Supporting Information

Histone Deacetylase inhibitory and cytotoxic activities of the constituents from the roots of three species of *Ferula*

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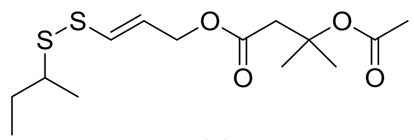
Table of Content



(2)

[1]H NMR (301 MHz, Chloroform-*d*) δ 6.39 (d, *J* = 14.9 Hz, 1H), 5.99 (dt, *J* = 14.8, 6.5 Hz, 1H), 4.62 (dd, *J* = 6.5, 0.9 Hz, 2H), 2.92 (s, 2H), 2.84 (h, *J* = 6.8 Hz, 1H), 2.01 (s, 2H), 1.82 – 1.47 (m, 7H), 1.32 (d, *J* = 6.8 Hz, 2H), 1.01 (t, *J* = 7.4 Hz, 2H).

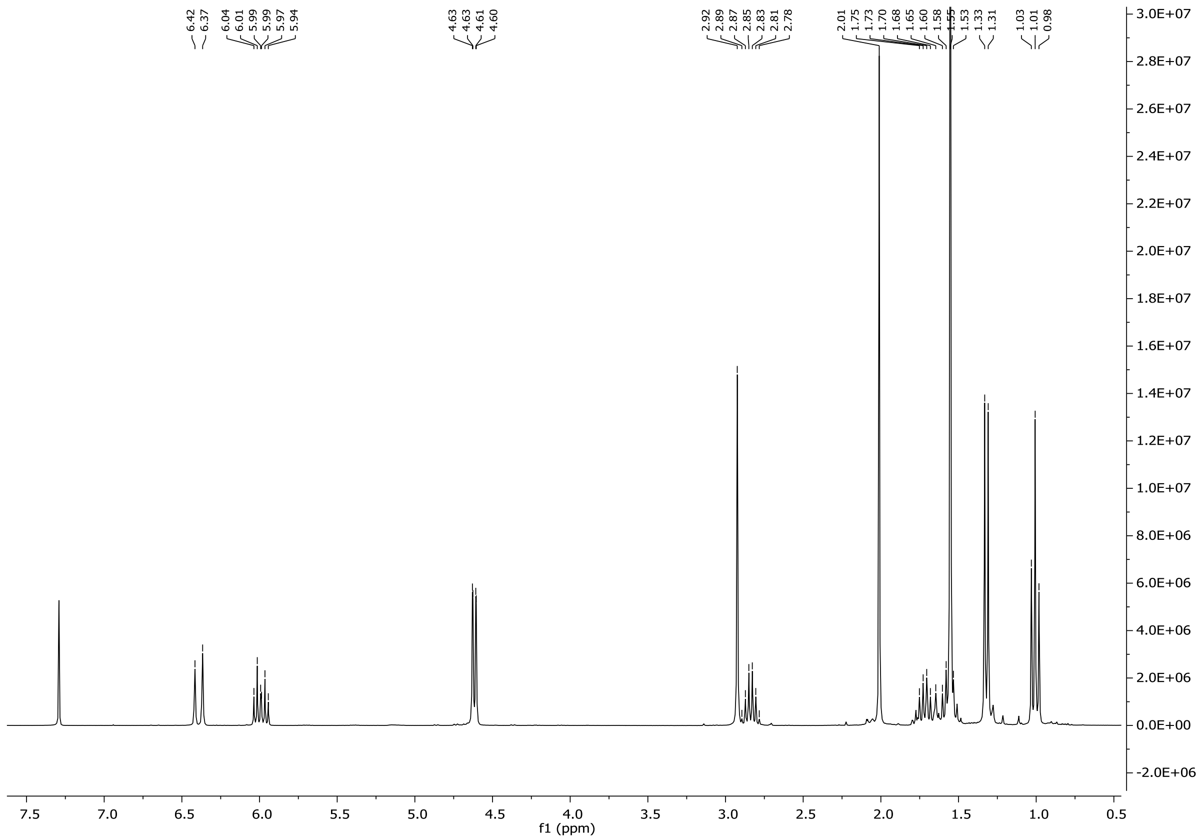
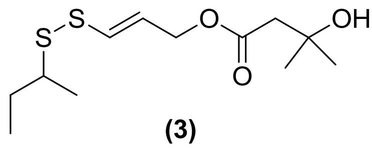


Figure S1. The [1]H-NMR spectrum of persicasulfide A.



(3)

^{1}H NMR (301 MHz, Chloroform-*d*) δ 6.32 (d, *J* = 14.8 Hz, 1H), 5.98 – 5.84 (m, 1H), 4.57 (d, *J* = 6.6 Hz, 2H), 3.40 (s, 1H), 3.24 (d, *J* = 2.9 Hz, 0H), 2.75 (h, *J* = 6.7 Hz, 1H), 2.44 (s, 2H), 1.71 – 1.40 (m, 7H), 1.23 (d, *J* = 6.6 Hz, 9H), 0.93 (q, *J* = 7.4, 6.9 Hz, 5H).

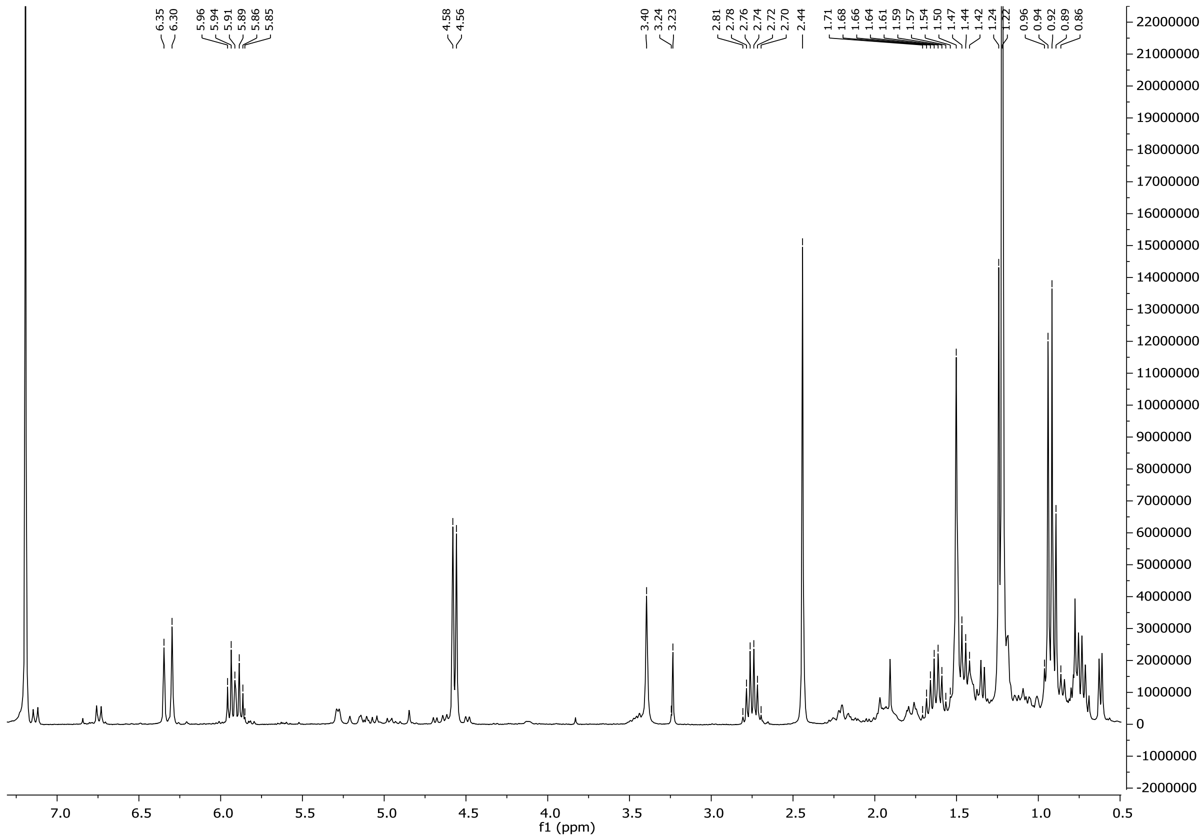
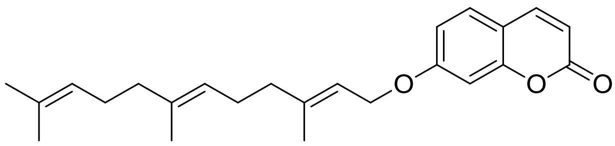


Figure S2. The ^{1}H-NMR spectrum of persicasulfide C.



(4)

^{1}H NMR (301 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 9.5 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 7.29 (s, 0H), 6.92 – 6.80 (m, 3H), 6.27 (d, *J* = 9.5 Hz, 1H), 5.49 (t, *J* = 6.2 Hz, 1H), 5.09 (dd, *J* = 9.4, 3.8 Hz, 3H), 4.63 (d, *J* = 6.6 Hz, 2H), 1.79 (s, 3H), 1.70 (s, 4H), 1.62 (s, 8H).

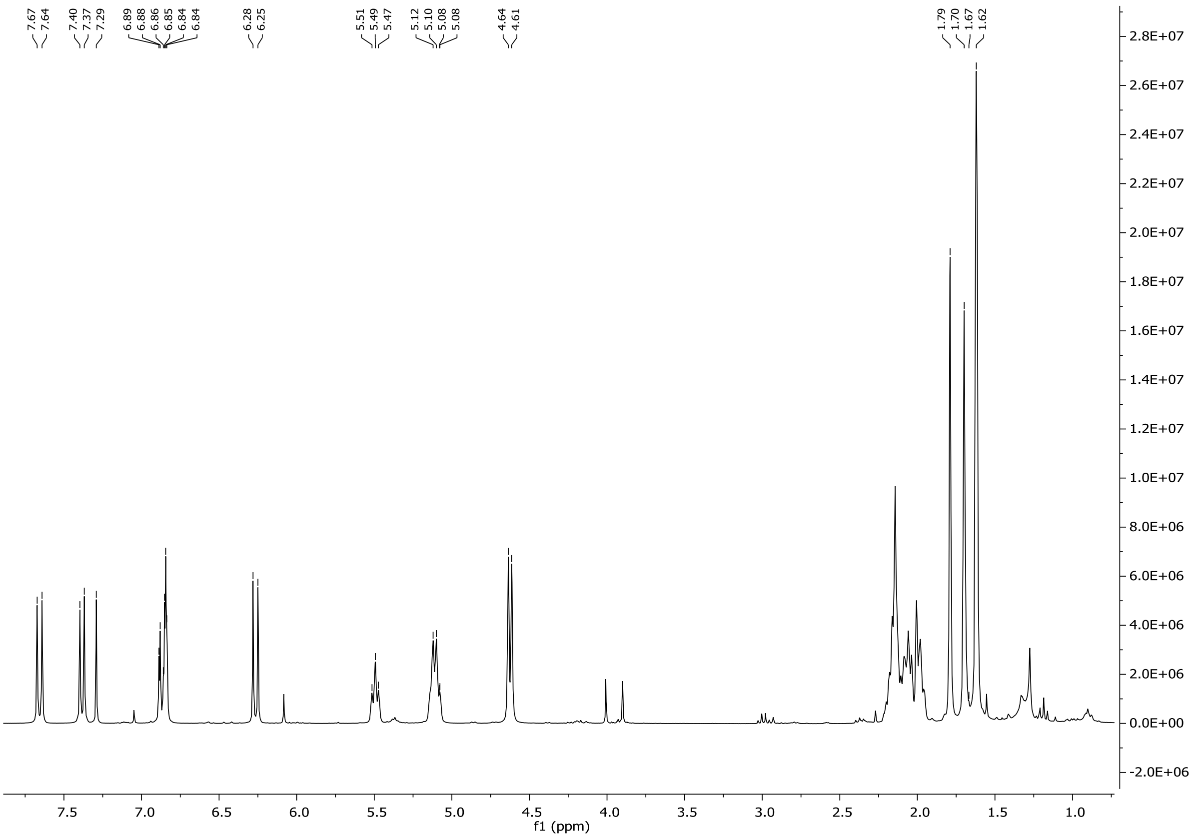
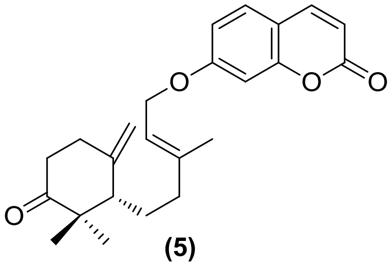


Figure S3. The ^{1}H-NMR spectrum of umbelliprenin.



