Taylor & Francis
Taylor & Francis Group

Natural Product Research
Formerly Natural Product Letters

ISSN: 1478-6419 (Print) 1478-6427 (Online) Journal homepage: http://www.tandfonline.com/loi/gnpl20

Four new phenolic constituents from the rhizomes of Gastrodia elata Blume

Zhi-Wei Wang, Yun Li, Da-Hui Liu, Yan Mu, Hong-Jing Dong, Hong-Lei Zhou, Lan-Ping Guo & Xiao Wang

To cite this article: Zhi-Wei Wang, Yun Li, Da-Hui Liu, Yan Mu, Hong-Jing Dong, Hong-Lei Zhou, Lan-Ping Guo & Xiao Wang (2018): Four new phenolic constituents from the rhizomes of Gastrodia elata Blume, Natural Product Research, DOI: 10.1080/14786419.2018.1460836

To link to this article: https://doi.org/10.1080/14786419.2018.1460836

NATURAL PRODUCT RESEARCH, 2018
https://doi.org/10.1080/14786419.2018.1460836

Taylor & Francis
Taylor & Francis Group

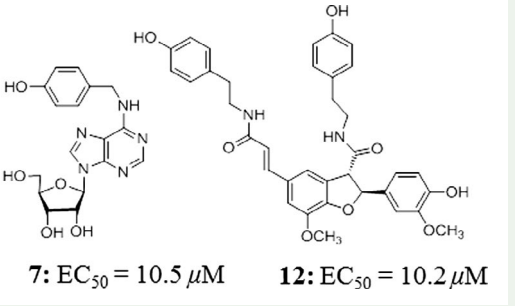
Four new phenolic constituents from the rhizomes of *Gastrodia elata* Blume

Zhi-Wei Wang[a§], Yun Li[a,b§], Da-Hui Liu[c], Yan Mu[a], Hong-Jing Dong[a], Hong-Lei Zhou[b], Lan-Ping Guo[a] and Xiao Wang[a]

[a]Shandong Key Laboratory of TCM Quality Control Technology, Shandong Analysis and Test Center, Qilu University of Technology (Shandong Academy of Sciences), Jinan, People's Republic of China; [b]College of Pharmacy, Shandong University of Traditional Chinese Medicine, Jinan, People's Republic of China; [c]Institute of Medicinal Plants, Yunnan Academy of Agriculture Science, Kunming, People's Republic of China

ABSTRACT

Four new gastrodin derivatives containing a *trans*-cinnamoyl unit (**1–4**) and nine known compounds (**5–13**) were isolated from the rhizomes of *Gastrodia elata* Blume. All these compounds were evaluated for their neuroprotective effects against 6-hydroxydopamine-induced cell death, and compounds **7** and **12** showed potent activities with EC_{50} values of 10.5 and 10.2 μM, respectively.



7: $EC_{50} = 10.5\ \mu M$ **12:** $EC_{50} = 10.2\ \mu M$

ARTICLE HISTORY
Received 7 February 2018
Accepted 1 April 2018

KEYWORDS
Phenolics; *Gastrodia elata* Blume; neuroprotective effects; N^6-(4-hydroxybenzyl) adenosine; grossamide

1. Introduction

Gastrodia elata Blume (*G. elata*), commonly called 'Tian-ma' in Chinese, is an extensively used traditional Chinese herbal medicine to treat neurological disorders, such as epilepsy, stroke and convulsion (Liu and Mori 1992; Chen and Sheen 2011). The neuroprotective effect of *G. elata* has been attracting more attentions. Indeed, pharmacological studies have demonstrated that *G. elata* extract, gastrodin, p-hydroxybenzaldehyde and parishin possessed neuroprotective effect through anti-inflammatory and anti-oxidative mechanism (Ng et al.

