SHORT REPORT

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A Novel Polyketide from the Endophytic Fungus *Aspergillus puniceus*

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Abstract: A novel polyketide, named Asperpropanol E, was found from the secondary metabolites of the endophytic fungus *Aspergillus puniceus* which was isolated from *Eupatorium chinense* L. In addition to this new compound, six known compounds were also identified. The structures of all compounds were elucidated through comprehensive chemical analysis utilizing nuclear magnetic resonance (NMR) and mass spectrometry (MS) spectroscopic techniques. All isolated compounds were evaluated for biological activity by the MTT assay, compound **1** exhibited moderate inhibitory activities against α-glucosidase and protein tyrosine phosphatase 1B (PTP1B), the IC_{50} (μg/mL) values of 31.63 $\pm$ 0.42 and 36.82 $\pm$ 0.54, respectively. Compound **3** demonstrated significant inhibitory activities against α-glucosidase ($IC_{50} = 12.3 \pm 0.56$ μg/mL). Notably, compound **6** displayed potent dual inhibitory activities against α-glucosidase and PTP1B with the IC_{50} (μg/mL) values of 26.72 $\pm$ 0.63 and 12.68 $\pm$ 0.87, respectively. However, none of the tested compounds showed significant inhibitory effects on HGC-27 gastric cancer cells and HepG2 liver cancer cells.

Keywords: *Aspergillus puniceus*; *Eupatorium chinense* L; Endophytic fungi; PTP1B Inhibition; α-Glucosidase.
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1. Fungus Source

The endophytic fungus *Aspergillus puniceus* was isolated from the roots of *Eupatorium chinense*. The plant species *Eupatorium chinense* L. was procured from Changyang Tujia Autonomous County, situated in Hubei Province, China. Its taxonomic identification was confirmed by Prof. Yu-Bin Wang, affiliated with China Three Gorges University. The identification of the fungal strain was confirmed through comparison of its internal transcribed spacer rDNA (ITS rDNA) gene sequences with those of a reference strain (MW111283) in the GenBank database (www.ncbi.nlm.nih.gov/genbank). The fungal strain is currently preserved at the Hubei Key Laboratory of Natural Products Research and Development, China Three Gorges University, China.

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2. Previous Studies

Endophytic fungi, which reside within the internal tissues of plants without causing visible harm, are known for their diverse secondary metabolites. These metabolites have garnered significant attention due to their potential applications in medicine and agriculture [1]. The genus *Aspergillus*, in particular, is renowned for producing a wide array of secondary metabolites, including polyketides, alkaloids, and terpenoids. These compounds have been reported to exhibit various bioactivities, such as antimicrobial, antitumor, and metabolic regulatory effects [2]. Literature reviews indicate that the fungus *Aspergillus puniceus* is rich in secondary metabolites, but here have been relatively few reports on the isolation and characterization of polyketide compounds from this fungus. Polyketides, a class of natural products derived from the polyketide pathway, are known for their diverse structural features and significant biological activities, including anti-inflammatory, antimicrobial, and antitumor properties [3]. Recent research has demonstrated a close correlation between PTP1B and the onset and progression of cancer [4]. Studies have reported that PTP1B serves as a therapeutic target for type 2 diabetes and obesity [5].

3. Present Study

The fungus *Aspergillus puniceus* was revitalized on Potato Dextrose Agar (PDA) medium at 28°C for 3 days. Subsequently, blocks of 0.5 cm × 0.5 cm from the activated culture were inoculated into flasks containing Potato Dextrose Broth (PDB) medium. These were incubated at 28°C with a rotary shaking speed of 150 rpm for 14 days. The resulting fermentation broth was extracted three times with ethyl acetate to yield extract A. The mycelium was then dried in a dryer at 45°C and subjected to extraction with a dichloromethane-methanol mixture (1:1, v/v) overnight for three consecutive times to obtain extract B. Finally, extracts A and B were combined to yield the crude extract (36.5 g).

