Records of Natural Products

Open Access
This article is licensed under CC-BY-NC-ND 4.0

www.acgpubs.org

SHORT REPORT

New polyketide and chromene derivative isolated from an endophytic *Diaporthe Phaseolorum* associated with *Polygonatum cyrtonema* Hua

Ling-ling Gan[1], Si-rui Wang[1], Gui-kai Wang[1,2], Xun-cui Wang[2*] and Yun-Peng Sun[1,2*]

[1]School of Pharmacy, Anhui University of Chinese Medicine, Hefei 230012, P.R. China
[2]Anhui Province Key Laboratory of Bioactive Natural Products, Hefei 230012, P.R. China

Abstract: Eight compounds were isolated from the ethyl acetate extract of the *Diaporthe phaseolorum* fermentation products, comprising five polyketide derivatives (**1**–**5**), one chromene (**6**), one chromone (**7**), and one tetralone (**8**). Among these, compounds **1** and **6** were identified as previously undescribed. Notably, compound **6** features a unique C12 chromone skeleton, representing only the second reported example of such a framework. The structures and spatial configurations of all compounds were elucidated through comprehensive analysis of HR-MS, NMR, and quantum chemical calculations supported by DP4+ analysis. In vitro anti-inflammatory activity screening revealed that none of the isolated compounds (**1**–**8**) inhibited nitric oxide (NO) production in mononuclear macrophages.

Keywords: *Diaporthe phaseolorum*, *Polygonatum cyrtonema* Hua, polyketide, chromene

Cite this article as:
Gan et al. New polyketide and chromene derivative isolated from an endophytic *Diaporthe Phaseolorum* associated with *Polygonatum cyrtonema* Hua. (2026). *Records of Natural Products*, 20(3):e26013781

Received: *04 January 2026*
Revised: *19 January 2026*
Accepted: *24 January 2026*
Published: *05 February 2026*

1 Fungal Source

The endophytic fungus was isolated from tubers of *Polygonatum cyrtonema* Hua. The plant material was collected in Huangshan City, Anhui Province, China, in July 2019 and taxonomically authenticated by Prof. Dongmei Xie (Anhui University of Chinese Medicine). Based on morphological characteristics, the fungal strain was preliminarily identified as *Diaporthe phaseolorum*. Molecular identification, based on analysis of the rDNA ITS region, confirmed this classification, and the corresponding nucleotide sequence was deposited in the GenBank database under accession number MN650843.1. A working stock of the axenic culture was preserved in 25% (v/v) glycerol at –80°C and deposited at the School of Pharmacy, Anhui University of Chinese Medicine.

2 Previous Studies

Polygonatum cyrtonema Hua is a perennial herb of the genus *Polygonatum* (Liliaceae family). Its rhizome serves as the primary source of the traditional Chinese medicine "Huangjing," which is listed in the Chinese Pharmacopoeia as a medicinal and edible plant with tonic properties (Zhao et al., 2023). Modern research has demonstrated that *P. cyrtonema* is rich in diverse bioactive constituents, including polysaccharides, saponins, flavonoids, alkaloids, and amino acids. These compounds contribute to a broad spectrum of pharmacological activities, such as hypoglycemic and hypolipidemic, antioxidant, immunomodulatory, antibacterial, antiviral, antitumor, and neuroprotective effects. Consequently, *P. cyrtonema* has been investigated for its potential in managing conditions like atherosclerosis, skin diseases, diabetes, and hypertension (Zhou et al., 2025; Lu et al., 2023; Pan et al., 2024).