CONTACT Xiao Wang wangx@sdas.org
§Z.-W. Wang and Y. Li contributed equally to this work.
Supplemental data for this article can be accessed at https://doi.org/10.1080/14786419.2018.1460836

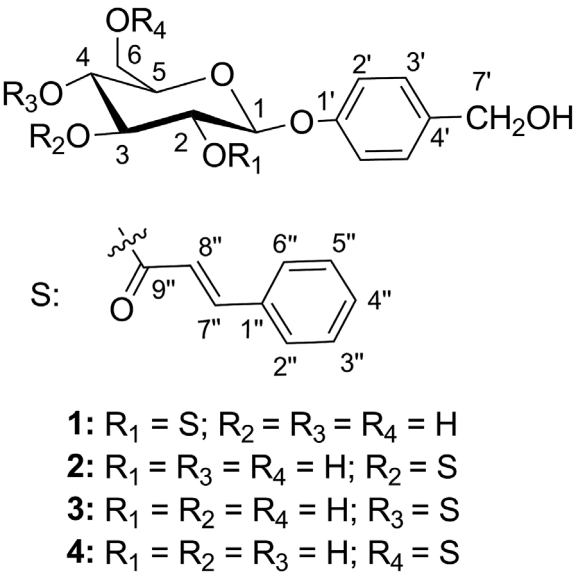
2016; Zhan et al. 2016; Tang et al. 2017). So far, more than 80 compounds (Li et al. 2015; Wu et al. 2017) have been isolated from *G. elata*, but only a few of them have been evaluated for their neuroprotective activity (Huang et al. 2007; Chen et al. 2016; Li et al. 2016). These results promoted us to continue to investigate the potential neuroprotective components of *G. elata*.

G. elata f. glauca S. Chow, *G. elata* f. elata, *G. elata* f. viridis Makino, *G. elata* f. flavida S. Chow, and *G. elata* f. alba S. Chow are the five varieties of *G. elata* cultivated in China, which are considered as the original plants of the traditional Chinese medicine 'Tian-ma' (Chen et al. 2015). Among these varieties, *G. elata* f. glauca S. Chow is the most widely cultivated. Here, we reported the isolation and structural elucidation of four new phenolic constituents from the ethanol extract of the rhizomes of *G. elata* (*G. elata* f. glauca S. Chow), together with nine known compounds. Neuroprotective effects of all isolated compounds against 6-hydroxydopamine-induced cell death were evaluated *in vitro*.

2. Results and discussion

Compound **1** was isolated as a light yellow powder. The molecular formula of **1** was determined as $C_{22}H_{24}O_8$ by HR-ESI-MS at *m/z* 439.1362 $[M + Na]^+$ (calcd. 439.1363 $[M + Na]^+$). The IR spectrum indicated the presence of ester (1711 cm^{-1}) and aromatic ring (1614 and 1512 cm^{-1}). The existence of a *p*-hydroxybenzyl alcohol moiety in **1** was evidenced by NMR signals (Table S1) at δ_H 7.20 (1H, d, J = 8.8 Hz, H-3′, 5′), 6.91 (1H, d, J = 8.4 Hz, H-2′, 6′), 5.07 (1H, t, J = 5.6 Hz, 7′-OH) and 4.39 (2H, d, J = 5.6 Hz, H-7′), and at δ_C 156.3, 137.0, 128.2 (2C), 116.5 (2C), 62.9; the presence of a *trans*-cinnamoyl group was supported by the observed proton signals at δ_H 7.72 (2H, m), 7.42 (3H, m), *trans*-olefinic proton signals at δ_H 7.70 and 6.66 (each 1 H, d, J = 16.0 Hz), and carbon resonances at δ_C 165.8, 145.3, 134.4, 131.0, 129.4 (2C), 128.8 (2C), 118.5. The proton resonance at δ_H 5.17 (1H, d, J = 8.0 Hz, H-1) and carbon signals at δ_C 99.0, 77.7, 74.5, 74.2, 70.4, 61.0 suggested the existence of a *β*-glucose. In the HMBC spectrum (Figure S0), the correlation from the anomeric proton δ_H 5.17 (1H, d, J = 8.0 Hz) to δ_C 156.3 (C-1′) confirmed the *p*-hydroxybenzyl alcohol moiety was linked to C-1. The HMBC correlation between δ_H 4.93 (H-2) and δ_C 165.8 (C-9″) was located the *trans*-cinnamoyl group at C-2. The detailed assignment of all NMR signals arising from **1** was performed by ^{1}H-^{1}H COSY, HSQC and HMBC spectroscopy. The absolute configuration of the sugar was determined to be D-glucose on the basis of GC-MS analysis of its chiral derivative. Thus, the structure of compound **1** (Figure 1) was determined to be 1-*O*-(4-hydroxymethylphenoxy)-2-*O*-*trans*-cinnamoyl-*β*-D-glucoside.

