Supplementary data for the article:

Šegan, S.; Penjišević, J.; Šukalović, V.; Andrić, D.; Milojković-Opsenica, D.; Kostić-Rajačić, S. Investigation of Lipophilicity and Pharmacokinetic Properties of 2-(Methoxy)Phenylpiperazine Dopamine D2 Ligands. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* **2019**, *1124*, 146–153. https://doi.org/10.1016/j.jchromb.2019.06.006

Supplementary data

Investigation of lipophilicity and pharmacokinetic properties of 2-(methoxy)phenylpiperazine dopamine D2 ligands

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Content

Table S1. R_F values of the investigated substances in chromatographic system MeOH/5%NH_3/H_2O

Comp.	92.5%MeOH	90%MeOH	87.5%MeOH	85%MeOH	82.5%MeOH
1	0.53	0.40	0.33	0.32	0.27
2	0.62	0.47	0.40	0.37	0.33
3	0.58	0.44	0.39	0.37	0.33
4	0.55	0.42	0.35	0.33	0.31
5	0.44	0.31	0.25	0.24	0.20
6	0.55	0.39	0.32	0.29	0.25
7	0.51	0.37	0.31	0.29	0.24
8	0.51	0.38	0.31	0.28	0.24
9	0.75	0.62	0.58	0.51	0.53
10	0.74	0.62	0.57	0.52	0.51
11	0.73	0.60	0.55	0.51	0.50
12	0.74	0.63	0.58	0.53	0.49
13	0.72	0.58	0.53	0.48	0.46
14	0.74	0.60	0.55	0.50	0.50
15	0.73	0.59	0.53	0.49	0.46
16	0.75	0.62	0.55	0.53	0.51
17	0.64	0.64	0.53	0.43	0.52
18	0.61	0.64	0.55	0.53	0.49
19	0.64	0.64	0.53	0.52	0.49
20	0.64	0.62	0.51	0.51	0.44
21	0.67	0.61	0.49	0.48	0.44
22	0.64	0.62	0.49	0.48	0.44
23	0.65	0.62	0.49	0.48	0.44
24	0.64	0.61	0.48	0.47	0.42
25	0.40	0.36	0.25	0.22	0.20
26	0.44	0.39	0.28	0.27	0.25
27	0.44	0.38	0.31	0.27	0.25
28	0.41	0.38	0.28	0.23	0.22
29	0.35	0.27	0.15	0.14	0.14
30	0.40	0.31	0.20	0.16	0.16
31	0.42	0.37	0.28	0.24	0.22
32	0.38	0.31	0.19	0.17	0.16

Table S2. R_F values of the investigated substances in chromatographic system Acetone/5%NH_3/H_2O

Comp.	85% Acetone	80% Acetone	75% Acetone	70% Acetone	65% Acetone
1	0.62	0.46	0.40	0.31	0.22
2	0.68	0.53	0.44	0.33	0.21
3	0.66	0.52	0.44	0.33	0.22
4	0.65	0.51	0.43	0.32	0.22
5	0.51	0.35	0.30	0.20	0.13
6	0.62	0.44	0.35	0.22	0.13
7	0.59	0.42	0.33	0.21	0.13
8	0.60	0.44	0.35	0.22	0.13
9	0.77	0.67	0.60	0.50	0.40
10	0.77	0.67	0.59	0.49	0.37
11	0.76	0.65	0.58	0.47	0.35
12	0.76	0.65	0.58	0.47	0.34
13	0.73	0.61	0.53	0.42	0.31
14	0.74	0.61	0.53	0.42	0.3
15	0.72	0.59	0.51	0.39	0.28
16	0.73	0.60	0.53	0.39	0.28
17	0.83	0.72	0.64	0.57	0.50
18	0.83	0.72	0.64	0.57	0.49
19	0.83	0.72	0.63	0.55	0.47
20	0.83	0.72	0.64	0.55	0.47
21	0.79	0.71	0.63	0.54	0.45
22	0.80	0.67	0.59	0.5	0.39
23	0.80	0.66	0.59	0.49	0.39
24	0.80	0.67	0.60	0.50	0.39
25	0.58	0.45	0.38	0.30	0.23
26	0.62	0.50	0.42	0.33	0.27
27	0.64	0.51	0.42	0.33	0.27
28	0.59	0.47	0.40	0.31	0.24
29	0.44	0.29	0.20	0.15	0.12
30	0.54	0.35	0.31	0.22	0.15
31	0.59	0.47	0.40	0.31	0.24
32	0.52	0.35	0.29	0.21	0.15

