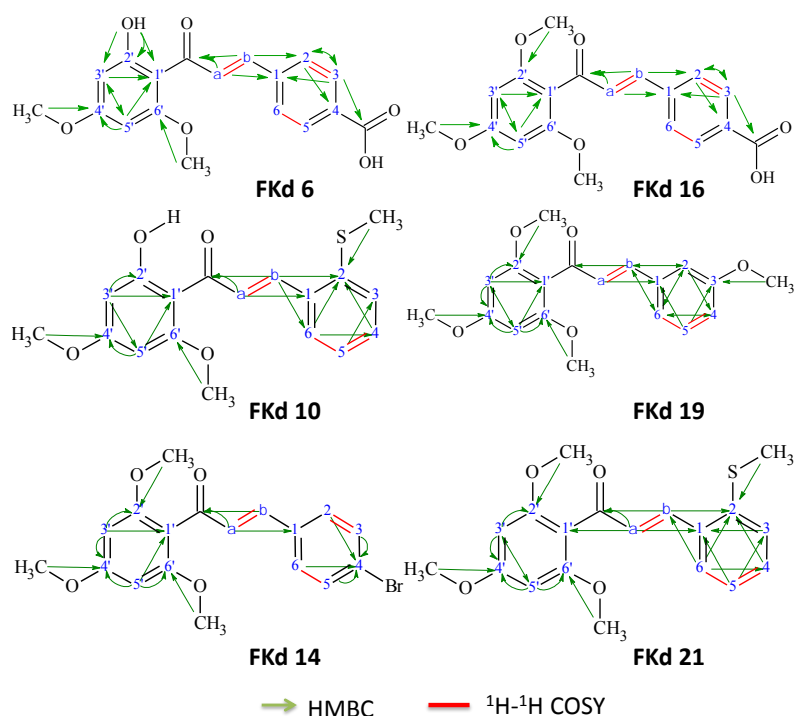


Supplementary Data

Supplementary Table S1. Percentages of cell survival (PS) after treatment by FKD at a unique concentration of 50 μ M; in grey, FKD inducing a PS \leq 50%

FKD	HuH7	CaCo-2	MDA-MB-231	HCT116	PC3	NCL-H727	HaCaT	Fibroblasts
1	50	32	58	20	43	40	35	67
2	10	1	19	0	27	2	7	32
3	> 80	> 80	> 80	> 80	> 80	> 80	> 80	> 80
4	> 80	> 80	> 80	> 80	58	72	66	> 80
5	66	45	69	25	56	54	36	> 80
6	> 80	> 80	> 80	> 80	> 80	> 80	> 80	> 80
7	> 80	> 80	> 80	> 80	> 80	> 80	> 80	> 80
8	13	1	11	0	22	1	7	44
9	39	43	37	8	32	11	30	71
10	38	23	39	1	35	8	22	65
11	39	32	26	19	33	14	21	62
12	6	5	13	1	29	1	20	74
13	8	3	13	0	15	1	11	68
14	3	0	6	0	10	2	6	57
15	8	3	12	1	26	4	21	78
16	38	25	68	7	39	23	59	57
17	66	68	> 80	> 80	75	58	> 80	> 80
18	4	1	3	1	6	1	4	51
19	3	2	4	0	19	1	18	66
20	6	5	11	0	32	1	23	77
21	4	17	36	0	30	1	6	74
22	45	24	32	17	33	42	16	65



Supplementary Figure F1. Structural elucidation of the new synthetic FKd **6**, **10**, **14**, **16**, **19** and **21** based on the NMR study (¹H-¹H COSY and key HMBC)

