SUPPORTING INFORMATION

Highly Potent and Selective Dopamine D_4 Receptor Antagonists Potentially Useful for the Treatment of Glioblastoma

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Table S1. Elemental analysis results for compounds **7-33**.

Compd	**Formula**	**Calcd**				**Found**			
		C%	**H%**	**N%**	**S%**	**C%**	**H%**	**N%**	**S%**
7	$C_{21}H_{24}N_3.H_2C_2O_4$	67.46	6.65	10.26		67.21	6.78	10.11	
8	$C_{20}H_{24}N_4.H_2C_2O_4$	64.37	6.38	13.65		64.66	6.17	13.82	
9	$C_{20}H_{24}N_4.H_2C_2O_4$	64.37	6.38	13.65		64.12	6.29	13.43	
10	$C_{20}H_{23}N_3O.H_2C_2O_4$	64.22	6.12	10.21		63.99	6.36	10.34	
11	$C_{20}H_{23}N_3S.H_2C_2O_4$	61.81	5.89	9.83	7.50	62.11	7.30	6.10	7.27
12	$C_{22}H_{29}N_3.H_2C_2O_4$	67.74	7.34	9.88		67.44	7.19	9.99	
13	$C_{21}H_{25}N_3O.H_2C_2O_4$	62.99	7.93	10.02		63.25	7.90	10.19	
14	$C_{23}H_{29}N_3O.H_2C_2O_4$	66.21	6.89	9.27		65.27	6.54	9.36	
15	$C_{24}H_{31}N_3O.H_2C_2O_4$	66.79	7.11	8.99		66.41	7.02	9.09	
16	$C_{23}H_{29}N_3O.H_2C_2O_4$	66.21	6.89	9.27		65.88	6.83	9.08	
17	$C_{23}H_{29}N_3O.H_2C_2O_4$	66.21	6.89	9.27		66.10	6.81	9.33	
18	$C_{23}H_{29}N_3O.H_2C_2O_4$	66.21	6.89	9.27		66.34	6.96	9.34	
19	$C_{23}H_{29}N_3O_2.H_2C_2O_4$	63.95	6.66	8.95		64.11	6.47	9.12	
20	$C_{23}H_{29}N_3O_2.H_2C_2O_4$	63.95	6.66	8.95		63.74	6.80	8.92	
21	$C_{23}H_{29}N_3O_2.H_2C_2O_4$	63.95	6.66	8.95		63.90	6.41	8.76	
22	$C_{22}H_{26}ClN_3O.H_2C_2O_4$	60.82	5.96	7.48		60.74	5.83	7.60	
23	$C_{22}H_{26}ClN_3O.H_2C_2O_4$	60.82	5.96	7.48		60.52	6.01	7.61	
24	$C_{22}H_{26}ClN_3O.H_2C_2O_4$	60.82	5.96	7.48		61.02	6.06	7.50	
25	$C_{22}H_{26}N_4O_3.H_2C_2O_4$	59.50	5.83	11.56		59.59	5.70	11.80	
26	$C_{22}H_{26}N_4O_3.H_2C_2O_4$	59.50	5.83	11.56		59.38	5.83	11.34	
27	$C_{22}H_{26}N_4O_3.H_2C_2O_4$	59.50	5.83	11.56		59.29	5.98	11.40	
28	$C_{23}H_{26}N_4O.H_2C_2O_4$	64.64	7.00	14.96		64.78	7.01	15.20	
29	$C_{21}H_{26}N_4O.H_2C_2O_4$	62.71	6.08	12.06		62.99	6.31	12.31	
30	$C_{20}H_{25}N_5O.H_2C_2O_4$	59.85	6.16	15.86		59.98	6.00	16.03	
31	$C_{22}H_{25}Cl_2N_3O.H_2C_2O_4$	56.70	5.35	8.27		56.60	5.24	8.38	
32	$C_{22}H_{25}Cl_2N_3O.H_2C_2O_4$	56.70	5.35	8.27		56.51	5.31	8.12	
33	$C_{22}H_{25}Cl_2N_3O.H_2C_2O_4$	56.70	5.35	8.27		56.62	5.20	8.38	

Table S2. Physico-chemical descriptors for compounds **5-33**.