Table S3. R_F values of the investigated substances in chromatographic system Dioxane/5%NH_3/H_2O

Comp.	80% Dioxane	75% Dioxane	70% Dioxane	65% Dioxane	60% Dioxane
1	0.64	0.56	0.41	0.34	0.25
2	0.68	0.62	0.44	0.33	0.23
3	0.68	0.64	0.45	0.37	0.28
4	0.66	0.63	0.44	0.36	0.27
5	0.48	0.42	0.26	0.19	0.13
6	0.57	0.50	0.43	0.20	0.11
7	0.59	0.53	0.31	0.22	0.13
8	0.59	0.53	0.34	0.23	0.14
9	0.81	0.77	0.67	0.60	0.51
10	0.83	0.79	0.68	0.61	0.53
11	0.81	0.78	0.67	0.58	0.50
12	0.83	0.78	0.65	0.61	0.50
13	0.75	0.72	0.57	0.49	0.39
14	0.80	0.72	0.61	0.53	0.42
15	0.80	0.72	0.58	0.49	0.39
16	0.80	0.72	0.59	0.49	0.4
17	0.74	0.74	0.64	0.59	0.48
18	0.77	0.75	0.67	0.60	0.50
19	0.78	0.76	0.67	0.60	0.49
20	0.79	0.77	0.67	0.6	0.49
21	0.69	0.67	0.55	0.48	0.35
22	0.73	0.70	0.58	0.49	0.35
23	0.73	0.70	0.58	0.48	0.35
24	0.74	0.71	0.58	0.50	0.38
25	0.50	0.45	0.31	0.23	0.18
26	0.56	0.52	0.37	0.28	0.20
27	0.56	0.52	0.38	0.29	0.20
28	0.57	0.54	0.39	0.29	0.18
29	0.39	0.34	0.21	0.14	0.07
30	0.46	0.40	0.25	0.18	0.09
31	0.56	0.52	0.38	0.28	0.18
32	0.47	0.41	0.25	0.18	0.11

Table S4. R_F values obtained by microemulsion thin-layer chromatography

Comp.	METLC1	METLC2
1	0.3	0.42
2	0.37	0.47
3	0.34	0.44
4	0.34	0.44
5	0.28	0.4
6	0.35	0.45
7	0.33	0.42
8	0.33	0.42
9	0.53	0.65
10	0.55	0.64
11	0.52	0.62
12	0.53	0.63
13	0.50	0.57
14	0.54	0.62
15	0.51	0.60
16	0.52	0.61
17	0.49	0.57
18	0.51	0.61
19	0.50	0.60
20	0.51	0.61
21	0.44	0.52
22	0.49	0.57
23	0.49	0.57
24	0.49	0.57
25	0.23	0.35
26	0.24	0.36
27	0.27	0.39
28	0.24	0.36
29	0.20	0.32
30	0.22	0.34
31	0.24	0.36
32	0.20	0.32

