Supporting Information

Discovery of a Hepatoprotective Trinor-Sesterterpenoid from the Marine Fungus *Talaromyces* sp. Against Hepatic Ischemia-Reperfusion Injury

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The physicochemical data of the known compounds 2 and **3**

Penitalarin A (**2**): yellow oil; ^{1}H NMR (500 MHz, DMSO-d_6) δ 6.26 (1H, dd, J = 15.2, 10.5 Hz, H-6), 6.17 (1H, dd, J = 15.1, 10.8 Hz, H-13), 6.03 (1H, dd, J = 15.3, 10.5 Hz, H-7), 5.75 (1H, d, J = 10.8 Hz, H-12), 5.66 (1H, dd, J = 15.3, 7.4 Hz, H-8), 5.60 (1H, dd, J = 15.2, 9.0 Hz, H-5), 5.43 (1H, dd, J = 15.1, 7.8 Hz, H-14), 4.50 (1H, s, H-1), 4.41 (1H, d, J = 9.0 Hz, H-4), 3.97 (1H, s, H-5), 3.69 (3H, s, H-19), 2.42 (1H, m, H-9), 2.06 (2H, dt, J = 13.5, 6.9 Hz, H-10), 1.95 (1H, m, H-15), 1.67 (3H, s, H-22), 1.33 (3H, s, H-20), 1.27 (2H, m, H-16), 0.93 (6H, m, H-23, 21), 0.81 (3H, t, J = 7.4 Hz, H-17); ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.5 (C, C-18), 141.6 (CH, C-8), 138.1 (CH, C-14), 134.2 (C, C-11), 134.0 (CH, C-6), 127.9 (CH, C-5), 127.3 (CH, C-7), 126.5 (CH, C-12), 124.9 (CH, C-13), 82.6 (CH, C-4), 76.3 (CH, C-1), 65.0 (C, C-3), 63.2 (CH, C-2), 52.1 (CH_3, C-19), 46.9 (CH_2, C-10), 38.0 (CH, C-15), 34.3 (CH, C-9), 29.3 (CH_2, C-16), 20.1 (CH_3, C-23), 19.8 (CH_3, C-21), 16.3 (CH_3, C-22), 13.7 (CH_3, C-20), 11.7 (CH_3, C-17).

Nafuredin (**3**): yellow oil; ^{1}H NMR (500 MHz, Chloroform-d) δ 6.34 (1H, dd, J = 15.3, 10.6 Hz, H-7), 6.14 (1H, dd, J = 15.2, 10.9 Hz, H-14), 5.99 (1H, dd, J = 15.3, 10.3 Hz, H-8), 5.77 (1H, dd, J = 15.2, 7.1 Hz, H-9), 5.73 (1H, d, J = 11.3 Hz, H-13), 5.47 (1H, dd, J = 14.8, 7.8 Hz, H-6), 5.42 (1H, m, H-15), 4.89 (1H, d, J = 7.6 Hz, H-5), 4.57 (1H, s, H-2), 3.49 (2H, s, H-3), 2.40 (1H, m, H-10), 2.05 (2H, m, H-16), 1.93 (1H, dd, J = 13.6, 8.1 Hz, H-11), 1.67 (3H, s, 12-CH_3), 1.42 (3H, s, 4-CH_3), 1.28 (3H, q, J = 7.1 Hz, H-17), 0.95 (6H, t, J = 7.0 Hz, 10, 16-CH_3), 0.82 (3H, m, H-18); ^{13}C NMR (125 MHz, Chloroform-d) δ 170.7 (C, C-1), 145.1 (CH, C-9), 138.9 (CH, C-15), 138.0 (CH, C-7), 133.7 (C, C-12), 127.1 (CH, C-13), 126.2 (CH, C-8), 124.7 (CH, C-14), 122.2 (CH, C-6), 80.3 (CH, C-5), 68.1 (CH, C-2), 58.8 (CH, C-3), 58.4 (C, C-4), 47.3 (CH_2, C-11), 38.7 (CH, C-16), 34.9 (CH, C-10), 29.9 (CH_2, C-17), 20.2 (CH_3, C-16), 19.5 (CH_3, C-10), 17.8 (CH_3, C-4), 16.6 (CH_3, C-12), 11.8 (CH_3, C-18).

