvent, the ethyl acetate extract (90 g) was subjected to silica gel CC using gradient mixtures of $CHCl_3$–CH_3OH (100:0 → 0:100) as eluent to give four fractions (Fr. 1–4). Fr. 2 (30 g) was separated by silica gel column using $CHCl_3$–acetone (100:0 → 0:100) as eluent to yield three subfractions (Fr. 2a–2c). Fr. 2a (14 g) was subjected to preparative HPLC [CH_3OH–H_2O (40: 60)] to give compounds **4** (188 mg), **5** (131 mg), and **6** (336 mg). Fr. 2b (11 g) was re-separated by Sephadex LH-20 column (CH_3OH) and preparative HPLC [CH_3OH-H_2O (25: 75)] to yield compounds **1** (84 mg), **2** (23 mg), **3** (34 mg), **7** (1170 mg), **8** (129 mg), **9** (12 mg), **10** (14 mg), **11** (20 mg), **12** (21 mg), **13** (150 mg), and **14** (30 mg), respectively.

3.3.1 Compound *1*

Colorless oil: $[\alpha]_D^{21}$ −34.8 (*c* 0.1, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 208 (3.88), 251 (2.58) nm; IR (KBr): ν_{max} 3325, 2932, 2886, 1724, 1637, 1455, 1383, 1318, 1210, 1160, 1079, 1046, 1019, 905, 751, 700 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS *m/z* 437.1423 $[M + Na]^+$ (calcd for $C_{19}H_{26}O_{10}Na$, 437.1418).

3.3.2 Compound *2*

Colorless oil: $[\alpha]_D^{21}$ −29.8 (*c* 0.2, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 211 (3.74), 258 (2.52) nm; IR (KBr): ν_{max} 3377, 2944, 2874, 1729, 1687, 1452, 1354, 1323, 1209, 1158, 1078, 1049, 1019, 912, 742, 700 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS *m/z* 451.1584 $[M + Na]^+$ (calcd for $C_{20}H_{28}O_{10}Na$, 451.1575).

3.3.3 Compound *3*

Colorless oil: $[\alpha]_D^{21}$ −12.9 (*c* 0.3, CH_3OH); UV (CH_3OH) λ_{max} (log ε) 212 (3.59), 258 (2.38) nm; IR (KBr): ν_{max} 3331, 2938, 2881, 1723, 1637, 1455, 1381, 1318, 1202, 1158, 1085, 1017, 908, 748, 700 cm^{-1}; ^1H and ^{13}C NMR spectral data, see Table 1; HR-ESI-MS *m/z* 451.1584

$[M + Na]^+$ (calcd for $C_{20}H_{28}O_{10}Na$, 451.1575).

3.4 Acid hydrolysis and GC analysis of 1–3

Each solution of compounds **1**–**3** (each 1.5 mg) was heated in an ampoule with 1.5 ml of 2 N HCl (CH_3OH-H_2O, 1:1) at 95°C for 2 h. The solution was evaporated with a stream of N_2. The reaction mixture was dissolved in H_2O and extracted with $CHCl_3$. The aqueous layer was evaporated to give a residue. Then, 2 ml of anhydrous pyridine and 3 mg of L-cysteine methyl ester hydrochloride were added to the residue, and the reaction mixture was heated at 60°C for 2 h. The solution was concentrated to dryness with N_2. Furthermore, *N*-(trimethylsilyl)imidazole (0.2 ml) was slowly added into the reaction mixture and then kept at 60°C for 1 h. Finally, H_2O (1 ml) was added to the solution to stop the reaction, and the aqueous layer was extracted with hexane (2 ml). The organic layer was analyzed using GC under the following conditions: column: HP-1701 (0.25 mm × 30 mm, 0.5 μm), detector: FID, column temperature: 200–250°C (5 °C/min), detector temperature: 280°C, injector temperature: 250°C, and carrier gas: N_2. The standard D-glucose and L-glucose were subjected to the same reaction and GC analysis under the above conditions [t_R (min): 32.231 (D-glucose), 34.863 (L-glucose)]. As a result, D-glucose [t_R (min): 32.185] was detected from the hydrolyzates of **1**–**3**, respectively.

Acknowledgements

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