# CHEMICAL CONSTITUENTS OF MAGNOLIA TIEPII LEAVES

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**Pham Van Huyen[1,2*], Nguyen Thi Thu Hien[1], Tran Thi Ngoc Hanh[1], Nguyen Thi Dieu Thuan[1], Nguyen Huu Huong Duyen[1], Nguyen Huu Toan Phan[1,2*]**

*[1]Tay Nguyen Institute for Scientific Research, Vietnam Academy of Science and Technology (VAST), 116 Xo Viet Nghe Tinh, Dalat, Viet Nam*

*[2]Graduate University of Science and Technology, VAST, 18 Hoang Quoc Viet, Cau Giay, Hanoi, Viet Nam*

*Email: pvhuyen@tni.vast.vn, nhtphan@tni.vast.vn

## TÓM TẮT

## THÀNH PHẦN HOÁ HỌC CỦA LÁ LOÀI MỘC LAN TIẾP

*Chi Magnolia thuộc họ Magnoliaceae, phân bố ở châu Mỹ và châu Á. Nhiều loài trong chi này có giá trị chữa bệnh và được đưa vào các bài thuốc dân gian. Mộc lan Tiếp (Magnolia tiepii) là một loài đặc hữu của Việt Nam, hiện có rất ít các nghiên cứu về thành phần hoá học. Quá trình nghiên cứu hoá sinh thực vật đã phân lập được năm hợp chất bao gồm (+)-pinorecinol (**1**), laricіresinol (**2**), blumenol A (**3**), dehydrovomifoliol (**4**) và eleutheroside B (**5**) từ dịch chết methanol của lá loài Mộc lan Tiếp. Cấu trúc của các hợp chất được làm sáng tỏ bằng các phương pháp phân tích phổ cộng hưởng từ (1D, 2D-NMR), phổ khối lượng (MS), quang phổ lưỡng sắc tròn (CD) và so sánh với các dữ liệu phổ. Đây là các hợp chất lần đầu tiên được công bố từ loài này.*

***Từ khóa*: *Magnolia tiepii, (+)-pinorecinol, laricirecinol, blumenol A, dehydrovomifoliol, eleutheroside B.***

## 1. INTRODUCTION

The family Magnoliaceae has over 300 species and 17 genus. Some of the genus with well-known include *Magnolia*, *Liriodendron*, *Alcimandra*, *Lirianthe*, *Manglietia*, *Michelia*, *Pachylarnax*, *Parakmeria*, *Talauma*, and *Yulania* [1]. The *Magnolia* has about 220 species of woody plants with simple blooms. These species are found across the tropics and subtropics, particularly in Southeast Asia and America [2]. Most members of the *Magnolia* genus have been utilized as traditional remedies. *M. officinalis* is used to treat phlegm, constipation, bloating, vomiting, diarrhea, food buildup, and asthmatic cough [3]. *M. kobus* cures colds and headaches [4]. *M. obovata* relieves tense muscles to increase energy and treats gastrointestinal issues, anxiety, allergies, and bronchial asthma [5, 6]. *M. virginiana* is used as a component in rheumatism and fever medications, among other uses [7].

*Magnolia tiepii* V. T. Tran & N. V. Duy sp. nov. (Magnoliaceae) is recognized in Khanh Vinh slope, Khanh Vinh District, Khanh Hoa Province. In this study, we present the structural elucidation and isolation of five known compounds (**1**–**5**) from the leaves of the species. The isolated compounds from this plant have never been reported before.

## 2. EXPERIMENTAL

### 2.1. General experimental procedures

Column chromatography (CC) was performed on silica gel (Kieselgel 60, 70–230 mesh and 230–400 mesh, Merck, Darmstadt, Germany) and reversed-phase silica gel (ODS-A, 12 nm S-150 mm, YMC Co., Ltd., Japan) resins, and Sephadex LH-20 gel (25-100 µm, Pharmacia Fine Chemical Co. Ltd.). TLC used pre-coated silica gel 60 F254 (1.05554.0001, Merck) and RP-18 F254S plates (1.15685.0001, Merck), and compounds were visualized by spraying with aqueous 10% $H_2SO_4$ and heating for 2–3 min. NMR spectra were recorded on a Bruker AVANCE III HD spectrometer (Bruker, Billerica, MA, USA) using TMS as an internal standard. ESI mass spectra were collected on Agilent 1100 LC/MS systems. A Chirascan CD spectrometer (Applied Photophysics Ltd., Surrey, UK) was used to measure circular dichroism (CD) spectra.

