Euphosantianane A-D: AntiproliferativePremyrsinaneDiterpenoids from the Endemic Egyptian Plant

Euphorbia sanctae-catharinae

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S82. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 10 serial dilutions as mentioned at the *Experimental* section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnifictaion=150×.

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Total magnification=150×.

S86. Photomicrographs showing morphological changes of A549 cells following 48 h exposure to serial dilutions of doxorubicin HCl as mentioned at the Materials and Methods section. Morphological signs of cytotoxicity include cell rounding, shrinking and complete loss of monolayer integrity compared to vehicle control. Total magnification=150×.

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S2. ¹³C NMR (150 MHz, CDCl₃) spectrum of 1





S2. ¹³C NMR (150 MHz, CDCl₃) spectrum of 1

S3. DEPT (150 MHz, CDCl₃) spectra of 1





S4. ¹H ¹H COSY spectrum of **1** in CDCl₃



S5.. HMBC spectrum of 1 in CDCl₃



S5.. HMBC spectrum of 1 in CDCl₃



S5. HMBC spectrum of 1 in CDCl₃

S6. HSQC spectrum of 1 in CDCl₃







S8. LR-EI-MS of 1



S9. . HR-EI-MS of 1

Note : 3-NOBA, CHCl3+NaIaq.
Inlet : DirectIon Mode : FAB+
Scan#: 3RT : 0.60 minScan#: 3Elements : C 34/0, H 60/0, O 12/0, Na 1/0
Mass Tolerance: 1000ppm, 3mmu if m/z < 3, 5mmu if m/z > 5Unsaturation (U.S.) : -0.5 - 30.0Observed m/z Int%Err[ppm / mmu]
+0.5 / +0.3U.S. Composition
9.5 C 34 H 50 O 12 Na

673.3203 10.7 +0.5 / +0.3 9.5 C 34 H 50 O 12 Na







S10. ¹H NMR (600 MHz, CDCl₃) spectrum of 2







S11. 13 C NMR (150 MHz, CDCl₃) spectrum of **2**





S13. ¹H ¹H COSY spectrum of **2** in CDCl₃



S13. ¹H ¹H COSY spectrum of **2** in CDCl₃



S14. HMBC spectrum of 2 in CDCl₃



S14. HMBC spectrum of 2 in CDCl₃



S14. HMBC spectrum of **2** in CDCl₃



S15. HMQC spectrum of 2 in CDCl₃






S16. HMQC spectrum of 2 in CDCl₃





S17, . LR-EI-MS of 2



728.3394

0.0006

Note : 3-NOBA, CHCl3+NaIaq. Inlet : Direct Ion Mode : FAB+ RT : 0.30 min Scan#: 2 Elements : C 38/0, H 60/0, O 12/0, Na 1/0 Mass Tolerance : 1000ppm, 3mmu if m/z < 3, 5mmu if m/z > 5Unsaturation (U.S.) : -0.5 - 30.0 Observed m/z Int% U.S. Composition Err[ppm / mmu] 721.3206 +0.9 / +0.613.5 C 38 H 50 O 12 Na 100.0

Page: 1 [Theoretical Ion Distribution] Molecular Formula : C38 H50 O12 Na (m/z 721.3200, MW 721.7976, U.S. 13.5) Base Peak : 721.3200, Averaged MW : 721.7921(a), 721.7928(w) m/z INT. 42.7220 ********************** 722.3234 11.2964 ****** 723.3262 724.3289 2.2277 * 725.3316 0.3584 726.3342 0.0492 727.3368 0.0059



S19. ¹H NMR (600 MHz, CDCl₃) spectrum of ${\bf 3}$











S22. ¹H ¹H COSY spectrum of **3** in CDCl₃

S23. HMBC spectrum of **3** in CDCl₃





S23. HMBC spectrum of $\mathbf{3}$ in CDCl₃



S24. HSQC spectrum of 3 in CDCl₃



S25. NOESY spectrum of $\mathbf{3}$ in CDCl₃

S26. LR-EI-MS of 3



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S27. HR-EI-MS of 3

Note : 3-NOBA, CHCl3+NaIaq. Inlet : Direct Ion Mode : FAB+ RT : 0.30 min Scan#: 2 Elements : C 41/0, H 50/0, O 12/0, Na 1/0 Mass Tolerance : 1000ppm, 3mmu if m/z < 3, 5mmu if m/z > 5Unsaturation (U.S.) : -0.5 - 30.0

