Supporting Information

Antitumor Agents 293. Non-toxic Dimethyl-4,4′-dimethoxy-5,6,5′,6′-dimethylenedioxybiphenyl-2,2′-dicarboxylate (DDB) Analogues Chemosensitize Multidrug Resistant Cancer Cells to Clinical Anti-cancer Drugs

Hsin-Yi Hung,[†] Emika Ohkoshi,[†] Kenneth F. Bastow,[‡] Kyoko Nakagawa-Goto,[†*] Kuo-Hsiung Lee[†*§]

[†] *Natural Products Research Laboratories, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599-7568*

[‡] *Division of Chemical Biology & Medicinal Chemistry, Eshelman School of Pharmacy, University of North Carolina, Chapel Hill, North Carolina 27599-7568*

[§] *Chinese Medicine Research and Development Center, China Medical University and Hospital, Taichung, Taiwan*

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Table S1. Cytotoxicity of DDB analogs

Cmpd	IC_{50} (μM)[a]			
	A549	DU145	KB	KBvin
1-5	>100	>100	>100	>100
6	98	>100	>100	>100
7-27	>100	>100	>100	>100
28	45	>100	88	71
29-31	>100	>100	>100	>100
32	>10	>10	>10	>10
33-36	>100	>100	>100	>100
TAX[b]	7.0 nM	2.9 nM	1.2 nM	1290.9 nM
VRP[c]	97.9	>100	49.2	77.2

[a] Antiproliferative activity as IC_{50} values for each cell line, the concentration of compound that caused 50% reduction in absorbance at 562 nm relative to untreated cells using the sulforhodamine B assay. Human lung carcinoma (A549), prostate cancer (DU145), epidermoid carcinoma of the nasopharynx (KB), and MDR expressing P-glycoprotein (KBvin). All compounds, besides **28** and **32**, exhibited no cytotoxicity. [b]Paclitaxel [c]Verapamil

Table S2. IC_{50} ± SD for reversal effects with paclitaxel (TAX), vincristine (VCR), and doxorubicin (DOX) in KBvin

Cmpd[a]	**IC_{50} of TAX (nM)**	**IC_{50} of VCR (nM)**	**IC_{50} of DOX (nM)**
	976.8 ± 163.4	2520.7 ± 719.4	1942.3 ± 404.1
4	82.93 ± 14.05	80.96 ± 4.69	507.5 ± 8.6
5	46.52 ± 9.19	41.42 ± 8.35	284.0 ± 55.3
6	26.15 ± 4.29	7.22 ± 0.75	42.6 ± 4.6
7	30.50 ± 3.22	50.81 ± 9.72	510.9 ± 55.9
8	37.06 ± 5.95	35.92 ± 7.71	93.9 ± 12.2
9	8.72 ± 2.07	31.75 ± 8.38	339.7 ± 62.5
10	40.74 ± 7.75	15.65 ± 2.43	221.5 ± 50.8
11	39.11 ± 3.06	47.31 ± 8.67	61.9 ± 4.7
13	48.65 ± 6.82	8.14 ± 1.13	86.3 ± 8.4
14	39.89 ± 2.65	10.55 ± 0.52	65.8 ± 15.9
15	9.55 ± 1.96	10.98 ± 0.63	547.8 ± 105.8
16	2.99 ± 0.21	4.50 ± 0.19	291.5 ± 1.5
17	47.45 ± 8.29	46.53 ± 0.81	573.9 ± 38.1
19	7.65 ± 0.96	20.21 ± 3.34	157.7 ± 13.9
20	46.82 ± 4.81	39.61 ± 4.61	130.8 ± 10.5
21	47.23 ± 2.04	40.53 ± 1.03	131.4 ± 7.3
22	14.25 ± 4.41	10.10 ± 0.92	68.80 ± 1.43
23	4.41 ± 0.89	4.45 ± 0.84	84.2 ± 14.6
VRP	31.87 ± 7.20	23.04 ± 4.78	219 ± 57.0

Table S3. Standardized P values of compounds **6**, **23**, and VRP.

	6		**23**		VRP	
Concentration (μM)	Cell viability[a]	P value	Cell viability[a]	P value	Cell viability[a]	P value
20	16.5 ± 4.8	<0.001	14.9 ± 8.2	<0.001	13.0 ± 10.0	0.002
10	22.0 ± 3.5	0.004	22.3 ± 5.2	0.001	23.9 ± 12.0	0.002
5	30.7 ± 2.6	0.007	25.9 ± 5.7	0.008	32.4 ± 10.4	0.005
3	47.0 ± 7.5	0.022	29.8 ± 4.8	0.002	45.8 ± 16.2	0.023
1	98.7 ± 5.7	0.294	76.6 ± 17.4	0.098	91.2 ± 21/3	0.426
0.1	112.5 ± 11.8	0.086	105.3 ± 15.1	0.112	103.7 ± 11.2	0.207

[a] Cell viability was presented by percentage of cell viability ± SD. P value was calculated for each concentration.

Table S4. Effect of compounds on P-gp function in KBvin cells

	Concentration (μM)				
Compound	0.1	0.3	0.5	1	5
6	4.6 ± 0.15	5.27 ± 0.38	5.68 ± 0.72	6.37 ± 0.2	9.43 ± 0.04
23	5.66 ± 0.22	6.66 ± 0.31	8.16 ± 0.62	12.6 ± 1.25	21.44 ± 1.95
Verapamil	4.69 ± 0.18	5.37 ± 0.07	5.78 ± 1.19	7.7 ± 1.3	12.65 ± 2.36

Cellular accumulation of calcein is represented by the relative fluorescent unit ($\times 10^4$ RFU). Data are expressed as mean ± SD of three independent experiments.