### 2.2. Plant material

*M. tiepii* leaves were gathered in Khanh Vinh slope, Khanh Vinh District, Khanh Hoa Province, Vietnam, in May 2021, and identified by Dr. Nong Van Duy, Tay Nguyen Institute for Scientific Research, VAST. The Tay Nguyen Institute for Scientific Research received a voucher specimen (No. TN3/227).

### 2.3. Extraction and isolation

The 10.0 kg of fresh *M. tiepii* leaves were dried at room temperature in the shade and crushed into a fine powder (4.1 kg). Three extractions of the powdered leaves were performed at room temperature using methanol (20 L/time). The methanol solvents were filtered, combined, and concentrated under reduced pressure to obtain MT-M residue (760 g). This was suspended in water (3 L) and partitioned in turn with *n*-hexane, chloroform, and ethyl acetate to give the corresponding extracts: *n*-hexane (MT-H, 7.3 g), $CHCl_3$ (MT-C, 7.8 g), EtOAc (MT-E, 14.5 g), and water layer (MT-W).

The MT-C (7.8 g) was loaded on silica gel CC with stepwise gradient elution of $CH_2Cl_2$/MeOH (1:0-0:1, v/v) to yield ten fractions, C1-C10. Fraction C9 (534 mg) was separated by silica gel CC with *n*-hexane/EtOAc (20:1-1:1, v/v) to give eight subfractions, C9A-C9H. Subfractions C9A (50 mg), C9B (45 mg), and C9D (70 mg) were purified by YMC column eluted with MeOH/$H_2O$ (1:1, v/v) to afford compounds **4** (15 mg), **3** (10 mg), and **2** (12 mg), respectively. Fraction C6 (238 mg) was separated on Sephadex LH-20 CC and eluted with MeOH/$H_2O$ (3:2, v/v) to afford five subfractions, C6A-C6E. Subfraction C6E (67 mg) was separated by RP-18 CC with MeOH/$H_2O$ (3:2, v/v) and purified by silica gel CC eluted with *n*-hexane/EtOAc (2:3, v/v) to obtain compound **1** (8 mg).

The MT-E (14.5 g) was chromatographed on a silica gel column with stepwise gradient elution of $CHCl_3$/MeOH (1:0-0:1, v/v) to yield eight subfractions E1-E8. Subfraction E6 (1.1 g) was further separated by sephadex LH-20 CC with MeOH/$H_2O$ (1:1-1:0, v/v) to give four subfractions E6A-E6D. Subfraction E6D (72 mg) was separated by silica gel CC eluting with $CHCl_3$/MeOH/$H_2O$ (3:1:0.1, v/v/v) and purified by YMC column using MeOH/$H_2O$ (3:2, v/v) as elution to yield compound **5** (6 mg).

**(+)-Pinoresinol (1):** white solid; molecular formula $C_{20}H_{22}O_6$; ESI-MS *m/z* 359.14 $[M+H]^+$; CD (MeOH) $\lambda_{max}$ 206 ($\Delta\varepsilon$+2.12), 284 ($\Delta\varepsilon$+0.18), 341 ($\Delta\varepsilon$+0.17) nm [8, 9]. $^1$H NMR (600 MHz, $CDCl_3$) and $^{13}$C NMR (150 MHz, $CDCl_3$): see Table 1.

**Lariciresinol (2):** colorless oil; molecular formula $C_{27}H_{30}O_{15}$; ESI-MS *m/z* 361.40 $[M+H]^+$. $^1$H NMR (600 MHz, $CDCl_3$) and $^{13}$C NMR (150 MHz, $CDCl_3$): see Table 1.