Supplementary Material M1. ¹H and ¹³C NMR data of already known FKd

(E)-1-(2-hydroxy-4,6-diméthoxyphényl)-3-(4-méthoxyphényl)prop-2-èn-1-one ou flavokavaine A (1)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.83 (s, 3H, 4-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.94 (d, *J*=2.4Hz, 1H, H-5'), 6.09 (d, *J*=2.4Hz, 1H, H-3'), 6.91 (d, *J*=8.7Hz, 2H, H-3,5), 7.54 (d, *J*=8.7Hz, 2H, H-2,6), 7.79 (d, *J*=15.3Hz, 2H, H-α,β)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.56 (4-OCH₃), 55.74 (4'-OCH₃), 56.00 (6'-OCH₃), 91.40 (C-5'), 93.99 (C-3'), 106.53 (C-1'), 114.52 (C-3,5), 125.31 (C-α), 128.50 (C-1), 130.27 (C-2,6), 142.42 (C-β), 161.52 (C-4), 162.62 (C-6'), 166.18 (C-4'), 168.53 (C-2'), 192.75 (-CO)

(E)-1-(2-hydroxy-4,6-diméthoxyphényl)-3-phénylprop-2-èn-1-one ou flavokavaine B (2)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.95 (d, *J*=2.4Hz, 1H, H-5'), 7.00 (d, *J*=2.4Hz, 1H, H-3'), 7.36 – 7.40 (m, 3H, H-3,4,5), 7.59 (d, *J*=7.9Hz, 2H, H-2,6), 7.77 (d, *J*=15.5Hz, 1H, H-β), 7.88 (d, *J*=15.5Hz, 1H, H-α)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.83 (4'-OCH₃), 56.09 (6'-OCH₃), 91.48 (C-5'), 94.02 (C-3'), 106.60 (C-1'), 127.78 (C-α), 128.58 (C-3,5), 129.09 (C-2,6), 130.26 (C-4), 135.78 (C-1), 142.54 (C-β), 162.73 (C-6'), 166.46 (C-4'), 168.63 (C-2'), 192.89 (-CO)

(E)-3-(4-diméthoxyphényl)-1-(2-hydroxy-4,6-diméthoxyphényl)prop-2-èn-1-one (3)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.95 (d, *J*=2.4Hz, 1H, H-5'), 6.09 (d, *J*=2.4Hz, 1H, H-3'), 7.35 (d, *J*=8.3Hz, 2H, H-3,5), 7.51 (d, *J*=8.3Hz, 2H, H-2,6), 7.69 (d, *J*=15.5Hz, 1H, H-β), 7.84 (d, *J*=15.5Hz, 1H, H-α)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.84 (4'-OCH₃), 56.12 (6'-OCH₃), 91.55 (C-5'), 94.05 (C-3'), 106.54 (C-1'), 128.29 (C-α), 129.36 (C-3,5), 129.68 (C-2,6), 134.34 (C-1), 136.09 (C-4), 140.96 (C-β), 162.68 (C-6'), 166.58 (C-4'), 168.66 (C-2'), 192.57 (-CO)

(E)-3-(4-bromophényl)-1-(2-hydroxy-4,6-diméthoxyphényl)prop-2-èn-1-one (4)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.89 (s, 3H, 6'-OCH₃), 5.94 (d, *J*=2.4Hz, 1H, H-5'), 6.09 (d, *J*=2.4Hz, 1H, H-3'), 7.43 (d, *J*=8.5Hz, 2H, H-2,6), 7.51 (d, *J*=8.5Hz, 2H, H-3,5), 7.67 (d, *J*=15.5Hz, 1H, H-β), 7.85 (d, *J*=15.5Hz, 1H, H-α)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.86 (4'-OCH₃), 56.13 (6'-OCH₃), 91.57 (C-5'), 94.07 (C-3'), 106.55 (C-1'), 124.40 (C-4), 128.40 (C-α), 129.89 (C-2,6), 132.33 (C-3,5), 134.76 (C-1), 141.02 (C-β), 162.68 (C-6'), 166.60 (C-4'), 168.67 (C-2'), 192.55 (-CO)

