

Chemical constituents isolated from the aerial parts of *Swertia pseudochinensis* and their potential neuroprotective effects

Ke Xiang¹, Qi He¹, Yanmei Chen¹, Dongxin Yang¹, Yanwei Duan¹, Hua Li^{1,2,*}, Lixia Chen^{1,*}

Abstract

Objective: *Swertia pseudochinensis*, an annual herb of the genus *Swertia* in the family Gentianaceae. Some constituents and extracts from the *Swertia* genus have been recently reported to possess neuroprotective effects, suggesting their potential utility in the prevention and treatment of Parkinson disease (PD). The aim of this work is to identify the chemical constituents and evaluate the potential biological activists of *Swertia pseudochinensis*.

Methods: The phytochemicals from the aerial parts of *S. pseudochinensis* were isolated and purified by silica gel, Sephadex LH-20 gel, semi-preparative high-performance liquid chromatography, and identified by the spectroscopic methods. All compounds were evaluated for their potential neuroprotective effects against 1-methyl-4-phenylpyridinium-induced apoptosis in the SH-SY5Y human neuroblastoma cell line using the 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide assay. Then, we performed an enrichment analysis using the Database for Annotation, Visualization, and Integrated Discovery and investigated the mechanisms by which bellidifolin regulates neurodegenerative disease.

Results: Two new anthraquinone, 1,5,6-trimethoxy-2-hydroxy-3-methy-anthraquinone (1) and 1,5,6,8-tetramethoxy-2-hydroxy-3-methyanthraquinone (2), together with nine known including 7-O- β -d-glucopyranosyl-1,8-dihydroxy-3-methoxyxanthone (3), gentisin (4), swertianolin (5), bellidifolin (6), gentiacaulein (7), norswertianolin (8), 5-O- β -d-glucopyranosyl-1,3,8-trihydroxyapatone (9), 1-hydroxy-3,5,8-trimethoxyxanthone (10), and aurantio-obtusin (11), were isolated and compounds 6–8 and 10 exhibited neuroprotective effects at a concentration of 50 μ mol/L. Among them, bellidifolin showed significant protective activity, and might have potential as a neuroprotective agent for the treatment of PD, possibly by acting on oxidative damage and reactive oxygen species.

Conclusions: These findings indicate that further research on the genus *Swertia* and its bioactive constituents toward neurodegenerative disorders could be extremely rewarding.

Keywords: Anthraquinone, Neuroprotective effect, Parkinson disease, *Swertia pseudochinensis*, Xanthone

1 Introduction

Swertia pseudochinensis, an annual herb of the genus *Swertia* in the family Gentianaceae, is mainly distributed

in northern China and northeast Asia, and the dried whole plant has been used to treat jaundice, dysentery, acute enteritis, rib pain, and loss of appetite in traditional medicine^[1]. In phytochemical studies, various types of compounds, including xanthenes, flavonoids, triterpenoids, and iridoid glycosides, have been isolated from the genus *Swertia*^[2–3]. These constituents have shown antitumor^[2,4], hepatoprotective^[5–7], hypoglycemic^[8–9], antibacterial^[10], gastrointestinal protective^[11–12], anti-inflammatory^[13–14], and other effects. In addition, some constituents and extracts from the *Swertia* genus have been recently reported to possess neuroprotective effects, suggesting their potential utility in the prevention and treatment of Parkinson disease (PD)^[15–16].

To identify more compounds with neuroprotective effects, we analyzed the 75% EtOH extract of the aerial parts of *S. pseudochinensis* and successfully isolated and identified Two new anthraquinone, 1,5,6-trimethoxy-2-hydroxy-3-methy-anthraquinone (1) and 1,5,6,8-tetramethoxy-2-hydroxy-3-methyanthraquinone (2), and nine known compounds (3–11), including 7-O- β -d-glucopyranosyl-1,8-dihydroxy-3-methoxyxanthone (3), gentisin (4), swertianolin (5), bellidifolin (6), gentiacaulein (7), norswertianolin (8), 5-O- β -d-glucopyranosyl-1,3,8-trihydroxyapatone (9) and 1-hydroxy-3,5,8-trimethoxyxanthone (10) and aurantio-obtusin (11). The anthraquinones 1, 2, and 11 have been isolated from the genus *Swertia* for the first time. Herein, we describe the isolation and

Ke Xiang and Qi He contributed equally to this work.

¹ Wuya College of Innovation, Key Laboratory of Structure-Based Drug Design & Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang, China; ² Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

* Corresponding author. Hua Li, Wuya College of Innovation, Key Laboratory of Structure-Based Drug Design & Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China; Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China, E-mail: li_hua@hust.edu.cn; Lixia Chen, Wuya College of Innovation, Key Laboratory of Structure-Based Drug Design & Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China, E-mail: syzclx@163.com.