Plant endophytic fungi have garnered considerable research interest owing to their unique ecological functions and their potential to yield novel bioactive compounds (Tiwari & Bae, 2022; Huang & Zhao, 2023). The genus *Diaporthe*, which is commonly found in medicinal plants, is a prolific producer of diverse secondary metabolites exhibiting a range of biological activities, including antibacterial and antitumor effects (Guo et al., 2019; Feng et al., 2025; Cui et al., 2017). To explore this potential further, we examined the chemical constituents of *Diaporthe phaseolorum*, an endophytic fungus isolated from *P. cyrtonema*. Chemical examination of its rice fermentation extract resulted in the isolation of eight compounds

*Corresponding Authors: Xun-cui Wang. Email: wangxuncui@163.com; Yun-Peng Sun. Email: sunyp@ahtcm.edu.cn

Copyright © 2026. Published by ACG Publications.

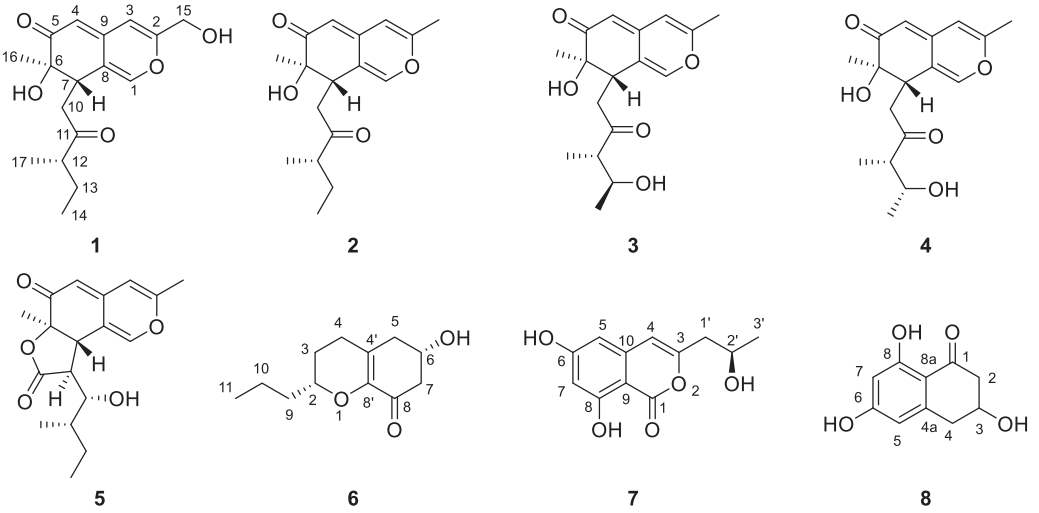

Figure 1. Structures of compounds **1–8**

(Figure 1), the anti-inflammatory activities of which were subsequently evaluated.

3 Present Study

Diaporthe phaseolorum was inoculated onto autoclaved rice medium (150 g rice, 90 mL water, 121°C) and cultured statically at 28°C in the dark for 25 days. The fermented material was homogenized and then exhaustively extracted with ethyl acetate (3–5 times, equal volume each). The combined ethyl acetate extracts were concentrated under reduced pressure, yielding 224.8 g of crude extract. This crude extract was fractionated by silica gel column chromatography (200–300 mesh) using a stepwise gradient of ethyl acetate/petroleum ether (100:0 → 0:1, v/v) to afford ten fractions (A–J).

Fraction D was fractionated on an ODS column using a CH_3OH–H_2O gradient (30:70 → 100:0, v/v) to afford 14 subfractions (Da–Dn). Subfraction Df was initially purified by Sephadex LH-20 (CH_3OH), followed by semi-preparative HPLC (CH_3CN–H_2O, 53:47, v/v), yielding **2** (4.9 mg, t_R = 23 min) and **5** (47.0 mg, t_R = 31 min). Fraction G was subjected to ODS column chromatography with a CH_3OH-H_2O gradient (40:60 → 100:0, v/v), providing eleven subfractions (Ga–Gk). Compound **7** (9.6 mg, t_R = 17 min) was obtained from subfraction Gc via semi-preparative HPLC (CH_3OH-H_2O, 56:44, v/v). Separation of Fraction H on an ODS column (CH_3OH-H_2O, 30:70 → 100:0, v/v) provided subfractions Ha–Hn. Subfraction Hd was purified sequentially by Sephadex LH-20 (CH_3OH) and semi-preparative HPLC (CH_3CN–H_2O, 40:60, v/v) to yield **8** (5.7 mg, t_R = 18 min), **3** (22.9 mg, t_R = 22 min), **4** (45.4 mg, t_R = 23 min), and **6** (4.6 mg, t_R = 32 min). Similarly, purification of subfraction Hg by semi-preparative HPLC (CH_3CN–H_2O, 27:73, v/v) afforded **1** (3.1 mg, t_R = 36 min).