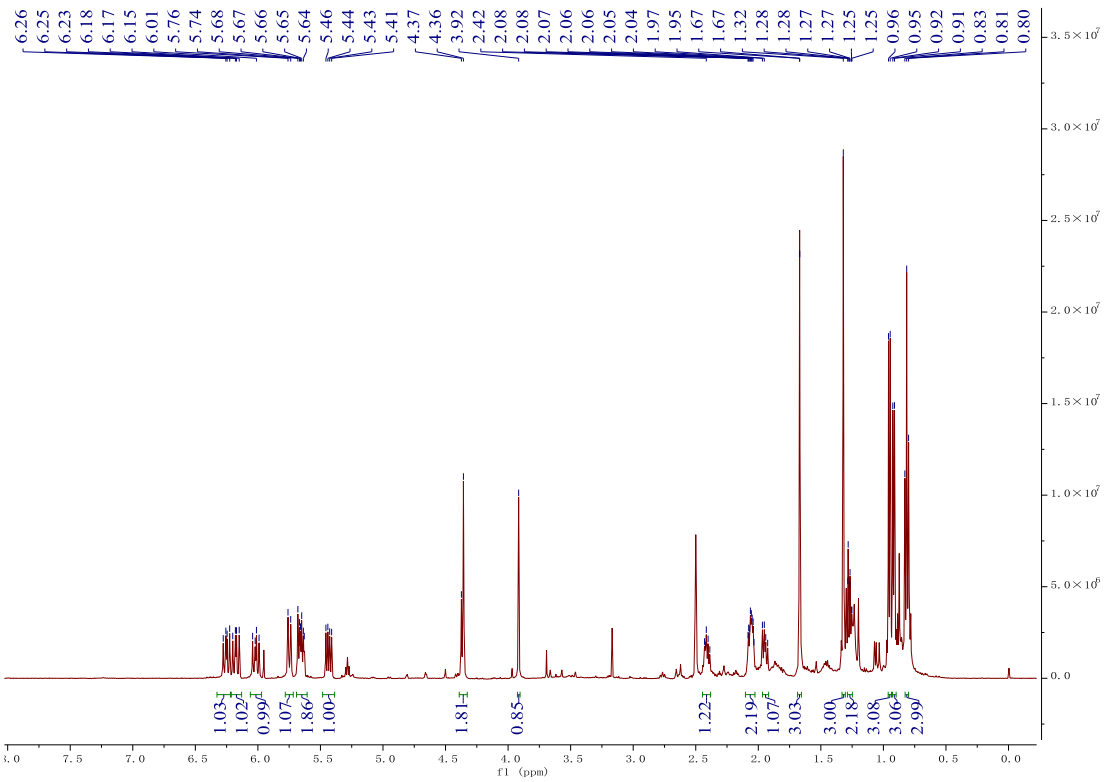


Figure S1. [1]H NMR (500 MHz) spectrum of **1** in DMSO-*d*6.