Copyright © 2021 Tianjin University of Traditional Chinese Medicine. This is an open access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

Acupuncture and Herbal Medicine (2021) 1:1

Received 30 July 2021 / Accepted 30 July 2021

<http://dx.doi.org/10.1097/HM9.000000000000010>

structural elucidation of these compounds, as well as the evaluation of their neuroprotective effects in SH-SY5Y cells damaged by 1-methyl-4-phenylpyridinium (MPP⁺). We performed an enrichment analysis using the Database for Annotation, Visualization, and Integrated Discovery (DAVID), a web-accessible program that integrates functional genomic annotations with intuitive graphical summaries^[17], and investigated the mechanisms by which 6 regulates neurodegenerative disease.

2 Materials and methods

2.1 General experimental procedures

UV spectra were measured on a Shimadzu UV 2201 UV-visible spectrophotometer (Shimadzu, Kyoto, Japan). Analytical high-performance liquid chromatography (HPLC) was performed on an Agilent 1260 system with a diode array detector (DAD) using a YMC-Triart C₁₈ column (4.6 × 250 mm², 5 μm). Preparative HPLC was carried out using a Shimadzu HPLC system was equipped with a reversed-phase C₁₈ column (250 × 20 mm², 5 μm, 120 Å; YMC Co. Ltd., Kyoto, Japan) and SPD-20A UV detector (Shimadzu). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AVANCE III 600 spectrometer (Bruker, Karlsruhe, Germany) with tetramethylsilane as an internal standard. High-resolution electrospray ionization mass spectrometry (HR-ESI-MS) was performed on an Agilent 6210 TOF mass spectrometer. Open column chromatography was carried out using silica gel (100–200 mesh, 200–300 mesh, Qingdao Marine Chemical Factory, China), Sephadex LH-20 (GE Healthcare, Australia), and octadecyl silica gel (Merck Chemical Company Ltd., Germany). Thin-layer chromatography was performed with silica gel GF254 plates (Qingdao Marine Chemical Factory, China) and visualization was accomplished with UV light.

2.2 Plant material

Air-dried aerial parts of *S. pseudochinensis* were collected from the cultivated area of Chengde, Hebei Province, China, in October 2016, and were authenticated by Dr. Jincai Lu, Shenyang Pharmaceutical University. A voucher specimen of this collection (No. 20160706) has been deposited at the Herbarium of Shenyang Pharmaceutical University, Shenyang, China.

2.3 Extraction and isolation

The air-dried aerial parts of *S. pseudochinensis* (40.0 kg) were extracted with 75% EtOH 30 L and 3 h for 3 times to yield an extract after the solvent was removed *in vacuo*. The extract (1.07 kg) was suspended in water (1.5 L) and extracted with EtOAc 1.5 L for 3 times. The EtOAc extract (500.0 g) was subjected to silica gel column chromatography eluted with a gradient of CH₂Cl₂–MeOH (100:1 to 1:1) to afford eight fractions (F1–F8). Fraction F3 (17.7 g) was subjected to silica gel column chromatography using cyclohexane–acetone (100:1 to 1:1) as an eluent to afford six subfractions (F31–F36). Fraction F34 (7.5 g) was purified by a Sephadex LH-20 column and eluted with CH₂Cl₂–MeOH (1:1) to yield compounds 6 (143.8 mg) and 7 (391.0 mg). Fraction F35 (6.2 g) was then applied to a Sephadex LH-20 column (CH₂Cl₂–MeOH, 1:1) to give four subfractions (F351–F354). Fraction F351 (24.8 mg) was purified by preparative HPLC (MeOH–H₂O, 70:30)

to yield compounds 1 (5.3 mg, *t*_R = 15.0 min) and 2 (6.4 mg, *t*_R = 21.0 min). Fraction F352 (1.0 g) was recrystallized with CH₂Cl₂–MeOH to afford compound 11 (21.9 mg). Fraction F354 (1.2 g) was separated by a Sephadex LH-20 column (CH₂Cl₂–MeOH, 1:1) to obtain five subfractions (F3541–F3545). Compound 10 (12.9 mg, *t*_R = 21.0 min) was obtained from fraction F3542 by preparative HPLC (MeOH–H₂O, 70:30). Fraction F4 (44.2 g) was subjected to silica gel column chromatography eluted with CH₂Cl₂–MeOH (90:1 to 15:1) to yield eight subfractions (F41–F48). Fraction F47 (13.7 g) was separated by a Sephadex LH-20 column (CH₂Cl₂–MeOH, 1:1) to obtain compound 3 (26.3 mg). Fraction F5 (63.2 g) was applied to a silica gel column using petroleum ether–acetone (from 80:1 to 1:1) as the eluent to yield ten subfractions (F51–F510). Fraction F54 (5.6 g) was crystallized with MeOH to afford compound 4 (419.9 mg). Fraction F6 (75.8 g) was separated with a silica gel column using CH₂Cl₂–MeOH (from 90:1 to 1:1) as the eluent to afford eight subfractions (F61–F68). Subfraction F64 (4.3 g) was separated by an octadecylsilane column (MeOH–H₂O, 1:9 to 1:0) to give seven subfractions (F641–F647). Fraction F642 (1.2 g) was crystallized with MeOH to afford compound 9 (10.1 mg). Fraction F7 (64.7 g) was isolated by silica gel column chromatography and eluted with CH₂Cl₂–MeOH (40:1 to 1:1) to afford ten fractions (F71–F710). Fraction F73 (15.1 g) was recrystallized with MeOH to afford compound 5 (3.357 g). Separation of fraction F75 (6.5 g) through preparative HPLC (MeOH–H₂O, 45:55) yielded compound 8 (14.1 mg, *t*_R = 12 min).

