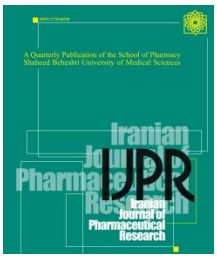

Supplementary Materials for

Molecular Insights of 1,2,3,4-tetrahydropyrimido[1,2-a]benzimidazole as CRF-1 Receptor Antagonists: Combined QSAR, Glide Docking, Molecular Dynamics, and *In-silico* ADME Studies

Sunil Kumar, Neeraj Kumar, Chandra Shekhar Sharma and Shashank Shekhar Mishra*

*To whom correspondence should be addressed. E-mail: shashankmedchem09@gmail.com

Volume 20, Issue 2 (Spring 2021)

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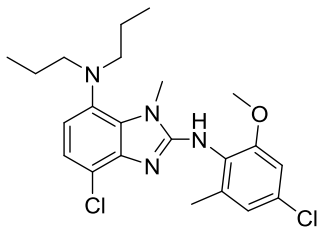
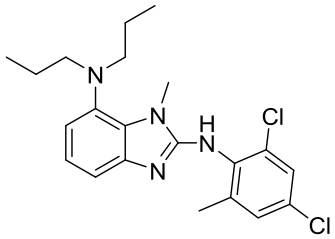
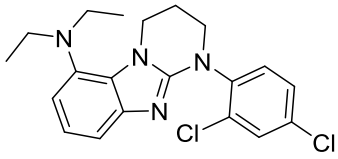
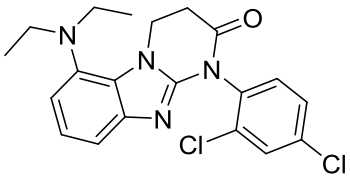
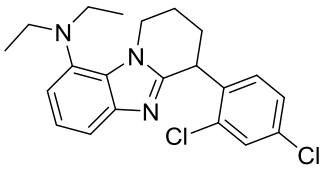
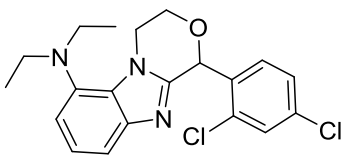
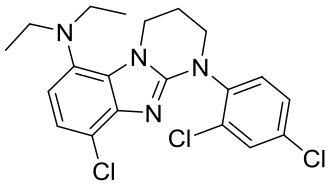
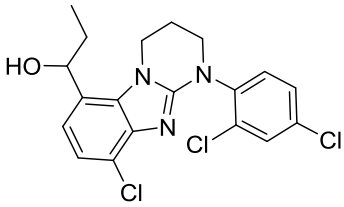
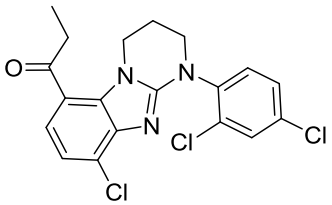
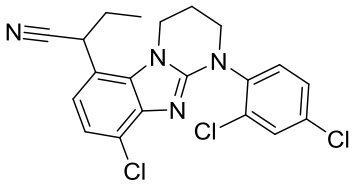
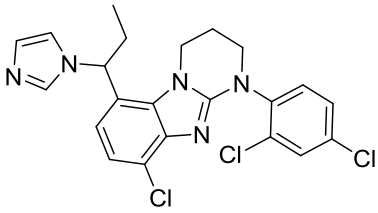
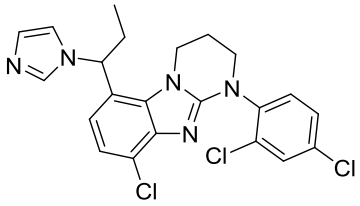
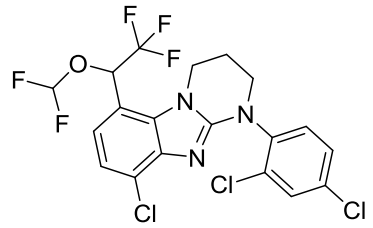
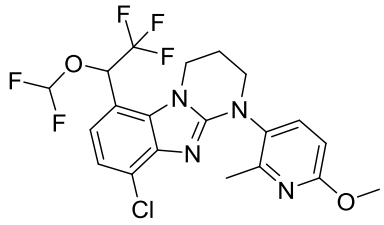
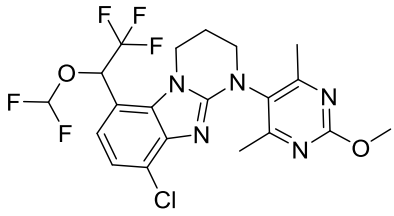
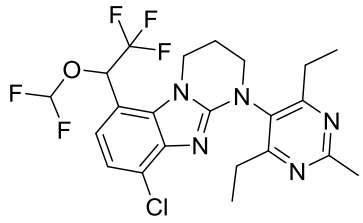
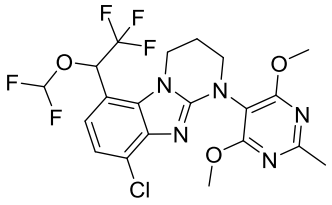
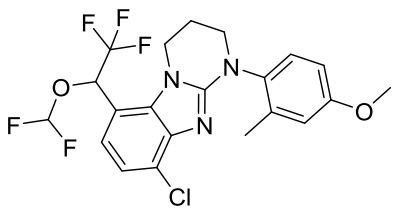
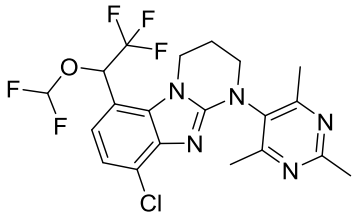
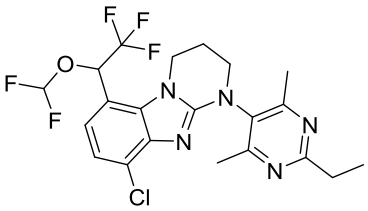
Tables S1-S3