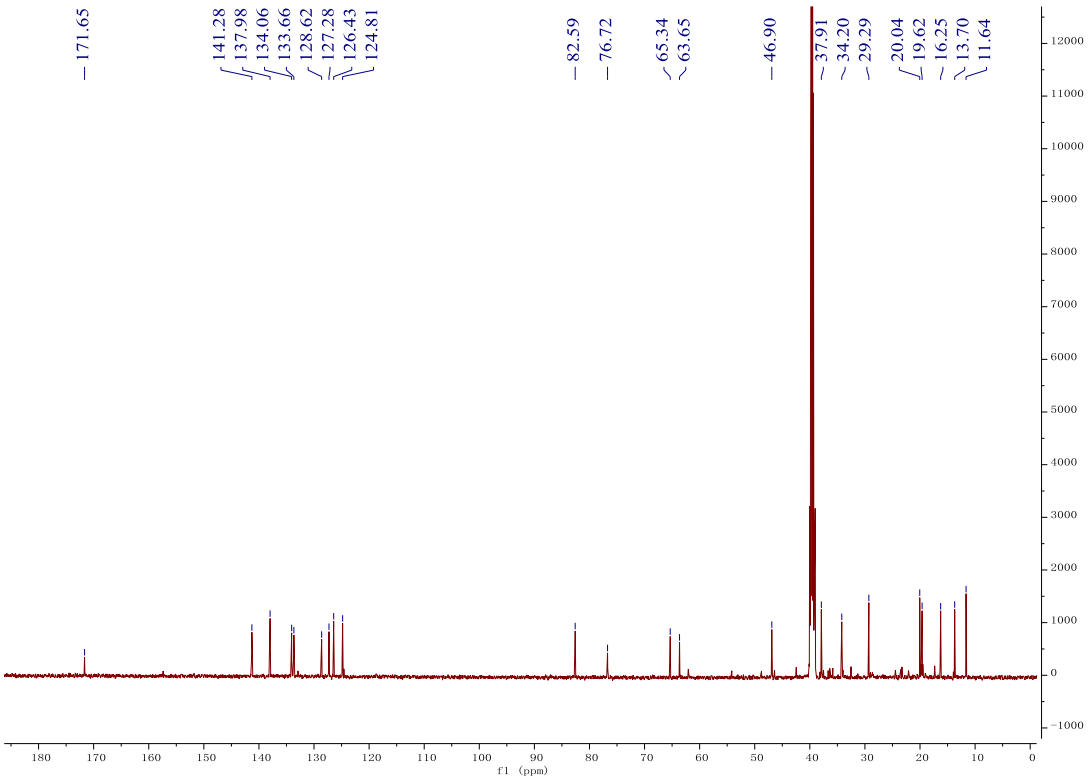


Figure S2. [13]C NMR (125 MHz) spectrum of **1** in DMSO-d_6.