2.4 1,5,6-Trimethoxy-2-hydroxy-3-methy-anthraquinone

Yellow amorphous powder (MeOH); UV (MeOH) $\lambda_{\max}$ (log ϵ): 220 (1.40), 281 (1.36) nm; ¹H (600 MHz, DMSO-*d*₆); and ¹³C-NMR (150 MHz, DMSO-*d*₆) (Table 1);

Table 1
¹H- and ¹³C-NMR data of compounds 1 and 2 (δ in ppm)

Pos.	1		2	
	δ_{H} (J in Hz)	δ_{C}	δ_{H} (J in Hz)	δ_{C}
1	–	146.3	–	146.6
2	–	156.8	–	159.4
3	–	126.6	–	130.4
4	7.69 s	124.8	7.67 s	125.1
4a	–	131.2	–	126.3
4b	–	128.7	–	122.7
5	–	147.7	–	146.9
6	–	158.0	–	153.3
7	7.45 d (8.5)	116.3	7.48 s	105.2
8	7.89 d (8.5)	123.6	–	156.5
8a	–	126.4	–	122.7
8b	–	123.6	–	126.3
9	–	182.9	–	179.9
10	–	180.2	–	181.9
1–OCH ₃	3.80 s	61.1	3.78 s	60.7
3–CH ₃	2.24 s	16.6	2.20 s	16.7
3–OCH ₃	–	–	–	–
5–OCH ₃	3.84 s	60.9	3.84 s	60.8
6–OCH ₃	3.93 s	56.3	3.86 s	61.5
8–OCH ₃	–	–	3.96 s	56.2

¹H-NMR spectrum recorded at 600 MHz and ¹³C-NMR spectrum recorded at 150 MHz in DMSO-*d*₆. NMR: nuclear magnetic resonance.

HR-ESI-MS m/z 329.1012 $[M+H]^+$ (calcd for $C_{18}H_{17}O_6^+$, 329.1020).

2.5 1,5,6,8-Tetramethoxy-2-hydroxy-3-methyl-anthraquinone

Yellow amorphous powder (MeOH); UV (MeOH) λ_{max} (log ϵ): 220 (2.60), 297 (3.73) nm; ^1H (600 MHz, DMSO- d_6); and ^{13}C -NMR (150 MHz, DMSO- d_6) (Table 1); HR-ESI-MS m/z 359.1132 $[M+H]^+$ (calcd for $C_{19}H_{19}O_7^+$, 359.1125).

2.6 Cell culture

SH-SY5Y cells (CBP60913; a human neuroblastoma cell line) were cultured in Gibco™ Dulbecco modified Eagle medium (DMEM) (HyClone, Logan, UT, USA) supplemented with 10% (v/v) heat-inactivated fetal bovine serum and 100 units/mL penicillin/streptomycin. Cells were maintained at 37°C in a humidified 95% air and 5% CO₂ atmosphere.

2.7 Cell viability assay

The viability of MPP⁺-treated SH-SY5Y cells was examined by the 3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide (MTT) (Sigma-Aldrich, St. Louis, USA) colorimetric assay, which was performed as previously described^[18]. After two generations, the cells were cultured in 96-well plates (8,000 cells/well) to study dose protection with the compounds at a concentration of

50 μ M for 6 h. The cells were treated with 1.2 mM MPP⁺ for 24 h. Next, the cells were incubated with DMEM containing 0.5 mg/mL of MTT at 37°C for 3 h, followed by treatment with dimethyl sulfoxide at 37°C for 10 min. At this point, the absorbance of the formation dye was measured at 490 nm using a microplate reader. This assay was repeated thrice.

2.8 Bioinformatics

First, compound 6 was analyzed using the similarity ensemble approach server (<http://sea.bkslab.org/>), building on the structural similarity of ligands^[19]. Then, these potential targets were submitted to DAVID, and the top 10 enrichment of Gene Ontology (GO) terms (biological process, cellular component, and molecular function) were obtained^[17,20].

2.9 Statistical analysis

Data were analyzed using GraphPad Prism 5.0 software (La Jolla, CA, USA). The results were processed by one-way analysis of variance, and $P < 0.05$ was considered statistically significant.