Compound **2** was obtained as a light yellow powder. The molecular formula of **2** was determined as $C_{22}H_{24}O_8$ by HR-ESI-MS at *m/z* 439.1366 $[M + Na]^+$ (calcd. 439.1363 $[M + Na]^+$). The absorption bands in the IR spectrum suggested the existence of ester (1712 cm^{-1}) and aromatic ring (1613 and 1512 cm^{-1}). Careful comparison of the NMR data (Table S1) of **2** and **1** demonstrated they possessed the similar structural moieties. The major differences were upfield shift at C-2 ($\Delta\delta_C$ −2.5 ppm) and C-4 (δ_C −2.4 ppm), and downfield shift at C-3 ($\Delta\delta_C$ +3.7 ppm). This revealed that the locations of *p*-hydroxybenzyl alcohol moiety or *trans*-cinnamoyl group in compound **2** may be changed. The HMBC correlations from δ_H 5.05 (1H, d, J = 7.2 Hz, H-1) to δ_C 156.5 (C-1′), and from δ_H 5.06 (1H, t, J = 9.6 Hz, H-3) to δ_C 166.2 (C-9″) confirmed *p*-hydroxybenzyl alcohol moiety and *trans*-cinnamoyl group was respectively connected to C-1 and C-3. The sugar moiety was identified as D-glucose in the same way to that of **1**. Thus, the structure of **2** was established as 1-*O*-(4-hydroxymethylphenoxy)-3-*O*-*trans*-cinnamoyl-*β*-D-glucoside.



1: R_1 = S; R_2 = R_3 = R_4 = H
2: R_1 = R_3 = R_4 = H; R_2 = S
3: R_1 = R_2 = R_4 = H; R_3 = S
4: R_1 = R_2 = R_3 = H; R_4 = S

Figure 1. Structures of compounds **1–4**.

Compound **3** was isolated as a light yellow powder. It was found to have the same molecular formula of $C_{22}H_{24}O_8$ as compound **2** from HR-ESI-MS at *m/z* 439.1368 $[M + Na]^+$ (calcd. 439.1363 $[M + Na]^+$). The absorption bands in the IR spectrum suggested the existence of ester (1695 cm^{-1}). The data of ^1H and ^{13}C (Table S1) were similar to those of **2** except for the upfield shift at C-3 ($\Delta\delta_C$ −3.9 ppm) and C-5 ($\Delta\delta_C$ −2.2 ppm), and downfield shift at C-2 ($\Delta\delta_C$ +2.1 ppm) and C-4 ($\Delta\delta_C$ +3.6 ppm), which suggested the different connections of *p*-hydroxybenzyl alcohol moiety or *trans*-cinnamoyl group in compound **3**. In the HMBC spectrum, the correlations of H-1 with C-1′, and of H-4 with C-9″ located the *p*-hydroxybenzyl alcohol moiety and *trans*-cinnamoyl group at C-1 and C-4, respectively. The sugar moiety was identified as D-glucose followed the same protocol for **1**. Thus, compound **3** was deduced to be 1-*O*-(4-hydroxymethylphenoxy)-4-*O*-*trans*-cinnamoyl-*β*-D-glucoside.