Observed m/zInt%Err[ppm / mmu]U.S.Composition755.3050100.0+0.9 / +0.617.5C41H48O12Na

[Theoretical Ion Distribution] Page: 1 Molecular Formula : C41 H48 O12 Na (m/z 755.3043, MW 755.8147, U.S. 17.5) Base Peak : 755.3043, Averaged MW : 755.8095(a), 755.8103(w) m/z INT. 46.0587 ******************** 756.3077 12.7591 ****** 757.3106 758.3134 2.6207 ** 759.3161 0.4370 760.3187 0.0620 761.3213 0.0077 762.3239 0.0009



S28. 1 H NMR (600 MHz, CDCl₃) spectrum of 4



S28. 1 H NMR (600 MHz, CDCl₃) spectrum of 4









S29. ¹³C NMR (150 MHz, CDCl₃) spectrum of 4













S32. HMBC spectrum of 4 in CDCl₃



S32. HMBC spectrum of 4 in CDCl₃







S34. NOESY spectrum of 4 in CDCl₃

S35. LR-EI-MS of 4



S36. HR-EI-MS of 4

Note: 3-NOBA, CHCl3+NaIaq.
InletIon Mode: FAB+
Scan#: 3RT: 0.60 minScan#: 3Elements: C 38/0, H 60/0, N 1/0, O 12/0, Na 1/0Mass Tolerance: 1000ppm, 3mmu if m/z < 3, 5mmu if m/z > 5Unsaturation (U.S.): -0.5 - 30.0Observed m/z Int%Err[ppm / mmu]U.S. Composition
13.5C 38 H 51 N O 12 Na





S38. 13 C NMR (150 MHz, CDCl₃) spectrum of **5**







S40 1 H 1 H COSY spectrum of 5 in CDCl₃



S40 $^1\mathrm{H}$ $^1\mathrm{H}$ COSY spectrum of $\boldsymbol{5}$ in CDCl_3



S41. HMBC spectrum of $\mathbf{5}$ in CDCl₃



S41. HMBC spectrum of 5 in CDCl₃


S41. HMBC spectrum of 5 in CDCl₃















S43. NOESY spectrum of 5 in CDCl₃

S44. LR-EI-MS of 5



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S45. HR-EI-MS of 5

Note : 3-NOBA, CHCl3+NaIaq. Inlet : Direct Ion Mode : FAB+ RT : 0.00 min Scan#: 1 Elements : C 34/0, H 60/0, O 12/0, Na 1/0 Mass Tolerance : 1000ppm, 3mmu if m/z < 3, 5mmu if m/z > 5Unsaturation (U.S.) : -0.5 - 30.0

Observed m/z Int% Err[ppm / mmu] U.S. Composition 673.3206 100.0 +0.9 / +0.6 9.5 C 34 H 50 O 12 Na

Page: 1 [Theoretical Ion Distribution] Molecular Formula : C34 H50 O12 Na (m/z 673.3200, MW 673.7536, U.S. 9.5) 673.3200, Averaged MW : 673.7479(a), 673.7486(w) Base Peak : m/zINT. 674.3234 38.2731 ******************* 9.5195 ***** 675.3261 676.3288 1.7753 * 677.3314 0.2721 678.3340 0.0357 679.3365 0.0041 680.3390 0.0004

S46. 1 H NMR (600 MHz, CDCl₃) spectrum of **6**





S47. ¹³C NMR (150 MHz, CDCl₃) spectrum of $\mathbf{6}$



S47. ¹³C NMR (150 MHz, CDCl₃) spectrum of **6**

0.3 0.20.1 -0.1 -0.2 abundance 80.0 60.0 70.0 10.0 50.0 40.0 20.0 30.0 // 70.6150 68.8246 63.4723 50.2974 78.2940 42.8386 14.8516 14.0856 8.8865 34.7958 34.1447 37.4097 29.5201 27.7680 24.6083 18.8443 18.7868 18.6240 X : parts per Million : 13C

S48. DEPT (150 MHz, CDCl₃) spectra of 6.



