3 Results

Studies on the constituents of the aerial parts of *S. pseudochinensis* yielded two new compounds (1, 2) and nine known compounds (3–11) (Figure 1), including

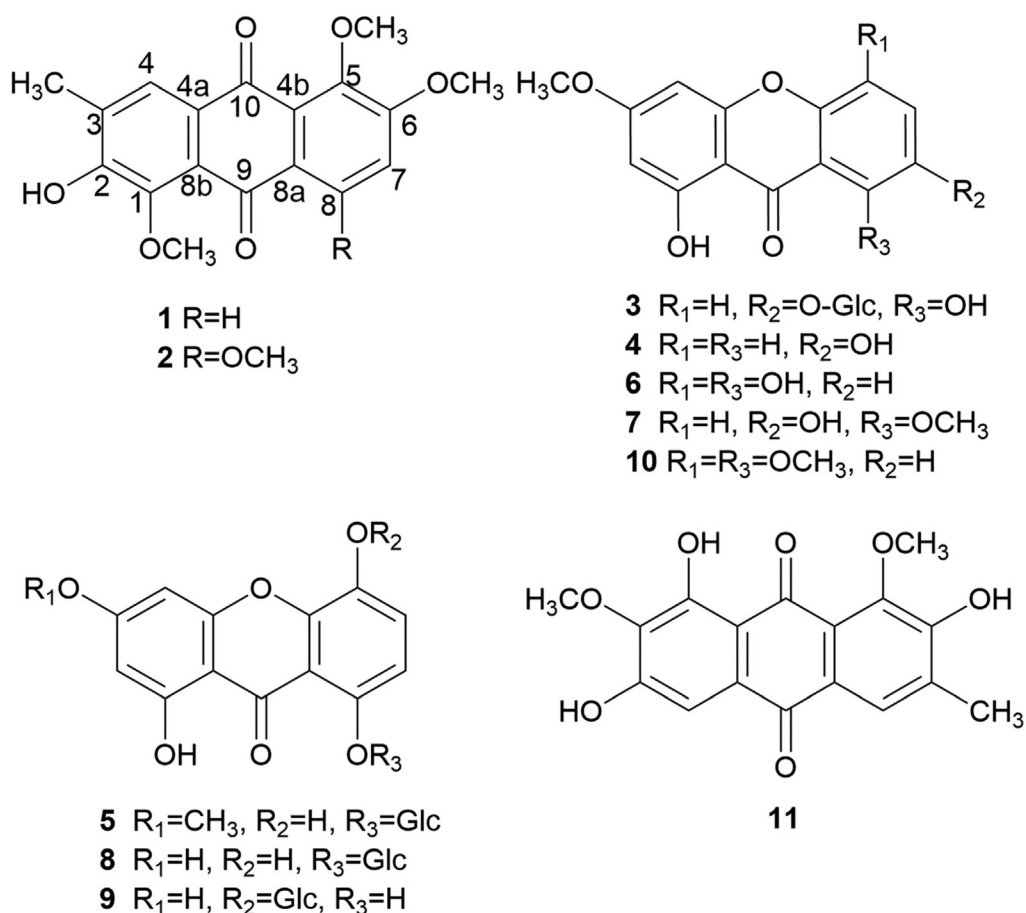


Figure 1. Structures of compounds 1–11 from *Swertia pseudochinensis*.

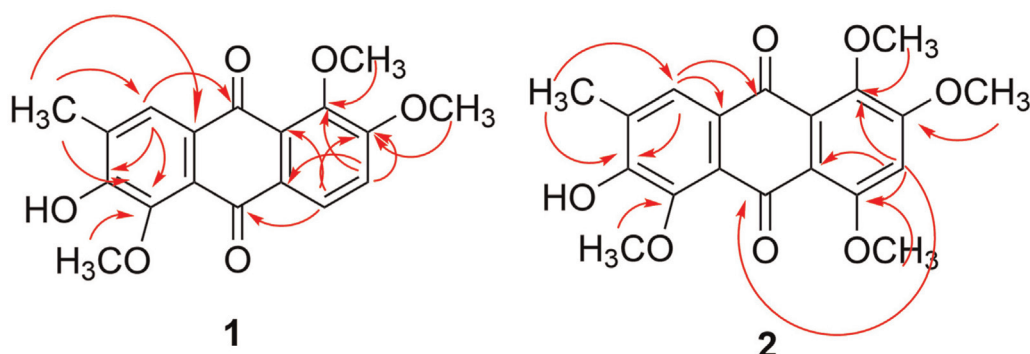


Figure 2. Key HMBC correlations of compounds 1 and 2. HMBC: heteronuclear multiple bond correlation.

7-O- β -D-glucopyranosyl-1,8-dihydroxy-3-methoxyanthone (3)^[21], gentisin (4)^[22], swertianolin (5)^[23], bellidifolin (6)^[24], gentiacaulein (7)^[25], norswertianolin (8)^[26], 5-O- β -D-glucopyranosyl-1,3,8-trihydroxyapatone (9)^[27], 1-hydroxy-3,5,8-trimethoxyanthone (10)^[28], and auranio-obtusin (11)^[29]. These known compounds were identified by comparison with the literature data.