The fermented and extracted concentrated extract was dissolved in methanol and mixed with normal phase silica gel (200–300 mesh) at a ratio of 1:1 to make the crude fermented extract sample into powder. The normal phase silica gel (200–300 mesh) of 500 g was soaked in dichloromethane overnight, and then loaded into a column with a volume of 1.0 L by wet method. Dry loading was adopted, and the column was eluted by wet method. Gradient elution was performed using dichloromethane-methanol (100:0, to 0:1), afford to 15 fractions (Fr.1–Fr.15).

Fraction Fr.2 was purified by HPLC using a mixture of ACN/H_2O (65:35, 2 mL/min), to yield compound **7** (0.8 mg).

Fractions Fr.3 was dissolved in methanol, and splitted into six fractions by semi-preparative high-performance liquid chromatography (HPLC) with ACN/H_2O (10:90-100:0-10:90, 2 mL/min) to yield compound **2** (1.4 mg), **3** (1.8 mg), **4** (1.3 mg) and **5** (1.2 mg).

Fraction Fr.7 was subjected to preparative separation by semi-preparative HPLC, with ACN/H_2O (60:40-100:0-60:40, 2 mL/min), three crude fractions were obtained. Subfraction Fr.7-2 was purified via HPLC with elution using ACN/H_2O (70:30, 2 mL/min) to obtain compound **6** (2.1 mg).

Fraction Fr.8 was dissolved in methanol and then roughly separated by HPLC with MeOH/H_2O (10:90-100:0-10:90, 2 mL/min) to obtain 5 fractions. Fraction Fr.8-3 was further purified using a semi-preparative RP HPLC eluted with ACN/H_2O (25:75, 2 mL/min) to obtain Compound **1** (1.3 mg).

*Asperpropanol E (**1**)*: Yellow oil; UV (MeOH) λ_{max} = 225, 281 nm; IR (KBr) ν_{max} = 3451, 3010, 1710, 1425, 1186, 1091, 731 cm^{-1}. ^{1}H-NMR (DMSO-d_6, 400 MHz) and ^{13}C-NMR (DMSO-d_6, 100 MHz) data (Table 1); HR-ESIMS *m/z* measured 197.0807 $[M+H]^+$ ($C_{10}H_{12}O_4$, calcd. 197.0807).

In this paper, all compounds (**1**–**7**) were isolated from the secondary metabolites of *Aspergillus puniceus* by various column chromatography methods. Structures of the new compounds **1** were identified by NMR and HR-MS data analyses. The known compounds were identified as Tyrosol (**2**) [6], 4-hydroxybenzal dehyde (**3**) [7], 1H-indole-3-carbaldehyde (**4**) [8], paracetamol (**5**) [9], 2, 4-dihydroxy-6-((3E,5E)-nona3,5-dien-1-yl) benzoic acid (**6**) [10] and 4, 6-dihydroxy-1(3H)-isobenzofuranone (**7**) [11], by comparing their spectroscopic data with literature values respectively (Figure 1).

The molecular formula of the novel compound **1** was determined to be $C_{10}H_{12}O_4$, with an unsaturation degree of 5. This was established through high-resolution electrospray ionization mass

spectrometry (HR-ESI-MS), which yielded an ion peak at m/z 197.0807 $[M+H]^+$ (calculated value: 197.0814).

Table 1. ^{1}H (400 MHz) and ^{13}CNMR (100 MHz) data of Compound **1** and the Compound in literature in DMSO-d6 (δ in ppm)

Position	Compound 1		Asperpropanol C	
	δ_C	$\delta_H J$ (Hz)	δ_C	$\delta_H J$ (Hz)
1	129.5	–	134.2	–
2	139.1	–	138.5	–
3	151.0	–	151.0	–
4	103.3	6.22 (d, 2.8)	104.1	6.27 (d, 2.9)
5	153.7	–	153.9	–
6	107.9	5.97 (d, 2.8)	105.2	6.12 (d, 2.9)
7	45.3	3.54 (d, 3.3)	74.7	5.10 (d, 4.7)
8	206.6	–	208.3	–
9	29.7	2.08 (s)	26.0	2.03 (s)
2-OMe	60.0	3.54 (s)	60.6	3.63 (s)
3-OH	–	–	–	9.27 (s)
5-OH	–	9.10 (s)	–	9.03 (s)
7-OH	–	–	–	5.59 (d, 4.7)

