Benzylphenethylamine Alkaloids from the Bulbs and Flowers of *Lycoris radiata*

WANG Huan1,2,3, WANG Yue-hu2, ZHAO Fu-wei2, HUANG Qiao-qin2,3, XU Jin-jin2,3, MA Li-juan1,2, LONG Chun-lin1,2*

1. College of Life and Environmental Sciences, Minzu University of China, Beijing 100081, China
2. Key Laboratory of Economic Plants and Biotechnology, Kunming Institute of Botany, the Chinese Academy of Sciences, Kunming 650204, China
3. Yunnan Agricultural University, Kunming 650201, China

Abstract: Objective To study the benzylphenethylamine alkaloids from the bulbs and flowers of *Lycoris radiata*. Methods Alkaloids were isolated by various column chromatographic methods and their structures were identified by spectral data. Results Fifteen known benzylphenethylamine alkaloids were isolated and identified as lycoramine (1), O-demethyllycoramine (2), N-demethyllycoramine (3), galanthamine (4), lycorine (5), caranine (6), ungerminorine (7), narciclasine (8), 5-hydroxy-10-O-demethyl-homolycorine (9), hippeastrine (10), ungerine (11), hippeastrine N-oxide (12), O-demethylhaemanthamine (13), haemanthidine (14), and 8-demethoxyhostasine (15). Conclusion Compound 15 is first isolated from the plants in Amaryllidaceae, compounds 3, 6, 9, and 11 are first reported from the plants in *Lycoris* Herb., and compounds 2, 7, and 14 are isolated from *L. radiata* for the first time. The 13C-NMR data of compounds 3, 7, and 12 are first reported in the present study. Furthermore, the galasine-type alkaloid is isolated from the plants of *Lycoris* Herb. for the first time. Key words: Amaryllidaceae; benzylphenethylamine alkaloids; bulbs and flowers; 8-demethoxyhostasine; *Lycoris radiata*

DOI: 10.3969/j.issn.1674-6384.2011.01.012

Introduction

*Lycoris* Herb. (Amaryllidaceae) is a genus endemic to East Asia, and plants in the genus are with medicinal values and ornamental values (Zhao et al., 2008). The plants of this genus are rich in benzylphenethylamine alkaloids, which have cytotoxic (Evidente and Kornienko, 2009), antimalarial (Sener, Orhan, and Satayavivad, 2003), antiviral (Szlávik et al., 2004), anticholinesterase (López et al., 2002), and other activities. *Lycoris radiate* (L’ Her.) Herb., a traditional Chinese medicine, is used to treat and cure sore throat, bromatoxism, boils, rheumatoid arthritis, snake bites, and other diseases (Editorial Committee of the Flora of China of Chinese Academy of Science, 1985). In previous researches, some benzylphenethylamine alkaloids, such as lycorine, lycorenine, and galanthamine, had been isolated from *L. radiata* (Geng, Lv, and Zhang, 2008; Wang et al., 2009). In the present study, fifteen known benzylphenethylamine alkaloids were isolated and identified from the bulbs and flowers of *L. radiata*.

Materials and methods

General

Analytical TLC: pre-coated silica-gel-F254 plates (Qingdao Meigao Chemical Co.); Spots were detected under UV light (254 and 365 nm), and by spraying with Dragendorff’s reagent or 5% H2SO4 in EtOH. Column chromatography (CC): silica gel G (80—100, 200—300, and 300—400 mesh; Qingdao Meigao Chemical Co.), C18 silica gel (40—75 μm, Fuji Silysia Chemical Ltd.), MCI gel (70—150 μm, Mitsubishi Chemical Corporation), D-101 resin (Qingdao Marine Chemical Ltd.), and Sephadex LH-20 gel (GE Healthcare Bio-Sciences AB). NMR spectra: Bruker AM—400, DRX—500,

**Plant material**

The bulbs and flowers of *Lycoris radiata* (L’ Her.) Herb. were collected from Liping County, Guizhou Province of China, in September 2009. The plant material was identified by Dr. HU Guang-wan at the Kunming Institute of Botany, the Chinese Academy of Sciences (CAS). A voucher specimen (No. DS09130) was deposited at the Key Laboratory of Economic Plants and Biotechnology, Kunming Institute of Botany, CAS, China.