Compound **4** was obtained as a light yellow powder. The molecular formula of **4** was deduced as $C_{22}H_{24}O_8$ based on a sodium adduct ion at *m/z* 439.1364 $[M + Na]^+$ (calcd. 439.1363 $[M + Na]^+$). The IR spectrum showed the characteristic absorptions for ester at 1696 cm^{-1} and aromatic ring at 1613 and 1512 cm^{-1}. The 1D NMR data (Table S1) of **4** showed similar to those of **3**. The major differences between **4** and **3** were the downfield shift of proton signals at δ_H 4.44 ($\Delta\delta_H$ +0.98 ppm, H-6a) and δ_H 4.22 ($\Delta\delta_H$ +0.85 ppm, H-6b), and of carbon resonance at δ_C 64.1 ($\Delta\delta_C$ +3.2 ppm, C-6), indicating that the position of C-6 may be substituted. The HMBC correlation from H-6 to C-9″ revealed that the *trans*-cinnamoyl group was linked to C-6. The position of *p*-hydroxybenzyl alcohol moiety at C-1 was further confirmed by the HMBC correlation of H-1 (δ_H 4.90) with C-1′ (δ_C 156.5). According to the same way as in compound **1**, the sugar was determined to be D-glucose. Thus, compound **4** (1-*O*-(4-hydroxymethylphenoxy)-6-*O*-*trans*-cinnamoyl-*β*-D-glucoside) was established as shown in Figure 1.

Additionally, the other previously reported compounds **5–13** were identified as 4-hydroxybenzyl ethyl ether (**5**) (Zhou et al. 1981), adenosine (**6**) (Huang et al. 2005),

N^6-(4-hydroxybenzyl) adenosine (**7**) (Huang et al. 2006), gastrodioside (**8**) (Taguchi et al. 1981), bis(4-hydroxybenzyl) ether (**9**) (Taguchi et al. 1981), 4,4′-dihydroxybenzyl sulfoxide (**10**) (Yun-Choi and Pyo 1997), bis(4-hydroxybenzyl) sulfide (**11**) (Huang et al. 2007), grossamide (**12**) (Lajide et al. 1995), and S-(4-hydroxybenzyl) glutathione (**13**) (Andersson et al. 1995) by comparing NMR and MS data reported in the literature.

All isolated compounds were evaluated *in vitro* for their neuroprotective effects against 6-hydroxydopamine-induced cell death, with curcumin used as a positive control (EC_{50}: 6.5 μM). Compounds N^6-(4-hydroxybenzyl) adenosine (**7**) and grossamide (**12**) exhibited potent activities with EC_{50} values of 10.5 and 10.2 μM, respectively, while the other compounds were inactive with EC_{50} far beyond 50 μM.

3. Experimental

3.1. General methods

NMR spectra were recorded on Varian INOVA-600 (^{1}H: 600 MHz, ^{13}C: 150 MHz) and Bruker Avance III 400 (^{1}H: 400 MHz, ^{13}C: 100 MHz) instruments, with tetramethylsilane as internal standard. Mass spectra were obtained on an Agilent Technology 6520 Accurate-Mass Q-TOF spectrometer. UV spectra were recorded using a Shimadzu UV-2550 spectrophotometer. IR (KBr disks) spectra were performed on Bruker Vertex 70 spectrometer. Optical rotations were measured on an Anton Paar MCP 200 polarimeter. Macroreticular resins (D101, Cangzhou Bon Adsorber Technology Co., Ltd., Cangzhou, China) were used for column chromatography. Medium pressure liquid (MPLC) was performed on an Agela CHEETAH^{TM} MP instrument using prepacked RP-C_{18} column (500 × 80 mm). Preparative HPLC was carried out using a RIGOL L-3000 series instrument with a YMC-PEAK RP-C_{18} column (250 mm × 10.0 mm, 5 μm). Gas chromatography analyses were performed using a Thermo Trace 1310 system equipped with a FID detector.

3.2. Plant material

The rhizomes of *G. elata* (*G. elata* f. glauca) were collected at the plantation field of Xiaocao Ba, Yunnan province, China, in December 2015, and were authenticated by Dr. Da-Hui Liu (Institute of Medicinal Plants, Yunnan Provincial Academy of Agricultural Sciences, China). A voucher sample (No. GE-201511) was deposited at Shandong Analysis and Test Center, Shandong Academy of Sciences, China.