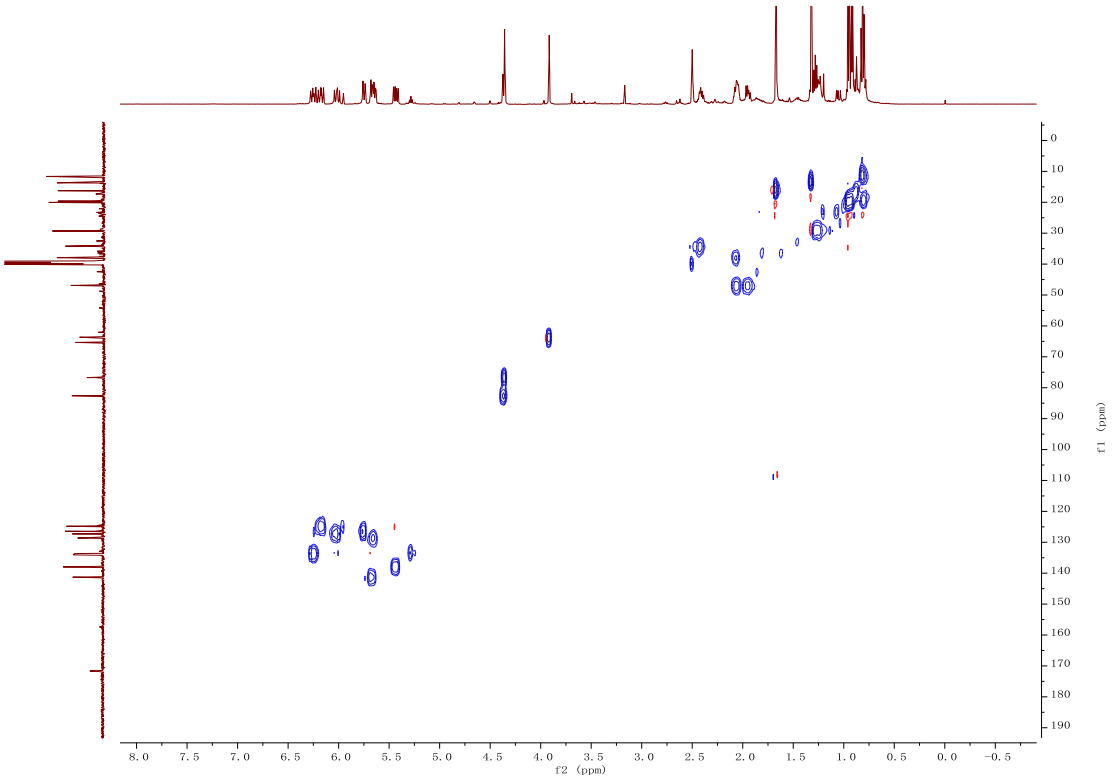


Figure S3. HSQC spectrum of **1** in DMSO-d_6.

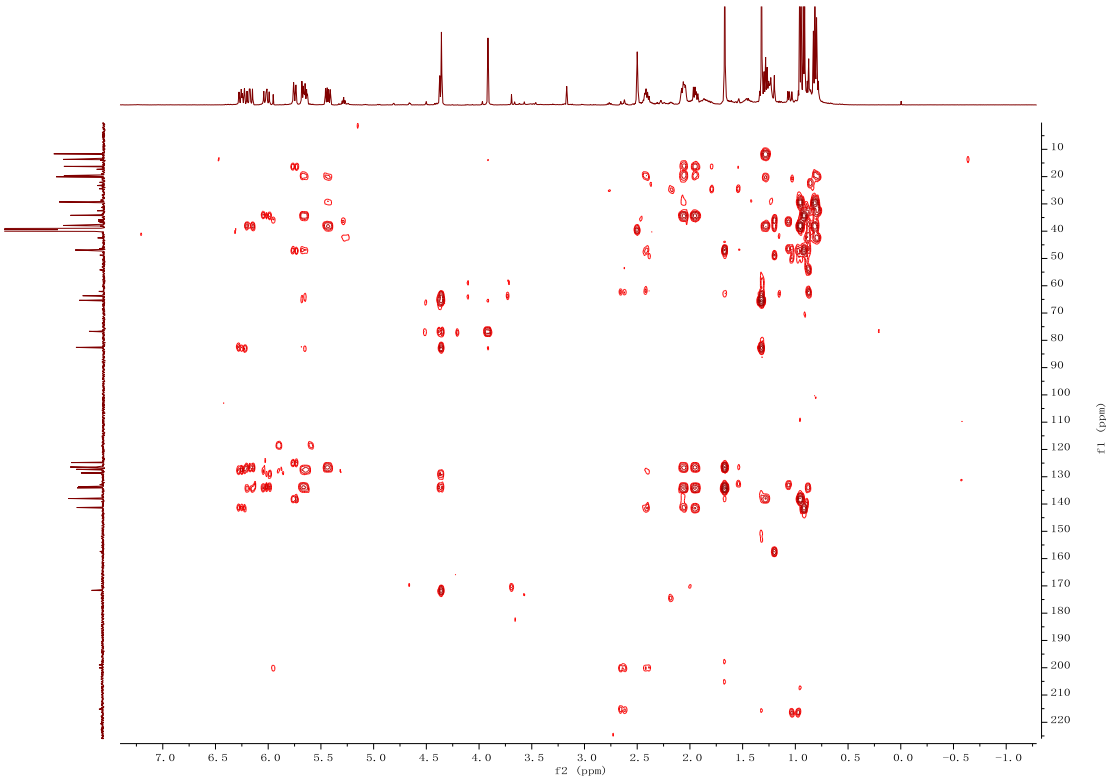


Figure S4. HMBC spectrum of **1** in DMSO-d_6.