**Blumenol A (3):** white amorphous powder; molecular formula $C_{13}H_{20}O_3$; ESI-MS: *m/z* 225.15 $[M+H]^+$. $^1$H NMR (600 MHz, $CDCl_3$): 5.91 (1H, t, *J* = 1.2 Hz, H-4), 5.85 (1H, dd, *J* = 5.4, 15.3 Hz, H-7), 5.79 (1H, dd, *J* = 1.1, 15.3 Hz, H-8), 4.41 (1H, t, *J* = 6.0 Hz, H-9), 2.44 (1H, d, *J* = 17.1 Hz, H-$2_a$), 2.24 (1H, d, *J* = 17.1 Hz, H-$2_b$), 1.90 (3H, d, *J* = 1.2 Hz, H-13), 1.30 (3H, d, *J* = 6.0 Hz, H-10), 1.08 (3H, s, H-11), 1.02 (3H, s, H-12); $^{13}$C

NMR (150 MHz, $CDCl_3$): 41.18 (C-1), 49.73 (C-2), 198.08 (C-3), 126.92 (C-4), 162.87 (C-5), 79.07 (C-6), 135.75 (C-7), 129.06 (C-8), 68.06 (C-9), 23.76 (C-10), 22.92 (C-11), 24.06 (C-12), 18.92 (C-13).

**Dehydrovomifoliol (4):** amorphous powder; molecular formula $C_{13}H_{18}O_3$; ESI-MS: *m/z* 223.04 $[M+H]^+$. $^1H$ NMR (600 MHz, $CDCl_3$): 6.83 (1H, d, *J* = 15.6 Hz, H-7), 6.47 (1H, d, *J* = 15.6 Hz, H-8), 5.96 (1H, s, H-4), 2.50 (1H, d, *J* = 17.1 Hz, H-$2_a$), 2.34 (1H, d, *J* = 17.1 Hz, H-$2_b$), 2.31 (3H, s, H-10), 1.89 (3H, d, *J* = 1.2 Hz, H-13), 1.11 (3H, s, H-11), 1.03 (3H, s, H-12); $^{13}C$ NMR (150 MHz, $CDCl_3$): 41.46 (C-1), 49.60 (C-2), 197.42 (C-3), 127.81 (C-4), 160.40 (C-5), 79.31 (C-6), 145.04 (C-7), 130.41 (C-8), 197.01 (C-9), 28.37 (C-10), 22.95 (C-11), 24.36 (C-12), 18.68 (C-13).

**Eleutheroside B (5):** white crystalline solid; molecular formula $C_{17}H_{24}O_9$; ESI-MS: *m/z* 373.37 $[M+H]^+$. $^1H$ NMR (600 MHz, $CD_3OD$) and $^{13}C$ NMR (150 MHz, $CD_3OD$): see Table 1.

## 3. RESULTS AND DISCUSSION

Compound **1** was isolated as a white solid. The $^1H$ NMR spectra revealed the signals of three ABX-type protons [$\delta_H$ 6.90 (*d*, *J* = 1.8 Hz, H-2), 6.89 (*d*, *J* = 8.4 Hz, H-6), and 6.82 (*dd*, *J* = 2.1, 9.0 Hz, H-5)]. The $^1H$ NMR also showed one oxymethine proton [$\delta_H$ 4.74 (1H, *d*, *J* = 4.8 Hz, H-7)], one methine proton [$\delta_H$ 3.10 (1H, *m*, H-8)], and two oxymethylene protons [$\delta_H$ 4.25 (1H, *dd*, *J* = 6.9, 9.0 Hz, H-$9_a$), 3.88 (1H, *dd*, *J* = 4.2, 10.8 Hz, H-$9_b$)], one methoxy group [$\delta_H$ 3.90 (3H, s, 3-$OCH_3$)]. The $^{13}C$ NMR and DEPT spectra of **1** showed the presence of 10 carbon signals, including six aromatic carbons [$\delta_C$ 132.97 (C-1), 108.67 (C-2), 146.75 (C-3), 145.29 (C-4), 144.31 (C-5), 118.99 (C-6)], one oxymethine carbon ($\delta_C$ 85.91, C-7), one methine carbon ($\delta_C$ 54.20, C-8), one oxymethylene carbon ($\delta_C$ 71.70, C-9), and one methoxy carbon ($\delta_C$ 56.00). In the COSY spectra of **1** showed the correlation between H-7 and two protons H-8 and H-9. Besides, in the HMBC spectrum, proton H-7 ($\delta_H$ 4.74) correlated with carbon C-1 ($\delta_C$ 132.97), confirmed the propylbenzene unit. The ESI-MS gave a molecular ion peak at *m/z* 359.14 $[M+H]^+$, which was suggested the molecular formula $C_{20}H_{22}O_6$. This demonstrated that structure of **1** was replicated, with the other part being fully symmetrical. By comparison of the NMR data of **1** with those of the published data [10] as well as the CD spectrum of **1** displayed the positive Cotton effects at 206 nm ($\Delta\varepsilon$+2.12), 284 nm ($\Delta\varepsilon$+0.18) and 341 nm ($\Delta\varepsilon$+0.17), compound **1** was identified as (+)-pinorecinol.