Table S1. 2D structures, observed and predicted values of the compounds according to the best model in 2D and 3D QSAR.

			pIC_{50}				
				2D QSAR		3D QSAR	
Com. no.	**Structure**	**IC_{50} (nM)**	**Exp. value**	**Predicted value**	**Residual value**	**Predicted value**	**Residual value**
B1		9.5	8.022	8.032	-0.01	7.946	0.076
B2		18	7.744	7.799	-0.055	8.085	-0.341
B3		11	7.958	7.721	0.237	7.741	0.217
B4		39	7.408	7.621	-0.213	7.231	0.177
B5		36	7.443	7.721	-0.278	7.309	0.134
B6		270	6.568	6.673	-0.105	6.979	-0.411

B7		7.1	8.148	7.821	0.327	7.540	0.608
B8		89	7.050	6.842	0.208	7.033	0.017
B9		210	6.677	6.642	0.035	6.632	0.045
B10		66	7.180	7.421	-0.241	7.164	0.016
B11		130	6.886	7.19	-0.304	7.312	-0.426
B12		20	7.698	7.196	0.502	7.032	0.666

B13		50	7.301	7.349	-0.048	7.328	-0.027
B14		48	7.318	7.080	0.238	7.372	-0.054
B15		110	6.958	6.780	0.178	6.784	0.174
B16		100	7.000	6.912	0.088	6.726	0.274
B17		46	7.337	6.912	0.425	7.309	0.028
B18		48	7.318	7.480	-0.162	7.269	0.049

B19		320	6.494	6.648	-0.154	6.979	-0.485
B20		210	6.677	6.780	-0.103	6.740	-0.063

pIC_{50} (Residual) = pIC_{50} (Experimental) - pIC_{50} (Predicted).

Table S2. Calculated relative binding energies of the compounds and reference molecules.