Table S5. Regression coefficients for chromatographic system MeOH/5%NH_3/H_2O

Comp.	R_M^0	-b	r	R^2	F	P	N
1	4.16±0.73	0.040±0.008	0.951	0.905	28.611	0.013	5
2	4.38±0.83	0.050±0.009	0.948	0.898	26.517	0.014	5
3	3.72±0.77	0.040±0.009	0.936	0.877	21.390	0.019	5
4	3.82±0.82	0.040±0.009	0.931	0.867	19.512	0.022	5
5	4.42±0.78	0.050±0.009	0.948	0.898	26.534	0.014	5
6	4.89±0.86	0.050±0.010	0.952	0.907	29.099	0.012	5
7	4.47±0.73	0.050±0.008	0.958	0.917	33.164	0.010	5
8	4.61±0.65	0.050±0.007	0.967	0.936	43.854	0.007	5
9	3.48±1.00	0.040±0.011	0.904	0.817	13.381	0.035	5
10	3.51±0.81	0.040±0.009	0.935	0.875	20.914	0.020	5
11	3.44±0.89	0.040±0.010	0.919	0.844	16.203	0.028	5
12	3.76±0.59	0.040±0.007	0.968	0.937	44.656	0.007	5
13	3.87±0.87	0.050±0.010	0.936	0.875	21.076	0.019	5
14	3.65±1.00	0.040±0.011	0.910	0.828	14.490	0.032	5
15	4.01±0.88	0.050±0.010	0.938	0.880	22.071	0.018	5
16	3.61±0.98	0.040±0.011	0.912	0.832	14.854	0.031	5
17	2.72±1.22	0.030±0.014	0.800	0.640	5.326	0.104	5
18	2.06±0.58	0.020±0.007	0.909	0.826	14.207	0.033	5
19	2.51±0.58	0.030±0.007	0.935	0.874	20.832	0.020	5
20	3.09±0.52	0.040±0.006	0.962	0.925	37.193	0.009	5
21	3.62±0.65	0.040±0.007	0.958	0.917	33.296	0.010	5
22	3.29±0.64	0.040±007	0.950	0.902	27.637	0.013	5
23	3.42±0.64	0.040±0.007	0.953	0.908	29.733	0.012	5
24	3.55±0.61	0.040±0.007	0.960	0.922	35.295	0.010	5
25	4.44±0.59	0.050±0.007	0.969	0.939	46.274	0.006	5
26	3.76±0.67	0.040±0.008	0.948	0.898	26.540	0.014	5
27	3.69±0.34	0.040±0.004	0.985	0.971	101.037	0.002	5
28	4.20±0.56	0.040±0.006	0.970	0.941	47.691	0.006	5
29	5.49±1.24	0.060±0.014	0.916	0.839	15.597	0.029	5
30	5.63±0.93	0.060±0.011	0.954	0.909	30.102	0.012	5
31	4.18±0.43	0.040±0.005	0.981	0.963	78.730	0.003	5
32	5.27±0.92	0.050±0.011	0.948	0.898	26.465	0.014	5