Compound **2** was obtained as a colorless oil. The molecular formula was established as $C_{20}H_{24}O_6$ by ESI-MS data (*m/z* 361.40 $[M+H]^+$). The $^{13}C$ NMR spectrum displayed signals of 20 carbons, including 12 aromatic carbons [$\delta_C$ 134.82, 108.37, 146.57, 145.08, 114.22, 118.79, 132.31, 111.26, 146.67, 144.04, 114.46, 121.23]; 4 carbons of the tetrahydrofuran ring [$\delta_C$ 82.86 (C-7), 52.62 (C-8), 42.44 (C-8' ), 72.92 (C-9' )], one methylene carbon [$\delta_C$ 33.35 (C-7)], one oxymethylene carbon [$\delta_C$ 60.96 (C-9)], and two methoxy groups [$\delta_C$ 55.95 (3-$OCH_3$), 55.97 (3' -$OCH_3$)]. The $^1H$ NMR spectrum of **2** showed the signals of two ABX aromatic proton systems [$\delta_H$ 6.87 (1H, *d*, *J* = 4.2 Hz, H-2), 6.86 (1H, *d*, *J* = 1.5 Hz, H-5), 6.80 (1H, *dd*, *J* = 1.5, 8.4 Hz, H-6)] and [6.69 (1H, *brs*, H-2' ), 6.83 (1H, *d*, *J* = 8.4 Hz, H-5' ), 6.70 (1H, *brs*, H-6' )], two protons of methylene [$\delta_H$ 2.91 (1H, *dd*, *J* = 5.4, 13.5 Hz, H-$7_a$' ), 2.55 (1H, *dd*, *J* = 10.5, 13.5 Hz, H-$7_b$' )], two protons of oxymethylene [$\delta_H$ 3.91 (1H, *dd*, *J* = 6.6, 10.8 Hz, H-$9_a$), 3.75 (1H, *dd*, *J* = 6.6, 9.0 Hz, H-$9_b$)], and a tetrahydrofuran moiety with four protons including: two methine protons [$\delta_H$ 2.40 (1H, *m*, H-8), 2.73 (1H, *m*, H-8' )], two oxymethylene protons [$\delta_H$ 4.05 (1H, *dd*, *J* = 7.2, 8.4 Hz, H-$9_a$' ), 3.77 (1H, *dd*, *J* = 6.6, 9.6 Hz, H-$9_b$' )], and one oxygenated methine proton [$\delta_H$ 4.79 (1H, *d*, *J* = 6.6 Hz, H-7)]. The HMBC data confirmed the correlation between protons and carbons: H-7 and C-2, C-6, C-8, C-9, C-8' , C-9' ; H-7' and C-1' , C-2' , C-6' , C-8' , C-9' , C-8, resulting in a lignan-type skeleton. By comparison of the NMR data of **2** with those of the published data [11], **2** was assigned as lariciresinol.