Compound code	dG_Bind	dG_Bind_ Coulomb	dG_Bind_ Covalent	dG_Bind_ Hbond	dG_Bind_ Lipo
B1	-57.086	-8.3222	11.3508	-2.318	-48.702
B2	-71.049	-3.947	6.7701	-1.261	-40.317
B3	-95.794	-9.981	11.293	-0.725	-55.523
B4	-98.359	-16.920	7.828	-1.412	-52.789
B5	-78.094	-7.439	6.736	-0.704	-41.420
B6	-75.203	-6.361	6.761	-0.618	-40.423
B7	-107.147	-8.044	6.653	-0.688	-60.386
B8	-105.352	-13.870	6.778	-2.030	-56.170
B9	-100.907	-13.201	4.377	-1.371	-52.132
B10	-101.52	-13.870	9.578	-0.986	-56.173
B11	-67.682	-25.223	8.800	-1.200	-42.427
B12	-67.682	-25.223	8.800	-1.200	-42.427
B13	-100.410	-9.423	8.916	-1.361	-55.225
B14	-86.128	-6.256	10.903	-2.024	-48.518
B15	-74.371	-7.610	9.027	-1.902	-49.256
B16	-49.253	-11.161	17.778	-1.038	-43.773
B17	-59.8133	4.539	18.596	-1.432	-46.620
B18	-89.375	-6.719	7.090	-1.620	-50.898
B19	-77.055	-5.085	8.0784	-2.123	-49.393
B20	-78.204	-6.336	10.599	-2.074	-53.344
Emicerfont	-62.828	29.558	3.827	-1.308	-29.557
CP-316,11	-32.491	-0.161	4.994	-0.125	-39.516
Verucerfont	-47.402	1.950	2.869	-2.113	-38.801
Pexacerfont	-47.443	-4.047	6.898	-1.015	-38.978

Table S3. Physicochemical parameters calculation results for selected data sets.

Compound code	CNS	Mol.wt.	Volume	QPlogPo/w	QPlogS	QPlogBB	QPPMDCK	Percent Human Oral Absorption
B1	1	435.395	1325.782	6.711	-7.343	0.382	10000	100
B2	1	405.369	1263.083	6.595	-7.272	0.354	10000	100
B3	2	389.327	1165.02	6.096	-6.883	0.581	10000	100
B4	1	403.31	1161.242	4.603	-5.436	0.248	9579.757	100
B5	2	388.339	1180.042	6.403	-7.243	0.564	10000	100
B6	2	390.311	1127.274	5.228	-5.784	0.559	10000	100
B7	2	423.772	1207.203	6.603	-7.407	0.803	10000	100
B8	1	410.73	1156.253	5.618	-7.15	0.391	10000	100
B9	2	408.714	1140.184	5.468	-6.745	0.54	10000	100
B10	0	419.74	1219.003	5.916	-8.947	-0.081	8393.701	100
B11	2	460.792	1282.862	6.515	-7.886	0.473	10000	100
B12	2	460.792	1282.862	6.515	-7.886	0.473	10000	100
B13	2	500.682	1219.149	7.901	-9.204	1.335	10000	100
B14	2	476.833	1245.375	6.943	-8.198	0.799	10000	100
B15	2	491.847	1253.281	6.318	-7.511	0.669	10000	100
B16	2	503.902	1357.462	7.07	-8.375	0.723	10000	100
B17	2	507.847	1300.24	6.656	-7.79	0.655	10000	100
B18	2	475.845	1252.133	7.192	-8.238	0.918	10000	100
B19	2	475.848	1262.128	6.399	-7.965	0.75	10000	100
B20	2	489.875	1319.843	6.825	-8.37	0.763	10000	100
Emicerfont	0	404.471	1282.752	4.985	-7.364	-0.393	777.348	100
CP-316,11	1	327.466	1214.753	6.221	-8.527	0.201	5888.187	100
Verucerfont	0	412.534	1375.869	4.567	-6.518	-0.322	1619.26	100
Pexacerfont	0	340.427	1163.7	4.547	-5.871	-0.066	2402.831	100
Reference values[a]	−2 to +2	130.0–725.0	500.0–2000.0	−2 to 6.5	−6.5 to 0.5	−3.0 to 1.2	<25 poor >500great	>80% high <25% poor

[a]Note: range for 95% oral drugs from qikprop.