(5)

^{1}H NMR (301 MHz, Chloroform-*d*) δ 7.64 (d, *J* = 9.5 Hz, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.80 (d, *J* = 2.3 Hz, 1H), 6.24 (d, *J* = 9.5 Hz, 1H), 5.42 (t, *J* = 6.0 Hz, 1H), 5.02 (s, 1H), 4.82 (s, 1H), 4.58 (d, *J* = 6.7 Hz, 2H), 2.66 – 2.58 (m, 1H), 2.48 (d, *J* = 4.1 Hz, 1H), 2.30 (dt, *J* = 13.5, 4.1 Hz, 1H), 2.14 (dd, *J* = 12.1, 3.8 Hz, 2H), 2.01 – 1.96 (m, 1H), 1.90 – 1.85 (m, 1H), 1.72 (s, 3H), 1.70 – 1.64 (m, 1H), 1.18 (s, 2H), 1.04 (s, 2H).

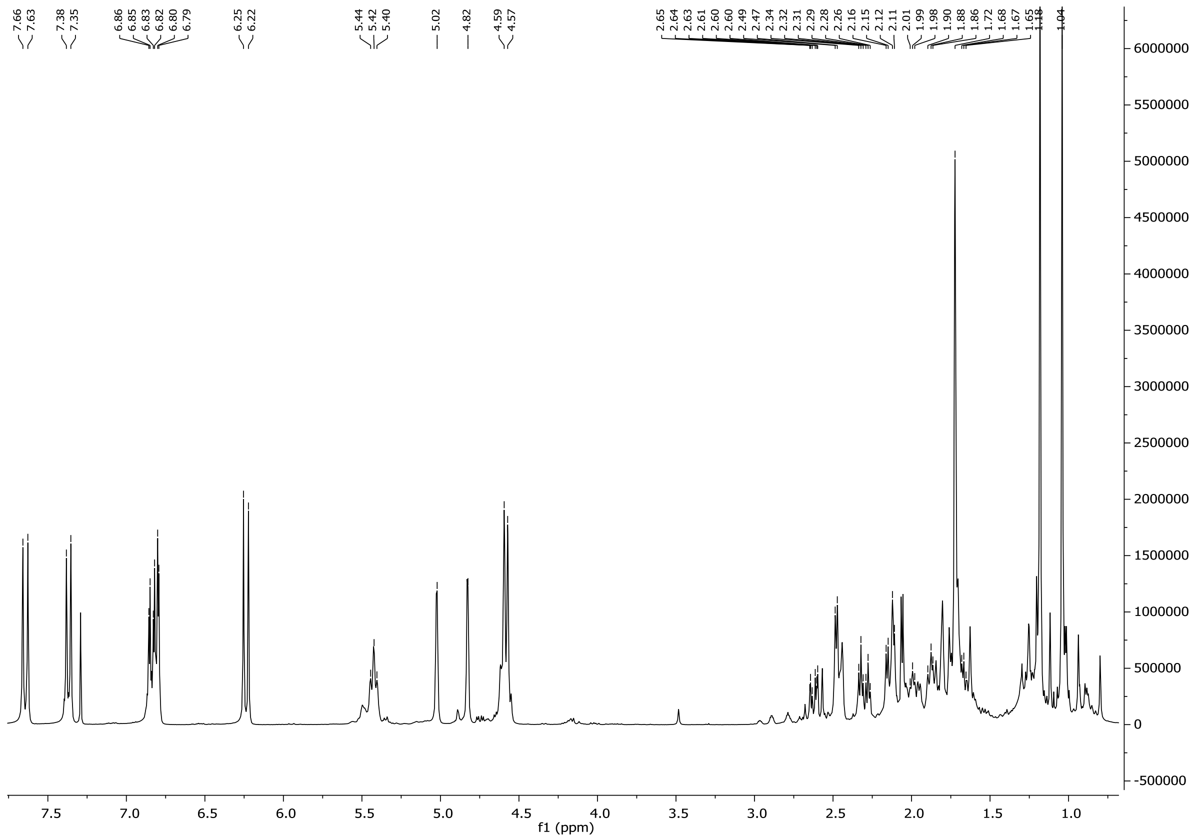
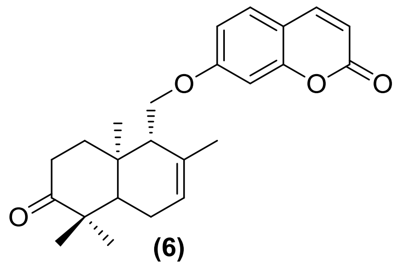


Figure S4. The ^{1}H-NMR spectrum of farnesiferone B.



(6)

^{1}H NMR (301 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 9.5 Hz, 1H), 7.39 (d, *J* = 8.4 Hz, 1H), 6.86 (d, *J* = 2.3 Hz, 1H), 6.82 (s, 2H), 6.26 (d, *J* = 9.5 Hz, 1H), 5.61 (s, 1H), 4.20 (dd, *J* = 9.9, 3.9 Hz, 1H), 4.09 (dd, *J* = 9.8, 5.3 Hz, 1H), 2.76 (td, *J* = 16.0, 14.6, 5.2 Hz, 1H), 2.37 – 2.29 (m, 3H), 2.29 (s, 2H), 2.23 – 2.07 (m, 2H), 2.01 (d, *J* = 17.3 Hz, 1H), 1.72 (s, 4H), 1.66 (dd, *J* = 8.2, 4.3 Hz, 2H), 1.15 (s, 3H), 1.14 (s, 3H), 1.10 (s, 3H).

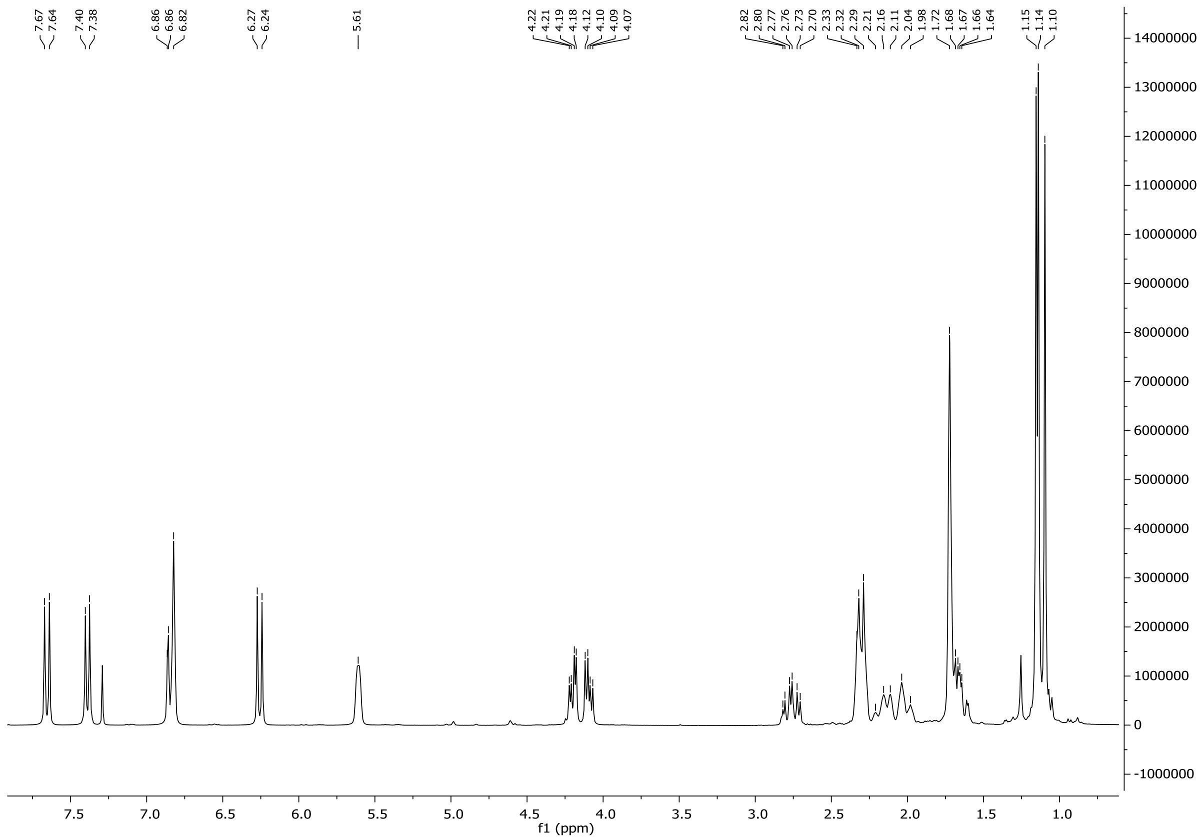
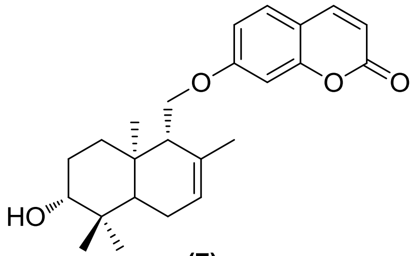


Figure S5. The ^{1}H-NMR spectrum of conferone.



(7)

[1]H NMR (301 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 9.5 Hz, 1H), 7.39 (d, *J* = 8.3 Hz, 1H), 6.87 (d, *J* = 2.2 Hz, 1H), 6.83 (s, 1H), 6.27 (d, *J* = 9.5 Hz, 1H), 5.58 (s, 1H), 4.19 (dd, *J* = 9.7, 3.2 Hz, 1H), 4.03 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.31 (dd, *J* = 10.5, 5.2 Hz, 1H), 2.25 (s, 1H), 2.06 (s, 3H), 2.03 (d, *J* = 3.4 Hz, 1H), 1.71 (s, 4H), 1.69 – 1.62 (m, 1H), 1.38 (dd, *J* = 13.2, 4.4 Hz, 1H), 1.30 (dd, *J* = 10.3, 6.0 Hz, 2H), 1.03 (s, 2H), 0.93 (s, 2H), 0.92 (s, 3H).