Table S6. Regression coefficients for chromatographic system Acetone/5%NH_3/H_2O

Comp.	R_M^0	-b	r	R^2	F	P	N
1	2.89±0.21	0.040±0.003	0.991	0.982	162.600	0.001	5
2	3.37±0.17	0.040±0.002	0.996	0.992	377.097	0.000	5
3	3.15±0.15	0.040±0.002	0.996	0.993	401.582	0.000	5
4	3.12±0.13	0.040±0.002	0.997	0.994	493.000	0.000	5
5	3.44±0.22	0.040±0.003	0.992	0.985	195.829	0.001	5
6	4.09±0.18	0.050±0.002	0.997	0.993	426.452	0.000	5
7	3.94±0.15	0.050±0.002	0.997	0.995	572.029	0.000	5
8	3.99±0.17	0.050±0.002	0.997	0.994	465.050	0.000	5
9	2.40±0.10	0.030±0.001	0.998	0.996	688.318	0.000	5
10	2.61±0.10	0.040±0.001	0.998	0.996	813.143	0.000	5
11	2.67±0.13	0.040±0.002	0.997	0.993	449.165	0.000	5
12	2.73±0.15	0.040±0.002	0.996	0.992	358.135	0.000	5
13	2.80±0.11	0.040±0.002	0.998	0.995	632.891	0.000	5
14	2.93±0.15	0.040±0.002	0.996	0.993	413.060	0.000	5
15	2.99±0.13	0.040±0.002	0.997	0.994	535.731	0.000	5
16	3.07±0.16	0.040±0.002	0.996	0.992	358.653	0.000	5
17	2.20±0.27	0.030±0.004	0.983	0.966	84.657	0.003	5
18	2.26±0.26	0.030±0.003	0.985	0.971	100.819	0.002	5
19	2.43±0.24	0.040±0.003	0.988	0.976	123.273	0.002	5
20	2.43±0.22	0.040±0.003	0.990	0.980	147.178	0.001	5
21	2.23±0.05	0.030±0.001	0.999	0.999	2666.539	0.000	5
22	2.68±0.22	0.040±0.003	0.992	0.983	176.414	0.001	5
23	2.68±0.25	0.040±0.003	0.989	0.978	131.085	0.001	5
24	2.67±0.21	0.040±0.003	0.992	0.984	186.726	0.001	5
25	2.63±0.13	0.030±0.002	0.996	0.991	335.950	0.000	5
26	2.53±0.13	0.030±0.002	0.996	0.992	366.109	0.000	5
27	2.66±0.16	0.030±0.002	0.994	0.988	250.488	0.001	5
28	2.60±0.10	0.030±0.001	0.997	0.995	577.633	0.000	5
29	3.37±0.30	0.040±0.004	0.984	0.968	89.707	0.002	5
30	3.26±0.30	0.040±0.004	0.984	0.969	92.787	0.002	5
31	2.60±0.10	0.030±0.001	0.997	0.995	577.633	0.000	5
32	3.21±0.23	0.040±0.003	0.990	0.981	151.628	0.001	5

Table S7. Regression coefficients for chromatographic system Dioxane/5%NH_3/H_2O

Comp.	R_M^0	-b	r	R^2	F	p	N
1	2.70±0.15	0.040±0.002	0.995	0.990	311.660	0.000	5
2	3.19±0.21	0.040±0.003	0.993	0.986	213.038	0.001	5
3	2.77±0.28	0.040±0.004	0.985	0.970	98.395	0.002	5
4	2.74±0.29	0.040±0.004	0.983	0.966	84.790	0.003	5
5	3.32±0.22	0.040±0.003	0.992	0.983	175.473	0.001	5
6	4.03±0.58	0.050±0.008	0.965	0.932	41.098	0.008	5
7	3.90±0.31	0.050±0.004	0.989	0.978	135.638	0.001	5
8	3.74±0.27	0.050±0.004	0.991	0.983	171.930	0.001	5
9	1.87±0.12	0.030±0.002	0.996	0.991	347.470	0.000	5
10	1.95±0.16	0.030±0.002	0.993	0.986	215.271	0.001	5
11	2.01±0.18	0.030±0.003	0.991	0.983	171.080	0.001	5
12	2.09±0.22	0.030±0.003	0.988	0.977	125.210	0.002	5
13	2.32±0.23	0.040±0.003	0.987	0.975	115.686	0.002	5
14	2.36±0.09	0.040±0.001	0.998	0.997	884.091	0.000	5
15	2.64±0.15	0.040±0.002	0.996	0.992	373.423	0.000	5
16	2.58±0.13	0.040±0.002	0.997	0.993	453.044	0.000	5
17	1.53±0.26	0.030±0.004	0.969	0.940	46.763	0.006	5
18	1.59±0.18	0.030±0.003	0.987	0.974	112.618	0.002	5
19	1.74±0.20	0.030±0.003	0.986	0.973	108.049	0.002	5
20	1.83±0.20	0.030±0.003	0.987	0.974	113.281	0.002	5
21	2.12±0.26	0.030±0.004	0.981	0.962	75.236	0.003	5
22	2.37±0.25	0.040±0.004	0.986	0.971	102.052	0.002	5
23	2.40±0.24	0.040±0.003	0.987	0.974	114.415	0.002	5
24	2.26±0.21	0.030±0.003	0.989	0.977	129.199	0.001	5
25	2.78±0.20	0.040±0.003	0.990	0.981	155.171	0.001	5
26	2.82±0.22	0.040±0.003	0.990	0.980	143.889	0.001	5
27	2.78±0.22	0.040±0.003	0.990	0.979	142.598	0.001	5
28	3.04±0.30	0.040±0.004	0.983	0.967	87.974	0.003	5
29	3.90±0.32	0.050±0.005	0.986	0.973	107.773	0.002	5
30	3.77±0.31	0.050±0.004	0.987	0.975	114.808	0.002	5
31	2.99±0.26	0.040±0.004	0.988	0.975	118.150	0.002	5
32	3.55±0.23	0.040±0.003	0.992	0.984	180.654	0.001	5