3.3. Extraction and isolation

The steamed and air-dried *G. elata* rhizomes (12 kg) were powdered, and extracted with 85% EtOH under reflux. The EtOH extract was evaporated under reduced pressure to yield a concentrated solution (2.6 L), which was subjected to macroporous resin column (D101, 12 cm × 70 cm), and eluted successively with 10% EtOH, 20% EtOH, 30% EtOH, 50% EtOH, 70% EtOH, 95% EtOH, to give six further fractions (Fr. MR-1–MR-6). Fr. MR-1 (37.4 g) was applied to a prepacked ODS MPLC column (500 × 80 mm) and eluted with MeOH-H_2O (5:95, 10:90, 15:85, 30:70, 40:60, 100:0) to give five sub-fractions (MR-1A–MR-1E). Sub-fraction MR-1B was purified by repeated preparative RP-HPLC (10% methanol in water containing

0.1% formic acid) to afford compound **1** (25 mg, 11.5 min). Compound **2** (2.6 mg, 14.5 min) was obtained from Fr. MR-1C by preparative HPLC (28% methanol in water containing 0.1% formic acid). Sub-fraction MR-1D was recrystallized by methanol to yield compound **4** (890 mg). Sub-fraction MR-1E was purified by RP-HPLC using MeOH-H_2O (28:72, containing 0.1% formic acid) as mobile phase to give compound **3** (11.9 mg, 11.9 min). Fr. MR-3 (35.8 g) was chromatographed on MPLC (ODS) successively eluted with 10, 25, 30, 35, 40% methanol in water to obtain seven sub-fractions (Fr. MR-3A–Fr. MR-3G). Compound **5** (528 mg, 17.1 min) was obtained from Fr. MR-3E by RP-HPLC (18% acetonitrile in water containing 0.1% formic acid). Fr. MR-4 (11 g) was chromatographed on silica gel eluted with CH_2Cl_2-MeOH (100:0 to 0:100) to afford six fractions (Fr. MR-4A–Fr. MR-4F). Compounds **10** (51 mg, 6.4 min) **11** (4 mg, 6.8 min) and **12** (10 mg, 14.5 min) was isolated from Fr. MR-4C by repeated preparative HPLC (MeOH-H_2O, 50:50, 0.1% formic acid). Fr. MR-4D was separated by preparative HPLC eluted with 50% methanol in water containing 0.1% formic acid to yield compounds **8** (29 mg, 11.0 min) and **9** (15 mg, 9.0 min). Fr. MR-4E was purified by repeated preparative HPLC (MeOH-H_2O, 50:50, 0.1% formic acid) to obtain compounds **6** (71 mg, 9.7 min) and **7** (8 mg, 12.4 min). Fr. MR-5 (18 g) was subjected to silica gel eluted with CH_2Cl_2-MeOH (100:0 to 0:100) to give six sub-fractions (Fr. MR-5A–Fr. MR-5G). Fr. MR-5C was purified by preparative HPLC with acetonitrile-H_2O (47:53, containing 0.1% formic acid) to obtain compound **13** (20 mg, 6.1 min).

3.4. Compound 1

Light yellow powder; $[\alpha]_D^{20}$: –4.6 (c = 0.1, methanol); UV λ_{max} (acetonitrile) nm (log ε): 277 (4.30), 217 (4.39); IR (KBr) cm^{-1}: 3395, 2922, 1711, 1637, 1614, 1512; ^{1}H- and ^{13}C-NMR spectral data: see Table S1; ESI-MS *m/z*: 439.1 $[M + Na]^+$; HR-ESI-MS *m/z*: 439.1362 $[M + Na]^+$ (Calcd for $C_{22}H_{24}O_8Na$: 439.1363).

3.5. Compound 2

Light yellow powder; $[\alpha]_D^{20}$: +26.5 (c = 0.1, methanol); UV λ_{max} (acetonitrile) nm (log ε): 276 (4.33), 217 (4.40); IR (KBr) cm^{-1}: 3416, 2920, 1712, 1636, 1613, 1512; ^{1}H- and ^{13}C-NMR spectral data: see Table S1; ESI-MS *m/z*: 439.1 $[M + Na]^+$; HR-ESI-MS *m/z*: 439.1366 $[M + Na]^+$ (Calcd for $C_{22}H_{24}O_8Na$: 439.1363).