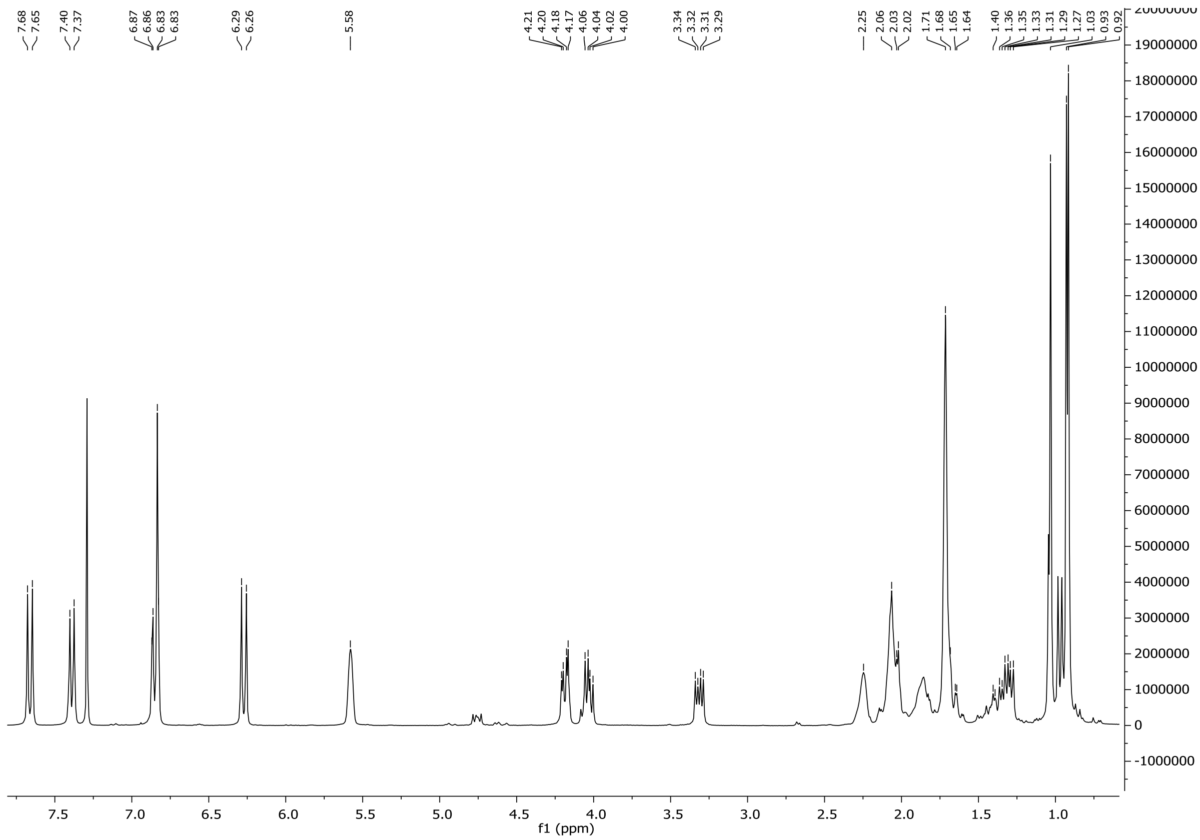
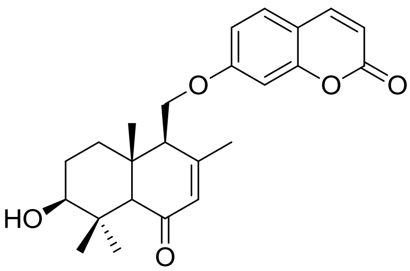


Figure S6. The ^{1}H-NMR spectrum of feselol.



(8)

^{1}H NMR (301 MHz, Chloroform-*d*) δ 7.68 (d, *J* = 9.5 Hz, 1H), 7.42 (d, *J* = 8.7 Hz, 1H), 6.88 (d, *J* = 2.3 Hz, 1H), 6.85 (s, 2H), 6.30 (d, *J* = 9.5 Hz, 1H), 5.94 (s, 1H), 4.29 (dd, *J* = 10.0, 3.0 Hz, 1H), 4.18 (dd, *J* = 10.0, 5.5 Hz, 1H), 3.28 (dd, *J* = 10.0, 5.0 Hz, 1H), 2.70 (s, 1H), 2.22 (s, 1H), 2.10 – 2.00 (m, 1H), 1.98 (s, 3H), 1.78 – 1.71 (m, 2H), 1.70 – 1.59 (m, 2H), 1.31 (s, 3H), 1.21 (s, 3H), 1.06 (s, 3H).

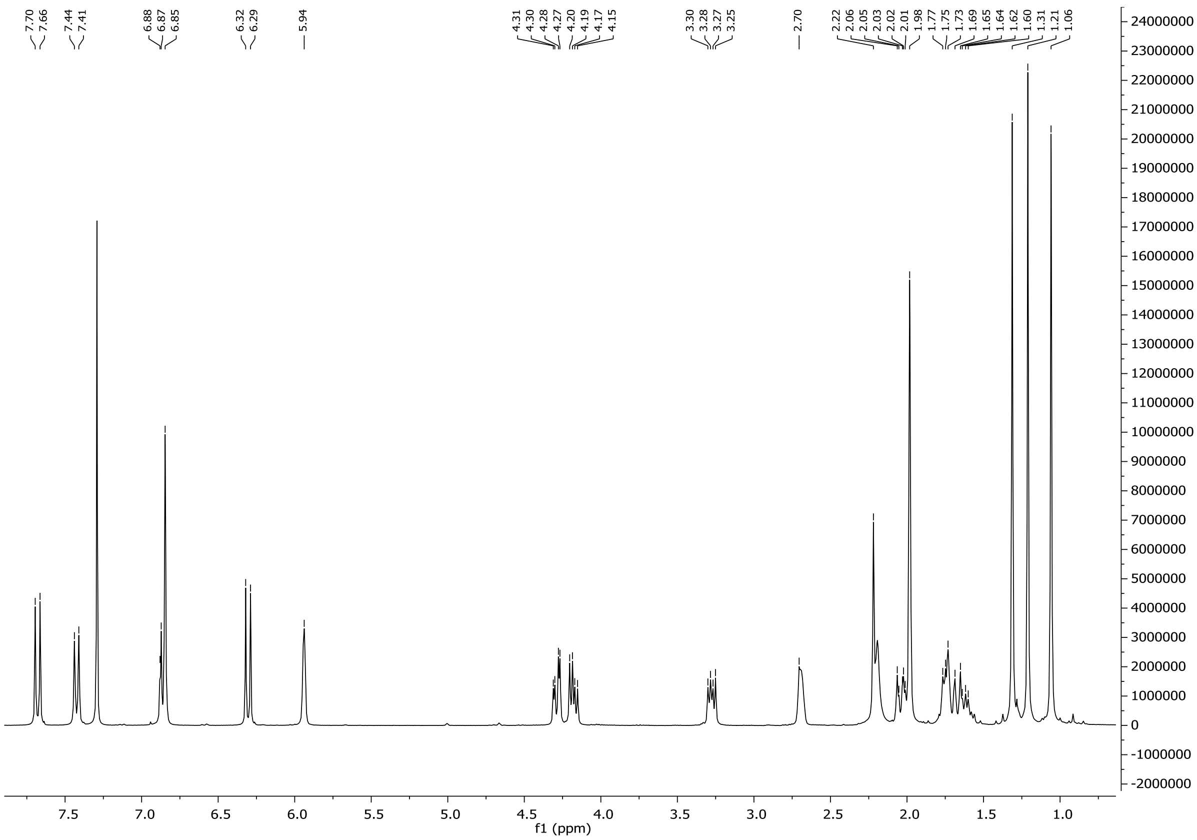
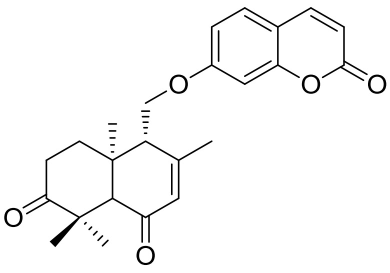


Figure S7. The ^{1}H-NMR spectrum of ligupersin A.



(9)

[1]H NMR (301 MHz, Chloroform-*d*) δ 7.67 (d, *J* = 9.5 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H), 6.88 (d, *J* = 2.4 Hz, 1H), 6.85 (s, 1H), 6.28 (d, *J* = 9.5 Hz, 1H), 6.01 – 5.94 (m, 2H), 4.33 (dd, *J* = 10.2, 3.3 Hz, 1H), 4.25 (dd, *J* = 10.2, 5.0 Hz, 1H), 2.84 (td, *J* = 15.5, 14.9, 5.9 Hz, 1H), 2.54 (s, 1H), 2.01 (s, 4H), 1.90 (td, *J* = 14.1, 13.2, 4.6 Hz, 2H), 1.45 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H).

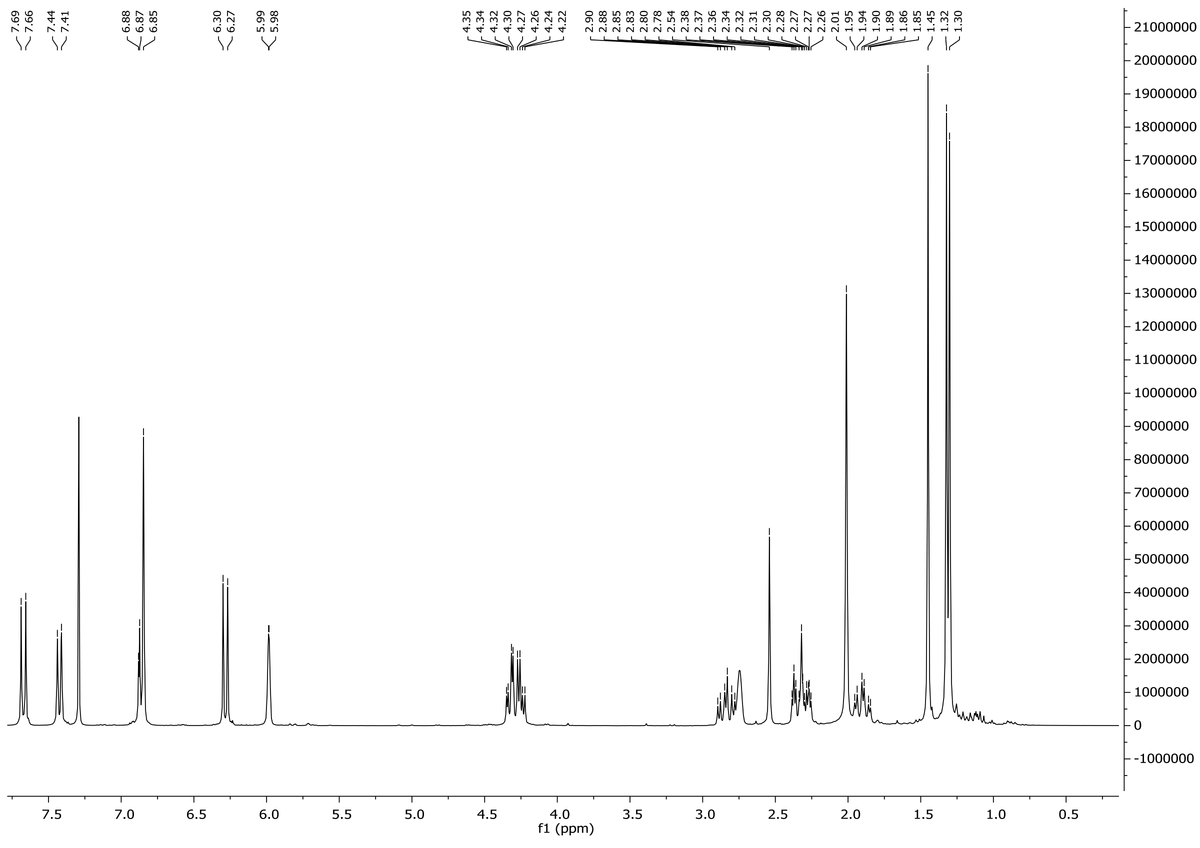
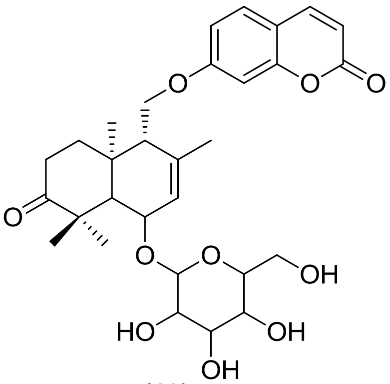


Figure S8. The ^{1}H-NMR spectrum of conferdione.