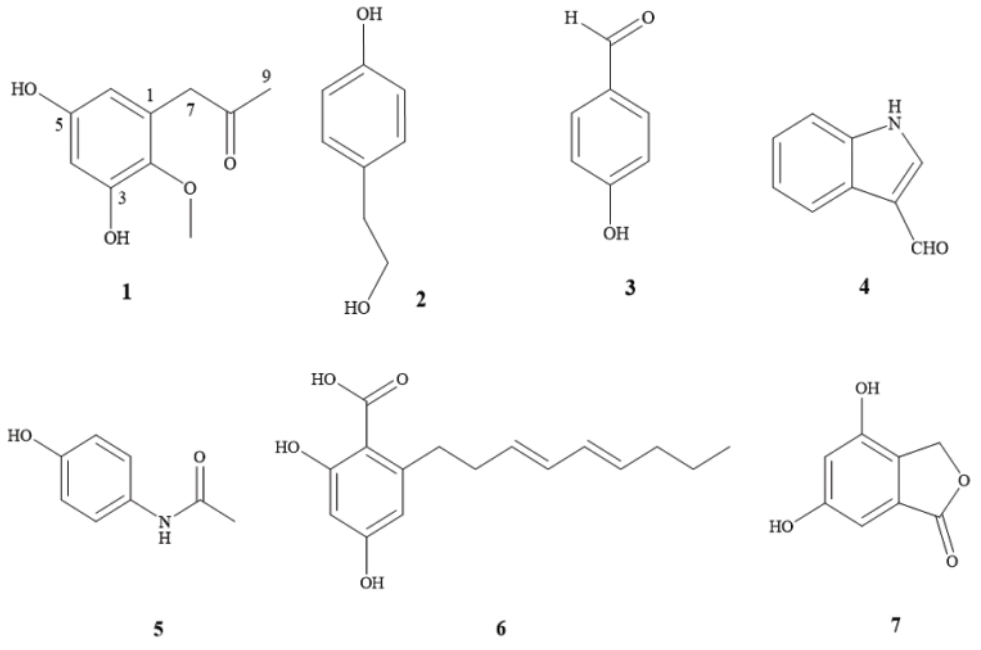

Figure 1. Chemical structures of compounds **1–7**

The ^{1}H-NMR spectrum of compound **1** (Table 1) exhibited several characteristic proton signals. Two methyl proton signals were observed at δ_H 3.54 (3H, s, J = 2.8 Hz, 2-OMe) and δ_H 2.08 (3H, s, H-9). A methylene proton signal appeared at δ_H 3.54 (2H, d, J = 3.3 Hz, H-7). Additionally, two aromatic proton signals were detected at δ_H 6.22 (1H, d, J = 2.8 Hz, H-4) and δ_H 5.97 (1H, d, J = 2.8 Hz, H-6).

The ^{13}C-NMR spectrum (Table 1) and DEPT135 spectra revealed a total of 10 carbon signals. These included six aromatic carbon signals at δ_C 153.67 (C-5), 150.97 (C-3), 139.09 (C-2), 129.45 (C-1), and 107.91 (C-6). Two methyl carbon signals were observed at δ_C 45.24 (C-7) and 29.73 (C-9). Two oxygen-bearing carbon signals were detected at δ_C 206.58 (C-8) and 60.01 (2-OMe).