Compound 1 was obtained as a yellow amorphous powder. Its molecular formula was determined to be $C_{18}H_{16}O_6$ by HR-ESI-MS analysis (m/z 329.1012 $[M+H]^+$, calcd for $C_{18}H_{17}O_6^+$, 329.1020) and ^{13}C -NMR spectroscopic data. The ^1H -NMR spectrum (Table 1) showed one singlet aromatic proton at δ_H 7.69 (1H, s, H-4); two aromatic protons at δ_H 7.89 (1H, d, $J=8.5$ Hz, H-8) and 7.45 (1H, d, $J=8.5$ Hz, H-7); three methoxy proton signals at δ_H 3.93 (3H, s, OCH₃-6), 3.84 (3H, s, OCH₃-5), and 3.80 (3H, s, OCH₃-1); and one methyl proton signal at δ_H 2.24 (3H, s, CH₃-1). The ^{13}C -NMR (Table 1) indicated 14 sp^2 carbon signals, including four oxygenated quaternary sp^2 carbon signals at δ_C 158.0 (C-5), 147.7 (C-6), 146.3 (C-1), and 156.8 (C-2), and two carbonyl carbon signals at δ_C 182.9 (C-9) and 180.2 (C-10). These data were similar to those of an anthraquinone, auranio-obtusin (11)^[29], except for the absence of two hydroxy signals and the presence of one methoxy signal. The ^1H -detected heteronuclear multiple bond correlation (HMBC) (Figure 2) correlations of H-8 [δ_H 7.89 (1H, d, $J=8.5$ Hz)] to C-4b (δ_C 128.7), C-6 (δ_C 158.0), and C-9 (δ_C 182.9), and H-7 [δ_H 7.45 (1H, d, $J=8.5$ Hz)] to C-5 (δ_C 147.7), C-6 (δ_C 158.0), and C-8a (δ_C 126.4) revealed a set of *ortho*-coupled protons on C-7 and C-8. The HMBC correlations of OCH₃-5 (δ_H 3.84) to C-5 (δ_C 147.7) and of OCH₃-6 (δ_H 3.93) to C-6 (δ_C 158.0) suggested the linkage of two methoxy groups at C-5 and C-6. In addition, the correlations of H-4 (δ_H 7.69) to C-3 (δ_C 126.6), C-9 (δ_C 180.2), and CH₃-3 (δ_H 2.24) to C-4 (δ_C 124.8) and C-2 (δ_C 131.2); and of CH₃-1 (δ_H 3.80) to C-1 (δ_C 146.3) revealed an aromatic proton at C-4, a methyl at C-3, and the other methoxy at C-1 (δ_C 61.1). Based on the above observations, as well as the known carbon and hydrogen numbers and HR-ESI-MS data, we deduced the presence of a hydroxy group at C-2, and the HMBC correlations of H-4 (δ_H 7.69) and CH₃-3 (δ_H 2.24) to δ_C 156.8 (C-2) confirmed the results. Therefore, the structure of compound 1 was established as 1,5,6-trimethoxy-2-hydroxy-3-methyl-anthraquinone.

The formula of compound 2 was established as $C_{19}H_{18}O_7$ based on the HR-ESI-MS (m/z 359.1132 $[M+H]^+$, calcd for $C_{19}H_{19}O_7^+$, 359.1125) and ^{13}C -NMR

data. The ^1H and ^{13}C -NMR spectra (Table 1) for compounds 1 and 2 showed very similar signals, except that the H-8 doublet at δ_H 7.89 and the carbon signal at δ_C 123.6 (C-8) in compound 1 was replaced by a new methoxy group at δ_H 3.96 (3H, s) and a carbon resonance at δ_C 156.5 in compound 2, respectively. These data indicated that the aromatic proton at C-8 in compound 1 was substituted by a methoxy group in compound 2. This assignment was supported by the HMBC (Figure 2) correlations of H-7 (δ_H 7.48) to C-5 (δ_C 146.9), C-8 (δ_C 156.5), C-8a (δ_C 122.7), and C-9 (δ_C 179.9), and of OCH₃-8 (δ_H 3.96) to C-8 (δ_C 156.5). Consequently, the full structure of compound 2 was confirmed and named 1,5,6,8-tetramethoxy-2-hydroxy-3-methyl-anthraquinone.

All the isolated compounds were evaluated for their neuroprotective effects. We first examined the cytotoxic effects of the compounds on SH-SY5Y cells using the MTT assay, and the results showed that none of the tested compounds had any apparent toxicity in the concentration range of 20 to 100 μ M. At the same time, cell viability against MPP⁺-induced SH-SY5Y cell death at a concentration of 50 μ M was determined by the MTT assay. Compared with the model group (Figure 3), compound