**Extraction and isolation**

The air-dried and powdered bulbs and flowers of *L. radiata* (4.5 kg) were exhaustively extracted with MeOH. The solvent was evaporated under reduced pressure to give a residue (120 g), which was suspended in water and extracted with petroleum ether. The pH value of water phase was adjusted to about 2 with 2 mol/L HCl, and extracted with EtOAc. The pH value of aqueous phase was adjusted to about 10 with 5% NaOH, and extracted with CHCl₃. Then the pH value of water part was adjusted to about 7 with 2 mol/L HCl.

The CHCl₃ fraction (Fr. A, 15 g) was subjected to MCI gel CC, silica gel CC, and preparative TLC (CHCl₃:MeOH = 2:1) to obtain compounds 2 (8.0 mg) and 6 (2.8 mg). Fr. A₂b was subjected to recrystallization (MeOH), Sephadex LH-20 (MeOH) and preparative TLC (CHCl₃:MeOH = 2:1) to yield compounds 7 (2.0 mg), 11 (2.1 mg), 13 (22.0 mg), and 14 (470 mg). Fr. A₂c was separated by a Sephadex LH-20 column (MeOH), then by silica gel CC to obtain compounds 1 (70.5 mg), 3 (13.1 mg), 4 (285.0 mg), 9 (2.5 mg), and 10 (45.0 mg).

The H₂O fraction (Fr. B) was chromatographed on a D-101 resin column, eluted with H₂O and 95% EtOH. The EtOH eluent was collected and concentrated to yield Fr. B’ (10 g). Fr. B’ was separated by silica gel CC to yield two parts, Fr. B’₁ (2 g, CHCl₃:MeOH = 5:1) and Fr. B’₂ (6 g, CHCl₃:MeOH = 1:2). Fr. B’₁ was subjected to MCI gel CC and preparative TLC to obtain compounds 12 (5.1 mg) and 15 (11.0 mg). Fr. B’₂ was chromatographed by MCI gel CC, silica gel CC, and recrystallization (MeOH) to give compound 8 (500 mg).

**Results and discussion**

Fifteen known benzylphenethylamine alkaloids were isolated and identified from the bulbs and flowers of *L. radiata*. These compounds belonged to six structure types, galanthamine- (1—4), lycorine- (5—7), narciclasine- (8), lycocline- (9—12), crinine- (13 and 14), and galasine-type (15). The structures were in Fig. 1.

Compound 1: white amorphous powder, was identified as lycoramine by comparison of the spectral data with the literature (Li et al, 1987).

---

**Fig. 1** Structures of benzylphenethylamine alkaloids from the bulbs and flowers of *L. radiata*
Compound 2: white amorphous powder, was characterized as O-demethyllycoramine by comparison of the $^1$H-NMR data with the literature (Kihara et al., 1991), and it was isolated from L. radiata for the first time.

Compound 3: white amorphous powder. $^{13}$C-NMR (100 MHz, CD$_3$OD) $\delta$: 146.6 (C-6), 146.2 (C-5a), 135.1 (C-8b), 124.0 (C-8a), 118.1 (C-8), 111.8 (C-7), 89.4 (C-4a), 64.6 (C-3), 58.1 (C-9), 55.9 (O-Me), 51.9 (C-11), 46.3 (C-12a), 31.4 (C-4), 29.7 (C-1), 27.3 (C-2), 23.9 (C-12). It was defined as N-demethyllycoramine by comparison of the $^1$H-NMR data with the literature (Kihara et al., 1987), and the $^{13}$C-NMR data of this compound was first reported in the present study. Besides, compound 3 was first isolated from the plants in genus Lycoris Herb.

Compound 4: white amorphous powder, was determined as galanthamine, for its NMR data was in agreement with literatures (Li et al., 1987; Zetta, Gatti, and Fuganti, 1973).

Compound 5: white crystals (MeOH), was identified as lycorine by comparing the spectral data with the literature (Wang, 2006).

Compound 6: white crystals (MeOH), was identified as caranine by comparison of the $^1$H-NMR data with the literature (Lamoral-Theys et al., 2009), and it was isolated from the plants in genus Lycoris Herb. for the first time.