The ^{13}C-NMR data of compound **1** closely resembled those of Asperpropanol C reported in the literature [12] (Table 1), suggesting that compound **1** is an analogue of the previously reported compound. However, a detailed comparison revealed distinct differences. Specifically, compound **1** lacked one oxygen-bearing carbon signal at δ_C 74.29 (C-7) and one hydroxyl proton signal at δ_H 5.59 (7-OH), which were characteristic of Asperpropanol C. Instead, compound **1** exhibited an additional methylene carbon signal at δ_C 45.24 (C-7). These observations led to the inference that the hydroxyl group at position 7 in Asperpropanol C was replaced by a methylene group in compound **1**.

Further structural confirmation was achieved through the analysis of the HMBC spectrum (Figure 2). The HMBC correlations between δ_H 2.08 (H-9) and δ_C 45.24 (C-7), as well as between δ_H 3.52 (H-7) and δ_C 129.5 (C-1)/139.1 (C-2), were observed. These correlations provided strong evidence supporting the proposed structure of compound **1**. A comprehensive literature search confirmed that compound **1** has not been previously reported. Therefore, it is designated as a novel compound and named Asperpropanol E.

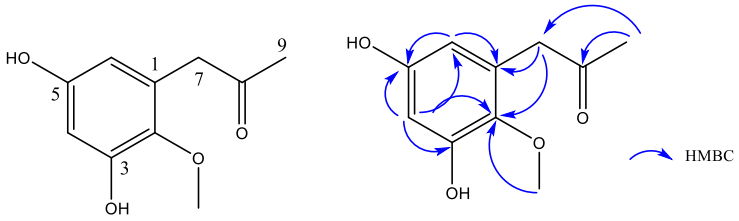

Figure 2. Structure of Compound **1**(L), and HMBC of Compound **1**(R)

Bioactivity Test: Experimental concentration screening of 7 compounds were tested for α-glucosidase [13,14], PTP1B inhibitory activities [15,16] according to the literature, also against two types of tumor cells, namely gastric cancer HGC-27 and liver cancer HepG2 by MTT colorimetric assay [17]. The IC_{50} values for those with inhibition rate more than 50% were further determined. Experiments were repeated three times and conducted in triplicate.

Compound **1** exhibited moderate dual activities against α-glucosidase and PTP1B with the IC_{50} (μg/mL) values of 31.63 $\pm$ 0.42, 36.82 $\pm$ 0.54, respectively. For comparison, the positive control acarbose had an IC_{50} value of 4.60 $\pm$ 0.12 against α-glucosidase, and the positive control sodium orthovanadate had an IC_{50} value of 1.27 $\pm$ 0.26 against PTP1B (Table 2).

Compound **3** demonstrated significant inhibitory activities against α-glucosidase with an IC_{50} (μg/mL) values of 12.3 $\pm$ 0.56 (Table 2).

Compound **6** showed potent dual inhibitory activities against α-glucosidase and PTP1B with the IC_{50} (μg/mL) values of 26.72 $\pm$ 0.63 and 12.68 $\pm$ 0.87, respectively. In contrast, compounds **2**, **4**, **5, 7** had no significant inhibitory effects on the activities of α-glucosidase and PTP1B (IC_{50} > 50 μg/mL) (Table 2).

Additionally, the cytotoxic effects of all compounds were evaluated against HGC-27 gastric cancer cells and HepG2 liver cancer cells using the MTT cytotoxicity assay. None of the tested compounds demonstrated significant cytotoxicity against these two tumor cell lines.

In this experiment, All compounds were docked with α-glucosidase and PTP1B [18]. The binding energies of compound **6** were both less than −6 kcal/mol, indicating strong interactions. These results suggest potential binding modes for compound 6 with the target proteins.

The complex of compound **6** and α-glucosidase was visualized using PyMOL 2.1. Compound **6** formed hydrogen bonds with residues ASP-327, ASP-382, and ILE-143, and hydrophobic interactions with MET-385 and TYR-63. π-π conjugations were also observed with PHE-144 (**Figure S16**). The binding energy was −6.397 kcal/mol.