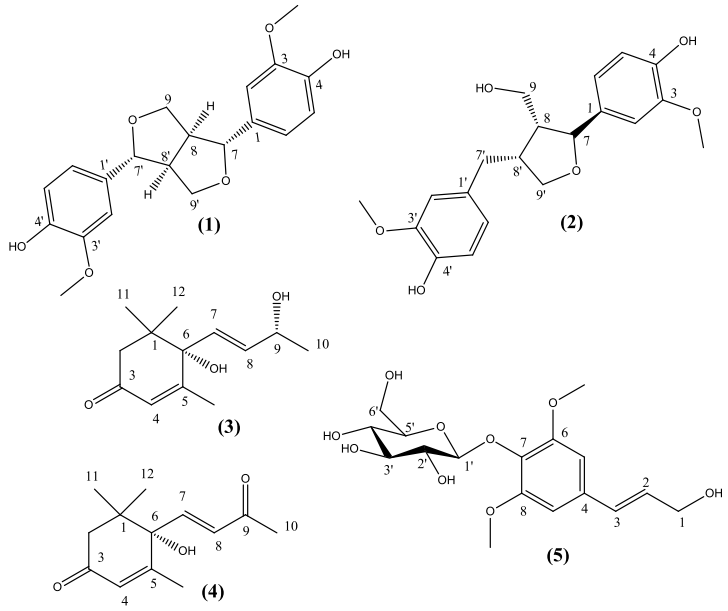


*Figure 1. Structure of compounds **1-5***

*Table 1. The NMR data of compounds **1-2** and **5***

| | **1** | | **2** | | **5** | |
|---|---|---|---|---|---|---|
| **C** | **$\delta_C$** | **$\delta_H$** | **$\delta_C$** | **$\delta_H$** | **$\delta_C$** | **$\delta_H$** |
| 1 | 132.97 | | 134.82 | | 63.57 | 4.24 dd 1.0, 5.5 |
| 2 | 108.67 | 6.90 d 1.8 | 108.37 | 6.87 d 4.2 | 130.05 | 6.35 dt 5.5, 16.0 |
| 3 | 146.75 | | 146.57 | | 131.27 | 6.57 d 16.0 |
| 4 | 145.29 | 5.62 brs (4-OH) | 145.08 | 5.61 brs (4-OH) | 135.27 | |
| 5 | 114.31 | 6.89 d 8.4 | 114.22 | 6.86 d 1.5 | 105.50 | 6.77 s |
| 6 | 118.99 | 6.82 dd 2.1, 9.0 | 118.79 | 6.80 dd 1.5, 8.4 | 154.36 | |
| 7 | 85.91 | 4.74 d 4.8 | 82.86 | 4.79 d 6.6 | 135.92 | |
| 8 | 54.20 | 3.10 m | 52.62 | 2.40 m | 154.36 | |
| 9 | 71.70 | 4.25 dd 6.9, 9.0<br>3.88 dd 4.2, 10.8 | 60.96 | 3.91 dd 6.6, 10.8<br>3.75 dd 6.6, 9.0 | 105.50 | 6.77 s |
| 3-$OCH_3$ | 56.00 | 3.90 s | 55.95 | 3.87 s | | |
| 6,8- $OCH_3$ | | | | | 57.04 | 3.88 s |
| 1' | 132.97 | | 132.31 | | 105.35 | 4.89 d 7.5 |
| 2' | 108.67 | 6.90 d 1.8 | 111.26 | 6.69 brs | 75.74 | 3.50 m |
| 3' | 146.75 | | 146.67 | | 77.84 | 3.44 m |
| 4' | 145.29 | 5.62 brs (4' -OH) | 144.04 | 5.53 brs (4' -OH) | 71.36 | 3.43 m |
| 5' | 114.31 | 6.89 d 8.4 | 114.46 | 6.83 d 8.4 | 78.36 | 3.24 m |
| 6' | 118.99 | 6.82 dd 2.1, 9.0 | 121.23 | 6.70 brs | 62.60 | 3.80 dd 2.5, 12.0<br>3.69 dd 5.0, 12.0 |
| 7' | 85.91 | 4.74 d 4.8 | 33.35 | 2.91 dd 5.4, 13.5<br>2.55 dd 10.5, 13.5 | | |
| 8' | 54.20 | 3.10 m | 42.44 | 2.73 m | | |
| 9' | 71.70 | 4.25 dd 6.9, 9.0<br>3.88 dd 4.2, 10.8 | 72.92 | 4.05 dd 7.2, 8.4<br>3.77 dd 6.6, 9.6 | | |
| 3' -$OCH_3$ | 56.00 | 3.90 s | 55.97 | 3.88 s | | |