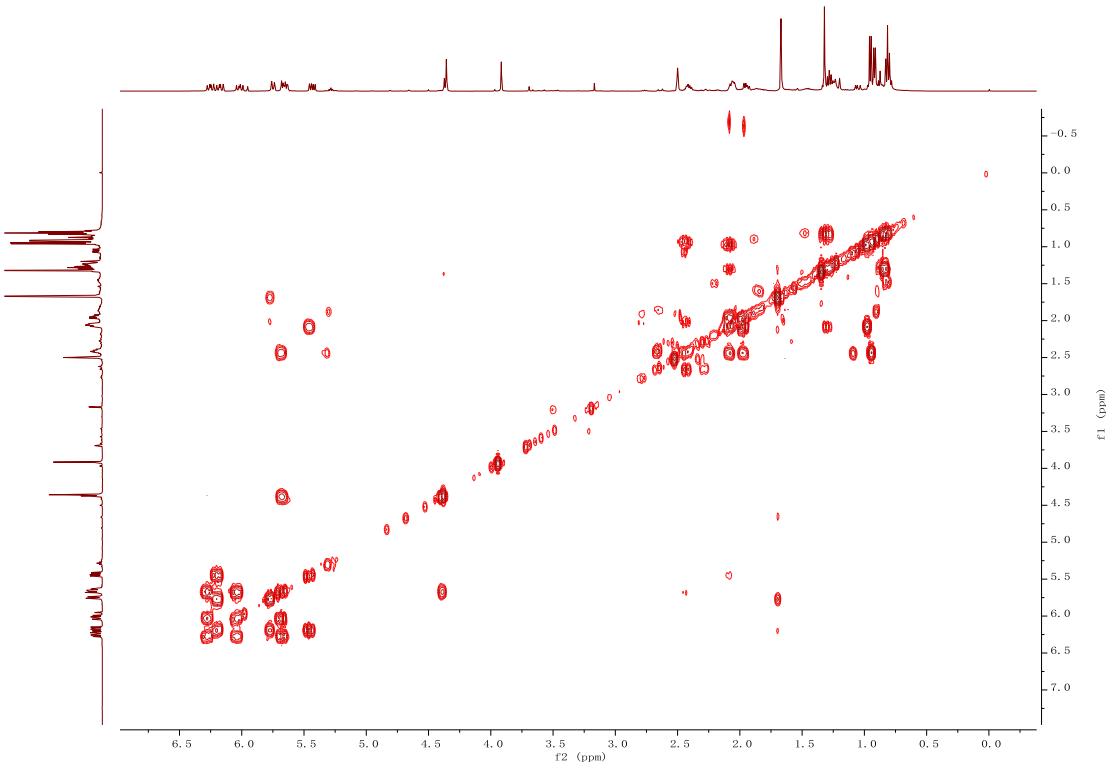


Figure S5. ^{1}H–^{1}H COSY spectrum of **1** in DMSO-d_6.