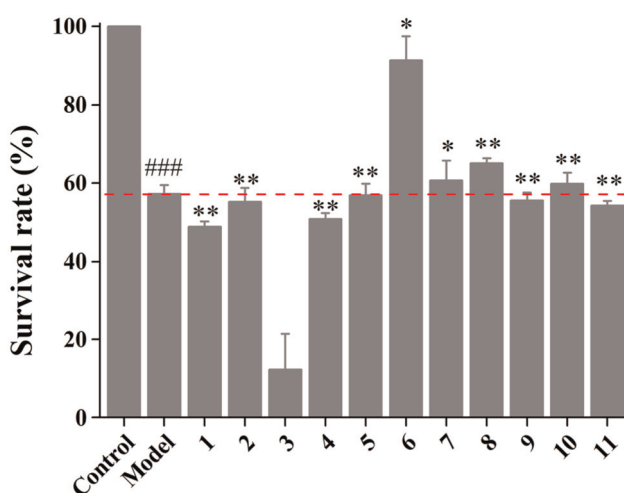


Figure 3. The protective effects of the isolated compounds (1–11) against MPP⁺-induced SH-SY5Y cells. "Control" refers to the value of SH-SY5Y cells that were not treated with MPP⁺. "Model" refers to the value of SH-SY5Y cells that were treated with 1.2 mM MPP⁺ for 24 h. Data are expressed as mean $\pm$ SEM ($n=3$ each); $P<0.05$ was considered statistically significant. (* $P<0.05$ and ** $P<0.01$, vs MPP⁺-treated model group; ### $P<0.01$, vs control group). MPP⁺: 1-methyl-4-phenylpyridinium.

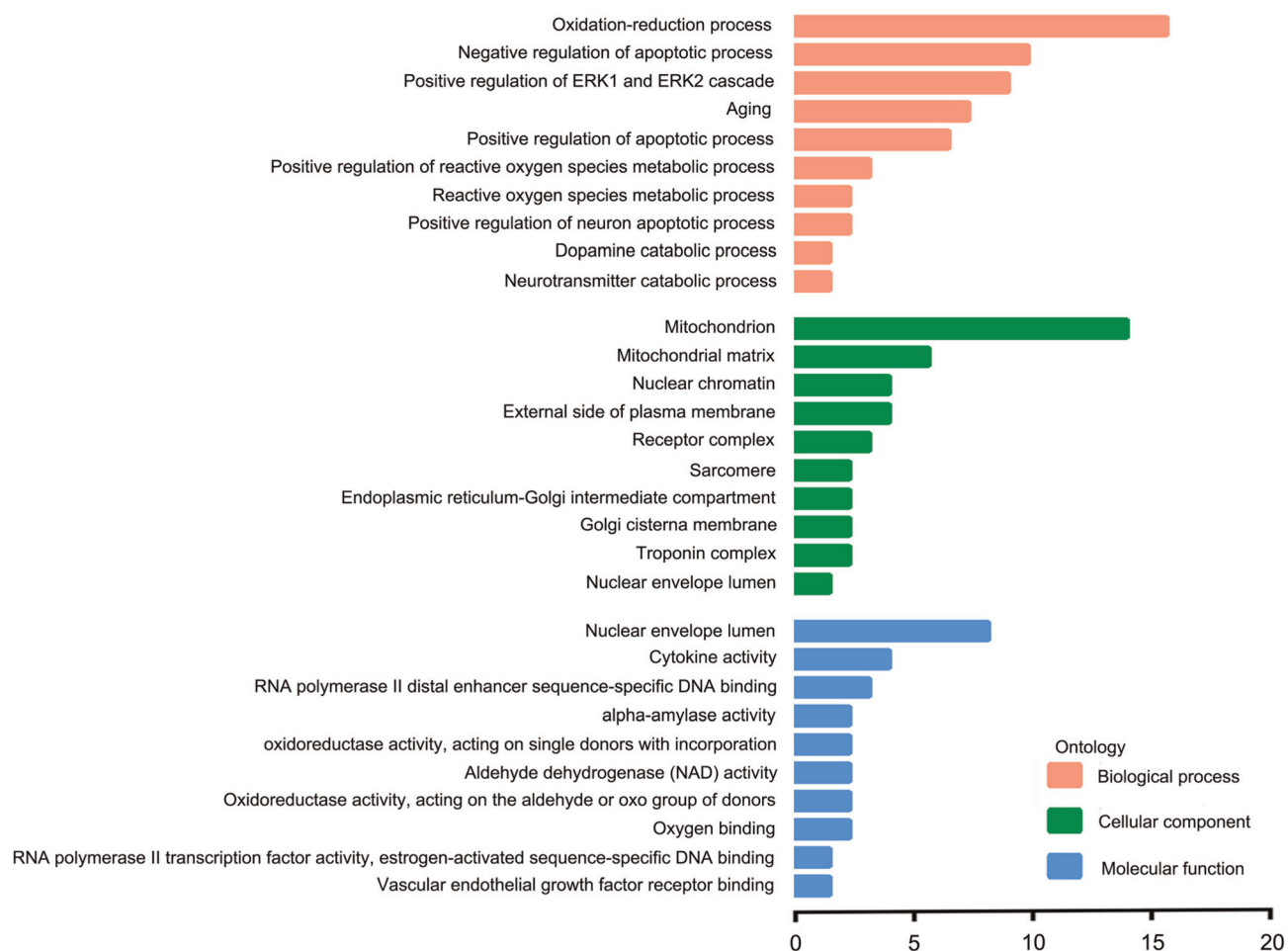


Figure 4. Bioinformatics analysis of potential targets of compound 6. The SEA server and DAVID were used to predict the potential targets. Functional clustering of GO was carried out on the biological process, cellular component, and molecular function. DAVID: Database for Annotation, Visualization and Integrated Discovery; GO: Gene Ontology; SEA: Similarity ensemble approach

6 markedly increased the survival rate (about 91%) of 1.0mM MPP⁺-treated SH-SY5Y cells ($P < 0.05$). The viability of cells treated with compounds 7, 8, and 10 was marginally enhanced. Curiously, cell viability after treatment with compound 3 was less than 20%, implying that it intensified the cytotoxicity effect together with MPP⁺. The remaining compounds showed no obvious protective effects on SH-SY5Y cells.