15-Hydroxy-chermesinones A (**1**): yellow oil; $[\alpha]_D^{20.0}$ = +256.0 (CH_3OH, 0.1); UV (CH_3OH) λ_{max} (log ε) 200 (4.42), 348 (4.84) nM; ECD (CH_3OH), λ_{max} ($\Delta\varepsilon$) 246 (−17.84), 320 (+24.71), 366 (+21.68) nM; ^1H and ^{13}C NMR see Table 1; HR-ESI-MS *m/z*: 307.1530 $[M+H]^+$ ($C_{17}H_{23}O_5$, calcd. for 307.1540).

6S-Hydroxy-2R-phomochromene (**6**): yellow oil; $[\alpha]_D^{20.0}$ = +86.3 (CH_3OH, 0.1); UV (CH_3OH) λ_{max} (log ε) 200 (4.19), 273 (4.40) nM; ECD (CH_3OH) λ_{max} ($\Delta\varepsilon$) 271 (+54.12), 308 (−33.70) nM; ^1H and ^{13}C NMR see Table 2; HR-ESI-MS *m/z*: 233.1148 $[M+Na]^+$ ($C_{12}H_{18}O_3Na$, calcd. for 233.1148).

Compound **1** was obtained as a yellow oil. Its high-resolution electrospray ionization mass spectrometry (HR-ESI-MS) data exhibited a quasi-molecular ion peak at *m/z* 307.1530 $[M + H]^+$ (calcd for $C_{17}H_{23}O_5$, 307.1540), corresponding to the molecular formula $C_{17}H_{22}O_5$ with seven degrees of unsaturation. The ^1H NMR spectrum revealed signals for three olefinic protons (δ_H 6.81, 1H, s; 6.25, 1H, s; 5.47, 1H, s), an oxygenated methylene group (δ_H 4.34, 2H, s), and three methyl groups (δ_H 1.15, 3H, d, *J* = 6.8 Hz; 1.09, 3H, s; 0.89, 3H, t, *J* = 7.3 Hz). The ^{13}C NMR spectrum displayed 17 carbon signals, including two carbonyls (δ_C 213.3, 199.5), six olefinic carbons (δ_C 159.4, 146.9, 144.5, 120.9, 106.2, 105.8), and two oxygenated carbons (δ_C 73.2, 61.3).

Careful analysis of the 1D NMR data for compound **1** (Table 1), in conjunction with HSQC, ^1H-^1H COSY, and HMBC spectra, indicated its structure is closely related to that of the known compound chermesinone A (**2**) (Huang et al., 2011). Comparison of the NMR data revealed the ^{13}C NMR spectrum of **1** contained an additional oxygenated carbon signal (δ_C 61.3), while the ^1H NMR spectrum lacked one methyl signal. In the HMBC spectrum, the oxygenated methylene protons (δ_H 4.34) correlated with C-2 (δ_C 159.4) and C-3 (δ_C 106.2) (Figure 2), suggesting that the C-15 methyl group in **2** is replaced by a hydroxymethyl group in **1**. Combined with the molecular weight established by HR-ESI-MS, this evidence allowed the planar structure of **1** to be elucidated, as depicted in Figure 1.