(10)

^{1}H NMR (301 MHz, DMSO-d_6) δ 7.99 (d, *J* = 9.5 Hz, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.12 (d, *J* = 2.2 Hz, 0H), 7.07 (d, *J* = 2.2 Hz, 1H), 6.95 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.29 (d, *J* = 9.5 Hz, 1H), 5.72 (s, 1H), 4.52 (s, 1H), 4.47 (s, 1H), 4.44 (s, 1H), 4.29 (dd, *J* = 10.4, 2.9 Hz, 2H), 4.14 – 4.10 (m, 1H), 3.72 (dd, *J* = 10.1, 4.8 Hz, 2H), 3.42 (s, 2H), 3.19 (s, 3H), 3.17 (s, 3H), 3.06 (dd, *J* = 8.9, 4.5 Hz, 2H), 2.95 (td, *J* = 8.3, 5.4 Hz, 2H), 2.61 (td, *J* = 15.2, 5.6 Hz, 2H), 2.31 (s, 2H), 2.30 (s, 1H), 2.28 (s, 0H), 2.26 – 2.22 (m, 1H), 2.20 – 2.11 (m, 2H), 1.84 (d, *J* = 10.2 Hz, 1H), 1.72 (s, 4H), 1.64 (dd, *J* = 13.3, 4.9 Hz, 2H), 1.28 (s, 4H), 1.26 (s, 3H), 1.02 (s, 3H).

(10)

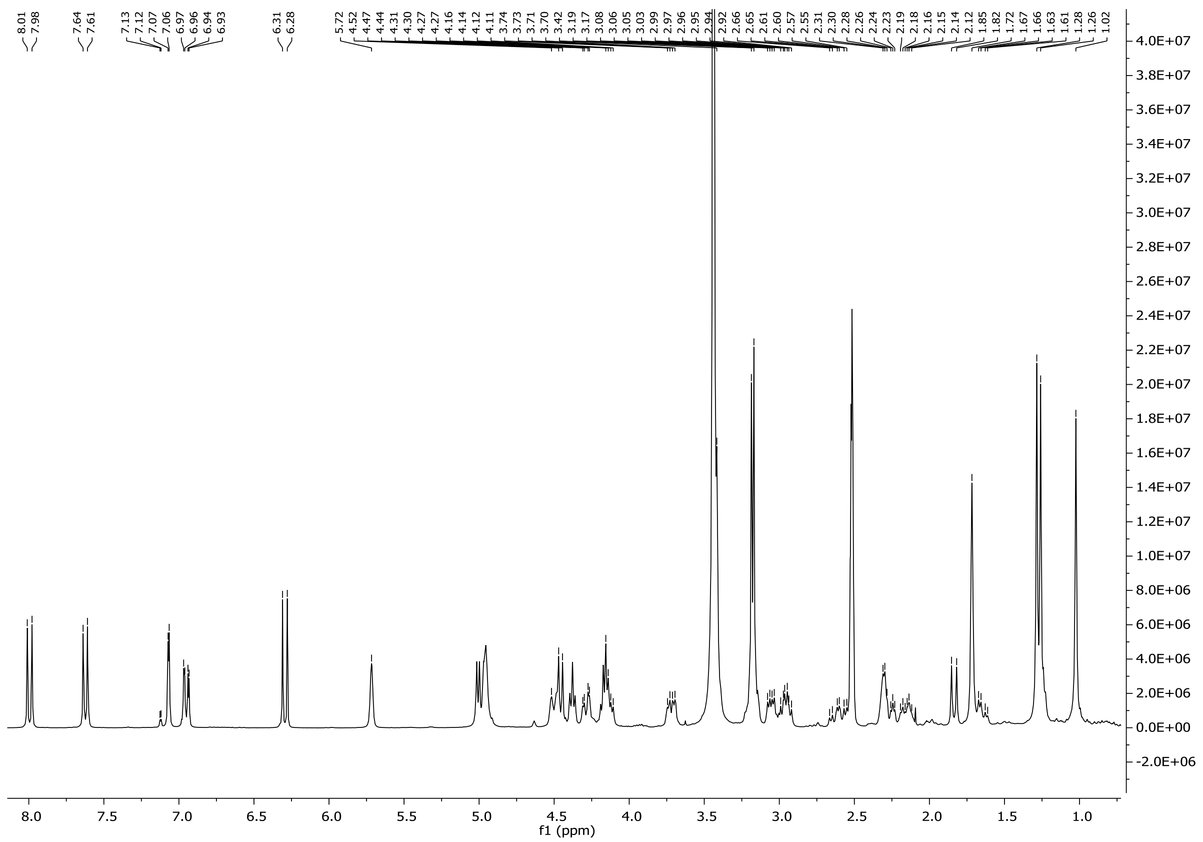
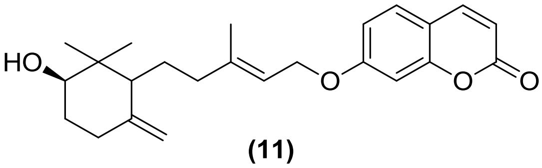


Figure S9. The ^{1}H-NMR spectrum of conferoside.



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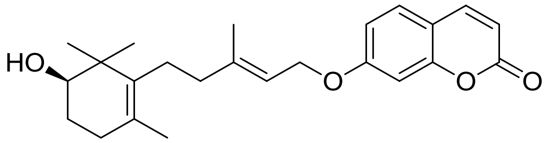


(12)

[1]H NMR (301 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 9.5 Hz, 1H), 7.38 (d, *J* = 8.5 Hz, 1H), 7.29 (s, 0H), 6.86 (ddd, *J* = 11.8, 5.9, 2.6 Hz, 3H), 6.26 (d, *J* = 9.5 Hz, 1H), 4.89 (s, 1H), 4.62 (d, *J* = 7.0 Hz, 3H), 2.16 (d, *J* = 10.6 Hz, 2H), 1.79 (d, *J* = 7.3 Hz, 3H), 1.66 (d, *J* = 10.4 Hz, 4H), 1.10 (s, 1H), 1.04 (s, 3H), 0.75 (s, 2H).

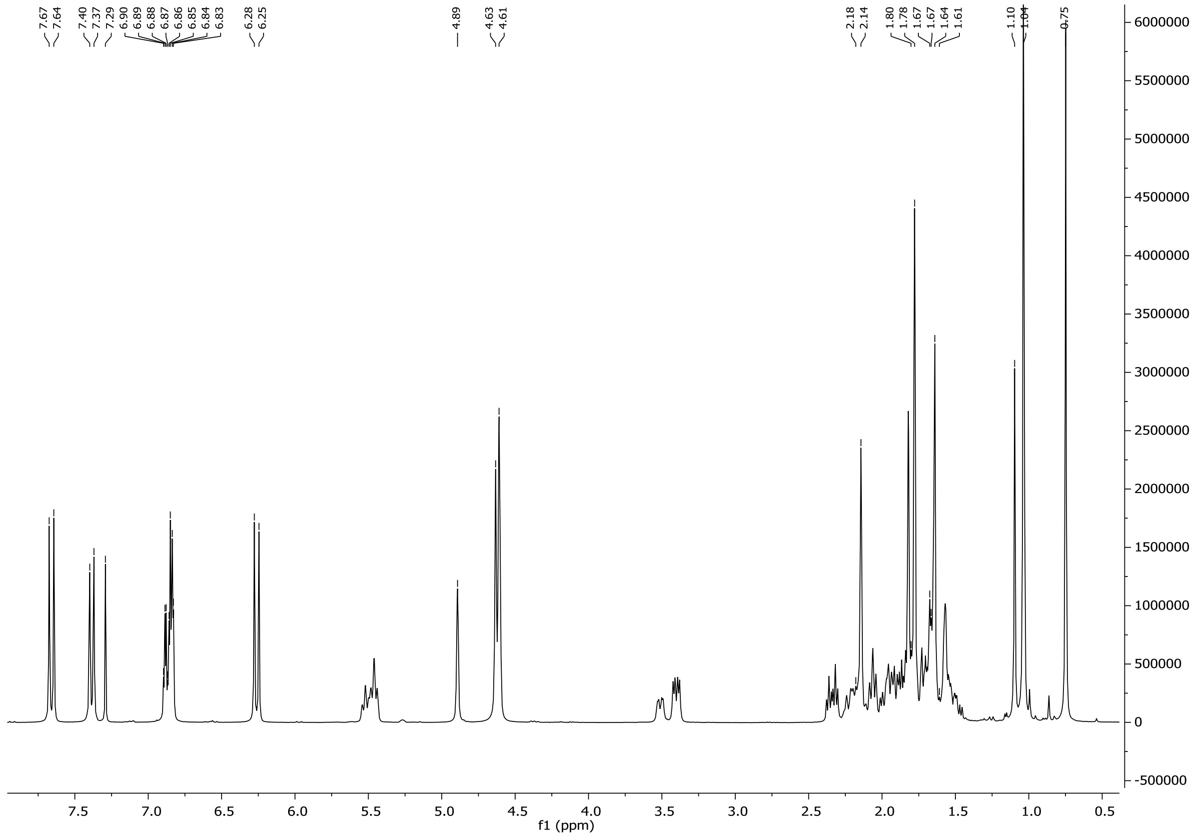
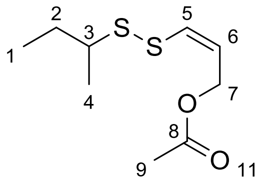


Figure S10. The ^{1}H-NMR spectrum of farnesiferol B and lehmferin.



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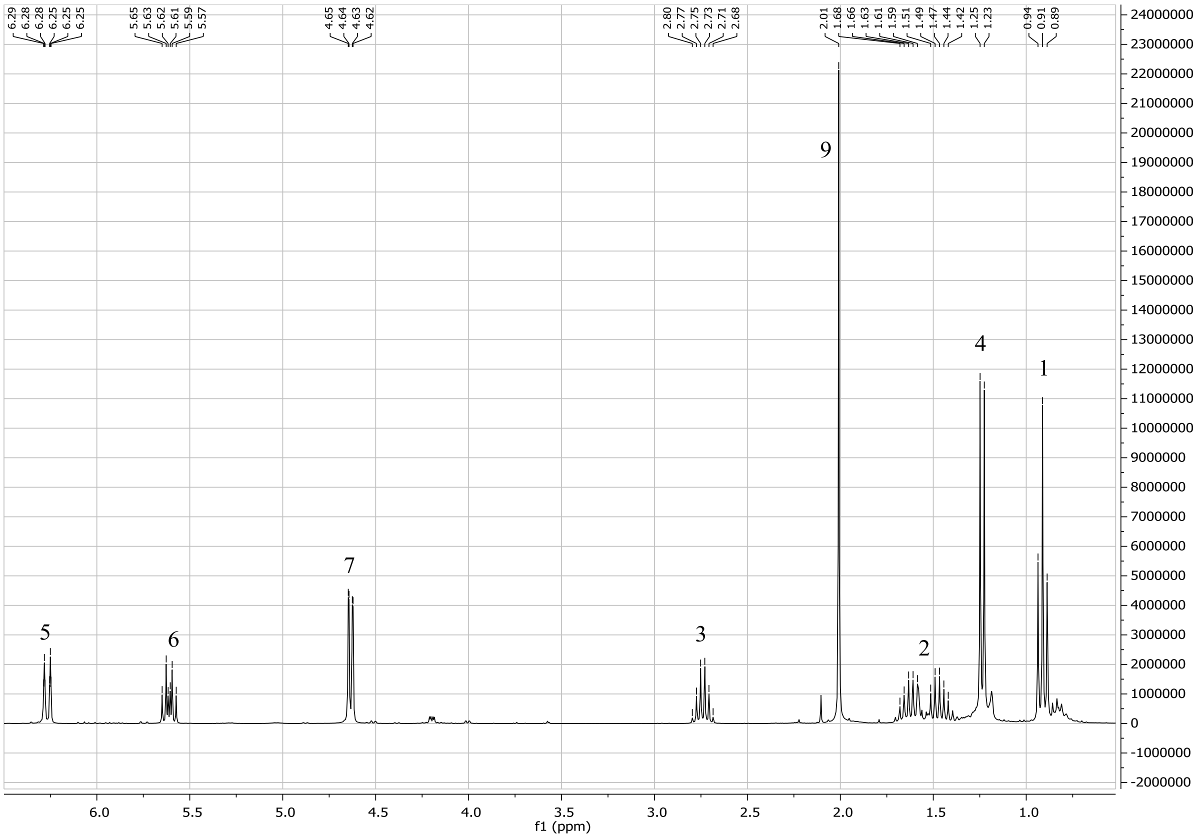
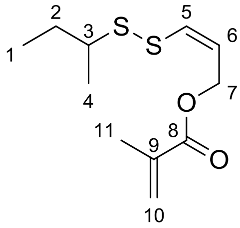


Figure S11. The ^{1}H-NMR spectrum of latisulfide A.