S52. ¹H NMR (600 MHz, CDCl₃) spectrum of 7



S53. 13 C NMR (150 MHz, CDCl₃) spectrum of 7

S54. LR-EI-MS of 7





S55. ¹H NMR (600 MHz, CDCl₃) spectrum of 8



S56. ¹³C NMR (150 MHz, CDCl₃) spectrum of 8

S57. LR-EI-MS of 8





S58. 1 H NMR (600 MHz, CDCl₃) spectrum of **9**



S59. ¹³C NMR (150 MHz, CDCl₃) spectrum of 9

S59. ¹³C NMR (150 MHz, CDCl₃) spectrum of 9





S60. . $^1\mathrm{H}$ $^1\mathrm{H}$ COSY spectrum of $\boldsymbol{9}$ in CDCl3





S62. HSQC spectrum of 9 in CDCl₃



S63. NOESY experiment of 9 in CDCl₃



S65. ¹H NMR (600 MHz, CDCl₃) spectrum of **10**



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S66. ¹³C NMR (150 MHz, CDCl₃) spectrum of 10







S68. ^{13}C NMR (150 MHz, CDCl₃) spectrum of 11





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S72. ¹³C NMR (150 MHz, CDCl₃) spectrum of 13



S 73. Photomicrographs showing morphological changes of Caco-2 cells following 48 h exposure to compound 1 serial dilutions as mentioned at the *Experimental* section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification= $150\times$.



S74. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 2 serial dilutions as mentioned at the *Experimental* section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification= $150 \times$.

А	Compound 2	В
	0.1% DMSO	
	6.25 μM	
	12.5 μM	
	25 μΜ	
	50 µM	
	100 µM	

S75. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 3 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

А	Compound 3	В
	0.1% DMSO	
	6.25 μM	
	12.5 μΜ	
	25 μΜ	
	50 µM	
	100 µM	

S76. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 4 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

Α	Compound 4	В
	0.1% DMSO	
	6.25 μM	
	12.5 μM	
	25 μΜ	
	50 µM	
	100 μM	

S77. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 5 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

А	Compound 5	В
	0.1% DMSO	
	6.25 μM	
	12.5 μM	
	25 μΜ	
	50 µM	
	100 μM	

S78. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 6 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

А	Compound 6	В
	0.1% DMSO	
	6.25 μM	
	12.5 μM	
	25 μΜ	
	50 µM	
	100 µM	

S79. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 7 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

Δ	Compound 7	D
A	0.1% DMSO	B
	6.25 μΜ	
	12.5 μΜ	
100 M	25 μΜ	
	50 µM	
	100 µM	

S80. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 8 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

A	Compound 8	В
	0.1% DMSO	
	6.25 μM	
	12.5 μM	
	25 μΜ	
	50 µM	
	100 μM	

S81. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 9 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.

А	Compound 9	В
	0.1% DMSO	
	6.25 μΜ	
	12.5 μΜ	
	25 μΜ	
	50 μΜ	
	100 μΜ	

S82. Photomicrographs showing morphological changes of Caco-2 cells (A) or A549 cells (B) following 48 h exposure to compound 10 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.



S83. Photomicrographs showing morphological changes of Caco-2 cells following 48 h exposure to compound 11 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.



S84. Photomicrographs showing morphological changes of Caco-2 cells following 48 h exposure to compound 12 serial dilutions as mentioned at the Experimental section. Morphological signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnification=150×.



S85. Photomicrographs showing morphological changes of Caco-2 cells following 48 h exposure to compound 13 serial dilutions as mentioned at the Materials and Methods section. Morphological

signs of cytotoxicity include cell rounding, shrinking and loss of monolayer integrity compared to vehicle control. Total magnifictaion=150×.



S86. Photomicrographs showing morphological changes of A549 cells following 48 h exposure to serial dilutions of doxorubicin HCl as mentioned at the Materials and Methods section. Morphological signs of cytotoxicity include cell rounding, shrinking and complete loss of monolayer integrity compared to vehicle control. Total magnification=150×.



S87. Photomicrographs showing morphological changes of Caco-2 cells following 48 h exposure to serial dilutions of doxorubicin HCl as mentioned at the Materials and Methods section. Morphological signs of cytotoxicity include cell rounding, shrinking and complete loss of monolayer integrity compared to vehicle control. Total magnification=150×.