(E)-3-(4-fluorophényl)-1-(2-hydroxy-4,6-diméthoxyphényl)prop-2-èn-1-one (5)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.95 (d, *J*=2.4Hz, 1H, H-5'), 6.09 (d, *J*=2.4Hz, 1H, H-3'), 7.05 – 7.10 (m, 2H, H-3,5), 7.54 – 7.59 (m, 2H, H-2,6), 7.78 (d, *J*=15.4Hz, 1H, H-β), 7.86 (d, *J*=15.4Hz, 1H, H-α)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.83 (4'-OCH₃), 56.10 (6'-OCH₃), 91.51 (C-5'), 94.03 (C-3'), 106.53 (C-1'), 116.15 (C-3,5), 127.49 (C-α), 130.35 (C-2,6), 132.02 (C-1), 141.26 (C-β), 162.69 (C-6'), 164.84 (C-4), 166.50 (C-4'), 168.55 (C-2'), 192.62 (-CO)

(E)-3-(4-(diméthylamino)phényl)-1-(2-hydroxy-4,6-diméthoxyphényl)prop-2-èn-1-one (7)

NMR ¹H (CDCl₃, 600 MHz): δ 3.03 (s, 6H, 4-N(CH₃)₂), 3.81 (s, 3H, 4'-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.94 (d, *J*=2.4Hz, 1H, H-5'), 6.09 (d, *J*=2.4Hz, 1H, H-3'), 6.72 (d, *J*=8.6Hz, 2H, H-3,5), 7.51 (d, *J*=8.6Hz, 2H, H-2,6), 7.74 (d, *J*=15.1Hz, 1H, H-α), 7.81 (d, *J*=15.1Hz, 1H, H-β)

NMR ¹³C (CDCl₃, 600 MHz): δ 40.68 (4-N(CH₃)₂), 55.77 (4'-OCH₃), 56.03 (6'-OCH₃), 91.38 (C-5'), 94.05 (C-3'), 106.65 (C-1'), 112.65 (C-3,5), 122.86 (C-α), 125.41 (C-1), 130.56 (C-2,6), 151.67 (C-4), 144.24 (C-β), 162.59 (C-6'), 165.87 (C-4'), 168.53 (C-2'), 192.67 (-CO)

(E)-1-(2-hydroxy-4,6-diméthoxyphényl)-3-(3-méthoxyphényl)prop-2-èn-1-one (8)

NMR ¹H (CDCl₃, 600 MHz): δ 3.82 (s, 3H, 4'-OCH₃), 3.83 (s, 3H, 3-OCH₃), 3.90 (s, 3H, 6'-OCH₃), 5.95 (d, *J*=2.2Hz, 1H, H-5'), 6.09 (d, *J*=2.2Hz, 1H, H-3'), 6.92 (dd, *J*=7.9Hz, *J*=2.3Hz, 1H, H-4), 7.10 (sl, 1H, H-2), 7.19 (d, *J*=7.9Hz, 1H, H-6), 7.30 (t, *J*=7.9Hz, 1H, H-5), 7.72 (d, *J*=15.6Hz, 1H, H-β), 7.86 (d, *J*=15.7Hz, 1H, H-α)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.53 (3-OCH₃), 55.83 (4'-OCH₃), 56.10 (6'-OCH₃), 91.49 (C-5'), 94.02 (C-3'), 106.61 (C-1'), 113.87 (C-2), 115.82 (C-4), 121.13 (C-6), 128.13 (C-α), 130.06 (C-5), 137.21 (C-1), 142.40 (C-β), 160.09 (C-3), 162.73 (C-6'), 166.50 (C-4'), 168.63 (C-2'), 192.84 (-CO)

(E)-1-(2-hydroxy-4,6-diméthoxyphényl)-3-(2-méthoxyphényl)prop-2-èn-1-one (9)

NMR ¹H (CDCl₃, 600 MHz): δ 3.81 (s, 3H, 4'-OCH₃), 3.89 (s, 3H, 6'-OCH₃), 3.91 (s, 3H, 2-OCH₃), 5.94 (d, *J*=2.5Hz, 1H, H-5'), 6.09 (d, *J*=2.5Hz, 1H, H-3'), 6.91 (brd, *J*=8.3Hz, 1H, H-3), 6.96 (t, *J*=7.6Hz, 1H, H-5), 7.33 (m, 1H, H-4), 7.59 (dd, *J*=7.6Hz, *J*=1.6Hz, 1H, H-6), 7.95 (d, *J*=15.7Hz, 1H, H-α), 8.13 (d, *J*=15.7Hz, 1H, H-β)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.73 (4'-OCH₃), 55.79 (6'-OCH₃), 55.99 (2-OCH₃), 91.40 (C-5'), 93.99 (C-3'), 106.68 (C-1'), 111.40 (C-3), 120.90 (C-5), 124.82 (C-1), 128.99 (C-6), 128.12 (C-α), 131.54 (C-4), 138.06 (C-β), 158.86 (C-2), 162.72 (C-6'), 166.24 (C-4'), 168.57 (C-2'), 193.28 (-CO)