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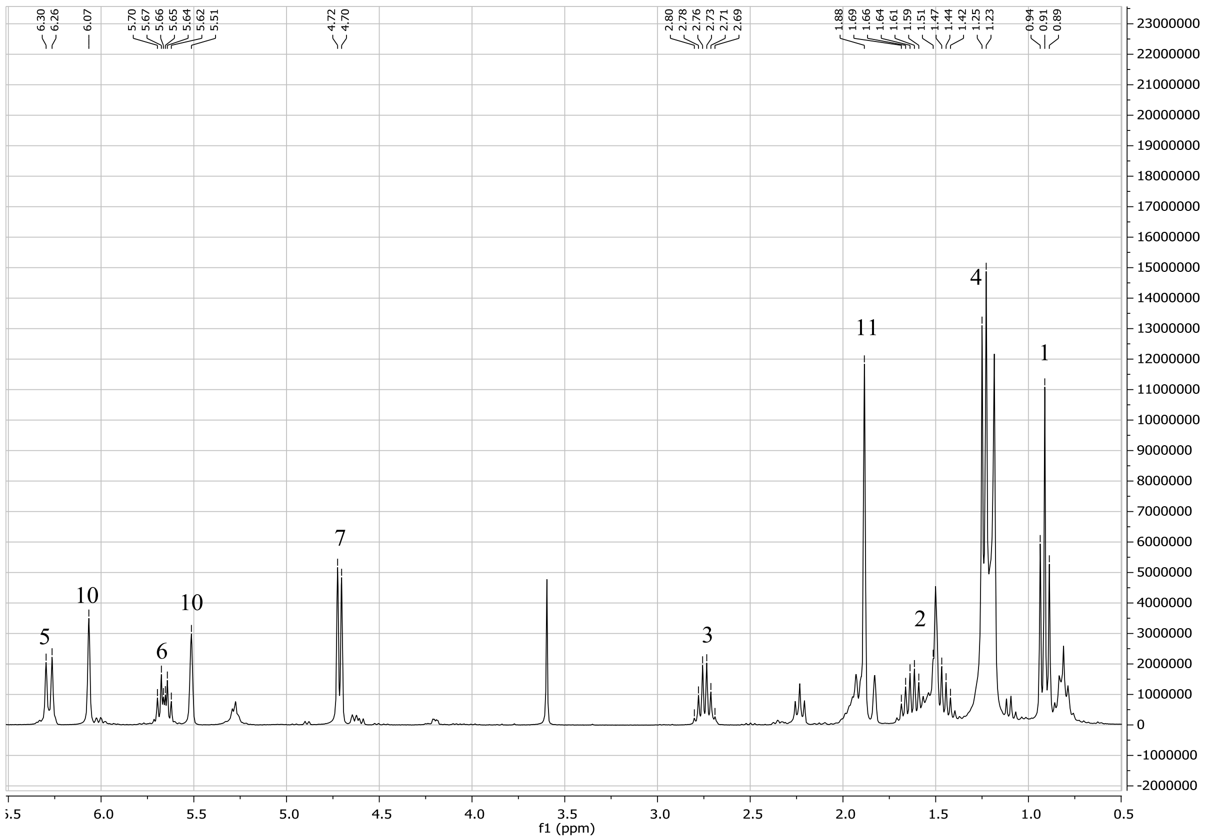
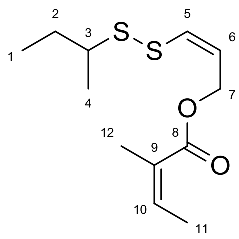


Figure S12. The ^{1}H-NMR spectrum of latisulfide B.



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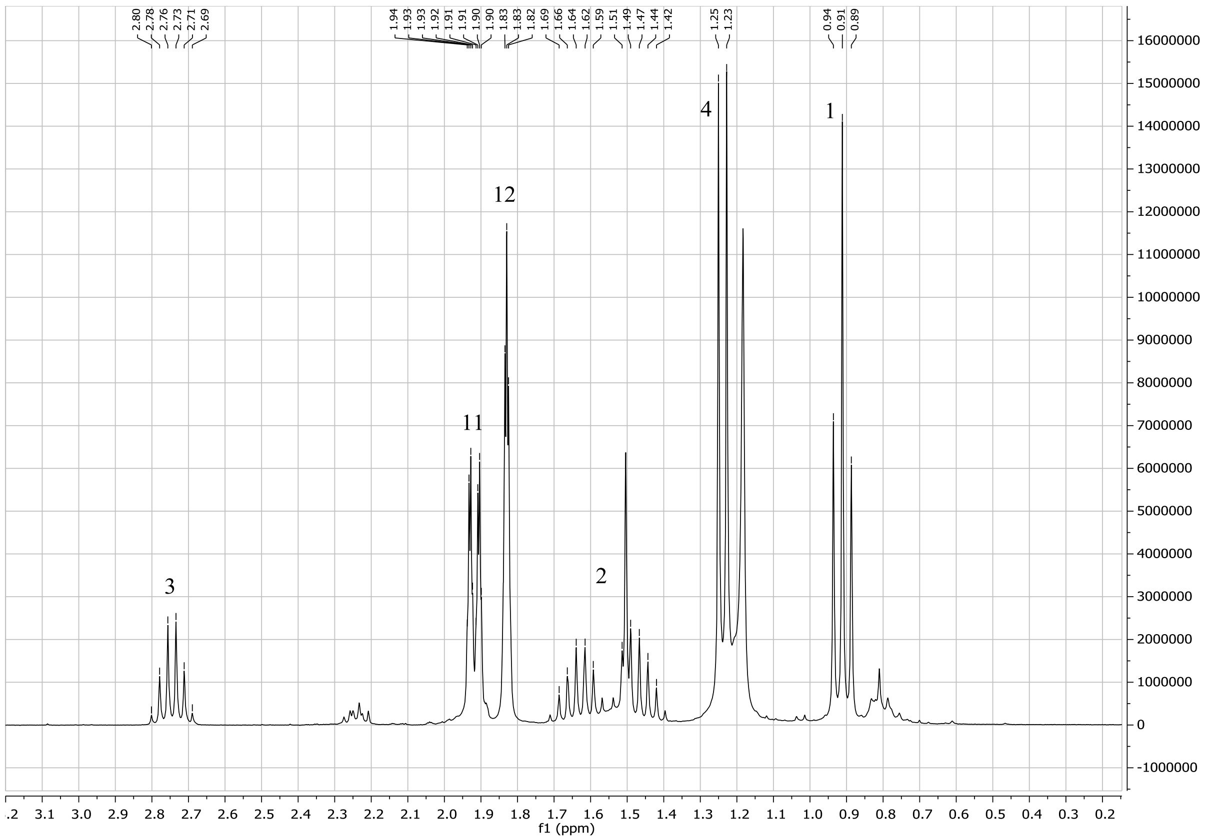


Figure S13. The ^{1}H-NMR spectrum of latisulfide C- expanded 1.

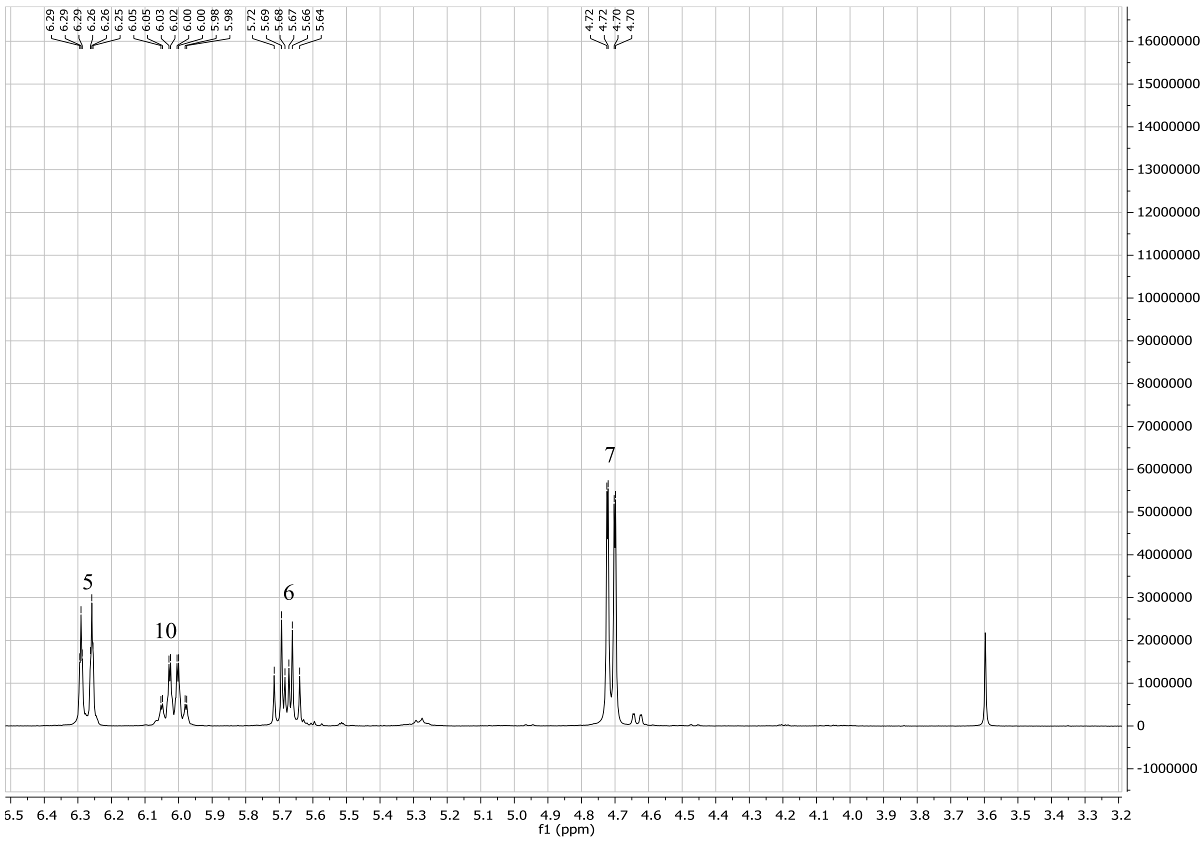
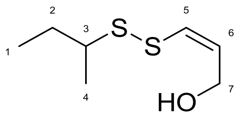


Figure S14. The [1]H-NMR spectrum of latisulfide C- expanded 2.