Table S8. R_M values of the investigated substances for chromatographyc systems METLC1 and METLC 2

Comp.	METLC1	METLC2
1	0.37	0.14
2	0.23	0.05
3	0.29	0.10
4	0.29	0.10
5	0.41	0.18
6	0.27	0.09
7	0.31	0.14
8	0.31	0.14
9	-0.05	-0.27
10	-0.09	-0.25
11	-0.03	-0.21
12	-0.05	-0.23
13	0.00	-0.12
14	-0.07	-0.21
15	-0.02	-0.18
16	-0.03	-0.19
17	0.02	-0.12
18	-0.02	-0.19
19	0.00	-0.18
20	-0.02	-0.19
21	0.10	-0.03
22	0.02	-0.12
23	0.02	-0.12
24	0.02	-0.12
25	0.52	0.27
26	0.50	0.25
27	0.43	0.19
28	0.50	0.25
29	0.60	0.33
30	0.55	0.29
31	0.50	0.25
32	0.60	0.33

Table S9. Correlations betwwen experimental and calculated lipophilicity values

	C^0 MeOH	R_M^0 MeOH	C^0 Ac	R_M^0 Ac	C^0 Diox	R_M^0 Diox	ME TLC1	ME TLC2	milogP	AlogPs	AClogP	AlogP	MlogP	XlogP2	XlogP3	QPlogPo/w
C^0 MeOH	1.00															
R_M^0 MeOH	0.76	1.00														
C^0 Ac	0.90	0.90	1.00													
R_M^0 Ac	0.47	0.70	0.69	1.00												
C^0 Diox	0.97	0.84	0.93	0.59	1.00											
RM0 Diox	0.81	0.90	0.91	0.86	0.89	1.00										
METLC1	0.98	0.73	0.87	0.38	0.94	0.76	1.00									
METLC2	0.98	0.74	0.87	0.43	0.96	0.79	0.99	1.00								
milogP	0.89	0.65	0.73	0.39	0.90	0.75	0.89	0.91	1.00							
AlogPs	0.85	0.69	0.73	0.42	0.89	0.78	0.84	0.87	0.96	1.00						
AClogP	0.58	0.61	0.63	0.10	0.57	0.46	0.61	0.56	0.44	0.55	1.00					
AlogP	0.89	0.84	0.89	0.60	0.95	0.89	0.86	0.89	0.91	0.93	0.61	1.00				
MlogP	0.86	0.83	0.88	0.56	0.90	0.87	0.83	0.84	0.84	0.91	0.75	0.95	1.00			
XlogP2	0.87	0.89	0.95	0.59	0.92	0.86	0.85	0.85	0.75	0.78	0.73	0.94	0.91	1.00		
XlogP3	0.95	0.80	0.89	0.39	0.94	0.78	0.96	0.95	0.86	0.85	0.76	0.92	0.90	0.94	1.00	
QPlogPo/w	0.67	0.69	0.70	0.27	0.73	0.56	0.67	0.67	0.59	0.57	0.58	0.75	0.62	0.84	0.81	1.00