The relative configuration of compound **1** was assigned based on ROESY correlations observed between H-10α (δ_H

http://doi.org/10.25135/rnp.2601.3781
Rec. Nat. Prod. 2026, 20(3):e26013781

Table 1. ^{1}H NMR (600 MHz) and ^{13}C NMR (150 MHz) data of **1** and **2** ($CDCl_3$, *J* in Hz)

No	1		2	
	δ_C	δ_H (*J* in Hz)	δ_C	δ_H (*J* in Hz)
1	144.5	6.81, s	144.9	6.81, s
2	159.4	–	158.5	–
3	106.2	6.25, s	107.2	5.97, s
4	105.8	5.47, s	104.0	5.39, s
5	199.5	–	199.3	–
6	73.2	–	73.1	–
7	40.5	3.28, d (9.4)	40.4	3.26, dt (9.9, 2.2)
8	120.9	–	120.5	–
9	146.9	–	147.9	–
10α	37.6	3.22, d (17.6)	37.7	3.21, dd (17.6, 2.0)
10β		2.75, dd (17.6, 9.8)		2.74, dd (17.6, 9.9)
11	213.3	–	213.4	–
12	47.9	2.61, m	47.9	2.61, m
13a	26.0	1.73, m	26.0	1.73, dt (14.1, 7.1)
13b		1.42, m		1.42, dt (14.3, 7.2)
14	11.8	0.89, t (7.3)	11.8	0.89, t (7.4)
15	61.3	4.34, s	19.5	2.12, s
16	21.3	1.09, s	21.4	1.08, s
17	16.5	1.15, d (6.8)	16.5	1.15, d (7.0)

Table 2. ^{1}H NMR (600 MHz) and^{13}C NMR (150 MHz) data of compound **6** and phomochromene in $CDCl_3$

No	6		Phomochromene	
	δ_C	δ_C (*J* in Hz)	δ_C	δ_C (*J* in Hz)
2	75.6	3.76, m	75.3	3.78, m
3α	26.8	1.62, m	26.7	1.88, m
3β		2.28, m		1.59, m
4α	26.9	2.15, dd (19.6, 5.1)	26.6	2.23, m
4β		1.91, m		2.10, m
4'	127.4	–	131.3	–
5α	38.7	2.39, dd (16.8, 8.4)	29.7	2.29, t (5.6)
5β		2.61, dd (16.8, 3.7)		
6	66.7	4.22, m	22.2	1.94, m
7α	47.4	2.54, dd (16.0, 10.4)	38.3	2.56, t (5.9)
7β		2.80, dd (16.0, 3.4)		
8	191.2	–	193.4	–
8'	146.2	–	145.7	–
9a	37.0	1.77, m	36.8	1.74, m
9b		1.54, m		1.50, m
10a	18.6	1.42, m	18.6	1.43, m
10b		1.50, m		
11	14.2	0.93, t (7.2)	14.1	0.93, t (7.3)

3.22) and H-16 (δ_H 1.09) and between H-10β (δ_H 2.75) and H-7 (δ_H 3.28)/H-1 (δ_H 6.81), in conjunction with the close similarity of its NMR data to those of compound **2**. The absolute configuration was subsequently determined as 6*R*, 7*S*, 12*S* by comparing the experimental ECD spectrum of **1** with that of **2** (Figure 3). Accordingly, the structure of compound **1** was elucidated and designated as 15-hydroxychermesinone A.