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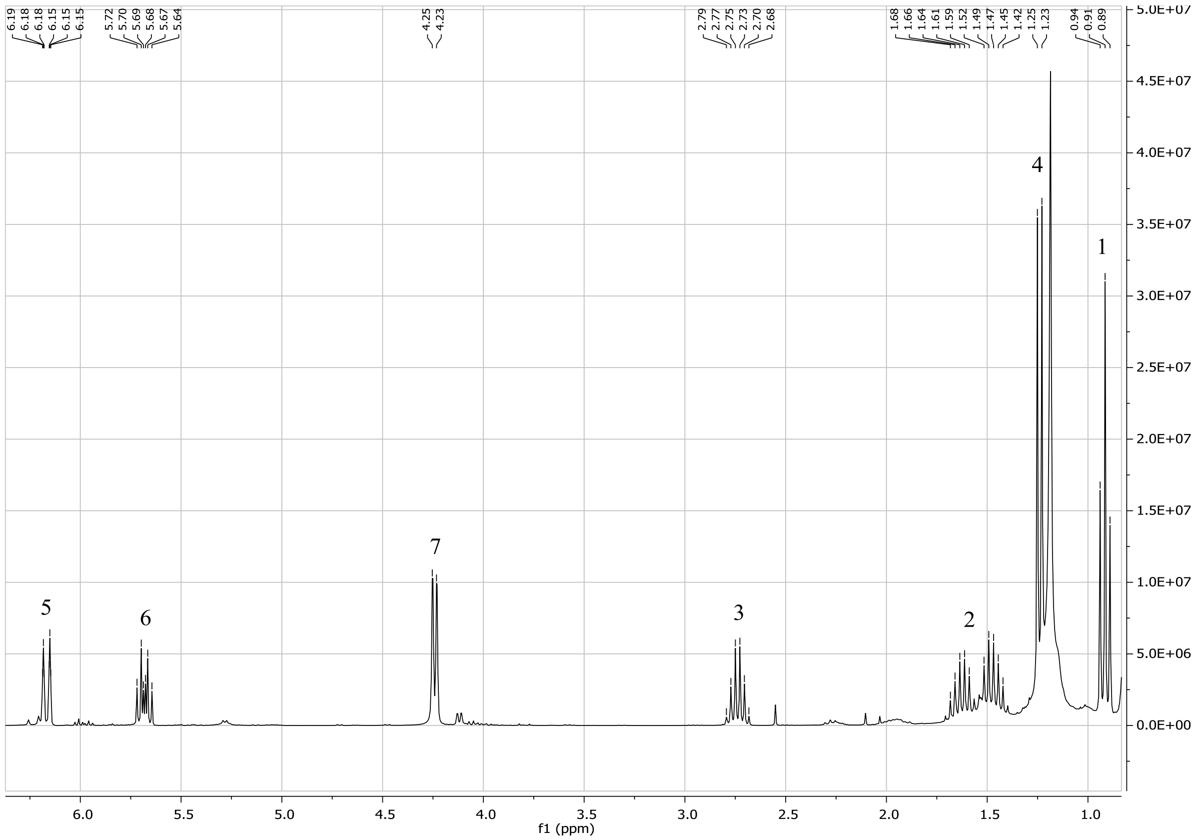
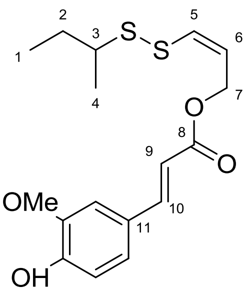


Figure S15. The ^{1}H-NMR spectrum of latisulfide D.



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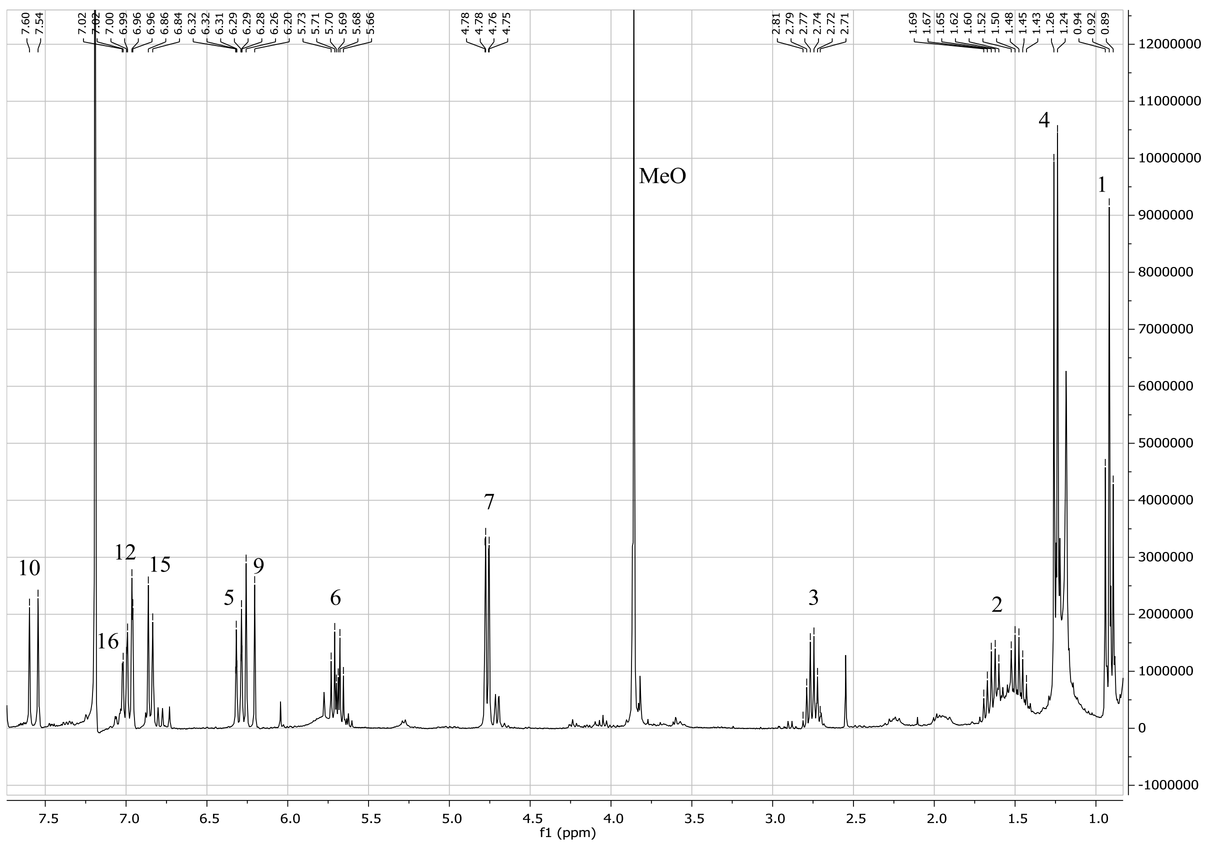
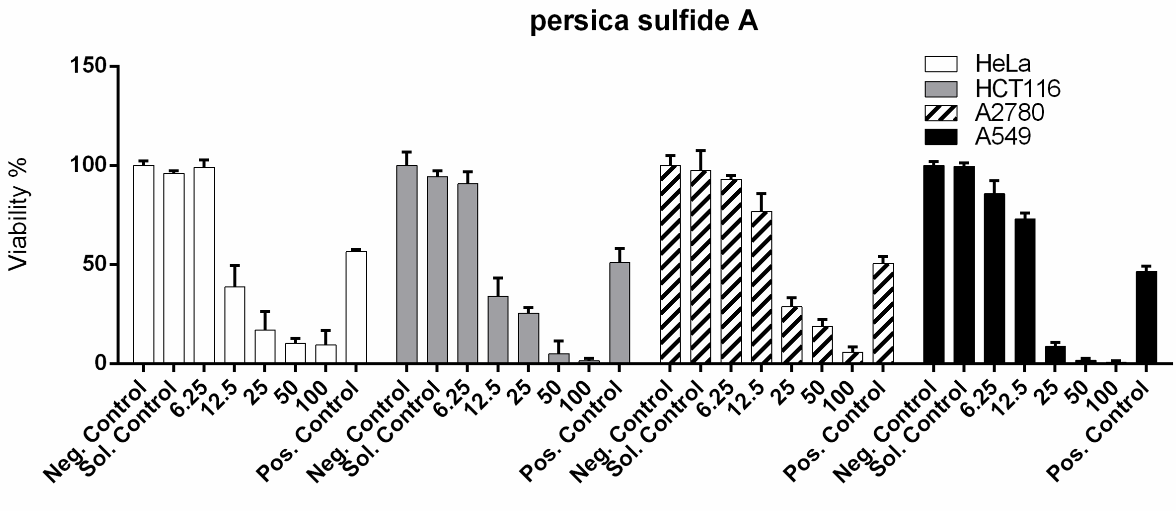