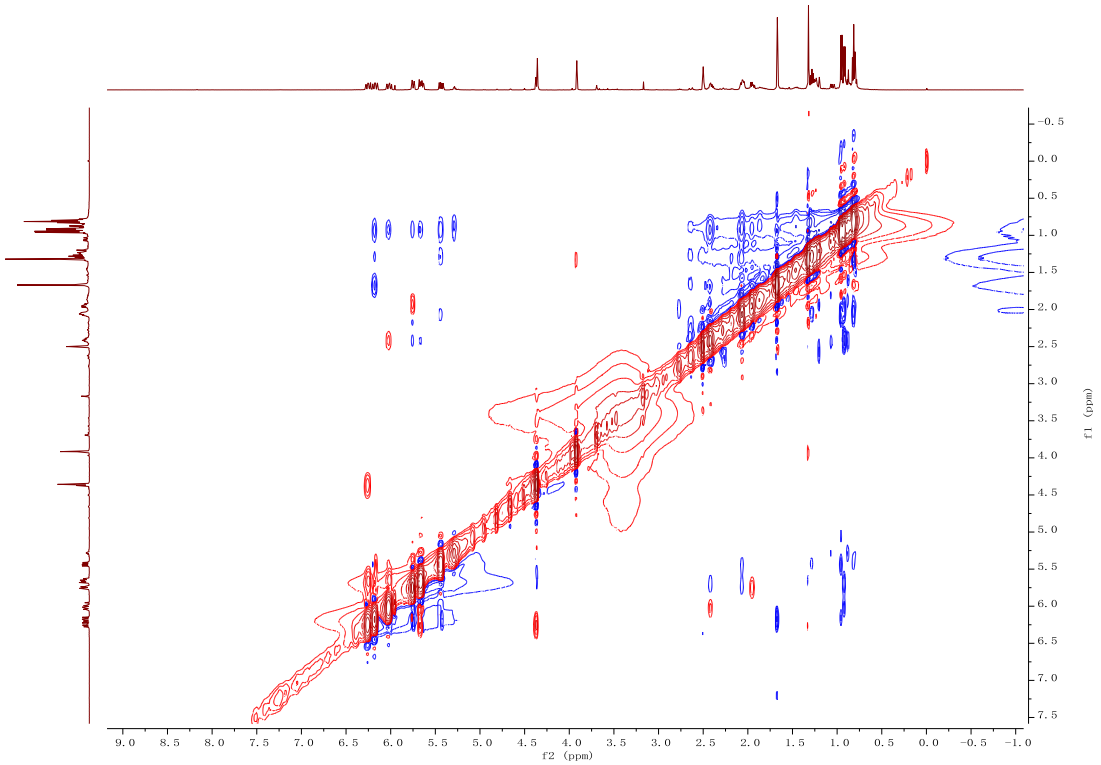


Figure S6. NOESY spectrum of **1** in DMSO-d_6.

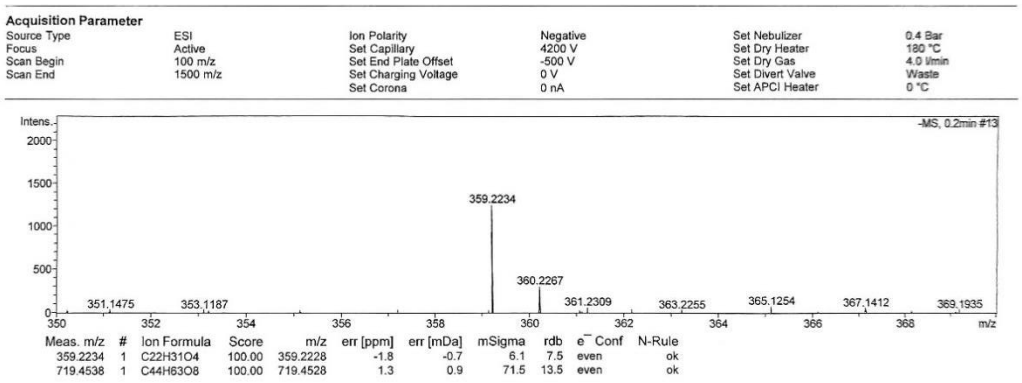


Figure S7. HRESIMS spectrum of **1**.