Table 2. The inhibitory activities against α-glucosidase and PTP1B for **1–7**.

Compounds	α-glucosidase (IC_{50}, μg/mL)	PTP1B (IC_{50}, μg/mL)
1	31.63 ± 0.42	36.82 ± 0.54
3	12.3 ± 0.56	>50
6	26.72 ± 0.63	12.68 ± 0.87
2,4,5,7	>50	>50
Acarbose	4.60 ± 0.12	–
Sodium orthovanadate	–	1.27 ± 0.26

Compound **6** formed multiple hydrophobic interactions with PHE-280 and PHE-196 at the PTP1B active site, and hydrogen bonds with GLU-200 and ASN-193 (**Figure S17**). These interactions stabilize Compound **6** in the PTP1B pocket and suggest effective enzyme modulation. The binding energy was −7.056 kcal/mol. The unsaturated side chain in compound **6** may enhance its inhibitory activity against PTP1B.

In summary, compound **6** could form a variety of interactions, including hydrogen bonds, hydrophobic interactions, and conjugations, with both α-glucosidase and PTP1B target proteins. It could form stable complexes with the proteins and exhibited strong binding affinity.

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Supporting Information

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

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References

[1] R. K. Dissanayake, P. B. Ratnaweera, D. E. Williams, C. D. Wijayarathne, R. L. C. Wijesundera, R. J. Andersen and E. D. D. Silva (2016). Antimicrobial activities of endophytic fungi of the Sri Lankan aquatic plant Nymphaea nouchali and chaetoglobosin A and C, produced by the endophytic fungus *Chaetomium globosum*, *Mycology* **7**(**1**), 1–8. https://doi.org/10.1080/21501203.2015.1136708.

[2] M. E. Elawady, A. A. Hamed, W. M. Alsallami, E. Z. Gabr, M. O. Abdel-Monem and M. G. Hassan (2023). Bioactive metabolite from endophytic Aspergillus versicolor SB5 with anti-acetylcholinesterase, anti-inflammatory and antioxidant activities: In vitro and in silico studies, *Microorganisms* **11**(**4**), 1062. https://doi.org/10.3390/microorganisms11041062.

[3] Y. B. Zeng, Z. Wang, W. J. Chang, W. B. Zhao, H. Wang, H. Q. Chen, H. F. Dai and F. Lv (2023). New azaphilones from the marine-derived fungus *Penicillium sclerotiorum* E23Y-1A with their anti-inflammatory and antitumor activities, *Mar. Drugs* **21**(**2**), 75. https://doi.org/10.3390/md21020075.

[4] X. Liu, Q. Chen, X. G. Hu, X. C. Zhang, T. W. Fu, Q. Liu, Y. Liang, X. L. Zhao, X. Zhang and Y. F. Ping (2016). PTP1B promotes aggressiveness of breast cancer cells by regulating PTEN but not EMT, *Tumour Biol.* **37**(**10**), 13479–13487. https://doi.org/10.1007/s13277-016-5245-1.

[5] V. R. Munoz, R. C. Gaspar, M. B. Severino, A. P. A. Macedo, F. M. Simabuco, E. R. Ropelle, D. E. Cintra, A. S. R. D. Silva, Y. B. Kim and J. R. Pauli (2021). Exercise counterbalances Rho/ROCK2 signaling

impairment in the skeletal muscle and ameliorates insulin sensitivity in obese mice, *Front. Immunol.* **12**, 702025. https://doi.org/10.3389/fimmu.2021.702025.

[6] A. Bianco, C. Melchioni, A. Ramunno, G. Romeo and N. Uccella (2004). Phenolic components of *Olea europaea*–isolation of tyrosol derivatives, *Nat. Prod. Res.* **18**(**1**), 29–32.

[7] H. Fujimoto, Y. Satoh and M. Yamazaki (1998). Four new immunosuppressive components, kobiin and kobifuranones A, B, and C, from an *ascomycete*, Gelasinospora kobi, *Chem. Pharm. Bull. (Tokyo)* **46**(**2**), 211–216.