Compd	Rotors	HbAcc	HbDon	PSA	LogP	MW
5	7	2	0	24.85	4.38	328.49
6	5	2	0	28.95	3.17	349.47
7	5	1	0	11.37	4.11	319.44
8	5	2	0	22.55	3.24	320.43
9	5	2	1	34.65	4.44	320.43
10	5	3	0	30.51	4.83	321.42
11	5	2	0	42.00	4.37	337.48
12	5	1	0	11.74	4.91	335.49
13	4	2	0	27.66	2.77	335.44
14	6	2	0	27.49	3.61	363.50
15	7	2	0	28.56	3.84	377.52
16	5	2	0	27.46	3.45	363.50
17	5	2	0	27.68	3.58	363.50
18	5	2	0	28.21	3.60	363.50
19	6	3	0	38.97	3.34	379.50
20	6	3	0	40.59	3.25	379.50
21	6	3	0	38.97	3.28	379.50
22	5	2	0	28.21	3.77	383.91
23	5	2	0	28.01	3.76	383.91
24	5	2	0	27.64	3.71	383.91
25	5	4	0	66.88	3.67	394.47
26	5	4	0	68.32	3.71	394.47
27	5	4	0	69.24	3.58	394.47
28	5	2	0	47.04	2.47	374.48
29	5	3	0	37.35	2.21	350.46
30	5	4	0	47.96	1.58	351.45
31	5	2	0	27.64	4.32	418.36
32	5	2	0	28.57	4.28	418.36
33	5	2	0	28.02	4.33	418.36

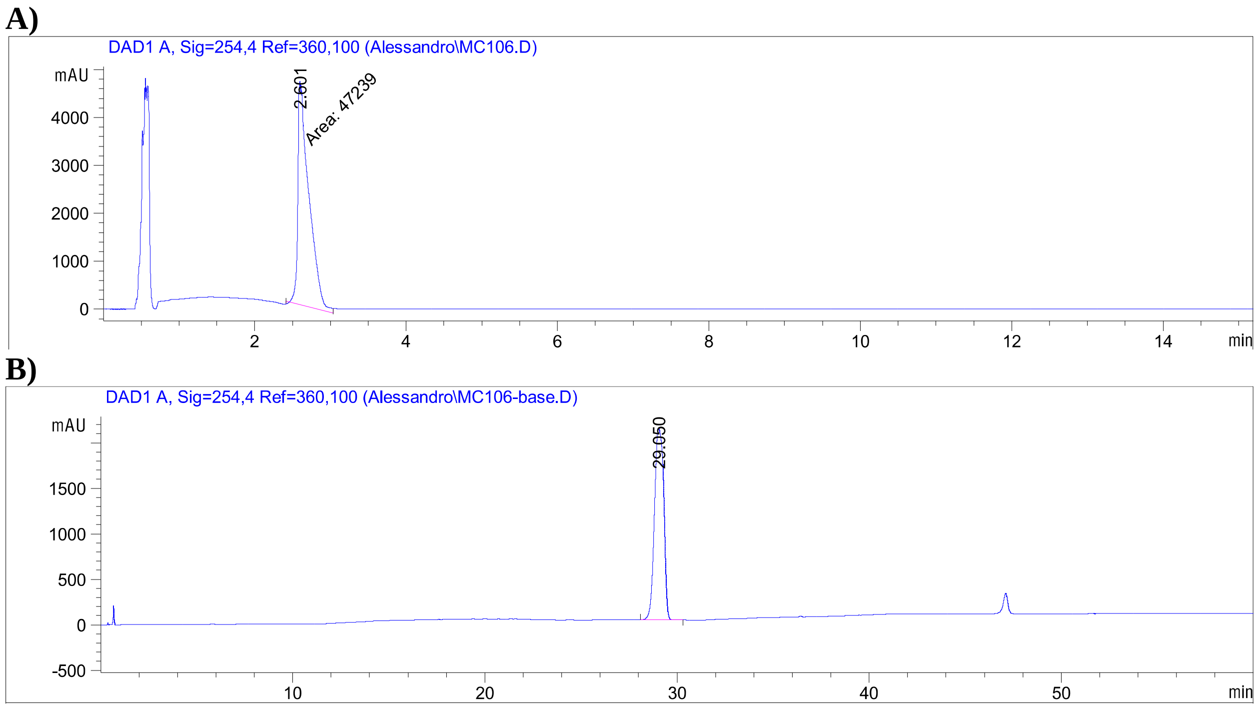
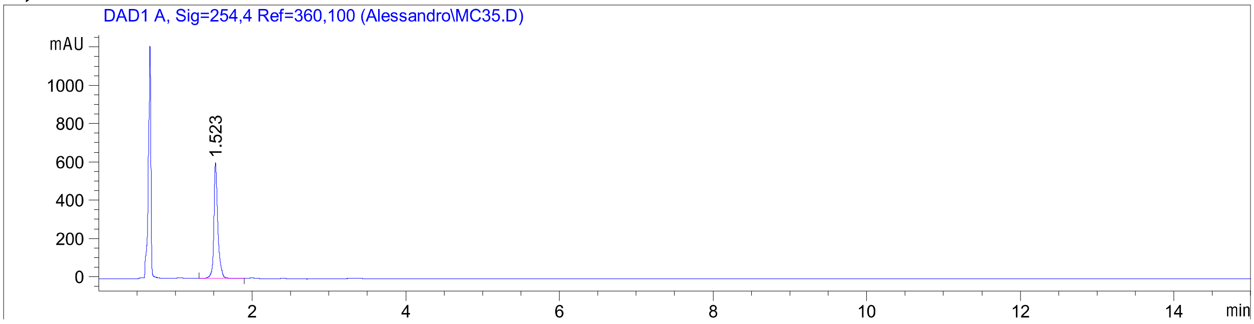