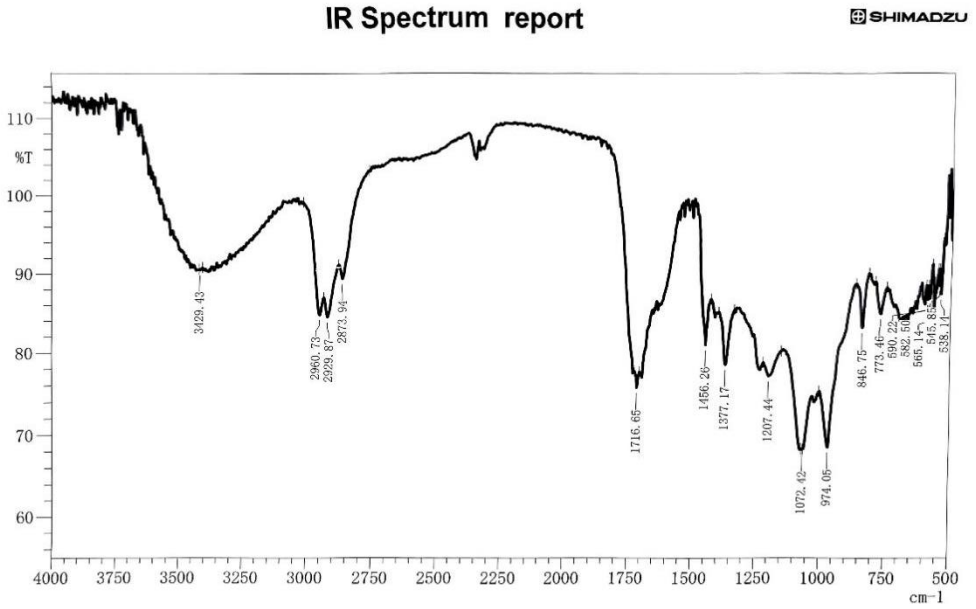


Figure S8. IR spectrum of **1**.

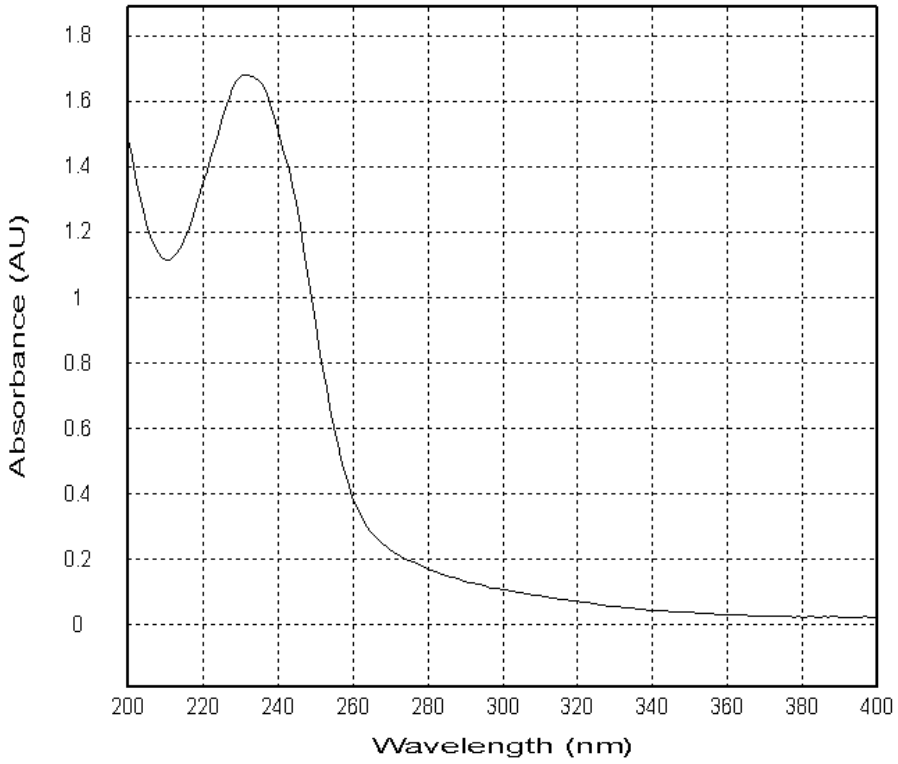


Figure S9. UV spectrum of **1** in MeOH.