A combination of bioinformatics methods was carried out to analyze and predict the possible mechanism of compound 6 regulating neurodegenerative disease. The biological process, cellular component, and molecular function of target genes were analyzed using DAVID^[18–20]. Although this remains to be experimentally verified, bioinformatic analysis suggests that oxidative damage and reactive oxygen species (ROS) are targeted by compound 6 (Figure 4).

4 Discussion

On basis of the above experimental results, we found that although compounds 3–10 belong to xanthenes, only compounds 6–8 and 10 displayed protective activity. Mounting evidence suggests that the presence and position of the hydroxy group could affect the activity of xanthenes, for example, cudratruxanthone P, cudratruxanthone R, and

gartanin have been shown to have neuroprotective effects^[30–31], and may act through the inhibition of the apoptosis pathway and oxidative stress injury. Compared to previously reported xanthenes, the presence of the trihydroxy group in compound 6 may also play an important role in neuroprotection. However, the effect of compound 6 on neuroprotection has not been reported in the literature. Through the prediction of bioinformatics analysis online, we found that compound 6 might have potential as a neuroprotective agent for the treatment of PD, possibly by acting on oxidative damage and ROS. Many studies have shown that oxidative stress plays an important role in the development of neurodegenerative diseases. Furthermore, this result to some extent confirmed the reliability of the screening experiments results.

In conclusion, compound 6 showed significant protective activity and might have potential as a neuroprotective agent for the treatment of PD, possibly by acting on oxidative damage and ROS. Our study further enriched secondary metabolites in the *Swertia* genus and also indicates that further research on the bioactive constituents toward neurodegenerative disorders could be extremely rewarding.

Supplemental Digital Content: 1D and 2D NMR, HR-ESI-MS, and UV spectra for the new compounds (1, 2), <http://links.lww.com/AHM/A3>.

Conflict of interest statement

The authors declare no conflict of interest.

Funding

This study was financially supported by the Liaoning Revitalization Talents Program (No. XLYC1807182) and the Liaoning Province Natural Science Foundation (No. 2019-MS-299).

Author contributions

Ke Xiang was involved in writing the paper; Qi He participated in the performance of the research; Yanmei Chen participated in data analysis; Dongxin Yang contributed analytical tools; Yanwei Duan participated in the performance of the research; Hua Li participated in research design; Lixia Chen participated in research design.

Ethical approval of studies and informed consent

Not applicable.

Acknowledgments

We are grateful for the experimental support of the Wuya College of Innovation public laboratory platform in Shenyang Pharmaceutical University.