(E)-3-(4-méthoxyphényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (11)

NMR ¹H (CDCl₃, 600 MHz): δ 3.74 (s, 6H, 2',6'-OCH₃), 3.81 (s, 3H, 4-OCH₃), 3.84 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.83 (d, *J*=15.8Hz, 1H, H-α), 6.87 (d, *J*=8.7Hz, 2H, H-3,5), 7.29 (d, *J*=15.8Hz, 1H, H-β), 7.45 (d, *J*=8.7Hz, 2H, H-2,6)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.61 (C-4), 55.87 (4'-OCH₃), 56.18 (2',6'-OCH₃), 90.98 (C-3',5'), 112.28 (C-1'), 114.49 (C-3,5), 127.26 (C-α), 127.96 (C-1), 130.31 (C-2,6), 144.46 (C-β), 161.62 (C-4), 162.49 (C-4'), 158.98 (C-2',6'), 194.59 (-CO)

(E)-3-phényl-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (12)

NMR ¹H (CDCl₃, 600 MHz): δ 3.75 (s, 6H, 2',6'-OCH₃), 3.84 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.94 (d, *J*=15.9Hz, 1H, H-α), 7.33 (m, *J*=8.7Hz, 3H, H-3,4,5), 7.34 (d, *J*=15.9Hz, 1H, H-β), 7.50 (dl, *J*=8.7Hz, 2H, H-2,6)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.64 (4'-OCH₃), 56.11 (2',6'-OCH₃), 90.94 (C-3',5'), 112.03 (C-1'), 128.54 (C-2,6), 128.96 (C-3,5), 129.23 (C-α), 130.32 (C-4), 135.21 (C-1), 144.25 (C-β), 159.04 (C-2',6'), 162.60 (C-4'), 194.39 (-CO)

(E)-3-(4-chlorophényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (13)

NMR ¹H (CDCl₃, 600 MHz): δ 3.75 (s, 6H, 2',6'-OCH₃), 3.84 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.90 (d, *J*=16.1 Hz, 1H, H-α), 7.30 (d, *J*=16.1Hz, 1H, H-β), 7.31 (d, *J*=8.7Hz, 2H, H-3,5), 7.43 (d, *J*=8.7Hz, 2H, H-2,6)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.70 (4'-OCH₃), 56.18 (2',6'-OCH₃), 90.98 (C-3',5'), 111.97 (C-1'), 129.29 (C-3,5), 129.66 (C-α), 129.71 (C-2,6), 133.82 (C-1), 136.20 (C-4), 142.49 (C-β), 159.16 (C-2',6'), 162.78 (C-4'), 193.96 (-CO)

(E)-3-(4-fluorophényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (15)

NMR ¹H (CDCl₃, 600 MHz): δ 3,75 (s, 6H, 2',6'-OCH₃), 3.84 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.86 (d, *J*=16.2Hz, 1H, H-α), 7.03 (dl, *J*=8.4Hz, 2H, H-3,5), 7.31 (d, *J*=16.2Hz, 1H, H-β), 7.49 (dd, *J*=8.9Hz, *J*=5.3Hz, 2H, H-2,6)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.69 (4'-OCH₃), 56.17 (2',6'-OCH₃), 90.97 (C-3',5'), 112.02 (C-1'), 116.22 (C-3,5), 129.03 (C-α), 130.45 (C-2,6), 130.48 (C-1), 142.87 (C-β), 159.10 (C-2',6'), 162.71 (C-4'), 164.89 (C-4), 194.15 (-CO)

(E)-3-(4-(diméthylamino)phényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (17)