[8] M. T. Gutierrez-Lugo, G. M. Woldemichael, M. P. Singh, P. A. Suarez, W. M. Maiese, G. Montenegro and B. N. Timmermann (2005). Isolation of three new naturally occurring compounds from the culture of *Micromonospora sp*. P1068, *Nat. Prod. Res.* **19**(**7**), 645–652. https://doi.org/10.1080/14786410412331272040.

[9] D. Wu, L. Dong, J. Y. Yin and Q. Meng (2012). Study on the antitumor active compounds of rhizoma typhonii(II), *Spec. Wild Econ. Anim. Plant Res.* **3**, 52–53.

[10] Z. J. Song, D. W. Chen and J. G. Dai (2024). Isolation of four new phenolic compounds from the fungus talaromyces cellulolyticus, *Phytochem. Lett.* **64**(**16**), 19–24. https://doi.org/10.1016/j.phytol.2024.09.003.

[11] M. J. Liu, V. Seidel, D. R. Katerere and A. I. Gray (2007). Colorimetric broth micro-dilution method for the antifungal screening of plant extractsagainst yeasts, *Methods* **42**, 325–329.

[12] J. L. He, X. Wu, S. H. Huang, J. Wang, S. Niu, M. X. Chen, G. Y. Zhang, S. Y. Cai, J. N. Wu and B. H. Hong (2022). Phenolic metabolites from a deep-sea-derived fungus *Aspergillus puniceus* A2 and their Nrf2-dependent anti-in flammatory effects, *Mar. Drugs* **20**(**9**), 575–585. https://doi.org/10.3390/md20090575.

[13] Y. Tao, Y. F. Zhang, Y. Y. Cheng and Y. Wang (2013). Rapid screening and identification of α-glucosidase inhibitors from mulberry leaves using enzyme-immobilized magnetic beads coupled with HPLC/MS and NMR, *Biomed. Chromatogr.* **27**(**2**), 148–155. https://doi.org/10.1002/bmc.2761.

[14] L. T. T. Anh, H. T. Dang, N. T. T. Ha, N. T. Tra, N. T. T. Linh, B. T. Cham, B. T. T. Luyen, H. H. Do and T. K. Nguyen (2024). α-Glucosidase inhibitors from *Polyscias serrata* roots in a parallel study of network pharmacology, *Rec Nat. Prod.* **3**, 363–368.

[15] J. Xu, J. Q. Cao, J. Y. Yue, X. S. Zhang and Y. Q. Zhao (2018). New triterpenoids from acorns of Quercus liaotungensis and their inhibitory activity against α-glucosidase, α-amylase and protein-tyrosine phosphatase 1B, *J. Funct. Foods* **41**(**21**), 232–239. https://doi.org/10.1016/j.jff.2017.12.054.

[16] Z. G. Yue, R. Zhou, Y. H. He, H. B. Xu, Y. L. Pan, L. Y. Lei, P. Xie, Z. S. Tang and J. N. Duan (2019). Protein tyrosine phosphatase 1B inhibitors from the root bark of *Pseudolarix amabilis* (Nelson) Rehd. (Pinaceae), *Rec. Nat. Prod.* **6**, 475–482.

[17] F. F. Lu, W. Song, H. Li and L. H. Cao (2024). Peniciloxatone A, a new polyoxygenated ergostane steroid isolated from the marine alga-sourced fungus *Penicillium oxalicum* 2021CDF-3, *Rec Nat. Prod.* **18**(**6**), 699–704.

[18] L. Güven, A. Ertürk, M. A. Yılmaz, S. H. Alwasel and İ. Gülçin (2024). Alchemilla pseudocartalinica Juz: Phytochemical Screening by UPLC-MS/MS, molecular docking, anti-oxidant, anti-diabetic, anti-glaucoma, and anti-alzheimer effects, *Rec. Nat. Prod.* **2**, 251–272.

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