Compound **6** was obtained as a yellow oil. Its molecular formula was determined as $C_{12}H_{18}O_3$ by HR-ESI-MS (quasi-molecular ion peak at *m/z* 233.1148 $[M + Na]^+$, calcd 233.1148), corresponding to four degrees of unsaturation. The

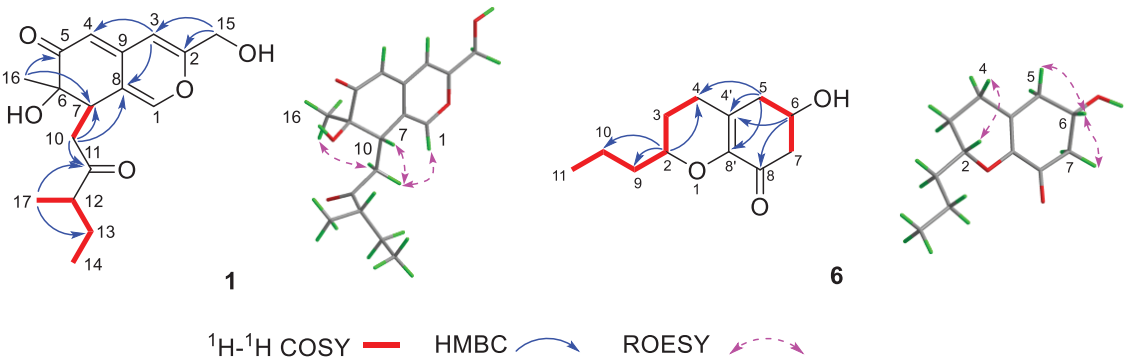

Figure 2. Key 2D NMR correlations of compounds **1** and **6**

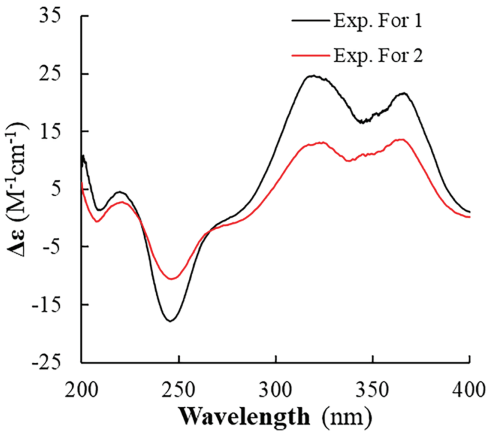

Figure 3. Experimental ECD spectra of compounds **1** and **2**

^{1}H NMR spectrum displayed signal overlap in the high-field region, including a methyl triplet (δ_H 0.93, 3H, t, J = 7.2 Hz). The ^{13}C NMR spectrum exhibited 12 carbon signals, featuring a carbonyl (δ_C 191.2), two olefinic carbons (δ_C 146.2, 127.4), and two oxygenated carbons (δ_C 75.6, 66.7) in the low-field region.

Comparison of the NMR data indicated that compound **6** closely resembles the known compound phomochromene (Yang et al., 2015) (Table 2). A key distinguishing feature was the significant downfield shift observed for C-6 in **6** (δ_C 66.7, $\Delta\delta$ +44.5). Analysis of the ^{1}H-^{1}H COSY spectrum revealed two spin–spin coupling fragments: fragment **a** [H-5 (δ_H 2.39, 2.61)/H-6 (δ_H 4.22)/H-7 (δ_H 2.54, 2.80)] and fragment **b** [H-4 (δ_H 2.15, 1.91)/H-3 (δ_H 1.62, 2.28)/H-2 (δ_H 3.76)/H-9 (δ_H 1.77, 1.54)/H-10 (δ_H 1.42, 1.50)/H-11 (δ_H 0.93)]. Furthermore, HMBC correlations from H-6 (δ_H 4.22) to C-8 (δ_C 191.2) and C-4′ (δ_C 127.4) confirmed oxygen substitution at C-6. In conjunction with the molecular formula established by HR-ESI-MS, these data led to the identification of compound **6** as 6-hydroxyphomochromene.