References

- [1] Yu CY, Zhao YM, Chen G. *Swertia pseudochinensis*, a new plant source of andrographolide. *Chem Nat Compd* 2013;49(1):119–120.
- [2] Balasundari P, Singh SK, Kavimani S. Free radical scavenging of xanthones from *Swertia chirata* Buchham and tumor cell growth inhibition. *Main Group Chem* 2005;4(3):177–185.
- [3] Geng CA, Jiang ZY, Ma YB, et al. Swerilactones A and B, anti-HBV new lactones from a traditional Chinese herb: *Swertia mileensis* as a treatment for viral hepatitis. *Org Lett* 2009;11(18):4120–4123.
- [4] Kumar S, Paul BN, Asthana R, et al. *Swertia chirayita* mediated modulation of interleukin-1 β interleukin-6, interleukin-10, interferon- γ , and tumor necrosis factor- α in arthritic mice. *Immunopharmacol Immunotoxicol* 2003;25(4):573–583.
- [5] Li JC, Feng L, Sun BH, et al. Hepatoprotective activity of the constituents in *Swertia pseudochinensis*. *Biol Pharm Bull* 2005;28(3):534–537.
- [6] Nagalekshmi R, Menon A, Chandrasekharan DK, et al. Hepatoprotective activity of *Andrographis paniculata* and *Swertia chirayita*. *Food Chem Toxicol* 2011;49(12):3367–3373.
- [7] Zheng XY, Yang YF, Li W, et al. Two xanthones from *Swertia punicea* with hepatoprotective activities in vitro and in vivo. *J Ethnopharmacol* 2014;153(3):854–863.
- [8] Suryawanshi S, Asthana RK, Gupta RC. Assessment of systemic interaction between *Swertia chirata* extract and its bioactive constituents in rabbits. *Phytother Res* 2009;23(7):1036–1038.
- [9] Tian LY, Bai X, Chen XH, et al. Anti-diabetic effect of methylswertianin and bellidifolin from *Swertia punicea* Hemsl. and its potential mechanism. *Phytomedicine* 2010;17(7):533–539.
- [10] Zhang YP, Yang YS, Liu Y, et al. Study on chemical composition and antibacterial activity of essential oil from tibetan folk medicine *Swertia mussotii* Franch. *Lishizhen Med Mater Med Res* 2010;20(3):595–597.
- [11] Zhang JS, Wang XM, Dong XH, et al. Studies on chemical constituents of *Swertia mussotii*. *J Chin Med Mater* 2009;32(4):511–514.
- [12] Kimura Y, Sumiyoshi M. Effects of *Swertia japonica* extract and its main compound swertiamarin on gastric emptying and gastrointestinal motility in mice. *Fitoterapia* 2011;82(6):827–833.
- [13] Banerjee S, Sur Kumar K, Mandal S, et al. Assessment of the anti-inflammatory effect of *Swertia chirata* in acute and chronic experimental models in male albino rats. *Indian J Pharmacol* 2000;32(1):21–24.
- [14] Hu TY, Ju JM, Mo LH, et al. Anti-inflammation action of xanthones from *Swertia chirayita* by regulating COX-2/NF- κ B/ MAPKs/Akt signaling pathways in RAW 264.7 macrophage cells. *Phytomedicine* 2019;55:214–221.
- [15] Zhou JJ, Sun Y, Zhao X, et al. 3-O-demethylswertipunicoside inhibits MPP $^{+}$ -induced oxidative stress and apoptosis in PC12 cells. *Brain Res* 2013;1508:53–62.
- [16] Guo YF, Wang C, Li W, et al. Neuroprotective effects of xanthone extract from *Swertia punicea* Hemsl against 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP)-induced mouse model of Parkinson's disease. *J Chin Pharm Sci* 2016;25(5):357–365.
- [17] Jones AR, Hubbard SJ. An introduction to proteome bioinformatics. *Methods Mol Biol* 2010;1549:1–5.
- [18] Chen YM, Sa YL, Wang G, et al. The protective effects of *Citrullus colocynthis* on inhibiting oxidative damage and autophagy-associated cell death in Parkinson's disease. *J Taiwan Inst Chem Eng* 2019;100:18–25.
- [19] Chen C, Huang H, Wu CH. Protein bioinformatics databases and resources. *Methods Mol Biol* 2017;1558:3–39.
- [20] Wooller SK, Benstead-Hume G, Chen X, et al. Bioinformatics in translational drug discovery. *Biosci Rep* 2017;37(4):7.
- [21] Inayat UR, Arfan M, Reinecke MG, et al. A new xanthone glucopyranoside from *Swertia ciliate*. *J Chem Soc Pak* 2000;22(2):142–150.
- [22] Ando H, Hirai Y, Fujii M, et al. The chemical constituents of fresh Gentian root. *J Nat Med* 2007;61(3):269–279.
- [23] Ishimaru K, Sudo H, Satake M, et al. Amarogentin, amaroswerin and four xanthones from hairy root cultures of *Swertia japonica*. *Phytochemistry* 1990;29(5):1563–1565.
- [24] Wang HX, Yuan X, Huang HM, et al. Chemical constituents from *Swertia mussotii* Franch (Gentianaceae). *Nat Prod Res* 2017;31(2):1704–1708.
- [25] Hajimehdipour H, Amanzadeh Y, Sadat Ebrahimi SE, et al. Three tetraoxygenated xanthones from *Swertia longifolia*. *Pharm Biol* 2003;41(7):497–499.
- [26] Zhou HM, Liu YL, Blaskó G, et al. Swertiabixanthone-I from *Swertia macrosperma*. *Phytochemistry* 1989;28(12):3569–3571.
- [27] Zeng GY, Tan GS, Xu KP, et al. Water-soluble chemical constituents of *Swertia davidi* Franch. *Acta Pharm Sin* 2004;39(5):351–353.
- [28] Li XS, Jiang ZY, Wang FS, et al. Chemical constituents from herbs of *Swertia mileensis*. *China J Chin Mater Med* 2008;33(23):2790–2793.
- [29] Xu LJ, Chan CO, Lau CC, et al. Simultaneous determination of eight anthraquinones in Semen Cassiae by HPLC-DAD. *Phytochem Anal* 2012;23(2):110–116.
- [30] Wang SN, Li Q, Jing MH, et al. Natural xanthones from *Garcinia mangostana* with multifunctional activities for the therapy of Alzheimer's disease. *Neurochem Res* 2016;41(7):1806–1817.
- [31] Kwon J, Hiep NT, Kim DW, et al. Chemical constituents isolated from the root bark of *Cudrania tricuspidata* and their potential neuroprotective effects. *J Nat Prod* 2016;79(8):1938–1951.

How to cite this article: Xiang K, He Q, Chen YM, Yang DX, Duan YW, Li H, Chen LX. Chemical constituents isolated from the aerial parts of *Swertia pseudochinensis* and their potential neuroprotective effects. *Acupunct Herb Med*. 2021;1(1):59–64. doi: 10.1097/HM9.0000000000000010