Compound **3** was obtained as an amorphous powder. The $^{1}$H NMR, $^{13}$C NMR, and DEPT spectra indicated that **3** was a megastigmane. The remaining 13 signals, including one carbonyl carbon ($\delta_C$ 198.08), four olefinic carbons ($\delta_C$ 126.92, 162.87, 135.75, 129.06), one oxygenated quaternary carbon ($\delta_C$ 79.07), one oximethine carbon ($\delta_C$ 68.06), one methylene carbon ($\delta_C$ 49.73), one quaternary carbon ($\delta_C$ 41.18), and four methyl carbon ($\delta_C$ 18.92, 22.92, 23.76, 24.06). The $^{1}$H NMR spectrum displayed signals for two tertiary methyl groups [$\delta_H$ 1.08 (3H, *s*), 1.02 (3H, *s*)], a secondary methyl [$\delta_H$ 1.30 (3H, *d*, *J* = 6.0 Hz)], a methyl attached to an olefinic carbon [$\delta_H$ 1.90 (3H, *d*, *J* = 1.2 Hz)], a pair of isolated methylene protons centered [$\delta_H$ 2.44 (1H, *d*, *J* = 17.1 Hz), 2.24 (1H, *d*, *J* = 17.1 Hz)], an oximethine proton [$\delta_H$ 4.41 (1H, *t*, *J* = 6.0 Hz)], and three olefinic protons [$\delta_H$ 5.91 (1H, *t*, *J* = 1.2 Hz), 5.85 (1H, *dd*, *J* = 5.4, 15.3 Hz), 5.79 (1H, *dd*, *J* = 1.1, 15.3 Hz)]. In the HMBC spectrum, the correlations were observed between the protons and carbons: H-2 and C-1, C-3, C-4, C-6, C-11; H-4 and C-2, C-6, C-13; H-7 and C-6, C-8, C- 9, C-10; H-8 and C-5, C-6, C-7, C-9; H-10 and C-7, C-9; H-11, H-12 and C-1, C-2, C-6; H-13 and C-4, C-5, C-6, indicated that the structure of **3** is 6,9-dihydroxy-4,7-megastigmadien-3-one. Thus, compound **3** was identified as blumenol A by comparison with the reported data [12].

Compound **4** was isolated as an amorphous powder. Its molecular formula, $C_{13}H_{18}O_3$, was determined by the ESI-MS quasi-molecular ion peak at *m/z* 223.04 $[M+H]^+$. Comparison of the $^{1}$H and $^{13}$C NMR data of **4** with those of **3** indicated that the structures of both compounds were similar, except for the replacement of the hydroxymethine group ($\delta_C$ 68.06) in **3** with a carbonyl group ($\delta_C$ 197.01) in **4**. By comparison of the NMR data of **4** with those of the published data [13], **4** was identified as dehydrovomifoliol.

Compound **5** was isolated as a white crystalline solid. In the $^{1}$H NMR spectrum of **5** showed the signals of two protons in a tetrasubstituted benzene [$\delta_H$ 6.77 (2H, *s*, H-5, H-9)], two methoxy groups [$\delta_H$ 3.88 (6H, *s*, 6,8-$OCH_3$)], two olefinic protons [$\delta_H$ 6.57 (1H, *d*, *J* = 16.0 Hz, H-3), 6.35 (1H, *dt*, *J* = 5.5, 16.0 Hz, H-2)], and two oxymethylene protons [4.24 (2H, *dd*, *J* = 1.0, 5.5 Hz, H-1)]. Besides, the $^{1}$H NMR of **5** also displayed the anomeric proton of *β*-glucopyranoside moiety at $\delta_H$ 4.29 (1H, *d*, *J* = 7.8 Hz, H-1' ). Furthermore, the $^{13}$C NMR displayed seventeen carbon signals, including six carbons in the aromatic region [$\delta_C$ 135.27 (C-4), 105.50 (C-5, C-9), 154.36 (C-6, C-8), 135.92 (C-7)], two olefinic carbon signals [$\delta_C$ 130.05 (C-2), 131.27 (C-3)], one oxygenated methylene [$\delta_C$ 63.57 (C-1)], two methoxy groups [$\delta_C$ 57.04 (6,8-$OCH_3$)], and six carbons of a glucose moiety (table 1). Moreover, the molecular formula was established as $C_{17}H_{24}O_9$ by ESI-MS data (*m/z* 373.36 $[M+H]^+$). By comparing the NMR data with those reported in the literature [14], suggested the structure of **5** to be eleutheroside B.

## IV. CONCLUSION

From *Magnolia tiepii* leaves collected in Khanh Vinh slope, Khanh Hoa Province, five compounds including (+)-pinorecinol (**1**), lariciresinol (**2**), blumenol A (**3**), dehydrovomifoliol (**4**), and eleutheroside B (**5**) were isolated. Their structures elucidation was confirmed by NMR, MS, and CD as well as comparison with published data. These compounds were isolated for the first time from this species.

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