Compound **6** contains two chiral centers (C-2 and C-6). While ROESY correlations were observed between H-2 (δ_H 3.76) and H-4β (δ_H 1.91) and between H-6 (δ_H 4.22) and both H-5β (δ_H 2.61) and H-7β (δ_H 2.80), these data alone were insufficient to assign the relative configuration unambiguously. Therefore, density functional theory (DFT) calculations were conducted for the two possible diastereomers (2*S**, 6*S**-**6** and 2*R**, 6*S**-**6**). Subsequent linear fitting and DP4+ probability analysis of the calculated versus experimental NMR data afforded a 100% probability for the 2*R**, 6*S** configuration (Figure 4A). Finally, comparison of the experimental ECD spectrum with the calculated ECD curves (Figure 4B) established the absolute configuration as 2*R*, 6*S*. Based on this elucidation, the compound is designated as 6*S*-hydroxy-2*R*-phomochromene, thereby establishing compound **6** as the first chromene of this type with an assigned stereoconfiguration.

Compound **6** possesses a unique C12 chromene skeleton, which has been reported only once previously among the fermentation products of *Phomopsis* sp. (Yang et al., 2015) Regarding its biosynthesis (Scheme S1), compound **6**, like typical polyketides, is derived from the acetate–malonate pathway. Heptanoyl-CoA and three malonyl-CoA units are condensed by a tetraketide synthase (TKS) to form a linear hexyltetra-β-ketide intermediate (C13). This intermediate is then cyclized by olivetolic acid cyclase (OAC) to yield the resorcylic acid scaffold (I) (Lee et al., 2022). Intermediate I subsequently undergoes decarboxylation, oxidation, and cyclization to afford the benzothiophene framework (IV). Finally, the aromatic ring is converted into compound **6** through keto–enol tautomerization and reductive hydrogenation.

Additionally, six known compounds were isolated and identified as chermesinone A(**2**) (Huang et al., 2011), 13*S*-hydroxy-chermesinone A(**3**) (Zhang et al., 2022), 13*R*-hydroxy-chermesinone A(**4**) (Zhang et al., 2022), 11-hydrochermesinone B(**5**) (Hu et al., 2021), de-*O*-methyldiaporthin (**7**) (Xiao et al., 2022), scytalone (**8**) (Li et al., 2012).

In this study, all compounds (**1**–**8**) were evaluated for their ability to inhibit NO production in LPS-stimulated RAW264.7 macrophages. At a concentration of 50 μM, none of the compounds exhibited significant anti-inflammatory activity, showing inhibition rates ranging from 5.36% to 20.54%. In comparison, the positive control, *L*-NMMA, demonstrated a 52.62% inhibition rate under the same conditions.