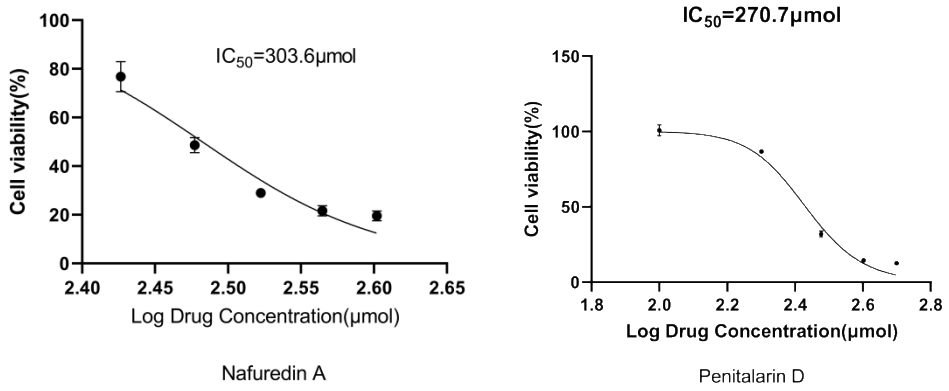


Figure S10. IC_{50} of penitalarin D (**1**) and nafuredin A (**3**) on HepG2 cells

Table S1. Primers of RT-qPCR

Primer	Sequence (5'→3')
H-HMOX1-F	AAGACTGCGTTCCTGCTCAAC
H-HMOX1-R	AAAGCCCTACAGCAACTGTCG
H-Nrf2-F	TCAGCGACGGAAAGAGTATGA
H-Nrf2-R	CCACTGGTTTCTGACTGGATGT
H-FTH1-F	CCCCCATTTGTGTGACTTCAT
H-FTH1-R	GCCCGAGGCTTAGCTTTCATT
H-SLC7A11-F	TCTCCAAAGGAGGTTACCTGC
H-SLC7A11-R	AGACTCCCCTCAGTAAAGTGAC
H-GCLC-F	GGAGGAAACCAAGCGCCAT
H-GCLC-R	CTTGACGGCGTGGTAGATGT
H-GCLM-F	GTCTTGGAATGCACTGTATCTC
H-GCLM-R	CCCAGTAAGGCTGTAAATGCTC

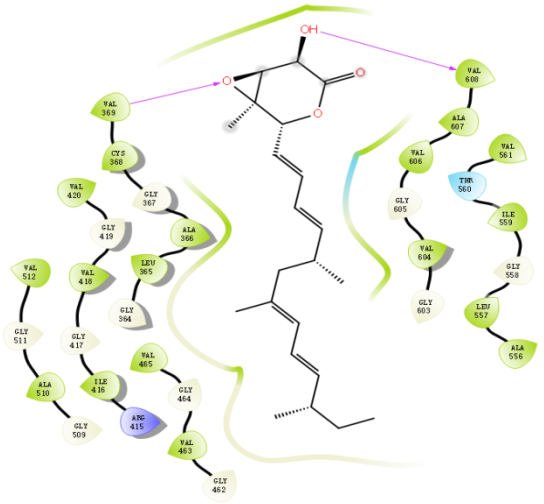


Figure S11. The docking site of the Nafuredin A complex with Nrf2-keap1

Table S2. The docking scores of the Nafuredin A complex with Nrf2-Keap1

Small-molecule ligands	Docking scores	PDB
nafuredin A	-5.352	5WHL
Hydroxyphenylpropionic acid	-6.012	5WHL