Figure S16. The 1H-NMR spectrum of latisulfide E.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A549
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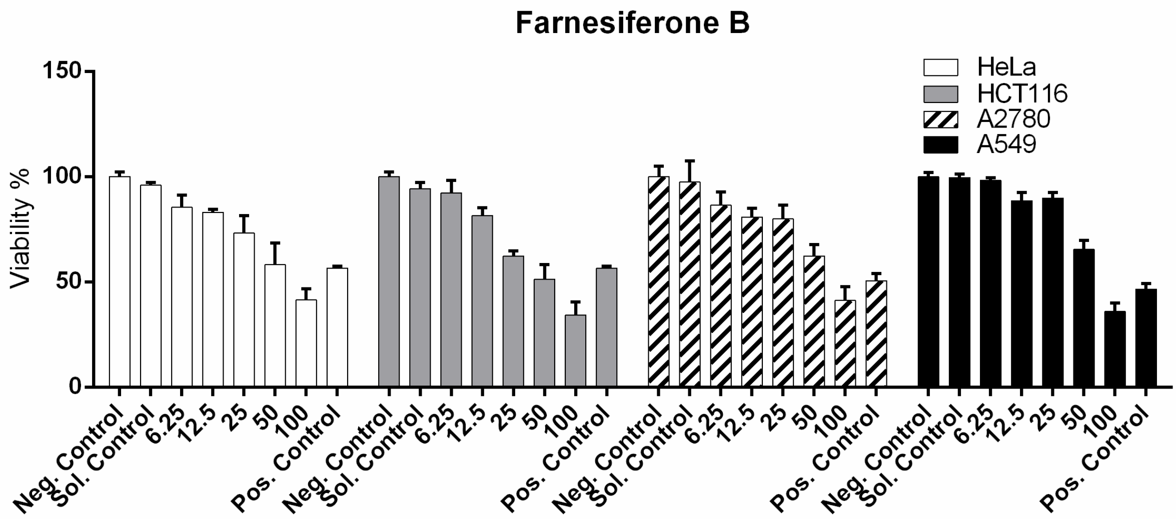
Sol. Control
6.25
12.5
25
50
100
Pos. Control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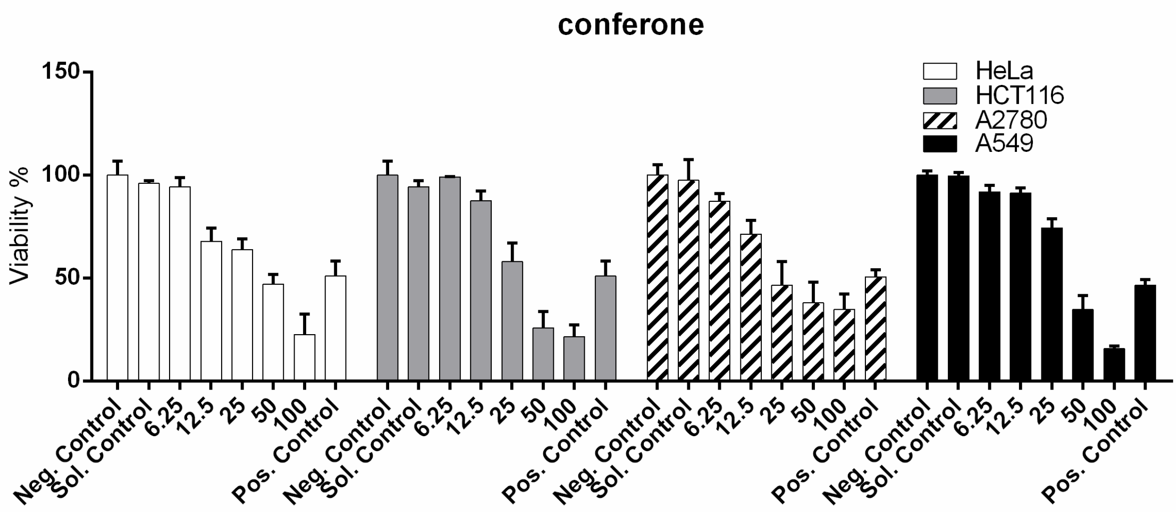
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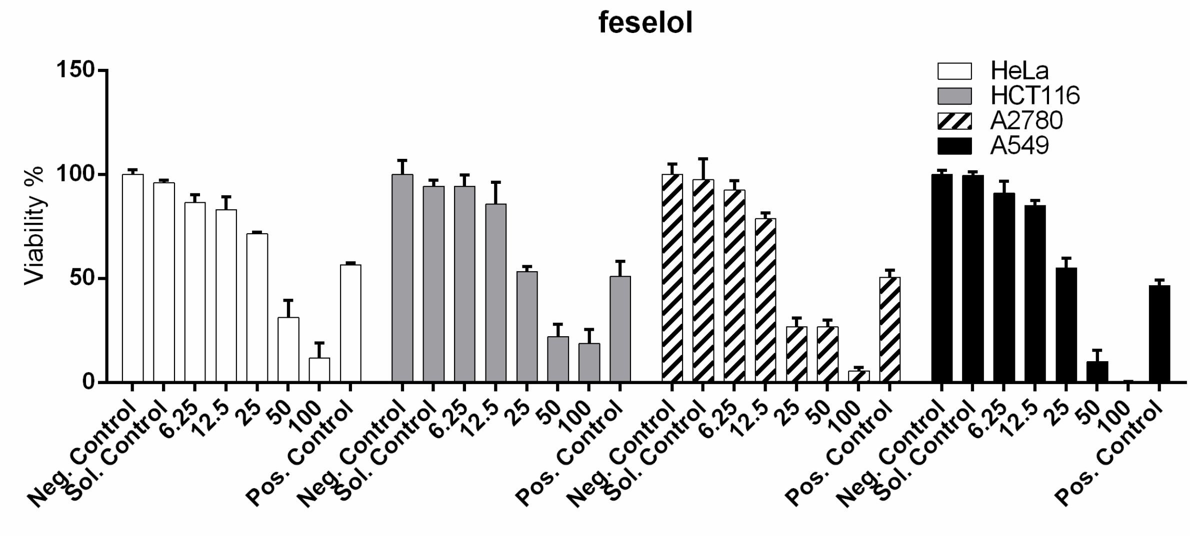
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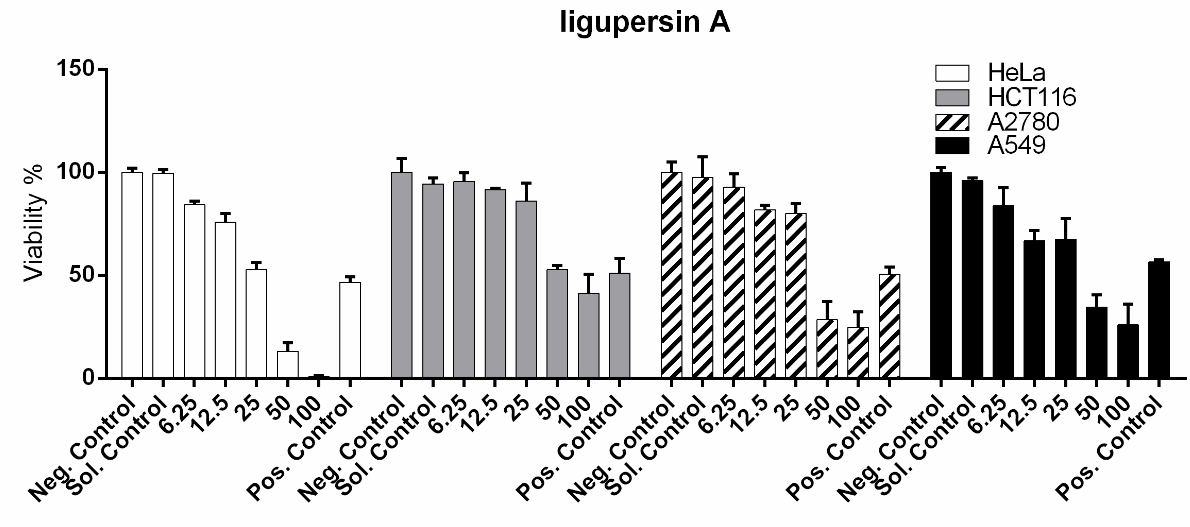
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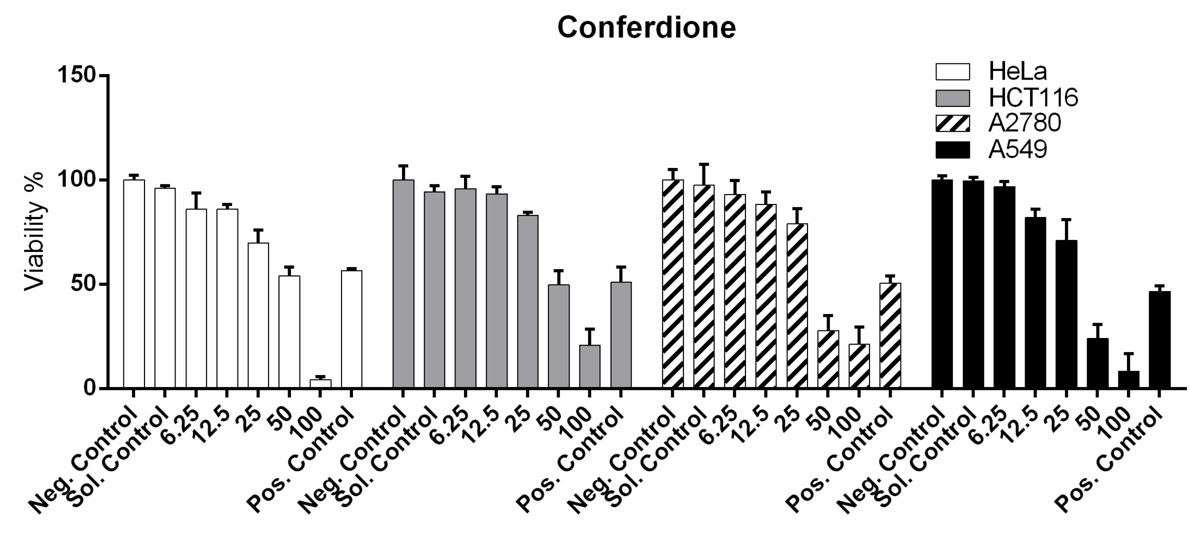
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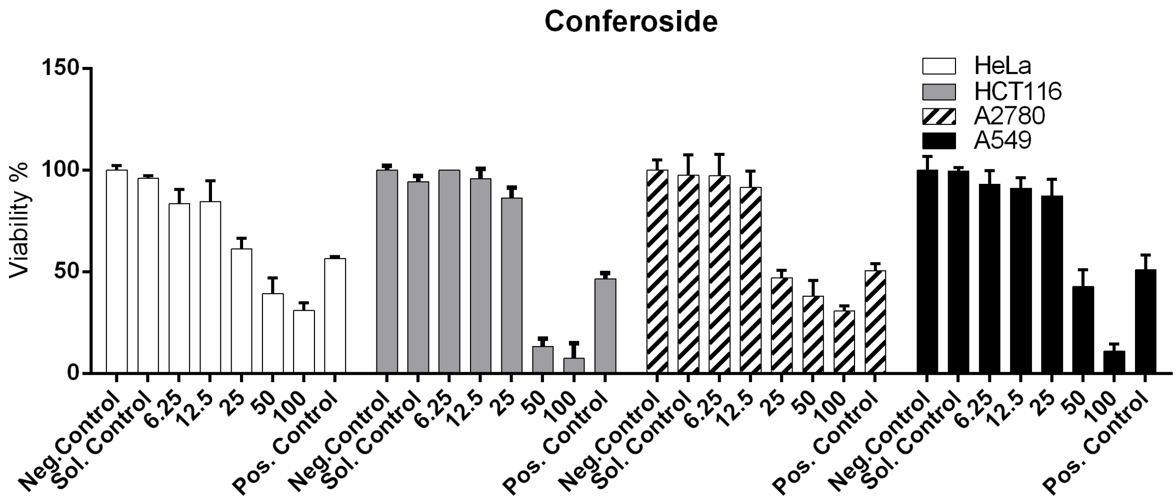
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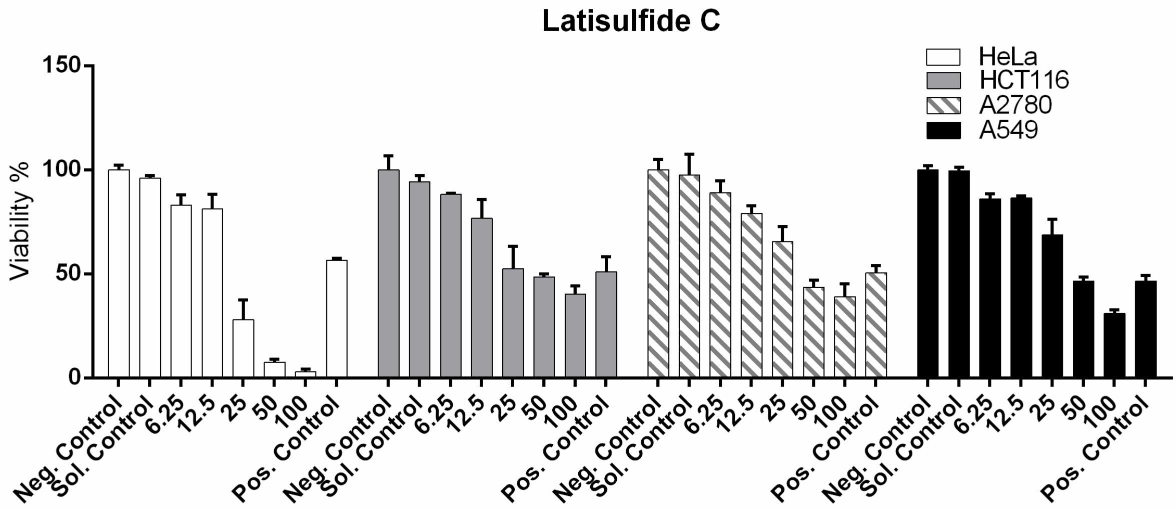
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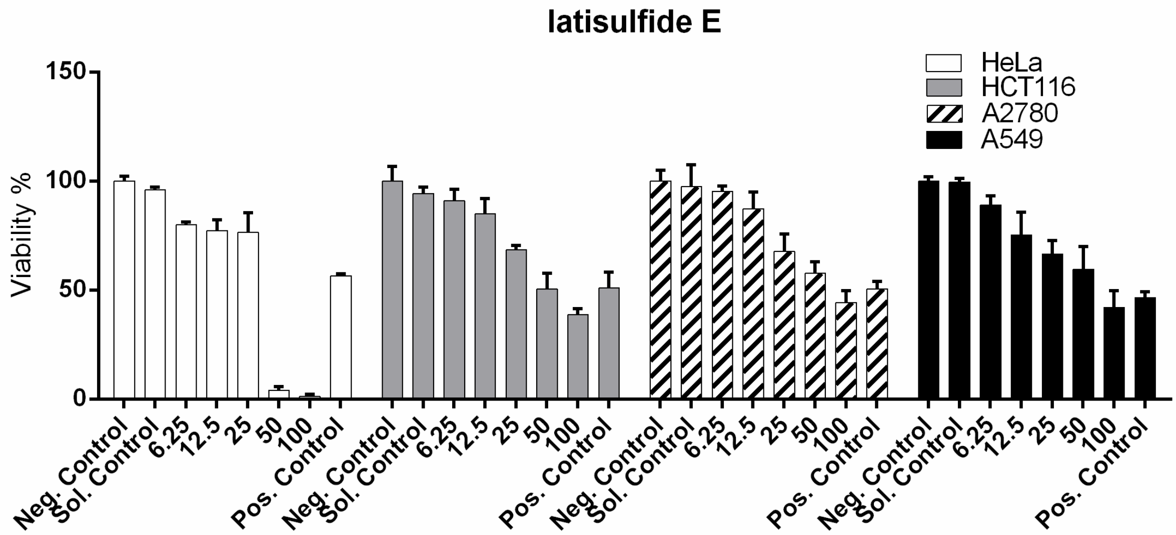
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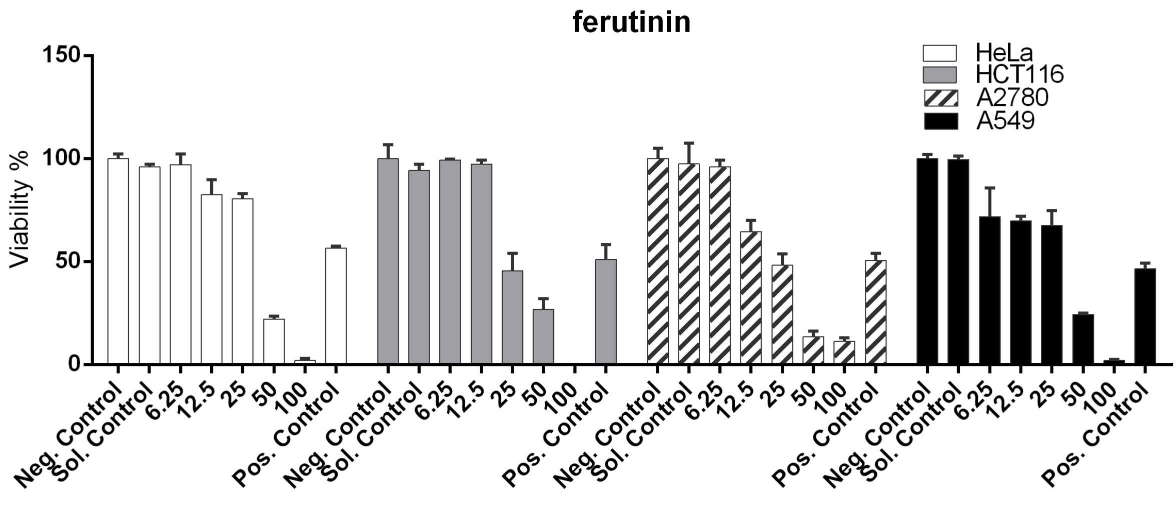
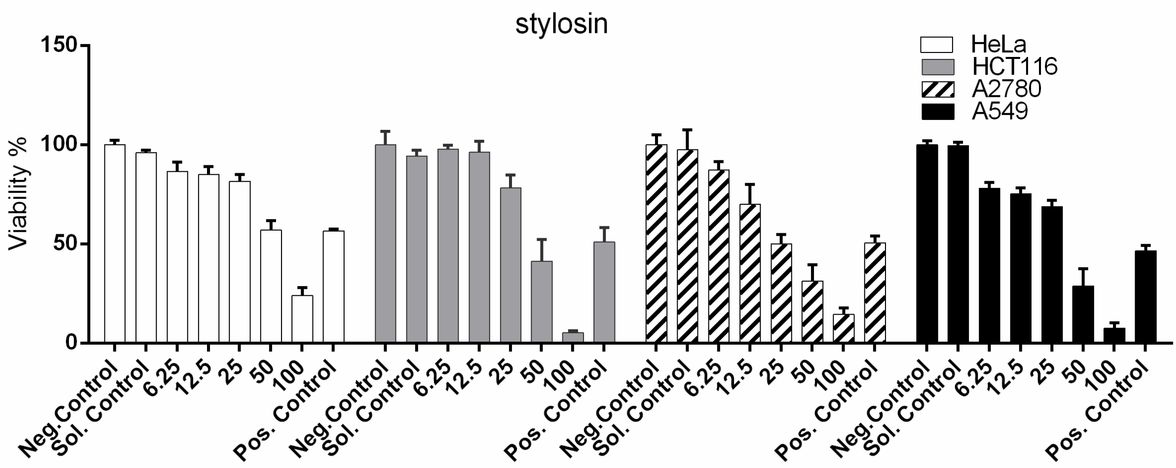
100
Pos. Control