http://doi.org/10.25135/rnp.2601.3781
Rec. Nat. Prod. 2026, 20(3):e26013781

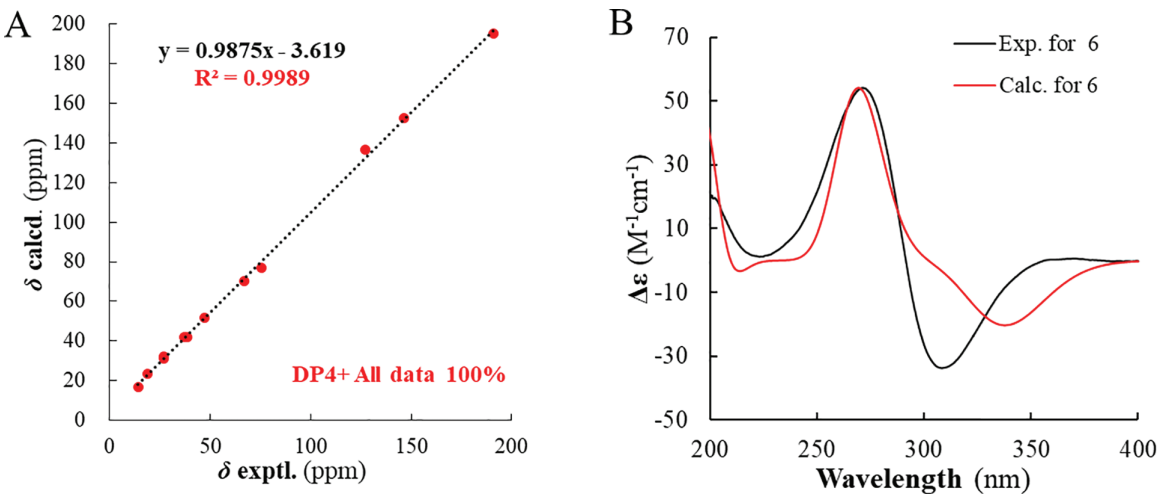

Figure 4. Linear relationship between experimental and calculated carbon spectra of compound **6** (A), curve between experimental and calculated ECD (B)

Funding Statement

This work was partially supported by the National Natural Science Foundation of China (32400324), the Open Fund of High-level Key Discipline of Chemistry of Chinese Medicine of the State Administration of Traditional Chinese Medicine, Anhui University of Chinese Medicine (HKD-CCM2024013), the Anhui Province University Discipline (Professional) Leader Training Project (DTR2023026), and the High-level Talent Project of Anhui University of Chinese Medicine (2023rcZD006).

Author Contributions

Ling-Ling Gan: Formal analysis, Investigation, and Writing original manuscript; Si-Rui Wang: Methodology, Investigation, and Data Curation; Guo-Kai Wang: Funding, and Supervision; Xun-Cui Wang: Methodology and Formal analysis; Yun-Peng Sun: Writing-review & editing, Funding, and Supervision.

Availability of Data and Materials

The authors declare that the data supporting the findings of this study are available within the paper and its Supplementary Information files. Should any raw data files be needed in another format they are available from the corresponding author upon reasonable request. Source data are provided with this paper.

Conflicts of Interest

The authors declare that they have no competing financial interests.

Supporting Information

Supporting Information accompanies this paper on http://www.acgpubs.org/journal/records-of-natural-products.

ORCID

Ling-ling Gan: 0009-0000-3539-4458
Si-rui Wang: 0009-0008-3856-4430
Guo-Kai Wang: 0000-0002-3924-6169
Xun-cui Wang: 0009-0001-5324-643X
Yun-Peng Sun: 0000-0001-6368-0427

References

Cui, H., Yu, J., Chen, S., Ding, M., Huang, X., Yuan, J. & She, Z. (2017). Alkaloids from the mangrove endophytic fungus *Diaporthe phaseolorum* SKS019. *Bioorganic & Medicinal Chemistry Letters*, *27*(14), 803–807. DOI: 10.1016/j.bmcl.2017.01.029.

Feng, T., Deng, X. L., Xu, Z. Y. & Xu, J. (2025). Diaporlabanoids A–C, Immunosuppressive dinorlabdane diterpene alkaloids with an unprecedented carbon skeleton from mangrove endophytic fungus *Diaporthe phaseolorum* H3-2. *Organic Letter*, *27*(27), 7267–7272. DOI: 10.1021/acs.orglett.5c01572.

Guo, H., Liu, Z. M., Chen, Y. C., Li, S. N., Li, H. H., Gao, X. X., Liu, H. X. & Zhang, W. M. (2019). Chromone-derived polyketides from the deep-sea fungus *Diaporthe phaseolorum* FS431. *Marine Drugs*, *17*(3), 182. DOI: 10.3390/md17030182.

Hu, C. Y., Li, S. N., Chen, Y. C., Huang, X. X., Liu, Z. M. & Zhang, W. M. (2021). Polyketides from the deep-sea-derived fungus *Diaporthe phaseolorum* FS459. *Chinese Journal of Organic Chemistry*, *41*(4), 1591–1598. DOI: 10.6023/cjoc202010046.

Huang, H., Feng, X., Xiao, Z., Liu, L., Li, H., Ma, L., Lu, Y., Ju, J., She, Z., & Lin, Y. (2011). Azaphilones and p-terphenyls from the mangrove endophytic fungus *Penicillium chermesinum* (ZH4-E2) isolated from the South China Sea. *Journal of Natural Products*, *74*(5), 997–1002. DOI: 10.1021/np100889v.