Figure S1. HPLC chromatograms of **24**. HPLC analysis was performed using an Agilent Technologies 1260 Infinity system coupled with DAD (Diode Array Detector). For each analytical HPLC run multiple DAD λ absorbance signals were measured in the range of 210-280 nm (representative chromatograms reported at λ254 nm). Separation of the analyte was achieved using a Phenomenex Gemini C18 4.6 x 50 mm. 3 μm column. **Method A)** mobile phase isocratic 30% ACN in water + 0.1% TFA; 15 min run; injection 20 μL (0.5 mg/mL); temperature 40 C; purity >95%; **Method B)** mobile phase gradient 10%-80% ACN in water + 0.1% DEA; 60 min run; injection 20 μL (0.5 mg/mL); temperature 40 C; purity >95%.

A)



B)

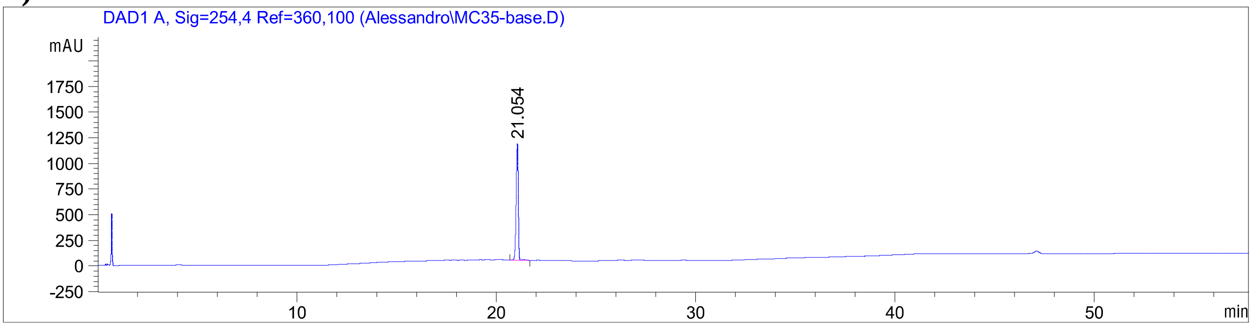


Figure S2. HPLC chromatograms of **29**. HPLC analysis was performed using an Agilent Technologies 1260 Infinity system coupled with DAD (Diode Array Detector). For each analytical HPLC run multiple DAD λ absorbance signals were measured in the range of 210-280 nm (representative chromatograms reported at λ254 nm). Separation of the analyte was achieved using a Phenomenex Gemini C18 4.6 x 50 mm. 3 μm column. **Method A)** mobile phase isocratic 15% ACN in water + 0.1% TFA; 15 min run; injection 20 μL (0.5 mg/mL); temperature 40 C; purity >95%; **Method B)** mobile phase gradient 10%-80% ACN in water + 0.1% DEA; 60 min run; injection 20 μL (0.5 mg/mL); temperature 40 C; purity >95%.