3.6. Compound 3

Light yellow powder; $[\alpha]_D^{20}$: –41.0 (c = 0.1, methanol); UV λ_{max} (acetonitrile) nm (log ε): 275 (4.20), 216 (4.32); IR (KBr) cm^{-1}: 3430, 2924, 1695, 1637, 1512; ^{1}H- and ^{13}C-NMR spectral data: see Table S1; ESI-MS *m/z*: 439.1 $[M + Na]^+$; HR-ESI-MS *m/z*: 439.1368 $[M + Na]^+$ (Calcd for $C_{22}H_{24}O_8Na$: 439.1363).

3.7. Compound 4

light yellow powder; $[\alpha]_D^{20}$: –50.2 (c = 0.1, methanol); UV λ_{max} (acetonitrile) nm (log ε): 275 (4.28), 217 (4.38); IR (KBr) cm^{-1}: 3428, 2922, 1696, 1637, 1613, 1512; ^{1}H- and ^{13}C-NMR spectral

data: see Table S1; ESI-MS *m/z*: 439.1 $[M + Na]^+$; HR-ESI-MS *m/z*: 439.1364 $[M + Na]^+$ (Calcd for $C_{22}H_{24}O_8Na$: 439.1363).

3.8. Sugar analysis

The absolute configuration of the sugar was determined according to the method previous reported (Wang et al. 2012). Compounds **1–4** (each 3 mg) dissolved in acetonitrile (3 mL) and 2 M HCl (3 mL) was respectively refluxed at 90 °C for 3 h. After this period, the reaction solution was concentrated under reduced pressure, and then the residue was suspended with H_2O and extracted with EtOAc (3 mL × 3). The aqueous layer was evaporated to dryness and then dissolved in 0.3 mL of anhydrous pyridine, to which 5 mg of L-cysteine methyl ester hydrochloride was added. The mixture was reacted at 60 °C for 2 h, and then hexamethyldisilazan (0.3 mL) and trimethylsilyl chloride (0.3 mL) were added, continued to react at 60 °C for 1 h. After partitioning between H_2O and *n*-hexane (each 0.4 mL), the *n*-hexane extract was analyzed with gas chromatography under the following conditions: column, HP-5MS (30 m × 0.25 mm × 0.5 μm); column temperature, initial temperature of 150 °C for 10 min, ramped up to 300 °C at a rate of 3 °C per minute followed by a hold at 300 °C for 5 min. In the acid hydrolysates of **1–4**, only D-glucose was detected by comparison of the retention time with that of authentic samples prepared in the same way (the t_R of D- and L-glucose was 39.47 and 40.06 min, respectively).

3.9. Determination of HT22 cell viability against 6-OHDA

The potential neuroprotective effects of all isolated compounds were conducted as previous reports (Kwon et al. 2016). HT22 cells (mouse hippocampal neuronal cells) were plated in a density of 5×10^3 cells/100 μL/well in 96-wellplates. After 24 h, the cells were treated with 6-OHDA (100 μM) and a series of concentrations of samples (50, 20, 10, 5 and 1 μM) for an additional 24 h. The cell viability was determined by SRB assay and curcumin was used as a positive control.

Supplementary material

1D, 2D NMR and MS spectra of the compounds **1–4** are available as supplementary material, alongside Table S1 and Figure S0.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This research work was financially supported by the Natural Science Foundation of Shandong [grant number ZR2016YL006]; the Shandong Province Taishan Scholar Program (Lanping Guo); and the Priority Research Program of the Shandong Academy of Sciences (Lanping Guo).

References

Andersson M, Bergendorff O, Nielsen M, Sterner O, Witt R, Ai J, Lu A, Wang AM. 1995. Inhibition of kainic acid binding to glutamate receptors by extracts of *Gastrodia*. Phytochemistry. 38:835–836.

Chen WC, Lai YS, Lu KH, Lin SH, Liao LY, Ho CT, Sheen LY. 2015. Method development and validation for the high-performance liquid chromatography assay of gastrodin in water extracts from different sources of *Gastrodia elata* Blume. J Food Drug Anal. 23:803–810.