Compound 7: white amorphous powder. $^{13}$C-NMR (100 MHz, CD$_3$OD) $\delta$: 150.1 (C-9), 148.1 (C-8), 141.1 (C-4), 125.6 (C-6a, 10a), 122.8 (C-11), 109.2 (C-7), 106.6 (C-10), 102.9 (OCH$_2$O), 81.1 (C-2), 72.5 (C-4a), 65.6 (C-3), 63.1 (C-12), 60.1 (C-1), 58.7 (O-Me), 53.8 (C-6), 38.5 (C-10b). Compound 7 was defined as unngunminorine by comparison of the $^1$H-NMR data with the literature (Ingkaninan et al., 2000). This compound was isolated from L. radiata for the first time, and its $^{13}$C-NMR data was first reported in the present study.

Compound 8: white amorphous powder, was identified as narcislasine by comparison of the spectral data with the literature (Evidente, 1991).

Compound 9: white solid, was identified as 5-hydroxy-10-O-demethyl-homolycorine, for its NMR data was in accordance with the literature (Bastida et al., 1988). Furthermore, it was first isolated from the plants in genus Lycoris Herb.

Compound 10: colorless crystals (MeOH), was identified as hippeastrine by comparison of the NMR data with the literature (Evidente et al., 2004).

Compound 11: colorless solid, was determined as ungerine by comparison of the $^1$H-NMR data with the literature (Yagudaev, Abduazimov, and Yunusov, 1970), and it was isolated from plants in the genus Lycoris Herb. for the first time.

Compound 12: white amorphous powder. $^{13}$C-NMR (100 MHz, CD$_3$OD) $\delta$: 165.1 (C-7), 152.2 (C-10), 150.0 (C-9), 139.6 (C-12), 139.0 (C-15), 123.6 (C-4), 119.8 (C-14), 110.6 (C-8), 110.3 (C-11), 104.1 (OCH$_2$O), 83.2 (C-17), 78.3 (C-13), 70.8 (C-2), 67.0 (C-5), 56.3 (N-Me), 34.3 (C-16), 26.5 (C-3). It was defined as hippeastrine N-oxide by comparison of the $^1$H-NMR data with the literature (Kihara et al., 1991), and this compound was the first report for its $^{13}$C-NMR data.

Compound 13: white solid, was identified as O-demethylhaemanthamine by comparison of the NMR data with literatures (Tato, Castedo, and Riguera, 1988; Wang, 2006).

Compound 14: colorless needles (MeOH). According to the literature (Hohmann et al., 2002), it was identified as haemanthidine. And this alkaid was isolated from L. radiata for the first time.

Compound 15: white crystals (MeOH), was identified as 8-demethoxyhostasine by comparison of the spectral data with the literature (Wang et al., 2007). This compound was isolated from the plants in Amaryllidaceae for the first time, and the galasine-type alkaloid was first reported from plants in the genus Lycoris Herb.

Many researches had been done to study the bioactivities of these alkaloids from the plants in Amaryllidaceae. Lycorine-, narcicasine-, and crinine-type alkaloids had noteworthy cytotoxic activities (Evidente et al., 2009; Evidente and Kornienko, 2009), whereas galanthamine- (Jokhadze et al., 2007) and lycorine-type (Evidente et al., 2009; Evidente and Kornienko, 2009) alkaloids only had weak activities. Galanthamine- (López et al., 2002), lycorine- (López et al., 2002), and galasine-type (Wang et al., 2007) alkaloids had remarkable anticholinesterase activity, but lycorine- and crinine-type alkaloids were inactive (López et al., 2002). Lycorine- and crinine-type alkaloids had stronger antimalarial activities than...
galanthamine-type alkaloids (Campbell et al., 2000; Sener, Orhan and Satayavivad, 2003; Torizuka et al., 2008). Besides, lycorine- and crinine-type alkaloids had notable antiviral activities (Li et al., 2005; Szlávik et al., 2004). As stated previously, these benzylphenethylamine alkaloids have excellent bioactivities, and their structure-activity relationship should deserve our attention.

References