Huang, X. Z. & Zhao, L. F. (2023). Mechanism of endophytes of medicinal plants in promoting the growth of host plants. *Microbiology China*, *50*(4), 1653–1665. DOI: 10.9734/air/2018/40014.

Lee, Y. E., Nakashima, Y., Kodama, T., Chen, X. & Morita, H. (2022). Dual engineering of olivetolic acid cyclase and tetraketide synthase to generate longer alkyl-chain olivetolic acid analogs. *Organic Letters*, *24*(1), 410–414. DOI: 10.1021/acs.orglett.1c04089.

Li, X. J., Gao, J. M., Chen, H., Zhang, A. L. & Tang, M. (2012). Toxins from a symbiotic fungus, *Leptographium qinlingensis* associated with *Dendroctonus armandi* and their in vitro toxicities to *Pinus armandi* seedlings. *European Journal of Plant Pathology*, *134*, 239–247. DOI: 10.1007/s10658-012-9981-9.

Lu, J. C., Xue, C. & Jiang, C. X. (2023). Research progress on anti-aging mechanism of extracts and active ingredients of *Polygonati Rhizoma*. *Chinese Traditional and Herbal Drugs*, *54*(14), 4732–4739. DOI: 10.4268/cjcmm20150610.

Pan, M., Wu, Y., Sun, C., Ma, H., Ye, X. & Li, X. (2024). *Polygonati Rhizoma*: A review on the extraction, purification, structural characterization, biosynthesis of the main secondary metabolites and anti-aging effects. *Journal of Ethnopharmacology*, *327*, 118002. DOI: 10.1016/j.jep.2024.118002.

Tiwari, P. & Bae, H. (2022). Endophytic fungi: key insights, emerging prospects, and challenges in natural product drug discovery. *Microorganisms*, *10*(2), 360. DOI: 10.3390/microorganisms10020360.

Xiao, Y., Liang, W., Zhang, Z., Wang, Y., Zhang, S., Liu, J., Chang, J., Ji, C. & Zhu, D. (2022). Polyketide derivatives from the endophytic fungus *Phaeosphaeria* sp. LF5 isolated from *Huperzia serrata* and their acetylcholinesterase inhibitory activities. *Journal of Fungi*, *8*(3), 232. DOI: 10.3390/jof8030232.

Yang, Z. J., Yin, Y. & Ge, M. (2015). A novel chromene with anti-tumor activities from fungus *Phomopsis* sp. *China Journal of Chinese Materia Medica*, *40*(4), 667–671. DOI: 10.4268/cjcmm20150418.

Zhang, S. Q., Wang, J. P., Zhang, F. M., Yao, L. L., Li, B. X., Li, Y. N., Gan, D., Mei, R. F., Cai, L., & Ding, Z. T. (2022). Investigations of specialised metabolites of endophyte *Diaporthe destruens* hosted in *Illigera orbiculata* C. Y. Wu. *Phytochemistry.*, *203*, 113357. DOI: 10.1016/j.phytochem.2022.113357.

Zhao, L. X., Xu, C. Y., Zhou, W. L., Li, Y. Y., Xie, Y. M., Hu, H. L. & Wang, Z. G. (2023). *Polygonati Rhizoma* with the homology of medicine and food: A review of ethnopharmacology, botany, phytochemistry, pharmacology and applications. *Journal of Ethnopharmacology*, *309*, 116296. DOI: 10.1016/j.jep.2023.116296.

Zhou, J., Guan, Y. M., Li, P., Li, Y. F., Peng, B., Fan, C. X. & Pan, H. P. (2025). Research progress on the anti-inflammatory active constituents and mechanisms of *Polygonati Rhizoma*. *Chinese Pharmaceutical Journal*, *60*(22), 2333–2338.