Chen WC, Lai YS, Lin SH, Lu KH, Lin YE, Panyod S, Ho CT, Sheen LY. 2016. Anti-depressant effects of *Gastrodia elata* Blume and its compounds gastrodin and 4-hydroxybenzyl alcohol, via the monoaminergic system and neuronal cytoskeletal remodeling. J Ethnopharmacol. 182:190–199.

Chen PJ, Sheen LY. 2011. Gastrodiae Rhizoma (tiān má): a review of biological activity and antidepressant mechanisms. J Tradit Complementary Med. 1:31–40.

Huang NK, Chern Y, Fang JM, Lin CI, Chen WP, Lin YL. 2007. Neuroprotective principles from *Gastrodia elata*. J Nat Prod. 70:571–574.

Huang ZB, Song DM, Chen FK. 2005. The chemical constituents isolated from *Gastrodia elata* BL. Chin J Med Chem. 15:227–229.

Huang ZB, Wu Z, Chen FK, Zou LB. 2006. The protective effects of phenolic constituents from *Gastrodia elata* on the cytotoxicity induced by KCl and glutamate. Arch Pharmacal Res. 29:963–968.

Kwon J, Hiep NT, Kim DW, Hong S, Guo Y, Hwang BY, Lee HJ, Mar W, Lee D. 2016. Chemical constituents isolated from the root bark of *Cudrania tricuspidata* and their potential neuroprotective effects. J Nat Prod. 79:1938–1951.

Lajide L, Escoubas P, Mizutani J. 1995. Termite antifeedant activity in *Xylopia aethiopica*. Phytochemistry. 40:1105–1112.

Li Z, Wang Q, Ouyang H, Huang L, Feng Y, Wang R, Yang S. 2016. New compounds with neuroprotective activities from *Gastrodia elata*. Phytochem Lett. 15:94–97.

Li Z, Wang Y, Ouyang H, Lu Y, Qiu Y, Feng Y, Jiang H, Zhou X, Yang S. 2015. A novel dereplication strategy for the identification of two new trace compounds in the extract of *Gastrodia elata* using UHPLC/Q-TOF-MS/MS. J Chromatogr B. 988:45–52.

Liu J, Mori A. 1992. Antioxidant and free radical scavenging activities of *Gastrodia elata* Bl. and *Uncaria rhynchophylla* (Miq.) Jacks. Neuropharmacology. 31:1287–1298.

Ng CF, Ko CH, Koon CM, Chin WC, Kwong HCST, Lo AWI, Wong HL, Fung KP, Lau CBS, Lam PK, et al. 2016. The aqueous extract of rhizome of *Gastrodia elata* Blume attenuates locomotor defect and inflammation after traumatic brain injury in rats. J Ethnopharmacol. 185:87–95.

Taguchi H, Yosioka I, Yamasaki K, Kim I. 1981. Studies on the constituents of *Gastrodia elata* Blume. Chem Pharm Bull. 29:55–62.

Tang C, Wang J, Yu J, Wang L, Cheng M, Cui W, Zhao J, Xiao H. 2017. Identification, characterization and *in vitro* neuroprotection of N^6-(4-hydroxybenzyl) adenine riboside and its metabolites. Phytochem Lett. 20:146–150.

Wang ZW, Wang JS, Luo J, Wei DD, Kong LY. 2012. Three new phenolic glucosides from the roots of *Rheum palmatum*. Chem Pharm Bull. 60:241–245.

Wu JY, Wu BC, Tang CL, Zhao JS. 2017. Analytical techniques and pharmacokinetics of *Gastrodia elata* Blume and its constituents. Molecules. 22:1137–1154.

Yun-Choi HS, Pyo MK. 1997. Isolation of 4,4′-dihydroxybenzyl sulfoxide from *Gastrodia elata*. Arch Pharmacal Res. 20:91–92.

Zhan HD, Zhou HY, Sui YP, Du XL, Wang WH, Dai L, Sui F, Huo HR, Jiang TL. 2016. The rhizome of *Gastrodia elata* Blume-An ethnopharmacological review. J Ethnopharmacol. 189:361–385.

Zhou J, Pu XY, Yang YB. 1981. Nine phenolic constituents from fresh *Gastrodia elata*. Chin Sci Bull. 26:1118–1120.