NMR ¹H (CDCl₃, 600 MHz): δ 2.99 (s, 6H, 4-N(CH₃)₂), 3.73 (s, 6H, 2',6'-OCH₃), 3.83 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.64 (d, *J*=8.5Hz, 2H, H-3,5), 6.76 (d, *J*=15.8Hz, 1H, H-α), 7.23 (d, *J*=15.8Hz, 1H, H-β), 7.39 (d, *J*=8.5Hz, 2H, H-2,6)

NMR ¹³C (CDCl₃, 600 MHz): δ 40.44 (4-N(CH₃)₂), 55.65 (4'-OCH₃), 56.16 (2',6'-OCH₃), 90.96 (C-3',5'), 112.09 (C-3,5), 112.57 (C-1'), 124.80 (C-α), 130.36 (C-1), 130.40 (C-2,6), 145.96 (C-β), 151.87 (C-4), 158.79 (C-2',6'), 162.18 (C-4'), 194.77 (-CO)

(E)-3-(4-nitrophényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (18)

NMR ¹H (CDCl₃, 600 MHz): δ 3.77 (s, 6H, 2',6'-OCH₃), 3.85 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 7.05 (d, *J*=16.2Hz, 1H, H-α), 7.41 (d, *J*=16.2Hz, 1H, H-β), 7.65 (d, *J*=8.8Hz, 2H, H-2,6), 8.20 (d, *J*=8.8Hz, 2H, H-3,5)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.73 (4'-OCH₃), 56.20 (2',6'-OCH₃), 91.00 (C-3',5'), 111.66 (C-1'), 124.27 (C-3,5), 129.01 (C-2,6), 132.67 (C-α), 139.99 (C-β), 141.70 (C-1), 148.51 (C-4), 159.46 (C-2',6'), 163.20 (C-4'), 192.93 (-CO)

(E)-3-(2-méthoxyphényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (20)

NMR ¹H (CDCl₃, 600 MHz): δ 3.75 (s, 6H, 2',6'-OCH₃), 3.80 (s, 3H, 2-OCH₃), 3.84 (s, 3H, 4'-OCH₃), 6.14 (s, 2H, H-3',5'), 6.90 (m, 1H, H-5), 6.92 (d, *J*=15.9Hz, 1H, H-α), 7.02 (m, 1H, H-6), 7.09 (dl, *J*=7.6Hz, 1H, H-3), 7.27 (m, 1H, H-4), 7.30 (d, *J*=15.9Hz, 1H, H-β)

NMR ¹³C (CDCl₃, 600 MHz): δ 55.57 (2-OCH₃), 55.71 (4'-OCH₃), 56.17 (2',6'-OCH₃), 90.06 (C-3',5'), 111.87 (C-1'), 113.36 (C-6), 116.38 (C-5), 121.37 (C-3), 129.57 (C-α), 130.01 (C-4), 136.57 (C-1), 144.21 (C-β), 159.11 (C-2',6'), 160.09 (C-2), 162.63 (C-4'), 192.44 (-CO)

(E)-3-(4-hydroxyphényl)-1-(2,4,6-triméthoxyphényl)prop-2-èn-1-one (22)

NMR ¹H (Acetone-d₆, 600 MHz): δ 3.74 (s, 6H, 2',6'-OCH₃), 3.86 (s, 3H, 4'-OCH₃), 6.30 (s, 2H, H-3',5'), 6.76 (d, *J*=15.9Hz, 1H, H-α), 6.88 (d, *J*=8.5Hz, 2H, H-3,5), 7.20 (d, *J*=15.9Hz, 1H, H-β), 7.50 (d, *J*=8.5Hz, 2H, H-2,6)

NMR ¹³C (Acetone-d₆, 600 MHz): δ 55.86 (4'-OCH₃), 56.23 (2',6'-OCH₃), 91.75 (C-3',5'), 113.01 (C-1'), 116.77 (C-3,5), 127.50 (C-α,1), 131.11 (C-2,6), 144.73 (C-β), 159.45 (C-2',6'), 160.63 (C-4), 163.18 (C-4'), 191.08 (-CO)