ferutinin
Viability %
HeLa
HCT116
A2780
A549
Neg. Control
Sol. Control
Pos. Control


stylosin
Viability %
HeLa
HCT116
A2780
A549
Neg.Control
Sol. Control
Pos. Control

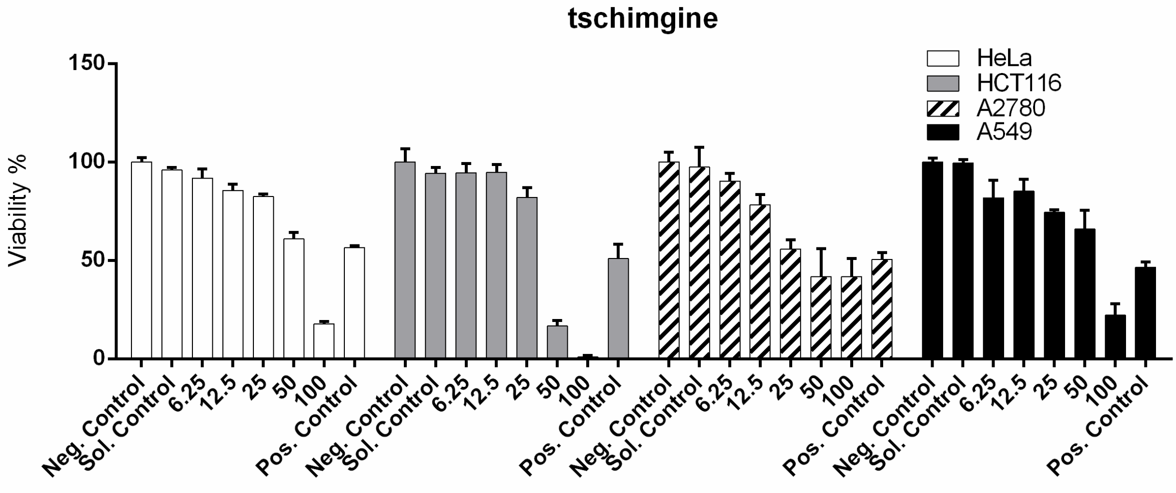

tschimgine
Viability %
HeLa
HCT116
A2780
A549
Neg. Control
Sol. Control
Pos. Control

Figure S17. Dose-dependent growth inhibition of HeLa, HCT116, A2780 and A549 cells by test compounds (6.25–100 µM) after 48 h. Viability was quantitated by AlamarBlue assay. Vorinostat was used as a positive control. Results are mean ± SD (n = 3).

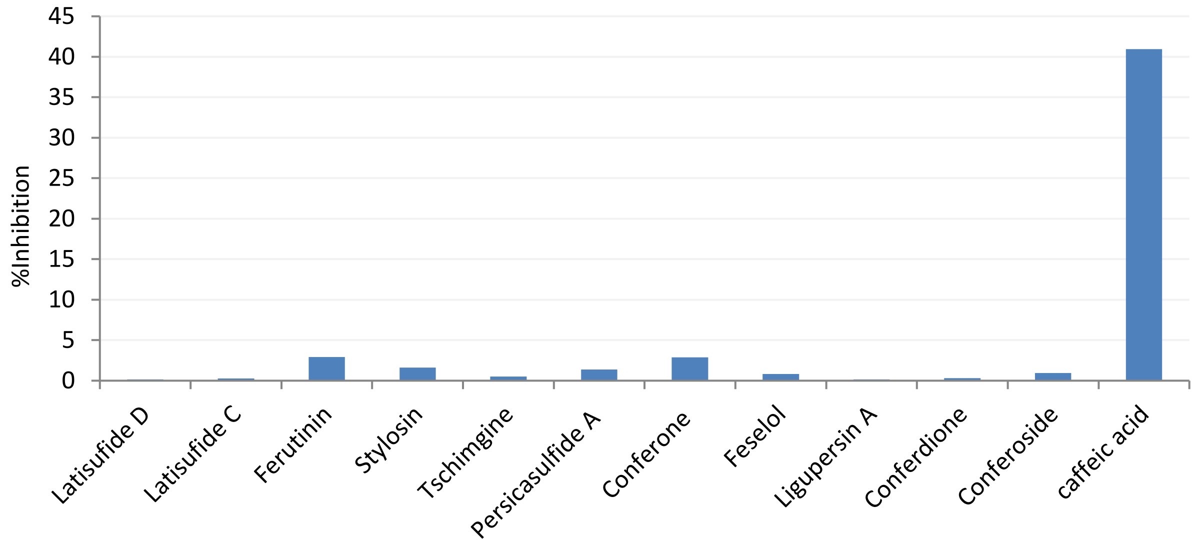


Figure S18. Trypsin inhibition of test compounds in the trypsin inhibitory assay at a maximum concentration of 70 µM.

Table S1. ^{1}H and ^{13}C NMR spectral data and coupling constants (in Hz) of ferutinin (18), stylosin (19) and tschimgine (20) (600 MHz in chloroform-d, δ, J in Hz).

	Ferutinin (18)		**Stylosin (19)**		**Tschimgine (20)**	
No.	^{13}C	^{1}H NMR	^{13}C	^{1}H NMR	^{13}C	^{1}H NMR
1	44.0	-	86.5	4.61 s	81.0	5.13 brd (9)
2	41.2	1.28 m 1.57 dd (12, 9)	39.8	-	49.1	-
3	31.4	1/65 m 1/97 m	48.4	1.80 brs	36.9	1.16 dd (13.8, 3) 2.51 m
4	87.0	-	41.4	1.26 1.68 brd (10.2)	28.1	1.33 m 1.82 m
5	60.1	2.03 d (10.8)	48.6	-	44.6	1.76 t
6	71.2	5.28 ddd (2.4, 10.8, 10.8)	26.9	1.24 1.94 m	27.4	1.43 m 2.15 m
7	41.4	2.30 dd (14.5, 3) 2.57 dd	25.9	1.54 m 1.80	47.8	-

		(10, 14.5)				
8	133.5	-	29.7	1.13 s	19.7	0.95 s
9	125.2	5.58 brm	19.5	0.87 s	18.8	0.98 s
10	40.9	1.96 m 2.07 m	29.7	1.20 s	13.1	0.96 s
11	37.0	1.95 m	-	-	-	-
12	17.5	0.96 d (6.6)	-	-	-	-
13	18.5	0.87 d (6.6)	-	-	-	-
14	26.3	1.84 s	-	-	-	-
15	20.2	1.12 s	-	-	-	-
1'	-	-	166.7	-	168.0	-
2'	-	-	122.8	-	122.2	-
3'	-	7.93 d (9)	111.8	7.61 d	131.9	8.01 d (8.4)
4'	-	6.91 d (9)	146.2	-	115.4	6.99 d (8.4)
5'	-	-	149.9	-	161.0	-
6'	-	6.91 d (9)	114.0	6.97 d (8.4)	115.4	6.99 d (8.4)
7'	-	7.93 d (9)	123.9	7.68 d (8.4)	131.9	8.01 d (8.4)
MeO	-	-	56.0	3.97 s	3.86 s	-